

18<sup>th</sup>  
dec 2025

# 15<sup>th</sup> ESRW

early stage researchers workshop  
in nanoscience

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INVESTIGACIÓN





# 15<sup>th</sup> ESRW



early stage researchers workshop  
in nanoscience

## Organizing Committee

Dr. Manuela Garnica  
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## Scientific Committee

Dr. Natalia Martín  
Dr. Vasileios Balos  
Dr. Zhen Zhan  
Dr. Atikur Rahman  
Dr. Paula Fernandez  
Dr. Mario Martínez

# Programme

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8:45 Reception

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9:15 Welcome

**Prof. Rodolfo Miranda**

IMDEA Nanociencia Director

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9:30 Invited talk

**Dr. Guillermo González Rubio**

Universidad Complutense de Madrid

*Wet-chemical synthesis of anisotropic gold nanocrystals*

## SESSION 1

**Chair:** Dr. Vasileios Balos

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10:15 Alejandro Martín Hoyas  
IMDEA Nanociencia

*Exploring rhenium half-sandwich complexes: from synthesis to reactivity and biological applications*

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10:30 Claudia Flórez Echavarría  
IMDEA Nanociencia

*Studying photosystem conformation landscape by protein loop engineering*

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10:45 Gabriel Alexandru Hrehoret  
IMDEA Nanociencia

*The fullerene flashlight: illuminating the path to single-particle antiviral dynamics*

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11:00 Jimena Pérez Maroto  
CIEMAT / IIS-FJD

*A non-viral nanodelivery platform for Cas9/Cas12a RNPs using dextran-coated magnetic nanoparticles*

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11:15 Coffee break / POSTER SESSION 1

*Even poster numbers*

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12:00 Invited talk

**Dr. Cristina Fornaguera Puigvert**

Institut Químic de Sarrià, Universitat Ramon Llull

*Engineering poly( $\beta$ -amino ester) nanocarriers: a modular platform for RNA therapeutics*

## SESSION 2

**Chair:** Dr. Atikur Rahman

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12:45 David M. Jiménez

IMDEA Nanociencia

*Chirality- and handedness-resolved mechanically interlocked derivatives of SWNTs via aqueous two-phase extraction*

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13:00 David Mateos Roncero  
Universidad Autónoma de Madrid

*Study of the polarization of plasmonic nanocavities*

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13:15 Iban Llamas  
IMDEA Nanociencia

*The effect of intercalated graphene on Fe-Ni superlattices*

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13:30 Marina Iglesias  
Universidad Complutense de Madrid

*Design and photophysical study of tetrahedral nanographenes exhibiting aggregation-induced emission*

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13:45 Comida

## 14:45 POSTER SESSION 2

*Odd poster numbers*

## SESSION 3

**Chair:** Dr. Natalia Martín

**15:30 Marion Le Meur**  
IMDEA Nanociencia

*Circadian resynchronizing molecules loaded into nanoparticles for enhanced brain delivery*

**15:45 Marta González**  
Universidad Complutense de Madrid

*Design of Janus nanoparticles for enzyme-activated and pH-responsive controlled drug release*

**16:00 Rafael Delgado García**  
Universidad de Castilla-La Mancha / INAMOL

*Critical field enhancement in nano-corrugated superconducting thin films*

**16:15 Guillermo Parra-Martínez**  
IMDEA Nanociencia

*Polarized phases and chiral superconductivity in multilayer graphene*

## 16:30 Coffee break / POSTER SESSION 3

*All posters*

## SESSION 4

**Chair:** Dr. Paula Fernández

**17:00 Jorge García Inglés**  
Universidad Autónoma de Madrid

*Conductance oscillations in helicene-based junctions*

**17:15 Chiara Crovara**  
Università della Calabria

*Modulating assemblies of monolayers of 4-n-alkyloxybenzoic acid on Au(111)*

**17:30 Elisa Collet**  
IMDEA Nanociencia

*Ultrafast hole dynamics in colloidal quantum dots revealed by femtosecond X-ray spectroscopy*

**17:45 Irene Pardo**  
IMDEA Nanociencia

*Gold nanoparticles functionalized with immune-modulatory microRNAs to reactivate antitumor immunity in melanoma*

**18:00 María Ortiz Rodríguez**  
IMDEA Nanociencia

*Single-molecule manipulation of genome integrity guardians*

**18:15 Closing remarks and award**

**18:30 Social gathering**

# Plenary Lectures

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# **Wet-chemical synthesis of anisotropic gold nanocrystals**

**Dr. Guillermo González Rubio**

*Universidad Complutense de Madrid*



Gold nanocrystals are intriguing materials displaying optical properties that vary according to the nanocrystal shape and size. This unique property makes them highly suitable for cancer diagnosis and treatment applications, optical devices, and photocatalysis. Gold nanorods, in particular, are especially attractive due to their ability to exhibit tunable and narrow extinction bands in the visible and near-infrared regions, depending on their volume and length-to-width ratio. In this presentation, I will discuss various methods for producing high quality gold nanorod colloids, focusing on surfactant-assisted seed-mediated growth routes and the application of pulsed laser irradiation to control size, morphology, and purity. We will explore fundamental concepts such as symmetry breaking, anisotropic growth, and the reshaping of nanocrystals through laser excitation, examining how different experimental factors impact the quality of the resulting colloids. I will also highlight recent advancements in the in-situ characterization of gold nanorod seeds, crucial for gaining insights into symmetry-breaking mechanisms.

## **Short biography**

Dr. González-Rubio studied Chemistry at the Complutense University (UCM) of Madrid, where he obtained his PhD in 2017 under the guidance of Prof. Luis Liz-Marzán (CIC biomaGUNE) and Prof. Andrés Guerrero-Martínez (UCM). His postdoctoral studies were conducted at the University of Konstanz under the mentorship of Prof. Helmut Cölfen, supported by a research fellowship from the Alexander von Humboldt Foundation. Since 2023, he has been an Atracción de Talento Research Fellow at the UCM. He was recently awarded an ERC Starting Grant to develop advanced methods to synthesize complex multielemental nanocrystals. His research interests focus on the development of colloidal routes and the use of ultrafast pulsed laser irradiation to synthesize, stabilize, and assemble high quality nanocrystals for optical and catalytic applications.

# Engineering poly( $\beta$ -amino ester) nanocarriers: a modular platform for RNA therapeutics

Dr. Cristina Fornaguera Puigvert

Institut Químic de Sarrià, Universitat Ramon Llull;



RNA medicines need delivery systems that can protect cargo, navigate biological barriers, and program intracellular fate. Poly( $\beta$ -amino ester)s (pBAEs) offer a biodegradable, chemically tunable platform in which backbone and end-group chemistry modulate complexation, stability, trafficking and release. I will discuss recent advances from our lab on pBAE nanocarriers for different types of RNA delivery, including oligopeptide-terminated and ligand-decorated libraries generation for selective transfection, as well as multilayer/hybrid designs aimed at crossing physiological barriers and shaping immune responses. Emphasis will be placed on structure–function rules, manufacturability, and translation-relevant assays that connect polymer design to potency and safety in vitro and in vivo. These examples illustrate how pBAE chemistry can be leveraged to build programmable RNA delivery systems with clear paths to application.

## Short biography

Cristina Fornaguera is an ICREA Academia Associate Professor in the Department of Bioengineering at Institut Químic de Sarrià (IQS), Universitat Ramon Llull (Barcelona), where she coordinates the NanoTher – Nano Therapies Lab, focused on nanomedicine engineering for targeted interactions with physiological barriers. Her research centers on polymeric and hybrid nanocarriers, particularly poly( $\beta$ -amino ester) (pBAE) systems, for RNA and gene delivery, immunomodulation, and barrier crossing. Only ten years after obtaining her PhD, Dr Fornaguera is currently leading a consolidated research group composed of almost 30 researchers of different levels. She is the principal investigator of national and international projects, funded under competitive calls. She was awarded last year with the ICREA Academia recognition.

# Oral Communications

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# Oral Communications

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- 1 Alejandro Martín Hoyas *IMDEA Nanociencia*  
**Exploring Rhenium Half-Sandwich Complexes: From Synthesis to Reactivity and Biological Applications**
- 2 Claudia Flórez Echavarria *IMDEA Nanociencia*  
**Studying photosystem conformation landscape by protein loop engineering**
- 3 Gabriel Alexandru Hrehoret *IMDEA Nanociencia*  
**The Fullerene Flashlight: Illuminating the path to Single-Particle Antiviral Dynamics**
- 4 Jimena Pérez Maroto *CIEMAT / IIS-FJD*  
**A Non-Viral Nanodelivery Platform for Cas9/Cas12a RNPs Using Dextran-Coated Magnetic Nanoparticles**
- 5 David M. Jiménez *IMDEA Nanociencia*  
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**Design and Photophysical Study of Tetrahedral Nanographenes Exhibiting Aggregation-Induced Emission**
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**Circadian resynchronizing molecules loaded into nanoparticles for enhanced brain delivery**
- 10 Marta González *Universidad Complutense de Madrid*  
**Design of Janus Nanoparticles for Enzyme-Activated and pH-responsive Controlled Drug Release**
- 11 Rafael Delgado García *Universidad de Castilla-La Mancha (UCLM), Departamento de Física and INAMOL*  
**Critical Field Enhancement in Nano-corrugated Superconducting Thin Films**
- 12 Guillermo Parra-Martínez *IMDEA Nanociencia*  
**Polarized phases and chiral superconductivity in multilayer graphene**
- 13 Jorge García Inglés *Universidad Autónoma de Madrid*  
**Conductance oscillations in helicene-based junctions**
- 14 Chiara Crovara *Università della Calabria (UniCal)*  
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- 15 Elisa Collet *IMDEA Nanociencia*  
**Ultrafast Hole Dynamics in Colloidal Quantum Dots revealed by Femtosecond X-ray Spectroscopy**
- 16 Irene Pardo Sierra *IMDEA Nanociencia*  
**Gold Nanoparticles Functionalized with Immune-Modulatory microRNAs to Reactivate Antitumor Immunity in Melanoma**
- 17 María Ortiz Rodríguez *IMDEA Nanociencia*  
**Single-molecule manipulation of genome integrity guardians**

# Exploring Rhenium Half-Sandwich Complexes: From Synthesis to Reactivity and Biological Applications

A. Martin-Hoyas<sup>a</sup>, and A. M. Pizarro<sup>a\*</sup>

<sup>a</sup>Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia), Spain.

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Following the discovery of cisplatin, organometallic half-sandwich complexes of Rh(III), Ir(III), Ru(II) and Os(II) have attracted attention due to their strong potency against cancer cells.<sup>1</sup> In particular, we are focused on the organometallic tethered half-sandwich structure of general formula  $[M(\eta^5:\kappa^1-Cp^*Z/\eta^5\text{-arene}Z)XY]^+$ , to explore new chemical reactivities inside cells. Metal-mediated chemistry is enabled by the vacancy created through the labile ligand Z, which is purposely the only metal bond in our structure susceptible to cleavage in aqueous media.<sup>2,3</sup> By extensive SAR analysis on Rh(III), Ir(III), Ru(II) and Os(II) half-sandwich tethered complexes, we have built a library of over 400 compounds with tunable metal-Z reactivity based on careful metal and ligand selection. We are now building on the knowledge have acquired to Re(Cp<sup>\*</sup>R) half-sandwich complexes.

In alignment with the  $d^6$  electronic configuration presented by the above-mentioned metals, we began exploring Re(I) half-sandwich complexes,  $[Re^I(\eta^5-C_5Me_4R)(CO)_3]$ , yet their inert tricarbonyl core limited the coordination of several bidentate ligands and functionalities. To overcome this challenge, we have expanded to Re(III), which successfully allows us to introduce a variety of ligands and to synthesise for the first time new families of four-legged piano-stool compounds with general formulae:  $[Re^{III}(\eta^5:\kappa^1-C_5Me_4R)X_2(CO)]^{2+}$ ,  $[Re^{III}(\eta^5-C_5Me_4R)X_2(CO)_2]$ ,  $[Re^{III}(\eta^5:\kappa^1-C_5Me_4R)X_2(CO)]$  and  $[Re^{III}(\eta^5:\kappa^1-C_5Me_4R)(en)(CO)]^{2+}$  ( $X = Cl, I$ ; Figure 1).

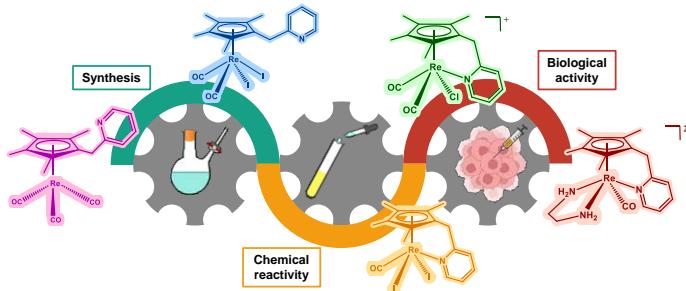


Figure 1. Re(I) and Re(III) complexes presented in this work.

Investigations into the reactivity in DMSO and the aqueous speciation of the new compounds corroborated the higher reactivity of Re(III) vs Re(I) towards substitution reactions. Additionally, biological studies demonstrated that Re(III) complexes exhibit greater cytotoxicity than their Re(I) counterparts, highlighting Re(III) as a promising candidate for further research.

## Notes and References

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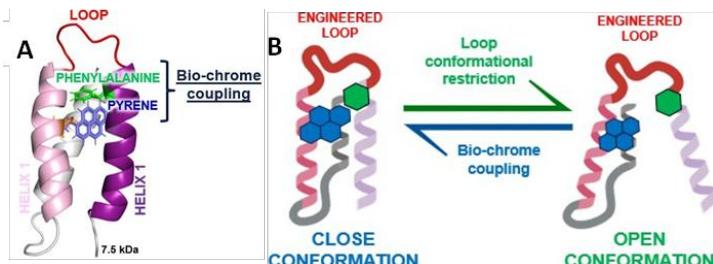
# Studying photosystem conformation landscape by protein loop engineering

Claudia Flórez Echavarría<sup>a</sup> and Sara H Mejías<sup>a</sup>

<sup>a</sup>IMDEA Nanociencia. Faraday 9, Cantoblanco, Madrid. Spain;

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Natural photosystems exhibit remarkable efficiency in light harvesting due to specific interactions between chromophores and protein structures. Protein conformational changes play a crucial role in modifying the chromophore's energy landscape to optimize it for efficient light harvesting.<sup>1</sup> These conformational changes are facilitated by the presence of unstructured protein structures, known as loops, which link different structural motifs, thereby providing flexibility and dynamics to the photosystem. The impact of the loops on shaping the protein conformation and their mechanistic role remains unknown due to the enormous complexity of natural photosystems. In this work, we propose an innovative approach to studying protein loops by developing easily manipulable biohybrid assemblies as model photosystems. The engineered biohybrids are formed by a de novo  $\alpha$ -helix protein and a covalently attached pyrene in the protein pocket (Figure 1A). A close interaction between phenylalanine in the protein pocket and the pyrene triggers a strong bio-chrome coupling in the bio-hybrid, which closes its conformation due to the flexibility of its loop.<sup>2</sup> Based on this biohybrid design, we modified the flexibility and length of one loop by adding from 1 to 4 glycines or prolines at different positions of the loop. Through spectroscopic methods, we demonstrated that long and rigid loops strengthen the bio-chrome coupling between the pyrene and phenylalanine, closing the conformation. In contrast, a short and rigid loop weakens it, leading to an open conformation (Figure 1B). Our study highlights the active role of the loop in the protein conformational landscape in photosystems. It demonstrates the potential of our engineered bio-hybrid as a model photosystem for studying unknown aspects of photosystem mechanisms.



**Figure 1.** **A.** Engineered biohybrid model with a closed conformation. **B.** The conformational equilibrium of the model. The conformation depends on the strength of the biochrome coupling and the conformational restriction imposed by the loop.

## References

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- 2 F. Echavarria C; Kocsi D; Abdellah M; Glover S; H Mejias; *ChemRxiv* **2025**; doi:10.26434/chemrxiv-2025-5krws.

# The Fullerene Flashlight: Illuminating the path to Single-Particle Antiviral Dynamics

Alexandru Hrehoret,<sup>\*a,b</sup> Cristina Flors,<sup>a</sup> Beatriz Illescas,<sup>b</sup> Nazario Martin.<sup>a,b</sup>

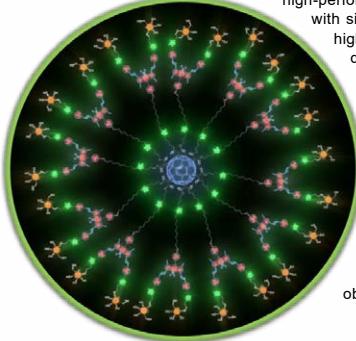
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Fullerene is a unique, spherical carbon-based nanomaterial that represents a promising biocompatible platform for biological activity and targeted molecular recognition. Its tunable structure is particularly promising for antiviral applications; specifically, **glycofullerenes** can mimic viral surfaces (e.g., Ebola, SARS-CoV-2) and effectively block infection by binding to cellular lectin receptors like DC-SIGN.<sup>[1, 2, 3]</sup> However, visualizing *how* and *when* these molecules inhibit viral entry at the single-particle level remains a significant challenge, as traditional bulk assays obscure these precise mechanisms.

To overcome this, we have designed and synthesized a series of novel **multichromophoric fullerenes** to act as high-performance fluorescent probes. These probes are specifically designed for use with single-particle microscopy (SPM) and single-particle tracking (SPT). These high-resolution techniques are critical for moving beyond population-level data to visualize the real-time, heterogeneous dynamics of individual molecules interacting with our biological receptors.<sup>[4]</sup> We employed click chemistry to symmetrically functionalize a fullerene core with 12 highly emissive BODIPY fluorophores. To confer lectin recognition and aqueous solubility, two of these derivatives were further decorated with 24 mannose moieties, creating trackable glycofullerenes.



Bulk and single-particle photophysical data confirm our molecules exhibit enhanced fluorescent brightness and photostability compared to the respective BODIPY precursor. Our data also suggest that by impairing chromophore aggregation and improving water solubility even further, these systems have the potential to enable direct, real-time observation of individual binding dynamics in living cells.

FIGURE:  
Visual representation of one of the fluorescent glycofullerene probes.

## Notes and References

- 1 Muñoz, A.; Sigwalt, D.; Illescas, B. M.; Luczkowiak, J.; Rodríguez-Pérez, L.; Nierengarten, I.; Holler, M.; Remy, J.; Buffet, K.; Vincent, S. P.; Rojo, J.; Delgado, R.; Nierengarten, J.; Martín, N. *Nature Chem.* **2016**, 8, 50–57.
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# A Non-Viral Nanodelivery Platform for Cas9/Cas12a RNPs Using Dextran-Coated Magnetic Nanoparticles

Jimena Pérez-Maroto<sup>1,2</sup>, Carmen Escalona-Noguero<sup>3</sup>, Nuria Lafuente-Gómez<sup>3</sup>, Mónica Dhanjani<sup>3</sup>, Gorka Salas<sup>3</sup>, Marta García<sup>1,4,5</sup>, Álvaro Somoza<sup>3</sup> and Begoña Sot<sup>1,2,3</sup>

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<sup>2</sup>Advanced Therapies Unit, Instituto de Investigación Sanitaria Fundación Jiménez Díaz (IIS-FJD, UAM), Av. Complutense, 40, Moncloa-Aravaca, 28040, Madrid, España. Tel: 913466000;

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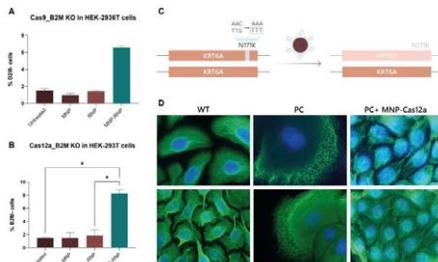
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\* These authors contributed equally to this work.

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CRISPR/Cas technology has revolutionized genome editing. The versatility of CRISPR/Cas-induced NHEJ, HDR and base editing offers the potential to treat most genetic diseases by disrupting or correcting harmful mutations, inserting therapeutic transgenes or introducing protective mutations<sup>1</sup>. However, delivery into target cells is still a matter of concern. Delivery of pre-assembled Cas endonuclease and guide RNA (gRNA) ribonucleoprotein (RNP) complex appears to be the easiest, most safety, cost-effective and efficient strategy<sup>2</sup>, although the large size and charge of the protein pose significant challenges for their delivery into cells. Integrating nanotechnology as vehicles for RNPs have shown great promise in genome editing. Several nanomaterials can be used, but magnetic nanoparticles (MNP) are particularly attractive because of their safety and tunability<sup>3</sup>. For these reasons, the present work aims to design a nanodelivery strategy through the conjugation of Cas9 or Cas12a RNPs with carboxymethyl dextran-coated iron oxide magnetic NP for the gene editing of different cell lines. To address this challenge, we first explored the delivery and gene editing efficacy of these nanocomplexes in HEK-uGFP and MEF-tdTOMO fluorescence-based reporter cells, respectively. We observed that nanocomplexes can be taken up by mammalian cells, decreasing the number of GFP+ cells and increasing the number of Tomato+ cells. Altogether, these findings indicate that MNPs are suitable vehicles for the intracellular delivery of Cas RNPs, which can display specific gene-knockout activity. Genetic disorders are the main objectives for CRISPR therapeutics, so we exploited the potential of MNP-RNP to target endogenous genes. To this end, we designed specific gRNA to target different endogenous genes in several human cell lines and evaluated the performance of our non-viral vector. Giving the promising results, we tested the therapeutic gene editing efficiency of MNP-RNP Cas12a in keratinocytes isolated from pachyonychia congenita patients, a rare, autosomal dominant genetic disorder<sup>4</sup>. Keratin immunostaining showed that cells treated with the nanonanocomplexes had undergone a partial recovery of wild-type intermediate filaments' structure and cell shape. To sum up, in this study we developed a novel strategy for the delivery of Cas RNP into target cells, which exhibit efficient gene editing and is likely to be used as a genome editing tool for the knock-out of disease-causing mutations.

**FIGURE.** Genome editing of B2M gene using the **A.** MNP-RNP Cas9 and **B.** MNP-RNP Cas12a nanocomplexes in a mammalian cell line. **C.** Schematic representation of the heterozygous N17K mutation in KRT6A, which can be harnessed for the selective KO of the mutant allele. **D.** MNP-RNP treated keratinocytes partially restored functional keratin.



## Notes and References

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# Chirality- and Handedness-Resolved Mechanically Interlocked Derivatives of SWNTs via Aqueous Two-Phase Extraction

David M. Jiménez,<sup>a</sup> Sylwia Parzyszek,<sup>a</sup> Dean Milanović,<sup>a</sup> María Luisa Ruiz-González,<sup>b</sup> Alejandro López-Moreno,<sup>a</sup> and Emilio M. Pérez<sup>a</sup>

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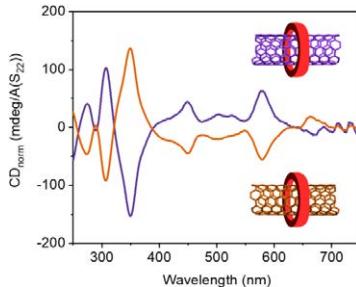
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Single-walled carbon nanotubes (SWNTs) are nanomaterials with exceptional properties set by their chiral vector ( $n,m$ ).<sup>[1]</sup> This vector determines the electronic behaviour, diameter, chirality of each nanotube. Moreover, each nanotube species (except armchair and zigzag) exists in two enantiomeric forms, left- and right-handed nanotubes, which show distinct chiroptical activity. Typical as-synthesized SWNT samples are inherently heterogeneous, which represents a major challenge for applications requiring determined SWNT species. Through the years, different strategies such as gel chromatography, conjugated polymers wrapping, and aqueous two-phase extraction (ATPE), have demonstrated effectiveness in isolating specific ( $n,m$ ) species.<sup>[2]</sup>

In parallel, functionalization of SWNTs has been explored as means to improve their processability and provide nanotubes with new functionalities. Conventional approaches consist of covalent modification, which disrupt the  $\pi$ -conjugated nanotube structure, and supramolecular functionalization, which is reversible and often labile. A decade ago, we introduced a new strategy which relies on the mechanical interlocking of SWNTs with macrocycles, introducing the concept of mechanically interlocked nanotubes (MINTs).<sup>[3]</sup> This approach maintains the tube structure while offering superior kinetic stability compared to other non-covalent approaches.

Despite the growing interest in functionalized SWNTs, current sorting techniques are more oriented to pristine nanotubes, requiring the isolation of specific ( $n,m$ ) species prior to functionalization. In this work, we demonstrate that ATPE can be directly extended to functionalized SWNTs, in particular MINTs, for the sorting and isolation of chirality- and handedness-enriched functional SWNT species. Typical ATPE workflows have been adapted for their application on MINT species, exploiting different approaches (e.g. trisurfactant systems and pH-driven sorting).

Comprehensive characterization confirms structural and optical integrity of the isolated MINT species: UV-Vis-NIR and photoluminescence excitation (PLE) spectroscopies indicate single-chirality enrichment; Raman spectroscopy shows preservation of the  $sp^2$  network; circular dichroism clearly shows the characteristic Cotton effect for each nanotube enantiomers. AFM and TEM micrographs are included which confirm the MINT structure. This general strategy enables the access to helicity- and enantiomer-defined MINTs, expanding the possible applications of these derivatives.



## Notes and References

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# Study of the Polarization of Plasmonic Nanocavities

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Nanocavities are resonant structures capable of confining the electromagnetic field of an optical mode within nanometer-scale dimensions, enabling the study of light-matter interactions at the atomic limit. Among these, nanocavities formed between the metallic tip of a scanning tunneling microscope (STM) and a metallic surface constitute an ideal platform for investigating plasmonic phenomena, owing to their high degree of tunability in both geometry and gap size<sup>1</sup>. Recent studies have demonstrated that the presence of atomic-scale defects within such nanocavities, thereby forming picocavities, can induce highly directional light emission, allowing these systems to behave as picoantennas with potential applications in nanoscale optoelectronics and sensing<sup>2</sup>. Beyond the angular distribution of the emitted radiation, the polarization state of the plasmonic emission provides additional insight into the multipolar nature of the confined optical modes. In this work, we investigate the polarization-resolved far-field emission arising from the radiative decay of localized surface plasmons generated in a nanocavity formed between a gold tip and a Cu(111) surface. The analysis reveals that the emitted light contains both linear and circular polarization components, whose relative amplitudes depend on the emission wavelength. Moreover, upon the deposition of cobalt islands, introducing magnetic order, on the Cu(111) surface, we observe a significant variation in the relative weights of the polarization components.

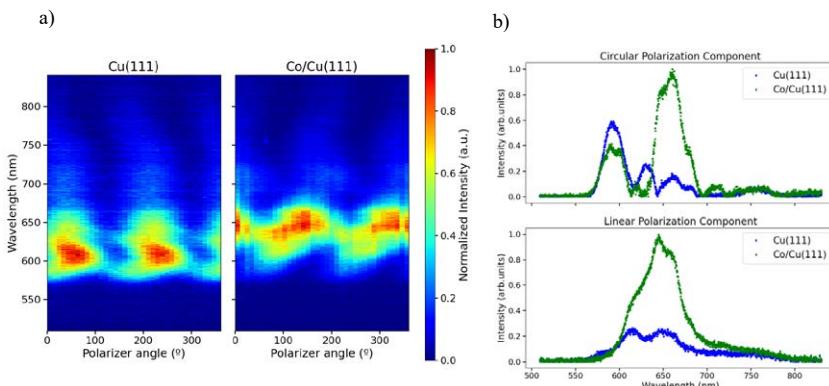


FIGURE 1: (a) STM nanocavity plasmonic raw light emission measured in the far field with the tip over a bare Cu(111) surface (left panel) and with the tip over a Cobal island on top of the Cu(111) surface (right panel). Acquisition settings: time/spectrum = 10s, bias voltage  $V_{\text{bias}} = 2.8\text{V}$ , and tunnelling current setpoint value  $I_{\text{sp}} = 3\text{nA}$ . (b) Decomposition of circular and linear polarization components of the emitted light as a function of the plasmonic emission wavelength.

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# The effect of intercalated graphene on Fe-Ni superlattices

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Nanocrystallites of the  $L_{10}$ -FeNi phase found in meteorites display a face-centered tetragonal structure with alternately stacked monoatomic layers of Fe and Ni along the c-axis. This "bulk" form of  $L_{10}$ -FeNi is characterized by intrinsic magnetic properties such as large saturation magnetization ( $M_s = 1270$  kA/m) and large uniaxial magnetic anisotropy energy ( $K_u$ ) of  $1.3$  MJ/m $^3$  [1-3], which are comparable to those of the best magnets containing rare earths. The origin of this large magnetic anisotropy was intriguing, since the material does not contain heavy metals (e.g. Pt or Au) or rare-earths providing high spin-orbit coupling (SOC), so fundamental studies of ideal  $L_{10}$ -FeNi will help on the understanding of this effect. This has resulted in a rush of interest in the possibility to create rare-earth-free strong magnets by synthesizing this phase on Earth.

Epitaxial, single-crystal Fe/Ni(100) superlattices with monolayer periodicity have been grown on graphene/Ir(100) by alternate monolayer-by-monolayer deposition under ultra-high vacuum (UHV). After every layer, the system was annealed in order to intercalate the metallic film under the graphene [4] so highly epitaxial and non intermixed Fe/Ni multilayer samples have been grown. We will discuss the effect of using graphene as a surfactant [4] to improve the structural perfection of the grown superlattice and its effect on the magnetic properties of the system.

All the samples have been characterized *in situ* by surface science techniques (XPS, UPS, LEED) and *ex situ* (XRD, SEM). The magnetic characterization has been done by Magneto Optic Kerr Effect (MOKE) magnetometry, Vibrating Sample Magnetometry (VSM), and Superconducting Quantum Interference Magnetometry (SQUID), which have helped on the identification of the  $L_{10}$ -FeNi phase and the unravelling of its intrinsic magnetic properties.

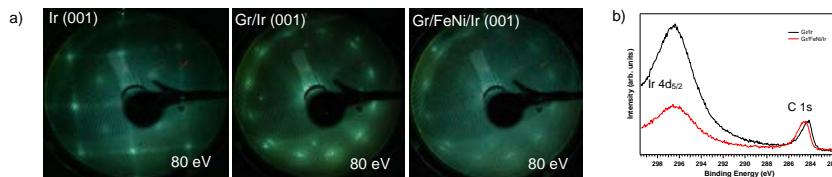


Fig. 1. a) LEED patterns of different steps of the growth, b) XPS core levels of Ir and C before and after intercalation

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# Design and Photophysical Study of Tetrahedral Nanographenes Exhibiting Aggregation-Induced Emission

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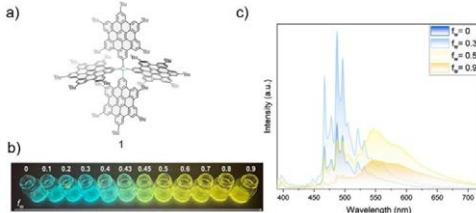
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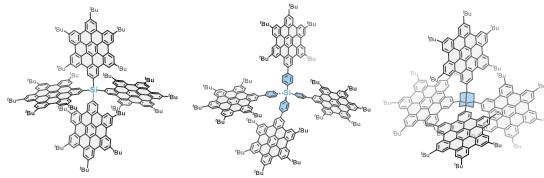
Graphene emerged in 2004 as a groundbreaking material with the potential to revolutionize the future of nanoelectronics. It exhibits exceptional mechanical strength, remarkable flexibility and high carrier mobility at room temperature. [1] However, as it is a zero-gap semiconductor, devices made of large area graphene are not suitable for conventional transistors. Among the strategies proposed to open a bandgap between the conduction and the valence bands, quantum confinement of the electrons in smaller fragments such as nanographenes has gained significant attention in the scientific community. [2]

The bottom-up benchtop synthesis by stepwise organic chemical transformations leads to monodisperse molecular nanographenes with a precise control over the size and the shape and, therefore, on the properties. Following this approach, our research group has recently developed the synthesis of tetrakis(penta-*tert*-butyl-hexa-*peri*-hexabenzocoroneny)methane, "tetrahedraphene" **1** (Figure 1a), a molecule composed of a central sp<sup>3</sup> carbon atom linked to four hexa-*peri*-hexabenzocoronenes (HBCs). This molecule showed aggregation-induced emission (AIE), observed as a fluorescence color change occurred between the solution and solid states [3].



**Figure 1.** a) Tetrahedraphene **1** b) Emission of **1** in THF with different volume fractions of water ( $f_w$ ). c) Emission spectra of **1** in THF with different volume fractions of water.

Encouraged by this result, we proceeded to design and synthesize a new series of tetrahedral nanographenes to gain deeper insight into the relationship between molecular structure and photophysical properties. Our efforts focused on three key structural modifications to investigate changes in the AIE. Firstly, by varying the central atom to Si, **2** (Figure 2). Then, by the introduction of rotational and vibrational freedom using a spacer between the HBC fragments and the central atom, compound **3**. Finally, by the modification of the central core employing molecular fragments such as adamantane, compound **4**, instead single atoms.



**Figure 2.** Tetrahedral nanographenes with a central silicon atom **2**, with a benzene spacer **3** and with a central adamantane moiety **4**.

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# Circadian resynchronizing molecules loaded into nanoparticles for enhanced brain delivery

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Disruption of the central circadian clock (CC) has shown to accelerate Alzheimer's disease (AD) progression. In preclinical models, CC-resynchronizing compounds have presented efficacy in AD, but their clinical success has been limited by poor brain penetration due to the presence of the blood-brain barrier (BBB) and unmet dosing time. Functionalized nanoparticles (NPs), by enhancing BBB crossing through passive and active transports, may offer a reliable solution to target CC dysfunctions in AD [1].

In this study, poly(lactic-co-glycolic) acid (PLGA) NPs were multifunctionalized with two brain-targeting peptides derived from angiotensin-2 and transferrin. NPs were orthogonally co-labelled with two fluorophores (C6 and Cy5) and their performance was evaluated by internalization studies in hCMC/D3 cells. Brain penetration ability was evaluated on a BBB-on-a-chip model. Different drugs targeting the CC with poor pharmacokinetics were encapsulated in the NPs, with encapsulation efficiency measured by UV or fluorescence. The drugs and the loaded-NPs effect on CC was evaluated using Per2-Luciferase U2O2 cellular system.

The NPs were monodisperse with hydrodynamic diameters of 100–150 nm. The fluorophores were colocalized in the cytoplasm during the internalization studies, confirming NP internalization and integrity. BBB permeability studies showed 55% BBB crossing enhancement when the NPs were functionalized with the transferrin derivative (Figure 1). The drug loading of the CC-targeting compounds reached up to 20%. Each drug had the same effect on the CC regardless if used as free compound or loaded into NPs. The nanoencapsulation did not impact negatively the activity of the compounds and for some them, even enhanced their efficacy.

Successful NPs functionalization lead to enhance BBB crossing ability in vitro. The encapsulation of CC-resynchronizing molecules was optimized and loaded-NPs were evaluated in a CC *in vitro* model with positive results. This work confirms the potential of NPs as a new strategy to increase brain CC resynchronization.

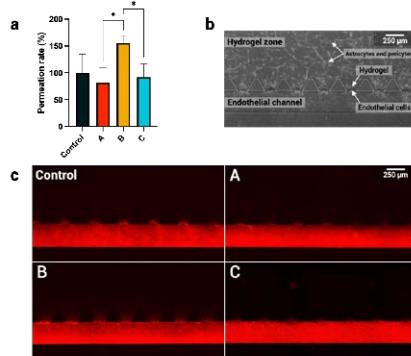


Figure 1: a) Permeation rate of NPs across the BBB-on-a-chip after 30 min incubation. Data displayed as mean  $\pm$  SEM. One-way ANOVA compared to control 95% CI: ns, non-significant; \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001. b) Bright field image of the BBB-on-a-chip at day 2. c) NP fluorescent images after 30 min incubation in the BBB-on-a-chip. Control: Cd-PLGA-Cy5; A: Cd-PLGA-Cy5-Angiotensin-2; B: Cd-PLGA-Cy5-Transferrin; C: Cd-PLGA-Cy5-Angiotensin-2-Transferrin. Scale bar is 250  $\mu$ m.

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# Design of Janus Nanoparticles for Enzyme-Activated and pH-responsive Controlled Drug Release

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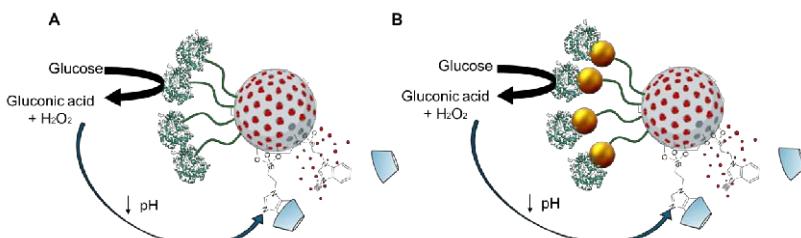
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In recent years, the development of smart drug delivery systems (DDS) capable of controlled release has grown exponentially. (1) A wide range of materials has been evaluated for DDS design, including liposomes, polymers, metal nanoparticles, micelles, and mesoporous silica nanoparticles (MSNs). Among them, MSNs stand out due to their unique properties, such as high loading capacity, low toxicity, and easy functionalization with stimulus-sensitive gate-like ensembles. (2)

One of the most promising research lines in this field is the development of anisotropic nanoparticles, known as Janus nanoparticles, which feature two distinct functionalities within a single structure. This duality allows for independent surface modification, enabling the incorporation of specific functional groups for targeted and controlled drug release. (3)

This work aims to design nanomachines capable of releasing antitumor drugs at the desired site and time, minimizing damage to surrounding healthy tissues and cells, and overcoming the limitations of current conventional cancer therapies. Furthermore, the integration of enzymes as recognition and transduction elements enhance the selectivity of these devices, enabling the construction of the nanomachines for autonomous drug release.

To this end, two types of Janus mesoporous silica nanoparticles were developed, both featuring asymmetric functionalization but differing in the nature of polyethyleneglycol (PEG) moiety -NH<sub>2</sub>-PEG-COOH (Fig. 1A) and NH<sub>2</sub>-PEG-SH (Fig. 1B)- used for enzymatic control. One face of each nanoparticle is modified with a distinct PEG derivative to support the immobilization of glucose oxidase, while the opposite face is functionalized with pH-sensitive gates based on a supramolecular complex between benzimidazole and β-cyclodextrin (CD). The nanomachine recognizes glucose as the input stimulus, which is enzymatically oxidized by glucose oxidase into gluconic acid and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). This reaction induces a localized drop in pH, protonating the benzimidazole and triggering the dissociation of the inclusion complex with β-cyclodextrin, thereby releasing the encapsulated drug in a controlled manner. (Fig 1)



**FIGURE 1:** Proposed mechanism of the nanomachines powered by the action of the enzyme glucose oxidase for controlled release. (A) Janus nanoparticle functionalized with NH<sub>2</sub>-PEG-COOH, and (B) Janus nanoparticle functionalized with NH<sub>2</sub>-PEG-SH.

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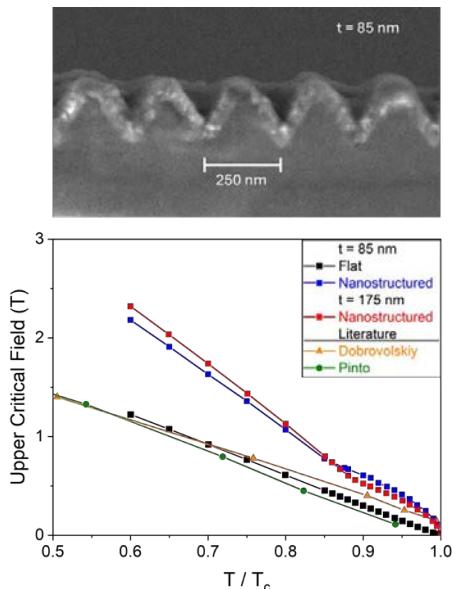
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# Critical Field Enhancement in Nano-corrugated Superconducting Thin Films

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We report an experimental study on the characterization of the superconducting properties of Niobium thin films grown over triangular-shaped nanostructured Silicon substrates with 250 nm periodicity [FIGURE]. At superconducting film thicknesses of 85 nm and 175 nm, we find changes in trend with the temperature in the upper critical field for the nanostructured thin films that are not observed in the flat non-nanostructured thin film of reference [FIGURE]. These changes of trend are related to a contribution of the parallel critical field to the measured upper critical field as a result of the nanostructuration.

In addition, we observe in the nanostructured thin films an increase in the upper critical field in a wide range of temperatures as compared to the flat film of reference and nanostructured<sup>1</sup> or flat<sup>2</sup> Niobium thin films from literature. These results can form a basis to develop new superconducting devices with potential applications in superconducting computing, magnetometry or superconducting electronics<sup>3</sup>.

FIGURE. (top) Lateral-SEM image of 85 nm thick Niobium thin film grown over nanostructured Silicon substrate with 250 nm periodicity. (bottom) Upper critical field as function of reduced temperature,  $T/T_c$ , where  $T_c$  is the critical temperature, of nanostructured Niobium thin films with 85 nm thickness (blue) and 175 nm thickness (red). Upper critical field of flat 85 nm thick Niobium thin film (black) is shown as comparison, as well as data of 52 nm thick nanostructured thin film from Dobrovolskiy et al.<sup>1</sup> (orange) and 33 nm thick flat thin film from Pinto et al.<sup>2</sup> (green).

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# Polarized phases and chiral superconductivity in multilayer graphene

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Rhombohedral multilayer graphene systems feature an abundance of correlated phases and superconducting states in experimental measurements. Some of the superconducting pockets can emerge from, or close to, one of these correlated states. This exotic superconductivity emerging from a spin-and-valley-polarized metallic phase has been recently discovered in 4,5 and 6 layer rhombohedral graphene. [1, 2]

In this work, Hartree-Fock calculations have been performed to build the phase diagram of rhombohedral graphene for different number of layers, in the presence of long-range Coulomb interactions. By varying the external displacement field and carrier density, a cascade of metallic partially-isospin-polarized phases that spontaneously break spin and/or valley (flavor) symmetries is found [3]. In addition, these states can present nematicity, stabilized by electron-electron interactions, exhibiting rich internal complexity.

Though mean-field correctly predicts the isospin flavors and reproduces the experimental phase diagram, it overestimates the band renormalization near the Fermi energy and suppresses superconducting instabilities. To address this, we introduce a physically motivated scheme that includes internal screening in the HF calculation. Using this formalism, we find superconductivity arising from the spin-valley polarized phase, on the electron-doped side. Our findings reproduce the experimental observations and reveal a p-wave, finite-momentum, time-reversal-symmetry-broken superconducting state, encouraging further investigation into exotic phases in graphene multilayers.

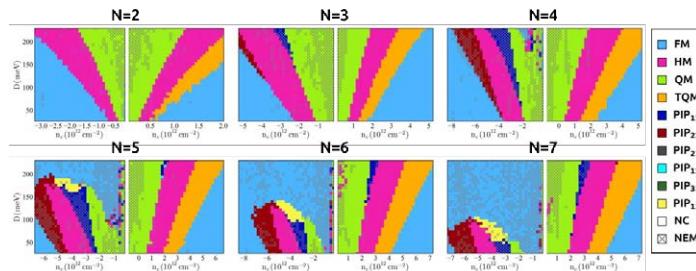


Figure 1: Hartree-Fock phase diagrams for rhombohedral multilayer graphene with different number of layers N.

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# Conductance oscillations in helicene-based junctions

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Helicenes have garnered significant attention over the past decade as molecular electronic devices due to exhibiting interesting phenomena related to their chirality, the conformational flexibility of their structures, and their optical, chemisorption, and self-assembly properties, among others [1-3].

With a few exceptions, theoretical studies of the electron transport through helicenes have been conducted mostly by tight-binding methods which, despite their inherent approximations, are known to work reasonably well for carbon-based materials and can provide valuable information.

In our study [4] we attempt to attain a more comprehensive overview of the electron-transport properties of helicenes by carrying out DFT simulations combined with Green's functions techniques for a wide range of [n]helicenes ( $n=7-30$  where  $n$  is the number of phenyl rings). We find that helicenes with an even number of phenyl rings tend to have lower conductances than their odd counterparts due to destructive quantum interference in through-bond transport. The odd-even effect on conductance is however modulated by the existence of through-space transport between layers of the helicene helix, leading to less pronounced conductance oscillations.

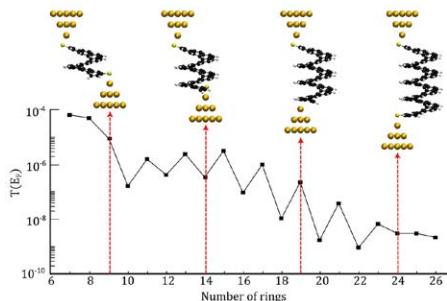


Figure 1. Transmission at the Fermi level as a function of helicene length obtained by tight-binding model.

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## Modulating assemblies of monolayers of 4-n-alkyloxybenzoic acid on Au(111)

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The design and synthesis of two-dimensional (2D) supramolecular assemblies with tailored functionalities represent key objectives in the field of molecular-based electronics, a research field that continues to advance rapidly [1-2]. Despite notable progresses, achieving uniformity and high order in 2D films remains a significant challenge [3-6]. In this work, we exploit the high affinity between carboxylic acid groups and the predictable packing behavior of nonpolar alkyl chains to obtain highly ordered, self-assembled monolayers of 4-n-alkyloxybenzoic acids forming micrometer-scale 2D supramolecular networks weakly interacting with the supporting substrate. Using scanning tunneling microscopy (STM) at both room and liquid-nitrogen temperatures, complemented by semi-empirical modeling, we reveal the formation of supramolecular assemblies of 4-heptoxybenzoic acid (4-HpBA) and 4-undecyloxybenzoic acid (4-Uba) on Au(111). [7] We find that both molecules, which possess an odd number of carbon atoms in their alkoxy chains (7 and 11, respectively), adopt identical supramolecular architecture. The structural properties and molecular packing density can be finely tuned by varying the alkoxy chain length, while preserving the parity of the carbon atom count. This precise control over molecular arrangement highlights the potential of these systems to act as tunable templates for hosting foreign atoms or molecules.

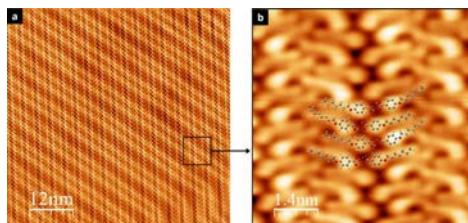


Figure: (a) STM image of 4-HpBA on Au(111) acquired at liquid nitrogen temperature ( $I=100\text{pA}$ ,  $V=-2\text{V}$ ); (b) Magnification view of the black rectangle in panel (a) ( $I=300\text{pA}$ ,  $V=2\text{V}$ ) with overlay of the supramolecular model obtained by semi-empirical calculations.

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# Ultrafast Hole Dynamics in Colloidal Quantum Dots revealed by Femtosecond X-ray Spectroscopy

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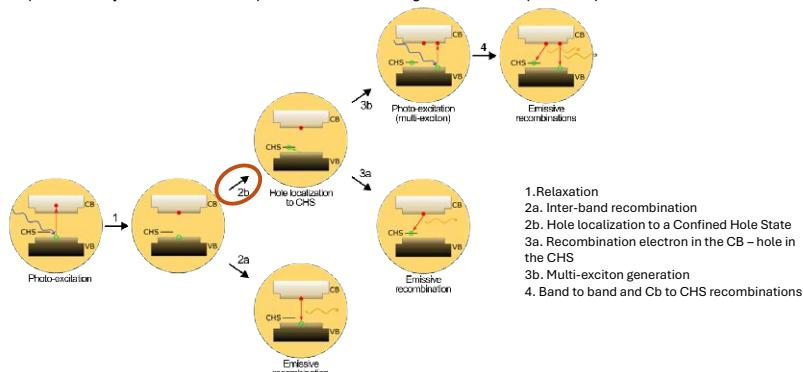
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Semiconductor CuInS<sub>2</sub> (CIS) quantum dots (QDs) exhibit low toxicity, excellent charge-transport properties, and remarkable photoluminescence features. These attributes make CIS QDs highly promising for a wide range of optoelectronic applications, such as highly efficient solar cells, luminescent solar concentrators and deep-tissue bioimaging<sup>1</sup>. To develop our fundamental understanding of nanoscale photophysics and to optimize the design of devices, several mechanisms of recombination in CIS QDs have been proposed, modelling the population dynamics of correlated electron-hole pairs (bound excitons). While most suggest that radiative recombination results from the interaction between an electron in the conduction band and a hole in the so-called confined hole state (CHS)<sup>2-3</sup>, no research has provided direct experimental evidence for the existence of this intra-gap state. The existence of such a state, arising from a defect of Cu<sup>+</sup> that can get oxidized to Cu<sup>2+</sup> by the hole, would explain the large Stokes shift and broad photoluminescence exhibited by the CIS QDs and has been theoretically predicted and postulated for a long time. We aim to understand and observe the formation process of the CHS and the localization of a hole in the CHS. We approached these questions through a combination of ultrafast optical and X-ray laser (XFEL) pump-probe techniques on Zn-doped core-shell CIS QDs of different composition. The element and oxidation state specificity of X-ray spectroscopies, both X-ray absorption (XAS) and X-ray emission (XES) spectroscopy, will serve as a direct probe to track recombination and localization dynamics of photogenerated holes, while optical probes will follow the electron dynamics. We probed the oxidation state of Cu fs-resolved K-edge XAS at two different light sources; PAL-XFEL in South Korea and LCLS in the USA, while we used non-resonant XES at the European XFEL. This extended study allowed us to gain insights and correlate the observed charge carrier dynamics, influenced by the laser fluence, with the underlying CIS QD structures, the degree of their surface passivation and the different Zn doping levels. This is then complemented by our time-resolved optical studies monitoring transient absorption and photoluminescence.



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# Gold Nanoparticles Functionalized with Immune-Modulatory microRNAs to Reactivate Antitumor Immunity in Melanoma

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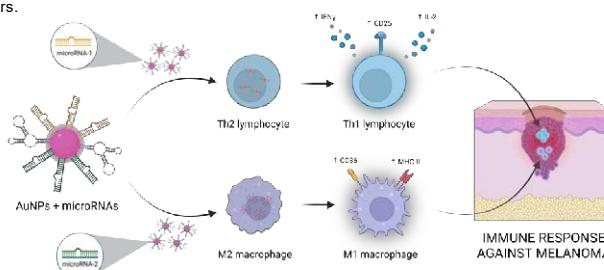
Melanoma is one of the most aggressive cancers, with poor survival in advanced stages due to its strong metastatic capacity and resistance to current therapies. Although immunotherapies have transformed treatment, only a minority of patients achieve durable responses, and toxicities remain a major limitation.

Nanoparticles capable of delivering immunomodulatory nucleic acids offer a promising way to overcome tumor-induced immunosuppression while reducing systemic side effects. Building on evidence that NK cell-derived extracellular vesicles carry microRNAs that enhance Th1/M1 responses and promote cytotoxic immunity, we developed gold nanoparticles (AuNPs) functionalized with immune-stimulatory microRNAs to mimic this natural signaling and enhance antitumor activity. These nanoparticles combine stability, biocompatibility, and nucleic acid protection, creating a versatile platform for miRNA-based immune modulation.

In this work, results show that the nanoparticles are stable, uniformly spherical, and efficiently internalized by both melanoma and immune cells without cytotoxicity. Among the candidates, the candidate AuNP-miR-1 triggered key immune signaling pathways and promoted Th1 polarization *in vitro*, while *in vivo* studies demonstrated that AuNP-miR-1 significantly reduced tumor growth in melanoma models, particularly when combined with PD-L1 blockade, where synergistic effects were observed. Immune profiling revealed increased cytotoxic T cells, Th1 cells, and NK cell infiltration, confirming systemic immune activation.

Overall, these results support that miRNA-functionalized AuNPs effectively reactivate antitumor immunity and provide a promising nanomedicine approach for complementing immunotherapy in melanoma and other treatment-resistant tumors.

FIGURE



## Notes and References

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# Single-molecule manipulation of genome integrity guardians

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DNA helicases of the Pif1 family are essential for maintenance of nuclear and mitochondrial genomes, acting as a guardian of its integrity. In coordination with other protein partners, Pif1 helicases work as molecular motors that unwind duplex nucleic acids and remodel nucleic acid-protein complexes driven by the energy from ATP hydrolysis. How these motor proteins open the DNA, how they couple chemical (ATP binding and hydrolysis) and mechanical (DNA unwinding) reactions, and how their behavior is modulated by protein-partners, such as single-stranded DNA binding (SSB) proteins, are questions under intense debate. To address these questions, we have developed an optical tweezers assay to follow in real-time and manipulate mechanically the DNA unwinding activity of individual Pfh1 helicase molecules. Here, we describe the effect of fork stability and ATP concentration on the real-time DNA unwinding kinetics of the Pfh1 helicase to unravel the mechano-chemical processes (energy conversion to work) that govern its operation. In addition, we show how binding of spRim1 SSB proteins to DNA modulates the real-time kinetics of the helicase.

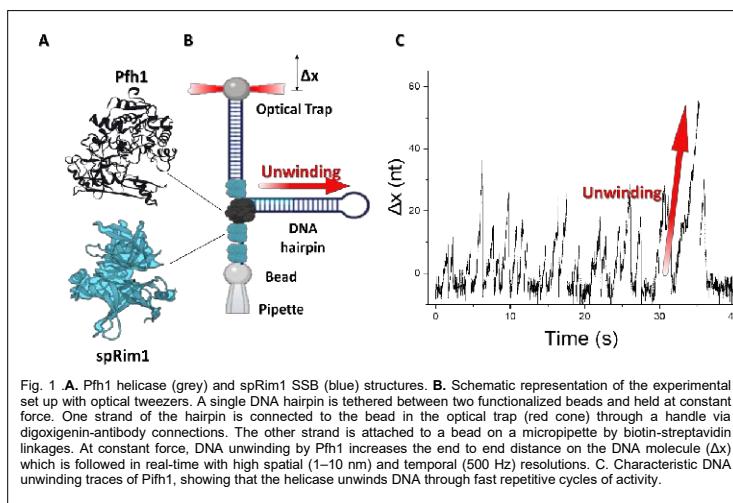


Fig. 1 A. Pfh1 helicase (grey) and spRim1 SSB (blue) structures. B. Schematic representation of the experimental set up with optical tweezers. A single DNA hairpin is tethered between two functionalized beads and held at constant force. One strand of the hairpin is connected to the bead in the optical trap (red cone) through a handle via digoxigenin-antibody connections. The other strand is attached to a bead on a micropipette by biotin-streptavidin linkages. At constant force, DNA unwinding by Pfh1 increases the end to end distance on the DNA molecule ( $\Delta x$ ) which is followed in real-time with high spatial (1–10 nm) and temporal (500 Hz) resolutions. C. Characteristic DNA unwinding traces of Pfh1, showing that the helicase unwinds DNA through fast repetitive cycles of activity.

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Temperature impact on the real-time dynamics of the human mitochondrial DNA polymerase
- 20 Dean Milanović *IMDEA Nanociencia*  
Exploring Supramolecular Diastereomers in Mechanically Interlocked Carbon Nanotubes

- |   |   |
|---|---|
| <p>21 Miguel Varea Martín <i>IMDEA Nanociencia</i><br/> <b>Spin-dependent Electron Scattering at Step Edges in Bi(111)</b></p> <p>22 Alejandro Martín Merinero <i>IMDEA Nanociencia</i><br/> <b>Fabrication &amp; photophysical characterization of deep blue-green organic microspheres</b></p> <p>23 Teresa Moreno Núñez <i>Universidad Complutense de Madrid</i><br/> <b>Antibody-controlled Janus nanomachine for targeted Drug Delivery</b></p> <p>24 Juan Manuel Hernández Gómez <i>Universidad Autónoma de Madrid</i><br/> <b>Electrochemical Detection of Chronic Obstructive Pulmonary Disease Biomarkers in Breath Samples Using a COF-Based Sensor</b></p> <p>25 Brishti Bagchi <i>IMDEA Nanociencia</i><br/> <b>Real-time kinetics of mitochondrial DNA replication reveal chaperone-mediated control by TID1–Mortalin</b></p> <p>26 Ignacio Ramos Aranda <i>IMDEA Nanociencia</i><br/> <b>High-loading polyglycerol-SWNT composites achieved via mechanical interlocking</b></p> <p>27 Alberto Martínez Bajo <i>IMDEA Nanociencia</i><br/> <b>On-Surface Synthesis of Porphyrinoid-Based Derivatives Comprising Exotic Macrocycles.</b></p> <p>28 Teresa Espinosa González <i>IMDEA Nanociencia</i><br/> <b>FRET-Based Approach to Study the Spatial Organization and Conformational Flexibility of Self-Assembling Proteins for 2D Nanobiomaterials</b></p> <p>29 Alba García <i>IMDEA Nanociencia</i><br/> <b>Driving multi-step regioselectivity in on-surface polymer synthesis by molecular coverage</b></p> <p>30 Gouri sahoo <i>IMDEA Nanociencia</i><br/> <b>On-Surface Self-Metalation of Porphyrins on 2D Ferromagnetic FeCl<sub>x</sub>/Au(111) Probed by STM</b></p> | <p>31 Marta Toldos <i>Universidad Autónoma de Madrid</i><br/> <b>Sensitive determination of p-cresol in human urine samples based on electrochemical tyrosinase biosensor for early Autism Spectrum Disorder (ASD) diagnosis</b></p> <p>32 Luis A Cobas <i>IMDEA Nanociencia</i><br/> <b>Single-Molecule Conductance of Pyrazine-Based OPEs</b></p> <p>33 Marina Castrillo Fernández <i>IMDEA Nanociencia</i><br/> <b>Development of flexible interfaces for neural electric stimulation based on nanostructured electrodes.</b></p> <p>34 Raquel Calvo Núñez <i>IMDEA Nanociencia</i><br/> <b>Nanofabrication of flexible Nanostructured Electrodes for Minimally Invasive Interfaces</b></p> <p>35 Adhil Kabeer <i>IMDEA Nanociencia</i><br/> <b>Modulating Delayed Emission Using Protein-Environment</b></p> <p>36 Gabriel Barrero Rodríguez <i>Universidad Complutense de Madrid</i><br/> <b>Engineering mesoporous bioactive glass nanocarriers for active biomolecules delivery in bone tissue regeneration</b></p> <p>37 Christiensen Rocha Aperador <i>IMDEA Nanociencia</i><br/> <b>Nonlinear THz Mobility in Doped Silicon</b></p> <p>38 Marina Luna Martínez <i>Universidad Complutense de Madrid</i><br/> <b>Proteomics Based Strategies to Optimize Therapeutic Nanoparticles Against Pathogens</b></p> <p>39 Cristina Sánchez Carrizo <i>IMDEA Nanociencia</i><br/> <b>Single Point -Photodynamic therapy: From making the tumor structure more permeable to inducing tumor cell death from within</b></p> <p>40 Laura Moreno Rodríguez <i>IMDEA Nanociencia</i><br/> <b>Enriching the structural design of anticancer Ru(II) and Os(II) half-sandwich complexes</b></p> |
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- .....
- 41 **Sebastián Mesa Pestegui** *IMDEA Nanociencia*  
**Bimolecular processes in bidimensional NiPS3**
- 42 **Francesco Petrone** *Università della Calabria (UniCal)*  
**Chain-length parity dictating molecular packing: odd–even effects of 4-n-alkyloxybenzoic acids on Au(111)**
- 43 **Jorge Gómez Olivares** *IMDEA Nanociencia/UCM*  
**Tailored design of new chalcogen-based spiro hole-transporting materials for perovskite solar cells**
- 44 **Paula Carreño Flores** *Universidad Complutense de Madrid*  
**Luminescent materials for hyperfluorescent OLED devices**
- 45 **Víctor Pastor Marcos** *Universidad Complutense de Madrid*  
**Harnessing Antiaromaticity in Molecular Nanographenes: Synthesis, Stability, and Electronic Modulation**
- 46 **Julieta Velasco Martínez-Pardo** *Universidad Autónoma de Madrid*  
**Magnetic Nanoparticles as Dual Nanoheaters and Nanothermometers: From Co\_Fe\_O to Synomag**
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**Hybrid iron oxide-metal nanoparticles against cancer**
- 48 **Vu Phong Dinh** *IMDEA Nanociencia*  
**Multifunctionalized gold nanoparticles for Duchenne muscular dystrophy treatment**
- 49 **Denise Maria Cuscela** *IMDEA Nanociencia*  
**Hybrid aptamer-magnetic nanoparticle tools for cancer therapy and diagnosis**
- 50 **Alejandro Venegas Gómez** *IMDEA Nanociencia*  
**Novel Methodologies for Monitoring Thermal Conformational Changes of Proteins Conjugated onto Magnetic Nanoparticles**
- 51 **Gonzalo Nicanor Molina** *IMDEA Nanociencia*  
**First-principles calculations of magnetic defects in rare-earth-doped Bi<sub>2</sub>Te<sub>3</sub>**
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**Machine-Learning Optimization of Antisense Oligonucleotides Targeting lncRNAs: from Rational Design to Delivery**
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# ELECTRICAL CHARACTERIZATION OF A LARGE-AREA SINGLE-LAYER OF Cu<sub>3</sub>BHT 2D CONJUGATED COORDINATION POLYMER

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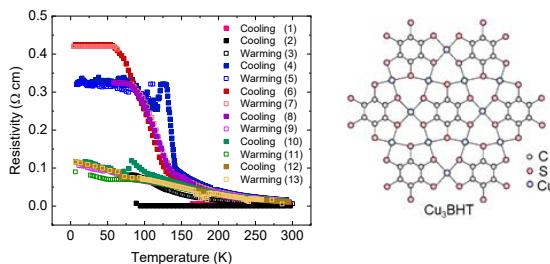
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Two-dimensional conjugated metal-organic frameworks (2D c-MOFs) are formed by the coordination of metal centers and planar organic conjugated building blocks. The modular nature of 2D c-MOFs make them highly advantageous for realizing materials with extensive tunability of their electrical and optical properties. In this contribution, I will discuss the synthesis and electrical characterization of a large-area, single-layer Cu<sub>3</sub>BHT 2D MOF. The Cu<sub>3</sub>BHT layer was synthesized at the water surface using the Langmuir-Blodgett technique and subsequently transferred onto SiO<sub>2</sub>/Si substrates with pre-patterned electrical contacts. Electrical measurements displayed ohmic behavior across areas as large as ~1 cm<sup>2</sup>. Cooling and heating cycles revealed hysteresis in the electrical response, indicating the formation of different current pathways as the samples underwent structural and chemical changes during the temperature sweeps. This hysteresis diminished after several cycles, with the conductivity stabilizing into an exponential temperature dependence, suggesting a tunnelling process governed the conduction mechanism in these polycrystalline single-layer Cu<sub>3</sub>BHT samples<sup>[1]</sup>.



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# Low-cost synthesis of hole transport materials for Improved Perovskite solar cells

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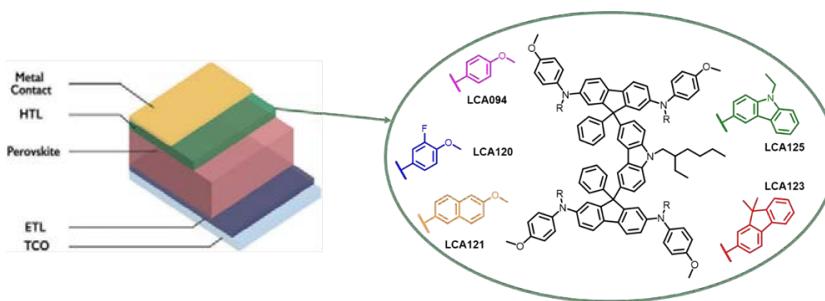
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Perovskite solar cells (PSCs) have attracted the attention of the scientific community since the first report of Miyasaka in 2009. Exhaustive efforts have been made to improve power conversion efficiencies, which nowadays have reached impressive values of 27,0%.<sup>1</sup> Nevertheless, stability is still the main challenge to solve, hindering the upscaling the PSCs into the photovoltaic market. One of the strategies followed to solve this lack of stability is devoted to the use of more stable and efficient charge transporting layers, able to transport the desired charges meanwhile protecting the perovskite layer.

In this work, we present a new family of organic hole transport material (HTMs). The role of these materials is to permit the movement of holes from the active layer (perovskite) directly to the metal electrode. At the same time, they prevent the transmission of electrons to that direction, avoiding the charge recombination and improving the energetic conversion yield.<sup>2</sup>

Based on our previous results,<sup>3</sup> the present work reports a new family of organic HTMs (Fig. 1) which incorporate a carbazole unit as central scaffold endowed with tailored diarylamines in the periphery. The chemical design is based on a simple synthetic route which permits us to obtain the different HTMs in a low-cost synthetic approach from commercially available starting materials, allowing an easy scale up for further applications. The new HTMs present adequate optoelectronic properties regarding their absorption in the UV-vis region, good alignment between their HOMO levels and the valence band edge of the perovskite, as well as an excellent thermal stability. The new HTMs have been implemented in planar perovskite solar cells for replacing the benchmark spiro-OMeTAD and the successful obtained results will be discussed in this presentation.



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# Unexpected $4 \times 4$ charge density wave in 1H-NbTe<sub>2</sub> monolayer

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NbTe<sub>2</sub> belongs to the family of tellurium-based transition metal dichalcogenides (TMDs), a class of materials well known for their diverse electronic and structural properties. They are nowadays the focus of intensive study because their quasi-two-dimensional nature enhances electron–electron and electron–phonon interactions, fostering the emergence of charge density waves (CDWs) and superconductivity. Unlike its sulfur and sulfide counterparts that stabilize in the hexagonal polymorph, bulk NbTe<sub>2</sub> crystallizes in the trigonal phase, which makes its electronic behavior particularly intriguing. Yet, when approaching the two-dimensional limit, the monolayer of NbTe<sub>2</sub> has remained the most elusive among the niobium compounds, leaving its structural stability and possible CDW phases completely unexplored.

In this work, we report the first successful growth of 2D islands of the metastable 1H-NbTe<sub>2</sub> phase via molecular beam epitaxy on epitaxial graphene on Ir(111). This phase is identified based on its hexagonal crystal structure, distinctive spectroscopic features, and the presence of mirror twin boundaries (MTBs). Scanning tunneling spectroscopy (STS) measurements show excellent agreement with the electronic band structure obtained from angle-resolved photoemission spectroscopy (ARPES) and density functional theory (DFT) calculations, confirming the phase's stability and metallic nature. Moreover, low-temperature STS measurements indicate the emergence of a  $4 \times 4$  CDW modulation, which is attributed to a phonon instability. These results pave the way for investigating the intricate phase behavior and electronic properties of NbTe<sub>2</sub> in the two-dimensional limit.

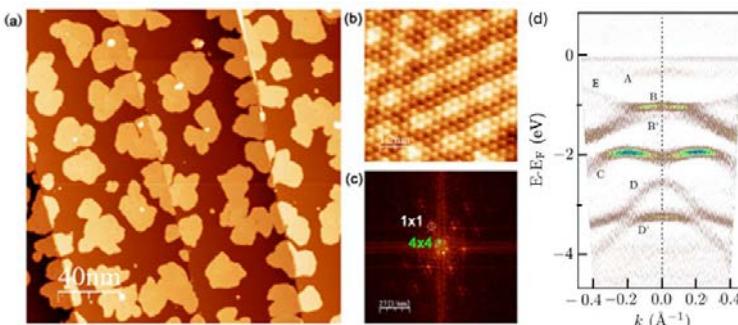


FIGURE - (a) Large STM image where 55% of the sample is covered with NbTe<sub>2</sub> islands ( $V_b=1\text{V}$ ,  $I_t=100\text{ pA}$ , 4.6 K). (b) High resolution image and its corresponding fast Fourier transformation (FFT) (c) of the most predominant phase of NbTe<sub>2</sub> were a  $4 \times 4$  CDW is observed. ( $V_b=-0.1\text{V}$ ,  $I_t=300\text{ pA}$ , 4.6 K). Measurements at  $T = 4.2\text{ K}$ . (d) Band dispersion around  $\Gamma$  measured by ARPES at room temperature and  $h\nu = 21.2\text{ eV}$ .

# DNA Nanostructure-Based Electrochemical Biosensing platforms for Interferon-Gamma Detection in Autism Spectrum Disorder patients

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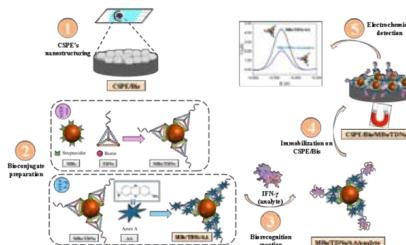
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Autism spectrum disorder (ASD) is a neurodevelopment condition characterized by difficulties in communication, social interaction, and repetitive behaviors. Early diagnosis is essential to improve patients' quality of life. However, current diagnostic methods are mainly observational and complex. Recent studies have reported immune system dysregulation in individuals with ASD, including elevated levels of the cytokine interferon-gamma (IFN- $\gamma$ ), suggesting its potential as a diagnostic biomarker. Nevertheless, conventional cytokine detection methods face limitations related to cost and time efficiency.

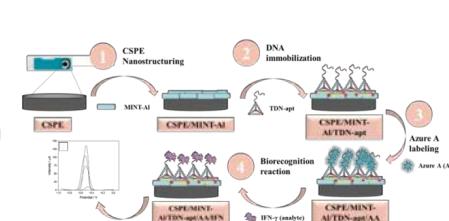
In this context, the present work focuses on the development of two electrochemical biosensing platforms for the detection of IFN- $\gamma$  (Scheme). The first strategy is based on a bi conjugate consisting of streptavidin-coated magnetic beads (MBs) functionalized with tetrahedral DNA nanostructures (TDNs). These TDNs incorporate a specific aptamer sequence for IFN- $\gamma$  recognition and biotin molecules at the basal vertices to enable immobilization onto the MBs. TDNs are also labeled with Azure A (AA) as an electrochemical indicator and finally the bi conjugate is immobilized onto a carbon screen-printed electrode (CSPE) modified with bismuthene nanosheets (Bis). The second strategy is also based on the use of TDNs which are immobilized over a CSPE modified with Mechanically Interlocked Carbon Nanotubes modified with alkenes (MINT-Al) through the thiol-ene click chemistry reaction. TDNs are again labeled with AA to be used as an electrochemical indicator.

In both cases, detection is carried out using differential pulse voltammetry (DPV, showing a decrease in the electrochemical signal after the specific interaction between aptamer-analyte. The first biosensing platform shows a detection limit of  $1.12 \text{ pg}\cdot\text{mL}^{-1}$  and a linear range from  $3.73 \text{ pg}\cdot\text{mL}^{-1}$  to  $1.00 \text{ ng}\cdot\text{mL}^{-1}$ ; whilst the second platform shows a detection limit of  $0.620 \text{ fg}\cdot\text{mL}^{-1}$  and a linear range from  $1.84 \text{ fg}\cdot\text{mL}^{-1}$  to  $1.00 \text{ pg}\cdot\text{mL}^{-1}$ .

## STRATEGY 1



## STRATEGY 2



# LNP-Mediated Delivery of CRISPR-Cas13b Ribonucleoproteins for Synergistic Oncological Therapy in Pancreatic Adenocarcinoma

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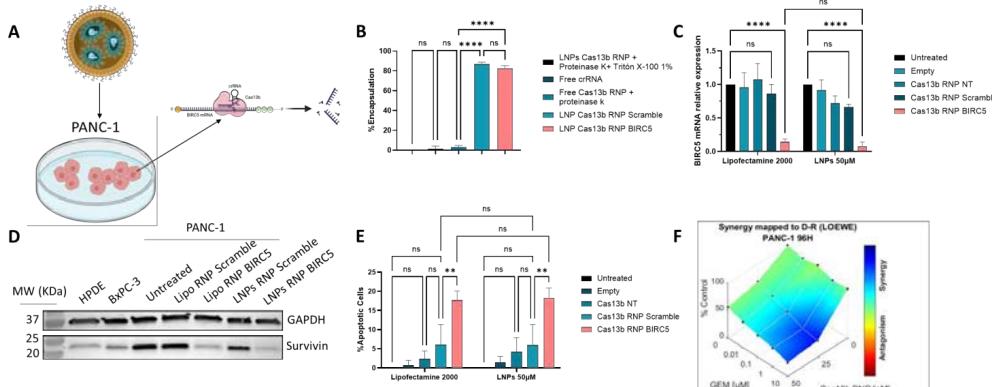
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The clustered regularly interspaced short palindromic repeats (CRISPR)-Cas system has produced a paradigm shift in gene editing, offering substantial prospects for therapeutic interventions. This study focuses on the application of an optimized lipid nanoparticle (LNP) formulation to facilitate the efficient *in vivo* delivery of CRISPR-Cas13b ribonucleoproteins (RNPs). Given the RNA-targeting capability of Cas13b, we explore its therapeutic utility for the transient knockdown of specific messenger RNAs (mRNAs) without inducing permanent genomic alterations.

We targeted Survivin (BIRC5), an inhibitor of apoptosis frequently overexpressed in pancreatic adenocarcinoma and implicated in chemoresistance<sup>1</sup>. We optimized an LNP formulation and encapsulation protocol to efficiently deliver the Cas13b RNP while preserving protein stability. We aimed to reduce Survivin expression, sensitize pancreatic cancer cells to gemcitabine<sup>2</sup>, and analyze its potential synergistic effect. Cas13b effectively reduced Survivin expression, leading to a direct cytotoxic effect in various pancreatic cancer cell lines. Furthermore, we established a synergistic and significant effect when combining gemcitabine with the LNP-Cas13b RNP treatments. Importantly, this specific knockdown was achieved without detectable trans-activity inside eukaryotic cells, suggesting a favorable safety profile for this therapeutic approach.

In conclusion, this research underscores the adaptability of LNP-mediated CRISPR RNP delivery for targeted gene knockdown in oncological therapies. The successful implementation of these strategies carries considerable translational potential for addressing currently unmet clinical imperatives in the treatment of pancreatic adenocarcinoma.



**Figure 1.** (A) Scheme of the treatment of PANC-1 (gemcitabine-resistant cell line) with LNPs encapsulating Cas13b RNP targeting BIRC5 mRNA. (B) Percentage of encapsulated CRISPR RNA (crRNA) within the LNPs is presented determined by Qubit RNA High Sensitivity assay (n=3). BIRC5 knockdown evaluated by RT-qPCR (C) and Western Blot (D) using RLP19 and GAPDH as housekeeping, respectively (n=3). Effects of this knockdown regarding cytotoxicity and cell viability was assessed by an Annexin V assay (E) and the synergistic effect evaluated by Alamar Blue assay in combination with different concentrations of Gemcitabine (GEM) (n=3) (G).

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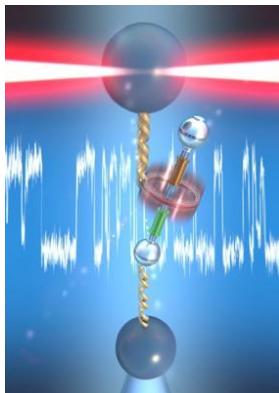
# Uncovering the dynamics of synthetic molecular motors at the single-molecule level

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Taking inspiration from the highly efficient molecular machinery found in nature, scientists have long sought to synthesize nanoscale machines and motors capable of performing work at the molecular level. Thanks to the proficiency of synthetic chemists, a variety of motors and machines have been developed that are capable of rotation and translation with defined directionality. However, many questions remain unanswered, as conventional bulk techniques yield ensemble-averaged information that obscures individual molecular behaviors. Our group has demonstrated that single molecule techniques, specifically optical tweezers, can directly probe the operation of synthetic molecular machines, revealing mechanical<sup>1</sup>, thermodynamic<sup>2</sup>, and kinetic<sup>3</sup> details inaccessible by bulk methods. Building on these advances, this project aims to investigate how environmental factors such as temperature and chemical environment affect the dynamics of molecular motors. Through this approach, we seek to understand the physical and chemical principles governing molecular motor function, ultimately guiding the design of more efficient molecular machines for applications in nanorobotics and materials science.

## FIGURE



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# 2D Lanthanide MOFs Composites

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Metal-organic frameworks (MOFs) are crystalline materials with bi- and tri-dimensional frameworks formed by the coordination of metal centres to organic molecules (ligands), which act as bridges for those ions. Such bonding makes MOFs exhibit high porosity and open channels, which are capable of taking up and storing gases and host molecules. Moreover, thanks to a rational choice (in both, metal and organic ligand), MOFs can be designed for specific functionalities[1],[2]. In this case, the correct selection of the ligand with a suitable functional group allows to obtain MOFs with a intermolecular interaction preference for certain molecules and their consequent detection. Furthermore, the selection of lanthanide ions allows the use of their widely studied photoemission intensity, spectral profiles and lifetimes[3],[4].

In this work, it has been demonstrated that is possible to correlate directly the photoluminescence (PL) intensity of the single crystal Ln-MOF with the absorption of host molecules. This leads, in some cases, to the perturbation of their spectra, a phenomenon that can be exploited for the detection of certain pollutants, making these materials excellent candidates for chemosensing. The response of two different Ln-MOFs containing Tb or Eu to two pollutants ( $\text{NO}_2$  and  $\text{SO}_2$ ) has been studied, resulting in two distinct detection patterns. Additionally, this materials were embedded in polydimethylsiloxane (PDMS) in order to obtain manageable composites with similar properties as the bulk. In this way, exposure to 50 ppm of  $\text{NO}_2$  or  $\text{SO}_2$  triggers a decrease in Tb-MOF luminescence while keeping the Eu-MOF luminescence unchanged. These markedly different luminescence responses are controlled by the specific gas, pollutant concentration and lanthanide, enabling the development of sensors for various pollutants.

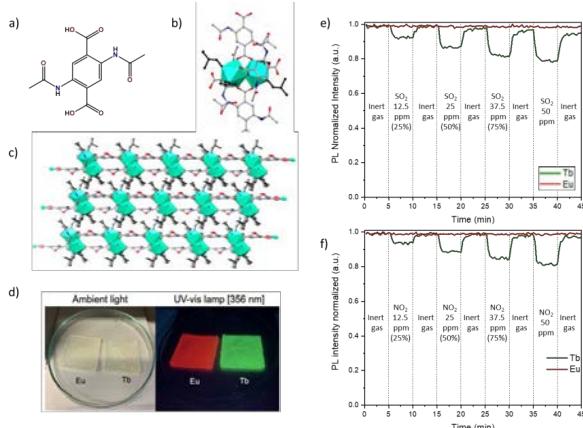


Figure 1.a) 2,5-bisacetylamido-terephthalic acid (AATA), b) Ln-MOF single crystal X-Ray diffraction binuclear cluster, c) Ln-MOF single crystal X-Ray diffraction structure, d) Ln-MOF@PDMS under ambient and UV-Vis light, e, f) Changes in the PL intensity at 543 nm (green) and 614 nm (red) upon three 50 ppm  $\text{NO}_2$  and  $\text{SO}_2$  exposure cycles and dilution exposure to  $\text{NO}_2$  and  $\text{SO}_2$  content.

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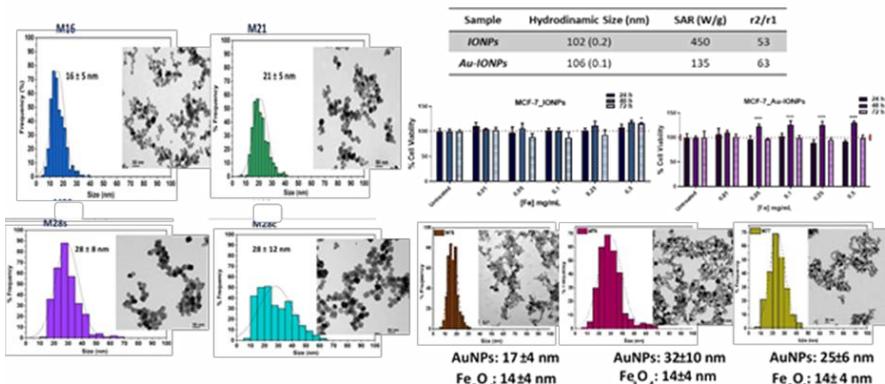
# Iron oxide nanoparticles and gold-iron oxide nanoaggregates for biomedical applications: evaluation in MCF-7 and PANC-1 cell cultures.

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Superparamagnetic iron oxide nanoparticles (IONPs) have been widely studied for biomedical applications as contrast agents in magnetic resonance imaging (MRI) and for magnetic hyperthermia (with application of alternating magnetic fields). Their size, shape and composition, are critical for these applications. It is also possible to combine them with other metals and obtain nanosystems with additive properties [1]. In this work, we present an environmentally friendly synthesis of IONPs and Au-IONPs with tunable and controlled shapes, compositions and sizes that can be useful for magnetic hyperthermia therapy, MRI diagnosis, in addition to having plasmonic properties. Characterization of the size, shape, composition, relaxation times for MRI and magnetic heating will be presented (Figure 1), as well as preliminary attempts to reduce the aggregation and improve cell internalization. The cytotoxicity has been studied in two different cells lines: MCF-7 (breast cancer) and PANC-1 (pancreatic cancer).



**Figure 1.** Selected TEM micrographs and size histograms of the nanoparticles and nanoaggregates. Table: hydrodynamic sizes, SAR values (29.9 mT, 202kHz) at  $[\text{Fe}] 1 \text{mg} \cdot \text{mL}^{-1}$  and r2/r1 relaxivity ratio. Right middle: cell viability at different iron concentration in MCF-7 (breast cancer line).

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# Spin-crossover 3D coordination polymers as tools for improving thermal efficiency

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In Europe, building thermalization accounts for approximately 40% of total energy usage, and 36 % of CO<sub>2</sub> emissions<sup>1</sup> with similar values observed globally. Despite increasing adoption of renewable energy sources, it is estimated that 75% of the world's primary energy is still derived from non-renewable and polluting sources, namely oil, coal and natural gas. This underscores the urgent need to enhance thermal regulation efficiency to mitigate climate change in the coming years.

In the context of materials science, spin-crossover (SCO) compounds are inorganic coordination materials that can reversibly switch between a Low Spin state and High Spin state by applying certain external stimuli such as a change in temperature, pressure or an irradiation with light. Recently, some of us demonstrated the potential of a 1D SCO coordination polymer (CP) ( $[\text{Fe}(\text{NH}_2\text{trz})_3](\text{OTs})_2$ ) integrated in a polymeric matrix (PMMA) to modify the albedo of surfaces and ultimately modulate interior temperature of buildings.<sup>2</sup>

In the present contribution, we extend on our previous work to 3D SCO CP with formula  $(\text{Fe}(\text{L})(\text{M}(\text{CN})_4))$  ( $\text{L}$  = bis monodentated nitrogen donor ligand,  $\text{M}$  = Ni, Pd, Pt). We will present our most recent developments regarding preparation, characterization and use of SCO materials to be used as thermo regulating materials to passively enhance the thermal efficiency profile of buildings in a passive and convenient manner.

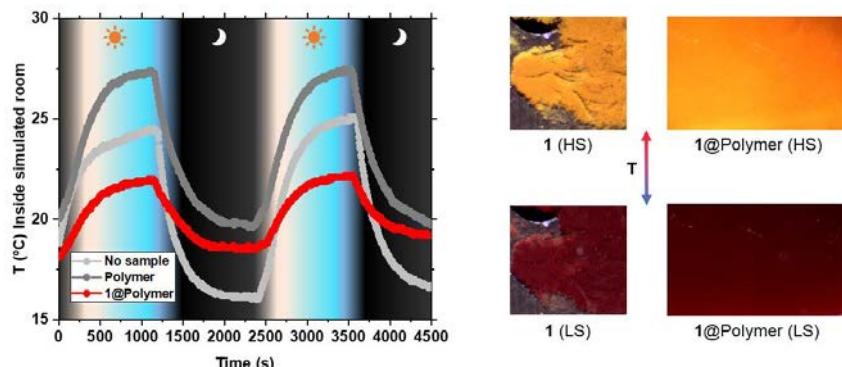


Figure 1.- Simulated day/night cycles and composite film SCO behaviour.

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# Integration of p-type-doped carbon nanostructures as additives for boosting spiro-OMeTAD performance in perovskite solar cells

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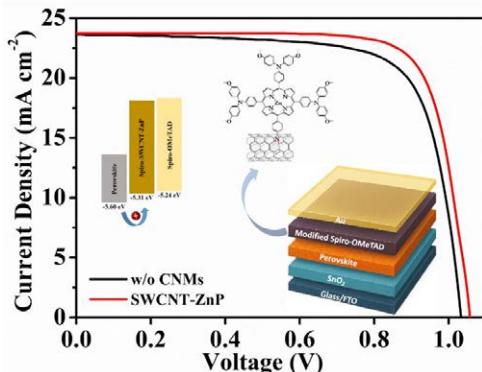
The rising demand for clean energy has led to an increased interest in sustainable energy sources, particularly photovoltaic (PV) technology. Significant efforts have been made to improve PV technologies that directly convert sunlight into electricity in an environmentally friendly way. Among various light-harvesting materials, perovskite solar cells (PSCs) have gained substantial recognition worldwide for their ease of fabrication and low production costs.<sup>1</sup> PSCs typically have a cubic structure, represented by the formula ABX<sub>3</sub>, and are built with a sandwich-like design that includes a light-absorbing hybrid halide perovskite layer between a semiconducting oxide (ETL) and an organic hole-transporting material (HTM). Among these HTMs, Spiro-OMeTAD has been extensively studied for its role in enhancing PV performance.<sup>2</sup>

In this study, we synthesized new functionalized carbon nanomaterials (CNMs) named as SWCNT-TPAO Me, SWCNT-ZnP, SWCNT-PdP, and CNH-TPAO Me, and integrated them into doped Spiro-OMeTAD. The chemical design include the incorporation of donor p-methoxytriphenylamines (TPAs) or porphyrin-substituted TPAs in combination with carbon nanotubes and carbon nanohorns. This integration improves, stability, charge extraction, optimizes the surface morphology and interface between Spiro-OMeTAD and the perovskite layer, and enhances energy level alignment with the perovskite material.<sup>3</sup>

PSCs fabricated using these functionalized CNMs achieved significant improvements in efficiency, short-circuit current density ( $J_{sc}$ ), fill factor (FF), and open-circuit voltage ( $V_{oc}$ ). The device incorporating SWCNT-ZnP achieved a power conversion efficiency (PCE) of 19.80%, while devices using SWCNT-TPAO Me, CNH-TPAO Me, SWCNT-PdP, and conventional Spiro-OMeTAD (without CNMs) reached PCEs of 18.95%, 17.91%, 17.11%, and 18.01%, respectively. This study demonstrates that the incorporation of functionalized CNMs into Spiro-OMeTAD can significantly enhance both the performance and stability of PSC devices, as it demonstrated with preliminary stability tests due to the enhanced hydrophobicity of the new HTM layer.

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# Designing model photosystem for tracking protein dynamics in chromophore's light harvesting properties

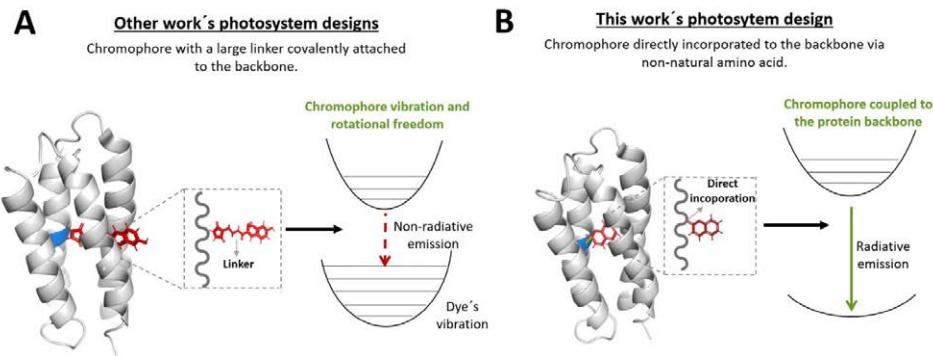
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Studies in natural photosystems suggest that a correlation between protein dynamics and chromophore's excited state relaxation is key for efficient light harvesting. However, showing the impact of these protein dynamics in chromophore's light-harvesting properties is challenging due to the huge complexity of the natural systems. Artificial photosystems have emerged as a solution to perform mechanistic studies by simplifying the effects that occur in natural light-harvesting processes. However, the chromophores used in most cases have linkers that attach them to the protein structure, giving flexibility and rotational freedom to the chromophore that obscures the role of protein dynamics in the photosystem.<sup>1</sup> In this work, I proposed a new approach to generate the artificial photosystem based on the incorporation of the chromophore as an unnatural amino acid (UAA). We hypothesize that the direct incorporation of the chromophores into the protein backbone will allow us to track protein dynamics in real-time. To show that, we designed two photosystem models one in which the chromophore is incorporated directly into the backbone as a UAA and the other where the chromophore is attached to the backbone via a linker (Figure 1). These designs will allow us to compare whether there are significant differences in the light-harvesting properties of the chromophore depending on whether a linker is present or not. This new approach will allow the development of mechanistic studies from a completely different angle, revealing how protein dynamics affect the light-harvesting properties of chromophores.



**Figure 1:** (a) Artificial photosystem model with an Alpha4 protein (grey) linked to coumarin-maleimide via click chemistry (red), implying weak coupling, less emission. (b) Alpha4 protein (grey) with coumarin bound as a non-natural amino acid (red), indicating strong coupling, more emission.

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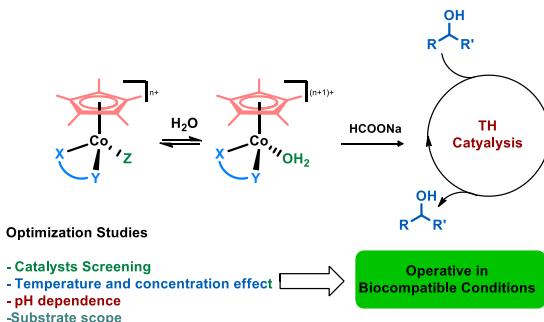
# Toward Intracellular Transfer Hydrogenation Catalysis Mediated by Half-Sandwich Cobalt(III) Complexes

Alfonso Annunziata,<sup>\*a</sup> Vanessa Rodríguez Fanjul<sup>a</sup> and Ana M. Pizarro<sup>a</sup>

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Intracellular transfer hydrogenation (TH) catalysis mediated by organometallic complexes of precious metals (Ru, Os, Rh, and Ir) has been affirmed as a powerful approach for the hydrogenation of substrates in biological systems, with broad potential applications in medicine, modulation of cell metabolism, and diagnostics.<sup>1</sup> Earth-abundant 3d metals are ubiquitous in nature and are involved in several enzymatic processes. Moreover, they are more available, cheaper, and more biocompatible than precious metals.<sup>2</sup> Biocompatibility is an important feature, considering that an intracellular catalyst should be non-toxic to human cells. However, the remarkable cytotoxicity of many precious metal complexes<sup>3</sup> can limit their use, while the higher biocompatibility of 3d metals is expected to enable broader applicability in living systems. Cobalt, an essential first-row transition metal present in numerous cofactors and redox-active enzymes, offers an appealing platform for expanding the scope of intracellular redox catalysts to 3d metals. In comparison with rhodium and iridium analogues, half-sandwich Co(III) complexes exhibit distinctive features: different thermodynamic and kinetic properties, higher electronegativity and harder Lewis acid character of the metal center, and a versatile redox profile encompassing oxidation states from 0 to +4 via one- and two-electron processes.<sup>4</sup> These characteristics make cobalt-based systems both an economical and biocompatible alternative to noble-metal counterparts, while also enabling access to unique redox pathways complementary to those achieved with heavier congeners.



Herein, we present the synthesis and characterization of a library of half-sandwich Co(III) complexes with the general formula  $[\text{CoCp}^*(\text{X}-\text{Y})\text{Z}]$ , incorporating diverse bidentate ligands ( $\text{X}-\text{Y} = \text{N}-\text{N}'$ ,  $\text{N}-\text{O}$ , or  $\text{N}-\text{C}$ ) and monodentate anions ( $\text{Z} = \text{Cl}^-$  or  $\text{I}^-$ ). Systematic variation of the ligand framework was employed to modulate the steric and electronic properties and to fine-tune the stability-reactivity balance in aqueous biological contexts. The complexes were evaluated for hydrolytic behavior and cytotoxicity across selected human cell lines to assess their biological compatibility. They were tested as TH catalysts using formic acid/formate as the hydrogen donor to convert carbonyl compounds to alcohols. Optimization studies involving catalyst screening, temperature and concentration effects, pH dependence, and substrate tolerance were performed, showing that some of the proposed catalysts work efficiently in aqueous solution under biocompatible conditions. These investigations lay the groundwork for translating Co-based redox catalysis into living cellular systems.

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# Linking Axonal Transport Defects to Extracellular Vesicle Signatures in ALS iPSC-Derived Motor Neurons

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the progressive loss of motor neurons, leading to muscle weakness and death within a short period of time. Currently, there are no effective treatments and reliable biomarkers are scarce, limiting both the monitoring of disease progression and the evaluation of potential therapies [1].

Motor neurons derived from induced pluripotent stem cells (iPSCs) represent a robust experimental model for studying ALS, as they allow the *in vitro* reproduction of disease-related features using patient-derived material. These models capture key aspects of ALS pathology, such as alterations in neuronal morphology and, in particular, in axonal transport — a process critical for neuronal communication and survival that is frequently impaired in ALS. In this context, extracellular vesicles (EVs) have emerged as mediators and potential indicators of these processes, as they participate in intercellular communication and can carry molecular signatures that reflect the functional state of motor neurons [2,3].

In this study, we used ALS patient-derived iPSC motor neurons, to characterize EVs and assess their potential as indicators of intracellular/axonal transport. Our preliminary results suggest that EVs secreted by motor neurons from ALS patients display differential characteristics that may correlate with alterations in axonal transport. These observations support the use of EVs as promising biomarkers for monitoring disease progression and treatment response.

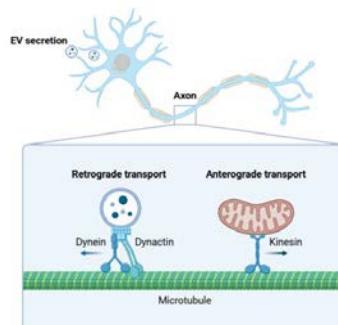


Figure 1. Schematic representation of axonal transport and extracellular vesicle (EV) secretion in motor neurons, highlighting anterograde (kinesin) and retrograde (dynein–dynactin) transport along microtubules.

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# Unraveling Metal-to-Ligand Charge Transfer Dynamics of Cu(I) and Fe(II) Complexes.

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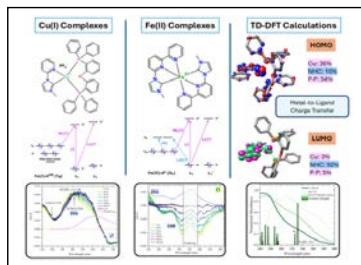
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Transition metal complexes play a central role in modern photophysics and photochemistry due to their ability to harvest light and mediate charge transfer processes<sup>1,2</sup>. However, many of the most efficient photoactive systems are based on scarce and expensive noble metals such as Ru, Ir, or Pt, which limits their large-scale application in photocatalysis, light-emitting devices, and solar energy conversion. In this context, first-row transition metals such as Cu and Fe have emerged as sustainable alternatives thanks to their earth abundance and tunable electronic properties<sup>3,4</sup>.

In this work, we investigate the ultrafast excited-state dynamics of Cu(I) and Fe(II) complexes bearing N-heterocyclic carbene (NHC) ligands. The Cu(I) systems are heteroleptic, containing bulky diphosphine co-ligands to stabilize the photoactive metal-to-ligand charge transfer (MLCT) state<sup>5</sup>, while the Fe(II) complexes are homoleptic, exclusively coordinated by NHC ligands to enhance ligand-field strength and suppress fast deactivation<sup>6</sup>.

Femtosecond transient absorption spectroscopy provides direct insight into the temporal evolution of the MLCT states, revealing their formation, nonradiative pathways, and decay on the tens of femtosecond up to millisecond timescales. Complementary time-dependent density functional theory (TD-DFT) calculations aid in interpreting the steady-state absorption spectra and assigning the nature of the excited states involved.

By combining experimental and theoretical approaches, this study elucidates the lifetimes of the involved excited states and the structural processes along the deactivation mechanism, thereby contributing to the rational design of efficient, earth-abundant photoactive coordination compounds for sustainable photochemical applications.



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# Immortalized human myoblasts for ALS research

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Traditionally, amyotrophic lateral sclerosis (ALS) has been viewed primarily as a neurodegenerative disease. However, it is now recognized as a multisystem disorder. Emerging evidence indicates that motor neuron (MN) degeneration may result from non-cell-autonomous mechanisms involving glial or muscle cells. Notably, skeletal muscle has been identified as a tissue with significant secretory activity that can exert toxic effects on MNs in the context of ALS. These findings support the “dying-back” hypothesis, which proposes that pathological alterations first occur distally—at the neuromuscular junction (NMJ) or within the skeletal muscle—and subsequently propagate toward the soma, preceding both clinical symptom onset and motor neuron death.<sup>1</sup>

The immortalization of human myoblasts is essential for advancing the study of muscular disorders due to the limited availability and accessibility of primary myoblast samples. Obtaining primary human myoblasts requires invasive muscle biopsies, which are often painful, carry medical risks, and can only yield small quantities of cells. Moreover, primary myoblasts have a restricted lifespan in culture, rapidly undergoing senescence and losing their proliferative and differentiation potential, which limits their usefulness for long-term experiments and reproducible studies. Using transduction with both telomerase-expressing and cyclin-dependent kinase 4 (CDK4)-expressing vectors, immortalized human muscle stem-cell lines can be acquired from patients with various neuromuscular disorders.<sup>2,3</sup>

In this study, myoblasts from both patients and ALS patients have been immortalized using lentiviral infection of both hTERT and CDK4. Further characterization of the cells has been carried out to determine if the differences between ALS and control myoblasts are preserved on the immortalized models.

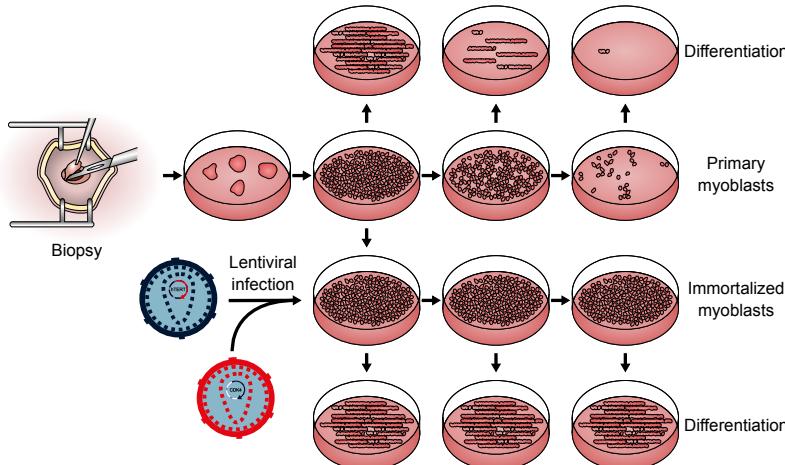


Figure 1. Schematic representation of myoblast immortalization from a skeletal muscle biopsy.

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# **Self-sustained oscillations in MoS<sub>2</sub> optomechanical resonators for VHF optical radio**

**Ruth Martínez-Temple<sup>a</sup>, Julia García-Pérez<sup>a</sup>,**

**Daniel Granados<sup>a</sup> and Ramón Bernardo-Gavito<sup>a</sup>**

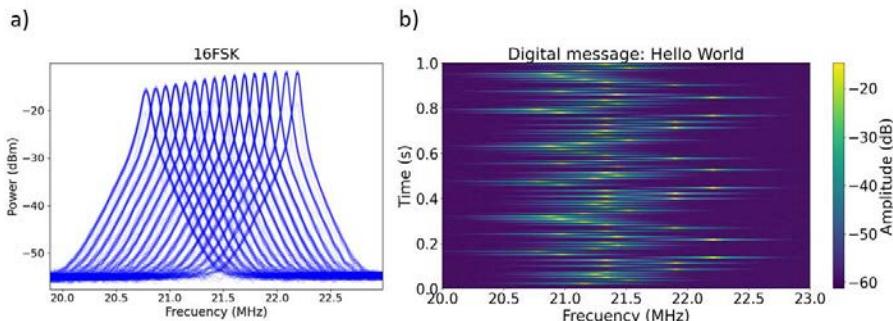
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Mechanical micro and nanoresonators can reach high resonance frequencies, which makes them attractive for the development of various applications, such as ultrafast sensors<sup>1</sup>. In recent years, introducing MoS<sub>2</sub> as an active oscillator in these kind of devices has been exploited due their outstanding properties such as large flexibility, ultralow weight and photoluminescence emission<sup>2</sup>.

In this work, we design and manufacture an optical cavity suspending a MoS<sub>2</sub> flake onto a circular well surrounded by electrical contacts, forming a microdrum resonator<sup>3</sup>. Since the MoS<sub>2</sub> is semitransparent, the system acts as a Fabry-Perot etalon. By applying a DC voltage, we can strain the membrane, changing the cavity length and, consequently, tuning the optical response. Additionally, the mechanical resonance frequency is also modified by strain and controlled via DC bias. This way, we can tune the cavity to the resonance condition of an incoming 488 nm CW laser. The radiation pressure exerted by the laser results in an optomechanical mode: the photons within the cavity transfer their momentum to the membrane upon impact, causing it to oscillate around its equilibrium position. In other words, we can induce self-sustained oscillations in the system by optical pumping.

Furthermore, we discover that there is a DC voltage range where the frequency of resonance of the OM mode linearly increases with the applied voltage. Exploiting this effect, we can send information through a frequency modulated message encoded into the laser beam. We send both analog and digital signals through the system and develop a simple protocol to decode the digital signal and obtain the original message. These results highlight the potential application of such devices in telecommunication systems, particularly in Radio over Fiber (RoF), underwater optical wireless communications or sensing.



**Figure 1:** a) Independent bit levels obtained and used for sending encoded digital messages using Frequency Shift Keying (FSK) protocol. Each curve corresponds to a bit level. We manage transmit a digital message using a 16-level modulation, which carries 4 bits of information per symbol

b) Frequencies for the digital message 'Hello World Hello World'. Each character corresponds to a specific frequency.

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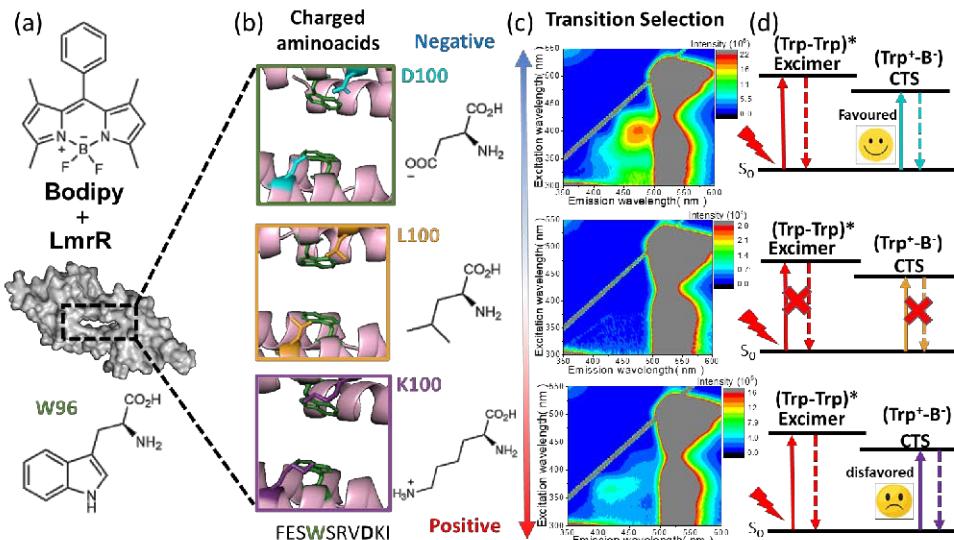
# Pocket Electrostatics Modulated Electronic-state Selection in Protein-Chromophore Biohybrids

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Attaching synthetic chromophores to the protein scaffold enables synergistic interactions, resulting in novel photonic responses that surpass the capabilities of current materials. A recent study demonstrated that the aromatic tryptophan (**W96**) residue of the lactococcal multidrug resistance regulator (**LmrR**) protein exhibits remarkable binding affinities and modulates the photophysics of Bodipy when embedded within the pocket [1] (Fig. 1a). The study showed that tryptophan plays a key role in modulating its properties. In this work, we aim to take a step further, demonstrating the impact of pocket electrostatics on interactions within the protein pocket and the excited-state dynamics of tryptophan and Bodipy after binding to it. For this purpose, we engineered the LmrR pocket including amino acids of different charges in its sequence (Fig. 1b). We performed spectroscopic measurements to study its photoresponse (Fig. 1c). Our results showed that the charge-transfer state (CTS) was stabilized in the negatively charged pocket **D100**. In contrast, the positively charged pocket **K100** exhibited favorable excimer decay pathways. On the other hand, a neutral-charged pocket **L100** has no impact on the photoresponse of bodipy. This demonstrated that the role of Bodipy is to select the excited-state transition modulated by the protein pocket charges (Fig. 1d). Our results can serve as a foundation for future design of *de novo* artificial photosystems.



**Fig.1:** (a) Structure of LmrR and Bodipy used in this study (b) from top to bottom close view render of the protein pocket for each LmrR mutant, (c) 2D excitation-emission maps of LmrR-Bodipy complexes and (d) Jablonski diagrams for the selected transition in each system.

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# Opto-electro-mechanical resonances in MoS<sub>2</sub> micro-drum cavities

Julia García-Pérez,<sup>\*a</sup> Daniel Granados<sup>a</sup> and Ramón Bernardo-Gavito<sup>a</sup>

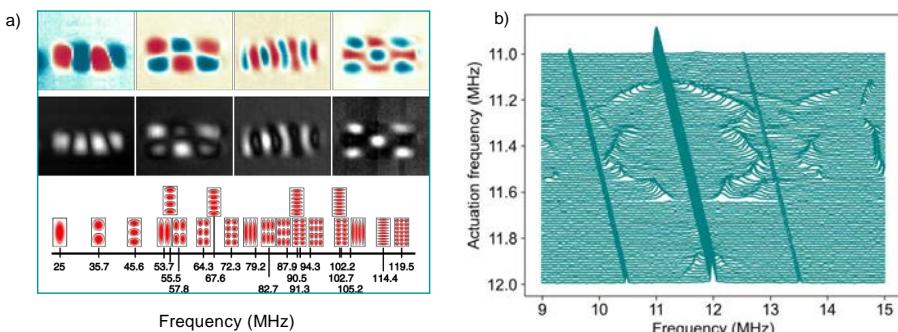
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Optomechanical devices are commonly used for the optical detection of displacements in the nanometric range, small masses or forces [1]. They have been employed as testbeds for the study of coherent light-matter interactions and have been proposed as building blocks for technological developments in quantum information processing [2].

In this work, we study the optomechanical behaviour of MoS<sub>2</sub> micro-drum resonators under different excitations schemes and at low temperatures. The radiation pressure and thermal effects of incoming CW laser light, result in the coupling between optical and mechanical drum modes, forcing the membrane to oscillate. The membrane response is readout optically by tracking the changes in the resonator's reflectivity. With the information gathered from this coupling, we can gather the displacement of the membrane's position and establish an analogy to a Fabry-Perot cavity with a moving output mirror. Employing lock-in amplification schemes, we can extract amplitude and phase maps of the optomechanical modes at 5 K under CW laser excitation.

The device design also allows us to excite the resonator electrically. Under RF electric fields between the drumhead membrane and the bottom of the cavity (doped substrate) we force electromechanical oscillations and study the coupling with the optomechanical resonances. In the range between 1 MHz up to 100 MHz, when the electrical driving and the optomechanical mode frequencies are close enough we observe an anti-crossing behavior characteristic of strongly coupled systems.



**Fig. 1** a) High resolution imaging of electrically actuated vibrational modes at 5 K. b) Spectrum analyser response of the optomechanical interference: the coupling between the optothermal resonance (at 12 MHz) as we increase the electrical resonance (driving frequency from 11 to 12 MHz). This interference leads to the upper and lower sidebands around the electrical actuation.

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# Temperature impact on the real-time dynamics of the human mitochondrial DNA polymerase

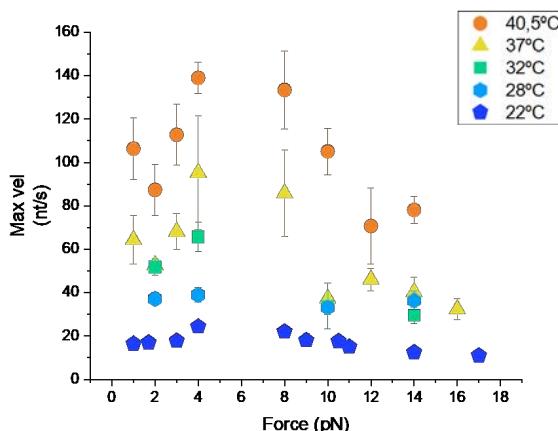
Lyra Zumeta<sup>a</sup>, Ismael Plaza-G. A.<sup>a</sup>, Grzegorz L Ciesielski<sup>b</sup>, Borja Ibarra<sup>a</sup>

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Mitochondria are eukaryotic organelles essential for energy generation. Mitochondria harbor their own DNA (mtDNA), which is replicated by the mitochondrial replisome (comprised of Pol $\gamma$ , Twinkle and SSBs) (1). mtDNA replication takes place inside the inner membrane of the mitochondria, a compartment that can reach temperatures of up to 50°C, some recent studies suggest (2). We aim to shed some light into the effects of increasing temperature on the real-time kinetics of the mitochondrial replisome operation. Here, we used optical tweezers with a temperature controller (3) to study at the single-molecule level the real-time kinetics of DNA replication activity of the DNA polymerase PolG, the effects temperature has on its pausing behavior and activation energy.



**Figure 1.** Higher temperatures increase the velocity of PolG. For each molecule held at a specific force, the highest polymerization speed is taken and averaged to give the points of the plot (each point with N:4-6). Different color curves indicate different temperatures.

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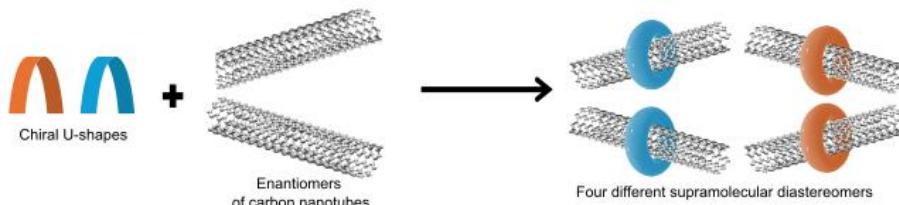
# Exploring Supramolecular Diastereomers in Mechanically Interlocked Carbon Nanotubes

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Single-walled carbon nanotubes (SWCNTs) have been extensively studied for over three decades due to their unique structural and electronic properties. One appealing method of functionalizing them without disrupting their structure is by mechanically interlocking them with macrocycles, forming mechanically interlocked nanotubes (MINTs) [1]. In recent years, several synthetic strategies toward MINTs have been developed, along with promising applications in areas such as polymer reinforcement [2] and catalysis [3] [4]. However, MINTs featuring chiral macrocycles have not yet been described. The synthesis of such species would open new avenues for exploring the interaction between chiral macrocycles and chiral nanotubes, potentially giving rise to diastereomeric MINTs with unique properties.

In this communication, we present examples of chiral U-shaped precursors used to prepare MINTs incorporating chiral macrocycles. We employed Aqueous Two-Phase Extraction (ATPE) to isolate the enantiomers of (6,5) SWCNTs [5] [6], and subsequently applied the same process to the corresponding MINTs. The resulting chiral MINTs were characterized using UV/Vis, PLE, CD, Raman spectroscopy, and thermogravimetric analysis. Future work may focus on leveraging this synthetic strategy for enantiomeric enrichment or separation of SWCNTs, offering a novel approach to chirality-based nanotube sorting.



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# Spin-dependent Electron Scattering at Step Edges in Bi(111)

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The Electron standing-wave patterns close to atomic scale defects yield information about their scattering potential. In surfaces with strong spin-orbit coupling, such potential can be spin-dependent even for non-magnetic impurities, a key effect in the development of spintronic devices. Simple Rashba systems show standing wave patterns with momentum-transfer vectors dictated by the nesting vectors of their circular constant-energy contours, corresponding only to backscattering processes. In such processes, the spin orientations can only be preserved or fully reversed, and interference can only take place in the former case, thus preventing the observation of spin-dependent scattering effects.

Bi(111) has spin-split surface states near  $\Gamma$ , with non-circular constant energy contours and a spin-texture with out-of-plane component, which might enable the observation of spin-dependent scattering in the standing-waves. In this contribution we indeed show that the scattering processes that contribute to standing waves close to monoatomic steps in Bi(111) are different for the upper and lower terraces. This effect can be rationalized in terms of the interaction between the out-of-plane spin component of the electrons and an effective magnetic field that originates from the repulsive interaction with the step edge through spin-orbit coupling. We believe that our observations and analysis constitute the first direct evidence of the spin-dependence of the scattering potential of step edges by Scanning Tunnelling Microscopy.

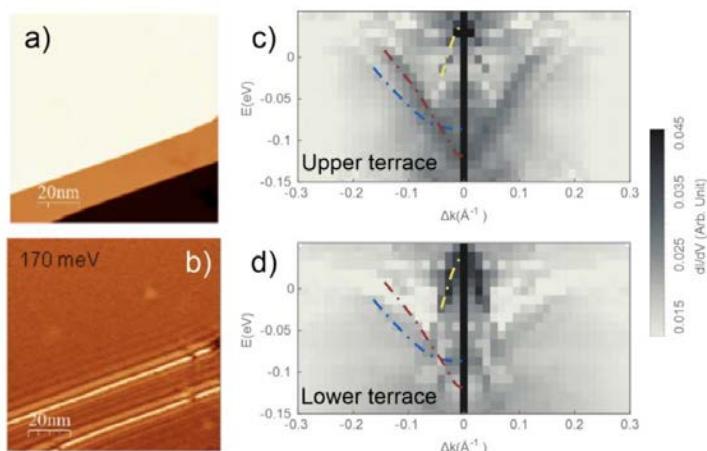


FIGURE 1: (a) STM topography of monoatomic step edges at the Bi(111) surface. (b)  $dI/dV$  map recorded at 170 mV showing the different standing wave patterns in the upper and lower terraces. (c) and (d) FFT of  $dI/dV$  lines perpendicular to a monoatomic step edge in the energy region close to the Fermi level. Three bands can be clearly distinguished in the upper terrace, whereas one of them is missing in the lower one.

**Fabrication & photophysical characterization of deep blue-green organic microspheres**

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Whispering-gallery-mode (WGM) micro-resonators are highly sensitive optical devices with outstanding photonic and optomechanical properties. The high-quality factor (Q) of the confined optical modes by strong light-matter interactions has raised interest in these devices for the detection of single molecules at low concentrations. In this work we have prepared micro-spherical WGM resonators based on an emulsion-solvent-evaporation method using polystyrene (PS), whereas PI2PhDPO and Coumarin 153 have been used as the luminescent gain material of these optical resonators. Structural characterization by SEM and AFM yields good sphericity and low surface roughness. When illuminated under continuous photoexcitation with a Hg lamp, microspheres exhibit spontaneous emission WGM resonant modes of narrow linewidth and high-quality factor ( $Q > 1800$ ). When pumped with a pulsed Nd:YAG laser ( $\lambda = 355$  nm), we observed stimulated emission for PI2PhDPO at low threshold fluences ( $\approx 1 \mu\text{J}/\text{cm}^2$ ) with instrumentally limited linewidths corresponding to  $Q > 18000$ . Both characterizations indicate that WGM resonators may be considered as promising candidates to develop low-threshold organic dye microlasers excited by diode lasers and to be used as high sensitive biochemical sensors.

# Antibody-controlled Janus nanomachine for targeted Drug Delivery

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Compared to conventional drugs, nanoparticle-based drug delivery has specific advantages such as improved stability and biocompatibility, and enhanced and precise targeting. Janus nanoparticles (JNs) have emerged as promising nanomaterials due to their anisotropic structure, which enables the combination of multiple functionalities within a single nanoparticle. In this study, we report the preparation and characterization of multifunctional Janus gold nanoparticles designed for controlled drug delivery applications<sup>1</sup>.

The approach was based on a site-selective modification strategy employing positive-charged  $\text{Fe}_3\text{O}_4@\text{SiO}_2$  core-shell nanoparticles (NanoCaptors) as support for the electrostatic adsorption of citrate-capped Au nanoparticles (AuNP). This magnetic support acted as masking element to protect one face of the AuNP toward further chemical modification, but also allowed easy purification of the resulting nanomaterial through magnetic detection<sup>2</sup>. The AuNPs were later asymmetrically functionalized, with one side capped with  $\beta$ -cyclodextrin-modified poly(amoidoamine) dendrimers ( $\beta$ -CD-PAMAM), to encapsulate model drugs like doxorubicin through supramolecular encapsulation<sup>3</sup>. The other side was conjugated with a biotinylated anti-p53 antibody linked through avidin-biotin interactions, providing a highly selective recognition that ensures targeted drug delivery in tumoral cells and minimizes side-effects<sup>4</sup>.

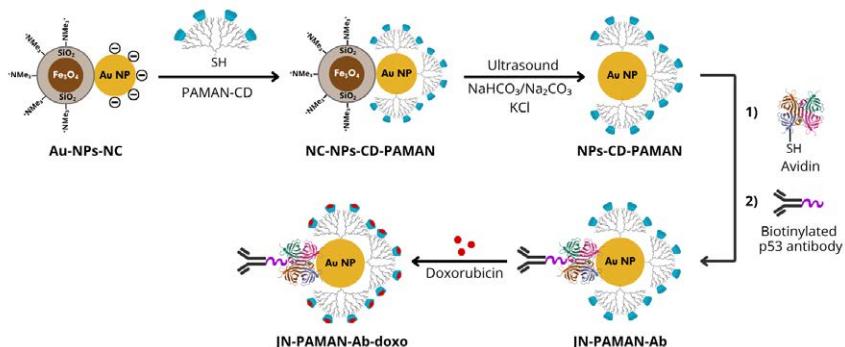


Figure 1: Assembly of the Janus nanoparticle loaded with doxorubicin

Successful modification of the nanoparticles was confirmed through transmission electron microscopy (TEM), UV-Vis spectroscopy, cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and atomic force microscopy (AFM). The loading capacity of the nanoparticles was evaluated with UV-Vis spectroscopy demonstrating that the  $\beta$ -CD moiety effectively formed inclusion complexes with the model drugs.

*In vitro* assays using HeLa cells were conducted to evaluate the performance of the Janus nanodevice as target drug release system. Doxorubicin-loaded JNs exhibited enhanced cytotoxicity when functionalized with the anti-p53 antibody, highlighting the potential of these nanoparticles for targeted drug delivery.

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# Electrochemical Detection of Chronic Obstructive Pulmonary Disease Biomarkers in Breath Samples Using a COF-Based Sensor

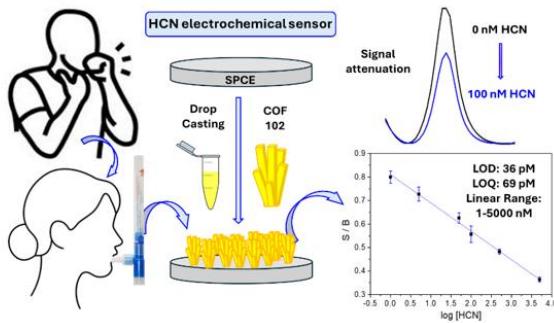
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Respiratory diseases pose a global health risk, and early detection methods are key to preventing them. Noninvasive and simple devices are the best tool for worldwide scale diagnosis. An encouraging COF-based electrochemical sensor has been developed in this work for the detection of HCN. This biomarker is associated with the presence of *Pseudomonas aeruginosa* which relates to cystic fibrosis. The novel COF consists of a nanostructured architecture with hydroquinone's in the surface which serve as the electrochemical beacon. HCN interacts with the hydroquinone's of the COF-based electrochemical sensor, attenuating the signal, hence a proposed sensor with 36pM limit of detection and 69pM limit of quantification is achieved. The system works in the presence of interfering compounds and its application in real exhaled breath sample has proven successful.



# REAL-TIME KINETICS OF MITOCHONDRIAL DNA REPLICATION REVEAL CHAPERONE-MEDIATED CONTROL BY TID1–MORTALIN

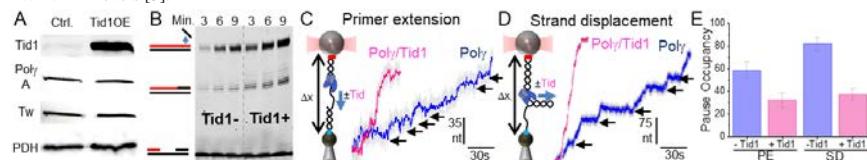
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Mitochondrial DNA (mtDNA) replication is catalyzed by a minimal replisome composed of DNA polymerase  $\gamma$  (Poly), the TWINKLE helicase, and mitochondrial single-stranded DNA-binding protein (mtSSB) [1]. Although sufficient for *in vitro* reconstitution, this core system does not recapitulate the high processivity observed *in vivo*. Using single-molecule optical tweezers with temperature control, our group at IMDEA Nanoscience revealed frequent, transient pausing during synthesis, with pause occupancies of ~60%, reducing net replication 76 velocity to ~3 nt/s. When inactive states are excluded, the pause-free rate reaches  $9 \pm 2$  nt/s closely matching *in vivo* estimates implicating stochastic pausing as a key kinetic bottleneck [2]. Such dynamic features remain hidden in ensemble assays, emphasizing the need for single-molecule approaches to resolve true replisome behavior [2,3]. The prevalence of pausing suggests the action of accessory factors that enhance processivity. Among these, the mitochondrial Hsp70 chaperone Mortalin and its Hsp40 partner Tid1, along with the nucleotide exchange factor GrpEL1, form a conserved chaperone system (KJE system) that regulates protein interactions and stability [4]. Tid1 localizes to replicating nucleoids, stimulates Poly activity, and is essential for mtDNA integrity [1,5]. Disruption of the Tid1–Mortalin axis destabilizes mtDNA, and Mortalin is required for replication in organisms such as *Trypanosoma brucei* [5]. Single-molecule and ensemble data reveal that Tid1, alone or in combination with Mortalin, reduces pausing and promotes strand displacement across structured templates. In cells, Tid1 overexpression increases mtDNA copy number ~3-fold and enhances Mortalin recruitment without altering Poly or TWINKLE levels [5].



A. *In vivo* assays. Western blotting analysis of levels of the catalytic subunit of Poly, PolyA, and Twinkle (Tw) in mitochondrial extracts of control (Ctrl.) and Tid1 overexpressing (Tid1 OE) cells. PDH (Pyruvate Dehydrogenase) is the loading control. B. *In vitro* assays. Primer extension time course assay by Pol without (left) or with Tid1 (right). Cartoons represent DNA substrate and products with fluorescently labeled fragments marked in red. C) and D) *In singulo* assays. Experimental set ups and representative primer extension (2 pN) (C) and strand displacement (6 pN) (D) replication traces of Pol without (blue) and with (magenta) Tid1. Tid1 reduces the frequency and duration of Pol pause events (arrows). E) Pause occupancy quantification during primer extension (PE) and strand displacement (SD) without (blue) and with (magenta) Tid1.

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# HIGH-LOADING POLYGLYCEROL-SWNT COMPOSITES ACHIEVED VIA MECHANICAL INTERLOCKING

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The chemical structure of single-walled carbon nanotube (SWNTs) makes them extremely strong, which, together with their dimensionality, makes SWNTs ideal to be used as polymer fillers. Nevertheless, the observed enhancements in mechanical properties of SWNT-polymer composites often fall significantly short of theoretical predictions, primarily due to challenges in individualizing SWNTs and achieving effective load transfer from the polymer matrix to the nanotubes. Mechanically Interlocked Carbon Nanotubes (MINTs), are rotaxane-type species where organic macrocycles are threaded around SWNTs. The functionalization in MINTs is as kinetically stable as a covalent bond, but without disrupting the native structure of the SWNTs.<sup>1</sup> MINTs are attractive SWNT derivatives to reinforce polymers, because as matrix and MINT filler can be directly linked through the mechanical bonds, it ensures both better dispersion of the SWNTs and enhanced load transfer.<sup>2,3</sup>

In this work, methyl alcohol functionalized MINTs and glycidol are used to grow a branched polyglycerol (PG-MINT) that will be further crosslinked with different agents. Different to other approaches in composite science, where polymer is mixed or reacts with CNTs, in this work the polymer is directly grown on the MINT ring, using the hydroxy groups of the macrocycle. This way a composite with a tensile strength of 15 MPa and with a young's modulus of 2.5 MPa is made. This composite has free hydroxy groups that will be further crosslinked using different crosslinking agents to make polyurethanes or other types of networks.

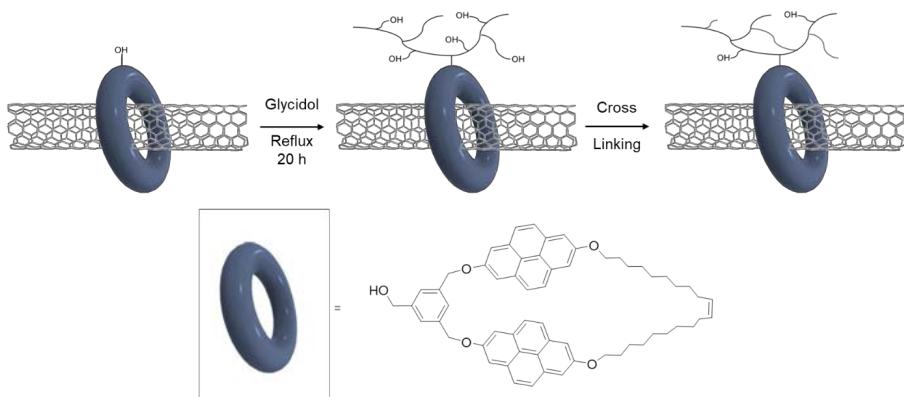


Figure 1. Preparation of PG-MINT and cross-linking.

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# On-Surface Synthesis of Porphyrinoid-Based Derivatives Comprising Exotic Macrocycles.

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The synthesis of porphyrinoid-based compounds has attracted the interest of many surface scientists during the last decades due to their intriguing electronic, optical and catalytic properties. In this work, porphyrinoid-based derivatives with exotic macrocycles (6 & 7 nitrogen hemiporphrazines) have been fabricated on Au(111) and studied with the use of Scanning Tunneling Microscopy (STM) and non-contact Atomic Force Microscopy (nc-AFM) under ultrahigh-vacuum conditions (UHV), complemented by theoretical modeling. Particularly, through surface-assisted synthesis, three carbahemiporphrazines of distinct dimensionality equipped with isopropyl groups have been studied. As shown in Figure 1, the macrocycle of precursors **P1** and **P2** comprises two pyrrole units and two benzene rings, while in precursor **P3** one of the benzene rings has been substituted by a pyridine.

First, an intermolecular carbon-carbon coupling between the carbahemiporphrazine precursors was achieved by thermal activation of their isopropyl substituents via a [3+3] cycloaromatization, giving rise to dimers (0D), one- and two-dimensional (1D and 2D) polymers. Second, the three low-dimensional free-base macromolecules, were exposed to an atomic flux of cobalt atoms, giving rise to cobalt-metallated macrocycles. The dicarbahemiporphrazines **1** and **2** showed that the metal atoms were coordinated only to the two pyrrolic nitrogens, in contrast to the typical four-fold coordination that occurs inside tetrapyrroles, while the monocarbahemiporphrazine **3** shows a three-fold coordination. This on-surface protocol renders atomically precise covalently-linked carbahemiporphrazine-based derivatives, and provides promising model systems toward the exploration of metallated, low-coordinated, porphyrinoid systems with utility in diverse technological areas.

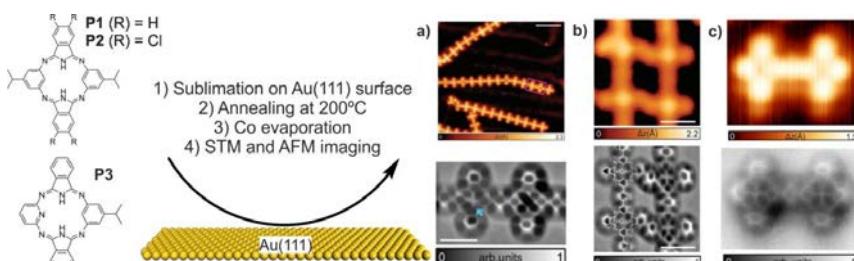


Figure 1. Scheme of work and characterization of: a)-b) STM and Laplace-filtered constant-height frequency shift nc-AFM images of evolved **P1** & **P2**. c) STM and constant-height frequency shift nc-AFM images of evolved **P1**.

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# FRET-Based Approach to Study the Spatial Organization and Conformational Flexibility of Self-Assembling Proteins for 2D Nanobiomaterials

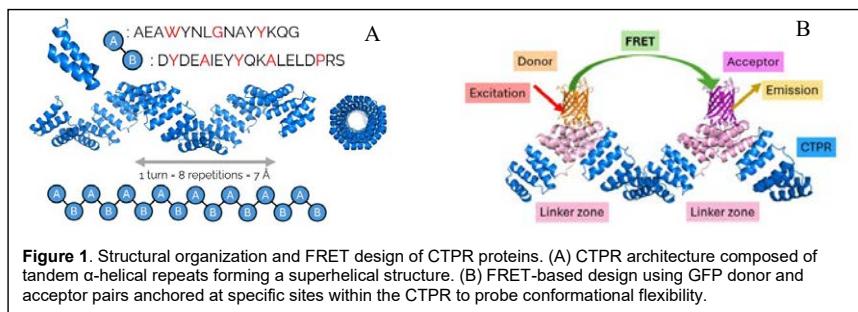
Teresa Espinosa González,<sup>\*a</sup> Angelo Berrato Ramos<sup>a</sup> and Sara Hernández Mejías<sup>a</sup>

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Consensus Tetratricopeptide Repeat (CTPR) proteins are 34–amino acid motifs arranged in tandem arrays that adopt a superhelical conformation<sup>1</sup> (Figure 1A). Through head-to-tail and side-to-side interactions, CTPRs can self-assemble into supramolecular structures such as solid films with hydration layers that preserve their native folding<sup>2</sup>. Despite their apparently rigid architecture, CTPRs possess a relatively flexible framework that tolerates sequence modifications, making them versatile building blocks for functional biomaterials. In this sense, they have been engineered with specific functionalities for applications in drug delivery<sup>3</sup> and bioelectronics<sup>4</sup>.

The next step would be to use them to create nanofunctionalized 2D materials through hierarchical assembly. However, to harness their potential in this direction, it is essential to understand the internal dynamics that govern their structure and assembly. To achieve this, I developed a methodology that uses Förster Resonance Energy Transfer (FRET) to investigate the spatial organization and conformational flexibility of CTPRs (Figure 1B). Using computational design, we created peptide sequences that can be incorporated into the CTPRs to anchor a GFP-based FRET pair. The anchoring sites can be positioned at various locations along the CTPR, allowing for precise control over the inter-GFP distances. This tunable functionalization allows us to study the relative orientation and flexibility of the proteins. Ultimately, the results of this study will enable more precise control over hierarchical assembly, promoting interactions between proteins and allowing the investigation of their collective photoresponse, thereby opening a new research direction.



**Figure 1.** Structural organization and FRET design of CTPR proteins. (A) CTPR architecture composed of tandem  $\alpha$ -helical repeats forming a superhelical structure. (B) FRET-based design using GFP donor and acceptor pairs anchored at specific sites within the CTPR to probe conformational flexibility.

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# Driving multi-step regioselectivity in on-surface polymer synthesis by molecular coverage

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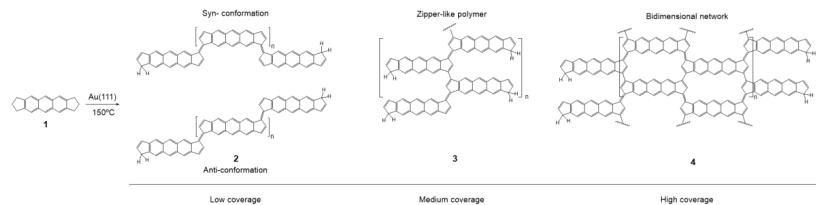
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Indenyl coupling refers to the reaction where molecular precursors equipped with indenyl ligands promote the formation of C-C bonds, thanks to deprotonation of indenyl groups and subsequent homocoupling. This leads to extended  $\pi$ -conjugated polymers along a polyacetylene backbone, expanding the electronic delocalization, which is crucial to obtain  $\pi$ -conjugated systems with broad applications in fields such as spintronics, sensing, optoelectronics and photovoltaics, among others.<sup>[1]</sup>

In this work, we present an on-surface chemical reaction in ultra-high vacuum conditions based on the regio- and stereo-selective covalent coupling of indenyl moieties<sup>[1]</sup> for fabricating  $\pi$ -conjugated systems whose dimensionality is directly driven by the initial molecular coverage of the precursor on the surface. The deposition of a dicyclopentaanthracene species (**1**) on Au(111) and its subsequent post-annealing at 150°C leads to the controlled formation of various  $\pi$ -conjugated polymers. When the coverage is low (less than 0.3 ML), 1D chains with –syn and –anti– bonding connections emerge (**2**). If the molecular coverage is around 0.5 ML, 1D extended zipper-like polymers are obtained (**3**). Finally, at very high coverage (almost 1 ML), small 2D patches are observed (**4**), whose size can be promoted by long annealing. By using scanning tunneling microscopy and non-contact atomic force microscopy, complemented by density functional theory simulations, the structural and electronic properties of the distinct polymers were rationalized. Notably the termini of the polymers are always doubly-hydrogenated as displayed in Figure 1. In addition we observe bandgaps of 3.2 eV for **1**, 2.03 eV for **2** and 3.5 eV eV for **3**, respectively.

Our results open avenues for the controlled design of molecular nanoarchitectures on surfaces, while exploiting a recently discovered reaction at interfaces, the indenyl coupling.



**Figure 1.** Dependence of the degree of polymerization on the molecular coverage.

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# On-Surface Self-Metalation of Porphyrins on 2D Ferromagnetic FeCl<sub>2</sub>/Au(111) Probed by STM

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## Abstract:

Metalloporphyrins are well-known in surface chemistry and are highly active catalysts for electrochemical reactions such as oxygen reduction and evolution reactions [1]. The self-metalation of porphyrins at solid–vacuum interfaces has become an unconventional protocol to study molecule–substrate coupling and to design metal–organic nanostructures. Previous studies have demonstrated that this process can be induced either by pre- or post-deposition of metal atoms or by direct incorporation of substrate atoms into the porphyrin macrocycle [2,3]. Here, we explore a distinct self-metalation pathway in which metal-free porphyrin molecules undergo spontaneous coordination on top of a two-dimensional (2D) ferromagnetic FeCl<sub>2</sub> material supported on an Au(111) surface. In our ongoing research, we successfully reproduced the growth of FeCl<sub>2</sub> on Au(111). The structural properties of this 2D magnetic support were characterized by scanning tunneling microscopy (STM). After preparing the FeCl<sub>2</sub>-based ferromagnetic surface on Au(111), we deposited 5,15-bis (2,6-dimethylphenyl) porphyrin using molecular beam epitaxy and followed stepwise annealing above room temperature. Upon annealing, the metal-free porphyrin molecules completely self-metallated at 325°C, thanks to dissolution of FeCl<sub>2</sub> and Fe incorporation into the macrocyclic cavity. We resolved the adsorption geometries of the porphyrin molecules and observed their transformation into metallated species. This process is clearly identified by the appearance of a central protrusion and modified intramolecular contrast in constant-current STM images. Our findings establish 2D transition-metal halides as active platforms for on-surface coordination chemistry, providing new opportunities for self-metalation of porphyrins molecules using 2D magnetic materials and paving the way for hybrid systems relevant to catalysis.

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# Sensitive determination of p-cresol in human urine samples based on electrochemical tyrosinase biosensor for early Autism Spectrum Disorder (ASD) diagnosis

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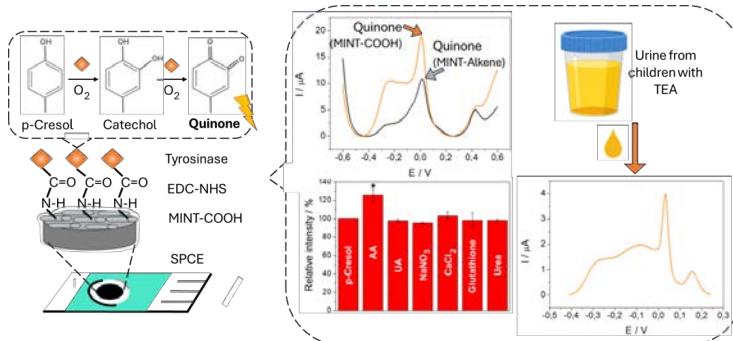
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Neurodevelopmental disorders are cognitive and behavioral disorders that involve significant difficulties in the acquisition and execution of specific motor, intellectual, social or language functions. They include disorders like autism spectrum disorder (ASD), which affects around 168 million people around the world [1]. This disorder is characterized by social communication deficits, difficulty in speech and unusual and repetitive sensory motor behaviors. Among this spectrum exist different levels of severity, but generally all ASD individuals need special support during their life. Currently, ASD individuals cannot be cured and most of them receive a diagnosis after 4 years in the best scenario [2]. To date, the diagnosis of ASD has been based on observation of daily functionality and behavioral characteristics of patients, and the standards to this diagnosis are complex, time-consuming and unpractical. Therefore, accurate clinical methods are needed for early detection of patients, which will allow the improvement of many deficits and communication and social skills, thus preventing social isolation and economic loss of their families.

p-cresol has been proposed as a biomarker of predisposition to autism in children [4] because there is accumulating research on the alteration of the microbiome and elevated levels of p-cresol in urine in autistic patients. With this aim, we have developed an electrochemical nanomaterial-based biosensor for p-cresol biomarker detection. In particular, we propose the use of carboxyl-functionalized Mechanically Interlocked Carbon Nanotubes (MINT-COOH) for enzyme tyrosinase immobilization to detect electrochemically this biomarker. Different strategies for nanomaterial optimal use, optimization of electrochemical parameters and characterization of the sensing platform were performed. The biosensor exhibited an excellent linear correlation from 100 pM ranging up to 200 μM with a limit of detection (LOD) of 0.117 μM and a limit of quantification (LOQ) of 0.392 μM. Its applicability on urine real samples was successfully tested.



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# Single-Molecule Conductance of Pyrazine-Based OPEs.

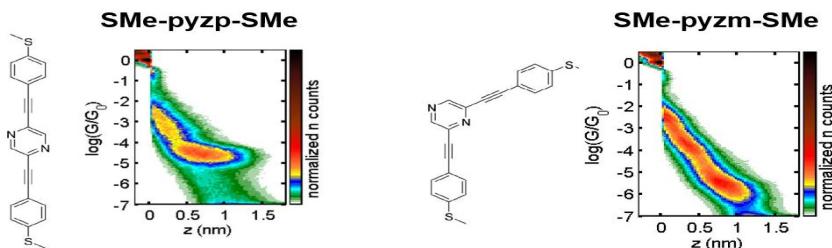
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## Abstract:

Molecular electronics has emerged from the need to characterize and study electron transport at the single-molecule level. This field benefits from organic chemistry, which allows the precise synthesis of molecules with specific structures to replicate the behavior of certain electronic components -such as wires, potentiometers and switches. In addition, the use of the scanning tunneling microscopy break-junction (STM-BJ) technique, allow to study the conductance on molecular circuits formed as a single molecule. Among the many molecular backbones studied, oligo(phenylene ethynylene) (OPE) derivatives have emerged as prototypical "molecular wires" due to their rigidity, linear  $\pi$ -conjugation, and predictable structure-conductance behavior. [1] Recent studies have shown that incorporating heterocycles into OPE backbones can significantly modify the electronic structure and create new conductance pathways [2], [3]. In parallel, Ortúñoz *et al.* [4] introduced a family of *stapled, chiral ortho*-OPE derivatives where conductance can be modulated through conformational changes within a locked helical scaffold. Together, these two approaches highlight complementary strategies for achieving molecular-scale potentiometers, where electronic properties can be adjusted through structural design.

The aim of this project is to focus on the studies of the electronic properties of a family of OPE3-like molecules in the central phenyl ring in the backbone is replaced by a pyrazine unit. To evaluate how structural modifications influence the electronic response of this family, we synthesized two compounds, one with the side chains connected in para-position to the pyrazine ring (**SMe-pyzp-SMe**) and another with the side chains connected in meta-configuration (**SMe-pyzm-SMe**). We performed STM-BJ measurements for these compounds and compared the results obtained for the two of them in order to determine how connectivity and conjugation pathways shape their electron transport characteristics. Several other molecules were also studied as models to fully characterized their potentiometer character. In addition, these experimental results are compared with theoretical simulations performed within the framework of the EIG-Concert Japan project DECOSMOL, in which this study is carried out.



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# Development of flexible interfaces for neural electric stimulation based on nanostructured electrodes

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Neurological disorders represent one of the leading causes of disability worldwide, often resulting in severe cognitive and motor impairments. Electrical stimulation of neural tissue using implantable electrodes has demonstrated promising therapeutic potential. However, current technologies still face critical challenges such as size reduction, limited biocompatibility, and mechanical mismatch with soft neural tissue.<sup>1,2</sup>

This project aims to design and develop flexible nanostructured neural interfaces capable of providing safe, efficient, and reliable long-term electrical stimulation. The electrodes will be fabricated using micro- and nanofabrication techniques such as sputtering, reactive ion etching, template-assisted electrodeposition, photolithography, and nanoimprint lithography to produce prototypes composed of flexible substrates and electrodes coated with vertically aligned metallic or polymeric nanowires. These nanostructures are expected to enhance the electrochemical surface area, decrease impedance, and improve the mechanical and biological compatibility with neural cells.<sup>1-4</sup>

Comprehensive electrical, mechanical, and stability characterizations will be performed under physiological conditions, along with the preparation of platforms for in-vitro biocompatibility and stimulation studies. Future stages will include the development of neural interface prototypes and the investigation of immune responses and in-vivo impedance behavior through collaborative studies.

By integrating nanotechnology, materials science, and neuroengineering, this project seeks to advance next-generation neural stimulation devices that combine high performance, long-term stability, and minimal invasiveness, ultimately contributing to safer and more effective neural therapies.

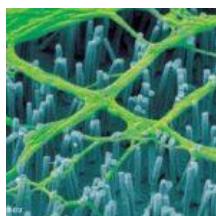


Figure 1. Neuronal culture on metallic nanowires.<sup>5</sup>

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# Nanofabrication of flexible Nanostructured Electrodes for Minimally Invasive Interfaces

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Neural interfaces are important devices to study, diagnose, treat, and stimulate neural activity [1]. However, implanted neural interfaces face different problems that shorten their life-time. There is a need of devices able to target only small specific areas, integrate well with the tissue, reduce inflammation, and stay stable in the long term.

In this work, we present our progress in developing nanostructured flexible electrodes for minimally invasive neural interfaces. The main goal is to fabricate implantable devices on flexible materials, with defined micrometric stimulation pads. On this active zone, metallic nanopillars are grown to increase the effective surface area of the electrode and decrease the impedance at the interface with neural tissue [2, 3]. Our strategy is based on a membrane-transfer method, using AAO membranes as nanoporous templates. First, we define the conductive paths on the template surface by metal sputtering using a mask. After this, electrodeposition is used to thicken the paths and cover their surface of vertical nanowires, as the electrodeposited metal fills the nanopores of the AAO template [1, 2, 3]. Finally, the so-prepared template is transferred to a flexible polyimide (PI) film, and the template is removed, exposing the nanowire-coated electrodes. Currently, we are using platinum as metal for the electrodes and we are working on optimizing the growth conditions with a homemade electrolyte, improving the nanostructuring process, and assembling all the fabrication steps into a complete and functional device.

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# Modulating Delayed Emission Using Protein-Environment

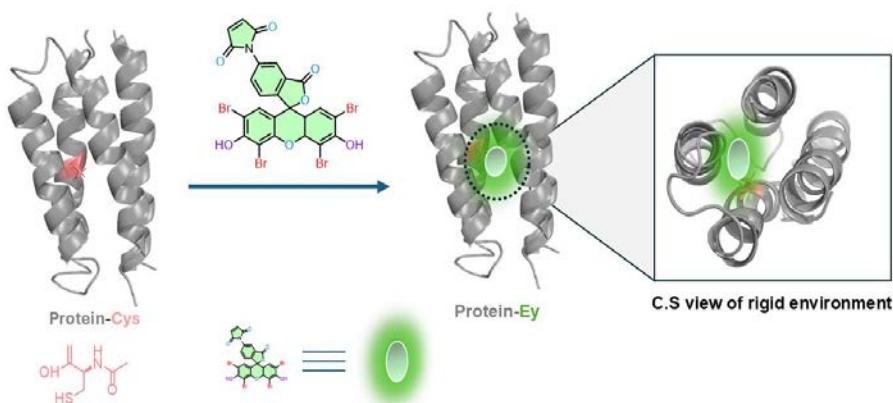
Adhil Kabeer,<sup>\*a</sup> Juan Cabanillas<sup>a</sup>, and Sara Hernandez<sup>a</sup>

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Thermally Activated Delayed Fluorescence Chromophores (TADF-C) have earned a burgeoning interest due to their interesting applications in light-emitting devices, photocatalysis, and sensing.<sup>[1,2]</sup> This is attributed to their phenomenal properties like prolonged luminescence lifetime and high quantum efficiency. Albeit to it, the non-radiative energy transfer to the host materials is a major bottleneck limiting their versatility and large-scale applications.<sup>[2]</sup> Herein, we advocate a novel approach to augment TADF properties enabled by a conformationally rigid chiral protein environment<sup>[3]</sup> (Fig. 1). In the protein cavity, the chromophore is confined, conferring nuanced control of the singlet-triplet energy gap and enhanced solubility. With the advent of site-specific mutagenesis, we infer the possibility of fine-tuning the local excited state by virtue of polar and charged amino acid residues in proteins.<sup>[4]</sup>

In the current work, we employ Eosin-Y (Ey) (Fig. 1) as a model molecule. Ey has a relatively small size and can fit into the cavity.<sup>[5]</sup> Based on this molecule, we infer the possibility of fine-tuning the energy gap (singlet-triplet) by using the protein environment using the cavity. We rely on Michael addition reaction to label the protein with Ey molecules in the cavity. Our initial results indicate the successful expression of protein with desired mutations together with their labeling. The temperature dependence studies indicate that the motion of Ey couples with the motion of the protein and enhances the phosphorescence decay rate. Taken together, this current work shall underscore a molecular understanding of how the protein environment influences the photo-physics of these molecules and hence can set directions towards new protein-based materials.



‡ Figure 1. Schematic of Protein-Ey biohybrids: Ey fits into the hydrophobic cavity.

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# Engineering mesoporous bioactive glass nanocarriers for active biomolecules delivery in bone tissue regeneration

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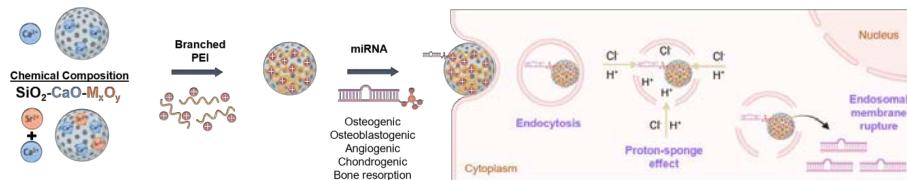
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Autograft bone remains the clinical gold standard for treating critical-sized and non-union bone defects. Each year, over ten million bone reconstruction surgeries are performed worldwide, underscoring the scale of the challenge. Conventional grafts—autografts, allografts, and xenografts—present significant limitations, including surgical complexity, immune rejection, limited availability, and infection risks. These constraints highlight the urgent need for innovative bone tissue engineering strategies to enable safer, more effective, and scalable regeneration solutions<sup>1</sup>.

In recent years, gene therapies have emerged as an alternative to grafts, prompting growing interest in their development. MicroRNAs (miRNAs) in particular are recognised as key regulators of gene expression. Consequently, they are considered essential for diagnosis and treatment. They have also demonstrated potential in angiogenesis, bone resorption and osteogenesis<sup>2</sup>. However, internalization and endosomal escape into the cytosol present significant biological barriers. Furthermore, nucleases and cellular immunity present an additional challenge in gene delivery. For this reason, efforts have focused on using nanocarriers to overcome these issues. Although viral vectors are widely used, they have drawbacks in terms of safety and load capacity. Consequently, there is increasing interest in developing non-viral vectors, such as inorganic nanoparticles<sup>3</sup>. Among inorganic nanocarriers, mesoporous materials possess distinctive properties, including elevated surface area, high pore volume, and the capacity for facile surface functionalization<sup>4</sup>. Specifically, mesoporous bioactive glass nanoparticles (MBGNs) possess enhanced properties, including rapid bioactive response and biocompatibility<sup>5</sup>.

MBGNs can be enriched with different therapeutic metal ions and loaded with biologically active molecules for controlled co-delivery and synergistic effects<sup>5</sup>. Calcium ion-containing MBGNs exhibit osteogenic response of osteoprogenitor cells<sup>6</sup>. Moreover, strontium ( $\text{Sr}^{2+}$ ) displays distinctive biological activity, supporting bone regeneration, cell metabolism, and tissue homeostasis. The combined effect of  $\text{Sr}^{2+}$  and  $\text{Ca}^{2+}$  further promotes bone mineralization and formation, reinforcing the overall osteogenic response<sup>7</sup>.

In this work, we present the optimized design and development of novel nanocarriers based on MBGNs with varying pore sizes and chemical compositions, functionalized with the cationic polymer polyethylenimine (PEI). This polymer enables the electrostatic condensation of nucleic acids, such as miRNA, shielding it from degradation and facilitating its intracellular delivery by overcoming biological barriers through the proton-sponge effect<sup>3,8</sup>.



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# Nonlinear THz Mobility in Doped Silicon

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Carrier mobility ( $\mu$ ) defines the proportionality between drift velocity and electric field in the low-field regime ( $v_d = \mu E$ ). At high fields, carriers gain excess energy, leading to enhanced scattering and energy relaxation processes that cause velocity saturation and nonlinear transport. Such high field behavior has been extensively studied in narrow-gap semiconductors such as GaAs, InSb, and InAs [1], where high-field terahertz (THz) excitation reveals pronounced intervalley scattering and velocity saturation effects. In contrast, the corresponding phenomena in silicon—despite its fundamental significance and central role in modern electronics—remain comparatively underexplored.

In this work, we conducted a research stay at the ELI-ALPS Research Institute (Szeged, Hungary) to investigate majority-carrier dynamics in crystalline silicon using nonlinear terahertz time-domain spectroscopy (THz-TDS), with high-energy THz pulses, able to promote intraband transitions [2]. To disentangle electron and hole contributions, we examined three silicon wafers: two with comparable carrier concentrations but opposite doping types (p- and n-type), and one highly resistive n-type sample. The field-dependent THz spectra exhibit a saturation of free-carrier absorption with increasing field strength (Figure 1), resulting in a decrease of the AC conductivity. This nonlinear behavior can be attributed either to intervalley carrier heating, which increases the effective mass due to band nonparabolicity [3], or to intervalley scattering processes.

Ongoing work aims to model the field-dependent spectral conductivity in order to extract key transport parameters—such as carrier mobility and effective mass—and to elucidate the distinct behaviors of electrons and holes in different valleys. Together, these results advance the microscopic understanding of high-field carrier dynamics in silicon.

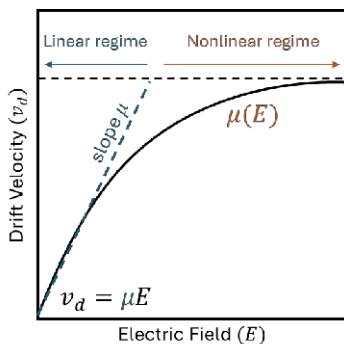


Figure 1. Drift velocity vs electric field strength. At low fields, the response is linear and the mobility  $\mu$  equals the slope. At higher fields, the velocity deviates from linearity,  $\mu$  becomes field-dependent, and eventually the drift velocity saturates.

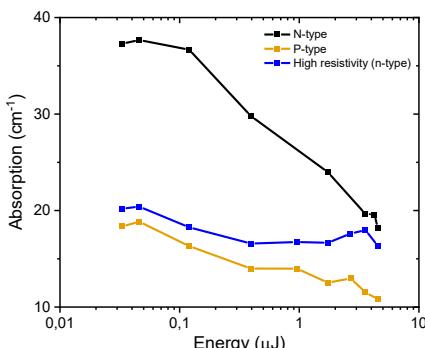


Figure 2. Spectrally averaged absorption versus THz pulse energy for three different silicon wafers at room temperature. The observed decrease in absorption with increasing THz field indicates the saturation of free-carrier absorption, consistent with nonlinear carrier transport at high fields.

## Notes and References

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# Proteomics Based Strategies to Optimize Therapeutic Nanoparticles Against Pathogens

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Antibiotic-resistant bacteria poses a serious threat to health worldwide, raising the urgent need for new therapeutic approaches.

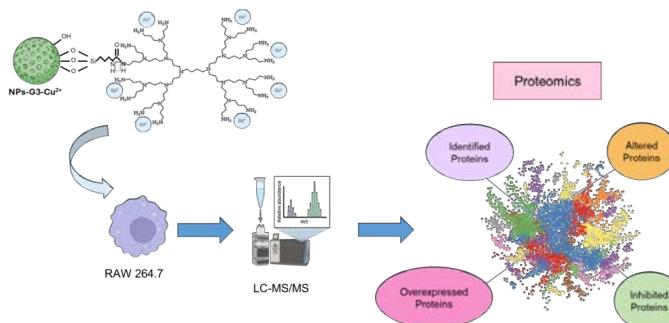
This study aims to develop an innovative solution to treat bacterial infections using multifunctional nanoplatforms that, in addition to acting as antibacterial drug carriers, exhibit intrinsic antimicrobial activity.

The proposed nanosystems are based on mesoporous glass nanoparticles in the SiO<sub>2</sub>-CaO system, which have excellent textural properties, biocompatibility and easy modification of their surface [1]. These nanomaterials are bioactive due to the calcium present in their composition and in addition the silanol groups present on the surface allow the anchoring of third generation poly(propylamine) type polycationic dendrimers (G3), making it easier for the nanosystem to effectively cross bacterial membranes [2]. The poly(propylamine) ligands allow the coordination of copper ions, conferring new angiogenic properties to the nanosystem. Furthermore, the presence of mesoporosity in the nanosystem allows a high loading capacity of therapeutic agents such as the antibiotics levofloxacin (LEVO) and rifampicin (RIF) that act on *Escherichia coli* y *Staphylococcus aureus*, Gram-negative and Gram-positive bacteria, respectively [3].

The main objective of this study is to demonstrate the immunomodulatory role of copper-loaded mesoporous bioactive glass nanoparticles (NPs-G3-Cu<sup>2+</sup>), which exhibit excellent antimicrobial and osteogenic properties. The assay was performed using the RAW264.7 cell line, evaluating how their intracellular presence promotes a pro-inflammatory or reparative phenotype.

For this purpose, the SILAC (Stable Isotope Labelling by Amino acids in Cell culture) technique was employed [4]. This technique allows for non-targeted and semi-quantitative analysis of the entire proteome through metabolic labelling with amino acids labelled with stable isotopes during cell culture. These amino acids are then quantified using molecular mass spectrometry techniques [5].

Microbiological studies confirm that these novel nanoplatforms are potential nanomaterials for the development of new, more effective and specific antimicrobial treatments that take advantage of the properties of copper and antibiotics to combat microbial activity.



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# Single Point - Photodynamic therapy: From making the tumor structure more permeable to inducing tumor cell death from within

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Photodynamic therapy (PDT) is a clinically approved anticancer approach that relies on the generation of reactive oxygen species (ROS) by a photosensitizer (PS) upon light irradiation. Despite advances in cancer therapy, the low permeability of tumors frequently restricts how effectively treatment agents can reach and act on them. To overcome this limitation, we developed Single-Point Laser Photodynamic Therapy (SPL-PDT), a focused irradiation approach capable of initiating cell death from within the tumor and promoting structural changes that enhance its permeability.

In single-cell experiments, SPL-PDT induced localized necrotic cell death by selectively disrupting the plasma membrane at the irradiation site. This precise and controllable injury provides the foundation for understanding how the damage can propagate in more complex models.

When applied to tumor spheroids, SPL-PDT triggered cell death that spread from the irradiation point throughout the spheroid (Figure 1, a), compromising its structural integrity and revealing a new mechanism of internal tumor disruption. Remarkably, this localized photodynamic activation not only induces death from the inside out but also modifies the tumor's architecture, increasing its permeability. The use of irradiation resulted in deeper penetration of fluorescent probes (Figure 1, b), showing that SPL-PDT can improve drug delivery to the core areas of tumor masses by increasing permeability.

Overall, SPL-PDT combines precision, selectivity, and the ability to reshape tumor structure, offering a dual therapeutic advantage: targeted tumor ablation and improved access for anticancer drugs. These results pave the way for new theranostic strategies, where light not only destroys from within but also is also capable of increase tumor's permeability.

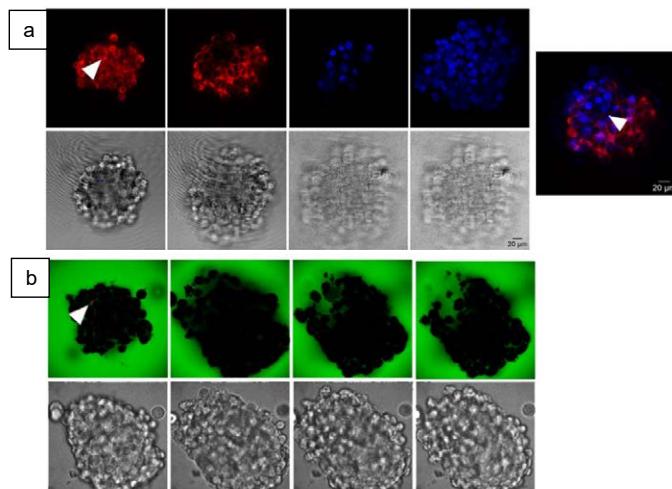


Figure 1 a) Confocal image showing progressive propagation of cell death (PI uptake) from the irradiation point toward the spheroid interior. b) Fluorescein (NaF) penetration before and after irradiation shows increased diffusion into the spheroid structure.

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# Enriching the structural design of anticancer Ru(II) and Os(II) half-sandwich complexes

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Cancer is still one of the main causes of death, and chemotherapy remains a central component of many treatment regimens. Cisplatin, a widely used chemotherapeutic, exhibits strong antitumour activity but is frequently limited by systemic toxicity and the emergence of acquired resistance. This underscores the need for new drugs, with metal-containing agents presenting opportunities for novel mechanisms of action.<sup>1</sup>

In the last decade, ruthenium and osmium complexes have attracted attention as potential anticancer agents, a status that is facilitated by the significant structural tunability these systems offer. Each building block of their characteristic piano-stool geometry – namely, the metal centre, the  $\eta^6$ -bound arene, the bidentate ligand ( $\kappa^2\text{-XY}$ ), and the monodentate ligand ( $\kappa^1\text{-Z}$ ) – can be varied systematically, allowing for fine-tuning of both thermodynamic and kinetic properties in substitution reactions.<sup>2</sup>

The arene plays a key role in stabilizing ruthenium in the +2 oxidation state and in providing a hydrophobic face to the complex, which facilitates membrane permeability and contributes to biological recognition processes.<sup>3</sup> It can also carry functional groups that enable the formation of tethered complexes. However, the arene is also the most difficult ligand to vary, particularly in osmium half-sandwich complexes.

We overcame these limitations by employing a novel approach based on the use of a cyclohexenol derivative instead of the usual cyclohexadiene, marking the first example of this strategy to yield half-sandwich complexes.<sup>4</sup> The reactions were carried out under focused microwave irradiation. To test reproducibility and scope, terpinen-4-ol and 2-cyclohexenol were employed as alternative precursors in the preparation of target complexes.

This new methodology is thought to proceed through a possible dehydration–arene formation mechanism, which may be promoted by methanol as a protic solvent, the elevated temperature and pressure of the microwave reaction, and the catalytic role of the metal centres, ruthenium and osmium, both well known for facilitating organic transformations. Preliminary experiments confirm that this microwave-assisted protocol is both efficient and reproducible for ruthenium and osmium complexes.

Overall, this work provides a practical and straightforward synthetic method that supports the development and diversification of half-sandwich metal–arene systems. It also enables easier access to arene precursors that are difficult to obtain through conventional methods.<sup>5,6</sup>

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# Bimolecular processes in bidimensional NiPS<sub>3</sub>

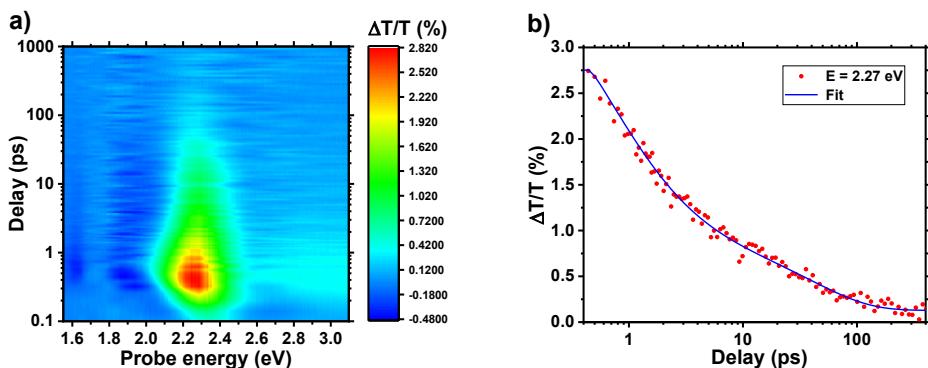
**Sebastián Mesa Apestegui\***<sup>a</sup>, Juan Cabanillas González<sup>a</sup>, Víctor Vega-Mayoral<sup>a</sup>

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NiPS<sub>3</sub>, a member of the metal phosphotrichalcogenide family, consists of crystalline layers strongly bonded within planes that are held together by weaker van der Waals forces. Quantum confinement effects promote the formation of tightly bound excitons, endowing NiPS<sub>3</sub> with properties of interest for applications in electrocatalysis and optoelectronic devices – such as transistors, photodetectors, and energy conversion systems – due to its tunable bandgap around 1.4 eV. Below its Néel temperature (150 K), the antiparallel alignment of nickel magnetic moments leads to antiferromagnetic ordering, opening opportunities for spintronic, magneto-optical, and magnetic storage applications, as well as for exploring two-dimensional magnetism. Notably, many-body phenomena such as collective excitonic states have also been observed below 150 K.

In this work, we employ time-resolved absorption spectroscopy (TAS) to investigate the ultrafast dynamics of charge carriers in NiPS<sub>3</sub>. The transient response reveals a bimolecular relaxation process followed by a slower exponential decay, providing insights into carrier recombination pathways in this layered antiferromagnetic semiconductor.



**FIGURE 1.** Transient absorption spectroscopy results for chemically exfoliated NiPS<sub>3</sub> nanosheets. a) 2D contour map of  $\Delta T/T$  value for all the energy and delay ranges of the experiment. b) Time trace of  $\Delta T/T$  for  $E = 2.27$  eV.

# Chain-length parity dictating molecular packing: odd–even effects of 4-n-alkyloxybenzoic acids on Au(111)

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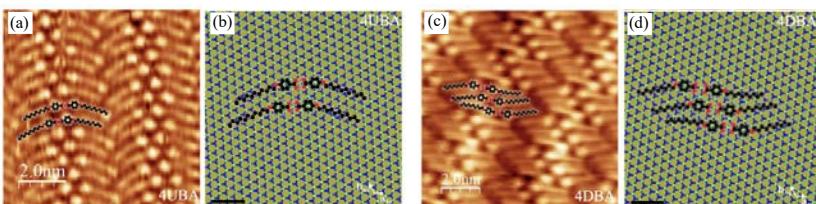
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The controlled fabrication of two-dimensional (2D) supramolecular architectures on solid substrates is a cornerstone of surface nanoscience, with implications spanning from molecular electronics to sensing, catalysis and nanophotonics. [1-3] At the heart of this approach lies the concept of molecular self-assembly via non-covalent interactions, among these, hydrogen bonding and van der Waals forces are particularly important for directing the structural organization of organic layers at the interface. [4-6]

The present contribution will be dedicated to scanning tunneling microscopy (STM) measurements and semi-empirical modeling, of two-dimensional self-assembled monolayers of 4-alkyloxybenzoic acids on the Au(111) surface with odd number of carbon atoms in the alkyloxy chain, compared with the obtained results reached through the deposition of corresponding acids with an even number of carbon atoms [7]. A clear odd/even effect is observed: the parity (even or odd) of the carbon number in the alkyloxy chain leads indeed to remarkably distinct packing geometries. This behaviour is attributed to a compromise between optimal intermolecular bonding, maximization of molecular packing, and substrate-adsorbate interaction, although we will show that in both cases interactions with the gold surface is rather weak. [8] These findings highlight the subtle balance of intermolecular and molecule-substrate forces in directing 2D crystal formation and offer a platform for engineering tunable supramolecular monolayers via chain-length control.



**Figure** STM images of (a) 4-undeyoxybenzoic acid (4UBA) and (c) 4-decyloxybenzoic acid (4DBA) self-assembled monolayers on Au(111). Proposed structural model of the unitary cell of (b) 4UBA and (d) 4DBA on the Au(111) substrate.

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# TAILORED DESIGN OF NEW CHALCOGEN-BASED SPIRO HOLE-TRANSPORTING MATERIALS FOR PEROVSKITE SOLAR CELLS

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The development of charge-transporting materials in order to improve the photovoltaic performance of perovskite solar cells (PSCs), especially their stability, has been widely investigated during recent years.<sup>1</sup> Our research group developed the preparation of new hole-transporting materials (HTMs) based on new spiro central units, reporting remarkable results both in efficiency and stability.<sup>2</sup> More recently, our group has demonstrated that using asymmetric diarylamines, including specially fragments such as dimethylfluorene, the PCE can be highly improved. Herein, the synthesis and characterization of three new HTMs based on spiranic cores including different chalcogen elements, these being 9H-quinophenoxazine (**spiro-POZ**), 9H-quinophenothiazine (**spiro-PTZ**) and 9H-quinophenoselenazine (**spiro-PSeZ**), are presented. The introduction of the chalcogen atoms has been reported to improve the interaction with the perovskite interface, enhancing the efficiency and stability of the devices. The reported materials have been incorporated in planar PSCs, showing promising values of power conversion efficiency (PCE) in the preliminary studies.

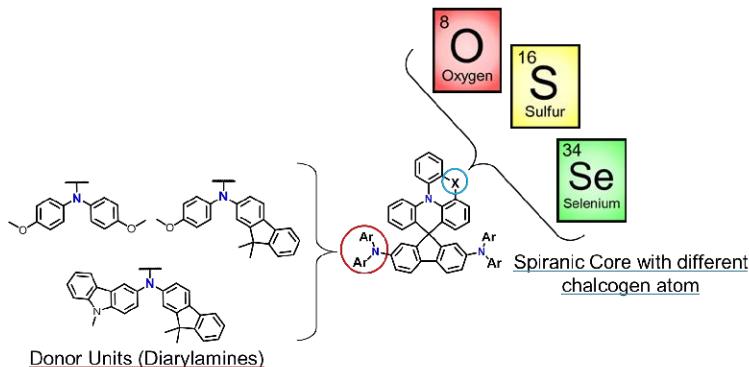


Figure 1. Chemical structure of chalcogen-containing spiro HTMs for Perovskite solar cells

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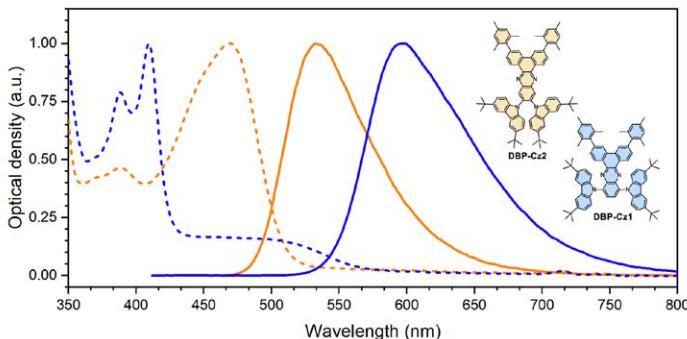
# Luminescent materials for hyperfluorescent OLED devices

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Thermally activated delayed fluorescence (TADF) has enabled the design of purely organic emitters capable of harvesting both singlet and triplet excitons in OLEDs, allowing the devices to achieve internal quantum efficiencies of 100%. Conventional TADF materials are based on donor–acceptor (DA) architectures, which promote charge-transfer excited states and reduce the singlet–triplet energy gap ( $\Delta E_{ST}$ ), facilitating reverse intersystem crossing (RISC) from triplet to singlet at room temperature.<sup>1</sup> Multi-resonant TADF (MR-TADF) materials provide an alternative by localizing frontier orbitals through rigid, fused polycyclic frameworks containing strategically placed heteroatoms (i.e. nitrogen, boron, oxygen). These induce a resonant distribution of frontier states, where HOMO and LUMO are segregated in an atomically alternating layout, that enables narrowband emission via second-order spin–vibronic coupling.<sup>2</sup> Hyperfluorescent OLEDs synergically exploit both types of emitters, where a DA-TADF molecule efficiently transfers excitonic energy via Förster resonance to an MR-TADF fluorophore, combining efficient triplet harvesting with high colour purity.<sup>3</sup>

In this work, we present two new emitters (**DBP-Cz1**,**DBP-Cz2**) that combine electron-poor dibenzo[a,c]phenazine (DBP) with electron-rich carbazole in a fashion that may facilitate the apparition of TADF. Both systems show strong emissions, which remarkably redshift from **DBP-Cz2** to **DBP-Cz1** by modifying the insertion position of the carbazoles into the DBP core (Figure 1). Singlet oxygen generation experiments suggest the accessibility to the triplet manifold which in turn is a precondition for enabling delayed fluorescence. Further experiments are still ongoing to evaluate the delayed fluorescence.



**Figure 1.** Normalized fluorescence (solid line) and absorption (dashed line) spectra of PC8 and PC16 in toluene.

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# Harnessing Antiaromaticity in Molecular Nanographenes: Synthesis, Stability, and Electronic Modulation

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Molecular nanographenes are well-defined graphene fragments whose size, topology, and electronic structure can be precisely engineered through bottom-up synthesis. This level of control has enabled strategies such as  $\pi$ -extension, heteroatom incorporation, and the introduction of non-hexagonal rings to tailor their optoelectronic behaviour.<sup>1</sup> Beyond these classical approaches, the incorporation of antiaromatic units provides a promising route to influence the electronic structure by narrowing the frontier-orbital energy gap and thereby modulating the overall optical and electronic response.<sup>2</sup>

In this work, we report the synthesis of molecular nanographene **1**, featuring a central dibenzo[a,e]pentalene unit, an eight- $\pi$ -electron antiaromatic motif (highlighted in yellow), covalently fused to two hexa-peri-hexabenzocoronene (HBC) subunits (in green). The molecule is assembled through a four-step sequence. Starting from precursor diketone **2**, a double nucleophilic addition of methylmagnesium bromide followed by intramolecular dehydration furnishes the antiaromatic dibromodimethylpentalene **3**. A subsequent twofold Sonogashira cross-coupling with 4-*tert*-butylphenylacetylene affords the bis(arylethynyl) derivative **4** with high efficiency. This intermediate undergoes a double Diels-Alder cycloaddition with tetraarylcyclopentadienone **5**, generating the bis(pentaryl)dibenzopentalene framework **6**. In the final step, oxidative Scholl cyclodehydrogenation establishes twelve new C-C bonds, completing the extended  $\pi$ -framework and preserving the embedded antiaromatic core.

Following its synthesis, the optoelectronic properties of nanographene **1** are being systematically investigated using UV-vis absorption, fluorescence spectroscopy, and cyclic voltammetry, with the aim of elucidating how the embedded antiaromatic unit shapes the electronic structure and optical behaviour.

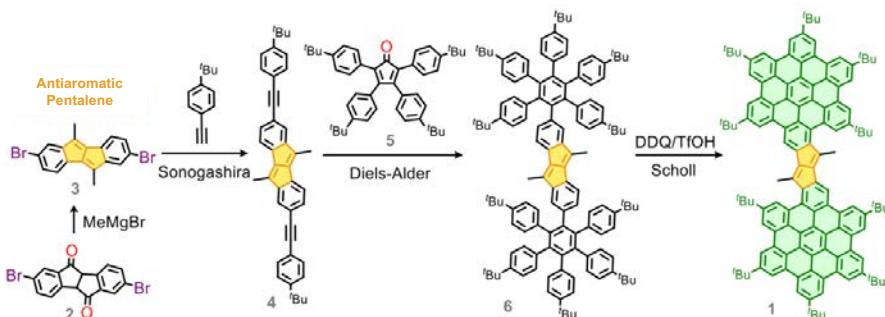


Figure 1. Synthetic sequence toward nanographene **1** with an embedded antiaromatic pentalene unit.

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# Magnetic Nanoparticles as Dual Nanoheaters and Nanothermometers: From $\text{Co}_{0.3}\text{Fe}_{2.7}\text{O}_4$ to Synomag

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In recent years, nanoscale systems capable of simultaneously generating and sensing heat have attracted growing interest [1]. Conventional dual-component constructs combining separate nanoheaters and fluorescent nanothermometers face major drawbacks in biological environments, including photobleaching, scattering, and biocompatibility issues.

To overcome these limitations, we previously demonstrated the label-free thermometric capability of magnetic nanoparticles (MNPs) functioning as both nanoheaters and nanothermometers. Specifically, commercial  $\text{Co}_{0.3}\text{Fe}_{2.7}\text{O}_4$  nanoflowers [2] (Micromod Nanopartikels GmbH) with a crystal size of 30 nm and a dextran coating, resulting in a hydrodynamic diameter of ~50 nm and PDI < 0.1. These MNPs were employed for their efficient photothermal conversion and magnetic relaxation properties. Under 780 nm LED irradiation, heat generation was achieved, and temperature readout was performed via AC magnetometry (10–100 kHz, up to 32 kA/m), exploiting Brownian relaxation for temperature transduction.

This enabled label-free heat generation and self-sensing of temperature variations at the nanoscale. Comparisons with bulk thermometry revealed nanoparticle–solution temperature differences, and MNP performance was further evaluated in protein-conjugated forms and biological media, with experimental data supported by theoretical simulations.

Building on these findings, we will now test the performance of this nanoheaters/nanothermometers in cell culture. In parallel, we will extend this approach to investigate the capacity of Synomag (Micromod Nanopartikels GmbH), a commercial iron oxide nanoparticle, to function as a nanothermometer/nanoheater. This next step aims to assess whether Synomag can replicate or improve upon the temperature-dependent magnetic behavior observed in  $\text{Co}_{0.3}\text{Fe}_{2.7}\text{O}_4$  nanoflowers.

This unified nanoheater/nanothermometer strategy provides a self-referenced and scalable platform for accurate magnetic nanothermometry, offering real-time thermal feedback and strong potential for biomedical applications such as magnetic hyperthermia and controlled drug delivery.

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# Hybrid iron oxide-metal nanoparticles against cancer

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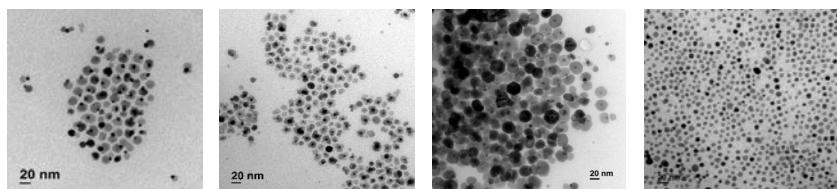
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The ability of magnetic nanoparticles' (MNPs) to transform electromagnetic energy into heat offers enormous promise as a robust and non-invasive therapeutic approach for use in biomedical applications. For tumor suppression, magnetic hyperthermia can be utilized to provide localized heating. The temperature at tumor areas can be raised significantly, lowering the viability of cancer cells[1] [2]. This therapy is minimally invasive, which makes it a promising alternative to other conventional therapies. In addition, it is possible to combine magnetic iron oxides with other materials that bring other interesting properties in hybrid nanostructures.

This study aims to explore the effects of various MNPs and hybrid M-MNPs (M = Au, Cu) on cells. The thermal decomposition of metal precursors was used to prepare MNPs and Au-MNPs with two different morphologies (Figure 1). The nanostructures were then transferred to water by surface modification and characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS), vibrating sample magnetometry (VSM), thermogravimetric analysis (TGA) and UV-Vis-NIR spectroscopy. The ability to generate heat under alternating magnetic fields (magnetic hyperthermia) and near infrared irradiation (phototherapy), as well as their efficiency to act as contrast agents in MRI, were also studied.

*In vitro* analyses were performed in two different cancer cell lines (PANC-1 and MCF-7). The cytotoxicity at different concentrations and incubation times were assessed. Additionally, reactive oxygen species (ROS) and internalization rates were also measured. Finally, cells were subjected to different conditions to assess the effect of hyperthermia on the cells and their mortality rates.



**Figure 1.** TEM micrographs of the MNPs and M-MNPs with different shapes and morphologies. **A)** Spherical shape  $\text{Fe}_3\text{O}_4$ -Au hybrid MNPs **B)** Nanoflowers of  $\text{Fe}_3\text{O}_4$ -Au MNPs. **C)** Spherical shape  $\text{Fe}_3\text{O}_4$ -CuAu hybrid MNPs. **D)** Spherical shape  $\text{Fe}_3\text{O}_4$  NPs.

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# Multifunctionalized gold nanoparticles for Duchenne muscular dystrophy treatment

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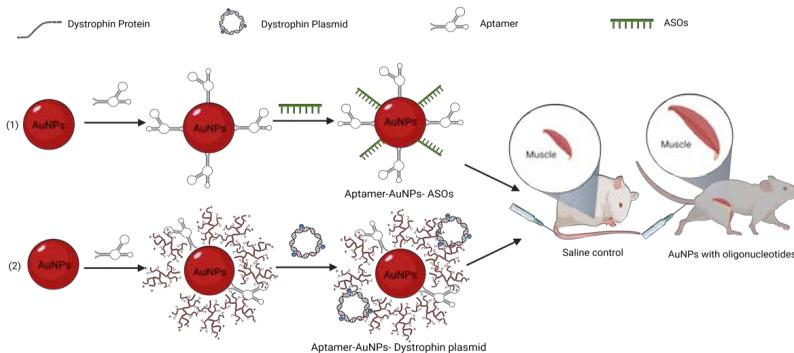
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Duchenne muscular dystrophy (DMD) is a severe X-linked genetic disorder caused by mutations in the dystrophin gene, leading to progressive muscle degeneration and loss of function. Nanoparticle-based oligonucleotide delivery has emerged as a promising strategy to modulate gene expression and restore dystrophin function. Among various nanocarriers, gold nanoparticles (AuNPs) are particularly attractive due to their tunable physicochemical properties and facile functionalization with diverse biomolecules for targeted delivery. In this study, AuNP-based delivery platforms were developed to enhance muscle regeneration in DMD. Citrate-stabilized AuNPs were synthesized and functionalized with thiol-derivative groups to enable electrostatic conjugation with a plasmid encoding a functional dystrophin gene. Remarkably, the AuNPs efficiently delivered dystrophin plasmid DNA (pDNA), resulting in elevated dystrophin mRNA expression. Conjugation with muscle-specific aptamers further enhanced mRNA expression, producing significantly higher levels compared to conventional transfection agents such as Lipofectamine in C2C12 cells. This increase in mRNA levels was confirmed by qPCR, and successful translation into dystrophin protein was validated by western blot analysis. Consistently, muscle regeneration was observed in vivo using immunofluorescence microscopy. In addition to plasmid delivery, AuNPs were applied for antisense oligonucleotide (ASO)-mediated exon skipping. Notably, in vivo administration in D2-mdx mice demonstrated effective exon skipping, confirmed by western blot, accompanied by enhanced muscle regeneration as observed through fluorescence microscopy. Overall, these findings highlight multifunctionalized AuNPs as a safe and efficient platform for both gene and oligonucleotide delivery, demonstrating their strong potential for DMD therapy.



**Figure 1.** Schematic illustration of gold nanoparticle (AuNP)-based delivery systems developed for Duchenne muscular dystrophy (DMD) therapy: (1) AuNP–antisense oligonucleotide (ASO) complexes and (2) AuNP–plasmid complexes.

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# Hybrid aptamer-magnetic nanoparticle tools for cancer therapy and diagnosis

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Magnetic nanoparticles (MNPs) have attracted considerable attention in the biomedical field due to their unique physicochemical properties, such as superparamagnetism, high surface area-to-volume ratio, and facile surface functionalization. Among their various applications, magnetic hyperthermia stands out as a promising cancer treatment modality, wherein MNPs generate localized heat upon exposure to an alternating magnetic field, selectively inducing cell death in tumor tissues while sparing surrounding healthy cells. However, the therapeutic efficacy and safety of magnetic hyperthermia critically depend on the precise accumulation of MNPs at the target site. To address this challenge, targeted therapy strategies have emerged, aiming to enhance the selective delivery of therapeutic agents to diseased tissues while minimizing off-target effects. In this context, we propose the functionalization of magnetic nanoparticles with a specific aptamer (nucleolin, AS1411) to achieve targeted magnetic hyperthermia, combining the heating potential of MNPs with the molecular recognition capabilities of aptamer-based targeting [1]. In this study, we will evaluate these systems in two distinct cancer models: pancreatic cancer (PANC-1) and breast cancer (MCF-7), which represent challenging malignancies with poor prognosis and a high need for improved targeted therapeutic strategies.

Iron oxide nanoparticles ( $\text{Fe}_3\text{O}_4$ , MNPs) were synthesized by the polyol method to obtain uniform nanoflowers with superparamagnetic properties [2]. The particles were coated with polyacrylic acid (PAA) to improve colloidal stability and introduce carboxyl groups (MNP@PAA2). The AS1411 aptamer with a terminal amine group (AS1411-NH<sub>2</sub>) was covalently attached through EDC-HCl/NHS activation of PAA carboxyl groups, forming MNP@PAA2@AS1411. Conjugation efficiency was determined by UV-Vis spectroscopy. Nanoparticles were characterized by TEM, DLS, zeta potential, VSM, TGA, and ICP to evaluate morphology, stability, magnetic behavior, and composition. Biocompatibility was assessed in MCF-7 and PANC-1 cancer cells using the resazurin assay with both bare and AS1411-functionalized nanoparticles. Functionalization of magnetic nanoparticles with aptamers (AS1411) may improve cellular internalization and selective accumulation in cancer cells [3].

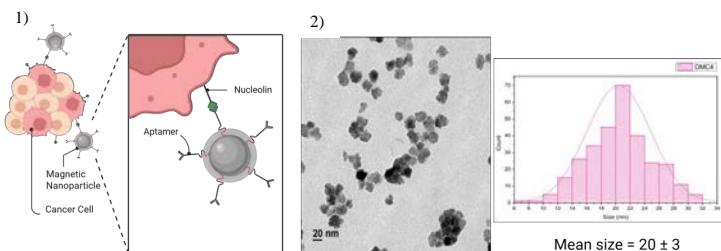


Fig. 1: Diagram illustrating the AS1411 targeted binding to Nucleolin

Fig. 2: TEM: Transmission electron microscopy

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# Novel Methodologies for Monitoring Thermal Conformational Changes of Proteins Conjugated onto Magnetic Nanoparticles

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Monitoring conformational changes in proteins is essential to understand their structure, function, and mechanisms of action. Structural transitions regulate ligand interactions, enzymatic processes, and cellular signaling, and play a crucial role in drug development and the study of illnesses, such as Alzheimer's disease and cancer. Several advanced techniques have been developed to investigate these changes. Circular dichroism (CD) spectroscopy provides insights into the secondary structure, whereas nuclear magnetic resonance (NMR) offers detailed atomic-level dynamics. X-ray crystallography reveals high-resolution structures, but only in crystalline states. The progress of material science is driving a huge interest in nanomaterials acting as protein carriers for different purposes. Traditional techniques fail to monitor conformational changes in the conjugated proteins due to the influence of the nanomaterial in the monitoring signal. Hence, novel methodologies are required to probe protein denaturation in biologically relevant settings. Here, we report the potential of dynamical magnetization measurements to track irreversible thermal conformational changes in the widely studied Bovine Serum Albumin (BSA), when conjugated onto magnetic nanoparticles in HEPES solutions. We achieved this by covalently binding BSA proteins in excess (500 BSA per MNP) using EDC/NHS protocols onto commercial Co<sub>0.3</sub>Fe<sub>2.7</sub>O<sub>4</sub> magnetic nanoparticles (MNPs) with a crystal size of 30 nm, coated with dextran with -COOH terminal groups with a hydrodynamic size of 50 nm. Magnetic measurements sensitively track BSA conformational phenomena during heating and cooling, indicating the irreversible BSA denaturation. We follow the thermal changes by heating from 20 °C up to 60 °C in 40 minutes, maintaining at 60 °C for 120 min, and returning to 20 °C in 40 minutes. These changes were corroborated by two other methodologies: circular dichroism and Fluorescent Polarization Anisotropy (FPA). To follow the changes induced by FPA, we employed differently functionalized BSA proteins by integrating 40 molecules of fluorescein per BSA (40F-BSA). Fluorescein is requested to analyze the optical anisotropy to continuously monitor thermal conformational BSA changes. AC magnetization loops were measured under AC magnetic fields (30 kHz and 24 kA/m) in 0F-BSA and 40F-BSA conjugated to the MNPs. In both cases, the AC magnetic hysteresis area was extremely sensitive to thermal denaturation (both heating and cooling), when measured every 15 min in the same dynamic temperature range employed for optical measurements. Our experimental evidence underlines the potential of dynamical magnetization measurements for monitoring denaturation phenomena in conjugated magnetic nanoparticles. These results offer a novel methodology to probe the thermal stability and functionality of conjugated proteins, which lack accurate techniques.

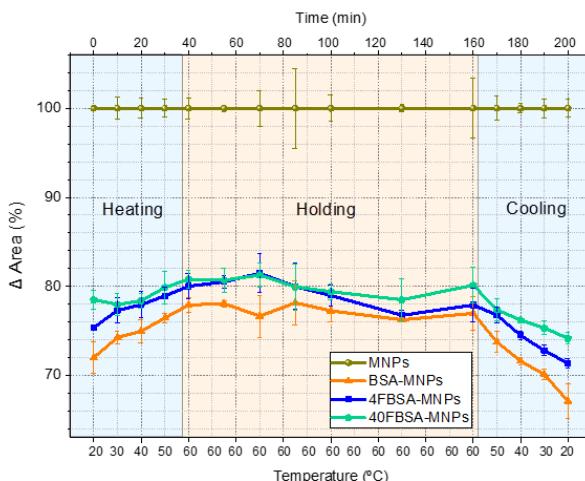


Figure: Magnetic hysteresis loop areas normalized to the MNP control. Each sample was measured in triplicate.

# First-principles calculations of magnetic defects in rare-earth-doped Bi<sub>2</sub>Te<sub>3</sub>

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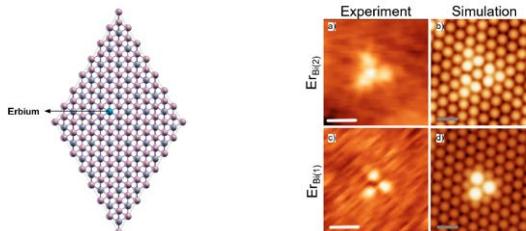
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Magnetic interactions at the surface of topological insulators (TIs) provide an effective route to manipulate the electronic structure and induce exotic quantum phases by breaking time-reversal symmetry (TRS). Opening a Dirac gap in the topological surface state (TSS) of Bi<sub>2</sub>Te<sub>3</sub> is a critical step toward realizing the quantum anomalous Hall effect (QAHE) [1-3]. This study investigates the microscopic origin of TRS breaking induced by submonolayer erbium (Er) deposition on Bi<sub>2</sub>Te<sub>3</sub>, combining scanning tunneling microscopy/spectroscopy (STM/STS), X-ray photoemission spectroscopy (XPS), angle-resolved photoemission spectroscopy (ARPES), X-ray magnetic circular dichroism (XMCD), and quasiparticle interference (QPI) mapping.

Experimentally, STM and XPS reveal the formation of substitutional defects and an additional Bi 5d component, signaling Er–Bi bonding. ARPES shows a dramatic transformation of the Fermi surface from a hexagonal “snowflake” to a “Star-of-David” geometry, accompanied by a Dirac-point gap opening and p-type doping, while XMCD confirms out-of-plane magnetic anisotropy of the Er moments.



**Figure.** Left: Schematic representation of the Bi<sub>2</sub>Te<sub>3</sub> supercell with an Er atom substituting a Bi atom in the second Bi layer. Right: Experimental and simulated STM images for two different substitutional configurations. (a,b) Correspond to the same defect configuration shown on the left. (c,d) Er atom substituting a Bi atom in the first Bi layer.

To interpret these observations at the atomic scale, we performed density functional theory (DFT) calculations using the SIESTA code [4]. Our simulations identify that Er atoms preferentially substitute Bi sites in the first quintuple layer, successfully reproducing the STM topographic contrasts and explaining the associated spectroscopic changes. The combined experimental and theoretical results demonstrate that local magnetic moments from Er adatoms couple strongly to the spin-polarized TSS, inducing a Zeeman-like symmetry breaking and electronic reconstruction, consistent with theoretical models of magnetic doping in TIs [5-7]. These findings are detailed in Ref. [8], which establishes a direct microscopic mechanism for the magnetic modification of topological states, confirming that rare-earth surface doping provides a robust and precise strategy to engineer magnetic topological phases.

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# Machine-Learning Optimization of Antisense Oligonucleotides Targeting lncRNAs: from Rational Design to Delivery

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Antisense oligonucleotides (ASOs) are a promising class of therapeutic agents capable of modulating gene expression through specific hybridization with target RNA sequences, leading to their degradation or functional inhibition via RNase H-mediated mechanisms [1]. In collaboration with Altenea Biotech, this project aims to develop a computational algorithm for the **identification and rational optimization of ASOs targeting long non-coding RNAs** (lncRNAs), a class of transcripts increasingly recognized for their critical regulatory roles in cancer and other diseases [2,3].

As a **proof-of-concept**, the lncRNA **MALAT1**, implicated in breast cancer proliferation, invasion, and metastasis, has been selected as the first target to validate the computational workflow. A foundational algorithm has been established to generate and prioritize 16-nucleotide candidate sequences based on **structural accessibility, thermodynamic stability, and sequence-specific parameters**. Top and Lower-ranked candidates have been synthesized and are currently being evaluated in **breast cancer cell lines** (e.g. MCF-7) to assess their silencing efficiency on MALAT1 expression. These results will provide the first dataset for training and refining the algorithm through **machine learning**, thereby improving its predictive performance and reducing off-target potential in subsequent ASO design iterations [4].

A central aspect of this work is the **rational design** of ASO sequences, **integrating biophysical modeling, RNA structural prediction, and data-driven optimization** to guide the selection of highly specific and effective target sites. This rational approach is key to overcoming the empirical limitations of traditional ASO screening, enabling a systematic and generalizable design strategy applicable to diverse lncRNA targets of therapeutic relevance.

In parallel, distinct **lipid nanoparticle (LNP)** formulations are being investigated as **delivery systems** to enhance ASO uptake, and stability [5]. This integrative framework, combining computational biology, molecular experimentation, and nanocarrier engineering, aims to establish a robust platform for the rational development of precision RNA-targeted therapeutics in oncology.

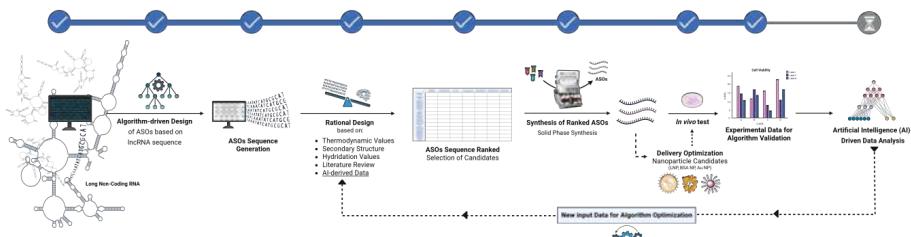


Figure 1. Schematic workflow of the rational design process for ASO synthesis

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# STRUCTURAL AND BIOLOGICAL APPLICATION OF IRON OXIDE NANOFLOWERS CONSTRUCTS FOR ADVANCED TISSUE REGENERATION STRATEGIES

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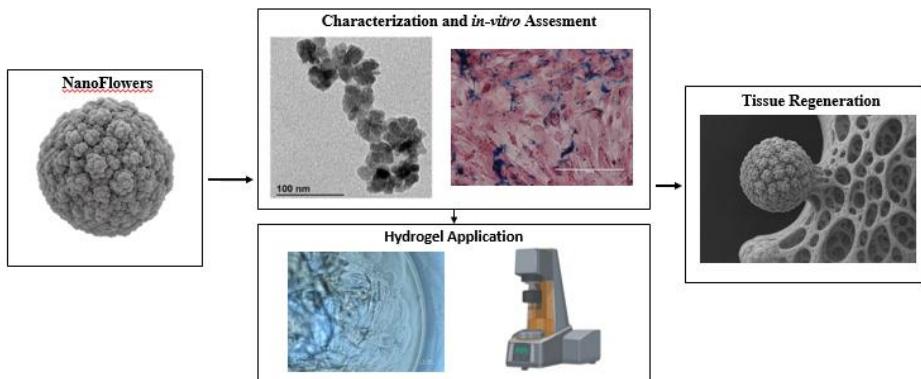
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Superparamagnetic iron oxide nanoparticles (SPIONs) have emerged as multifunctional agents in a wide range of biomedical applications, notably in bone tissue engineering. Their capacity to elicit targeted cellular responses and promote bone regeneration underscores their potential as candidates for bone repair therapies<sup>1</sup>. The synthesis method of SPIONs plays a critical role in defining their structural and magnetic properties, which in turn influence their biomedical performance<sup>2</sup>.

Among SPION variants, Nanoflowers (NFs) are distinguished by their flower-like morphology and typical size of approximately 40 nm, exhibiting highly desirable superparamagnetic behavior<sup>3</sup>. Parameters such as particle size, surface coating, and functionalization have a significant impact on their interactions with cellular environments.

To verify these properties and evaluate their biological response, extensive characterization and *in vitro* studies were performed. Magnetization and chemical composition analyses were conducted to define the synthesized material, while cell viability and internalization assays using mesenchymal stem cells (MSCs) revealed valuable insights into cellular dynamics. These findings are pivotal for the future application of NFs in bone tissue engineering, particularly through mechanotransduction processes<sup>4</sup> and integration with complementary biomaterials.



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Keywords: SPIONs, Nanoflowers, Tissue Engineering, Mechanotransduction

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# A Purely Electromagnetic Explanation Behind the Angle-Dependent Terahertz Photoconductivity of a Nanometric Silicon Grating

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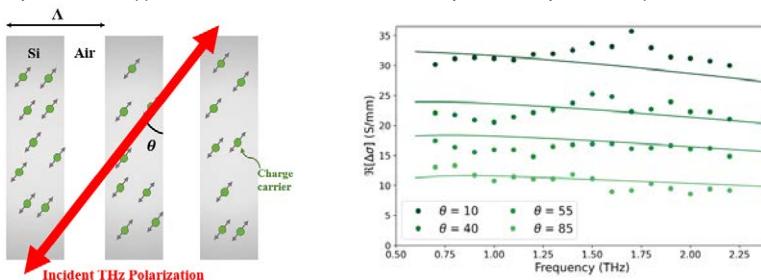
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The charge transport mechanisms in semiconductor nanostructures are a fundamental aspect of modern technology, and understanding them is critical for the design and optimization of electronic devices. To this end, Optical-Pump-Terahertz-Probe (OPTP) spectroscopy has proven to be a powerful technique for investigating the behavior of charge carriers in nanoscale systems [1]. In contrast with contact-based measurements, the optical nature of this approach avoids perturbing the electrical properties of the sample. Moreover, this method enables the determination of the photoconductivity in a spectral range that is highly sensitive to carrier motion in nanostructures, where nanoscale level size effects usually manifest as features in the terahertz response function.

The microscopic physics governing carrier transport can vary significantly depending on the characteristic dimensions of the structure, eventually leading to localization effects as the sample size decreases. Such localization manifests as deviations from the Drude-like behavior expected for free charge carriers. However, as an additional effect in OPTP experiments, purely electromagnetic phenomena can also influence the macroscopic response function of nanometric samples in ways that may be mistakenly attributed to carrier confinement effects [2].

A silicon grating provides an interesting system with a well-defined geometry to study these effects. By using a linearly polarized terahertz electric probe pulse, we vary the angle between the polarization and the grating axis, enabling the investigation of carrier response along paths with varying boundary separation distances. In our OPTP experiment, even in the case of a grating with dimensions large enough to prevent localization, we observe a sizeable modulation in the amplitude of a Drude-like response as a function of the polarization angle. This result can be properly explained within an effective medium approach that takes into account only geometrical factors and bulk properties of silicon. These findings highlight the role of electromagnetic effects in our OPTP experiments on nanoscale systems and supports the use of effective medium theory in the analysis of the spectral data.



**Fig 1. (Left)** Schematic top-view of the photoexcited silicon grating of period  $\Lambda$  and normally incident THz probe pulse. The angle between the polarization direction of the pulse and the grating axis defines the path along which the photojected charge carriers (green dots) are driven by the THz electric field. **(Right)** Real part of the complex-valued effective photoconductivity of the silicon grating for different polarization angles. Solid lines represent the effective medium theory fits considering solely free charge carriers and geometrical factors.

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# Revealing the Delicate Dance of Hydrogen Evolution at Catalytic Interfaces with Time-resolved Vibrational Sum Frequency Generation Spectroscopy

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The direct conversion of sunlight and water into hydrogen fuel represents one of the most promising routes toward a carbon-neutral energy economy, placing photocatalytic water splitting (PCWS) at the centre of global decarbonisation strategies.<sup>1</sup> Molybdenum disulfide ( $\text{MoS}_2$ ) is a promising earth-abundant hydrogen evolution reaction (HER) catalyst, with good band alignment, tunable electronic structure, and nearly ideal hydrogen adsorption energetics.<sup>2</sup> Yet, despite decades of research, the performance of  $\text{MoS}_2$  remains far lower than its theoretical potential. Its limitations arise not solely from its electronic structure but from something far more elusive - the dynamic behaviour of water molecules at its catalytic surface.<sup>3</sup>

At the heart of HER lies a highly complex, transient interplay between charge transfer, proton motion, hydrogen-bond rearrangement, and solvent orientation, all confined to just one or two molecular layers at the solid-liquid interface. These processes occur on femtosecond to picosecond timescales and directly influence reaction barriers and catalytic efficiency, and conventional experimental methods struggle to probe buried interfaces with sufficient temporal, spatial, and chemical specificity. While optical and electrochemical approaches reveal thermodynamics, they cannot capture the real-time molecular dynamics that ultimately govern catalytic performance, creating a blind spot in the rational design of next-generation photocatalysts.

This project addresses that challenge by pioneering the application of time- and phase-resolved vibrational sum-frequency generation spectroscopy (HD-VSFG) to HER-active  $\text{MoS}_2$ . HD-VSFG uniquely combines ultrafast time resolution with vibrational specificity and inherent surface sensitivity, and uses a heterodyne detection method to retrieve both the phase and amplitude of the molecular signals, overcoming long-standing limitations of conventional (homodyne) SFG. In this work, we will apply HD-VSFG to pristine and defect-engineered  $\text{MoS}_2$  crystals while systematically varying pH and temperature - two parameters that strongly modulate proton availability, interfacial fields, and hydrogen-bond structures. By capturing femtosecond snapshots of the interfacial water network during illumination, we will directly observe how solvent dipoles reorient, how hydrogen bonds reorganise, and how interfacial structure couples to electronic processes relevant to HER. Complementary optical pump–terahertz probe measurements will quantify photoexcited carrier dynamics, enabling us to link the observed solvent behaviour to the underlying electronic driving forces.

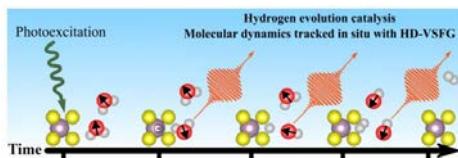


Figure 1: Representation of time-resolved vibrational spectroscopy following pump-induced photocatalysis.

Together, these experiments will establish the first quantitative molecular-level framework describing how interfacial water structure and dynamics limit HER at  $\text{MoS}_2$  active sites, and demonstrate a powerful and broadly applicable methodology for studying buried interfaces in photocatalysis, electrochemistry, and energy conversion. This work aims to unlock new strategies for rational photocatalyst design and contribute meaningfully to the advancement of clean hydrogen technologies.

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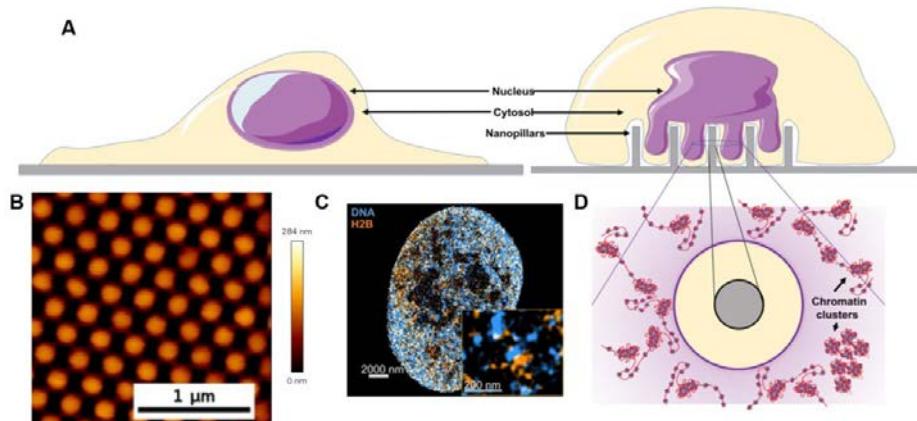
# Using nanofabrication and single molecule localization microscopy to map chromatin remodelling under mechanical stimuli

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Cells respond to physical stimuli from their environment, drastically changing the organization of their DNA and its associated proteins (chromatin). Mechanical stimuli upon the nucleus of the cells (nuclear mechanotransduction) affect cell behaviour, but this mechanism is still not fully understood. This unsolved link is due to the difficulty of finding tools to generate precise mechanical signals and observe changes in chromatin at the nanoscale level. We have used Single Molecule Localization Microscopy (SMLM), a fluorescence imaging strategy that provides a spatial resolution of about 20 nm, to examine the alterations of higher order chromatin folding in cells subjected to local mechanical stimuli provided by nanopillars. We show that primary human fibroblasts easily adhere and proliferate on nanopillars, nanoimprinted from a curable resin, without significant loss of viability. We prove that the optical properties of these nanofabricated surfaces are compatible with SMLM. Quantitative SMLM data show that cells grown on nanopillars present a distinct clustering distribution of key chromatin structure players such as cohesin, when compared to their counterparts grown on flat surfaces. Cohesin proteins aggregate in discrete clusters, which become bigger, denser and further apart upon local mechanical stimuli. This observation points towards a global alteration of topologically associated domains (TADs), the genomic regions in which chromatin interactions are preferentially confined, as a direct effect of the mechanical stimuli. Overall, we show that the combination of nanofabrication and advanced fluorescence microscopy can provide novel insights into the effect of local mechanotransduction on nuclear architecture.



**Figure 1:** A. Effect of nanopillars in nuclear structure B. AFM image showing the nanopillar distribution. C. SMLM imaging of chromatin in somatic cells unveils the nanometric distribution of chromatin. D. Combination of nanopillars and SMLM allows the measurement of the local alterations in chromatin around the nanopillar-induced nuclear mechanotransduction.

# Superconductivity in Twisted Bilayer Graphene

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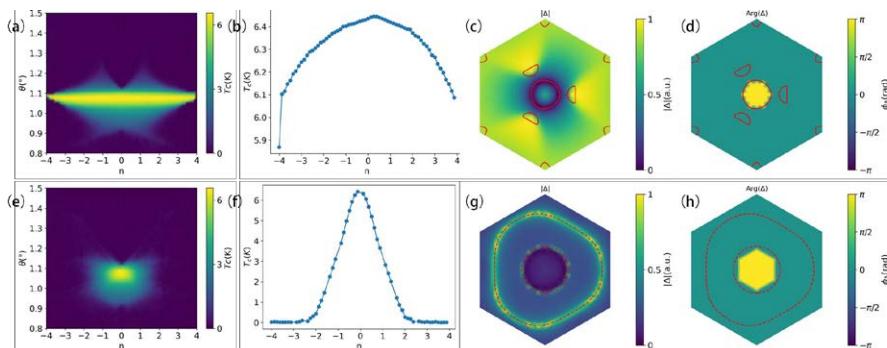
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This work aims to systematically investigate the dependence of the superconducting transition temperature on the twist angle in twisted bilayer graphene (TBG), as well as the influence of the Hartree–Fock effect on its electronic structure and superconducting properties. Within the Kohn–Luttinger theoretical framework, we calculate and analyze the superconducting transition temperature and the corresponding order-parameter symmetry under different twist angles and electron filling conditions. Our results provide theoretical insights into correlated-electron effects and the unconventional superconducting mechanism in TBG systems.



(a) and (b) Results without Hartree correction and (c–h) results including Hartree correction. Panels (a) and (e) show the superconducting transition temperature  $T_c$  map as a function of filling (horizontal axis) and twist angle (vertical axis), where the color scale indicates the magnitude of  $T_c$ . Panels (b) and (f) display the  $T_c$  vs filling line cuts at the magic-angle points corresponding to (a) and (e), respectively. Panels (c) and (d) present the order-parameter amplitude and phase at filling  $n=0$ , while (g) and (h) show the order-parameter amplitude and phase at filling  $n=-2$ , respectively.

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# Measurement of ultrafast spin dynamics and birefringence in quantum materials

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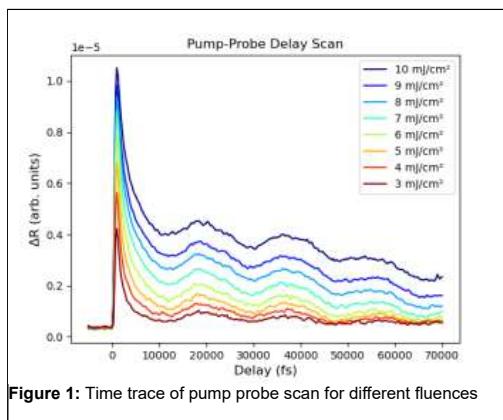
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Ultrafast measurements in quantum materials can capture the dynamic interplay between electrons, spins, and lattice structures revealing hidden phases, transient states, and the underlying mechanisms that give rise to phenomena like superconductivity and exotic forms of magnetism<sup>1</sup>. Magnetism in turn has been used to develop numerous contemporary technologies in the fields of health science, magnetic memory and data storage<sup>2</sup>.

In order to measure the dynamic response of magnetic materials, different experimental techniques have been developed. Time Resolved Magneto Optical Kerr (TR-MOKE) measurement is a powerful pump probe technique capable of measuring magnetization dynamics in materials having magnetic order with femtosecond time resolution via changes the probe polarization<sup>3,4</sup>. Using a newly constructed TR-MOKE we have measured out of plane spin dynamics of multilayer like Pd/Co/Al, and Co/Ta/Pt under different magnetic fields and observed fast magnon dynamics in the multilayer systems. These measurements reveal a strain-spin coupling response in magnetic multilayers and open the possibility of controlled manipulation of magnon excitation through tunable external parameters. We also show that by slight adjustment of the system we can study crystal symmetry breakings in a nonmagnetic transition metal oxide; a single crystal Vanadium Dioxide (VO<sub>2</sub>).

## FIGURE



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# Extracellular temperature measurements

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Nanoscience has been groundbreaking in a wide range of fields, enabling the development of new technologies. One of these fields is biomedicine, where the use of nanothermometers has improved cancer treatment by facilitating the measurement of intracellular temperature [1–3]. Nonetheless, in recent years, the extracellular environment has emerged as a key factor in the development and aggressiveness of tumors such as glioblastoma [4–6]. This has sparked growing interest within the scientific community in studying the extracellular environment, leading to an expansion of current techniques such as hyperthermia and immunotherapy modulation beyond the intracellular level [7–9]. Therefore, understanding the extracellular environment is crucial, as well as developing suitable instruments for this purpose.

Using the nanothermometers developed by Dr. Thompson, we are able to obtain temperature information from the extracellular environment of cells through the fluorescence polarization anisotropy (FPA) signal. In this way, we can achieve a better understanding of cellular behavior under different conditions.

Furthermore, these nanothermometers can be employed in the study of spheroids—three-dimensional cell colonies that more closely resemble real physiological conditions. Finally, the solution developed by Dr. Thompson can also be used in Single-Point Photodynamic Therapy (SP-PDT), a novel laser-based cancer treatment.

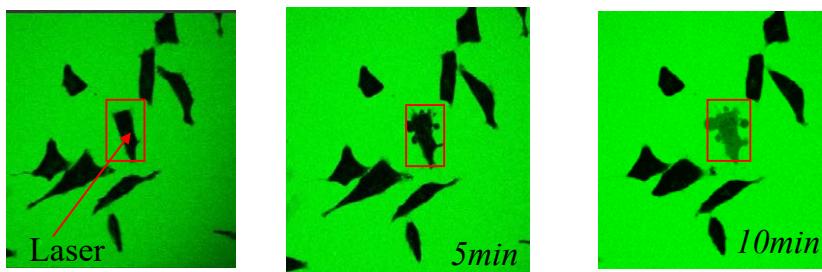


Fig 1. Evolution of the cell death after SP-PDT treatment.

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# Efficient CO<sub>2</sub> optical sensor based on europium 3D MOF/PDMS composite

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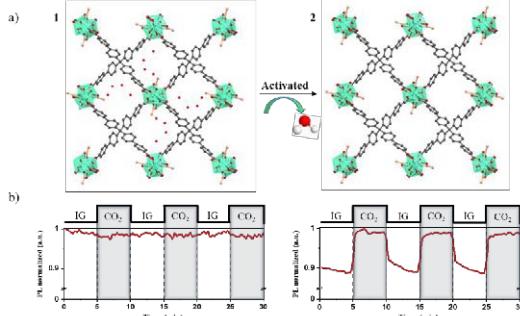
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Nowadays, the increasing concentration of Green House Effect gases (GHGs), and specially, carbon dioxide due to anthropogenic activities has led to concerns about global warming, climate change, and health impacts. Therefore, the detection and monitoring of CO<sub>2</sub> levels are of paramount importance in various domains, including environmental monitoring, industrial process control, and indoor air quality management. So on, the development of effective and reliable CO<sub>2</sub> sensors will be one of the most important challenges for the upcoming generations [1], [2]. Herein, the synthesis and physicochemical characterization of a 3D porous luminescence europium-based MOF for the efficient detection and straightforward quantification of CO<sub>2</sub> molecules have been described.

Exposure of the porous structure to CO<sub>2</sub> triggers a fast Eu<sup>3+</sup> luminescence intensity increase, which is fully reversed upon inert gas purging at room temperature, a process that can be repeated several times without signs of hysteresis, demonstrating the compound's high robustness. Furthermore, the compound was successfully embedded in a PDMS matrix, resulting in a composite material that exhibits a similar luminescence intensity profile to the original compound when exposed to CO<sub>2</sub>, but with even better results. All these results reveal that this compound is a promising candidate for the design of future reusable luminescent sensors for some atmospheric pollutants.



**Figure 1.** a) Crystalline structure of **1** and **2** (after activation, without solvents) b) The PL response of **1** and **2** to CO<sub>2</sub> after activation following exposure to three consecutive inert gas/CO<sub>2</sub> cycles.

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# Development of magnetoresistive sensors in the body temperature range for neural activity detection

Giuseppe Junior Mosca<sup>a</sup>, Paolo Perna<sup>a</sup> and María Teresa González<sup>a</sup>

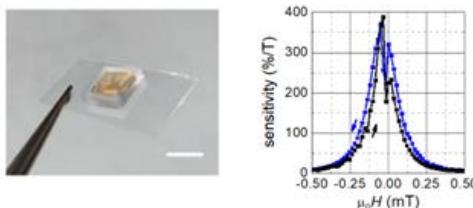
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Magnetoresistive sensors offer the possibility of detecting magnetic fields in wide ranges and with different sensitivities depending on the materials employed, the physical principle exploited for the sensing and, finally, the manufacturing techniques. Many steps have been made to develop sensors with higher sensitivities, higher robustness and lower noise<sup>1</sup> in many fields such as automotive, energy and medicine<sup>2</sup>. In the latter, magnetoencephalography uses big SQUIDS (Superconducting Quantum Interference Devices) to map the brain neural activity through magnetic readings with femtoTesla resolution. However, unfortunately, there is a lack of implantable devices with sufficient sensitivity for detecting neural magnetic signals, which leaves electric sensors as the only available option for implantable applications. Nowadays, these electric sensors, which rely on the change interchange at the tissue-device interface, fail frequently in the medium term, which hinders scientific progress in the diagnosis and treatment of disorders such as Parkinson's disease and epilepsy.

Therefore, the aim of this project, as part of the NeuroNanotech Doctoral Network, is the complete characterization of new high-sensitive magnetoresistive sensors from room to body temperature, including the development and optimization of implantable prototype devices. The properties of the sensors developed in IMDEA as well as by the other researchers of the Doctoral Network will be studied and compared to state-of-the-art commercial sensors of high performance but not suitable for implantation.

Characterization will be carried out with nanomagnetism, spintronics and advanced low-noise electronics techniques, while the manufacturing of prototype devices and the study of their biocompatibility will require nanofabrication and cleanroom microfabrication techniques, essential for the integration of the sensors into soft substrates. Coatings in the developed prototype devices, special care will be taken to encapsulate the sensors with soft biocompatible polymeric to ensure smooth integration in living tissues probes, as sensors and electrodes will be prepared to be used in biological environments. Through recordings of neural magnetic signals under in-vitro and in-vivo conditions, the goal is to correlate the electrical signals recorded by electrodes with the corresponding magnetic signals, and determine how magnetic recordings can complement the former, bringing new information, and improve their stability over time.



**Fig.1.** On the left, example of a magnetic sensor prototype on a thin layer soft substrate. On the right, example of the variation of the sensitivity and AMR of the sensor with the applied magnetic field<sup>3</sup>.

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# Harnessing Nanotechnology to Boost Immunotherapy Against Cancer

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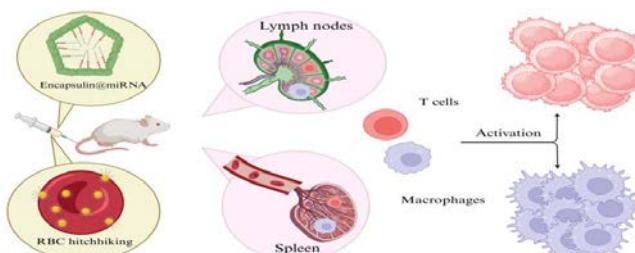
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Tumors employ diverse and coordinated immune-evasion strategies that suppress T-cell activation and skew macrophage polarization, establishing an immunosuppressive tumor microenvironment (TME) that limits the efficacy of immune checkpoint blockade and other immunotherapies (1). Although immunotherapy has transformed cancer treatment, clinical outcomes remain variable due to factors such as T-cell exhaustion, low neoantigen load, and resistance driven in part by dysregulated non-coding RNAs (2). MicroRNAs (miRNAs) have emerged as potent immunomodulators capable of simultaneously regulating T-cell differentiation, macrophage polarization, and immune-checkpoint pathways (3, 4).

We are developing two nanobiocarriers for immune-organ delivery of immune-stimulatory miRNAs: Encapsulin protein nanocompartments (5), which naturally accumulate in the liver; Erythrocytes conjugated with gold nanoparticles (RBC-AuNPs), which traffic to the spleen without requiring targeting ligands and have shown strong potential for immune priming (6, 7).

We have purified *Thermotoga maritima* encapsulin; TEM confirmed well-defined nanocage morphology, and encapsulation assays showed high miRNA loading efficiency. Additionally, biophysical studies are currently being carried out on both carriers to evaluate how miRNA and/or AuNP loading may modulate their dynamics and deformability, key factors for biodistribution and targeting, with the aim of enhancing accumulation in immune niches. These platforms will be evaluated *in vitro* on both cancerous and immune cells before *in vivo* testing in an immunotherapy-resistant colorectal cancer (CRC) model, a malignancy characterized by minimal neoantigen presentation and poor response to checkpoint blockade (8, 9).

By activating innate and adaptive immunity within secondary lymphoid organs, we aim to expand functional cytotoxic T-cell and M1-like macrophage populations capable of overcoming the immunosuppressive TME. This immune-organ-priming strategy represents a departure from conventional tumor-targeted nanotherapies and offers a promising approach to bypass tumor-induced immune exhaustion. Ultimately, our encapsulin- and RBC-based miRNA nanodelivery platforms aim to redefine immune modulation in cancer therapy, providing a technologically advanced route to overcome major limitations of current immunotherapies.



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# Engineering Flow in Wall-less channels: 3D Transient Modelling of Liquid Tube Technology

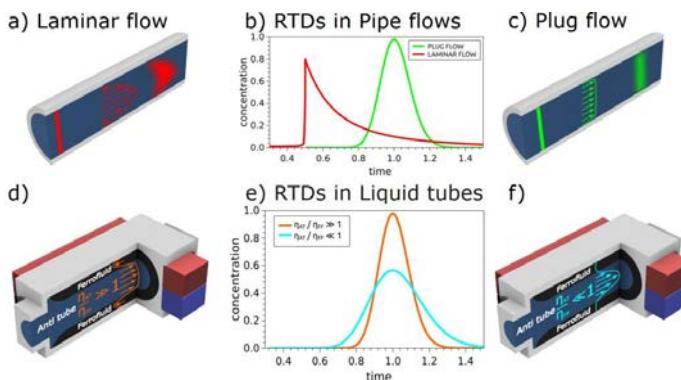
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Flow reactors are essential in the modern chemical industry, since they offer significant advantages, including enhanced control over key reaction parameters such as temperature, mixing, and residence time. These features leads to improved yields, product quality, production costs, therefore their importance is growing rapidly as the fine chemical sector shifts toward more sustainable, efficient, and digitally controlled manufacturing processes. Despite their beneficial features, flow reactors also have their drawbacks. For example, in laminar flow reactors (Fig. 1a), the parabolic velocity profile causes a wide residence time distribution (RTD, Fig. 1b), which decreases the selectivity and yield. In the turbulent regime (Fig. 1c) in contrast, plug flow can be achieved with narrow RTD (Fig. 1b), but this only works at high flow rates (and elevated pressure drop), which increases operational costs and is not applicable to long residence times.

Liquid tube technology is a recent innovation based on a completely new fluidic paradigm, where a central liquid channel is surrounded by an immiscible magnetic fluid confined by a quadrupolar magnetic field<sup>1</sup>. By strategically applying magnetic fields, it is possible to create truly wall-less inner channels. In these nearly frictionless channels, highly viscous fluids can be flowed, and challenging reactions can be carried out that clog traditional flow reactors<sup>2</sup>. Besides proving that such devices are ideal for flow chemistry applications due to their advantageous features like no clogging, self-healing and high drag reduction, our group has also shown that the flow profile inside the liquid-walled channels is plug flow-like (Fig. 1d), even though the Reynolds number is low<sup>3,4</sup>.

In this work, computational fluid dynamics is used to develop a ferrohydrodynamics model that couples the motion of two immiscible phases in a magnetic field. This enables fully 3D transient simulations, allowing the liquid tube technology to be studied in unprecedented detail. By modelling the system not only the exploration but also the engineering of the flow in wall-less channels become possible. Several such systems has been designed and experiemntally validated, demonstartng that the flow profile, and with it the residence time distribution, can be tailored by changing the viscosity ratio of the ferrofluid and inner channel fluid (Fig. 1d,e,f).



**Figure 1** The velocity profile and the concentration distribution in case of a) laminar flow and c) plug flow, and the resulting RTDs b). Velocity flow profiles if the viscosity of the ferrofluid (FF) is d) lower, f) larger than the liquid of the anti-tube (AT) and e) the expected RTDs of liquid tube devices.

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