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CHEMISTRY FOR THE FUTURE 2022

BOOK OF ABSTRACTS

Società Chimica Italiana

June 29 - July 1, 2022
Via Moruzzi, 13 – 56124
Pisa, Italy

JASCO

SCIENTIFIC PROGRAM

Wednesday - June 29th

14.00-14.45	**REGISTRATION**
14.45-15.00	**WELCOME AND OPENING**
15.00-15.45	**Giovanni Maria Pavan |** Politecnico di Torino *Innate Dynamics, Molecular Communication Networks & Emergent Bioinspired Properties in Complex Supramolecular Systems*
15.45-16.15	**Carlotta Pieroni |** Università di Pisa *Quantum and quantum-classical studies of photo-induced ultrafast processes*
16.15-16.30	**Giulia Bononi |** Università di Pisa *Design, synthesis and biological evaluation of benzylpiperidine-based reversible MAGL inhibitors*
16.30-17.00	**COFFEE BREAK**
17.00-17.45	**Matthew Fuchter |** Imperial College London *Chiral polymers for chiral light emission in optoelectronic devices: a curiosityled journey of discovery*
17.45-18.15	**Eduarda Sangiogo Gil |** Università di Pisa *Surface hopping dynamics with exciton models in a semiempirical framework*
18.15-18.30	**Rosarita D'Orsi |** Università di Pisa *Lignin: a bio-based dielectric polymer for organic field-effect transistors*

Thursday - June 30th

9.00-9.45	**Sophie Guillaume |** Rennes Institute of Chemical Sciences (ISCR) *Stereoregular to Sequence Controlled Poly(Hydroxyalkanoate)s (PHAs): A Matter of β-Lactone Substituent and Catalyst Tuning*
9.45-10.15	**Simona Braccini |** Università di Pisa *Polymeric scaffolds for 3D in vitro tumour modelling*
10.15-10.30	**Damiano Cirri |** Università di Pisa *Oxygen introduction on phosphor-gold linear complexes as an effective way to enhance thioredoxin reductase inhibition in cancer cells.*
10.30-11.00	**COFFEE BREAK**
11.00-11.45	**Aoife Morrin |** Dublin City University *Harnessing the Scent of Disease for Wearable Biodiagnostics*
11.45-12.15	**Alessandra Recchimurzo |** Università di Pisa *Chiral analysis by NMR spectroscopy*
12.15-12.30	**Marco Carlotti |** Istituto Italiano di Tecnologia *How I turned my kitchen in a lab during the pandemic and its (non-)icy outcomes*
14.30-15.00	**Alberto Gobbo |** Università di Pisa *Adding diversity to the ruthenium-tris(pyrazolyl)methane scaffold: new complexes for biological and catalytic applications*
15.00-15.45	**Mauro Ravera |** Università del Piemonte Orientale "Amedeo Avogadro" *Is there any future for platinum-based anticancer drugs?*
15.45-16.15	**Cosimo Micheletti |** Università di Pisa *Mechanochromic polymers based on aggregachromic fluorophores*
16.15-16.45	**COFFEE BREAK**
16.45-17.15	**Francesca Binacchi |** Università di Pisa *Beyond platinum compounds: studies on the potential cytotoxic activity of new coinage metal complexes*
17.15-17.30	**Matyas Ripszam |** Università di Pisa *A novel method for the analysis of sweat volatiles using evaporative dynamic headspace and comprehensive GCxGC high resolution MS*
17.30-19.00	**POSTER SESSION + HAPPY HOUR**

Friday - July 1st

9.15-10.00	**Dominik Kubicki |** University of Warwick *New approaches to determining the atomic-level structure of advanced materials*
10.00-10.30	**Elena Pulidori |** Università di Pisa *Gelatin/waste keratin-based biomaterials: keratin green extraction, manufacturing, protein structure investigation, mechanical performance, and cell proliferation*
10.30-11.00	**COFFEE BREAK**
11.00-11.45	**Federico Bella |** Politecnico Torino *Energy electrochemistry: conversion, storage and integration strategies for a self-powered society*
11.45-12.15	**Oykum Naz Avci |** Università di Pisa *Mechanism and Surface Structural Study for Oxygen Evolution Reaction (OER) on Spinel Oxides (AB2O4)*
12.15-12.30	**Francesca Nardelli |** Università di Pisa *Influence of Sulfur-Curing Conditions on the Dynamics and Crosslinking of Rubber Networks: A Time-Domain NMR Study*

Invited Speakers

Keynote lectures by PhD students

Short Oral Communications

ABSTRACTS

INVITED SPEAKERS

Energy electrochemistry: conversion, storage and integration strategies for a self-powered society

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Keyword: Batteries, Solar cells, Supercapacitors, Solar fuels, Integrated devices

Efficiency, stability, sustainability and integration of energy devices are milestone targets towards world electrification and renewable sources-dependent society.
In this talk, new strategies for materials design, use of biosourced components, unconventional device architectures and structure-propriety-performance correlation will be shown for the design of different energy devices for the storage and conversion of energy.
In particular, the lecture will cover these intriguing aspects in the current energy scenario:

- The design of stable cell components for Li and post-Li batteries, at the basis of large-scale research initiatives in the European framework;
- Solar fuels from emerging conversion technologies.
- The use new materials for allowing the design of integrated conversion/storage systems for people, cities and industries.

The importance of considering sustainability, stability and industrial scalability as main targets in the research work will be stressed, along with a real consideration of efficiency results presented in the literature.

This project has received funding from the European Union's Horizon 2020 Research and Innovation programme (grant agreement No. 952169, project title: SYNERGY).

Chiral polymers for chiral light emission in optoelectronic devices: a curiosity-led journey of discovery

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We have an ongoing interest in the use of chiral materials to control function in technological application areas.[1] This includes the development of conjugated materials which can emit and detect circularly polarized (CP) light – a chiral polarization state – within organic electronic devices. CP light is central to many applications, including data storage, quantum computation, biosensing, environmental monitoring and display technologies. Such technologies require the generation of device compatible materials, but the identification of organic materials which emit light that is strongly CP remain a challenge.[2] Almost 10 years ago we developed a method to induce strong CP electroluminescence from the active layer of polymer light emitting diodes (PLEDs) by blending achiral polymers with chiral small molecule additives.[3] This talk will build on that early result, presenting our recent analysis on the optical origins of the large induced chiroptical activity,[4,5] curious dependencies on CP light handedness and film/device parameters[6,7,8] and ongoing theoretical work to understand our experimental data.[9] We strongly believe these polymeric materials present multiple opportunities to the rapidly emerging field of chiral optoelectronic materials and devices.

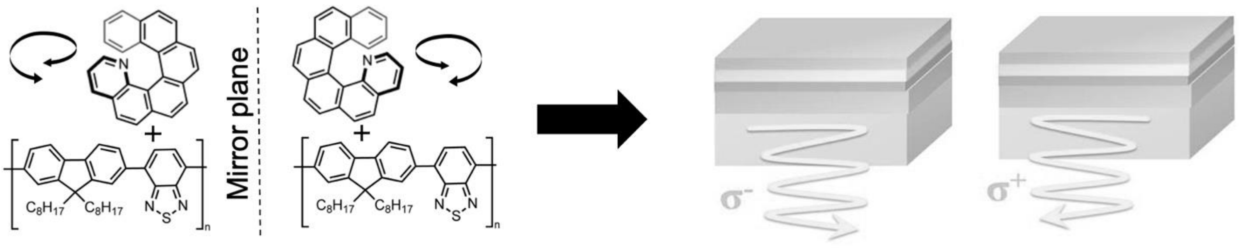

Figure 1. The use of induced chiral polymers to develop devices that emit CP light

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Stereoregular to Sequence Controlled Poly(Hydroxyalkanoate)s (PHAs): A Matter of *β*-Lactone Substituent and Catalyst Tuning

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Poly(hydroxyalkanoate)s (PHAs) are a class of natural or synthetic aliphatic polyesters which feature the same three-carbon backbone structure, only differing by their substituent (R) in β-position. PHAs have attracted considerable interest as “green” engineering plastics. These biodegradable and biocompatible polymers represent a targeted choice for in particular single-use plastics, packaging, and biomedical applications in tissue engineering and as drug delivery systems.

Recent highlights of research at Rennes University in the field of 1) tunable catalytic systems for the ring-opening (co)polymerization (ROP) of functional β-lactones, namely β-butyrolactone (BL), β-malolactonates (MLACO2Rs; R = CH2Ph (Bn), (CH2)2=CH2 (All)), or 4-alkoxymethylene-β-propiolactones (BPLCH2ORs; R = Me, Ph, Allyl, Bn) into their corresponding PHAs, that is (poly(3-hydroxybutyrate) (PHB), poly(alkyl β-malolactonate)s (PMLACO2Rs), poly(alkoxymethylene-β-propiolactone)s (PBPLCH20Rs), respectively), 2) original sequence controlled PHAs featuring a high degree of control over molecular and microstructural characteristics[1-3], and 3) PHA copolymers as promising drug delivery systems[4], will be presented.

Our most significant achievements in this endeavor include the development of strategies that enable the synthesis of alternated PHA-based copolymers, and evidences of the relationship between the catalytic system, the chemical structure and the composition of the macromolecules.

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New approaches to determining the atomic-level structure of advanced materials

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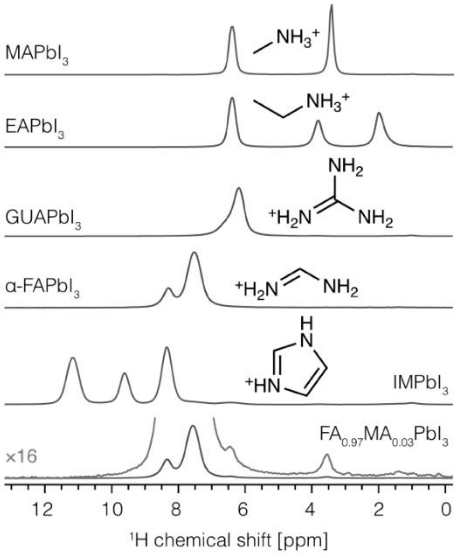
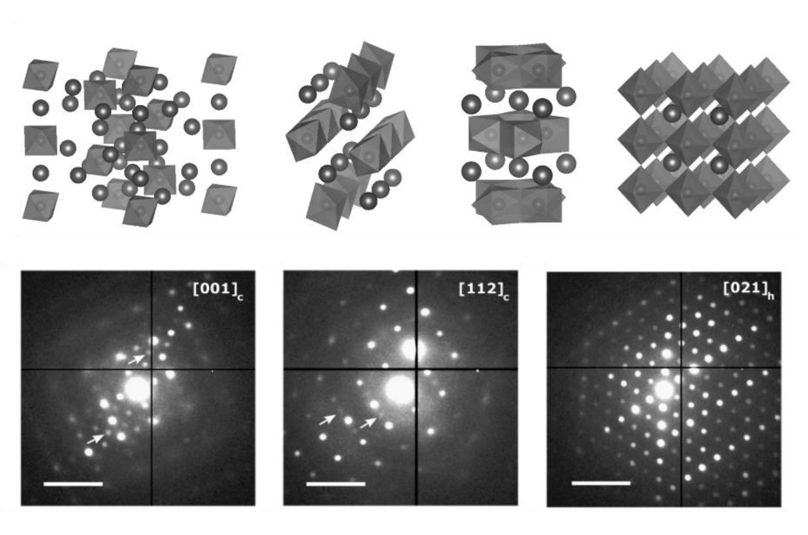
Determining the structure-property relationships at multiple length scales is one of the key tenets of rational design of new materials. While diffraction techniques offer insight into the long-range structure of solids, many properties are determined by local structure, which can be accessed using approaches based on, e.g., total scattering (PDF), XAFS, and magnetic resonance (NMR and ESR).

I will use the example of metal halide perovskites to discuss how we can determine the atomic-level structure of solids in an element-specific manner using solid-state NMR spectroscopy. The range of research problems includes quantifying dopant incorporation, phase segregation, decomposition pathways, passivation mechanisms, and structural dynamics.[1] I will also show how electron diffraction allows us to study structural phenomena inaccessible with X-rays.[2]

I will then show some areas where solid-state NMR will be key to answering the open questions in our understanding of these multifaceted materials. These strategies will be key to elucidating the performance-limiting factors in devices such as solar cells, light emitting diodes, and X-ray detectors. I hope that sharing these ideas will stimulate a productive and inspiring discussion.





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Harnessing the Scent of Disease for Wearable Biodiagnostics

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For the last number of years, ours and other research groups have been looking at ways to undertake continuous monitoring of health in non-invasive ways. While some exciting innovations in this field related to continuous or semi-continuous biomarker monitoring in sweat and interstitial fluid has been reported, our approach has focussed on capturing and analysing the volatile compounds that are coming from our skin. The skin surface emits many classes of volatile organic compounds (VOCs), as well as ammonia, which are derived directly from glandular secretions and also from their interactions with resident skin bacteria. These VOC emissions have the potential to offer insights into cutaneous and systemic physiology. However, in general, and in contrast to breath volatile research, research into skin-emitted VOCs as they relate to pathological state is at an early stage. Skin volatile profiles of healthy individuals have been shown to be influenced by gender and other genetic traits. However, little consistency has been seen across studies with regards to the compounds observed, likely due to the wide variety of sampling and analysis approaches being used but also the highly variable nature of the skin matrix itself. More research is required to more deeply understand the healthy skin volatile profile and the impact of disease on this emission.

This talk will cover the work that we have contributed to understanding the skin volatile emission, how we are translating what we know for future wearable biosensor devices and what we believe is still required of the field in order to exploit our knowledge and methodologies for clinical volatilomics in disease monitoring. Specifically, we are interested in skin volatilomics in the context of skin barrier disruption and also clinical wound volatilomics for pathogen detection. I will discuss our work to date and our perspectives on monitoring the skin volatile emission as a potential diagnostic tool for addressing needs in these specific application areas.

Innate Dynamics, Molecular Communication Networks & Emergent Bioinspired Properties in Complex Supramolecular Systems

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Supramolecular polymers, composed of monomers that self-assemble *via* non-covalent interaction into 1D, 2D, or 3D structures (or materials) are attracting increasing interest in many fields.[1] In such self-assembled systems, the constitutive building-blocks obey to a well-defined supramolecular equilibrium.[2] This imparts an intrinsically dynamic character to the assemblies that populate the system, which exist as exquisitely statistical/dynamical entities in continuous communication with each other and with the external environment, generating *de facto* a complex molecular system.

While typical experimental approaches allow to obtain average ensemble information on the dynamics of the entire system,[3] advanced simulation approaches may provide submolecular resolution insights into the origin of the dynamics of the (individual) assemblies.[4] However, the key molecular factors that control the communication networks and emergent properties in these complex molecular systems remain most often unclear. Learning how to master such complex molecular systems requires to enter into their innate dynamics at a submolecular resolution, and to obtain information on the molecular processes that control them.

In this talk, I will provide an overview of the computational approaches that we are recently adopting to reconstruct the intrinsic dynamics of self-assembling molecular systems. This journey brought us into the study of their complexity,[5] of their fluctuations,[6] and into the design and development of data-driven approaches to compare and classify them.[7] We are coming out with a new perspective, which contains general concepts that can be transferred to a variety of complex molecular systems and holds great potential for many applications.

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Is there any future for platinum-based anticancer drugs?

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The pandemic events have only temporally diverted the efforts of the scientific community from the cure of cancer, a leading cause of death worldwide, accounting for nearly 10 million of deaths in 2020 according to WHO.

Targeted- and immuno-therapy represent a new roadmap in cancer treatment to obtain high therapeutic effects with low systemic toxicity. Nevertheless, the traditional cytotoxic drugs (especially the DNA-damaging ones) maintain an immeasurable clinical value against several aggressive solid tumors. Among these compounds, cisplatin [(*SP*-4-2)-diamminedichloridoplatinum(II)] and its relatives (*e.g.*, the clinically approved carboplatin and oxaliplatin) remain the main component in several clinical trials despite their low appeal. Unfortunately, the numerous drawbacks associated to the use of these complexes pose a number of practical problems: low bioavailability and stability, severe side effects, inherent or acquired resistance).

Two different alternative philosophies were (and are) actively explored in the attempt to find a worthy alternative to cisplatin: *i)* non-traditional Pt(II) complexes (including Pt compounds that can be selectively activated by or in the tumor tissue, *e.g.*, prodrugs, stimuli-responsive, photoactivatable complexes) and *ii)* nanosized vectors (*guided missiles* designed to transport and release on demand the Pt warhead).

Moreover, the drug discovery paradigm has gradually shifted during the years from a “black box” approach that relies mainly on animal studies to the simplistic “one-target-one-disease” philosophy of today. This approach of producing highly selective “*magic bullets*” has provided notable successes, but it is probably inadequate for a multifactorial disease as cancer is. There is now an increasing realization that modulating a multiplicity of targets can be an asset in the treatment of a range of disorders (*e.g.*, multi-target compounds, bi- or multi-functional drugs).

It clearly turns out that young chemists with fresh ideas can still play a role in the proposal of new ways to increase the war potential of Pt-based drugs to fight cancer. For this reason, some historical and seminal examples will be discussed and critically analyzed in this presentation to provide food for thought useful to design molecules with increased efficacy and, in general, better patient compliance.

KEYNOTE LECTURES BY PhD STUDENTS

Beyond platinum compounds: studies on the potential cytotoxic activity of new coinage metal complexes

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The still actual key role of cisplatin, despite platinum's high toxicity and poor selectivity for cancer cells, is mainly due to the substantial lack of new metallodrugs drugs that could have better properties for possible clinical use [1]. On this ground, the interest in different metal centres has grown up together with the in-deep study of their mechanistic behaviour and cytotoxic activity. Au(I), Au(III), Ag(I) and Pd(II), are only some examples of the wide promising possibilities thatcould be explored.

Gold complexes are commonly accounted for as thioredoxin reductase inhibitors and binders for other biologically-relevant proteins, but it could be interesting to find gold complexes able to bind also genomic targets, especially non-canonical ones [2,3]. The study of d^8 planar Au(III) complexes that share the same geometry as Pt(II) complexes, or Au(I) carbene complexes endowed with an organic planar moiety which can intercalate into the strands of DNA or RNA, could be a starting point. N-heterocyclic carbenes (NHCs) ligands turned out of particular interest in medicinally relevant gold complexes [4]. Also, silver(I)-NHC complexes have been tested, and a recent scientific paper reported on an antitumor activity comparable and, in some cases, greater than that of gold carbenes [5]. Moreover, square-planar Pd(II) complexes represent an interesting alternative for Pt-based compounds. In this case, given the much faster hydrolysis of Pd(II) complexes with respect to the Pt(II) analogues, there is the need for a very strong nitrogen ligand (e.g. polydentate ligands), able to ensure enough stability to reach its biological target [6,7].

As for the type of substrates the metal complex needs to target, there is interest in studies on species that are supposed to prefer genomic targets but for which information on the binding to RNAs and non-canonical structures of DNA and RNA like G-quadruplexes, i-motifs and four-way junctions are still missing or incomplete.

This contribution involves different metal complexes that can be divided into four groups: (i) diphenyl-(anthracen-9-ylmethyl)phosphine-Au-X where X=Cl, Br, I; (ii) Ag(I) and Au(I) N- heterocyclic bis carbenes; (iii) Au(III), Pt(II), and Pd(II) square-planar complexes with tetradentate ligands; (iv) 1,10-Phenanthroline/Pd(II) complexes bearing arene ligands with N or O coordinating groups.

A comparison study, based on a multi-technique approach, will be presented, highlighting the role of the metal centre or the ligand in the mechanism of action of the metal complexes and their cytotoxic activity.

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Polymeric scaffolds for 3D *in vitro* tumour modelling

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In the last decades, three-dimensional (3D) cell culture systems based on a polymeric matrix (scaffold) have gained increasing interest in drug discovery and tissue engineering due to their ability in providing a more reliable biological environment for the long-term *in vitro* maintenance of cell phenotype. Considering the great influence of tumour microenvironment on the development and progression of cancer, 3D culture models have become essential for improving cancer physiology investigations [1]. The implementation of materials science and technology into cancer research and the application of innovative fabrication approaches (e.g., additive manufacturing and replica moulding techniques, Figure 1) represent a powerful route to develop 3D constructs with a variety of potential biomedical applications, such as scaffolds for 3D *in vitro* tissue models [2,3].
In this contribution, polymeric materials to be employed for biomedical scaffolds fabrication were selected among polysaccharides, i.e., chitosan-based polyelectrolyte complexes, and aliphatic polyesters, i.e., poly(lactic-*co*-glycolic acid), in virtue of their well ascertained biocompatibility and biodegradability. The design and fabrication of polymeric scaffolds with predefined geometry, controlled porosity, tailored stiffness and suitable physical-chemical properties, were optimized in order to develop novel approaches to *in vitro* 3D models of ovarian and hepatic cancer. Ongoing experimental investigations are dedicated to evaluating *in vitro* the response of the developed 3D tissue models to conventional and novel chemotherapeutics.

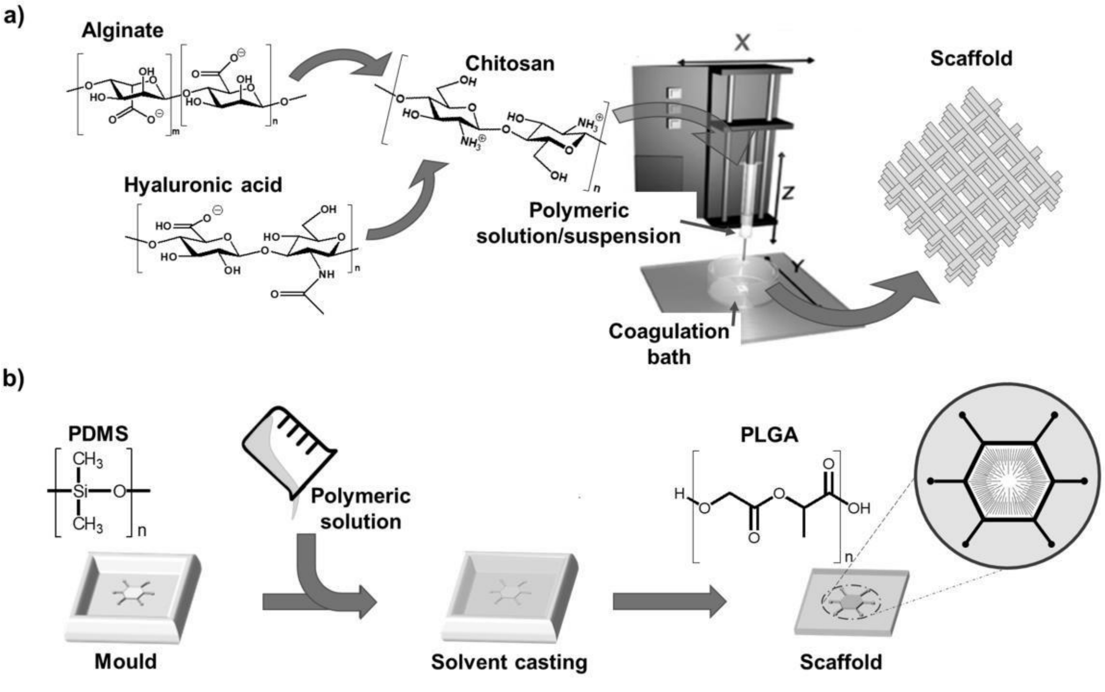

Figure 1. Schematic representation of the two investigated scaffold fabrication approaches: a) the additive manufacturing technique computer-aided wet-spinning, and b) replica moulding technique.

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Adding diversity to the ruthenium-tris(pyrazolyl)methane scaffold: new complexes for biological and catalytic applications

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Half sandwich ruthenium(II) complexes containing a η 6 -arene ligand have aroused a huge interest for their medicinal and catalytic application. [1] Conversely, the potential of homologous compounds containing a tridentate tris(1-pyrazolyl)methane ligand (tpm) has been sparingly explored. [2] A general method to access a family of novel ruthenium(II)-tpm complexes was developed. The synthesis of the precursor [RuCl(κ 3 -tpm)(PPh3)2]Cl was improved with respect to a reported procedure;[3] then, straightforward substitution reactions afforded the complexes [RuCl(κ 3 - tpm)(PPh3)(L)]Cl, which differ from each other in one key ligand (L). Moreover, esterification of 4- pyridinemethanol ligand allowed to incorporate different bioactive molecules, including ethacrynic acid, chlorambucil and NSAIDs (cyclooxygenase inhibitors). Most products are robust in water solution and pseudo-physiological conditions, undergoing a partial and reversible chloride/water exchange process. The antiproliferative activity of selected complexes was determined on a panel of cancer cell lines and a nontumoral one, evidencing a promising cytotoxicity and a significant selectivity against the cancer cells. An accurate choice of L modulates the biological properties of the complexes; the most potent candidates were selected for deeper experiments, including cytotoxicity analyses on 3D spheroids. In addition, the conjugation of the bioactive fragment with the Ru-tpm moiety provided a synergistic enhancement of enzyme inhibitor potency and antiproliferative activity of the functionalized complexes. On another side, the catalytic potential was investigated in transfer hydrogenation reactions from isopropanol of a range of ketones. The results suggest that dissociation of labile neutral ligands favours the formation of the catalytic active species.

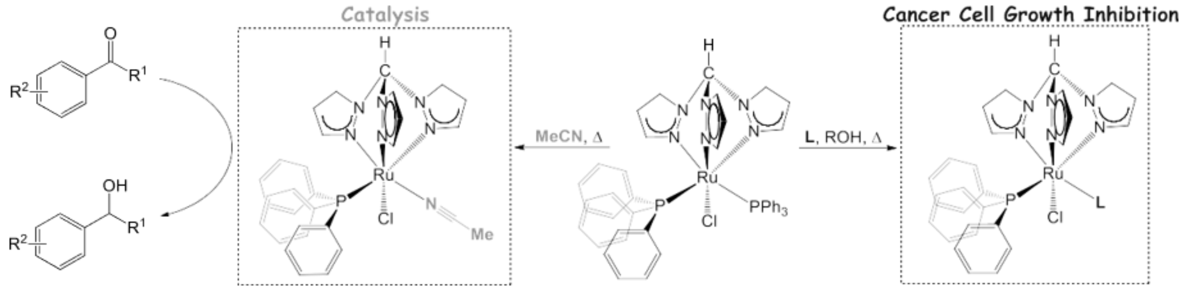

Figure 1. Synthesis of Ru(II)-tris(1-pyrazolyl)methane complexes investigated in this work.

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Mechanochromic polymers based on aggregachromic fluorophores

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In polymeric materials, mechanical forces can lead to the rupture of macromolecular chains,[1–3] which may ultimately lead to macroscopic failure of the material.[4] In order to prevent these potentially catastrophic events, it is useful to understand how, when, and where such degradation processes occur. To this aim, several mechanophores incorporated into polymeric materials have been proposed. Mechanophores are chromogenic molecules that display optical variations to mechanical stimuli, e.g. by compression or tensile deformation. Two distinct procedures are reported and based on the physical dispersion of the mechanophore in the form of supramolecular aggregates in a preformed polymer matrix or involves the covalent insertion of chromophoric units in the macromolecule backbone or side chains. In this last case, the mechanical solicitation induces selective chemical transformations of the mechanophore at the atomic level and the consequent colour change. However, being the mechanochromic response irreversible, it may limit their utility. Dispersed mechanophores that, on the basis of weak and reversible non-covalent interactions, operate in a non-sacrificial and potentially reversible manner are thus attractive alternatives.[5] Examples include the disassembly of associated non-covalent excimer-forming fluorophores (aggregates), which can be easily blended with a multitude of polymers.[6–8] Among them, aggregation-induced emission (AIE) molecules and aggregation-induced enhanced emission (AIEE), are attractive examples. Upon aggregation, the restriction of the intramolecular motions turnson or enhances fluorescence. The combination of AIE/AIEE emitters with polymeric materials is an attractive strategy for the in-situ auto-detection of mechanical stress since their aggregation extent varies during deformation.[9]

In this contribution, we explored several mechanochromic systems based on different AIE and AIEE emitter combined with elastomeric and thermoplastic polymer matrices. Functionalized tetraphenylethylene, pyrene and perylene AIE and AIEE fluorophores displayed interesting chromogenic response towards uniaxial deformation. Both elastomeric matrices such as poly(styrene-*b*-(ethylene-*co*-butylene)-*b*-styrene) (SEBS) and poly(ethylene-*co*-octene), a polyolefin elastomer (POE) was employed to confer reversible mechanochromism, whereas thermoplastic matrices like linear low density polyethylene (LLDPE) or poly(vinyl acetate) (PVAc), poly(D,L-lactide-*co*-glycolide) 75:25 (PLGA) and poly(butyl methacrylate) (PBMA) were utilized for endowing with an irreversible chromogenic response after drawing.

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Mechanism and Surface Structural Study for Oxygen Evolution Reaction (OER) on Spinel Oxides (AB_2O_4)

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Water electrolysis is a well-established method to produce hydrogen from the renewable energysources. The oxygen evolution reaction (OER) and hydrogen evolution reaction (HER) are the two important processes that are involved in electrochemical water splitting process that, incase of large-scale, is greatly hindered by the sluggish anodic OER. Even with state-of-the-art precious catalysts (i.e. RuO_2 and IrO_2) a substantial over-potential is required to drive the OER. Anion Exchange Membrane Water Electrolysis (AEMWE) has several advantages such as the use of non-noble metals as catalysts, low ohmic resistance, and good gas separation characteristics of membrane electrolyte.[1] Ni, Fe, Co based oxides are chemically stable in alkaline media and they show a OER performance relatively comparable to the Ru and Ir oxides.[2] Furthermore, combinations of these metals to obtain bimetallic catalysts, such as spineloxides, have demonstrated to be highly active and stable for this electrochemical reaction.[3] Throughout this study, we extensively investigate and quantitatively model the mechanism and energetics of the oxygen evolution reaction (OER) on the $NiFe_2O_4$, and $CoFe_2O_4$ inverse-spinel structures. We catalogue a wide set of intermediates and mechanistic pathways, including lattice oxygen mechanism (LOM) and adsorbate evolution mechanism (AEM), along with critical (rate-determining) O-O bond formation barriers[4]. Moreover, the structure/shape of large catalyst nanoparticles will be analyzed with employed DFT approach.

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Quantum and quantum-classical studies of photo-induced ultrafast processes

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The interpretation of photo-induced processes relies nowadays strongly on numerical simulations. Many theories and algorithms for excited state molecular dynamics have been developed over the years, but are still in continuous development. Widely used methods are quantum-classical algorithms, which introduce a description of nuclear dynamics based on classical trajectories coupled to a quantum description of electronic dynamics [1]. However, as a consequence of such aclassical approximation, some effects can be lost, as the lack of (or incorrect account for) decoherence in the trajectory surface hopping method. In the context of electronic nonadiabatic processes, these problems can result in wrong predictions for quantum populations and in unphysical outcomes for the nuclear dynamics. A solution to these issues was proposed by approximating the coupled electronic and nuclear equations within the framework of the exact factorization of the electron−nuclear wave function [2], deriving a simple quantum-classical schemebased on coupled classical trajectories. The algorithm was dubbed coupled-trajectory mixed quantum−classical, CT-MQC, scheme. Motivated by the appeal of a surface hopping-like scheme and by the success of CT-MQC we proposed and tested new strategies to improve the performance, in terms of computational efficiency and accuracy, of coupled-trajectory schemes derived from the exact factorization. In particular, we introduced the coupled-trajectory trajectory surface hopping (CT-TSH) scheme, where coupled trajectories are evolved adiabatically and are subject to stochastic hops between electronic states. The new CT algorithm has been tested on a one-dimensional two-state system using different model parameters which allow one to induce different dynamics. The benchmark is provided by the numerically exact solution of the time dependent Schrodinger equation [3]. We also studied the effect of various sampling schemes for the initial conditions of trajectories in combination with quantum-classical approaches to nonadiabatic dynamics. The analysis is based on the relaxation process through a conical intersection of a photo-excited retinal chromophore model [4]. Each of the trajectory-based methods used there have its strengths and drawbacks: the main obstacle to the wide application ofCT-MQC or CT-TSH is their numerical cost, because they require to propagate a large number of trajectories in parallel, contrary to standard trajectory surface hopping, for which the trajectories can be propagated independently. This numerical cost also prevents the use of CT-MQC/TSH with ab initio techniques for high-level electronic structure calculations. As a consequence, the ultimate goal of this thesis is to interface CT-MQC/TSH with semi-empirical electronic structure methods as implemented in the MOPAC package [5]. The high computational efficiency of using a semi- empirical method will make it possible to easily compute many trajectories for long timescales for medium to large molecular systems, as the photo-fragmentations process in azomethane.

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Gelatin/waste keratin-based biomaterials: keratin green extraction, manufacturing, protein structure investigation, mechanical performance, and cell proliferation

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The exploitation of waste biomasses to produce innovative biomaterials is one of the main goals of research aimed to replace fossil fuel-based materials [1,2]. Poultry feathers are among the most abundant and polluting keratin rich waste biomasses [3]. In this study, we developed microwave (MW)-assisted keratin extraction using MW-coaxial dipole antenna to apply energy inside the extraction medium. The soluble extracted keratin was directly mixed with gelatin and (3-(Glycidyloxypropyl)trimethoxysilane) (GPTMS) as crosslinker, and the blend was used to produce gelatin/keratin-based biomaterials by electrospinning process (ES). Gelatin film samples containing different amounts of GPTMS were also prepared by solvent casting for comparison. A detailed infrared spectroscopy study was performed aimed to evaluate the effect on gelatin secondary structure of (i) the process used to obtain the biomaterials (solvent casting *vs* electrospinning), (ii) the concentration of GPTMS, and (iii) the keratin added. The gelatin conformation has been related to the mechanical properties of electrospun samples and to their properties as substrate for cell proliferation and growth after 2 weeks of MC3T3-E1 pre-osteoblastic cells seeded on them.

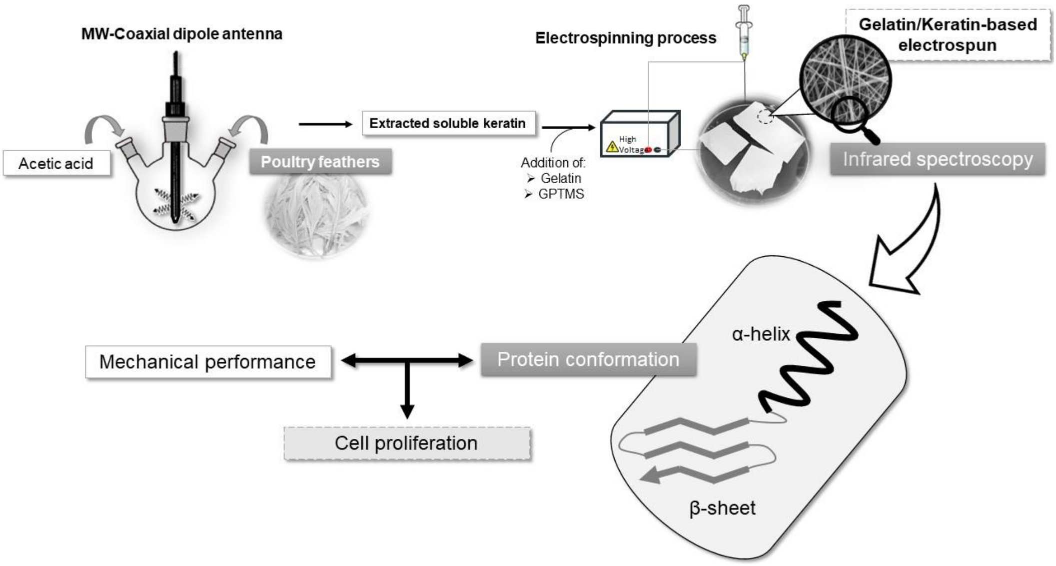

Figure 1. Schematized process which summarized (i) the MW-assisted extraction of keratin from poultry feathers; (ii) the production of gelatin/keratin-based electrospun by ES; (iii) the protein conformation study and its correlation with mechanical performance and cell proliferation.

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Chiral analysis by NMR spectroscopy

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Divergent pharmacological behaviour of two enantiomers of an active ingredient[1] has urged many research areas to develop increasingly reliable methods for monitoring and quantifying stereoisomeric products.[2-4] In this field, chiral solvating agents (CSAs) for NMR spectroscopy have gained increasing popularity.[3,4] Several classes of CSAs have been reported, spanning from synthetic chiral products to enantiomerically pure natural products. Among chiral natural products great potentialities of quinine (**Qui**, Fig.1) have been recognized since long time both as underivatized and derivatized system. We exploited here **Qui** for the enantiodiscrimination of *N*-trifluoroacetyl (TFA, Fig.1) amino acid derivatives, enantiomers of which were not only detected and differentiated by ^{19}F spectroscopy, but also in the presence of substoichiometric amounts of CSA, which is quite unusual for the most common CSAs.[5]

In the area of synthetic CSAs, we developed a new C2-symmetric bis-thiourea CSA (**TFTDA**, Fig.1), for the efficient enantiodiscrimination of *N*-amino acid derivatives with free carboxyl function, particularly acetylates (Ac) and TFA. **TFTDA** led to higher enantiodifferentiations, both at ^{1}H and ^{19}F nuclei, with respect to its monomeric counterpart **TFTMA** (Fig.1), suggesting thus the cooperativity between the two thiourea arms. Ternary mixtures were analyzed, by employing DABCO as third achiral additive, even in diluted conditions or in substoichiometric conditions (0.3 equiv. of CSA). The active role of DABCO in enantiodiscrimination processes has been demonstrated.

Among macrocyclic receptors, specifically cyclodextrins (CDs) largely employed in the gas-chromatographic separation of pharmaceutical relevance α-, β- and γ- acetylated-silylated CDs (**AcSiCDs**, Fig.1) were tested for the enantioseparation of fluorinated anesthetics, the nonequivalences of which were strongly dependent on the macrocycle size and on the solvent. The greatest enantioseparations at ^{19}F nuclei were observed for isoflurane and compound B (the volatile degradation product of sevoflurane) in C_6D_{12} by employing **γ-AcSiCD** as chiral agent, also in substoichiometric conditions.

Partially and exhaustively methylated β-cyclodextrins, such as **MCD**, **DIMEB** and **TRIMEB** (Fig.1) were instead used and compared in the hydrolysis and enantiodiscrimination of benzodiazepine derivative (*R*)- or (*S*)-oxazepam hemisuccinate (OXEMIS, Fig.1). Among methylated cyclodextrins, **DIMEB** proved to be most suitable to interact with the two enantiomers of OXEMIS and differentiate them, without hydrolysis of the hemisuccinic arm.[6]

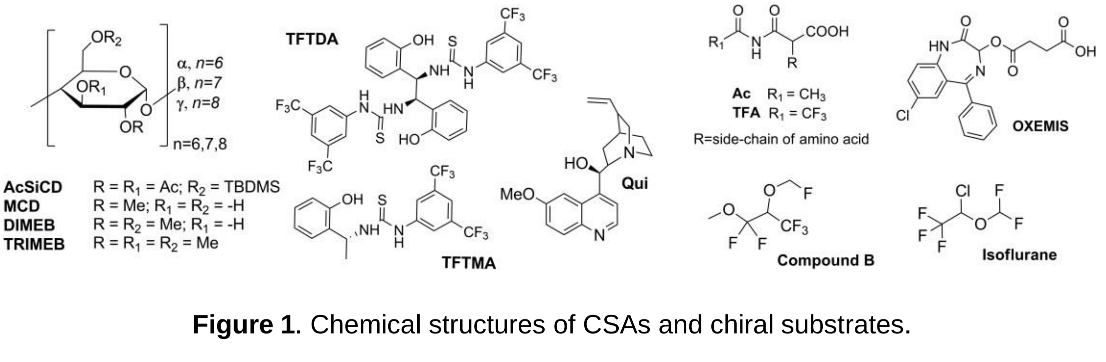

Figure 1. Chemical structures of CSAs and chiral substrates.

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Surface hopping dynamics with exciton models in a semiempirical framework

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The electronic excitation energy transfer (EET) is a fundamental process, in which electronic excitation is transferred from a donor fragment to an acceptor. This process normally starts with a chromophore (the donor) being optically excited, and then the excitation is transferred to a nearby acceptor. The study of EET and other aspects of nonadiabatic dynamics in multichromophoric systems calls for employing some sort of “divide and conquer” strategy. In this respect, one of the most successful schemes is offered by the Frenkel exciton model, where the electronic excited states of the multichromophoric system are represented by linear combinations of localized excitations. Thus, we will present an implementation of the *Frenkel exciton model* in the framework of the semiempirical floating occupation molecular orbitals-configuration interaction (FOMO-CI) electronic structure method to simulate the dynamics of multichromophoric systems, in which excitation energy transfer can occur, by a very efficient approach [1]. We will also show an application of our implementation in the study of the self-assembled monolayers (SAMs) of 4- (biphenyl-4-ylazo)-biphenyl-4-thiol (ABPT) molecules, where the excitonic interaction among 12 azobenzene chromophores were considered during the surface hopping dynamics. However,Frenkel exciton models are designed to describe local excitations, which makes its use not suitablefor systems where, for instance, charge transfer (CT) effects play an important role. To improve this shortcoming, we will present the formulation and implementation of an *extended exciton model*which was designed to include CT states, multiple excitations belonging to two different chromophores, or, for instance, singlet states which are the combinations of two triplets.

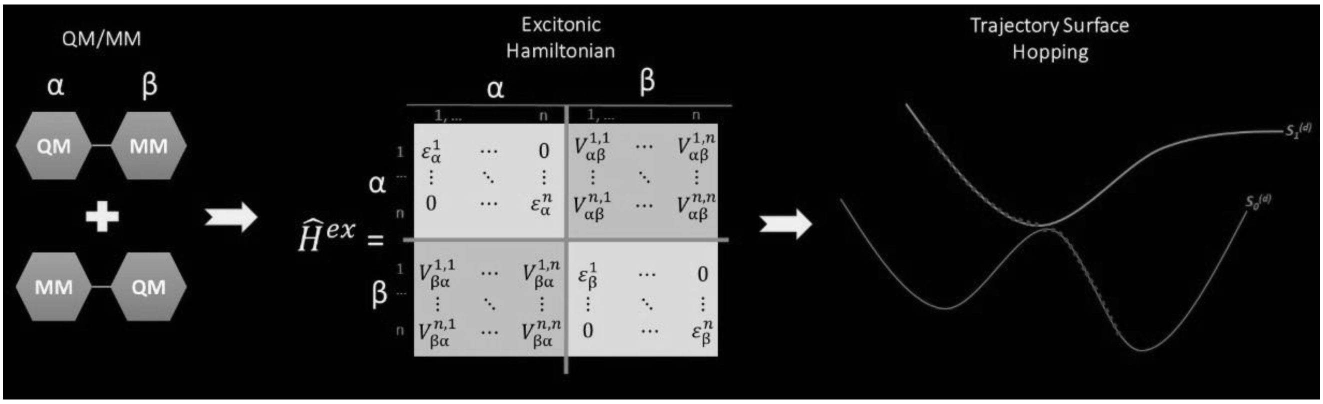

Figure 1. Schematic representation of our Frenkel exciton model implementation.

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SHORT ORAL COMMUNICATIONS

Design, synthesis and biological evaluation of benzylpiperidine-based reversible MAGL inhibitors

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Monoacylglycerol lipase (MAGL) is a cytosolic serine hydrolase which represents one of the most interesting enzymes of the endocannabinoid system (ECS). MAGL is the major responsible of the hydrolysis of brain 2-arachidonoylglycerol (2-AG), an endocannabinoid neurotransmitter involved in many physiological and pathological processes, such as cancer progression. This enzyme is overexpressed in aggressive cancer cells and primary tumors, where it provides a lipolytic source of free fatty acids, and promotes cancer aggressiveness.[1] Thus, MAGL can be considered as a suitable target to be inhibited in order to develop new potential anti-cancer agents. So far, almost all MAGL inhibitors reported in literature irreversibly inhibit this enzyme, causing a chronic MAGL inactivation which determines many side effects in animal studies.[2] At present, only few reversible and selective MAGL inhibitors have been developed and therefore this still remains an unexplored and appealing research field.

We designed a new class of benzylpiperidine-based reversible MAGL inhibitors among which compound **1** proved to be the most potent derivative of this series (IC_{50} value of 2.0 nM).[3] Benzylpiperidine **1** demonstrated to be selective towards other targets of the ECS such as fatty acid amide hydrolase (FAAH) and α/β hydrolase-6 and -12 (ABHD6 and ABHD12). In preliminary pharmacological assays on pancreatic cancer cells, compound **1** showed a good antiproliferative activity on SUIT-2 immortalized cancer cells and on PDAC2 and PDAC3 primary cell cultures (IC_{50} values ranging from 7.25 to 12.61 µM) compared to normal cells HPNE ($IC_{50} > 20$ µM). Additionally, compound **1** not only remarkably enhanced apoptosis induction in PDAC cells, but it also notably reduced cell migration and exerted a synergistic effect when combined with the chemotherapeutic drug gemcitabine.

In conclusion, the newly developed benzylpiperidine **1** is a potent, selective and reversible MAGL inhibitor that could be used as anti-cancer agent for PDAC treatment.

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How I turned my kitchen in a lab during the pandemic and its (non-)icy outcomes

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In the past two years, the national lockdowns and the unusual working conditions that came with the Covid-19 pandemic, have dramatically impacted the life of researchers. In the case of experimentalists, whose job cannot be fully done remotely, the impossibility to physically access laboratory and other facilities meant a slower pace of data production and testing.
While many took this opportunity to perform other tasks – such as writing, organizing future work, and studying –, a serendipitous encounter with an improbable manuscript about ice adhesion, inspired me in trying a new idea and convinced me to set up a small laboratory in my house to develop my own homemade anti-icing solution.

In particular, with the help of colleagues, we developed and characterized a series of slippery lubricant-infused porous surfaces (SLIPSs) realized by impregnating with silicone oil a candle soot layer deposited on double-sided 3M adhesive tape. These former consists of highly porous nanostructured materials where a lubricant fills the cavities and covers the surface, resulting in an interface which can be considered liquid and that prevents the adhesion of different materials. Capillary forces hold the lubricant in place and the porosity of the material act as a reservoir.

Despite the use of common household items, these SLIPSs showed anti-icing performance comparable to other systems described in the literature (ice adhesion < 20 kPa) and a good resistance to mechanical and environmental damages.
Moreover, the use of a flexible and functional substrate as tape allowed these devices to be stretchable without suffering significant degradation and highlights how these systems can be easily prepared and applied anywhere needed. The stretching and bending also provides an extremely efficient way to deliver the force necessary to detach the ice, showing the good performances of flexible SLIPS as actual mechanical ice removal technology.

Figure 1. Cartoon showing the working principle and the fabrication procedure of SLIPS on tape.

Oxygen introduction on phosphor-gold linear complexes as an effective way to enhance thioredoxin reductase inhibition in cancer cells.

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A panel of four gold(I) complexes, inspired to the clinically established compound auranofin, was prepared and characterized. All compounds possess an $[AuP(OCH_3)_3]^+$ cationic moiety, in which the triethylphosphine of parent compound auranofin was replaced with an oxygen-rich trimethylphosphite ligand. The gold(I) linear coordination geometry was completed by Cl^-, Br^-, I^- and the thioglucose tetracetate moiety. This "ligand exchange approach" has been already tested in our laboratories with some interesting results [1,2]. Despite its close similarity to auranofin, the panel compounds exhibited some peculiar and distinctive features, such as the weaker P-Au bond strength. Moreover, the replacement of triethylphosphine with a polar trimethylphosphite group, significantly improved the panel hydrophilicity. These differences might confer to the new molecules significant pharmaceutical and therapeutic advantages over auranofin itself, first of all, due to the better solubility in aqueous media. The solution behavior of the whole panel, as well as the compounds' interactions with some biologically relevant proteins, were comparatively analyzed through ^{31}PNMR and ESI-MS. Remarkable differences with respect to auranofin were disclosed upon interaction with model biomolecules. In particular, the novel complexes showed improved inhibition capabilities towards key enzyme thioredoxin reductase. Finally, the cytotoxic effects produced by the panel toward the A2780 ovarian cancer cell line were measured and found to be strong and nearly superimposable to those of auranofin.

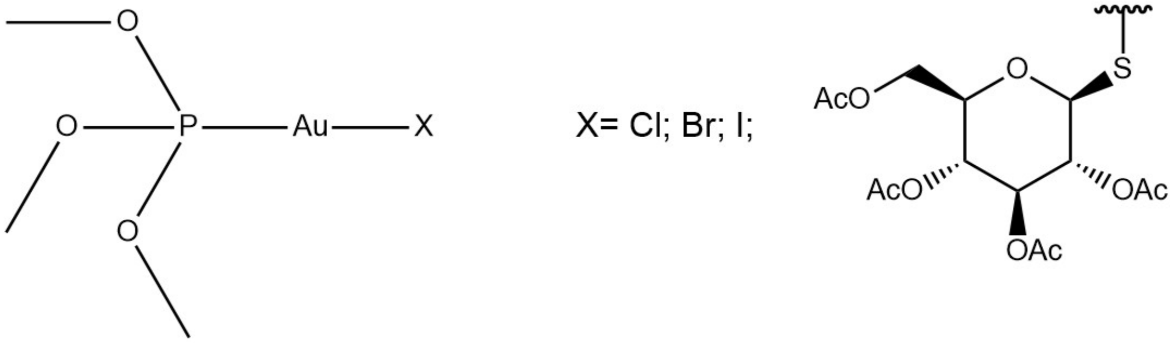

Figure 1. The investigated compounds

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Lignin: a bio-based dielectric polymer for organic field-effect transistors

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Lignin is a biopolymer, recovered as a waste product of industrial pulping processes of lignocellulosic biomass. Lignin displays a complex structure, poor solubility in common solvents, broad distribution of molecular weight, and properties that depend on natural origin and isolation procedure [1]. This makes the lignin valorization a challenging point for chemists and materials scientists, especially in device fabrication where materials with regular and definite molecular structures are required [2]. In this communication, we present the structural and chemical-physical characterization of two kraft lignins, named **L1** and **L2**, and we describe which structural characteristics will affect lignin efficiency in serving as an excellent gate dielectric polymer for OFET devices. Our promising results demonstrate the effectiveness of **L1** and **L2** as gate dielectric layers in pentacene or C60-based bottom gate top contacts OFET devices [3]. In addition, we present the solvent fractionation of **L1** and **L2** by Soxhlet or Kumagawa methods, supporting a deeper characterization of their chemical structures [4].

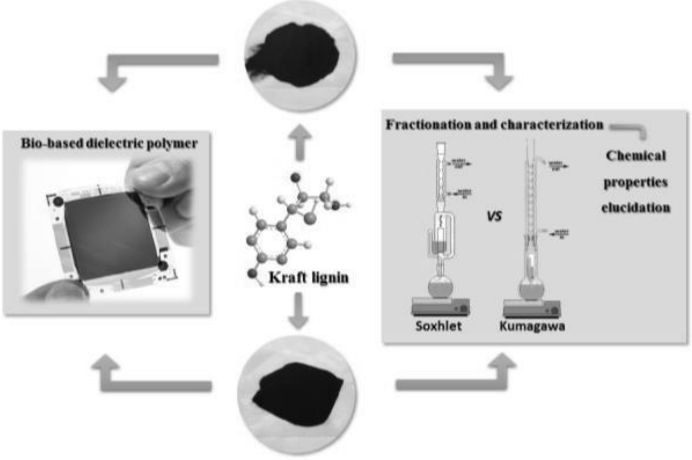

Figure 1. Fractionation, characterization, and application of two types of Kraft lignin

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Influence of Sulfur-Curing Conditions on the Dynamics and Crosslinking of Rubber Networks: A Time-Domain NMR Study

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Elastomers are polymeric materials extensively used for manufacturing a wide range of products for industrial applications, especially in the tire industry. These materials are obtained by vulcanization of one (or more) polydiene polymer(s) in the presence of sulfur and other additives (accelerators, activators, plasticizers, reinforcing fillers, etc.). During this process, chemical crosslinks are formed between the polymeric chains, which provide elasticity and durability to the final product. Furthermore, depending on the formulation and the vulcanization conditions, other mechanical properties required for industrial applications can be obtained. Importantly, such macroscopic properties are strongly related to the microscopic structure of the polymeric network [1]. Consequently, the investigation of microscopic and macroscopic properties giving access to information on the network structure in relation to the vulcanization conditions is fundamental for the optimization of processing and performance of elastomeric materials.

In this context, ^{1}H time-domain NMR (TD-NMR) represents a valuable tool to gain insights into the molecular dynamics of the polymeric chains. In fact, this technique allows to measure NMR observables (^{1}H T_1 and T_2 relaxation times and ^{1}H-^{1}H residual dipolar couplings (D_{res})), which depend on the modulation of ^{1}H-^{1}H dipolar couplings by segmental motions. These motions are quite fast in elastomers above glass transition temperature, but are anisotropic, resulting in residual ^{1}H-^{1}H dipolar interactions, which depend on the amount and distribution of topological constraints in the polymeric network [2].

In this work, natural and isoprene rubbers vulcanized at different curing temperatures and different sulfur contents have been investigated by exploiting ^{1}H TD-NMR techniques, including ^{1}H multiple-quantum experiments for the measurements of D_{res}, Carr–Purcell–Meiboom–Gill pulse sequence for the evaluation of ^{1}H T_2 relaxation times, and field cycling NMR relaxometry for the measurements of ^{1}H T_1 relaxation times on a wide range of Larmor frequencies (10 kHz-35 MHz). The NMR observables were compared with the crosslink density or macroscopic properties of the material that depend on this quantity, obtained using routinely employed methods in industrial analyses, allowing to gain insight into the effects of the formulation and the vulcanization conditions on the structure and dynamics of the polymeric networks [3].

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A novel method for the analysis of sweat volatiles using evaporative dynamic headspace and comprehensive GCxGC high resolution MS

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The POTION project investigates whether different human emotional states induce the excretion of specific sweat volatiles that may convey information about the emotive state of the individual. To elucidate this process, a sensitive and powerful analytical method was necessary. In this study, sweat samples from 40 volunteers were collected using sweat pads. We used dynamic headspace extraction, which mimics the volatilization of these chemicals from the skin. And to ensure high chromatographic peak purity and identification power, we have used comprehensive GCxGC interfaced with a high-resolution time-of-flight (TOF) mass spectrometer.

Volatile organic compounds (VOCs) in sweat have been studied before combining a diverse set of sampling methods, predominantly liquid extraction of sweat pads and in-situ sampling using solid phase microextraction (SPME) and stir-bar sorptive extraction (SBSE)[1]. Dynamic headspace extraction (DHS) is a very powerful extraction and enrichment technique for the sampling of aqueous matrix-based samples to be analysed by gas chromatography, very commonly used for flavour and fragrance analyses[2]. Due to its exhaustive nature, the combination of DHS with the superior chromatographic resolving power of comprehensive GCxGC[3] is almost a necessity due to the enormous complexity of the VOC profile of human sweat samples. Similar studies have been carried out in the past but lacked the detailed information on chemical identification that is presented in our study[4]. Our method shows a good overlap (581 *vs* 366 chemicals – perfectly matching about a third) with the combined coverage of all other reported sweat volatiles by Costello's group[1] (**Figure 1**), its drawbacks are the lack of detectability of organic acids and very volatile chemicals both due to methodological considerations. By performing such powerful and reliable identification work we hope to reach a better understanding of which chemicals or chemical groups may be responsible for emotional chemosignaling.

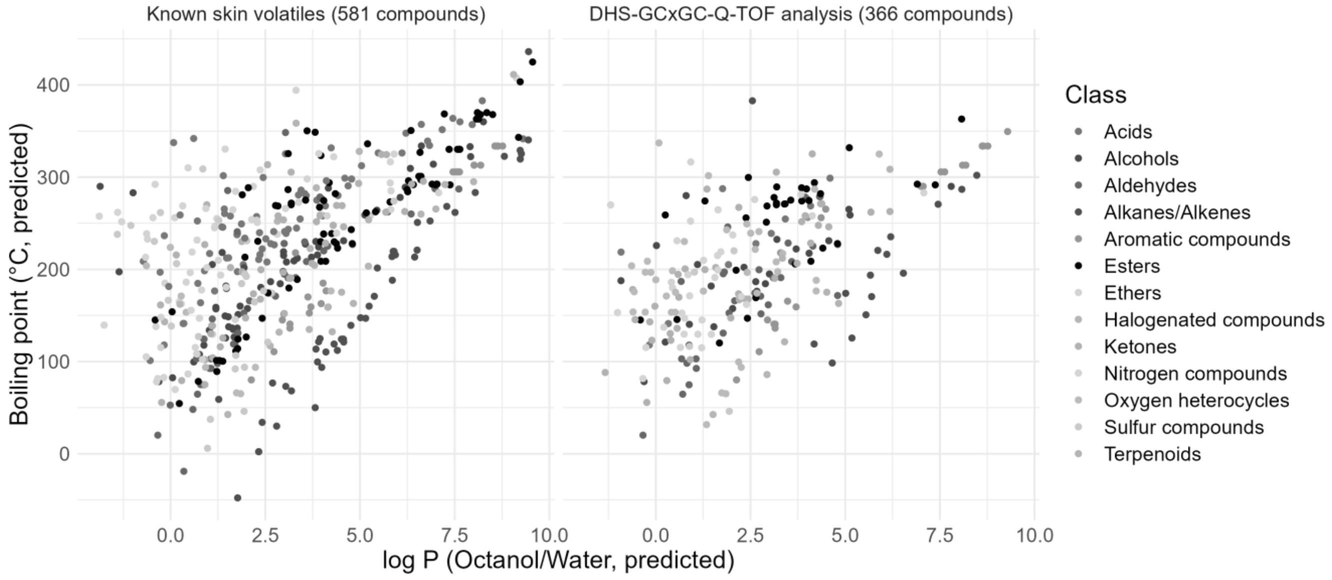

Figure 1. A comparison between the detected sweat volatiles reported in the literature by Costello[1] (left) and the presented DHS-GCxGC-HRMS method (right). The chemicals are presented in the two-dimensional space defined by their boiling points and their hydrophobicity (log*P*).

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POSTER COMMUNICATIONS

P1 D. ACCOMASSO, A. ARCIDIACONO, L. CUPELLINI, B. MENNUCCI. *The simulation of excited state dynamics of cantaxanthin in the Orange Carotenoid Protein.*

P2 V. ALBANO, M. TADDEI. *Aliovalent doping in Zr-based MOF UiO-66 with* Y^{+3} *cations.*

P3 I. BERTELLI, M. MATTONAI, J. LA NASA, E. RIBECHINI. *Study of thermal behaviour and response to accelerated aging process on pine resin and beeswax mixtures found as adhesives in archaeological finds.*

P4 G. BIALE, J. LA NASA, M. MATTONAI, A. CORTI, V. CASTELVETRO, F. MODUGNO. *Detection of potentially harmful compounds leaching out from microplastics in seawater during accelerated aging.*

P5 L. BIZZARRO, A. GIOVANELLI, M. TADDEI. *Synthesis of new fluorinated CeIV-based metal-organic frameworks with MIL-40 topology.*

P6 A. BOTTO, I. BONADUCE, M. CAPULA, E. GIOVANNETTI, L. A. MCDONNELL. *Bio-orthogonal non-canonical amino-acid tagging (BONCAT) of pancreatic ductal adenocarcinoma.*

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P14 G. D'ARCANGELO, S. LEGNAIOLI, B. CAMPANELLA, F. LIPPARINI. *DFT Raman and SERS vibrational analysis of pharmaceuticals.*

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P43 G. SALVADORI, V. MACALUSO, G. PELLICCI, L. CUPELLINI, G. GRANUCCI, B. MENNUCCI. *Uncovering transient intermediates in a bacteriophytochromephotocycle.*

P44 G. SARDELLI, G. SIGNORE, F. BALESTRI, M. CAPPIELLO, U. MURA, A. DEL CORSO, R. MOSCHINI. *Effect of hyperglycemic conditions on a cultured human lensepithelial cell line: the involvement of aldose reductase.*

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P47 L. SEMBRANTI, A. BONINI, F. VIVALDI, A. G. CAROTA, N. POMA, A. TAVANTI, F. DI FRANCESCO*. Laser-induced graphene electrode for aptamer-based sensingof bacteria.*

P48 L. SPAGNUOLO, R. D'ORSI, N. DI FIDIO, C. ANTONETTI, A. M. RASPOLLI GALLETTI, A. OPERAMOLLA. *Extraction of cellulose nanocrystals from lignocellulosic biomass: application of chemical and enzymatic hydrolysis.*

P49 A. TADDEUCCI, G. SILIGARDI, L. DI BARI, G. PESCITELLI, F. ZINNA. *Circular Dichroism Imaging of two novel Chiral Organic Dyesin Thin Film.*

P50 V. TEMPESTI, G. MANNINI, G. PECORINI, A. GABBANI, A. GRANDONI, A. PETRI, F. PINEIDER, D. PUPPI. *Validation of an automated dispensing system of epoxyadhesives for ultrasound probes manufacturing.*

P51 S. VOLANTE, JAN DEMEL, G. BRESCIANI, F. MARCHETTI, M. TADDEI. *Metal carbamate complexes for the synthesis of metal-organicframeworks (MOFs).*

P52 O. G. WILLIS, F. PETRI, G. PESCITELLI, C. MICHELETTI, A. MANDOLI, F. ZINNA. *Remarkable near-infrared chiroptical properties of chiral Yb, Tm and Er complexes.*

P53 F. CORDELLA, G. ALONCI, G. ANGELICI, R. MOCCHI, N. ZERBINATI*. De novo design and sustainable synthesis of new green materials based on cross-linked hyaluronic acid for surgical application.*

P54 E. EREMEEVA, F. M. VIVALDI, A. CERCHIAI, F. DI FRANCESCO. *UV-activated metal oxide ZnO/ZnO:Ni based hydrogen gas sensor.*

The simulation of excited state dynamics of cantaxanthin in the Orange Carotenoid Protein

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The orange carotenoid protein (OCP) is a water-soluble photoactive protein consisting of two domains, the N-terminal and the C-terminal domains (NTD and CTD), which embed a keto-carotenoid chromophore at their interface. The main function of OCP is the photoprotection of cyanobacteria [1]: in high-light situations, OCP can bind to the phycobilisomes (PBS), the light-harvesting complexes of cyanobacteria, and quench their excited states. In this way, the dangerous excess of light arriving at the PBS is dissipated into heat.

In order to perform its photoprotective function, OCP must be converted from the inactive orange form (OCP^O) to the active red form (OCP^R). The $OCP^O \rightarrow OCP^R$ conversion starts with the electronic excitation of the carotenoid chromophore by absorption of strong blue-green light and its excited state relaxation leading to a first intermediate (P1) which precedes a translocation of the carotenoid into the NTD domain [2]. Here, we present some preliminary simulations of this excited state dynamics for cantaxanthin, a keto-carotenoid naturally found in OCP. Our simulations are performed using the surface hopping method and a semiempirical quantum mechanics/molecular mechanics (QM/MM) scheme [3].

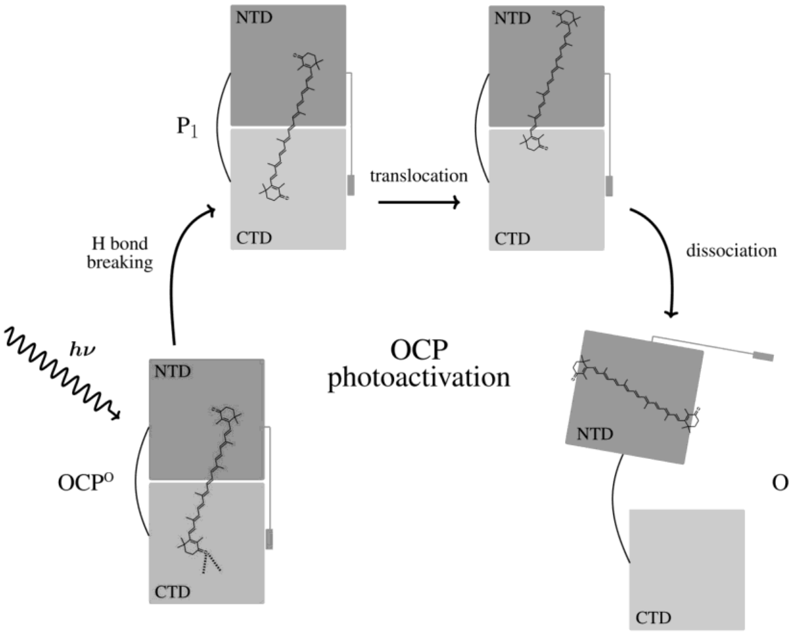

Figure 1. Schematic representation of the OCP photoactivation.

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Aliovalent doping in Zr-based MOF UiO-66 with Y^{+3} cations

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Metal-organic frameworks (MOFs) are a new class of crystalline and porous materials consisting of ions or metal clusters held together by a multitopic organic ligand forming a 2D or 3D crystalline structures. Their structural and functional diversity, synthetic versatility, large surface area, ease of tailoring the pore size and structure, make them promising materials for a wide range of applications such as gas storage and separation[1,2], catalysis[3] and others[4].
UiO-66(Zr)[5], a MOF based on Zr(IV) and terephthalic acid (BDC), has achieved resounding success due to its cheap and easy synthesis, high thermal and hydrolytical stability, high porosity and high chemical versatility. The inorganic unit of UiO-66 is a metal oxo-hydroxo cluster with the same local Zr-O connectivity found in cubic zirconia, a metastable form of zirconia at room temperature. Doping ZrO_2 with Y(III)[6], alias **aliovalent doping**, leads to the stabilization of cubic topology at room temperature yielding yttria-stabilised-zirconia (YSZ), with general formula $Y_xZr_{1-x}O_{2-x/2}$. The charge imbalance caused by the introduction of a lower valent cation in the structure leads to the formation of oxygen vacancies, as a result of charge compensation in the material, giving anionic conductivity of O^{2-} ions.
Based on this premise, it can be expected that doping of UiO-66(Zr) with Y(III) might alter the material's chemical-physical properties. We explored doping by direct synthesis, screening a wide range of synthetic parameters, such as different Zr and Y precursors and Zr/Y ratio, with and without the addition of crystallization modulators. The highest Y loading (xx%) was achieved using $ZrCl_4$ and $YCl_3 \cdot 6H_2O$ as metal precursors, in *N,N*-dimethylformamide as the solvent and in the presence of 2-fluorobenzoic acid and 2,6-difluorobenzoic acid as modulators. Because of the large difference in ionic radii between Y (1.02 Å) and Zr (0.84 Å), we believe that Y causes an excessive strain in the structure, leading to a low incorporation of Y in the MOF and the formation of a secondcrystalline phase at higher amount of dopant.

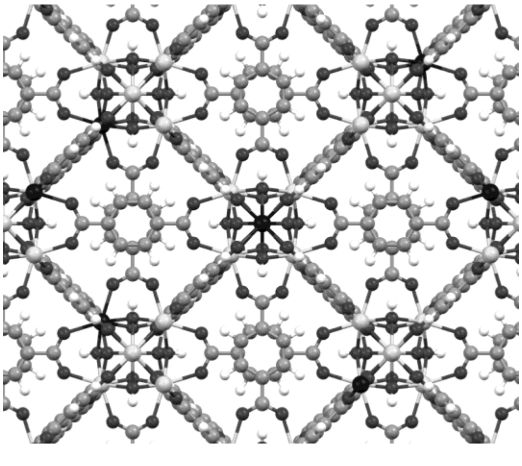

Figure 1. Representation of UiO-66 (Y/Zr). Yttrium and Zirconium ions are respectively depicted in grey and black

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Study of thermal behaviour and response to accelerated aging process on pine resin and beeswax mixtures found as adhesives in archaeological finds

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Resins are among the most common organic materials used as adhesives in archaeological finds [1]. In particular, pine resin can be found either in its natural form or as tar and pitch, products that were obtained by subjecting resinous materials to hard-heating (pyrolysis) processes [2], [3]. The adhesives found at archaeological sites are frequently constituted of mixtures of resin (or pitch) and other materials. In order to modify the physical and chemical properties of a resinous adhesive, a variety of organic materials, such as waxes or animal fats, were often also added [1], [4], [5]. Given that in the case of mixtures there is a significant change in the properties of the adhesive, it is not only important to identify its constituents, but also to understand how they interact with each other and what these interactions imply. In this work, reference mixtures of beeswax and pine resin were studied to investigate the effect of their interactions on the composition and properties of the resulting adhesives. The mixtures were also heated to simulate the most common ancient processes used in adhesives manufacturing. The acquired data has been then compared with those obtained from the analysis of archaeological samples, to obtain information on ancient technological knowledge.

Different analytical techniques were employed: flow injection analysis-high resolution mass spectrometry (FIA-HRMS), evolved gas analysis coupled with mass spectrometry (EGA-MS) and analytical pyrolysis combined with gas chromatography/mass spectrometry (Py-GC/MS).

EGA-MS was used to investigate the thermal behaviour of the mixtures and obtain information on production techniques and ageing processes. EGA-MS data were processed by isoconversional methods [6] to estimate the activation energies associated with the thermal degradation process of the adhesives. The results suggested that archaeological mixtures were subject to a thermal pre-treatment before their use as adhesives; the heating led to a material with new thermal characteristics, occurred from the formation of hybrid species between the diterpenes of resin and the compounds of beeswax. FIA-HRMAS analyses [7] showed the formation of hybrid resin-beeswax compounds after heating of the reference mixtures. To study the aging of these mixtures, a double step pyrolysis-gas chromatography/mass spectrometry (Py-GC/MS) was performed using an online UV-irradiator. The gas chromatographic analysis highlighted that the terpenes of pine resin did not act as antioxidant on the beeswax components, which underwent chemical degradation to produce short-chain alkenes and aldehydes, as well as other oxidized species.

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Detection of potentially harmful compounds leaching out from microplastics in seawater during accelerated aging

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Microplastics (MPs) have been detected almost everywhere as environmental contaminant being a major threat to both the ecosystem and human health. Moreover, studies have confirmed that MPs should not be considered chemically stable pollutants; in fact, plastic debris in the environment undergo chemical and physical fragmentation/degradation processes that lead to the release of low-molecular weight degradation products, besides additives and adsorbed organic pollutants, potentially toxic. In this work we systematically studied the organic compounds leached out from MPs upon aging. We performed accelerated photo-oxidative aging of four reference MPs, namely high-density and low-density polyethylene, HDPE and LDPE, polypropylene PP, and polystyrene PS, directly in artificial seawater and we applied gas chromatography/mass spectrometry (GC/MS), after selective solvent extraction and derivatization, to study the water-soluble organic fraction leached out from MPs. GC/MS analyses enabled us to characterize different chemical species and to detect more than 60 different compounds; in particular linear and branched mono- and dicarboxylic acids along with linear and branched hydroxy acids were detected mainly for PP, HDPE, and LDPE (Figure 1), while benzoic acid and phenol derivatives were detected for PS. The results for reference MPs were then compared with those obtained by analyzing the leachates in artificial seawater from aged plastic debris collected in the environment. The differences between the leachates from reference MPs and environmental plastic debris were mainly related to the abundances of the chemical species detected, with higher amounts of dicarboxylic acids and oxidized species for environmental MPs. Finally, through bibliographic research, we evaluated the toxicity of the chemical species released upon aging. These results provided an investigation of theextent of the molecular fragments that leach out from MPs in the aqueous environment as a result of photo-oxidative degradation, giving a preliminary overview of the effectiveness and extent of macromolecular fragmentation into low and medium molecular weight oxidation products upon photo-oxidative aging.

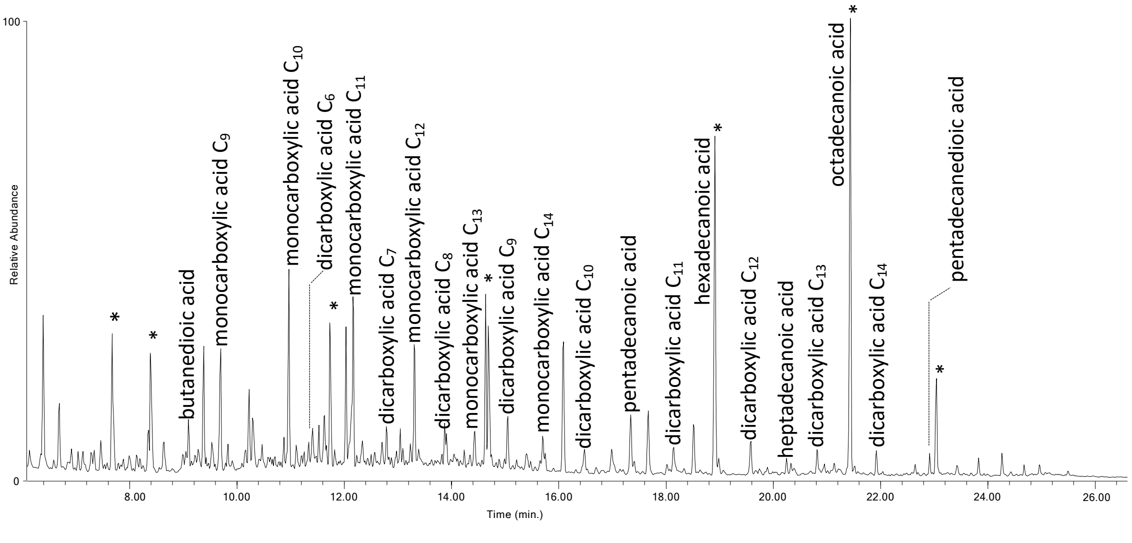

Figure 1. Chromatogram of the soluble organic fraction of reference LDPE after artificial aging.

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Synthesis of new fluorinated Ce^{IV}-based metal-organic frameworks with MIL-140 topology

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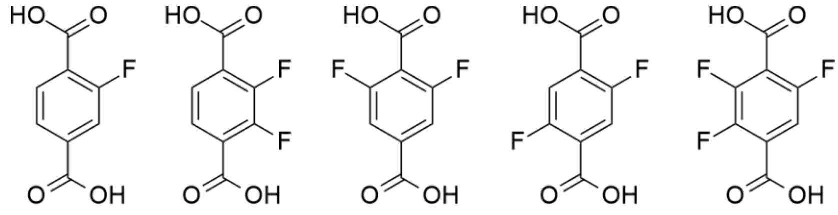
Metal organic frameworks (MOFs) are a class of crystalline materials that consist of metal ions or clusters connected by organic linkers to form porous structures. These materials are suitable for many applications (e.g., gas separation [1], gas storage [2] and catalytic reactions [3]) due to their tuneable pore sizes, the high surface area, and the possibility of modifying properties of the material by changing the metal centre or the organic linkers. In the MIL-140 topology, well known for tetravalent metals, edge-sharing CeO_7 units, carboxylate groups and μ_3-oxide bridges form the Inorganic Building Units (IBUs). These IBUs are connected to each other through terephthalate ions (BDC^{2-}) to form a 3D network characterised by 1D pores with triangular shape.

It is known that the presence of four fluorine atoms in the terephthalic moiety imparts a unique CO_2 step-shaped adsorption isotherm that enhances the selectivity over N_2 [4]. To investigate how fluorine influences adsorption properties, we have synthesized a series of new Ce^{IV}-based MOFs with MIL-140A topology characterized by a different degree of fluorination of the organic linker (**figure 1**).

F3_MIL-140A(Ce), *o*F2_MIL-140A(Ce), *p*F2_MIL-140A(Ce) and F1_MIL-140A(Ce) were obtained from the reaction of the organic linker and cerium^{IV} ammonium nitrate (CAN, 1 eq) in MeCN [5] at 140°C. The obtained MOFs were characterised by powder X-ray diffraction (PXRD), attenuated total reflectance infrared (ATR-IR) spectroscopy, and ^1H and ^{19}F nuclear magnetic resonance (NMR) spectroscopy. F3_MIL-140A(Ce) and *o*F2_MIL-140A(Ce) structures have also been investigated by solid-state NMR.

While regarding linker *m*F2-BDC, we are currently studying the ideal synthetic pathway to obtain phase-pure *m*F2_MIL-140A(Ce) with high crystallinity.



F1-BDC *o*F2-BDC *m*F2-BDC *p*F2-BDC F3-BDC

Figure 1. Organic linkers used in the synthesis of new MIL-140A(Ce) MOFs.

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Bio-orthogonal non-canonical amino-acid tagging (BONCAT) ofpancreatic ductal adenocarcinoma

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Pancreatic ductal adenocarcinoma (PDAC) has a very poor prognosis, with less than 10% of patients alive 5 years after diagnosis. The prognosis of cancer patients is much improved through earlier detection. A recent study reported 5- and 10-year survival rates of 49% and 31%, respectively, for T1-2, N0 and R0 tumors.[1] Earlier diagnosis enables treatment to begin when the tumour is in its earlier stages, and so improve patient prognosis. Early diagnosis requires the identification of characteristic markers of PDAC.

PDAC is characterized by a robust fibroinflammatory response, widespread vascular collapse, and hypoperfusion that make the tumor highly hypoxic and nutrient deprived. This microenvironment promotes tumor invasion, progression, leads to chemotherapy or radiotherapy resistance and eventual mortality. Within the nutrient deprived environment autophagy is central to PDAC metabolism. It has been demonstrated that autophagy shares molecular machinery with exosome biogenesis.[2,3] Exosomes are extracellular vesicles that are secreted from all cells and are present in all body fluids. These vesicles contain molecules characteristic of their cell of origin. Accordingly, the highly hypoxic/nutrient-deprived regions of PDAC are expected to be characterized by altered exosomal molecular signatures, and importantly exosomal surface markers, that would enable the specific isolation of PDAC exosomes from patient serum/plasma.

To isolate exosomes from hypoxic cells I will develop a protein labelling approach that is cell type/phenotype specific, and will enable exosome isolation through the labelled exosome-surface proteins. Bio-orthogonal non-canonical amino-acid tagging (BONCAT) is a technique that labels proteins with an azido moiety; this moiety is introduced during protein synthesis using methionine surrogates, then with a simple click chemistry reaction only the proteins that contain the azido moiety will be enriched.[4]

Cell-specific BONCAT labelling can be achieved using azidonorleucine (Anl) as the Met surrogate. Anl is only incorporated into proteins by a specific mutant form of the protein methionyl-tRNA synthetase (MetRS*). Accordingly, Anl labelling can be restricted to cells equipped with this mutant form. The DNA of MetRS* is introduced into cells by transfection, using specific promoters to target specific cell phenotype (e.g. hypoxia-response elements for hypoxia). Once Anl is added to the media all methionines in the newly synthesized proteins from MetRS* transfected cells will be substituted for Anl, importantly this also includes exosome surface proteins.

Here we will show progress in method development, including results showing incorporation of BONCAT labels into PDAC tumor cells and their enrichment.

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Small Unsaturated Molecules Activation on a Diruthenium μ-Allenyl Scaffold

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The C-C coupling between organic reactants and unsaturated hydrocarbyl fragments on transition metal complexes still arousing great interest both in academia and in industry.[1] In this context, the activation of hydrocarbyl moiety bridged coordinated in dinuclear ruthenium complexes bearing ancillary cyclopentadienyl and/or carbonyl ligands, has been widely investigated.[2] Indeed, the cooperativity effects due to the two metal centres working in concert often lead to an unconventional reactivity and the formation of new bridging ligands.[3]

Here, we demonstrate that an allenyl ligand, bridging coordinated in a diruthenium carbonyl cyclopentadienyl complex, easily reacts with substituted alkenes and ethylene undergoing facile C-C coupling via hydrogen migration (**Fig. 1A**).[4] Cross experiments with deuterated reagents,allowed us to reveal the reaction mechanism.

Moreover, we have found that reaction of the above-mentioned diruthenium complex with internal alkynes, and involving a CO ligand, lead to obtaining η^6-coordinated ruthenabenzenes[6] (arenes with a CH group formally replaced by a ruthenium atom[5]) (**Fig. 1B**). DFT calculations on these new complexes showed a six-membered ruthenacycle with a Shannon aromaticity index in line with related compounds. Despite the formation of ruthenium-coordinated ruthenabenzenes from a pre-existent diruthenium scaffold being a versatile method exploiting the cooperative effects typical of a bimetallic core, this method is still scarce investigated.

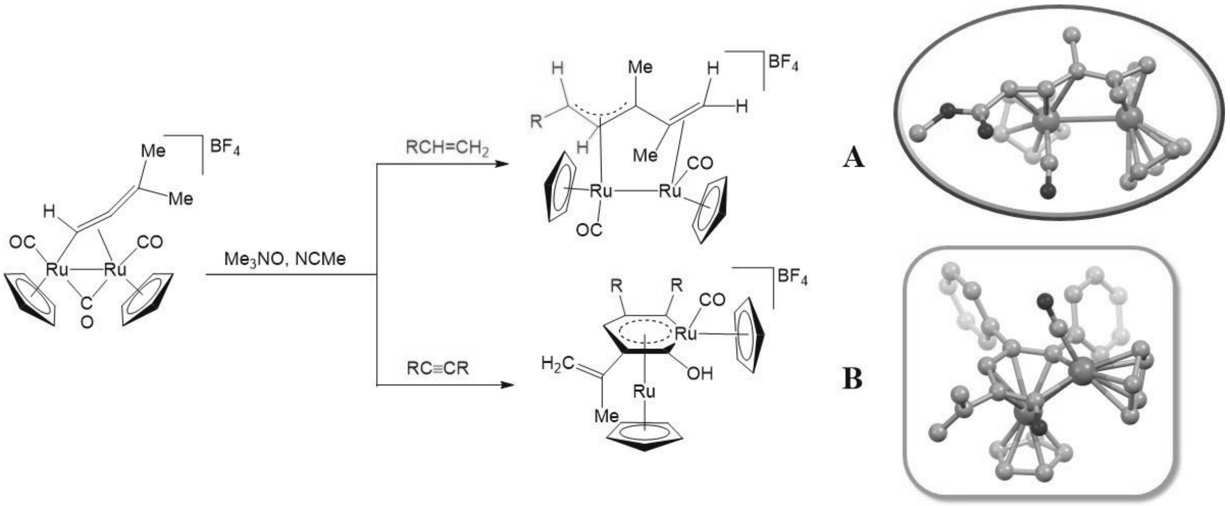

Figure 1. Diruthenium allenyl complex reactivity towards alkenes and alkynes.

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Computational Caracterization of dicationic ionic liquids

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Ionic liquids (ILs) gain a high relevance in the last decades and have been extensively studied as alternatives solvents due to their properties such as negligible vapor tension, thermal and chemical stability, and the possibility to recycle [1]–[4]. In this context, we use the computational technic to characterize and determine the stability of the IL-based on the two imidazolium rings connected by a xylene spacer with ortho (**Figure1a**), meta (**Figure1b**), and para (**Figure1c**) isomers with bromide, tungstate (**Figure1d**). The program gaussian 16 and XTB [8] was used for the analyses.

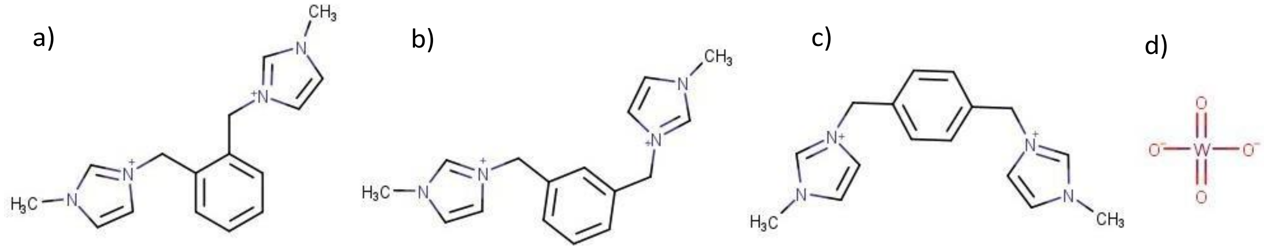

Figure 1: Structure a) orto; b) meta, c) para and d) tungstate anion.

The characterization using the gaussian program with the DFT theory, method B3PW91 and the base SDDall to calculate the IR and RMN spectrums from the IL with both anions. The simulation using molecular dynamics founded that the system based on WO_4^{2-} anion are more stable than those with the Br^- anion. These calculations demonstrate that the presence of the WO_4^{2-} anion creates strong ionic bonds between the cation and the anion leading to stable ionic pairs.

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Optimization of Luminescent Solar Concentrators with NIR-reflective nanoparticles

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Photovoltaic solar technologies are attracting an increasing interest [1], as they enable a significant reduction in the environmental impact compared to other traditional energy sources. In this perspective the concentration of sunlight is a promising approach. Compared to classic large geometric concentrators, luminescent solar concentrators (LSC) have the advantage of being more easily integrated in the urban architecture [2]. LSCs [3] are flat optical devices that use a high quantum yield fluorophore, embedded in a polymer matrix, capable of absorbing incident solar radiation by concentrating most of the fluorescence emitted on the edges of the device by total internal reflection [4]. This makes it possible to conveniently transmit sunlight to the photovoltaic (PV) cells placed on the edges even in cloudy sky conditions. Although significant advances in LSC technology and performance have been made in recent years, power conversion values (PCEs) around 7% and a life-span dependent on the stability of the fluorophore are considered limiting factors for a industrial diffusion of technology. In light of these observations, the goal of this work is the **creation of an innovative LSC,** defined as "**cold LSC**", capable of maximizing the generation of electric current in PV, while filtering the near infrared (NIR) radiation through the incorporation of metal oxide nanoparticles (NPs) able to block NIR radiation. If the transmission of the NIR radiation is blocked by the LSC, the internal environment would not undergo excessive heating phenomena, limiting consumption of energy for its cooling. Furthermore, the reflection of NIR radiation would not cause any overheating of the device, which would not undergo potential degradation phenomena, guaranteeing a useful life of the device compatible with an industrial application. In this work, In_2O_3 NPs were synthesized by thermal decomposition of organometallic precursors [5], aiming at testing their ability to block NIR radiation when incorporated in the LSC.
The NPs were characterized by transmission electron microscopy (TEM) and powder x-ray diffraction (XRD) techniques to determine their morphological and structural characteristics. The optical properties have been studied in transmission and reflection geometry, both in the form of colloidal dispersion and within polymeric nanocomposites, in the UV-visible-near infrared spectral range, to assess their ability to reflect NIR radiation.

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CRISPR/Cas based biosensor for the detection of waterborne pathogens

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Water resources contaminated with pathogen microorganisms are a vectors for the propagation and transmission of diseases, which represent one of the most common causes of mortality and morbidity worldwide and especially in developing countries. Currently, the main approaches for the pathogens detection in drinking water are represented by the traditional microbiological methods, but these techniques are time consuming and require highly trained personnel, expensive reagents and instrumentations [1].In the recent years, the newly discovered *Clustered Regularly InterspacedShort Palindromic Repeats* (CRISPR) and *CRISPR associated protein* (Cas) system seem to have revolutionised the gene editing and molecular diagnostic fields. Indeed, thanks to its programmability selectivity and specificity this endonuclease enzyme system can be used torecognize a specific portion inside of a nucleic acid target, developing a new class of biosensing[2]. In this scenario, the aim of this work is the integration of the innovative CRISPR/Cas12asystem with the advantages of the electrochemical transduction techniques, to develop a portable, low cost and highly specific point of need electrochemical biosensor for the detection of bacteria in drinking water. Briefly, the programmed CRISPR/Cas12 system specifically binds and cuts the target DNA (tDNA), thus triggering the CRISPR/Cas12 collateral activity (trans-activity) that will cleave the methylene blue modified ssDNA probes (ssDNA-MB) immobilized on the electrode surface. Square Wave Voltammetry (SWV) was used as a transduction technique and the difference between of the height peak before and after the enzymatic activity, represented the sensor signal (Figure 1). This work presents the possibility to use the CRISPR/Cas12a system coupled with the electrode surface functionalization for the electrochemical biosensor developing, showing the enzyme cleavage ability in different condition such us: different incubation times, temperatures and concentration of tDNA and ssDNA-MB.

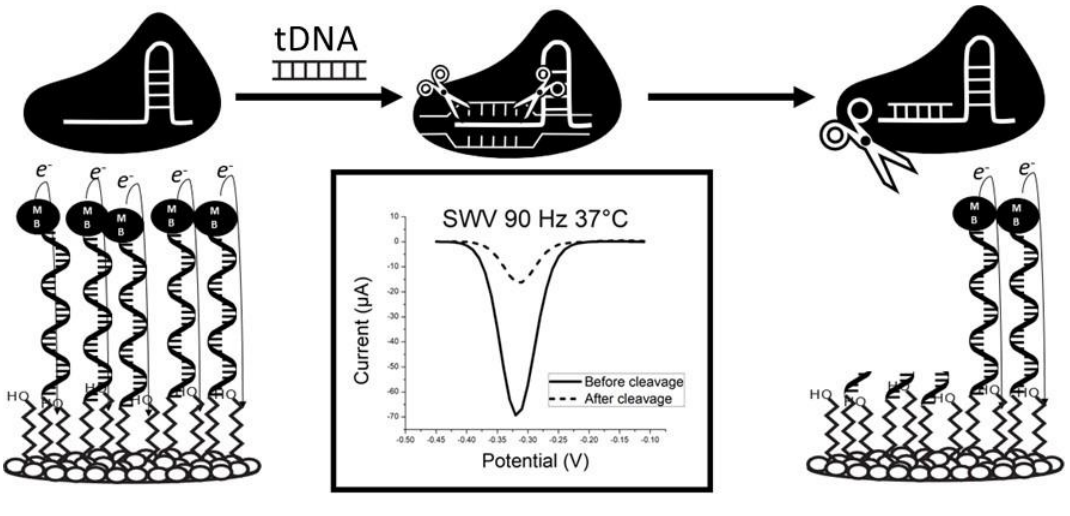

Figure 1. Working principle of the sensing system: recognition of the tDNA, *cis*-activity and *trans*-activity by CRISPR/Cas12a on the electrode surface.

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The derivatization of amino acids

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The analysis of proteins is fundamental in several research fields, such as food, health, environment and cultural heritage. In paintings, animal proteins such as egg, casein and glue were frequently used as binders for pigments.[1]
Gas chromatography coupled with mass spectrometry is particularly useful for the detection of proteinaceous materials in paint media thanks to its high sensitivity and specificity. GC-MS requires low molecular weight molecules and so the macromolecular nature of proteinaceous materials means that pretreatments of the sample are required. In particular a hydrolysis step is necessary in order to free amino acids.[2]
Amino acids can't be directly analyzed by GC-MS, as they are not volatile, they have low thermal stability and they may interact with the column stationary phase. A derivatization step is thus required.
This work presents the study of two different types of derivatization: acylation with ethyl chloroformate (ECF) and silylation with N-tert-butyldimethylsilyl-N-methyl-trifluoroacetamide (MTBSTFA) with 1% of tert-butyldimethylchlorosilane (TMCS).
Acylation is an instantaneous reaction, which proceeds without heating in aqueous media. Amino acids are treated with ethyl chloroformates in the presence of ethanol and pyridine, and the ethyl chloroformate derivatives are subsequently extracted from the reaction mixtures with organic solvents.[3] The major advantage of this protocol is its speed and the great stability of the derivatized amino acids, enabling the automatization of the analysis step.
Silylation requires more time than the acylation (30-40 min) and it must be conducted in anhydrous solvent. Amino acids are mixed with a silyl agent and heating of the reaction mixture is required (60°C).[4] The main drawbacks of the silylation are the low stability of the derivatives in thepresence of environmental humidity, and the sensitivity towards inorganic salts, making purificationsteps prior derivatization necessary. On the other hand, the sensitivity of MS analysis is greater when silyl derivatives are concerned in comparison to ethyl chloroformate derivatives.
This work discusses the optimisation of the conditions of reaction, and presents a systematic comparison and critical evaluation of the advantages and disadvantages the two analytical approaches.

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Selective separation of nitrate and chloride by tuning the hydrophobicity of anion-exchange membranes

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The selective removal or recovery of elements from a multicomponent aqueous stream is relevant for many industrial and agricultural applications. For instance, in closed horticulture irrigation systems the aim is to retain the nutrient nitrate in the recirculating water but to selectively remove the chloride. The technological challenge of this separation is related to the slight difference between these two equally charged ions (NO_3^- and Cl^-) in terms of their size and hydration energy. Epsztein *et al*. [1] explored ion permeation in ion-exchange membranes. Ions were shown to have an activation behaviour of transport – attributed to ion dehydration – according to an Arrhenius-type equation and smaller and more strongly hydrated ions showed a higher energy barrier for transport. Sata *et al*. [2] showed how the presence of a longer alkyl chain bonded to the quaternaryammonium functional group in the polymeric structure of the membrane increases the nitrate's permeation.
Building further on these previous contributions, we studied the selective separation of nitrate and chloride by increasing the hydrophobicity of manufactured anion-exchange membranes (AEMs). Polyvinylidene fluoride (PVDF) was used as a polymer to enhance the hydrophobicity, while a polyaromatic anion-exchange polymer solution (Fumion FAS solution) was used as binder. Different membrane compositions have been manufactured via a facile casting process followed byfurther characterization (permselectivity, bi-ionic potential, selectivity under dynamic conditions). The membrane selectivity under dynamic conditions has been determined in a six-compartment electrodialysis cell, while varying the experimental conditions (ionic strength, current density). The experimental results show that increasing the PVDF concentration in the membranes increases the nitrate transport by a factor of 1.7. Moreover, experimental data indicated that ionic strength and current density also play a role in membrane selectivity.

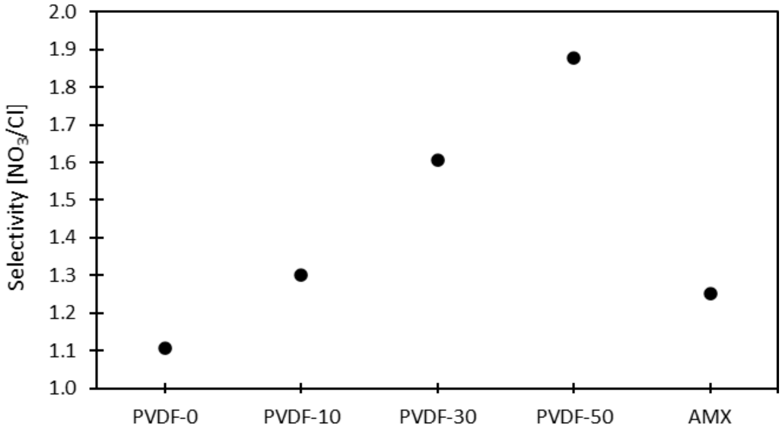

Figure 1: nitrate selectivity of manufactured membranes (PVDF-0, PVDF-10, PVDF-30, PVDF-50) and commercial available membrane (AMX Neosepta) under dynamic condition at 20 A m^{-2}.

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A Fast Method for Electronic Couplings in Embedded Multichromophoric Systems

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Electronic couplings are key to understanding excitation energy transfer and exciton delocalization in natural and artificial light harvesting processes [1]. Here we develop a method to compute couplings in multichromophoric aggregates embedded in complex environments, such as light-harvesting complexes, avoiding expensive quantum chemical calculations. First, we employ a transition charge approximation to represent the quantum mechanical transition densities of the chromophores coupled with a polarizable atomistic classical model to describe the environment (protein, membrane, and solvent) [2,3]. This approach is shown to be as accurate as performing a full TD-DFT QM MMPol calculation, but its computational cost is still comparable with the full QM calculation. We then extend our framework to estimating transition charges directly from the chromophore geometry through a regression approach. This allows bypassing completely the quantum mechanical calculations, except for training the model. Our method allows inexpensive and accurate calculations of couplings, both in vacuo and in environment, for a large number of geometries along molecular dynamics trajectories [4].

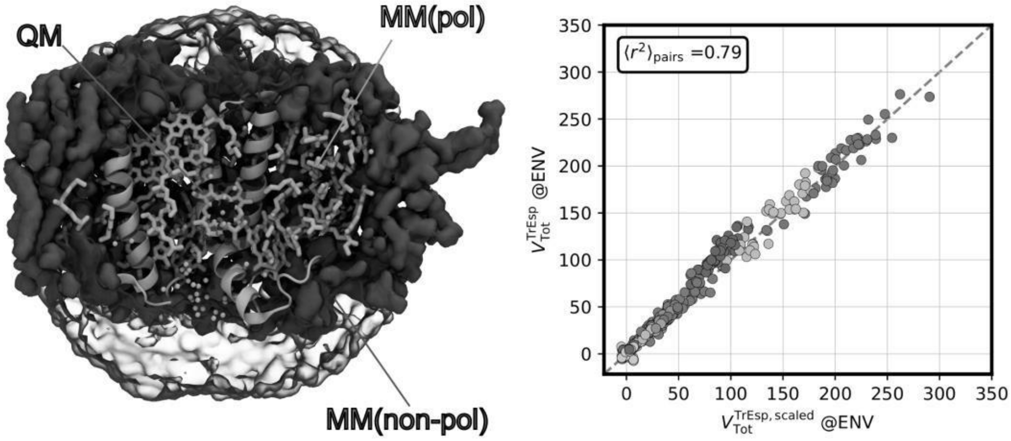

Figure 1. (left) QM MMPol calculation on a chlorophyll in light-harvesting complex II (LHCII). Evidenced are the QM part (the chlorophyll ring), the polarizable MM part (cartoon and licorice representations) and the non-polarizable MM part. (right) Prediction of the trained regression model of the coupling for several chlorophyll pairs in the presence of the environment (horizontal axis) versus the target TD-DFT QM MMPol coupling.

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DFT, Raman and SERS vibrational analysis of pharmaceuticals

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Pharmacologically active compounds, designed for medical and veterinary use, can be dispersed in nature during their manufacture, consumption and disposal. The greatest threat of this class of pollutants is due to the absence of a complete overview of their toxicological effects; however, there is some evidence confirming the fact that exposing the environment to this kind of contaminants leads to deleterious effects to ecosystems and human health [1]. It is therefore evident the importance of developing and validating analytical methodologies for the determination of these compounds in the environment.

In the present work, three commonly used active pharmaceutical ingredients (paracetamol, indomethacin and acetazolamide) have been selected and studied by Raman and surface enhanced Raman spectroscopy both from the qualitative and the quantitative point of view in solution. At the same time, the spectroscopic properties of the compounds were calculated by DFTmethods.

The theoretical study allowed not only to explore the potential energy surface and to identify stable structures in a solvated environment, but also to accurately predict the relative positions and intensities of Raman signals. The calculated spectral predictions supported the entire analytical process. Furthermore, in the case of indomethacin, it was possible to rationalize the evident spectral variations following its hydrolysis reaction at pH>12.

For the quantitative analysis linear multivariate regression models were built, correlating the spectral information to the concentration level of the sample under examination.

The quality of the obtained SERS spectra should be highlighted respect to those available in the literature, and the S/N ratios allow immediate recognition of the characteristic signals of each analyte. The detection limits of the technique were determined, reaching concentrations of theorder of 10^{-4} M for paracetamol and indomethacin, while for acetazolamide it was possible todetect concentrations down to 10^{-8} M.

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Development of a green biodegradable starch-based electrochemical sensor

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The focus of research is currently moving towards biomaterials capable of replacing plastic derivatives in various fields, including sensor industry. Such effort depends on the ever-increasing warning associated with the environmental and economic burden of plastic wastes. In this context, starch-based materials may represent an interesting alternative for the development of biodegradable and green products, as being easily produced from a naturally available starting material [1]. In this work, a crosslinked thermoplastic starch film is used for the first time as a substrate for the development of a set of electrochemical sensors (Figure 1a). The electrodes were produced by physical vapor deposition of gold (working and counter electrodes) and silver (reference electrode), and successfully used in cyclic voltammetry and electrochemical impedance spectroscopy on solutions containing potassium ferrocyanide as an electrochemical probe (Figure 1b). The sensors showed linear correlations between peak current and square root of the scan rate, and between peak current and probe concentration, in accordance with Randles-Ševčík equation. The electroactive/geometric area ratio was calculated in the order of ~1. The sensors proved to biodegrade insidedomestic compost within one week.

These preliminary results pave the way for applying starch-based products in sensing technologies, e.g. for the recognition of biomolecules after the functionalization of the working electrode surface.

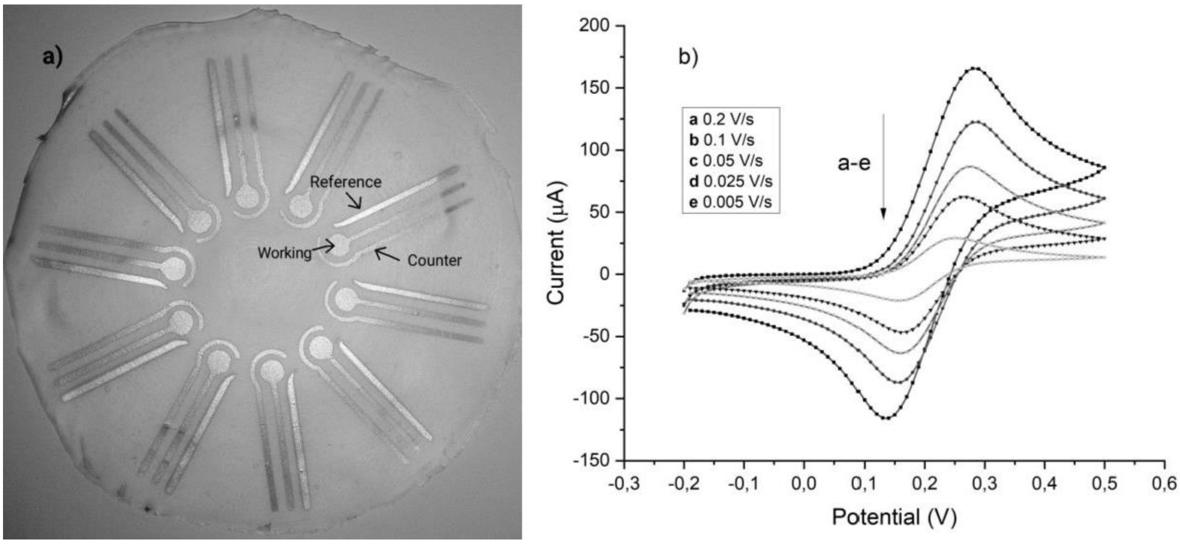

Figure 1. a) Electrodes obtained by physical vapor deposition on thermoplastic starch film; b) cyclic voltammetry of ferrocyanide solution at different scan rates (a-e); ferrocyanide concentration 5 mM in phosphate buffer saline solution 0.14 M, pH 7.4.

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Study of porous polymers for gas separation by means of Solid-State NMR

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Polymer-based membranes are very promising for gas separation, indeed they are appealing alternative systems to industrial energy-intensive processes. Polymers of intrinsic microporosity (PIMs) are a unique class of amorphous polymers, which, because of their rigid structure, cannot pack efficiently leaving free volume, and in particular generating micropores [1]. Since these systems proved to be very effective for gas separation, the development of materials with higher performances is of current interest [2,3]. Obviously, the design of new materials requires a deeper understanding of their structure and dynamics, but also of the interaction between polymers and gases. Solid-State NMR (SSNMR) is one of the most powerful techniques for the structural and dynamic characterization of solid materials, serving as a guidance for the development of new systems with improved gas separation properties. In this work we present a study of triptycene-based polymers containing fluorinated aromatic rings (Fig.1) by means of SSNMR.
The structure was investigated through ^{1}H, ^{19}F Direct Excitation (DE)/Magic Angle Spinning (MAS), ^{13}C{^{19}F} and ^{13}C{^{1}H} Cross-Polarization (CP)/MAS spectra. To get insight into the dynamics of the polymer, ^{1}H and ^{19}F spin-spin (T_2) and spin-lattice (T_1) relaxation times were measured by low-resolution experiments. Moreover, spin-lattice relaxation times of carbon-13 were measured under MAS conditions and high power decoupling from either ^{1}H or ^{19}F nuclei. The analysis of the SSNMR results allowed the main structural and dynamic features of the material to be unravelled.

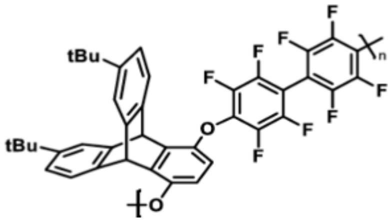

Figure 1. Chemical structure of the repeating unit of a triptycene-based polymer

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Discovering iron gall ink recipes by liquid chromatography coupled to diode array detector and tandem mass spectrometry

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Inks are liquid, semi liquid or solid materials used for writing or drawing on a support. Throughout history, inks have been obtained from many different coloured extracts of plant and animal origin [1]. Iron gall inks have been among the most important inks of the historical and artistic heritage of our society. From an analytical point of view, the identification of inks in drawing or manuscript samples is challenging. This can be due to the variations of both the ink composition and the numerous empirical formulations used over the centuries [2]. To date, most research has been performed by non-destructive analytical methods, which only provide limited information on degradation processes and minor components, which can be of interest in dating an ink [3]. Thus, analytical investigation in heritage science requires new protocols for the analysis of writing inks. Inthis work, we developed an analytical procedure based on High Performance Liquid Chromatography coupled with diode array and tandem mass spectrometric detectors (HPLC-DAD- MS^2) for analyzing iron gall inks. In order to establish the best experimental conditions, we have optimized both the sample pre-treatment and the chromatographic method starting from ink’s formulations reproduced in the laboratory according to historical recipes [2]. This allowed us to identify the molecular markers of iron gall inks, such as *gallic acid*, *ellagic acid*, *digallic acid* and *poly-galloylglucose*, and to reveal different chemical profiles depending on the historical ink recipesadopted. Furthermore, by performing ageing tests on the reference materials under different conditions (natural and artificial ageing) two degradation mechanisms were observed: hydrolysis oftannins and auto-oxidation of gallic acid. The semi-quantitative analysis of the molecular markers detected allowed us to highlight a different impact of the ageing mechanisms in relation to the ink’s recipes. Our studies devised a methodology that permits the identification of molecular markers of both the dyes/pigments in inks, thus introducing ultra-sensitive chromatographic and mass spectrometric methods in the array of analytical tools available in this field. This optimized approach can be expanded to other categories of dyes, both of natural and synthetic origin, such as *hematein* extracted from the logwood bark.

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Magnetoplasmonics beyond metals: Transparent Conductive Oxide Nanocrystals for High Performance Sensing

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Active modulation of the plasmonic response of nanostructures employing an external magnetic field can potentially improve the performance of plasmonic sensors or optical modulators. The use of magnetic field presents several advantages: it is a fast stimulus, easy to implement in devices, and its action on free charge carriers is fully reversible as it does not damage or modify the plasmonic material. However, achieving large magnetic modulation of the plasmonic resonance while maintaining a sharp optical response represents a great challenge in material choice for magnetoplasmonics. Indeed, noble metal nanocrystals (NCs) have sharp optical resonances, but weak magneto-optical signal, proportional to the cyclotron frequency (ω_C) [1]; on the other hand, nickel ferromagnetic nanodisks [2] or hybrid bimetallic nanostructures [3] have large magnetic modulation, but suffer from the high optical losses due to the magnetic metal, thus broadening the plasmonic resonance.

To overcome such limitations, we propose a paradigm shift in material choice by employing transparent conductive oxides (TCO) NCs, which are able to support a plasmonic resonance in the infrared, due to their lower carrier density than metals. Among TCOs we synthesized Sn-doped In_2O_3 (ITO) and F- and In- co-doped CdO (FICO) colloidal NCs, revealing a 20-fold and 40-fold enhanced magnetoplasmonic response compared to Au NCs. The enhancement is ascribed to the reduced effective mass (m*) of free carriers in such TCOs with respect to most metals, which in turn boosts the cyclotron frequency. FICO NCs are characterized by a sharper resonance, which increases the magnetoplasmonic response with respect to ITO, while having a comparable m* [4]. Finally, by using FICO NCs in a proof of concept magnetoplasmonic refractometric sensing experiment we achieved a superior refractive index sensitivity with respect to metal-based magnetoplasmonic systems reported in the literature [1-3]. Remarkably, our approach is competitive with the current state of the art of plasmonic refractometric sensing employing extinction spectroscopy [5], with the advantage of not requiring complicate curve fitting.

Considering that non-magnetic TCOs have been used in this work, further enhancement of the magnetoplasmonic response is potentially achievable by introducing magnetic dopants in plasmonic TCO NCs, exploiting the interaction between free charges and the introduced dopants. Such carrier-mediated magnetic interactions have been reported in the literature for several magnetically doped TCO films at low carrier concentration regimes [6]. If successful, the use of magnetic TCOs can represent a dramatic innovation in magnetic field modulated active plasmonics.

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VenomPred: A Machine Learning Based Platform for Molecular Toxicity Predictions

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A rapid and efficient in-silico assessment of the potential toxicity methods plays an important role in the selection of lead compounds and in ADMET studies since in vitro and in vivo methods are often limited by ethics, time, budget and other resources.[1] In this context, we present our new web tool VenomPred, a user-friendly platform for evaluating the potential mutagenic, hepatotoxic, carcinogenic and estrogenic effects of small molecules. VenomPred platform employs several in-house Machine Learning (ML) models developed with datasets derived from VEGA QSAR [2], a software that includes a comprehensive collection of different toxicity models and has been usedas a reference for building and evaluating our ML models. The results showed that our models achieved equal or better performance than those obtained with the reference models included in VEGA QSAR. In order to improve the predictive performance of our platform, we adopted a consensus approach combining the results of different ML models, which was able to predict chemical toxicity better than the single models. This improved method was thus implemented in theVenomPred platform, a freely accessible webserver that takes the SMILES (Simplified Molecular- Input Line-Entry System) strings of the compounds as input and sends the prediction results providing a probability score about their potential toxicity.

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A new chiral solvating agent for the configurational assignmentof *N*-TFA amino acids derivatives by NMR spectroscopy

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The assignment of absolute configuration of chiral compound is still a challenging task, some methods are available based on X-ray measurements [1], circular dichroism [2] and nuclear magnetic resonance (NMR) spectroscopy [3,4]. Regarding NMR, most methods are based on the use of chiral derivatizing agents (CDAs) [5]; only few cases of chiral solvating agents (CSAs) are reported [6]. We describe here the use of a new bisthiourea CSA (**TFTDA,** figure 1) for the assignment of the absolute configuration of *N*-trifluoroacetyl (*N*-TFA) derivatives of amino acids (figure 1). Mosher's method [5,7] was applied by comparing the complexation shifts underwent by each enantiomer of amino acid derivative in the presence of the two enantiomers of the CSA ($\Delta\delta^{RR}$and $\Delta\delta^{SS}$).

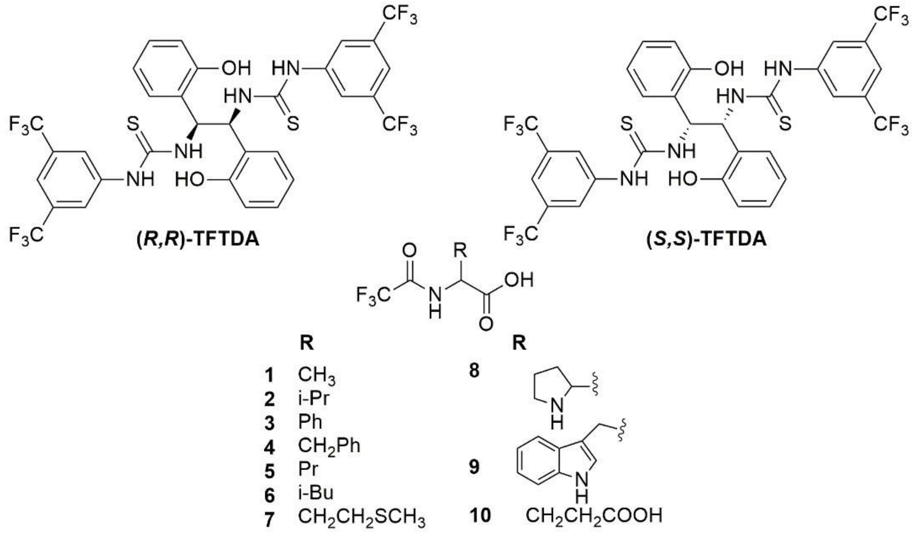

Figure 1. Structure of **TFTDA** enantiomers and substrates analyzed in the present work

In every case a positive value of $\Delta\delta^{RR}$-$\Delta\delta^{SS}$ for the ^{19}F resonances has been correlated to the (*R*) enantiomer of *N*-TFA amino acid, whereas a negative value has been correlated to the (*S*) enantiomer.

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New Au(I)-NHC complexes designed and synthesized as anticancer targeting agents.

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The extensive study of the antiarthritic drug Auranofin (AF) as a possible anticancer agent triggered growing attention towards Au-based complexes as promising candidates for new anticancer therapeutic strategies.[1] Gold complexes can activate apoptosis response in cancer cells mainly through inhibiting mitochondrial thioredoxin reductase (TrxR), a flavoenzyme involved in maintaining cellular redox homeostasis and often overexpressed in several cancer cell lines.[2] Thus, the inhibition of TrxR may represent an advantageous way to induce the cellular apoptosis by overcoming, at least in principle, the cellular cisplatin-induced pharmacoresistance. Anticancer targeting strategies involve the synthesis of conjugates where the bioactive molecule is bound to a targeting vector, which provides recognition of a specific cancer biomarker present oroverexpressed on the cancer cell's membrane. The potential advantages are higher selectivity, fewer side effects and less acquired/intrinsic resistance mechanisms. This project aims to synthesise, characterise, and evaluate the biological activity of a panel of Au(I)-based complexes conjugated to various targeting moieties, which exhibit targeting activity towards different tumour cell components. In particular, the complexes will be conjugated to three targeting agents: a glucose-mimetic thiosugar for a selective action exploiting the Warburg effect,[3] a peptide able to selectively recognise integrin receptors overexpressed on tumour cells and, finally, a peptoid for a mitochondrial targeting activity. On this basis, we synthesised two new gold(I) N-heterocyclic carbene complexes and their respective conjugates with 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranose, according to the first targeting strategy. In addition, all four gold(I) complexes are labelled with an anthracenyl residue as a fluorescent tag. This contribution is focused on theresults obtained by the interaction studies between the new compounds and a biologically relevant biomolecule, the human serum albumin (HSA). The studies were performed by means of fluorescence spectroscopy and high-resolution ESI-MS experiments. Moreover, preliminary testson A2780 cell lines showed cytotoxic activity for all four Au(I)-complexes, especially for thethiosugar-conjugates, with IC50 values falling in the low micromolar range.

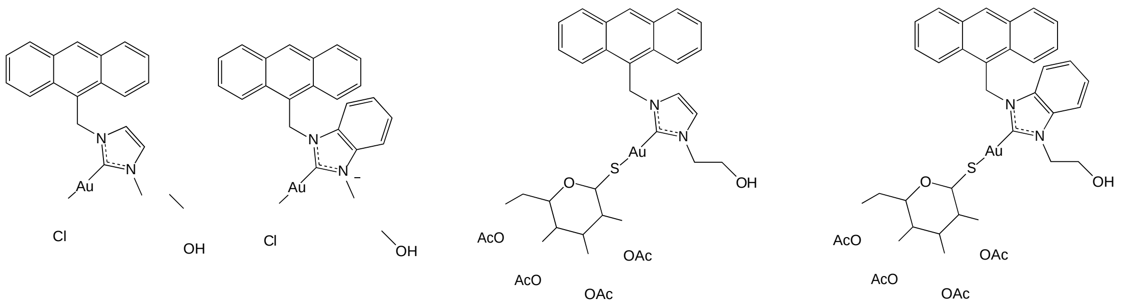

Figure 1. Structures of the four new Au(I) NHC-complexes

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Structural properties of Fluorinated Metal Organic Frameworks (MOFs) by Solid State NMR

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Metal-Organic Frameworks (MOFs) are a class of crystalline compounds whose scaffolding derives from metal clusters or ions that are interconnected by organic linkers. The high number of possible combinations of metals and ligands leads to high tunability of macroscopic properties and thus it is possible to employ MOFs in many fields of applications, including gas storage, gas separation, and catalysis [1,2]. During the design and development of a new MOF, it is extremely important to completely understand every macroscopic property of the compound and to relate it toits microscopic origin.

Many techniques can be exploited and combined to characterize the structural and dynamic molecular properties of a MOF. Among them, Solid State Nuclear Magnetic Resonance (SSNMR) spectroscopy is certainly one of the most important because it can shed light on many aspects of the MOF at a molecular level, such as 3D structure, porosity [3], local dynamics [4], and host-guest interactions [5].

In this work, ^{1}H, ^{13}C, and ^{19}F SSNMR spectroscopy has been employed to characterize two novel MOFs prepared with trifluoroterephthalic acid as the organic ligand: F3-UiO66(Ce) and F3-MIL140A(Ce). The former is characterized by a face-centered cubic topology in which hexanuclear clusters of Ce^{IV} are interconnected by ligands. In the latter, chain-like inorganic building units of Ce^{IV} are interconnected by ligands.

SSNMR 1D and 2D correlation spectra have been used to obtain, also by comparison with powder X-ray diffraction results, a detailed characterization of the framework structure both in the presence and after removal of crystallization water. On the other hand, dynamic processes involving the fluorinated aromatic rings have been investigated through the analysis of variable-temperature ^{19}F spin-lattice relaxation times.

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Development of a targeted top-down proteomic approach for determining natriuretic peptides in biological fluids

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Cardiac natriuretic peptides (NPs), i.e., ANP, BNP, and CNP, are hormones initially synthesized from cardiomyocytes, as prohormones. Once they are released from the heart, prohormones are split into two fragments: a longer N-terminal fragment (NT-proBNP and NT-proANP) and a shorter C-terminal fragment (BNP and ANP) [1]. In pathological conditions as heart failure (HF), heart induces the stretching of myocytes due to pressure overload, leading to the release of NPs in blood. Thus, NPs plasma levels increase progressively with the severity of HF and represent the main biomarkers for prognosis and diagnosis of HF [2]. NPs are normally determined in blood using commercial immunoassay kits [3]. This approach is affected by cross-reactions due to the presence of several NP forms showing homologous structures [3], as those with oxidized methionine [4]. Nowadays, immunoassay kits used in the clinical practice can detect only a single NP at a time based on the type of antibody present in the kit.

In this work we developed a reliable and innovative analytical workflow based on targeted top- down proteomics and UHPLC-MS/MS analysis for the determination of NPs in biological fluids (saliva and plasma samples). Peptides' ionization efficiency was improved by the addition of a supercharger agent into mobile phases, which allowed to enhance up to 5-times the sensitivity of the method, depending on the analyte. In the optimized conditions, the instrumental detection limitswere in the range 10-1000 pg/mL. At first, particular attention was paid to the evaluation of analyte stability in standard solutions. NPs were found to be stabilized at 4°C in aqueous solutions by the presence of both human serum albumin, as displacement agent, and methionine as oxygenscavenger up to 24h. Ultrafiltration, fractional protein precipitation, and micro-extraction by packed sorbent (MEPS) will be tested as sample treatment procedures and the optimized analyticalprotocol will be employed for the monitoring of patients suffering from HF.

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Sustainable exploitation of paper mill wastes: a resource to re-use in the paper factory

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In the papermaking industry, billions of tonnes of paper mill wastes are globally produced as wastes every year [1]. These include cellulosic and inorganic sludges, which are traditionally landfilled, leading to environmental and economic issues [2]. For these reasons, it is urgent to develop new sustainable strategies to exploit these fractions. Up to now, these sludges have been exploited *i)* for land application (as soil amendment/substrate), *ii)* for energy recovery and *iii)* for theproduction of bio-composites [3]. However, the above possibilities involve the direct use of the bulk wastes, without fractionating/exploiting each feedstock component.

In the perspective of the valorisation of the different components, the present investigation has considered different strategies: *i)* a thermal treatment, *ii)* an alkaline and *iii)* a mechanical one, aimed at the fractionation and recovery of the two main components of cellulosic and inorganic sludge, cellulose and calcium carbonate, respectively, that could be advantageously reused within the same papermaking process. A preliminary compositional analysis of these wastes has been carried out and a pyrolysis approach has been developed for the fractionation of the calcium carbonate from the bulk inorganic sludge. This is a thermochemical process where the feedstock is converted/fractionated under nitrogen atmosphere to give a liquid bio-oil, a solid biochar and non-condensable gases. A preliminary phisico-chemical characterization of the recovered fractions has been performed in order to propose their exploitation within the context of a more sustainable and integrated process, in agreement with the principles of the circular bio-economy.

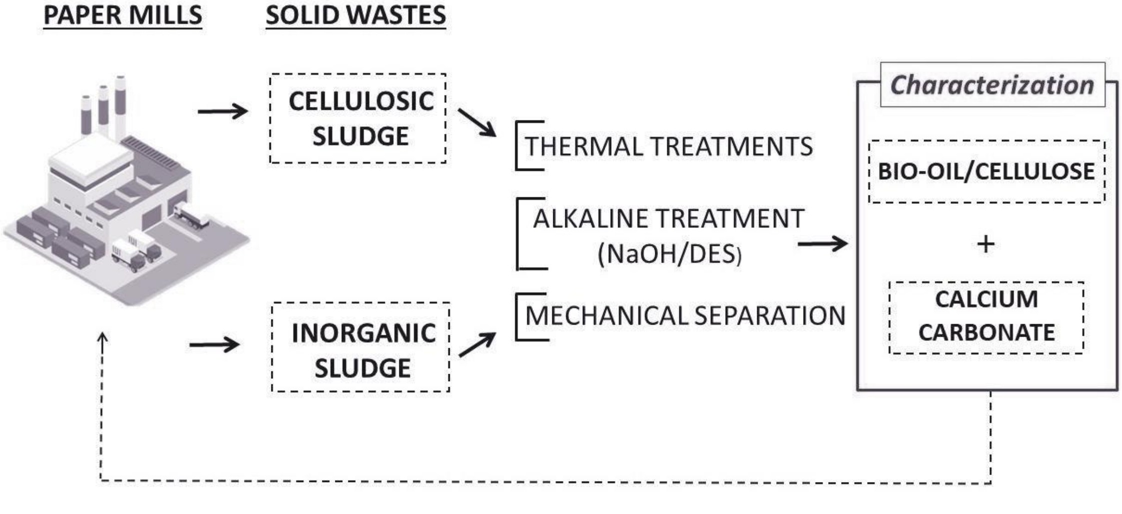

Figure 1. Proposed strategies for the exploitation of industrial paper mill wastes.

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New Pt-based anticancer prodrugs conjugated with mitochondria-targeting agents

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Nowadays, cancer is still one of the main responsible of death worldwide. Against this disease, traditional DNA-damaging drugs, such as Cisplatin and its derivatives (namely Carboplatin and Oxaliplatin) still represent the first choice in the clinical treatment of this disease. However, these drugs possess several drawbacks, ranging from their low bioavailability, the insurgence of acquired resistance and oto- and nephrotoxicity which dramatically lower the patients' quality of life. In order to overcome these problems, one possible approach is based on the use of Pt(IV) prodrug complexes. Indeed, these prodrugs are more kinetically inert than their Pt(II) counterparts, and thus less prone to off-target reactivity.[1] These prodrugs are activated inside cancer cells through reduction, thus restoring the Pt(II) drug and releasing the two axial ligands.[2] The Pt(II) species are responsible for the cytotoxicity, but the introduction of bioactive axial ligands might further enhance the pharmacological properties of these compounds.[3] In this frame, mitochondria-targeting agents appear to be interesting candidates to increase the anticancer properties of these complexes.

One such agent is the α-tocopherol succinate (α-TOS), an analogue of Vitamin E, which was proved to be cytotoxic in many different cancer cell lines by targeting the aforementioned cellular organelles.[4] Indeed, this molecule was shown to be able to trigger mitochondria-mediated apoptosis by inhibiting some anti-apoptotic proteins.[4] In this context, we propose new Pt(IV) complexes conjugated with α-TOS in the axial position. Such compounds should be able both to damage the DNA (thanks to the Pt-containing moiety) and to disrupt the mitochondrial function (thanks to α-TOS).

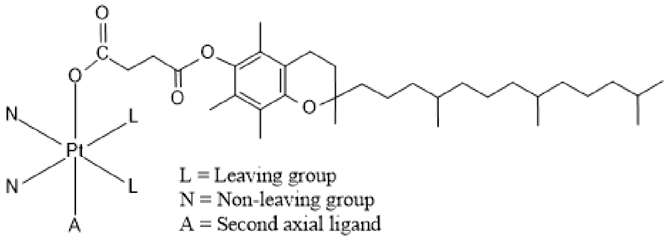

Figure 1. Structure of a general Pt(IV) complex conjugated with α-TOS in the axial position.

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Magnetically co-doped Indium Tin Oxide nanoparticles (ITO-NPs) for magnetoplasmonic refractometric sensing

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Magnetoplasmonics is a subfield of active plasmonics where the Surface Plasmon Resonance is actively controlled by an external magnetic field.[1] Magneto-optical properties of plasmonic materials can be analysed and used in refractometric biosensing. The Localized Surface Plasmon Resonance (LSPR) present in gold nanoparticles (Au-NPs) was studied and the magnetic modulation amplitudes are found to be weak [2]. Indium Tin Oxide nanoparticles (ITO-NPs) exhibit LSPR in the NIR region and are optically transparent. Interestingly ITO-NPs show a strong magnetic modulation compared to Au-NPs since the effective mass of electron (m*) is lower than that in Au-NPs. Our group has assessed the superior magnetoplasmonic response of non-magnetic ITO NPs compared to metal-based NPs. [3]. For ITO-NPs it is possible to be co-doped with magnetic cations improving the magnetic modulation of LSPR provided that there is coupling between the magnetic cations and the charge carriers. Magnetic cations Fe, Tb, Gd and Cr were used for co-doping. The process was developed in our laboratory as a refinement of previously reported synthetic procedures [4]. Two series of ITO NPs are compared with 5% and 2.5% of co-dopant. The sizes of particles are in the range 8-10 nm in all cases (Fig.1). From UV-Vis-IR spectrophotometry, it's found that the Fe-ITO NPs present the lowest LSPR energy in both the series and it can be seen that Fe-doping has introduced a red shift in the LSPR energy in comparison with that of pristine 10% ITO-NPs. This could be result of the reduction of Fe (III) to Fe (II)absorbing free electrons, lowering the plasma frequency. All other dopants introduce a blue shift in theLSPR with respect to the Pristine sample. The highest LSPR energy are those of Gd-ITO (2.5%) and Cr-ITO (5%). The Q factor of the LSPR signal, an important metric for potential application inrefractometric biosensing follows the trend: Fe<Tb<Cr<Gd. Interestingly, the Q factor of Gd-ITO NPs isslightly higher than that of pristine ITO NPs. Magnetic Circular Dichroism spectra (MCD) at room temperature were acquired using the 5% series. Fe-ITO NPs have the highest effective doping in bothconcentrations but broadening of the MCD signal is a disadvantage (Fig.2) The MCD results denote thepossibilities of co-doping of Gd and Tb cations in ITO for better magnetic modulation. Low temperatureMCD experiments are needed to study the magneto-optical nature of these particles to determine if magnetic coupling occurs between dopants and free carriers, which would result in a strong, temperature dependent magnetoplasmonic effect. A paramagnetic nature is observed in the magnetometry analysis (Fig.3).

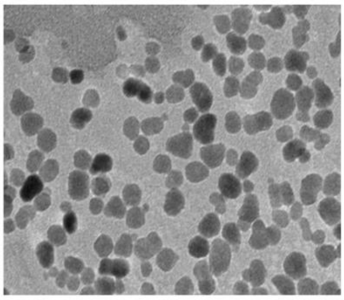

Fig.1: TEM image Gd-ITO 5%

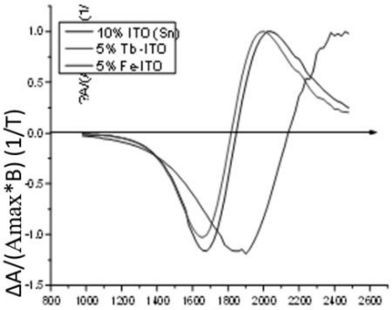

Fig.2: MCD spectra comparison of ITO, Fe-ITO & Tb-ITO

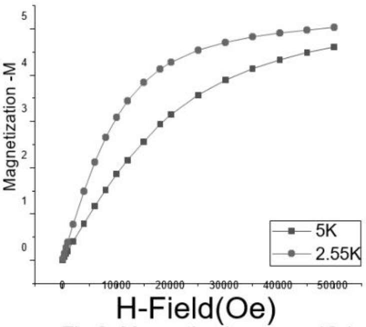

Fig.3: Magnetization curve (Gd-ITO at2.5K & 5K)

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Paints from Simon Hantaï

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Advancements in industrialization accelerated and complexified oil paint fabrication in the post-war era and therefore, paint formulas used by contemporary painters are little known causing difficulties in the fields of conservation and restoration. These formulas are more chemically sensitive due to the inclusion of additives such as dispersants, surfactants, and drying agents, and also, replacing traditional pigments with organic colorants. The formulas are often secret and continuously being modified for visual aspects such as brilliance and glossiness and practicality such as faster drying times. Moreover, conservation issues of those oil painting are very challenging and one of them is the competition between oxidation and cross-linking process duringthe curing.

This project is centered around a unique sample set of oil paints from the contemporary painter Simon Hantaï (1922–2008), an influential artist of the 20th-century post-war era in Paris (Warnock, 2012). Hantaï's most notable artworks were his abstract paintings dating from 1962-early 1980s, made using his original technique called *pliage* or “folding as a method” to create patterns of paint on canvas (Chevalier, 2011). At the end of his career, Hantaï worked closely with the restorer Aurélia Chevalier, with whom he shared his techniques and materials used in the present study. Materials used by Hantaï are representative of his contemporaries during the post-war era in Paris,including Soulages, Riopelle, de Staël, and Mondrian.

The sample-set for this study consists of oil paint samplings from Lefebvre-Foinet, Lefranc-Bourgeois and others brands paint tubes fabricated with various pigments. Here we present the results of the initial characterization of these paints: the characterization of the paint binder used and indications of polymerization mechanisms of the aged paints using Py-GC-MS as well as complementary chemical speciation using ATR-FT-IR and SEM-EDX. We also use a two-step GC-MS procedure using N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) and 1,1,1,3,3,3-hexamethyldisilazane (HMDS) for the qualitative and quantitative analysis of free fatty and dicarboxylic acids and metal soaps in those samples. The glyceride fraction of the paint samples was characterized using liquid chromatography coupled with high resolution mass spectrometry (HPLC-ESI-Q-ToF) for the identification of the vegetable oils present.

This project is funded by the Ecole Normale Supérieure Paris-Saclay in collaboration with the University of Pisa (Dipartimento di Chimica e Chimica Industriale Università di Pisa). We also thank the teams at the IPANEMA laboratory for their laboratory and instrumentation. I would also like to thank Giulia Caroti and Silivia Pizzimenti who helped me for the analytical procedure and the experimental work.

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Investigating the composition and photodegradation of commercial wet wipes by Py-GC-MS and EGA-MS

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Wet wipes are spunlace nonwoven fabrics obtained through the binding of fibres only with water jets [1]. The absence of proper binders makes them safe to use in skin-touching products. Nowadays, they are used for several cleaning purposes and their composition is also various. In fact, wet wipes can be composed of cellulose fibres (e.g. viscose fibres), synthetic fibres (e.g. polyester, polypropylene), or blends of the two [2]. In the last few years wet wipes have been extensively used as disposable sanitary tools, leading to an increase in their production. The global wipes market size is expected to grow from $18.09 billion in 2021 to $19.67 billion in 2022 and reach $26.45 billion in 2026 [3]. The intensive usage of wet wipes has increased the concern of the scientific community about microfibre pollution [4,5] and the release of additives in the environment [6]. To date, analytical pyrolysis techniques have not been applied for the study of this type of fabrics.

The present work aims at characterizing the composition of different classes of commercial wet wipes by Evolved Gas Analysis coupled to Mass Spectrometry (EGA-MS) and analytical Pyrolysis coupled to Gas Chromatography and Mass Spectrometry (Py-GC-MS). The samples were classifiedin three categories: flushable according to UK certification (FC), biodegradable but not flushable (B), and conventional (C). Preliminary EGA-MS analysis allowed us to study the thermal behaviour of the wet wipes, while their composition and the presence of additives were assessed by multi-shot Py-GC-MS.

Moreover, the samples were immersed in distilled water and subjected to artificial photoageing with UV light in SolarBox for 2 and 4 weeks to monitor possible changes in their composition. At the end of the experiment, each artificially photoaged tissue was dried and analysed by Py-GC-MS, while the water was filtered through a quartz fibre filter to collect the microfibers released during the irradiation. The dried filters were also analysed in order to study the composition of the released microfibres. All the samples showed significant releases of microfibres in water, with FC and B samples being the ones to release the greatest amount after irradiation. In the case of the sample composed of cellulose and polypropylene, a tendency to release preferentially cellulose microfibres was observed.

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Synergistic effects and estimation of elemental composition of pyrolysis oil from biomass and plastic co-pyrolysis by Py-GC/MS

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Pyrolysis bio-oil is a promising material to replace fossil fuels even though its physicochemical features reduce its applicability [1]. Several strategies have been developed in the past decades to reduce the content of oxygenated species found in bio-oil. The co-pyrolysis of lignocellulose with hydrogen-rich materials such as plastics is a promising method to upgrade bio-oil [2]. The interaction of the two components during pyrolysis produces synergistic effects which affect the thermal behaviour and the composition of the bio-oil, leading to improvements of its yield and quality [3,4]. In this frame, analytical pyrolysis-based techniques have become essential, as they reveal the chemistry of the substates and their decomposition pathways by replicating co-pyrolysis under controlled experimental conditions and using small amounts of material [5].

In present work, the pyrolytic behaviour and the synergistic effects arising from the co-pyrolysis of lignocellulose with plastic (polyethylene, PE and polystyrene, PS) were investigated by analytical pyrolysis-gas chromatography-mass spectrometry (Py-GC/MS). The study was performed both on model systems and on waste materials. Principal component analysis (PCA) was employed to highlight the differences in the chemical composition of the pyrolysates due to the addition of plastics. The occurrence of synergistic effects was also evaluated from Py-GC/MS data by estimating experimental and theoretical values of H/C and O/C of the identified compounds.

The presence of plastic promoted multiple dehydration of holocellulose and secondary pyrolysis reactions, while secondary pyrolysis of the lignin fraction was inhibited in favour of depolymerization. In addition, the pyrolysis products of plastic were influenced by the presence of biomass. The average chain length of PE oligomers increased as the plastic amount in the system decreased. On the other hand, biomass hindered intramolecular hydrogen transfer in PS to give mainly styrene monomers. The elemental analysis based on the compounds identified in the pyrograms provided reliable values of H/C and O/C. The values obtained for the feedstocks investigated were improved by the addition of plastic indicating that lower amount of oxygen is present in the pyrolysates.

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Optimization of cell surface protein biotinylation on Pancreatic Ductal Adenocarcinoma cells and exosomes

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The study of membrane proteins is of particular interest in clinical research, since they are involved in many biological processes such as cellular communication and flux control.[1] Their location on the cell surface makes them attractive targets for pharmaceutical intervention, indeed they represent the majority of targets for pharmaceutical drugs.[2]
This work is focused on the analysis of PDAC (Pancreatic Ductal Adenocarcinoma) cells and exosomes. PDAC is the most common pancreatic cancer. It has a five-year survival rate below 10% due to the fact that is usually diagnosed in an advanced state and the therapeutic treatments are largely ineffective. It has been estimated that this type of neoplasm could become the second leading cause of death in Western countries.[3] The investigation of PDAC cell surface proteins can lead to the identification of new drug targets, and the identification of exosome surface proteins specific to PDAC, could enable the development of new biomarker assays for earlier diagnosis.

The hydrophobicity of membrane proteins and the embedding of the transmembrane domains within the phospholipid bilayer of the membrane means their extraction is more difficult with respect to the total cellular proteome. For this reason, specific methods of extraction and identification are required. The aim of this work is the optimization of a method for cell surface proteomics. The method consists in the use of a cell-impermeable biotinylation agent that chemically derivatizes the lysines of membrane proteins (when the cells are still intact). At the end of the reaction and after cell lysis, a neutravidin resin is used to isolation the biotinylated proteins. Neutravidin is a protein that can form a stable complex with biotin ($K_d \approx 10^{-5}$).[4] Finally, biotinylated denatured proteins are converted into peptides after proteolysis using trypsin and bottom-up proteomics analysis are carried out.
This technique has been applied to commercial immortalized tumor cells of PDAC called SUIT 2-028 and PANC 1 and their exosomes.

Cell surface biotinylation is well established and the materials needed are readily available. The challenge is the large number of cells typically used (~ 10^7 cells)[5] makes it difficult to apply to exosomes; when applied to cells endocytosis leads to the biotinylation of cytosolic proteins, and aspecific binding of proteins can lead to low specificity. The optimization was focused on the decreasing the number of cells used in the analysis, so that the method could be applied to exosome preparations, and to minimize the non-specific labeling.

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NEXT-GENERATION COMPOSITE POLYMERIC MEMBRANES FOR SEMI-ORGANIC REDOX FLOW BATTERIES

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Increasing focus on renewable energy production and storage is paramount as environmental and materials sustainability issues become more prevalent considerations in current and next- generation technologies. Energy sources, including solar and wind are inherently intermittent; thus,it is desirable to pair renewable energy generation with batteries so that the energy can be stored for optimal use. In this realm, redox flow batteries (RFBs) are promising candidates for large scale energy storage thanks to their long service lifetimes, relatively low capital costs, and independent scaling of energy and power density.[1] The membrane is a pivotal component of RFBs as it determines the performance as well as the economic viability of the batteries.[2] The present work aimed at the development of polymeric membranes for semi-organic RFBs based on 9,10- anthraquinone-2,6-disulfonic acid disodium salt (AQDS)/bromine (Fig.1). Nafion-based proton exchange membranes (PEMs) are regarded as the benchmark for many RFBs because of their high ionic conductivity and high stability in chemically aggressive environments.[3] However, disadvantages, including the exceptionally high cost and crossover of unwanted species (e.g. Br_2/Br^- in AQDS/Br_2 RFBs) prevent their use for large-scale energy storage. On the basis of these rationales, we developed composite membranes starting from a micro-porous polymeric substrate on which a polymerizable solution of *N*-vinylpyrrolidone (VP), a complexing agent for bromine species[4], was deposited. After the deposition, the membrane underwent a polymerization reaction and the experimental conditions were systematically varied to modulate the amount of incorporatedPVP. Ion conductivity and exchange, chemical and mechanical stability, and crossover of unwanted species of the membranes were evaluated by different analytical techniques. A RFB single cell with a composite membrane functionalized with 22 wt% of PVP showed a low-capacity loss, high coulombic efficiency and good ohmic resistance compared to the benchmark Nafion- based PEMs.

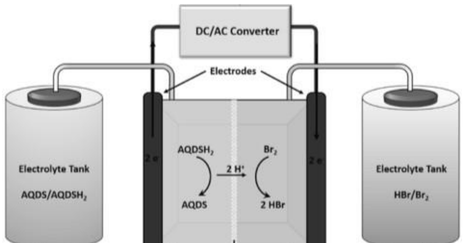

Figure 1. Representation of a semi-organic RFB.[5]

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Computation of NMR shieldings at the CASSCF level using gauge-including atomic orbitals and Cholesky decomposition

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We present an implementation of the coupled-perturbed complete active space – self-consistent field (CP-CASSCF) equations [1] that exploits gauge-including atomic orbitals (GIAO) and Cholesky decomposed (CD) two-electron integrals [2,3] for the calculation of nuclear magnetic resonance (NMR) chemical shifts [4]. The CP-CASSCF equations are solved using a direct algorithm where the magnetic Hessian matrix-vector product is ultimately expressed in terms of one-index transformed quantities.

Numerical tests on systems with up to about 1300 basis functions provide information regarding both the computational efficiency and limitations of our implementation.

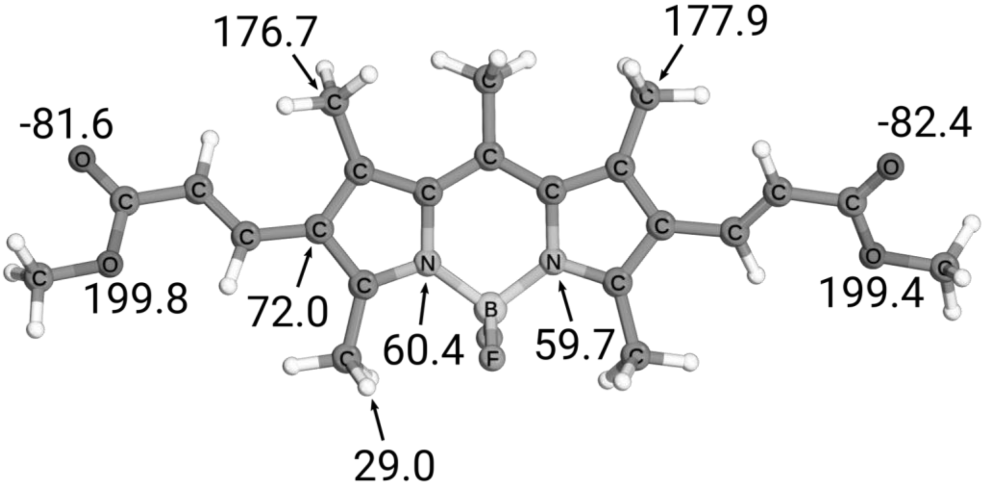

Figure 1. NMR chemical shifts of a BODIPY dye molecule computed at the CD-GIAO-CASSCF(8,8)/*cc*-pVTZ level of theory. In the figure, only a few representative NMR isotropic shieldings (in ppm) are reported. The basis set used consisted of 1280 basis functions, and the whole calculation took about 11 hours on a single cluster node equipped with 4 Intel Xeon Gold 6140 M CPUs, running at 2.30 GHz. Shared-memory parallelization was exploited sharing the work among 28 threads.

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Additive manufacturing of poly(lactide-*co*-glycolide)-based composite scaffolds loaded with functionalized hydroxyapatite for bone tissue engineering

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The application of synthetic biodegradable bone substitutes, referred to as scaffolds, represents a valuable alternative to current clinical treatments of bone defects, such as the grafting of a living tissue or the application of a permanent prosthesis [1]. One of the most commonly used polymer in bone tissue engineering is poly(lactide-*co*-glycolide) (PLGA) which is a biocompatible and bioresorbable aliphatic polyester. Its combination with osteoinductive calcium phosphate ceramics, such as hydroxyapatite (HA), has been explored as a means to obtain a composite material with increased bioactivity and mechanical properties. However, calcium phosphates are often not stable in organic solvents, as well as poorly compatible with hydrophobic polymeric matrices, causing a decrease of the strength of the resulting material. In this work HA microparticles were functionalized using a PLGA direct grafting method to increase their processing properties, as well as their compatibility with a PLGA matrix [2]. The successful grafting of PLGA to the HA surface was confirmed by FT-IR analysis and quantified by thermogravimetric analysis. Dynamic light scattering analysis revealed that the functionalization increased the stability of PLGA-g-HA particles suspensions in chloroform, enhancing their processability by computer-aided wet-spinning (CAWS). HA particles and the functionalized particles (PLGA-g-HA) were employed for the fabrication of composite PLGA scaffolds by means of CAWS, a 3D printing technique which is based on the extrusion of a polymeric solution into a coagulation bath for the computer-controlled deposition of the resulting polymeric fiber [3]. PLGA, PLGA/HA and PLGA/PLGA-g-HA scaffolds were fabricated. Scanning electron microscopy analysis carried out on the fabricated scaffolds confirmed the presence and the homogeneous distribution of particles in the fiber composite matrix, and that the fiber cross-section presented a diffused porosity. Tensile and compression tests showed a significant increase of the elastic and the compressive modulus for the composite scaffolds in comparison with those of PLGA scaffolds. Tensile tests also revealed for PLGA/PLGA-g-HA scaffolds a higher elongation at break in comparison with PLGA/HA scaffolds. An *in vitro* degradation test carried out on the fabricated scaffolds showed that PLGA/PLGA-g-HA scaffolds maintained better mechanical properties in comparison with the other scaffolds after 9 weeks of incubation in phosphate buffer saline (PBS, pH=7.4, 37°C) despite the reduction of the polymer molecular weight to 40% of its original value according to gel permeation chromatography measurements.

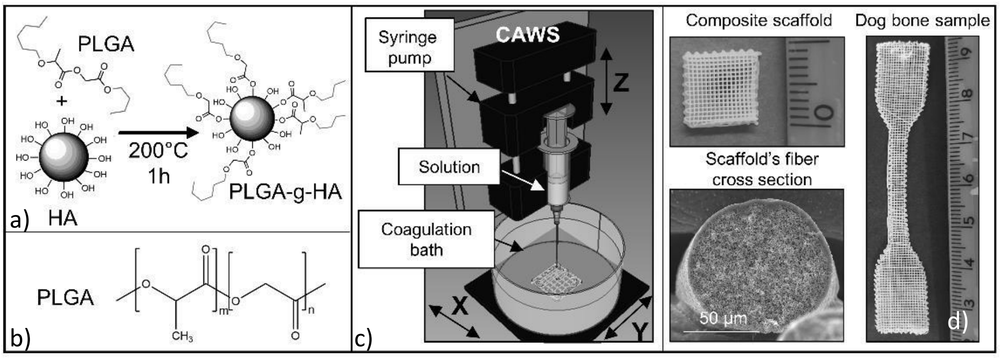

Figure 1. Schematic representation of a) PLGA grafting to HA particles surface, b) chemical structure of PLGA, c) CAWS processing; d) pictures and SEM micrographs of representative samples.

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Exploring pH-induced conformational changes involved in photoprotective quenching in the Light Harvesting Complex Stress-related 1

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In plants, mosses and algae, sunlight is collected by light harvesting pigment-protein complexes (LHCs) and rapidly funneled to the reaction centers of photosystems. In response to varying light conditions, LHCs can also play photoregulation and photoprotection roles. By sensing the pH change in the thylakoid membrane, which is induced in excess light conditions, LHCs can switch to a quenched state where the excitation energy is dissipated into heat, in a process called nonphotochemical quenching (NPQ). Here, we present a multi-step computational protocol to elucidate the pH-sensing of a stress-related LHC of mosses (LHCSR1) [1]. In Step 1, we identify the most likely protonation microstates (pMS) of the complex at different pH, via constant-pH Molecular Dynamics [2]. In Step 2, we explore the conformational space for selected pMSs, via Gaussian Accelerated MD [3]. Finally, in Step 3, the different conformations are characterized in terms of their NPQ-related properties.

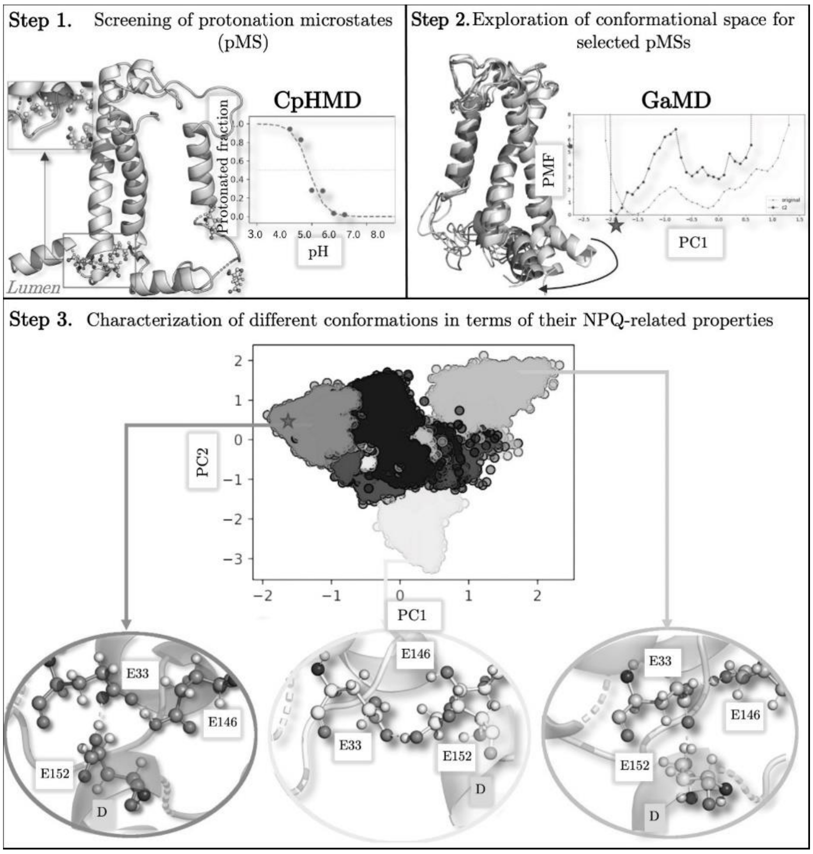

Figure 1. General workflow of the computational protocol used to elucidate the pH-sensing of the LHCSR1

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Thermal investigation of choline chloride-based deep eutectic solvents

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Deep eutectic solvents (DES) are a promising class of versatile and green solvents, with a melting point lower than the one of the ideal eutectic mixture of the precursor salts [1]. The investigation of thermal properties of DES made by choline chloride and a hydrated salt of alkali-earth metal (potential phase change materials [2,3] and green solvents for dissolution of lignin [4]) is reported.
The DES preparation was optimized, trying to have a high control of the quantity of water molecules involved, important to define their properties. After the preparation step, High Resolution thermogravimetry and thermogravimetry coupled with Infrared Fourier Spectroscopy (TGA-FTIR) was applied for the first time on this kind of systems to evaluate their thermal stability and the decomposition mechanism of both the precursor and the DES samples. The microwave absorption capability of DES, compared with the one of the precursor salts, was also tested in view of future applications in the extraction and treatment of biomasses.

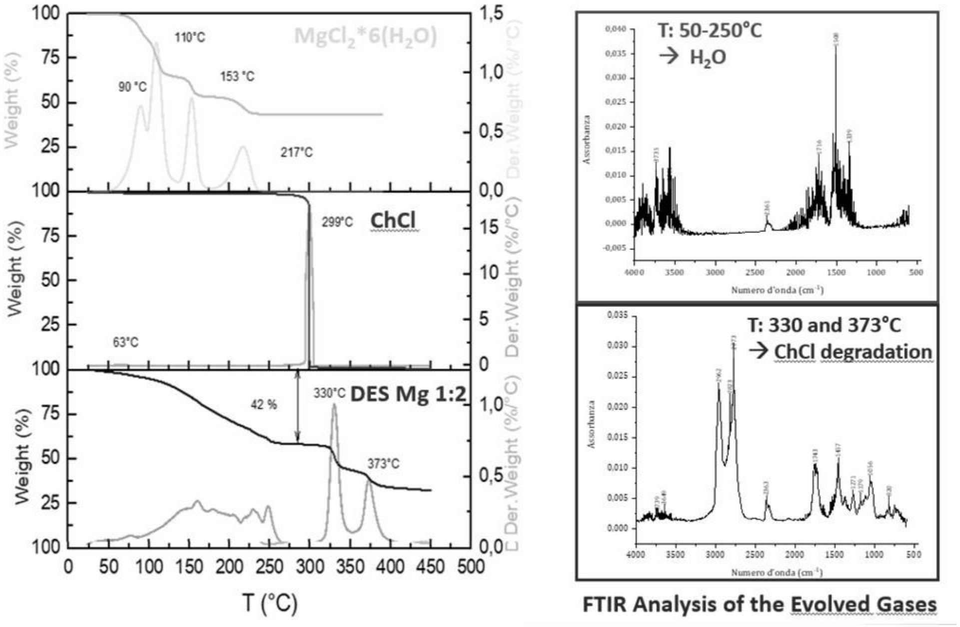

Figure 1. Hi-resolution TGA (on the left) and TGA-FTIR analysis (on the right) of the DES made with choline chloride (ChCl) and $MgCl_2*6H_2O$.

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Poly(cyclohexyl methacrylate-co-methyl methacrylate) as Host Polymer Matrices for Luminescent Solar Concentrators

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A major challenge in the field of Luminescent Solar Concentrator (LSC) research is to find a highly transparent waveguide and a great fluorophore dispersibility to enhance solar harvesting. In commonly used matrices such as poly(methyl methacrylate) (PMMA), less polar repeating units might more effectively stabilize organic fluorophores and allow their use at higher concentrations, thus improving LSCs efficiencies. Here we report the use of methyl methacrylate (MMA) and cyclohexyl methacrylate (CHMA) as comonomers in a polymeric host material for thin-film LSCs. In addition to the two homopolymers, i.e. PMMA and poly(cyclohexyl methacrylate) (PCHMA), composition of 75:25, 50:50 and 25:75 were studied, using Lumogen F Red 305 (LR) as the state-of-the-art fluorophore in the 0.4-2 wt% concentration range. The performance of these LSCs was evaluated in terms of internal quantum efficiency (IQE), external quantum efficiency (EQE), fluorophore quantum yield (QY) and electrical efficiency of the device (η_{dev}) when coupled to a silicon photovoltaic cell. Notably, the highest η_{dev} was recorded for the 50:50 P(MMA/CHMA) LSC at 1.6 wt% LR concentration, whereas maximum photon efficiencies were reached by using the 25:75 P(MMA/CHMA) matrix and compared to those gathered from LR/PMMA LSC. The trend of increasing optical and electronic properties of 25:75 P(MMA/CHMA) LSCs throughout the fluorophore concentration range under investigation can be considered promising and paves the way for exploration of these devices at higher LR concentrations, e.g. 2-5 wt%.

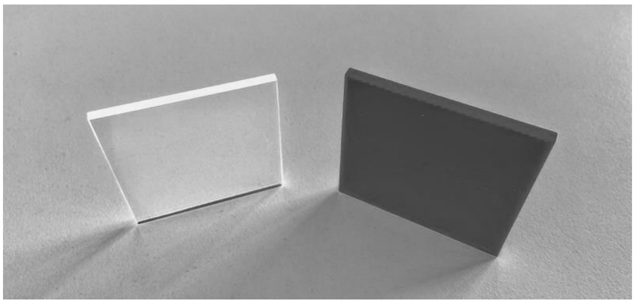

Figure 1. Examples of LSC containing high QY fluorophores

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Elastomeric Materials for Tyre Production Containing Resins of Natural Origin: A Time-Domain Solid-State NMR Study

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Elastomers are polymeric materials widely used in the tyre industry. The peculiar properties of these materials, such as high viscosity and elasticity, are obtained through vulcanization in the presence of sulfur and other additives, including accelerators, activators and antireversion agents. In addition to curing agents, blends contain other additives, such as fillers and plasticizers, which are necessary to obtain specific mechanical requirements. Among them, resins are needed to improve tensile strength or fatigue resistance of the final products, as well as to facilitate the processing steps.[1] Generally, resins used in the tyre industry are based on petroleum-derived compounds, which are not sustainable and often carcinogenic. Environmental and health requirements impose the substitution of petroleum-based plasticizers with biocompatible and non- toxic alternatives in the production of elastomeric materials of interest for the tyre industry, while achieving comparable or even improved properties of the final products. To obtain this goal, it is important to understand the compatibility and miscibility between the new resins and the polymeric matrix at the molecular level,[2] which are strictly related to the macroscopic properties of the final products. For this type of study, it is possible to exploit Time Domain Nuclear Magnetic Resonance (TD-NMR) spectroscopy, which is particularly useful for investigating elastomers' dynamics and structure.[3] NMR observables, such as longitudinal and transversal relaxation times (T_1 and T_2) and ^{1}H-^{1}H residual dipolar couplings (D_{res}), depend on the modulation of the homonuclear dipolar interaction between protons mediated by molecular motions. As a result, these parameters allow phases with different mobility to be distinguished and the presence of topological constraints, such as cross-links and entanglements, to be highlighted. More specifically, T_2 measurements allow to identify and quantify molecular environments with different mobility. From the analysis of T_1, information about the mixing degree between different phases in multiphase systems can be achieved.[4] Other important information can be obtained from the average ^{1}H-^{1}H D_{res} which are directly proportional to the cross-link density.[5]

Here, we studied styrene-butadiene rubbers vulcanized in the presence of natural origin or petroleum-based resins. Magic Sandwich Echo and Carr-Purcell-Meiboom-Gill experiments were acquired for the measurement of ^{1}H T_2 relaxation times to evaluate the molecular mobility of the polymeric and resin phases, also at different temperatures. Inversion Recovery experiments were performed to measure ^{1}H T_1 relaxation times in order to evaluate the homogeneity of the samples as a function of temperature. Moreover, Double-Quantum NMR experiments were acquired for the measurement of ^{1}H-^{1}H D_{res} to monitor the cross-link density in all vulcanized samples.

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Synthesis of Magnetoplasmonic Co-doped Al-ZnO Nanoparticles using continuous growth approach

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Magnetoplasmonics employs magnetic field as external stimulus to actively modulate the plasmonic properties. For efficient magnetoplasmonic response, materials with large magnetic modulation and sharp optical resonances are needed.

Within this framework, our group demonstrated promising magnetoplasmonic response in non-magnetic transparent conductive oxide (TCO) nanoparticles (NPs), due to their sharp resonances and improved magnetic modulation with respect to noble metals [1]. To further improve the magnetoplasmonic response, doping of TCOs with magnetic metal cations represent a promising strategy.

Among this class of materials we chose ZnO doped with cobalt, as carrier-mediated magnetic coupling between Co^{2+} cations in ZnO films have been observed in previous works, leading to room temperature ferromagnetism [2]. This phenomenon is expected to improve the magnetic modulation of the plasmonic resonance [3].

In highly doped semiconductors NPs, charge carriers can be introduced through insertion of aliovalent atoms in the lattice. To this purpose Al is selected as electron donor dopant in zinc oxide NPs, resulting in carrier densities lower than metals, thus shifting the plasmonic resonance in the infrared range while maintaining transparency in the visible range [4]. Co-doping of ZnO with Aluminum and Cobalt cations presents several synthetic challenges as the reactivity of the two precursors may be different, thus affecting the efficiency of dopant incorporation [5]. On the other hand, the introduction of cations in the semiconductor lattice is known to cause plasmon broadening due to electron scattering with the introduced charged impurities [6].

Continuous growth synthesis is a promising approach to obtain these materials because it allows the production of NPs with tailored shape, size and composition through continuous and controlled injection of metal oleates as precursors. The synthesis proceeds through an esterification between metal oleate complexes, which are added to a hot oleyl alcohol solution. M-OHx species are formed, followed by their condensation and formation of the M-O-M network of the metal oxide NPs[7].

To optimize the synthetic method, a design of experiment (DoE) approach has been used to correlate the synthetic conditions with the materials features obtained with various characterization techniques (such as ICP-OES, TEM, XRD, FTIR), especially regarding the optical and structural properties. The use of a DoE approach represents a more efficient way than the usual “one variable at a time” approach that requires more experiments and therefore more time and materials.

In the future the magneto-optical properties will be further studied as a function of the chargecarrier density and the effective amount of cobalt incorporated to achieve the optimal conditions for applications in magnetoplasmonics.

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Sampling human skin volatiles to investigate mother-infant dyad

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Body odours have a great importance in chemical communication. It is widely known that breastfeeding women emit olfactive signals that elicit a response of newborns influencing their behaviour. In particular, it has been supposed that women may develop a peculiar chemical profile through pregnancy and childbirth that enables the identification of the mother by the newborn [1]. From an analytical point of view, one of the hardest challenges in identifying these potential chemosignals is to develop reliable sampling and analytical approaches for an effective chemical characterization of the mother odours since the concentration of most of these compounds ranges in the ppt-ppb levels.

In this work, we present two simple, non-invasive, and robust analytical workflows for the collection and analysis of odours released from the breast area. The first approach involves the use of thin film solid phase micro-extraction (TF-SPME, Figure 1A) probe to passively collect a broad range of volatile and semi-volatile analytes due to its high porosity and to the use of a combination of sorbent materials. Such a probe can be placed directly in contact with the skin, or it can sample the headspace inside a 3D printed chamber placed onto the breast area (Figure 1B). The second approach entails the dynamic head-space analysis of the chemical profile over the breast area using needle trap devices (NTDs) packed with 3 cm of Tenax GR [2]. The headspace sample is obtained with the same chamber used for TF-SPME that contains a luer-lock adapter for an easy and robust insert of the NTDs. The sampling flow rate is controlled through a mass flow controller (MFC). The collection system is operated through an ATMega328-pu for the precise control and reading of the MFC (Figure 1C). The readout of the system is achieved through Bluetooth and an OLED display. Chemical analysis was performed by thermal desorption of the samplers into a gas chromatography coupled with a mass spectrometer (GC/MS). Preliminary results suggest the capacity of the devices to collect chemicals that can be differentiated from the blank samples. The chemical characterization of the chemical volatile signals may represent an interesting point in the research of human pheromones during pregnancy paving the way for new medical tools to better manage the pre- and post-partum period for both the mother and the baby.

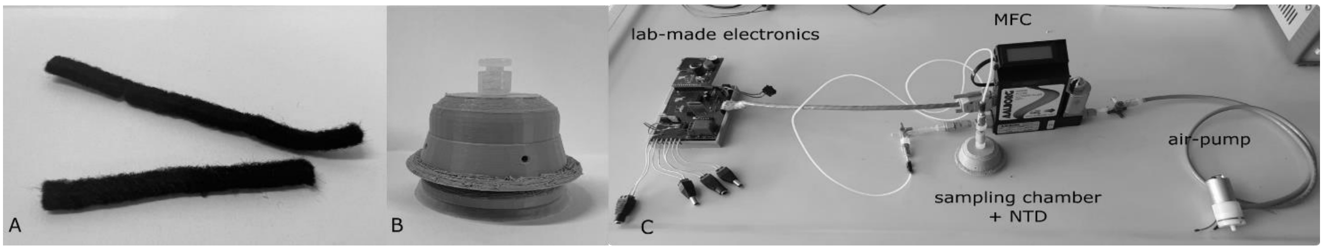

Figure 1 A) TF-SPME sampling device, B) 3D printed sampling chamber and C) lab-made prototype for the active collection of the breast samples.

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SBC-BASED ANION EXCHANGE MEMBRANES FOR GREEN HYDROGEN PRODUCTION

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Producing hydrogen by using anion exchange membrane (AEM) water electrolysis is a promising approach to address the severe energy crisis facing human society. AEM electrolysis can be integrated with renewable energy sources and utilizes low-cost electrocatalysts and other inexpensive components in stacks. To enable commercially viable hydrogen generation, improvement of the AEM component is imperative, [1,2] and the goal of fabricating a membrane, in which the chemical, mechanical and electrochemical requirements are combined and optimized in a synergistic way, still represents a challenging task.[2,3] The present work was, therefore, aimed at addressing several unique features of AEMs for implementation in an industrially scalable and sustainable energy- production process through a suitable synthetic strategy that involves the post-modification of a commercially available poly(styrene)-*b*-poly(butadiene (SBC) block copolymer matrix by grafting vinylbenzyl chloride (VBC). The synthesized SBC-*g*-VBC copolymers were, therefore, used for the fabrication of AEMs by solution casting followed by quaternization reaction with trimethylamine (TMA) for the quantitative conversion of $–CH_2Cl$ into $–CH_2(CH_3)_3N^+$ groups. Obtained films were thermally, mechanically and electrochemically characterized. By varying the VBC functionalization degree of the copolymers it was possible to modulate the ionic exchange capacity, conductivity, water uptake and mechanical properties of the membranes derived therefrom. The most promising AEM was selected for testing in electrolytic cells and was found to resist to real operating conditions for more than 2200 hours.

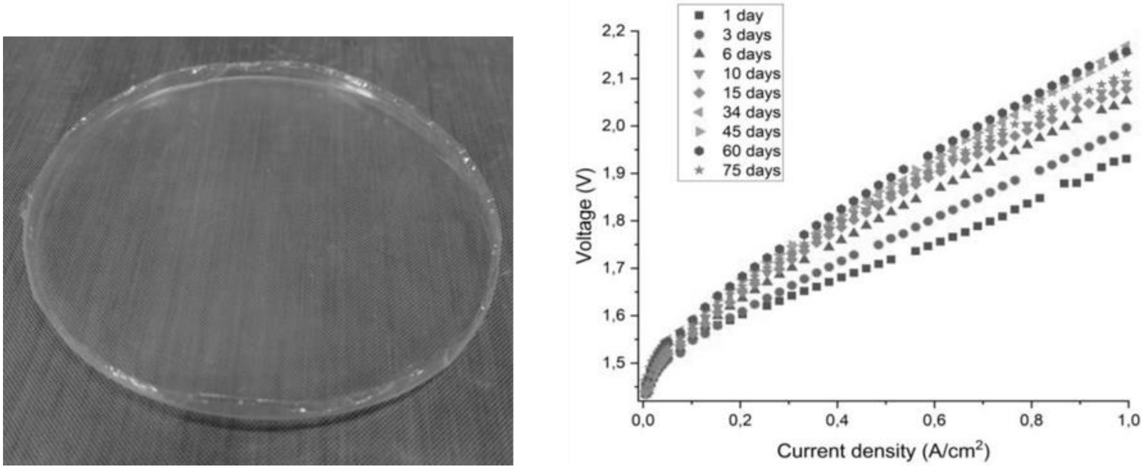

Figure 1. SBS-*g*-VBC based AEM (left) and polarization curves of the AEM as a function of residence time in an electrolytic cell (KOH 1 wt % at 55 °C) (right).

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Chemical depolymerization of polyethylene terephthalate by hydrolysis using Lewis-Brønsted acid mixtures

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The global demand for plastics continues to rise. The number of plastics in circulation is projected to increase from 236 to 417 million ton per year by 2030. Transition to a circular economy through reuse or recycle of plastics is essential to prevent increased accidental or purposeful release of polymeric materials into the environment, and thus curb environmental pollution. Mechanical recycling of waste plastic is an essential tool in an environmentally and economically sustainable economy of plastics, but current mechanical recycling processes are limited by cost, degradation ofmechanical properties, and general production of downgrading materials. Chemical recycling is gaining interest, as complementary to traditional recycling methods, especially when it is a selective process capable of returning the polymer to its monomeric feedstocks. [1] Unfortunately, all the protocols require harsh conditions, carrying out the reactions at least at 160 °C. In the present study we propose the use of a series of sustainable Lewis-Brønsted acid mixtures for the chemical depolymerization of post-consumer PET bottles. The effects of process parameters, suchas time, temperature, and water content are examined. The maximum conversion of PET and yieldfor monomer product, terephthalic acid, was observed as 100% and 89% respectively, after one hour at atmospheric pressure and at the reaction temperature of 100 °C (Figure 1).

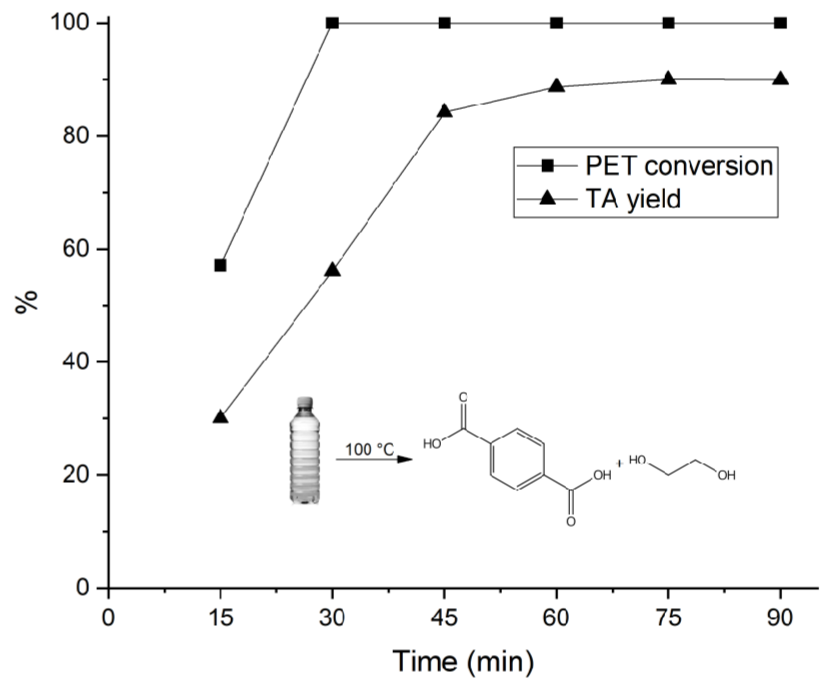

Figure 1. Effect of reaction time on the degradation of PET

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Computational insights into the carbon dioxide- promoted polyethylene terephtalate depolymerization

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Chemical recycling of plastic waste materials is an important tool for the transition to a real circular economy. Indeed, it overcomes some of the problems arising in the mechanical recycling process, as the downgrading of the recycled items. Among the polymers, one of the most common for applications certainly is the polyethylene terephtalate (PET). The large amount of PET produced each year (about 30.5 Mmt in 2019 with the expectation to increase to 35.3 Mmt by 2024)[1] combined to its non-biodegradability in nature, led to waste polymer recycling becoming an urgent issue. Various methods have been proposed and, among them, chemical recycling is the most promising in terms of 'sustainable development'[2]. In fact, it leds to the formation of raw materials ormonomers which allow the further high value added utilization. In the view of environmental protection, the conditions throughout PET depolymerization is performed are crucial, for example the energy consume, catalyst recovery and reuse, ect[2]. In this context, organocatalysis could be a potential solution to make chemical recycling more appealing in the waste treatment process. In the present study, we explore carbon dioxide as a cheap and traceless catalyst to afford PET depolymerization from post-user PET items, as beverage bottles, via aminolysis. Indeed, the CO_2- catalyzed degradation of polymer was already demonstrated to be promising for Nylon-6,6 degradation via transamidation reaction[3]. In particular, we focus our attention on the reaction mechanism to elucidate both CO_2 and amine roles in the reaction mechanism.

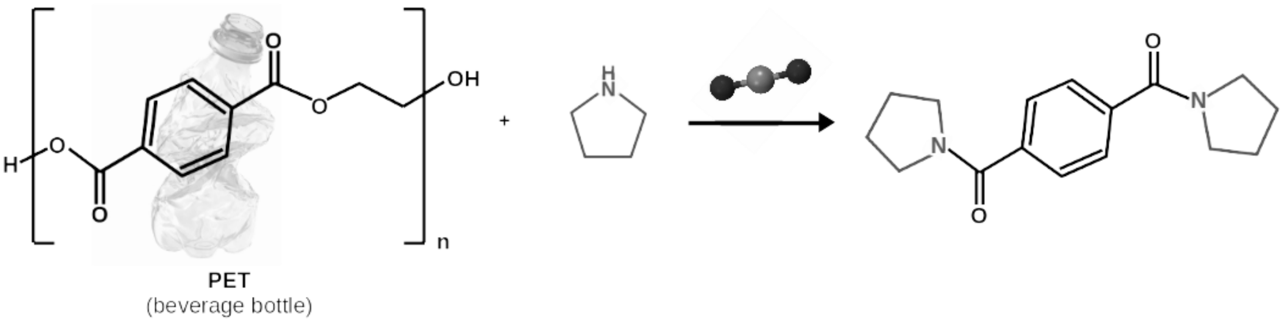

Figure 1: scheme for the CO_2-promoted depolymerization, via aminolysis, of PET from beverage bottle.

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Uncovering transient intermediates in a bacteriophytochrome photocycle

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Phytochromes are photoreceptors responsible for sensing light in plants, fungi, and bacteria. Their photoactivation is initiated by the photoisomerization of an embedded chromophore, which triggers a large conformational change in the entire protein structure[1,2]. Although phytochromes have been the subject of numerous studies[3-7], the photoisomerization mechanism and the following reaction path leading to the final active state remain elusive. Our work[8] shows an integrated computational approach that combines non-adiabatic surface hopping and adiabatic ground-state molecular dynamics simulations to unveil the photoactivation mechanism of *Deinococcus radiodurans* bacteriophytochrome. Our simulations[8] show that the ps-scale photoisomerization of the chromophore proceeds through a hula-twist mechanism that forces a counterclockwise rotation of the D-ring. The initial photoproduct rapidly evolves in an early intermediate characterized through IR spectroscopy simulation.

The early intermediate then evolves on the ns-to-μs scale to a late intermediate, characterized by a more disordered binding pocket and a clear weakening of the aspartate-to-arginine salt bridge interaction, whose cleavage is essential to interconvert to the final active state. The much longer time scales involved in this last transition[7] (ms and beyond) are extremely challenging for simulations and surely are not accessible without introducing enhanced-sampling methods.

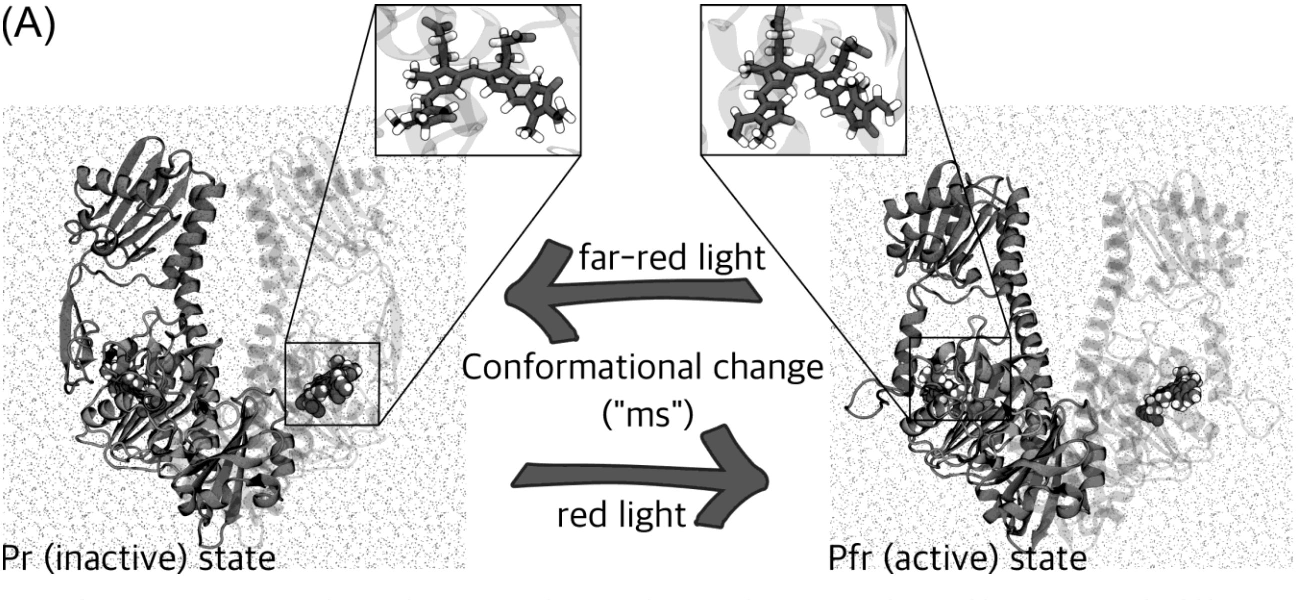

Figure 1. Representation of the PSM of the two photoproducts: Pr and Pfr, with a zoom on the bilin chromophore

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Effect of hyperglycemic conditions on a cultured human lens epithelial cell line: the involvement of aldose reductase

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Alteration in glucose homeostasis can result in hyperglycemia, which refers to high blood glucose levels, typical of diabetes. Among different metabolic alterations induced by high glucose concentrations, the increased flux of glucose through polyol pathway is one of major responsible of glucotoxicity. In this context, Aldose Reductase (AR) plays a central role [1]. AR is an NADPH-dependent enzyme belonging to a superfamily of enzymes (AKRs) involved in the metabolism of carbonyl substrates such as lipid aldehydes, ketosteroids and keto-prostaglandins [2]. AR acts as first enzyme of the polyol pathway, reducing glucose to sorbitol, which is then converted to fructose by the NAD+-dependent sorbitol dehydrogenase (SDH). The accelerated glucose flux through this metabolic pathway leads toward the reduction in the ratio NADPH/NADP+, as well as the accumulation of sorbitol and fructose. Overall, oxidative, osmotic and glycative stress increase in cells, culminating in a strong state of inflammation [3]. For this reason, AR is considered a target to be inhibited in order to counteract the deleterious events connected to hyperglycemic conditions.

Here we report the effect on cultured human lens epithelial (HLE) cells of the exposure to hyperglycemic conditions. A fluorimetric method, able to evaluate the intracellular content of sorbitol based on its enzymatic detection through the use of recombinant sorbitol dehydrogenase was optimized for HLE cells extracts. It was thus possible to demonstrate the occurrence in HLE cells of an increased flux through the polyol pathway which induced a marked and time dependent intracellular sorbitol accumulation. The addition of the aldose reductase inhibitor Sorbinil completely abolished sorbitol accumulation. In HLE cells exposed to hyperglycemic conditions an increase in COX-2 expression was also observed. The availability of a HLE cell line stable transfected with the luciferase gene under the control of NF-kB expression allowed to demonstrate that COX-2 expression was mediated by NF-kB transcription. However, any significant effect of Sorbinil was observed neither on NF-kB nor on Cox-2 expression, suggesting the contribution of additional metabolic alterations to the inflammatory response induced by hyperglycemic conditions.

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Trinuclear Iron Complexes for Biological Applications

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A variety of diiron complexes with a variable bridging hydrocarbyl ligand is easily available on multigram scale from commercial [$Fe_2Cp_2(CO)_4$] by stepwise assembly of small molecular units. In general, the dinuclear organometallic scaffold offers a wide structural variability, allowing to modulate the physicochemical properties of the compounds through an appropriate choice of the substituents on the bridging ligand. In particular, cationic complexes with aminocarbyne or vinyliminium ligands are air-stabile, amphiphilic and generally robust in aqueous media, which are important prerequisites for biological applications;[1] moreover, the biocompatibility and rich redox chemistry of iron make its complexes suitable for drug development.[2] Indeed, some complexes of the two families mentioned above recently displayed promising antiproliferative activity against 2D and 3D human cancer cell systems.[3]

To investigate further possibilities of functionalization, in this work we synthesized new aminocarbyne complexes decorated with a ferrocenyl unit, via incorporation of isocyanoferrocene as a terminal ligand or as part of the bridging aminocarbyne moiety (Figure 1). The new complexes contain three iron atoms in different oxidation states (i.e., +I and +II), possibly enhancing the redox properties. Furthermore, CO substitution enables the introduction of selected terminal ligands (e.g. isocyanides, ammonia) and the formation of vinyliminium derivatives. All triiron products were structurally characterized by spectroscopic, X-ray and DFT studies, and assessed for their behaviour in aqueous solutions.

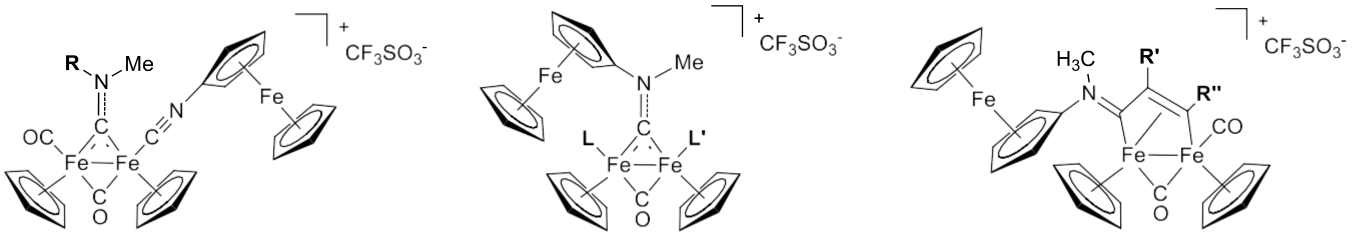

Figure 1. Structures of new trinuclear iron complexes obtained in this work (**R** = Me, C_6H_{11}, 4-C_6H_4-OMe. **L** = CO, **L'** = isocyanide, ammonia; **L** = **L'** = isocyanide. **R'** = H, **R''** = Me, Ph, Fc; **R'** = **R''** = Me).

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SSNMR Spectroscopy Study of Cubic $CsPbBr_3$ Perovskite Nanoparticles

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In recent years, metal halide perovskites (MHPs) have aroused a lot of enthusiasm in the materials science community due to their unique tunability, which allows a fine regulation of the desired properties. Indeed, MHPs show interesting properties making them promising candidates for optoelectronic applications, especially in photovoltaic and light emitting fields. $CsPbBr_3$ perovskite nanocrystals (Figure 1) have shown highly attractive light emitting properties, thanks to their narrow emission bandwidths, high quantum-yield values, and the possibility to perform a fine tune of the emission wavelength by controlling the size of the nanocrystals [1]. In the last few years, Solid-State NMR spectroscopy (SSNMR) has emerged as one of the main techniques for an in-depth structural and dynamic characterization of MHPs thanks to its ability to investigate over a broad spatial and temporal range, and to the possibility to perform different experiments on many different nuclei with non-null nuclear spin [2-4].

In this work, a multinuclear SSNMR approach was adopted for a structural study of cubic $CsPbBr_3$ nanoparticles stabilized with oleic acid and oleylamine. High-resolution SSNMR experiments on ^{1}H, ^{13}C, ^{207}Pb and ^{133}Cs nuclei confirmed the successful incorporation of different ions into the crystal lattice and the lack of phase segregation. ^{133}Cs MAS spectra allowed the observation of different signals of ^{133}Cs nuclei ascribable to inner and surface Cs atoms. In addition, a wider distribution of ^{133}Cs local environments was observed near the surface of the nanoparticles, probably associated with an increased disorder in the crystal structure. Relaxometric experiments showed interesting ligands effects on spin-lattice relaxation time values (T_1) of the ^{133}Cs nuclei.

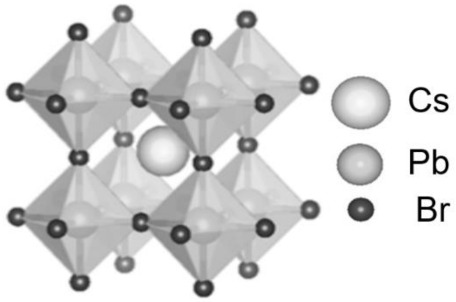

Figure 1. Structure of $CsPbBr_3$ perovskite

References:
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Laser-induced graphene electrode for aptamer-based sensing of bacteria

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Detection of bacteria during infectious is a key element in many different areas of interest, such as food safety, human health and environmental analysis. The traditional techniques for the detection for bacteria are ELISA, PCR methods or cultures.

However, these methods are time consuming, require qualified personnel, and expensive reagents. Additionally, these are not suitable for point-of-care testing applications.

In the recent years, the advancements in material science have brought to light a novel, interesting material called, Laser-Induced Graphene (LIG), that have attracted interest due to properties that include: its mechanical resistance, its high surface area and the relative ease in terms of production processes [1]. These characteristics have opened possibilities to develop low-cost and portable electrochemical devices that can respond to point-of-care applications.

In this work all the steps of functionalization process of LIG and standard Glassy carbon electrode (**Fig. 1A**) with two different aptamers, specifically designed for the ATC 25922 *E. coli* strain, will be described. The response of the biosensors developed were evaluated by using square wave voltammetry technique (**Fig. 1B**) and their selectivity was evaluated against *E. coli* and twopossible interferents such as *S. aureus* and *P. aeruginosa.* The biosensor showed a significative response toward *E. coli* over its interferents, specifically in the 0-10^4 CFU/mL. In particular, the biosensor prepared with 12-55 aptamer showed higher sensitivity and selectivity compared to the 12-31 aptamer ***(Fig. 1C)***.

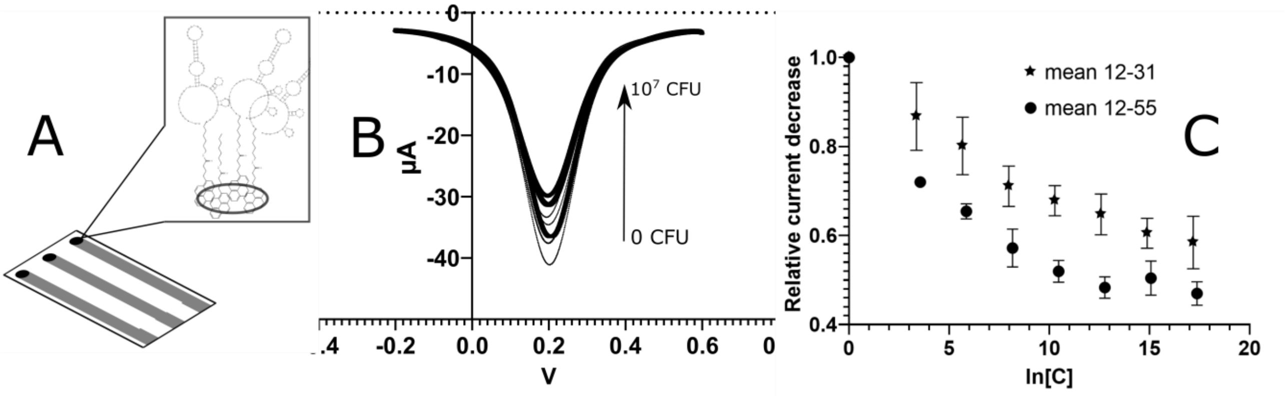

Figure 1. (A) A graphical representation of the fully functionalized electrode surface. (B) Square wave voltammograms performed in solutions with increasing concentration of E. coli (0 to 10^7 CFU). (C) Comparison between two aptamer-based biosensors (12-31 and 12-55) toward *E. coli*.

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Extraction of cellulose nanocrystals from lignocellulosic biomass: application of chemical and enzymatic hydrolysis.

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Biomasses have received increasing attention because of their availability and because they are a source of energy and chemicals.[1] The three main components of the lignocellulosic cell wall are cellulose, lignin, and hemicellulose. Hydrolysis of lignocellulosic biomass is useful for various applications, such as the synthesis of intermediates for the chemical and pharmaceutical industries, food additives, surfactants, solvents, and polymers. The most used strategy for obtaining cellulose nanocrystals (CNCs) is acid hydrolysis at moderate temperatures in the presence of strong acids, such as H_2SO_4 or HCl, which can degrade hemicellulose and the amorphous parts of cellulose, allowing crystalline parts to be isolated.[2] This strategy allowed to isolate CNCs from *Cynara cardunculus* (Figure 1), after mild organosolv delignification. However, acid hydrolysis may be a source of environmental concern, taking into account the large volumesof acid solution used to prepare the nanocrystals. A greener preparation procedure is based on enzymatic hydrolysis, which has a low environmental impact if compared with the previous method.[3] A commercially available enzyme such as cellulase from *Aspergillus niger* was used in this strategy. Here we show the hydrolysis results of cellulase attack on microcrystalline cellulose (Avicel PH10.1). Future developments of this work will entail the use of the enzymatic degradation strategy to enable cellulose nanocrystal synthesis from delignified biomass.

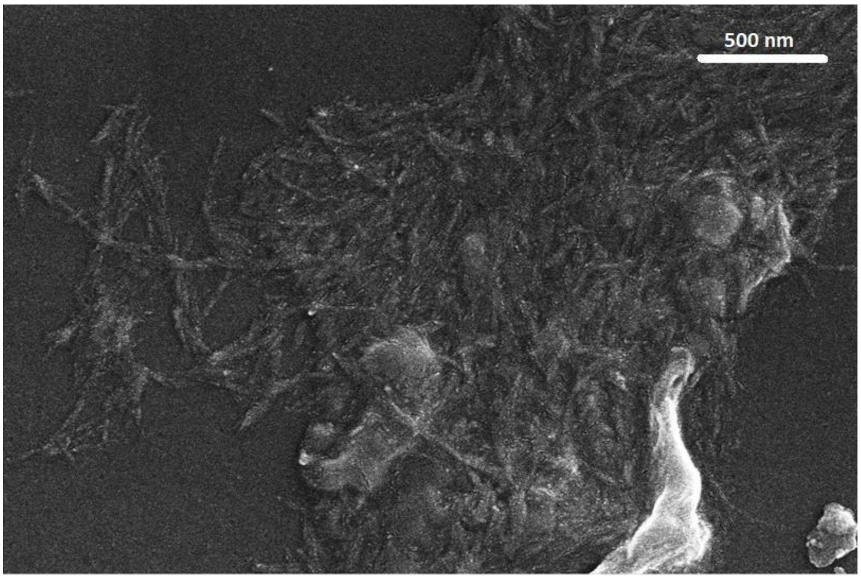

Figure 1. SEM micrograph of CNCs from *Cynara cardunculus* isolated by HCl hydrolysis

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Circular Dichroism Imaging of two novel Chiral Organic Dyes in Thin Film

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Thin films of chiral π-conjugated organic compounds[1] with semiconductive properties open the possibility to the fabrication of new generation chiroptoelectronic devices, such as CP-OLEDs[2] and circularly polarised light detecting OFETs[3]. In general, the homogeneity of the active layer hasa profound impact on charge mobility and overall device efficiency[4], that is why identifying inhomogeneities associated with local domains can lead to a more appropriate choice for the active material to be used in the device or to define the optimal protocol for its deposition. Optical and electron microscopies are the primary tools to investigate thin film textures, but they may not capture and cannot account for differential supramolecular order of the constituent molecules. To this end, spatially resolved chiroptical spectroscopies using highly collimated synchrotron radiation, such as Diamond Light Source B23 Circular Dichroism Imaging[5] (CDi), has been demonstrated to be able to furnish insights on the distribution of possibly diverse supramolecular structures down to 50 μm spatial resolution, when required even as a function of temperature. The potentialities of CDi will be herein presented with the analysis of two different chiral π-conjugated small molecules (a 9H-carbazole derivative and a hydroquinone derivative) in thin films created by spin coating. Thethin layers were guided to more stable supramolecular arrangements through post-deposition treatments (thermal or solvent annealing). We have previously demonstrated that the emergent CDsignals which are recorded with a benchtop spectrophotopolarimeter are identical to the average ofthe individual CDi signals over the same sample area. Here, we reinforced this concept bypositioning a square hole mask on top of the film, which ensures perfect correspondence between the measurements with CDi and conventional CD. In conclusion, we shall demonstrate that the supramolecular architectures of the thin layers studied are almost perfectly spatially homogeneous for the 9H-carbazole derivative, while for the hydroquinone derivative present intermolecular order degree discontinuities highlightable with CDi. Furthermore, we shall highlight again the good agreement between averaged CDi signals and bulk CD on the two systems studied, reconfirming the expected correlation and the reliability of B23 Circular Dichroism Imaging technique.

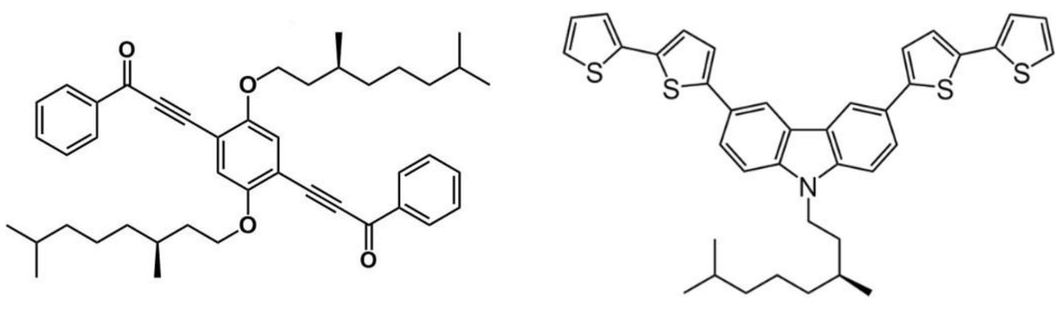

Figure 1. Structures of the two chiral organic molecules studied.

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Validation of an automated dispensing system of epoxy adhesives for ultrasound probes manufacturing

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In the last few years, the concept of robotic island is rapidly spreading within factories, representing a new vision of the industrialization of manufacturing processes. The transducer of an ultrasound probe is made by layering and gluing materials with decreasing acoustic impedance on a piezoelectric ceramic. The bonding layer should be as thin as possible and free from trapped air, in order to avoid acoustic wave reflections amongst the active material (piezo ceramic) and the passive layers (backing and front matching layers) and to ensure the performance of the probe. In the framework of A-Promise project funded by Tuscany Region, one of the goals is to redesign the current manual bonding process into an automated one, while improving the adhesion of the joined components, reducing the thickness of the glue layer and enhancing its homogeneity. The lamination part of the robotic cell is formed by an automated dispensing system which sums up three processes: dosing, mixing and dispensing of a bicomponent adhesive (epoxy resin). The feasibility of the automated dispensing process with different glues was investigated and the optimized operative parameters were established during tests by taking into account the viscous behaviour of the mixed adhesive and its temperature dependence. The dispensing pattern was carefully tailored to completely cover the piezo ceramic without overflowing [1; 2]. All surfaces were treated with atmospheric pressure plasma jet to enhance wettability and adhesive properties [3]. Dispensed amounts of resin were characterized through attenuated total reflection infrared spectroscopy (ATR-IR) [4] and differential scanning calorimetry (DSC) [5] to evaluate optimal dosing and mixing conditions. The reproducibility and repeatability of the process were assessedby weighting the dispensed resin. Mock-ups were also made to be characterized by scanning acoustic microscopy, which is a reliable method to discover flaws in the bonding layer and therefore the propagation of acoustic waves [6].

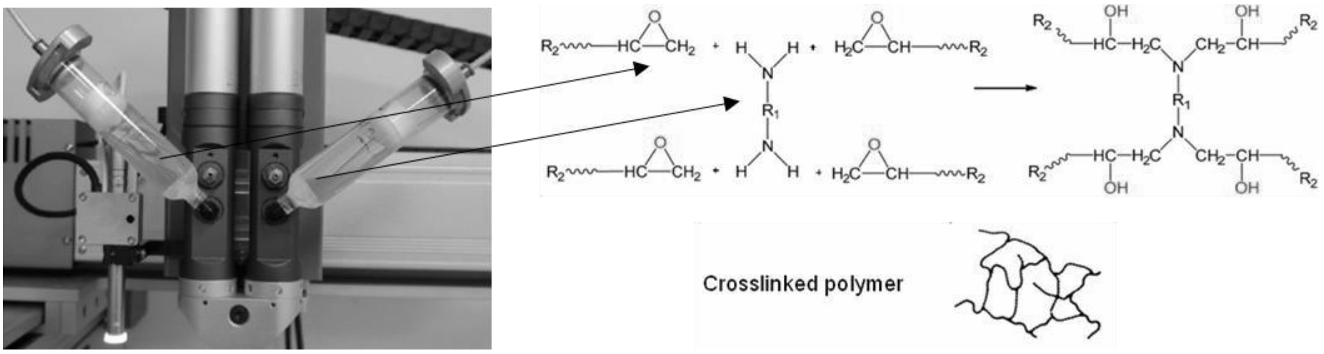

Figure 1. Dispensing system and chemical reactions between prepolymer and catalyst [1; 2]

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Metal carbamate complexes for the synthesis of metal-organic frameworks (MOFs)

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Metal-organic frameworks (MOFs) are crystalline materials belonging to the class of coordination polymers consisting of metal ions or clusters coordinated to organic ligands to form two- or three-dimensional structures with very high porosity. The synthesis of MOFs is usually performed by mixing a commercially available metal salt with the desired organic linker and by heating the reaction mixture to induce the self-assembly process that leads to formation of the porous framework. In most cases, the reaction proceeds upon organization of metal ions into secondary building units (SBUs), which are then connected via the organic linkers to form crystal structure. Metal carbamate complexes have been investigated in homogeneous catalysis and as precursors of nanostructured metal oxides, but there are only a handful of reports so far of their use as precursors of MOFs. Yet, many metal carbamates display structures analogous to SBUs commonly found in MOFs and could therefore be suitable precursors thereof.
In present work, complexes based on metal carbamates (Cu^{II}, Zr^{IV},)[1,2] (Figure 1) were synthesized and characterized by IR and NMR spectroscopy. These complexes were then used as precursors for the synthesis of MOFs, HKUST-1[3] and UiO-66[4], in combination with carboxylic ligands such as trimesic acid and terephthalic acid, respectively. The effect of various experimental parameters, such as the addition methods, linkers protonation state, solvents and reaction temperature, on the MOFs formation was investigated. The resulting MOFs were characterized by Powder X-raydiffractometry (PXRD), NMR spectroscopy, scanning electron microscopy (SEM), thermogravimetric analysis (TGA) and nitrogen adsorption measurements at 77 K. The results obtained suggest that metal-carbamato complexes are suitable precursors for the synthesis of MOFs. The high reactivity of these complexes allows to perform syntheses at room temperature that afford products in good yields and comparable quality to those obtained with literature procedures and from classical precursors.

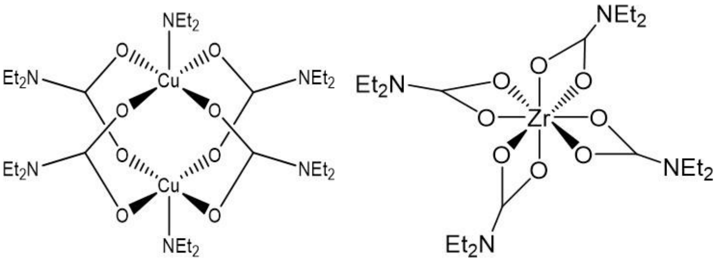

Figure 1- Structure of $Cu_2(OOCNEt_2)_4{\cdot}2NHEt_2$ and $Zr(OOCNEt_2)_4$.

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Remarkable near-infrared chiroptical properties of chiral Yb, Tm and Er complexes

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In recent years, a renewed interest in the study of chiroptical properties in both absorption and emission has occurred. Compounds showing significant optical activity have applications in chiral electronics and photonics, such as circularly polarized OLEDs,[1] polarization sensitive phototransistors and spin filters, as a few examples. Thanks to the nature of f–f transitions, lanthanide complexes prove effective in displaying significant chiroptical properties.[2] Beyond the UV-Vis domain, where most chiroptical properties are studied, it is possible to prepare lanthanide complexes endowed with effective CD (circular dichroism) and CPL (circularly polarized luminescence) in the NIR region.[3-7] Indeed, NIR wavelengths are of high interest in view of potential applications, such as in vivo imaging and telecommunications, as well as many others. In this work we aimed at demonstrating that selected transitions of certain chiral complexes of Yb, Tm and Er can show almost complete selective absorption of circularly polarized light in the 900–1600 nm region, while also emitting a significant degree of either left- or right-circular polarization.[8]

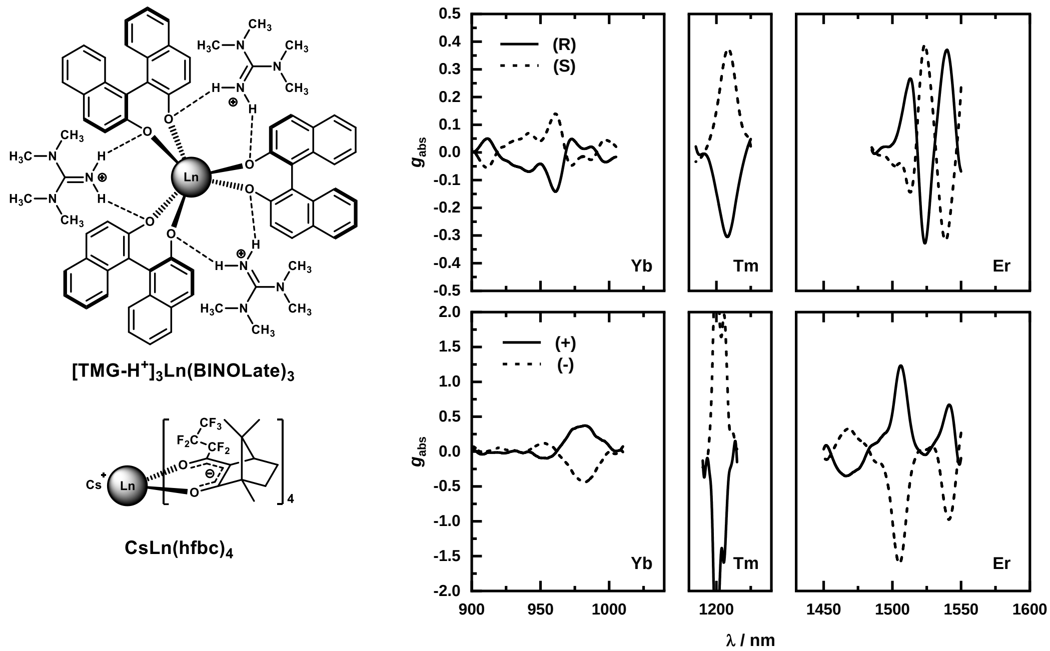

Figure 1. Top: The structure and plot of g_{abs}-vs.-wavelength for [TMG-H$^+$]$_3$Ln(BINOLate)$_3$ (Ln = Yb, Tm, Er). Bottom: The structure and g_{abs}-vs.-wavelength plot for CsLn(hfbc)$_4$ (Ln = Yb, Tm, Er).

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De novo design and sustainable synthesis of new green materials based on cross-linked hyaluronic acid for surgical applications

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Hyaluronic acid (HA) is one of the main components of extracellular matrix and human connective tissues. Its biocompatibility, biodegradability and viscoelasticity make it a good candidate for the development of soft-materials, which are used in several medical fields, such as ophthalmology, aesthetic medicine and arthrology.[1] The main limit of HA is its low durability so, modification of hyaluronic acid through cross-linking reactions, with different cross-linkers, or derivatization with biopolymers, oligomers or biomolecules (peptides, peptidomimetics, natural molecules etc.) can improve its properties and can lead to the synthesis of different materials, with new properties.[2] Such modifications should follow the principles of sustainable and green synthesis, to avoid the dispersion of these materials in environment and to guarantee the use of non-toxic materials for biomedical and surgical applications.[3,4]

The first part of the project deals with the synthesis and conformational analysis (NMR, CD, and theoretical calculations) of oligomers of natural and unnatural molecules, which could be used to derivatize HA. For example, we want to synthesize mimetics of oligoprolines, interesting for their folding and self-assembling properties, and oligomers based on N-functionalized glycine peptides (peptoids), which allows the synthesis of highly diversified molecules for the selective chelation of heavy metals. The synthesis will be performed both in solution and in solid-phase synthesis, while the chelating properties will be analysed through ICP, NMR and CD techniques. The other part of the project deals with the synthesis of cross-linked HA with different cross-linkers (PEG, collagen, peptides) and with the oligomers synthesized in the previous part of the project. These materials are designed for applications in biomedicine, so starting materials and products must comply with regulatory laws. Therefore, we are performing analysis of reagents and final products. Furthermore, a careful chemical characterization of the synthesized materials will be performed during the period at Matex Lab SA (Geneva), while mechanical and rheological properties, biological activity and toxicity will be studied during a period at UB-Care (Pavia, Italy).

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UV-activated metal oxide ZnO/ZnO:Ni based hydrogen gas sensor

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Ni-doped ZnO films were fabricated on an ITO glass substrate by sol-gel spin coating. Their properties were characterized by the UV-Vis (UV-vis spectrophotometer; JASCO-V750, spectral range of 300– 600 nm) measurements, revealing changes in the band gap width depending on Ni concentration, and the resistivity under the UV light. The performed ZnO-based films showed sensitivity to the H_2 gas under UV irradiation.

In the present work, ZnO and Ni:ZnO thin films were successfully synthesized using low-cost sol-gel spincoating on glass substrate. The band gap of ZnO is tuned from 3.17 eV to 3.07 eV with increasing Ni doping due to sp-d hybridization and exchange parameter. The present sensor with ZnO:Ni 10% showed sensitivity to the H_2 gas. Further research will include a more precise sensor calibration and a study of hydrogen sensing in the presence of other interference gases.

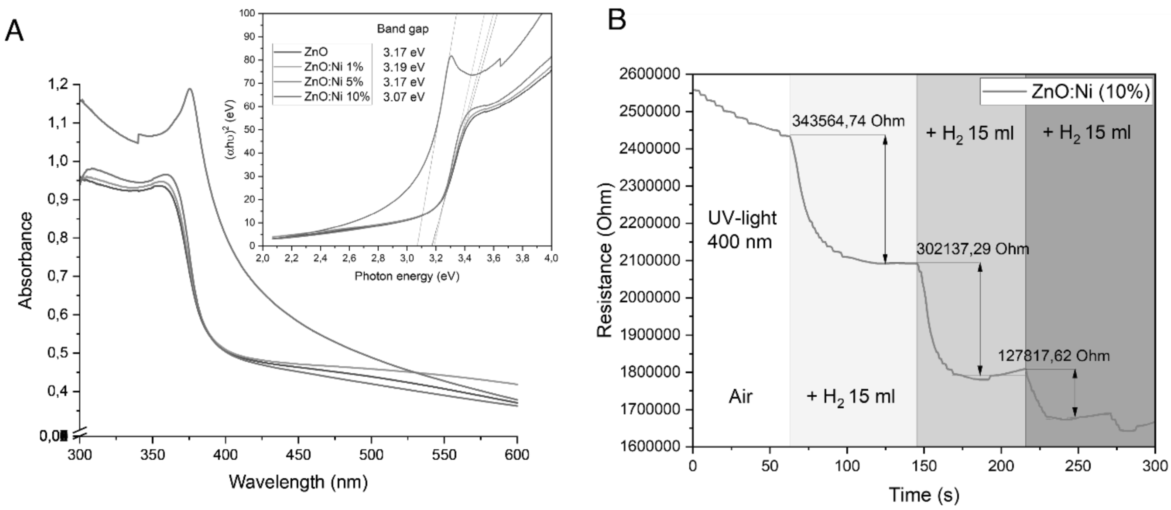

Figure 1. A – Absorbance spectra and the optical direct band gap (inset) of ZnO, ZnO:Ni (1, 5, 10%) films, respectively. B - Resistance response curve for UV-photoactivated (at room temperature) ZnO:Ni 10% film measured for hydrogen gas subsequent injections.

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