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2018

# 8th early stage researchers workshop in nanoscience

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EXCELENCIA SEVERO OCHOA 2017 - 2021
AGENCIA ESTATAL DE INVESTIGACIÓN
GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD
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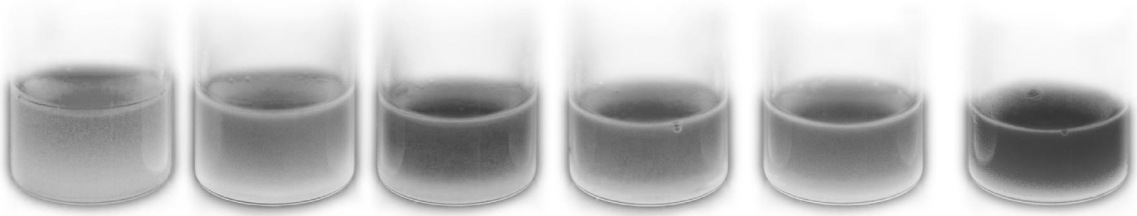

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# 8th ESRW in Nanoscience
# Madrid (Spain), June 13−14, 2018

Organized by the Madrid Institute for Advanced Studies in Nanoscience (IMDEA Nanoscience)

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# PROGRAM

# Wednesday, June 13

**9:00- 9:45** Registration

**9:45-10:00** **OPENING**
***Prof. Nazario Martín**, Universidad Autónoma de Madrid, (UAM)*

**10:00-11:00** **INVITED LECTURE** *(Sponsored by Fisher)*
***Dr. Javier Ramón Azcón,** Institute for Bioengineering of Catalonia (IBEC)*
*Title: Metabolic Cross-talk Approach by Multi-Organ-on-a-Chip*
*Chair: Alvaro Somoza*

**11:00-11:30** **Coffee Break & Photo** *(Sponsored by Bruker)*

***SESSION 1***
*Chair:*
*Ana Espinosa*

**11:30-11:45** **O1 – Patricia Bondia Raga,** *IMDEA Nanociencia,* Nanoscale imaging of light-induced damage in amyloid fibers

**11:45-12:00** **O2 – Aritz García Arribas,** *Instituto Biofisika (CSIC, UPV/EHU),* Ceramide effects on lipid bilayer heterogeneity under the AFM

**12:00-12:15** **O3 – Alberto Hidalgo,** *UCM*, Pulmonary surfactant and drug delivery: to alveoli and beyond

**12:15-12:30** **O4 – Julene Madariaga-Marcos,** *CNB-CSIC,* Characterization of protein kinetics at the single-molecule level combining microfluidics, Lateral Magnetic Tweezers and TIRF Microscopy

**12:30-12:45** **O5 – Natalia Martín González,** *UAM,* Understanding the Role of DNA condensing proteins in viral chromatin with Atomic Force Microscopy

**12:45-13:45** **POSTER SESSION 1**

**13:45-15:15** **Lunch**

***SESSION 2***
*Chair:*
*Marco Cordani*

**15:15-15:30** **O6 – Alejandro Martín González,** *CNB-CSIC*, Atomic Force Microscopy shows DNA-bridging by human CtIP

**15:30-15:45** **O7 – Juan Luis Paris,** *UCM,* NANOparticles for antiVAscular Multimodal therapy: Photothermal, photodYnamic and dual drug RElease (NANOVAMPYRE)

**15:45-16:00** **O8 – Carmen Suay-Corredera,** *CNIC,* Calibration-independent Atomic Force Microscopy

**16:00-16:15** **O9 - María Rocío Villegas Díaz,** *UCM,* Hybrid Nanocarriers for the Treatment of Cancer

**16:15-16:45** **Coffee Break** *(Sponsored by Bruker)*

***SESSION 3***
*Chair:*
*Andrew Norris*

**16:45-17:00** **O10 – Elena Beltrán de Heredia Rodríguez,** *UCM,* Curvature Induces Cardiolipin Sorting

**17:00-17:15** **O11 – Daniel Casaleiz,** *IMDEA Nanociencia,* Synthesis and Advanced 3D-printing of Polymerized Composites Based in Metallic Particles

**17:15-17:30** **O12 – Paula Corte Leon,** *UPV/EHU*, Engineering of magnetic properties of Co-rich microwires by Joule heating

**17:30-17:45** **O13 – Christin David,** *IMDEA Nanociencia,* Plasmonic properties of electrolytes beyond classical nanophotonics - Nonlocal soft plasmonics

**17:45-18:00** **O14 – Leticia de Melo Costa,** *IMDEA Nanociencia,* Exchange coupling effects in hybrid Gr-4f RE systems

# Thursday, June 14

**10:00-11:00** **INVITED LECTURE**
***Dr. Nair López Martínez,*** *Universidad Autónoma de Madrid, (UAM)*
*Title: 4-colours/2-junctions solar cells: 4 SUNS project*
*Chair: Borja Ibarra*

**11:00-11:30** **Coffee Break** *(Sponsored by Bruker)*

**11:30-11:45** **O15 – Fernando Jiménez,** *IMDEA Nanociencia,* Towards Fabrication of MoS2 P-N Homo-junctions via Pulsed Focused eBeam Induced Etching

**11:45-12:00** **O16 – Sergio Ramirez,** *IMDEA Nanociencia,* Reaction Products obtained in the Hydrothermal Synthesis of Carbon Dots

**12:00-12:15** **O17 – Beatriz Rodilla,** *IMDEA Nanociencia,* Nanowire interfaces as nanoelectrodes for neural electrical stimulation at the spinal cord

**12:15-12:30** **O18 – Victor Rollano García,** *IMDEA Nanociencia,* Topological protected superconducting ratchet effect produced by spin ice magnet

**12:30-12:45** **O19 – Chen Sun,** *IMDEA Nanociencia,* The Influence of β-Phase Conformation on Transient Absorption and Light Amplifying Properties of Polydiarylfluorene

***SESSION 4***
*Chair:*
*Manuela Garnica*

**12:45-13:45** **POSTER SESSION 2**

**13:45-15:15** **Lunch**

**15:15-15:30** **O20 – Arturo Gamonal,** *IMDEA Nanociencia,* Divergent Sorption Behaviour of Isostructural Luminescent Lanthanide-based Metal-Organic Frameworks as Key for the Design of Novel, Selective and Sensitive Gas Sensors

**15:30-15:45** **O21 – Juan Gurruchaga Pereda,** *Donostia International Physics Center,* Bioorthogonal Photocatalysis for prodrugs activation

**15:45-16:00** **O22 – Sonia Infante Tadeo,** *IMDEA Nanociencia,* Osmium(II) tether complexes with a coordinatively bound oxygen atom capable of hijacking and releasing a proton

**16:00-16:15** **O23 – Yurena Luengo,** *IMDEA Nanociencia,* Evaluation of antibacterial activity of magnetite/Ag nanocomposites with different silver content synthesized by an aqueous route

***SESSION 5***
*Chair:*
*Jose Santos*

**16:15-16:45** **Coffee Break** *(Sponsored by Bruker)*

**16:45-17:00** **O24 – Paloma Martínez Martín,** *UAM,* Pyridine/Diazine derivatives to access a new lanthanide luminescent materials

**17:00-17:15** **O25 – Lucía Palomino Ruiz,** *Universidad de Granada***,** Synthesis of non-planar nanographenes

**17:15-17:30** **O26 – Michele Pisarra,** *IMDEA Nanociencia,* Nanostructured graphene catalyzes the reaction between two organic molecules

**17:30-17:45** **O27 - Sonia Romero Perez,** *UAM,* Oligonucleotide-Templated Stacking of Semiconductors

**17:45-18:00** **O28 – Julia Villalva,** *IMDEA Nanociencia,* Band gap opening in metallic single-walled carbon nanotubes by encapsulation of an organic salt

***SESSION 6***
*Chair:*
*Amalía*
*Rapakousiou*

**18:00-18:15** **AWARDS & CLOSING REMARKS**

# POSTER SESSION 1, 13 June

**P1 –** New Hole Transporting Material for Perovskite Solar Cells
**Abasi Abudulimu,** *IMDEA Nanociencia*

**P2 -** Design of bactericidal surfaces by using micro-nano hierarchical topographies
**María Teresa Alameda Felgueiras***, IMDEA Nanociencia*

**P3 -** Mechanical softening of lipid membranes by the rotating motor protein F1F0 ATP synthase
**Víctor G. Almendro Vedia,** *UCM*

**P4 -** Magnetic microwires for contact-less sensing application
**Diego Archilla***, Instituto de Magnetismo Aplicado (IMA) [UCM-ADIF-CSIC]*

**P5 -** Carbon nanodots for the oxygen reduction reaction electrocatalysis
**Iria Bravo,** *UAM*

**P6 -** Organometallic iridium(III) cyclopentadienyl complexes bearing a structural strain as potential anticancer
**Ana Carrasco,** *IMDEA Nanociencia*

**P7 -** The many faces of the topological insulator BiTeCl
**Pablo Casado Aguilar,** *IMDEA Nanociencia*

**P8 -** Functionalized gold nanoparticles for the detection of uveal melanoma miRNAs
**Catarina Coutinho,** *IMDEA Nanociencia*

**P9 -** Biomedical application of novel magnetic detection methodology based on AC magnetometry
**Lucía Cremades,** *IMDEA Nanociencia*

**P10 -** Interfacing porphyrins and carbon nanotubes through mechanical links
**Leyre De Juan,** *IMDEA Nanociencia*

**P11 -** Simultaneous AFM nanoindentation and fluorescence microscopy of soft materials and individual bacteria
**Adrián Del Valle,** *IMDEA Nanociencia*

**P12 -** Protein engineering for improved delivery in CRIPSR-based gene editing strategies
**Carmen Escalona Noguero***, IMDEA Nanociencia*

**P13 -** Computational studies of core protonated and β-brominated of meso-tetraphenylporphyrin: High saddle shape structure properties
**Mortaza Eskandari***, Institute for Advanced Studies in Basic Sciences (IASBS)*

**P14 -** A Robust and Unique Iron (II) Mosaic-like MOF Architecture
**Estefanía Fernández Bartolomé***, IMDEA Nanociencia*

**P15 -** Alveolar dynamics: implication on drug delivery assisted by pulmonary surfactant
**Cristina García Mouton,** *UCM*

**P16 -** Synthesis of ferrite nanoparticles for biomedical applications
**David García Soriano***, IMDEA Nanociencia*

**P17 -** Smart self-immolative polymers as pH-responsive gatekeepers for mesoporous carbon nanoparticles
**Miguel Gisbert Garzarán,** *UCM*

**P18 -** Superconductivity in tungsten carbide nanostructures and its importance in STM experiments performed on metal-supported graphene
**Cosme Gonzalez Ayani,** *IMDEA Nanociencia*

**P19 -** Graphene/Ferromagnetic epitaxial stacks grown on oxides with tuned spin orbit coupling
**Adrián Gudín Holgado***, IMDEA Nanociencia*

**P20 -** Influence of ball milled pyrex free magnetic microwires on strontium ferrite, BHmax
**Papa Gorgui Birame Gueye,** *Instituto de Magnetismo Aplicado, UCM*

**P21 -** Moth-eye antireflective and self-cleaning surfaces with enhanced mechanical properties
**Alejandra Jacobo Martín**,*IMDEA Nanociencia*

**P22 -** Study of phase separation in a negatively charged colloid / polymer system
**Mikheil Kharbedia***, UCM*

**P23 -** Reaction of platinum(II) complexes with bismuth−halides: Pt−C(sp3) or Pt−C(sp2) bond cleavage
**Maedeh Koohi***, Institute for Advanced Studies in Basic Sciences (IASBS)*

**P24 –** Functionalization of Magnetic Nanoparticles with Gemcitabine and Doxorubicin via disulfide bonds
**Nuria Lafuente Gómez,** *IMDEA Nanociencia*

**P25-** Advanced Therapies Based on Nanoparticles: efficient drug delivery and CRISPR/Cas9 gene editing
**Ana Belén Latorre Lozano,** *IMDEA Nanociencia*

**P26-** Continuously modulate Förster energy transfer from fluorescein to rodamin 6G by electrical doping graphene
**Yansheng Liu***, IMDEA Nanociencia*

**P27 -** In vitro study of the thermal stress mediated by iron oxide nanoparticles sujected to infrared irradiation and/or alternating magnetic fields
**Claudia Lozano***, IMDEA Nanociencia*

# POSTER SESSION 2, 14 June

**P28 -** Interaction of L-Alanine and L-Dialanine with Aluminium Oxide surfaces
**Juan Carlos Martín,** *IMDEA Nanociencia*

**P29 -** Antimonene 2D single layers as supercapacitors
**Emiliano Martínez Periñán,** *UAM*

**P30 -** Towards graphene-based field effect transistors
**Victor Marzoa,** *IMDEA Nanociencia*

**P31 -** Carbon Dots Modified Electrodes for Catalysis of Hidrazine
**Mónica Mediavilla Supe,** *UAM*

**P32 -** Towards the Synthesis of a Nanoswimmer
**Sofía Mena Hernando***, IMDEA Nanociencia*

**P33 -** Uveal Melanoma Treatment Based on Gold Nanoparticles: Oligonucleotide Therapy Combined with Chemotherapy
**Paula Milan Rois,** *IMDEA Nanociencia*

**P34 -** Genetherapy for Osteoporosis using Mesoporous Silica Nanoparticles to Deliver sost siRNA and Osteostatin
**Patricia Mora Raimundo,** *UCM*

**P35 -** Nanocarrier for a controlled protein delivery to tumoral cells
**Victor Moreno Zafra,** *UCM*

**P36 -** Magnetic Composites: Strontium Ferrite with Magnetic Microwires and the dependence of its magnetic properties with the proportions
**Alberto Moya,** *Instituto de Magnetismo Aplicado (UCM)*

**P37 -** Advantages of carbon-coated superparamagnetic nanoflowers for lateral flow immunoassays
**Amanda Moyano Artime,** *Universidad de Oviedo*

**P38 -** A neural bypass for sensing and stimulating at the spinal cord
**Vicente Muñoz Martínez,** *IMDEA Nanociencia*

**P39 -** Efficient expression of OPA1 mitochondrial membrane fusion protein in in vitro and in vivo experiments by using Gemini/DOPE - based Lipoplexes
**Mónica Muñoz Úbeda,** *Instituto de Investigación Biomédica Hospital 12 de Octubre*

**P40 -** Loading capacity and stability of Gold Nanoparticles conjugated with oligonucleotides
**Demian Pardo Filippidis***, IMDEA Nanociencia*

**P41 -** In vitro Catalytic Transfer Hydrogenation Studies of Organoiridium Complexes
**Sonia Paz,** *IMDEA Nanociencia*

**P42 -** Endosomal escape of plasmonic gold nanoparticles mediated and quantum dots by Listeria monocytogenes Listeriolysin O toxin LLO
**Ismael Plaza García-Abadillo***, UCM*

**P43 -** Electrically conducting coordination polymer as an acetonitrile chemical sensor
**Esther Resines Urien,** *IMDEA Nanociencia*

**P44 -** A single-molecule manipulation assay to study the transcriptional dynamics of Influenza A virus
**Carlos Rodríguez Pulido,** *IMDEA Nanociencia*

**P45 -** In silico magnetic hypethermia: insights for a treatment planning platform
**Irene Rubia,** *IMDEA Nanociencia*

**P46 -** Enhancement of magnetic lateral flow immunoassays by means of a magnetic field gradient
**María Salvador Fernández,** *Universidad de Oviedo*

**P47 -** Fundamentals of detection methodology based on the AC magnetization signal of functionalized magnetic nanoparticles in biological fluids
**Elena Sanz de Diego,** *IMDEA Nanociencia*

**P48 -** MOF:PDMS Composites as a Promising Luminescent Chemosensors: Photophysics and Sensing Characterization
**Ahmad Sousaraei,** *IMDEA Nanociencia*

**P49 –** Preliminary study on a thermoresponsive drug delivery system based on the combination of magnetite NPs and liposomes
**Andrea Tabero,** *UAM*

**P50 -** Optimization of the resolution of pauses in biological motors
**Andrés Tejedor Reyes,** *UCM*

**P51-** Single Molecule Spectroscopy of Key Protein-Protein Interactions in the Pyruvate Dehydrogenase (PDH) Multienzyme complex
**Cintia Vequi-Suplicy,** *IMDEA Nanociencia*

**P52**- High coercive MnBi magnets for high temperature applications, from quasi-isotropic particles to textured films
**Melek Villanueva,** *IMDEA Nanociencia*

**P53 -** Entropy reduction by information in feedback flashing ratchets
**Daniel Villarrubia Moreno,** *UCM*

# ABSTRACTS

# Metabolic Cross-talk Approach by Multi-Organ-on-a-Chip

**Javier Ramón-Azcón**

*Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Baldiri Reixac 10-12, 08028 Barcelona Spain*

The pharmaceutical industry relies heavily on in vivo animal models and in vitro two-dimensional (2D) cell cultures to develop therapeutic strategies. There are many ethical issues surrounding animal studies and serious concerns also exist regarding their biological relevance to humans. The ability to extrapolate animal model data to human conditions is limited. Current in vitro tissues are useful for studying the molecular and cellular basis of physiological and pathological responses of biological processes. Integration of human cells in these tissues and their applications in vitro drug discovery processes increase the potential for success in pharmaceutical development. However, current in vitro tissue models are 2D and do not consider the complexity of physiological microenvironment in which the cells grow. Particularly, current 2D tissue models often do not simulate complex cell-cell and cell-matrix interactions, which are crucial for regulating cell behaviours in vivo. Due to these shortcomings, there is now substantial interest in developing fully functional 3D tissues that mimic the in vivo system closely as possible for the disease modelling and chemical testing.

Microscale fabrication technologies have emerged as potentially useful tools in tissue engineering and biological applications. As such, organ-on-a-chip devices have the potential to revolutionize the pharmaceutical industry by enabling reliable and high predictive in vitro testing of drug candidates. The capability to miniaturize biosensor systems and advanced tissue fabrication procedures have enabled researchers to create multiple tissues on a chip with a high degree of control over experimental variables for high-content screening applications. Most of the existing on-chip tissue models represent a single organ, preventing investigations on a drug's systemic effect. Microscale tissue systems attempt to improve the prediction of the effects of drugs and toxicity on various organs or tissues. This is especially important if both tissues are closely related with the disease, as are skeletal muscle and pancreatic islets for diabetes type II. The goal of Biosensors for bioengineering group (Bfb) is the fabrication of a biomimetic multi organ-on-a-chip integrated device composed of different functional tissues and study the metabolic cross talk within them. We aim to design a novel therapeutic tool to test drugs with a multi organ-on-a-chip device. Such finding would improve drug test approaches and would provide for new therapies to monitor complex disease.

# Organo- and Photo-Catalytic Materials in Organic Synthesis

*José Alemán*

[a]*Departamento de Química Orgánica (Módulo 1), Facultad de Ciencias, Universidad Autónoma de Madrid, 28049 Madrid, Spain. E-mail: jose.aleman@uam.es; webpage: www.uam.es/jose.aleman* [b]*Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, 28049 Madrid, Spain.*

***Photocatalysis*** or Photo-induced transformations have been at the forefront of chemical research for many years, yet lately they have received enormous interest.[1] The basis for modern photocatalytic methodologies is set on the transmission of photons to a specific molecule - a photosensitizer, which can be parlayed into the population of the molecule's excited state. This energy can then be transferred to other substrates via energy or electron transfer, wherein the pairing of excited-state energies and of redox potentials, respectively, of the sensitizer and the reactive substrate is crucial for a successful outcome in photochemical reactions. On the other hand, ***Organocatalysis***, the use of small organic molecules as catalyst for organic transformations, have been stablished as a new tool in organic synthesis. Although, these two catalysis, organo- and photo-catalysis, have been well-developed in a homogenous fashion, the use in heterogeneous catalysis have been less explored.

Very recently, our group has started a new research line concerning the use of photocatalytic and organocatalytic materials. Different advantages of these materials in comparison with the homogeneous catalysis will be shown in this communication. Among others, COF, MOF and mesoporous silica have been selected as materials for carrying out photo- and organo-catalysis.

# ORAL COMMUNICATIONS

# Nanoscale imaging of light-induced damage in amyloid fibers

**Patricia Bondia,*[a] Adrián del Valle,[a] Begoña Sot,[a] Youhei Sohma,[b] Motomu Kanai,[b] and Cristina Flors [a]**

[a]*Madrid Institute for Advanced Studies in Nanoscience (IMDEA Nanoscience), C/Faraday 9, Madrid 28049, Spain, Tel: +34912998700*
[b]*Graduate School of Pharmaceutical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan, Tel: +81358414830*

*E-mail: patricia.bondia@imdea.org*

The misfolding and aggregation of proteins into amyloid fibers is generally toxic and is involved in many neurodegenerative disorders. Photochemical strategies are becoming an interesting alternative to degrade amyloid aggregates and fibers. In our studies we use a thioflavin T derivative (Figure 1), which is able to target pathogenic aggregates in the presence of non-pathogenic proteins [1]. In addition to fluorescence, this compound produces reactive oxygen species upon blue light exposure, affecting amyloid structures through oxidation [1]. We investigate the photodynamic damage induced by this compound on model amyloid fibers using a combination of spectroscopic tools and correlative fluorescence and atomic force microscopy. Our results provide a nanoscale view of light-induced amyloid breakage, and are relevant to improve phototherapeutical strategies for amyloid-related disorders.

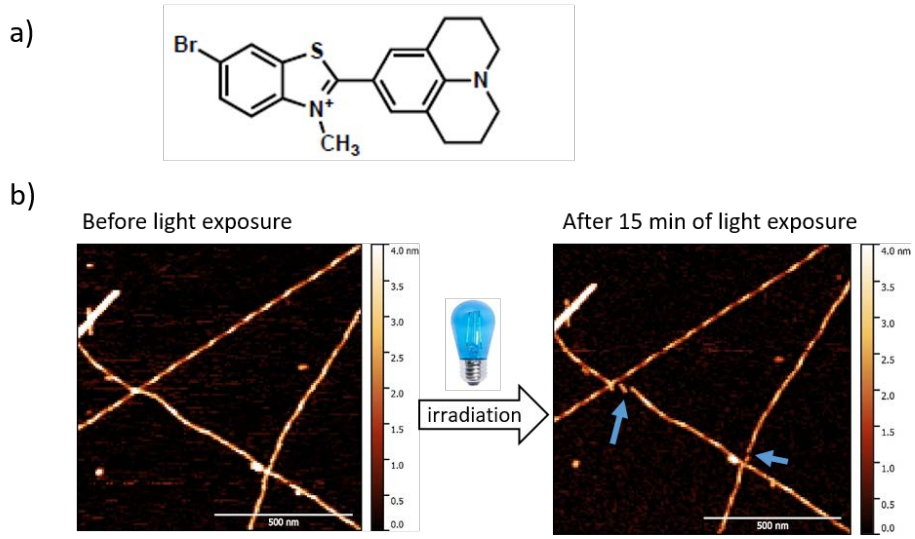


FIGURE1. a) Thioflavin T derivative structure. b) AFM images of β-lactoglobulin amyloid fibers labeled with compound a) before and after blue light irradiation. On the right panel fiber breakage was detected.

## References

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# Ceramide effects on lipid bilayer heterogeneity under the AFM

**Aritz B. García-Arribas*[a,b], Jesús Sot[a.b], Alicia Alonso[a,b] and Félix M. Goñi[a,b]**

[a]*Instituto Biofisika (CSIC, UPV/EHU), Barrio Sarriena s/n, 48940, Leioa, Spain*

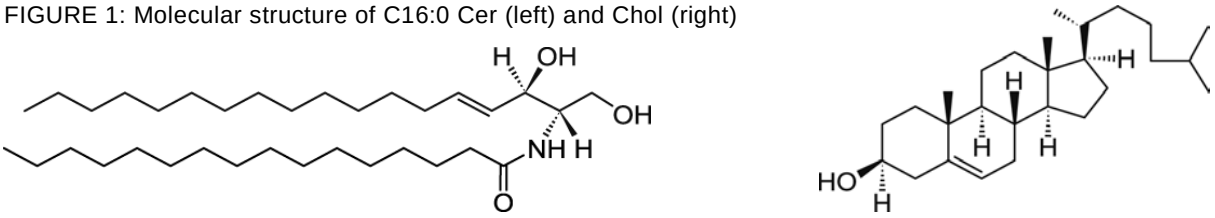
[b]*Departamento de Bioquímica y Biología Molecular (UPV/EHU), Barrio Sarriena s/n, 48940, Leioa, Spain*

** E-mail: aritzgarciaar@hotmail.com*

Our understanding of lipid membranes has improved dramatically over the last three decades. From Singer & Nicolson's fluid mosaic-model in the 70s to our current view on biomembranes, the level of knowledge has evolved thanks to the advances in new techniques and their applications to membrane biophysics [1]. The capacity of lipids to appear in different physical phases in a single membrane was a decisive finding thanks to techniques able to monitor and characterize lipid membranes, including all the different phases present. Atomic Force Microscopy (AFM) is one of these techniques as it allows direct measurements under nearly physiological conditions. In addition AFM gives information at both topographical and nanomechanical level, with the capacity to measure the fluidity of different phases in a localized manner.

One of the most intriguing subfamilies of lipids that have received widespread attention of lipid biophyisicists is arguably ceramide (Cer). Cer are a subfamily of sphingolipids that became truly relevant when their role as cell-death signaling molecules was detailed [2]. Some years later, their unique biophysical properties were observed as long-chain Cer (particularly C16:0) induced phase segregation in gel-like domains, while membanes became more permeable as well, with an increase in inter-layer lipid movement (flip-flop) [3]. These special features are considered to be caused by the high hidrophobicity of Cer (small polar headgroup) and because of their –NH-group (Figure 1), while other highly hidrophobic molecules such as cholesterol (Chol) do not present the same behavior. However, the capacity of Chol and Cer to compete for the same interaction spots in the membranes has been well documented [4, 5] and their tendency to displace each other has been an interesting research topic in the field. While high concentrations of Chol can definitely override the effects of Cer and solubilize the domains [6], in certain situations of high concentration of both Chol and Cer different intermediate phases can appear, with distinct biophysical properties [7, 8]. This speaks in favor of a Chol:Cer ratio as a way for cells to fine tune biophysical properties of their membranes [9]. Finally, as mitochondrial cholesterol has been involved in tumour cell behavior [10, 11], the possibility of cell death being regulated as well by an equilibrium of Chol and Cer must also be considered.

FIGURE 1: Molecular structure of C16:0 Cer (left) and Chol (right)

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# Pulmonary surfactant and drug delivery: *to alveoli and beyond*

**Alberto Hidalgo,*[a] M. Naeem Islam,[b] Sunita Bhattacharya,[2] Jahar Bhattacharya,[2] Antonio Cruz[a] and Jesus Perez-Gil[a]**

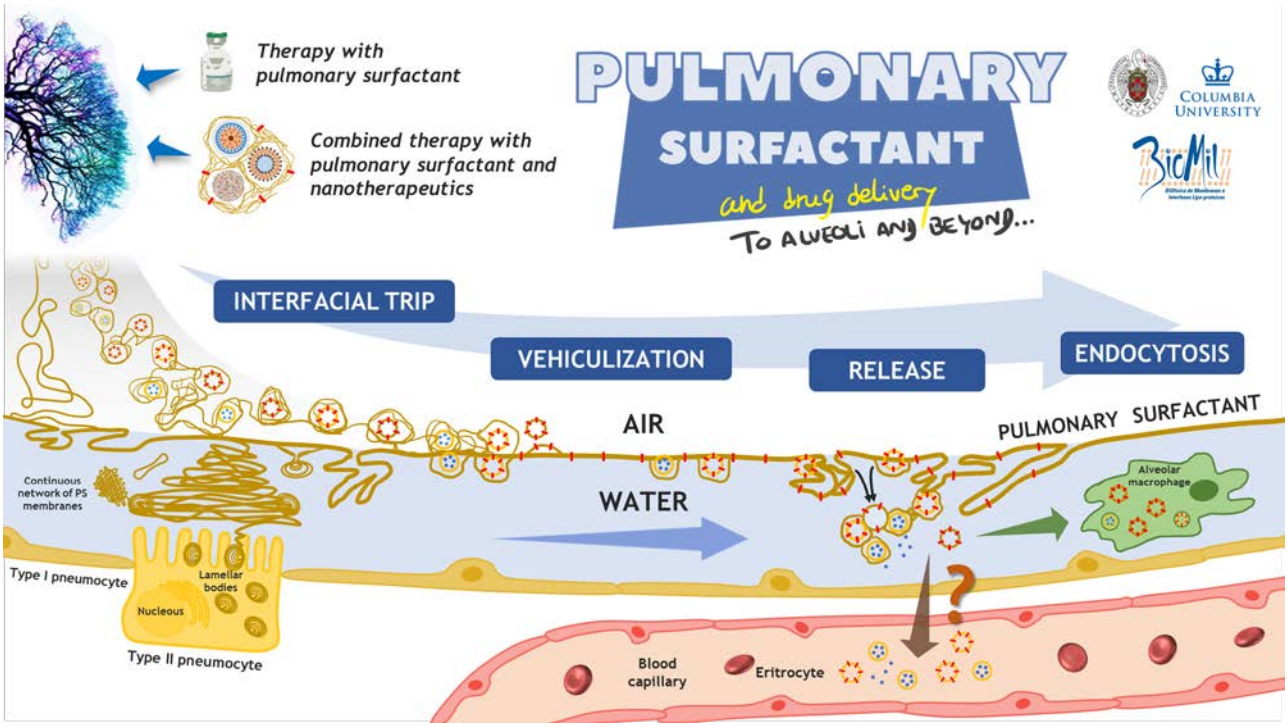
[a]*Department of Biochemistry, Faculty of Biology, and Research Institute "Hospital 12 de Octubre", Complutense University, Madrid, SPAIN. Tel. 91 394 5032*

[b]*Lung Biology Laboratory, Division of Pulmonary, Allergy, and Critical Care, Department of Medicine, Department of Pediatrics, Columbia University Medical Center, New York, US. Tel. +01 212-305-7310*

E-mail: albertohidalgo@ucm.es

The respiratory system has favourable properties that improve the delivery and pharmacokinetics of drugs intended for both local and systemic therapies. Pulmonary surfactant (PS), a membrane-based lipid-protein material coating the respiratory surface in charge of preventing pulmonary collapse during breathing and minimizing the entrance of undesirable entities, offers greater opportunities for drug delivery. According to our previous biophysical investigations, PS is able to travel interfacially while carrying hydrophobic drugs, such as corticosteroids or Tacrolimus, or nanomaterials without affecting its functionality. However, it is essential to evaluate whether this process also happens in the lungs, where different barriers and obstacles, such as mucus, air and liquid flows or the immune system are present. Therefore, we used LPS-induced inflammation mouse models and unique live lung imaging techniques to observe, describe and demonstrate the vehiculizing potential of PS directly on proper lungs.

The *in vivo* results confirmed our biophysical findings. PS is able to travel along the respiratory surface and share the interfacial trip with a drug like Tacrolimus to reach the alveolar region. Once there, in a process facilitated by breathing cycles, the drug is excluded from the interface to the aqueous alveolar lining layer, where alveolar macrophages uptake it and revert more efficiently the inflammation. This opens the use of pulmonary surfactant to vehiculize different therapeutic agents through the airways (drugs, nanocarriers, RNA or stem cells) and to develop novel strategies in medicine targeting the lungs (tuberculosis, acute lung injury, lung cancer or fibrosis) and peripheral locations.



# Characterization of protein kinetics at the single-molecule level combining microfluidics, Lateral Magnetic Tweezers and TIRF Microscopy

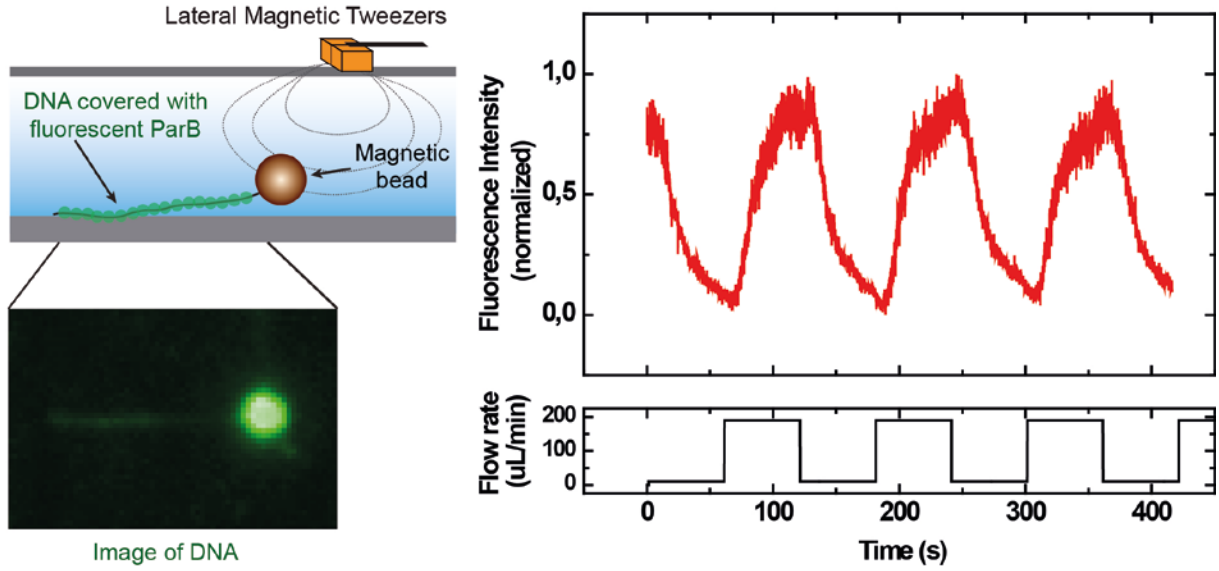
**Julene Madariaga-Marcos[a], Cesar L. Pastrana[a], Gemma L. M. Fisher[b], Mark S. Dillingham[b], and Fernando Moreno-Herrero[a].**

[a] *Department of Macromolecular Structures, National Center of Biotechnology, CSIC, Madrid, Spain*

[b] *DNA:Protein Interactions Unit. School of Biochemistry, Biomedical Sciences Building, University of Bristol, Bristol, BS8 1TD, UK.*

*E-mail: jmadariaga@cnb.csic.es*

Combining single-molecule techniques with fluorescence microscopy permits correlating mechanical measurements with directly visualized DNA:protein interactions. Specifically, the combination of magnetic tweezers (MT) with total internal reflection fluorescence (TIRF) microscopy is advantageous because one can follow many DNA molecules taking advantage of the high signal-to-noise ratio this fluorescence technique achieves. We have previously shown how to calibrate forces in this experimental configuration as well as its imaging capabilities to study ParB, a protein involved in bacterial chromosome segregation[1]. We have recently combined this hybrid setup with a double-channel laminar flow microfluidic device that is able to alternate between reagents (ie., buffer, protein, ATP) in a very precise way. This allows to study the binding/unbinding of proteins in a repetitive way at the single-molecule level, and we anticipate that it will allow to calculate binding and unbinding rates ($k_{on}$, $k_{off}$). Ongoing experiments include calculating binding and unbinding rates for ParB and the C-terminal domain of ParB ($ParB^{CTD}$), which plays an important role in unspecific DNA-binding[2]. Our results support previously proposed models on ParB and $ParB^{CTD}$.




On the right, schematics of the experiment of ParB binding and the actual TIRF image. On the left, fluorescence intensity for a single DNA molecule as a function of time when protein/buffer is introduced. Intensity peaks are correlated with the introduction of protein and binding/unbinding rates can be extracted from the curves.

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# Understanding the Role of DNA condensing proteins in viral chromatin with Atomic Force Microscopy

**Natalia Martín-González**[1], Gabriela N. Condezo[2], P. Ostapchuk[3], P. Hearing[3], Carmen San Martín[2] and Pedro J. de Pablo[1]

[1]Departament of Condensed Matter Physics. Universidad Autónoma de Madrid, 28049 Madrid, Spain
[2]Department of Macromolecular Structures, Centro Nacional de Biotecnología (CNB-CSIC), Madrid, Spain
[3]Department of Molecular Genetics and Microbiology, School of Medicine, Stony Brook University, Stony Brook, NY 11794-5222 USA

natalia.marting@uam.es

**Type of contribution**: Oral

Adenovirus, a human pathogen and a potential therapeutic tool, has an icosahedral shell enclosing the dsDNA genome associated with positively charged proteins VII, V and µ. To understand the function of core protein VII, we are using Atomic Force Microscopy to analyze the mechanical properties of a mutant where this protein is absent (VII-). First, we measure the elasticity and fragility of VII- particles; then, we carry out mechanical fatigue experiments [1] to assess the stability of the particles compared to wildtype; finally, by cracking open individual VII- particles, we access the nucleoprotein core to probe its mechanics [2]. Our results will help us understand the role of protein VII in core organization and capsid stability modulation.

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# Atomic Force Microscopy shows DNA-bridging by human CtIP

***A. Martín-González[1], O. Wilkinson[2], S. Northall[2], M. Dillingham[2], and F. Moreno-Herrero[1].***

[1] Dept. of Macromolecular Structures, National Center of Biotechnology, CNB-CSIC, Madrid, Spain

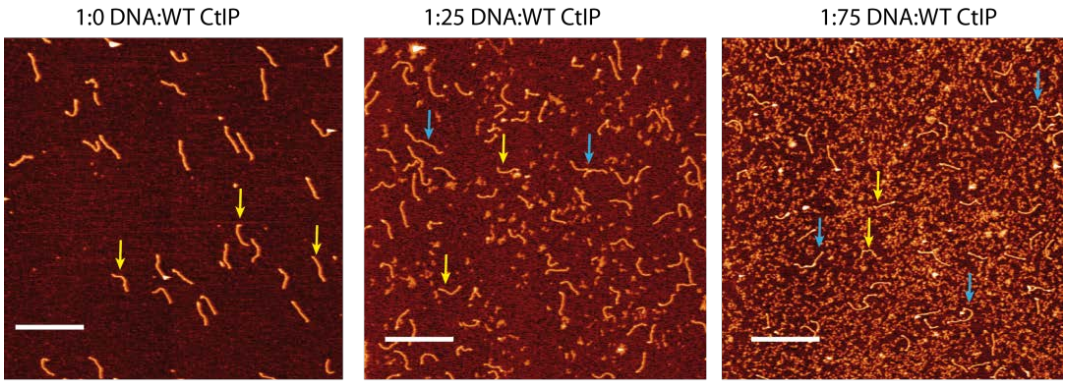
[2] School of Biochemistry, Medical Science Building, University of Bristol, Bristol, United Kingdom.

alejandro.martin@cnb.csic.es

Homologous recombination (HR) has been described as one of the main cellular mechanism for DNA damage-repair [1]. HR mechanism requires an identical copy of the damaged DNA and so is the most fail-proof repair mechanism in eukaryotic cells. It is a complex and many-step process carried by different proteins and thus the whole process is not widely understood. In this work, we have studied one of the proteins present in the first steps of HR in humans, hCtIP. Little is known about this protein apart from its role in the initial steps of HR and its tetrameric oligomeric state in in solution [2] responsible for the damaged-DNA resection. Previous biochemical assays have revealed a possible binding of CtIP to linear pieces of DNA related to a DNA-bridging event.

Here we have studied the oligomeric state of the human protein, hCtIP, and its binding interaction with DNA using Atomic Force Microscopy. AFM volumetric analysis of hCtIP correlates with a tetrameric structure in equilibrium with other oligomeric states mainly formed by the N-terminal tetramerization domain of the protein. This was confirmed by experiments using a mutant hCtIP that disrupts this domain. In addition, AFM images of reactions including CtIP and DNA show the formation of long molecules as a consequence of joining DNA from their ends by CtIP acting as a bridge. These bridging events were dependent on hCtIP concentration and on the oligomeric state of the protein, as corroborated with mutants that affects the dimerization interface and an additionally putative DNA binding region. The data from the CtIP domains arrangement along with the bridging experiments have permitted us to elaborate a model on CtIP structure. In this model we propose a structure for the different CtIP oligomeric states and its relation with bridging events.

FIGURE

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# NANOparticles for antiVAscular Multimodal therapy: Photothermal, photodYnamic and dual drug RElease (NANOVAMPYRE).

**Juan L. Paris,[a,b,*] Gonzalo Villaverde[a,b] and María Vallet-Regí[a,b]**

[a] *Dpto. Química en Ciencias Farmacéuticas (Unidad Docente de Química Inorgánica y Bioinorgánica), Facultad de Farmacia, UCM, Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), 28040-Madrid, Spain.*

[b] *Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.*

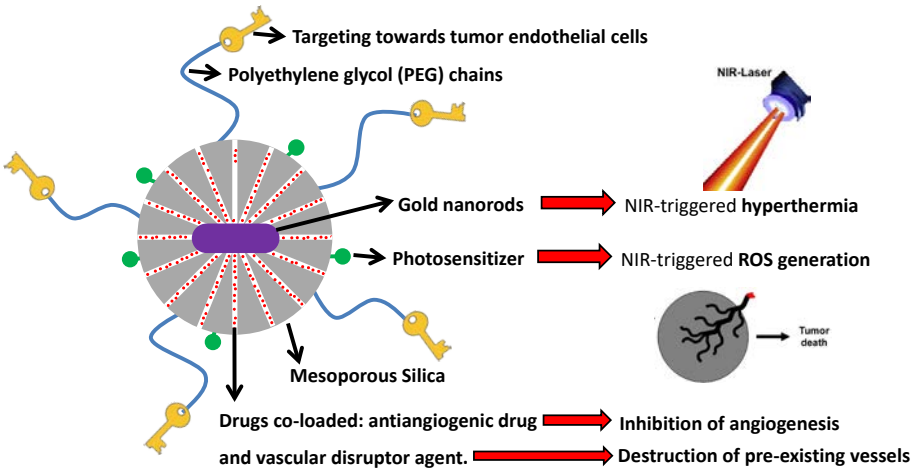
*E-mail: juanluisparis@ucm.es*

Cancer remains one of the leading causes of death worldwide. Anticancer chemotherapeutics present severe side effects that limit the dosage that can be applied and drastically decrease the quality of life of the patients, even putting their lives at risk. Cancer nanomedicine has emerged as a promising approach to decrease chemotherapy side-effects by achieving a selective distribution of the drug towards the desired site, since nanostructures undergo passive accumulation in tumor tissues due to the enhanced permeability and retention (EPR) effect.[1]

In spite of the wonderful potential of cancer nanomedicine, a large gap in its translation to the clinic can still be found. One of the main issues hindering nanomedicine translation is the poor penetration of nanoparticles in solid tumors, due to their high interstitial pressure. An alternative tactic could be selecting as a target a part of the tumor that is readily available for nanoparticles: the tumor blood vessels. If an efficient destruction of the tumor blood vessels is achieved, an antitumor response could be obtained by removing the nutrient source needed for cancer cell growth.[2]

Antiangiogenic drugs (AAD, which inhibit the formation of new blood vessels) are employed in the clinic to treat different tumors, although usually in combination with other therapeutic modalities to enhance their effectiveness. Vascular disruption agents (VDA, which are capable of destroying pre-existing vasculature) are also under clinical evaluation, and their combination with antiangiogenic agents appears especially promising.[3] The possiblity of combining two drugs in a single nanoparticle to ensure their combined delivery to the desired target site is regarded today as a key advantage of nanomedical approaches.

In the NANOVAMPYRE project, a tumor endothelium-targeted nanoparticle (employing the RGD peptide sequence) capable of co-delivering an AAD and a VDA has been designed, obtained and evaluated (*in vitro* and in an *ex ovo* chicken embryo model). Furthermore, the nanodevice has been provided with two additional anti-vascular capabilities, both of them activated by the application of an external stimulus (Near Infrared light): generating local hyperthermia (thanks to the inclusion of gold nanorods in the system) and the generation of toxic reactive oxygen species (by the presence of a photosensitizer).[4] The combination of these four therapeutic modalities could allow for a highly efficient destruction of tumor blood vessels, which appears as a potentially useful tool for cancer treatment.

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# Calibration-independent Atomic Force Microscopy

**Carmen Suay-Corredera*, Carolina Pimenta-Lopes*[,a], Diana Velázquez-Carreras, David Sánchez-Ortiz and Jorge Alegre-Cebollada**

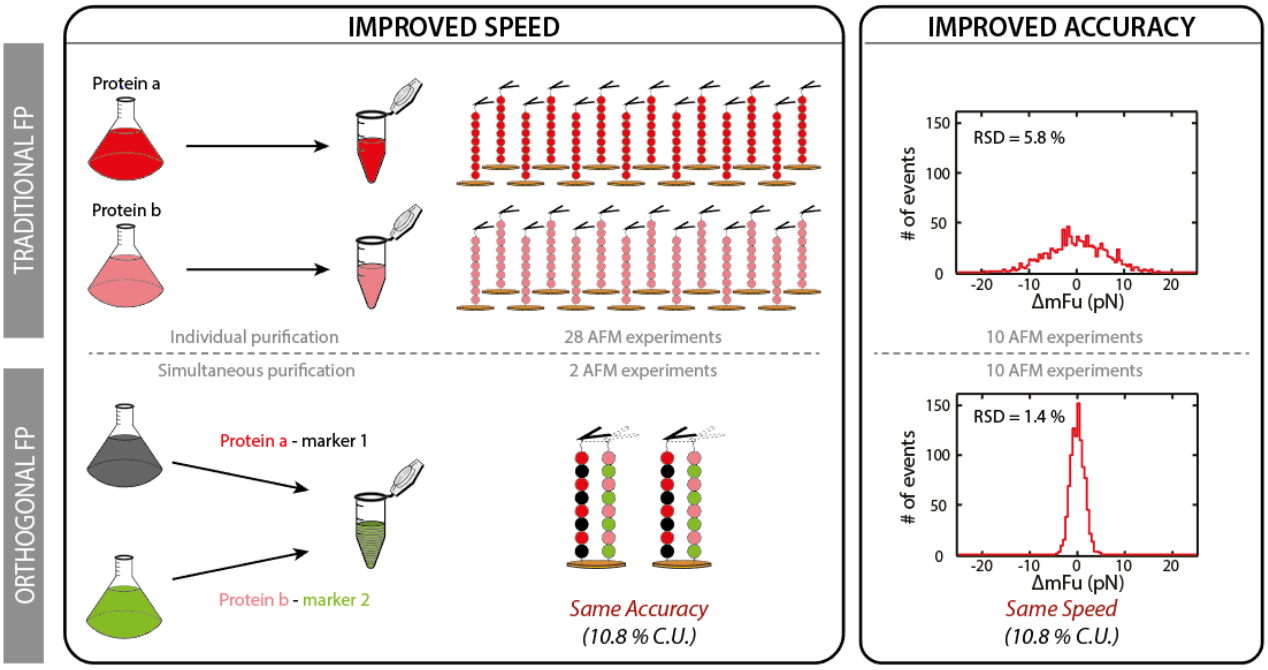
** Equal contribution*

*Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Melchor Fernández Almagro, 3, 28029. Madrid, Spain. Tel (+34) 914531200 - 2021*

*[a]Current address: Department of Physiological Sciencies, University of Barcelona, Feixa Llarga, s/n, 08907. L'Hospitalet Ll., Barcelona, Spain. Tel (+34) 934024268*

*E-mail: jalegre@cnic.es*

Atomic Force Microscopy (AFM) is the technique of choice to measure mechanical properties of molecules, cells, tissues and materials at the nano and micro scales. However, unavoidable calibration errors of AFM make it cumbersome to quantify modulation of mechanics. Here, we show that concurrent AFM measurements enable relative mechanical characterization with an accuracy that is independent of calibration uncertainty. To demonstrate calibration-independent AFM, we have achieved concurrent single-molecule nanomechanical profiling of two different proteins. Using orthogonal fingerprinting strategies to sort individual unfolding events, differences in mechanical unfolding forces can be obtained with a 6-fold improvement in accuracy and a 30-fold increase in throughput. Importantly, the performance of calibration-independent AFM is maintained even when averaging data from multiple, independent experiments.



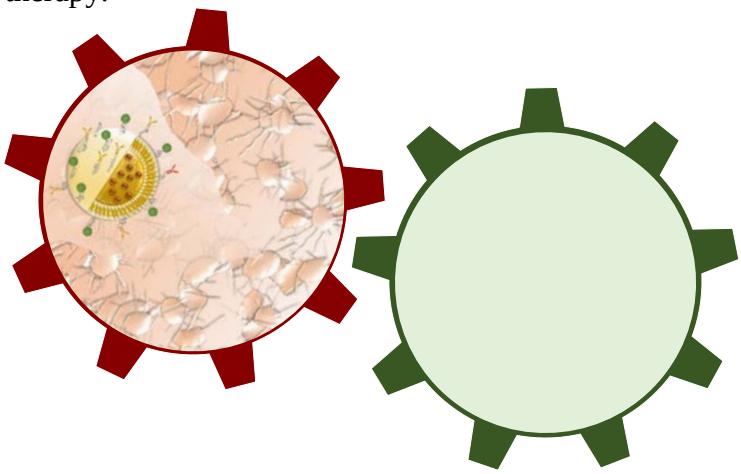

**Overview of concurrent single-molecule force-spectroscopy AFM.** In the traditional approach, comparison of the mechanical stability of *Protein a* and *Protein b* involves independent purification and several AFM experiments to compensate for inaccurate calibration of the AFM. Orthogonal fingerprinting (OFP) strategy is based on the production of heteropolyproteins composed of the proteins of interest fused to marker domains. Since the markers provide unequivocal fingerprints in single-molecule pulling experiments, OFP enables simultaneous purification and concurrent measurement in the AFM, circumventing errors in force calibration. Concurrent measurements can achieve the same accuracy as conventional single-molecule AFM with much better throughput (*left*). Alternatively, by keeping the speed of data acquisition constant, concurrent AFM by OFP considerably improves the accuracy of single-molecule AFM (*right*). The improvement in throughput and accuracy are estimated from Monte Carlo simulations at 10.8% calibration uncertainty (C.U.) (100 events per experiment and protein).

# Hybrid Nanocarriers for the Treatment of Cancer.

**M.R. Villegas,[a,b] A. Baeza[a,b] and M. Vallet-Regí [a,b]**

[a]*Departamento de Química en Ciencias Farmacéuticas, Facultad de Farmacia, Universidad Complutense de Madrid, España.*
[b]*Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain*
*E-mail: mr.villegas@ucm.es*

Drug nanocarriers are selectively accumulated in solid tumors by Enhanced Permeability and Retention effect. However, the use of these nanodevices are strong limited by the abnormally dense tumoral extracellular matrix that prevents their penetration and reduces the therapeutic effect of drug transported to the periphery. Our approach has been to design of a nanosystem capable of penetrating into tumoral matrix models, being engulfed selectively by cancer cells and destroy them. This multitasking system is formed by mesoporous silica nanoparticle loaded with a potent antitumoral and covered with a lipid bilayer. This bilayer avoids the premature release of the drug carrier and provides the system with colloidal stability. It was decoded with a targeting moiety, by selective endocytosis by lung tumoral cell line. Finally, the system was functionalized with collagenase nanocapsules. Collagenase nanocapsules were designed to protect the host enzyme against external insults and release it in slightly acidic environment, typical of solid tumors, in order to degrade the extracellular matrix and allow the penetration of carrier.[1],[2] Another approach to address oncologic therapy is based on intracellular trafficking of drug nanocarriers to important organelles. We are designed an asymmetric nanocarrier with a cellular targeting moiety on one hemisphere and other organelle targeting moiety to mitochondria on the opposite hemisphere. The "Janus" functionalization avoids undesirable interactions between moieties and allows the system achieves a better therapeutic effect due to closed localization of the drug on mitochondria membrane.[3]. Both strategies are interesting since they address important limitations of nanomedicine, because one of them allows treat of all the malignant tissue due to the homogeneous distribution or, on other hand, the other allows potent the effect of the drug carrier reducing the dose required for the therapy.



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# Curvature Induces Cardiolipin Sorting

**Elena Beltrán-Heredia*[a,b], Feng-Ching Tsai[c], Francisco J. Cao[a,d], Patricia Bassereau[c], and Francisco Monroy[b,e]**

[a]*Dpto. de Estructura de la Materia, Física Térmica y Electrónica, Universidad Complutense de Madrid, Plaza de Ciencias 1, 28040 Madrid, Spain Tel: 91 394 4742;*

[b]*Dpto. de Química Física, Universidad Complutense de Madrid, Avda. Complutense s/n, 28040 Madrid, Spain Tel: 91 394 4128;*

[c]*Laboratoire Physico Chimie Curie, Institut Curie, PSL Research University, CNRS UMR168, 75005 Paris, France;*

[d]*Instituto Madrileño de Estudios Avanzados en Nanociencia, IMDEA Nanociencia, Calle Faraday, 9, 28049 Madrid, Spain;*

[e]*Unit of Translational Biophysics. Instituto de Investigación Sanitaria Hospital Doce de Octubre (imas12), Avda. de Cordoba s/n, 28041 Madrid, Spain;*

*E-mail: elenabel@ucm.es*

Cardiolipin (CL) is a negatively charged lipid found predominantly in the inner mitochondrial membrane of eukaryotic cells and in the plasma membranes of certain bacteria. It is composed of two phosphatidic acid joined by a central glycerol resulting in a large molecule with inverted conical shape. Previous estimations based on crystal structure suggest that CL curvature is between 1 and 5 $nm^{-1}$ [1], making it favorable for this lipid to localize in highly curved regions of the membrane. Indeed, CL-enriched domains have been observed in bacterial poles and division sites as well as in mitochondrial cristae, tightly curved regions of the mitochondrial inner membrane. The proposed mechanism of these domains is geometry-driven: a coupling between membrane composition and CL shape would minimize the curvature frustration of the curved regions of the membrane [2]. However, no data are available yet on curvature-induced CL sorting *in vitro*. To test this hypothesis, we isolate the effects of membrane curvature by using cell-sized giant unilamellar vesicles (GUVs) made of mixtures EPC/CL and connected to a curved nanotube of controlled radii (see Fig. 1). The membrane was marked with a red fluorescent reference lipid (Bodipy TR-Ceramide), whereas the CL was labelled with a green fluorescent lipid (Top-Fluor CL). Interestingly, we find that CL becomes enriched in the tubes, with higher enrichment in more highly curved membranes. This relative CL enrichment can be quantified by the sorting ratio $S$, defined as

$$S = \frac{(I_{\mathrm{CL}}/I_{\mathrm{BOD\text{-}TR}})_{\mathrm{tube}}}{(I_{\mathrm{CL}}/I_{\mathrm{BOD\text{-}TR}})_{\mathrm{GUV}}}, \#(1)$$

where $I_{\mathrm{CL}}$ is the fluorescence of CL. According to this definition, $S > 1$ implies that CL is enriched in the tube as compared to the GUV, while $S < 1$ means that it is depleted from the tube. Sorting at high CL densities is observed, despite unexpected in an ideal mixing model (with non-CL interactions), but it can be explained by assuming the existence of self-associating CL finite-sized clusters. The fit to a model based on membrane elasticity and nonideal solution theory that includes CL-CL attractive interactions reproduces our data and predicts an intrinsic curvature of CL of 1.1 $nm^{-1}$ (in accordance with previous estimates [1]). We also show that CL molecules are able to freely diffuse through the neck between the tube and the GUV by measuring the fluorescence recovery after photobleaching. This work contributes to a better understanding of the sensitivity of CL to membrane shape and provides key insights into understanding mitochondrial and bacterial organization.

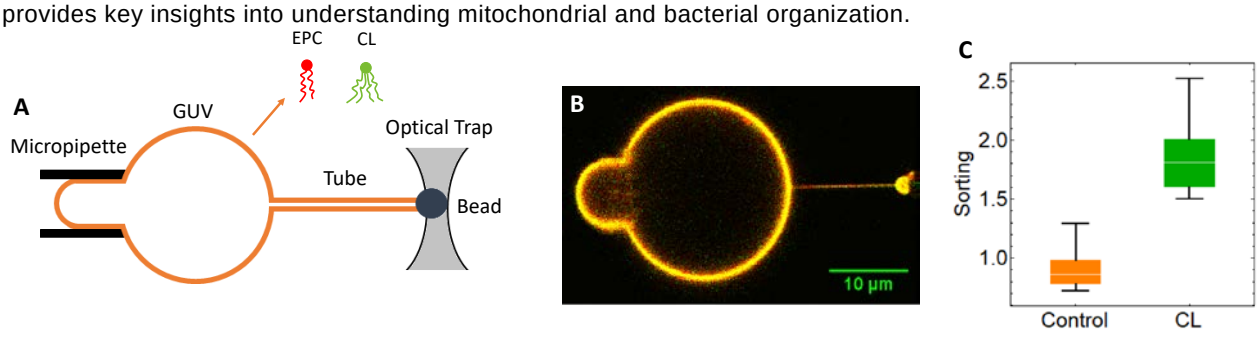


***Fig. 1. CL is enriched in curved membranes.*** *(A) Schematic of tube assay. A bead in an optical trap is used to pull a membrane tube from a GUV held by a micropipette. The pressure in the micropipette controls the membrane tension and resultant tube radius. (B) Confocal image of a tube pulled from a GUV containing CL. (C) Box plots comparing the sorting ratio (1) for curved tubes ($C \approx 0.1\ nm^{-1}$) containing green fluorescent lipids: control and CL.*

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# Synthesis and advanced 3D-printing of polymerized composites based on metallic particles

**Daniel Casaleiz,*[a] Ester M. Palmero,[a] Javier de Vicente,[a] Juan Hernández,[b] Silvia López,[b] Emilio Ramiro[b] and Alberto Bollero[a]**

[a]*Division of Permanent Magnets and Applications, IMDEA Nanoscience, 28049 Madrid, Spain*

[b]*RAMEM S.A., 28850 Torrejón de Ardoz, Madrid, Spain*

*E-mail: daniel.casaleiz@imdea.org*

Additive manufacturing is one of the most innovative manufacturing technologies with potential applications in sectors such as aeronautics, aerospace, energy and automotive. The most relevant characteristic of additive manufacturing is that it allows a rapid and precise fabrication of functional elements with no restriction in geometry and size [1], i.e. making possible optimized designs and more efficient devices. Different materials can be combined into tuneable composites depending on the final application allowing for a reduced amount of material used in the production.

In this work, composites based on metallic (stainless steel) spherical particles have been synthesized by solution casting [2], using ABS as matrix. The initial steel powder was prepared by gas-atomization, which is an excellent synthesis technique in view of 3D-printing technology because it delivers quasi-spherical particles with control on composition and particle size [2,3]. Measurement of the magnetic response (hysteresis loop) of steel in the composite allowed for a precise determination of the metal content [2] (Fig. 1(a)).The composite was extruded into filament, which was used for the fabrication of 3D-printed elements. Figure 1(b) shows an example of the products obtained in the different stages of the fabrication: synthesized composite, extruded filament and 3D-printed hollow columns with hexagonal shape. SEM image of the particles distribution in a printed column is shown in Figure 1(c).

We have obtained a continuous steel/polymer filament (4 m long) suitable for printing with a particle content of 33 wt% for stainless steel. Columns with different cross section (circular and hexagonal) and height have been printed demonstrating the potential of the 3D-printing technique for manufacturing elements with no restriction in the materials, shape and dimensions. The complete process (filament extrusion and 3D-printing) has been adapted for aluminum particles achieving an increased filling factor of 80 wt% due to the different density and the higher dispersion in particle size (increased filling factor).

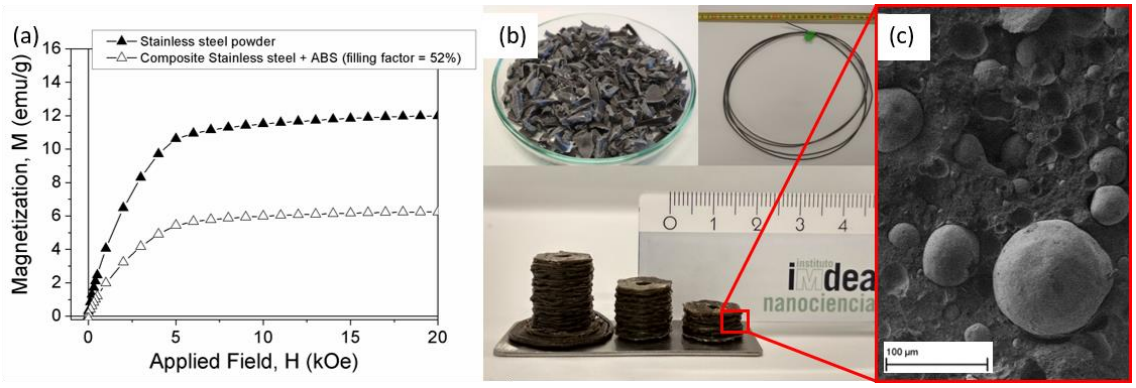


**Figure 1**: (a) Magnetic response of the starting stainless steel powder and the composite (filling factor of 52 wt%) (b) Composite pellets, filament and 3D-printed hexagonal columns of stainless steel/ABS (33 wt%). (c) Cross section SEM image of a 3D-printed column shown in Figure 1 (b).

**Acknowledgement**: This work has been done with the financial support from the Industrial Innovation Grant “Cheque Innovación” [Ref. 45/421504.9/17] by Regional Government “Comunidad de Madrid”.

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# Engineering of magnetic properties of Co-rich microwires by Joule heating

**P. Corte-León,*[a,b] V. Zhukova,[a,b] M. Ipatov,[a,b] J.M. Blanco,[b] J. González[a,b] and A. Zhukov[a,b,c]**

[a]*Departamento de Física de Materiales, Fac. Químicas, UPV/EHU, 20018 San Sebastián, Spain;*
[b]*Dpto. Física Aplicada I, EUPDS, UPV/EHU, 20018 San Sebastián, Spain;*
[c]*IKERBASQUE, Basque Foundation for Science, 48011 Bilbao, Spain;*
*Email: paula.corte@ehu.eus*

The performance of magnetic devices can be significantly improved if the used materials will present higher GMI effect. Considering that the predicted theoretical maximum GMI ratio (about 3000%) [1] is few times superior to the experimentally reported it is expected that technology improvement involving development of effective post-processing method will allow achievement of higher GMI ratio. Consequently considerable efforts have been paid to studies of the post-processing on GMI ratio of various magnetic materials, such as wires, ribbons, thin films and multilayers [2].

It is expected that Joule heating due to the induced magnetic anisotropy [3] can further improve the GMI effect. Up to know only limited number of experimental results on effect of current annealing on GMI effect are reported [2].

Up to now the best GMI performance is observed in amorphous magnetic wires exhibiting excellent magnetic softness. Current annealed $Co_{67}Fe_{3.9}Ni_{1.5}B_{11.5}Si_{14.5}Mo_{1.6}$ microwires present excellent magnetic softness with low magnetic anisotropy field of about 25 A/m and coercivity of 2 A/m.

We have investigated the GMI response of the current-annealed glass-coated microwire. From the obtained dependence we determined the optimal current annealing conditions and obtained considerable improvement of ΔZ/Zmax –values from 550% to about 650% after appropriate current annealing conditions as can be seen in the Figure.

The analysis of the GMI ratio as a function of the frequency opens new lights to understand the distribution of the magnetic anisotropy inside the microwire.

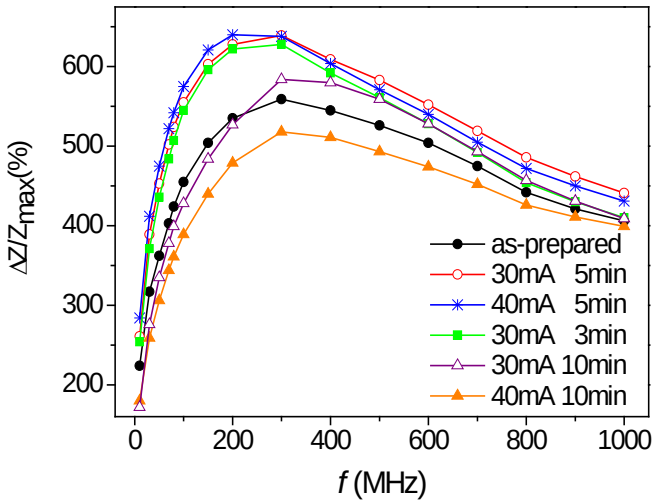


FIGURE. ΔZ/Zmax(f) dependences observed in as-prepared and current annealed microwire at different annealing conditions.

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# Plasmonic properties of electrolytes beyond classical nanophotonics - Nonlocal soft plasmonics

**Christin David**

*Madrid Institute for Advanced Studies in Nanoscience (IMDEA Nanoscience), Madrid, Spain;*
*christin.david@imdea.org*

Electrolytes consist of positively and negatively charged ions even in an equilibrium situation. Hence, plasmonic behavior can be observed in ionic systems and interaction effects between the charge carriers may play a sizable role as compared to the quantum effects observed for metal nanoparticles beyond a classical Maxwellian description [1-5].

We study ionic plasmon effects [6,7], i. e. collective charge oscillations, in electrolytes in the scope of a nonlocal, two-fluid model using the hydrodynamic theory of charges [8]. Notably, nonlocal quenching is observed for particle sizes spanning orders of magnitude, tunable via ion concentration and their mass and charge through choice of material.

A plasmonic theory for ions in solution can bridge hard and soft matter theory and allow studying interaction effects from a photonic perspective in full analogy to solid metal particles, see Fig. 1. The semi-classical approach presented here can be fully integrated into standard nano-optic simulation frameworks and is considered to be of great interest for plasmonic photo-catalysis [9] introducing nonlocal aspects into electrolyte-metal interactions.

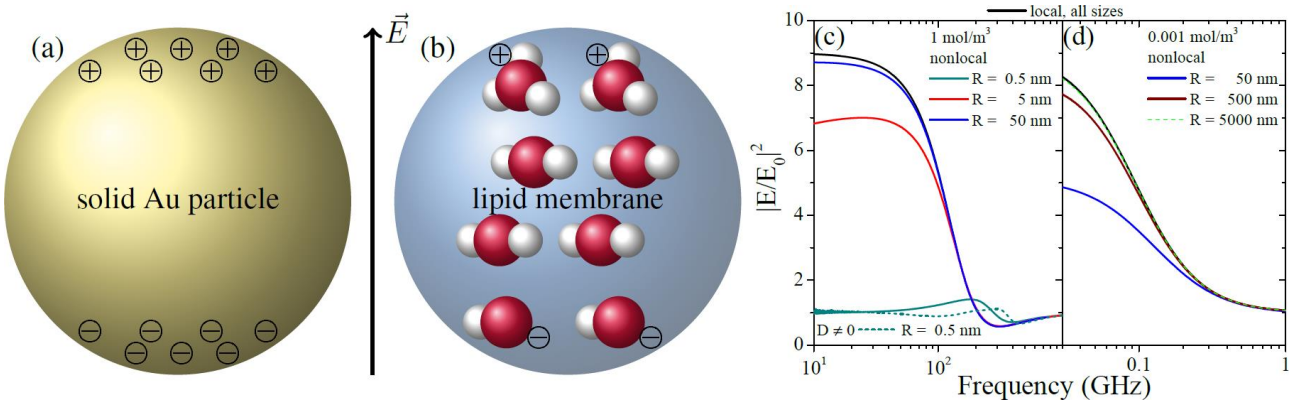


Figure 1. Concept of soft plasmonics: Illustration of charge carrier displacement in a (a) metal solid and (b) confined ionic fluid. (c), (d) Quenching of field enhancement at the particle surface for different ion concentration levels and several orders of magnitude in particle size.

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# Exchange coupling effects in hybrid Gr-4f RE systems

**Letícia de Melo Costa*[a,b] , Pierluigi Gargiani[b] , Julio Camarero[a] , Rodolfo Miranda[a], Miguel Pruneda[c], Stefan Blügel[d], Paolo Perna[a] and Manuel Valvidares [b]**

[a] *Instituto Madrileño de Estudios Avanzados en Nanociencia, Calle Faraday 9, Madrid, Spain. Tel: +34 91 299 87 00*

[b] *ALBA Synchrotron Light Source, Carrer de la Llum 2-26, Barcelona, Spain. Tel: +34 93 592 43 00*

[c] *Institut Catala de Nanociencia i Nanotecnologia (ICN2), Campus UAB, edifici ICN2, Barcelona, Spain. Tel: +34 937 372 649*

[d] *Forschungszentrum Jülich GmbH, Wilhelm-Johnen-Straße, Jülich, Germany. Tel: +49 2461 61-4249*

*E-mail:* leticia.demelo@imdea.org

Hybrid Ferromagnetic/Graphene (FM/Gr) systems enclose remarkable technological opportunities by bridging spintronics with promised ultra-fast Gr-based electronics and photonics. These are also of fundamental relevance since Gr actively interacts with the neighboring materials determining a modification of the electronic and magnetic properties of the system [1,2]. In particular, Graphene-spaced magnetic systems with antiferromagnets offer exciting opportunities for the investigation of exchange-coupling phenomena in spintronics.

We have recently shown that ultra–thin graphene/Co films grown on Ir(111) or Pt(111) templates exhibit robust perpendicular magnetic anisotropy (PMA) [1,2] and antiferromagnetic exchange-coupling when Fe is deposited on top of Gr [1]. These results gather a collection of magnetic properties well-suited for applications. However, one drawback in 3d-FM/Gr systems, is that the FM-Gr hybridization is so strong that impact Graphene´s electronic properties, for example, the presence of Dirac´s cone. Instead, the weak interaction between 4f-FM and Gr preserves Gr unique electronic structure and particularly Dirac´s cone.

Here, by resorting to X-ray absorption and magnetic dichroism (XAS-XMCD) measurements we investigate the magnetic configurations, the nature of the Gr mediated exchange coupling and the magnetic anisotropy in 4f-FM/Gr hybrid systems such as Eu and Dy as an extension of Gr- synthetic antiferromagnetic (SAF) systems [3].

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# Fabrication of $MoS_2$ P-N Homojunctions via Pulsed Focused eBeam Induced Etching

**Fernando Jiménez Urbanos,[a] Jorge Trasobares,[a] *Victor Marzoa Camarero,[a] Rodolfo Miranda,[a] Daniel Granados*[a]***

[a]*IMDEA Nanociencia, Calle Faraday 9, 28049, Madrid, Spain.*
*E-mail: daniel.granados@imdea.org*

Mono-Layer and few-layer Transition Metal Dichacolgenides (TMDCs) have attracted great due to their outstanding optoelectronic properties. Recent studies have shown the capability of fabricate P-N both homo and heterojunctions using different approaches, like material stacking or chemical doping.[1,2] The burden of these methods lies in involving several fabrication steps, like resist deposition, chemical manipulation and aligning or lithography procedures. This increases production time, cost and the probability of damaging the devices during the fabrication steps, which reduces the production yield.

In our group we developed a direct nanolithography method: Pulsed Focused Electron Beam Induced Etching (PFEBIE). It allows the scissoring of TMDCs materials on field effect transistor devices, once their fabrication steps have been completed. This method enables the possibility to fine tune the device's geometry and thus its optoelectronic properties. We have recently demonstrated that a p-doping mechanism occurs after the nanopatterning via PFEBIE, mainly in the exposed/etched region.[3] Taking advantage of this doping phenomenon, we have fabricated a lateral P-N homojunction from an intrinsically N field effect transistor (FET).

FET devices were fabricated from mechanically exfoliated $MoS_2$ flakes employing optical laser beam lithography, followed by a metal evaporation and a lift-off process to define the gate-contact structures. PFEBIE was utilized to fabricate a lateral P-N homojunction with bar geometry. The devices were characterized employing Raman and Photoluminescence (PL) mapping spectroscopy, transport measurements, AFM and SEM microscopy, before and after the PFEBIE nanopatterning. The original devices showed typical FET behavior, while a clear rectifying IV was demonstrated in the after etched samples. Photoresponse was also observed in the PN junction devices.

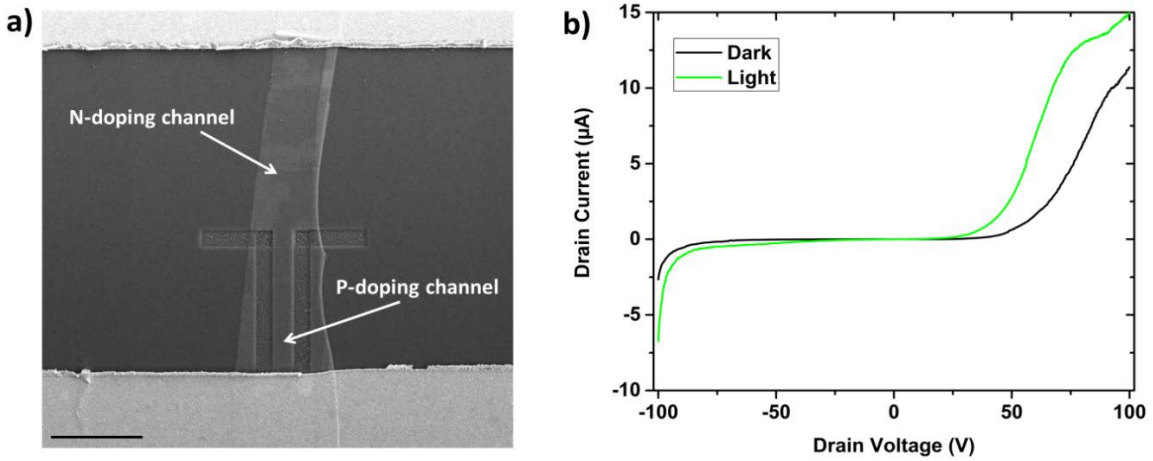


**Figure 1. a)** SEM image of the patterned device after PFEBIE. The upper zone remains intrinsically n-doped while the bottom channel is p-doped. Scale bar is 2 μm. **c)** Electric characterization of the device after the formation of the homojunction showing a diode response in dark and under white light illumination.

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# Reaction Products obtained in the Hydrothermal Synthesis of Carbon Dots

**Sergio Ramírez, Jennifer Sánchez, Alejandra Jacobo, Iván Navarro, Isabel Rodriguez, and Reinhold Wannemacher**

*IMDEA Nanociencia, Cantoblanco, Spain. Tel: 912998781;*
*E-mail: sergio.ramirez@imdea.org*

Carbon Dots (CDs) and graphene quantum dots (GQD) are quasi-zerodimensional analogues of quasi-one and quasi-twodimensional carbon allotropes, carbon nanotubes and graphene, respectively, and have been found to be ubiquitous in nature. In particular, hydrothermally synthesized CDs have received enormous interest (approaching 4000 publications) due to their easy, cheap and green metal-free synthesis, high fluorescence quantum yield (QY) and high photostability, good solubility in water, good biocompatility and low cytotoxicity, their strong tendency to charge transfer and corresponding photocatalytic properties, as well as their applications in sensing. It has been realized recently, however, that high QY photoluminescence, as observed mainly in nitrogen-containing CDs, is not due to the CDs themselves, but to small molecules produced actually as main products in the hydrothermal synthesis[1,2]. The exact composition of the materials produced depend critically on reaction parameters such as starting materials, temperature and reaction time. Polyaromatic hydrocarbons and polymeric by-products coexist with the CDs.

We produced fluorescent CDs from citric acid and ethylene diamine followed by dialysis in 1 kDa and 25 kDa dialysis bags and have applied high resolution transmission electron microscopy (TEM), liquid chromatography coupled to mass spectrometry (LC-MS), Fourier-transform infrared spectroscopy (FTIR), surface-enhanced Raman scattering (SERS), atomic force microscopy (AFM) and fluorescence correlation spectroscopy (FCS) to shed light onto the chemical composition of the reaction products and the size distribution of the fluorescent emitters. We support the experimental findings by quantum-chemical calculations.

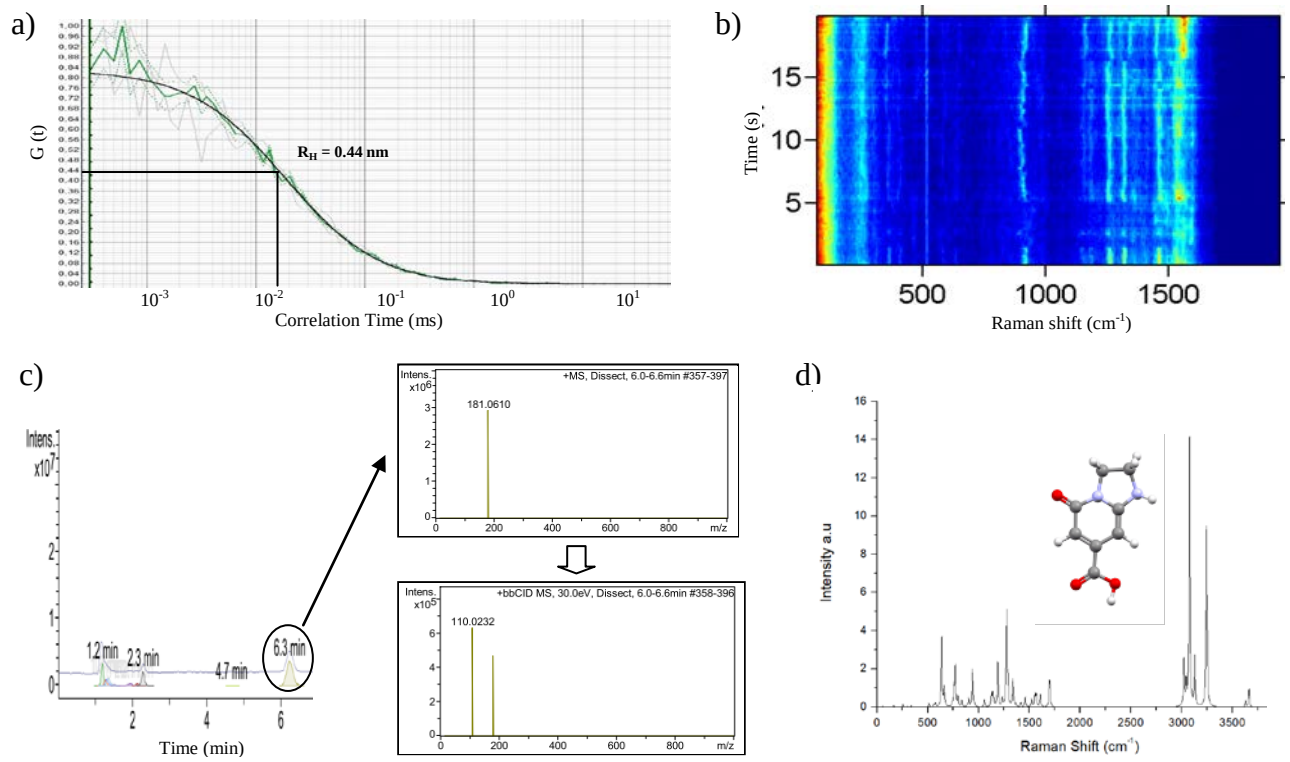


Figure 1: a) Averaged fluorescence autocorrelation of CDs, b) two-dimensional SERS spectrum of CDs, c)liquid chromatography coupled with tandem mass spectrometry of CDs, and d) the Raman spectrum of IPCA predicted by quantum chemical calculations (DFT).

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# Nanowire interfaces as nanoelectrodes for neural electrical stimulation at the spinal cord

**Beatriz L. Rodilla*[a,b], Ana Arché[c], Lucas Pérez[a,b], Ana Domínguez-Bajo[c], Ankor González-Mayorga[d], María Concepción Serrano[c], Rodolfo Miranda[a,e], María Teresa González[a]**

*[a]IMDEA Nanociencia, Campus Cantoblanco, 28049 Madrid, Spain, [b]Depto. Física de Materiales, Universidad Complutense de Madrid, 28040, Madrid, Spain, [c]Instituto de Ciencia de Materiales de Madrid, Consejo Superior de Investigaciones Científicas (ICMM-CSIC), 28049, Madrid, Spain, [d]Hospital Nacional de Parapléjicos, Servicio de Salud de Castilla-La Mancha, Toledo, Spain, [e]Depto. Física de la Materia Condensada-IFIMAC, Universidad Autónoma de Madrid, 28049, Madrid, Spain*

*E-mail: Beatriz.rodilla@imdea.org*

Accidents and trauma that occur directly at the spinal cord usually have devastating consequences as permanent paralysis due to the fact that, in a spinal cord injury, the neural connections are interrupted. Nowadays, material science, neuroscience and nanotechnology, work together developing neuronal interfaces designed at the nanoscale [1], that allow enhanced biological interactions with neural cells and tissues and, with the right stimulus, the recovery of the lost nervous connection.

We are currently developing a new generation of biocompatible stimulating nano-electrodes to allow a local bypass of the neuronal signals, directly at the spinal cord [2]. These nanostructured electrodes, consisting on an interface of metal nanowires, are grown by template-assisted electrodeposition over a gold base that works as the contact (Figure 1a). We have varied the composition, arrangment and length of our nanowires and tested biocompatibility, studying the behaviour of neural progenitor cells from rat embryos at E18 when cultured in vitro on the nanowire interfaces, with focus on cell adhesion, morphology and differentiation [3]. Neural cells are found to properly adhere and spread on the substrates (Figure 1b), with a significant differentiation toward neuronal phenotypes.

These results demonstrate the promising potential of our designed nanowire interfaces as nanotechnology-based neural interfaces aiding to stimulate the injured spinal cord.

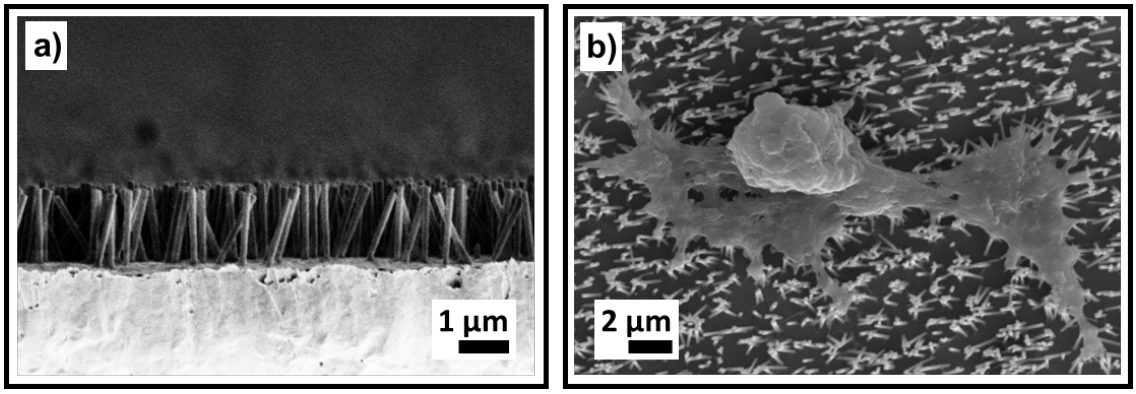


***Fig. 1**. SEM images of a) a vertical nanowire nanostructured interface and b) embryonic neural progenitor cells cultured on the nanowire interface.*

**FUNDING SOURCES:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 737116.

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# Topological protected superconducting ratchet effect produced by spin ice magnet

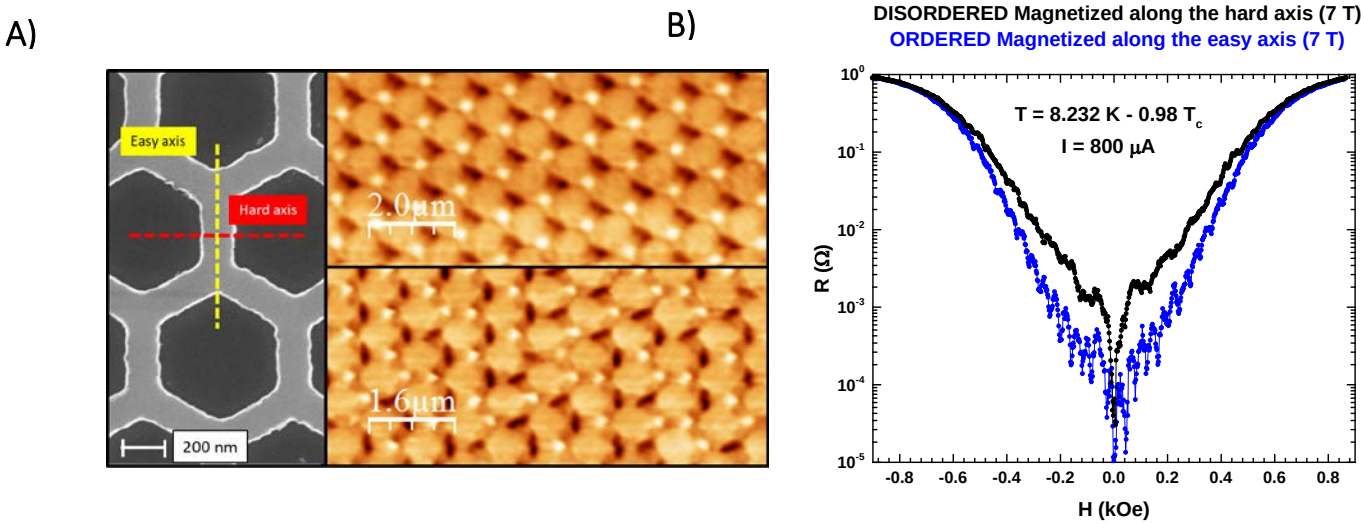
V.Rollano[1*], A. Gomez[2], A. Muñoz[3], M. R. Osorio[1], D. Granados[1], F. Valdés-Bango[4], M. Velez[4], J.I. Martin[4], E.M. Gonzalez[1,3], J.L. Vicent[1,3]

[1] *IMDEA-Nanociencia, Cantoblanco, 28049 Madrid, Spain.*
[2] *Centro de Astrobiología (CSIC-INTA), Torrejón de Ardoz, 28850 Madrid, Spain.*
[3] *Departamento Física de Materiales, Facultad CC. Físicas, Universidad Complutense, 28040 Madrid, Spain.*
[4] *Departamento de Física, Universidad de Oviedo – CINN, 33007 Oviedo, Spain.*

**E-mail: victor.rollano@imdea.org*

Magnetic frustrated systems known as spin ices have been the focus of intense research in the last years. Due to their non-trivial topology, these systems present a macroscopic degeneracy state in which a wide number of magnetic configurations are equivalent. These configurations create an interesting magnetic landscape potential that, when interacting with superconducting vortices, can completely change their dynamics.

In this work, we have fabricated an artificial Cobalt honeycomb spin ice as shown in figure A. Superconducting vortices will be used to explore the different configurations of the system at the nanoscale. We will show that, depending on the magnetic history of the system, an ordered o disordered magnetic charge distribution can be achieved. When the system is ordered, magnetotransport measurements show the fingerprint of the well-known matching effect (see figure B). Moreover, taking into account the domain wall chirality at the hexagons vertices, a magnetic asymmetry is always present in the sample. We will show that this topologically protected asymmetry will produce ratchet effect, even when the spin ice is a disordered state and there is not matching effect.




(A) *Left*: SEM image of the honeycomb spin ice. *Right*: MFM image of the ordered state (*top*) and disoredered (*bottom*). (B) Magnetorresistance measurement of the ordered state (blue) and disordered state (black).

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# The Influence of *β*-Phase Conformation on Transient Absorption and Light Amplifying Properties of Polydiarylfluorene

**Chen Sun,[a] Bin Liu,[b] Jinyi Lin[b] and Juan Cabanillas-Gonzalez *[a]**

[a]*Madrid Institute for Advanced Studies in Nanoscience, IMDEA Nanociencia, Calle Faraday 9, Ciudad Universitaria de Cantoblanco 28049, Spain.*

[b]*Centre for Molecular Systems and Organic Devices (CMSOD), Institute of Advanced Materials (IAM), Nanjing University of Posts & Telecommunications, 9 Wenyuan Road, Nanjing 210023, China*

[c]*Key Laboratory of Flexible Electronics (KLOFE) & Institute of Advanced Materials (IAM), Nanjing Tech University (NanjingTech), 30 South Puzhu Road, Nanjing 211816, China*

*E-mail: chen.sun@imdea.org, juan.cabanillas@imdea.org*

Organic semiconductors have been extensively applied as active layer in organic light emitting diodes (OLEDs) for different applications, such as displays, or as source of ambient illumination. During the past decades, π-conjugated polymers (CPs) and oligomers have attracted extensive attentions on account of their peculiar optical properties, high conductivities and low-cost fabrication process. Poly(9,9-dioctylfluorene) (PFO) is a typical blue light emitting polymer which can form β-phase conformation, resulting in an enhanced effective conjugation length, close molecular chain packing, and larger Förster radius of excitation transfer. From the study of the emission properties of PFO, it comes out that inter-molecular interactions play a major role in emission. Control of such interactions is crucial in order to hinder formation of low emissive aggregates, formation of charge-transfer states with strong photoinduced absorption associated, and exciton-exciton annihilation process, which becomes important at large exciton densities. However, PFO is not very stable and easy to form green band by photo-oxidation process. Therefore, in this work, we focus on a brand new polyfluorene, poly[4-(octyloxy)-9,9-diphenylfluoren-2,7-diyl]-co-[5-(octyloxy)-9,9-diphenylfluoren-2,7-diyl] (PODPF) whose diphenyl moieties lied at the 9-positon of fluorene and the alkyl side chains substituted at 4-position of fluorene. β-phase conformation of PODPF spin-coated film could be obtained only by using thermal heating above 230 ℃. We use femtosecond transient absorption (fs-TA) to trace the dynamic of the polymer chain plannerization process and find that the time-zero crossing point has a large red-shift in pump probe spectra in the film which cotains more β-phase conformation. This can be translated in remarkable optical gain properties in terms of low thresholds for amplified spontaneous emission (ASE) and effective laser action in surface emitting distributed feedback lasers based on β-phase PODPF.

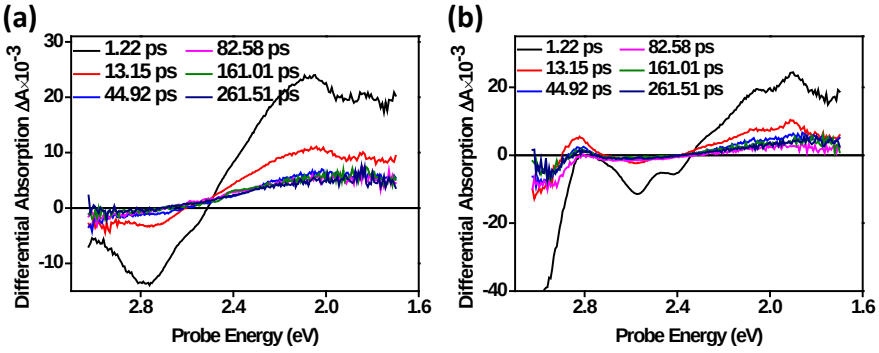


Figure 1. Differencial absorption spectra of PODPF (a) untreated and (b) annealed at 240 ℃ in film at different delay time.

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# The Influence of *β*-Phase Conformation on Transient Absorption and Light Amplifying Properties of Polydiarylfluorene

**Chen Sun,[a] Bin Liu,[b] Jinyi Lin[b] and Juan Cabanillas-Gonzalez *[a]**

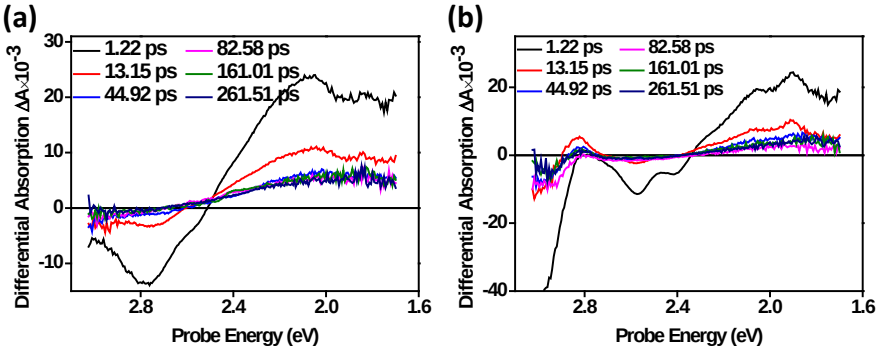
[a]*Madrid Institute for Advanced Studies in Nanoscience, IMDEA Nanociencia, Calle Faraday 9, Ciudad Universitaria de Cantoblanco 28049, Spain.*

[b]*Centre for Molecular Systems and Organic Devices (CMSOD), Institute of Advanced Materials (IAM), Nanjing University of Posts & Telecommunications, 9 Wenyuan Road, Nanjing 210023, China*

[c]*Key Laboratory of Flexible Electronics (KLOFE) & Institute of Advanced Materials (IAM), Nanjing Tech University (NanjingTech), 30 South Puzhu Road, Nanjing 211816, China*

*E-mail: chen.sun@imdea.org, juan.cabanillas@imdea.org*

Organic semiconductors have been extensively applied as active layer in organic light emitting diodes (OLEDs) for different applications, such as displays, or as source of ambient illumination. During the past decades, π-conjugated polymers (CPs) and oligomers have attracted extensive attentions on account of their peculiar optical properties, high conductivities and low-cost fabrication process. Poly(9,9-dioctylfluorene) (PFO) is a typical blue light emitting polymer which can form β-phase conformation, resulting in an enhanced effective conjugation length, close molecular chain packing, and larger Förster radius of excitation transfer. From the study of the emission properties of PFO, it comes out that inter-molecular interactions play a major role in emission. Control of such interactions is crucial in order to hinder formation of low emissive aggregates, formation of charge-transfer states with strong photoinduced absorption associated, and exciton-exciton annihilation process, which becomes important at large exciton densities. However, PFO is not very stable and easy to form green band by photo-oxidation process. Therefore, in this work, we focus on a brand new polyfluorene, poly[4-(octyloxy)-9,9-diphenylfluoren-2,7-diyl]-co-[5-(octyloxy)-9,9-diphenylfluoren-2,7-diyl] (PODPF) whose diphenyl moieties lied at the 9-positon of fluorene and the alkyl side chains substituted at 4-position of fluorene. β-phase conformation of PODPF spin-coated film could be obtained only by using thermal heating above 230 ℃. We use femtosecond transient absorption (fs-TA) to trace the dynamic of the polymer chain plannerization process and find that the time-zero crossing point has a large red-shift in pump probe spectra in the film which cotains more β-phase conformation. This can be translated in remarkable optical gain properties in terms of low thresholds for amplified spontaneous emission (ASE) and effective laser action in surface emitting distributed feedback lasers based on β-phase PODPF.

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3 Lin, J. Y.; Zhu, W. S.; Liu, F.; Xie, L. H.; Zhang, L.; Xia, R. D.; Xing, G. C.; Huang, W., *Macromolecules* **2014**, 47, 1001−1007

# Divergent Sorption Behaviour of Isostructural Luminescent Lanthanide-based Metal-Organic Frameworks as Key for the Design of Novel, Selective and Sensitive Gas Sensors

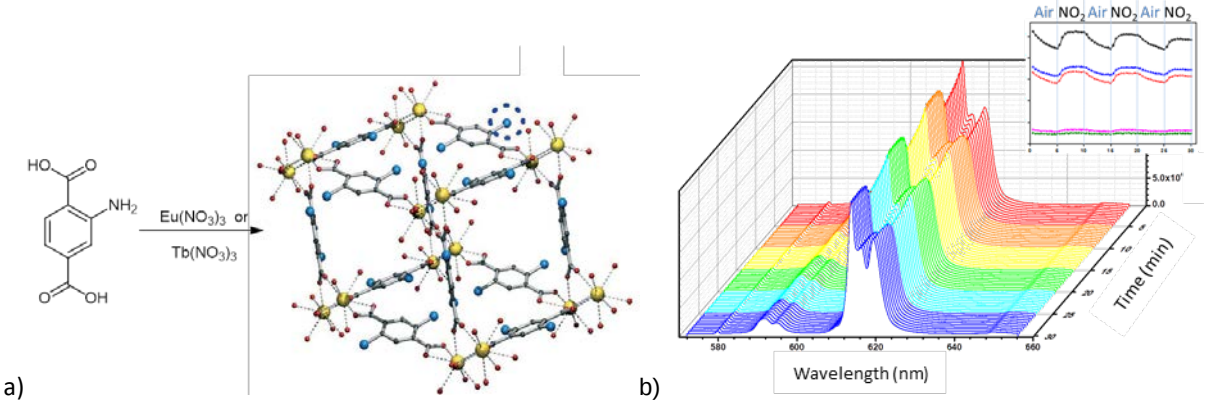
**Arturo Gamonal,[a] Chen Sun, [b] Elena San Vicente, [a] Estefania Fernandez-Bartolome,[a] Reinhold Wannemacher,[c] Juan Cabanillas-Gonzalez [b] and Jose Sanchez Costa[a]**

[a]*Switchable Nanomaterials Group at IMDEA Nanociencia, Ciudad universitaria de Cantoblanco 28049, Madrid. Spain*
[b]*Organic Photophysics and Photonics Group at IMDEA Nanociencia; Ciudad universitaria de Cantoblanco 28049, Madrid. Spain*
[c]*Nano-Optics and Nano-Acoustics, IMDEA Nanociencia; Ciudad universitaria de Cantoblanco 28049, Madrid. Spain*
*E-mail: arturo.gamonal@imdea.org*

Lanthanide-based metal organic frameworks (Ln-MOFs) have attracted special interest because of their rich coordination geometry, leading to fascinating architectures and interesting topologies, relatively high stability, and their unique and remarkable luminescent and magnetic properties. Due to sharp emissions and long lifetimes of the excited states the luminescence of Ln (III) ions in Ln-MOFs has a wide range of applications, e.g. as sensors, displays, fluoroimmunoasssays, adsorbents, etc.[1]

Moreover, MOFs exhibit porosity and open channels, which are capable of taking up and storing gases and guest molecules. In case of Ln-MOFs the perturbation from adsorbed guest molecules can alter the photoemission intensities, spectral profiles and lifetimes, making them excellent candidates for chemosensing.[2] Furthermore, the right selection of the ligand and its functional groups within the framework may be used to further promote preferred guest binding for selective detection. Based on these considerations, our research is mainly focused on synthesis of Ln-MOFs capable to take up and exchange guest molecules and to understand the relationship between their luminescent properties and sorption behaviour.

This communication describes the synthesis of two isostructural Ln-MOFs,[3] employing the ligand 2-amino-1,4-benzene dicarboxylic acid, which acts as a recognition center in order to provide an increased selectivity. The photo-physical study shows an interesting and unexpected behaviour of the luminescent intensity Eu-MOF versus Tb-MOF when exposed to air containing 5 ppm of $NO_2$ (see figure below). The study of the opposite effect of $NO_2$ on the luminescence efficiencies of Eu and Tb, is providing a better understanding of the nature of MOF/$NO_2$ interactions. The results suggest a powerful new approach for the development of new luminescent sensors for volatile compounds with increased selectivity and sensitivity.




## Notes and References

‡ a) Synthesis scheme; b) Emission spectra of Eu-MOF over three consecutive cycles (dry air- dry air w. 5ppm of $NO_2$)

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# Bioorthogonal Photocatalysis for prodrugs activation

**Juan Gurruchaga Pereda,[a,b] Silvia Alonso-de Castro,[b] Aitziber L. Cortajarena[*b,c] and Luca Salassa[*a,c]**

[a] *Donostia International Physics Center: Paseo Manuel de Lardizabal 4, Donostia, 20018, España, Inorganic Photochemistry Lab. Tel: 943 015346*
[b] *CIC biomaGUNE: Paseo de Miramón 182, Donostia, 20014, España, Biomolecular Nanotechnology Group. Tel: 943 00 54 27*
[c] *Ikerbasque, Basque Foundation for Science: Bilbao, 48011, España.*
E-mail: j.gurruchaga@dipc.org

Cancer, the second leading cause of death worldwide, was responsible for 8.8 million deaths in 2015. Since the discovery of cisplatin in 1969, platinum drugs have been employed effectively in the clinics for the treatment of different types of cancers. Despite the success of this family of chemotherapeutic agents, they present low selectivity against tumor tissues, producing undesired systemic side effects on patients. To overcome these drawbacks, a widely-investigated strategy consists of changing the oxidation state of the platinum ion from 2+ to 4+, hence obtaining low-toxicity prodrug complexes that can be activated by cellular reductants.
More recently, several research groups have also shown that the biological effects of platinum(IV) complexes can be switched on by light irradiation in a localized manner, potentially improving their therapeutic effectiveness. (1)

This contribution will discuss how our group has developed a novel strategy which allows using low doses of visible light for the selective photoactivation of platinum(IV) anticancer prodrugs in biological environments. We will describe new bioorthogonal reactions in which flavin cofactors (2) and the artificial flavoprotein miniSOG (mini singlet oxygen generator) (3, 4) act as highly selective photocatalysts for the in situ generation of platinum(II) anticancer agents. This chemistry is unique since the use of biocatalysis has been so far limited to organic reactions. Indeed, there are not available examples where biological catalysts such as flavins or flavoproteins convert inorganic complexes in biological active species.
Catalytic transformations of platinum prodrug candidates by flavins may expand the scope of bioorthogonal chemical reactions in the field of medicinal inorganic chemistry.

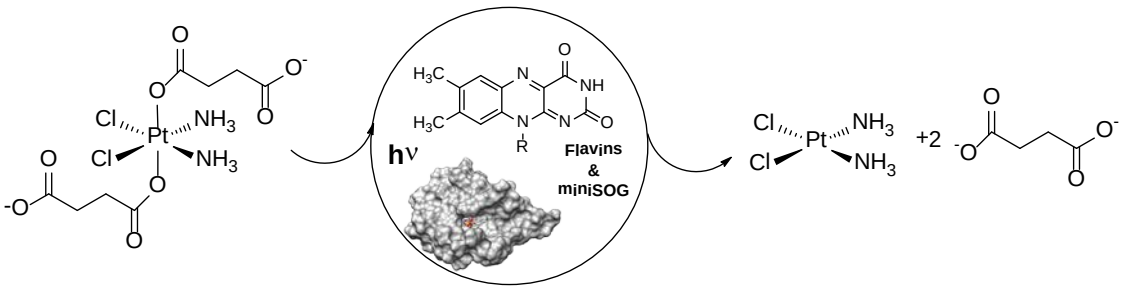


**Figure 1**. Photoactivation strategy of platinum (IV) produgs by photocatalysts based on falvins or flavoproteins

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# Osmium(II) tether complexes with a coordinatively bound oxygen atom capable of hijacking and releasing a proton.

**Sonia Infante*[a] and Ana M. Pizarro[a]**

[a]*IMDEA Nanociencia, Faraday 9, Ciudad Universitaria de Cantoblanco, Madrid, 28049, Spain*

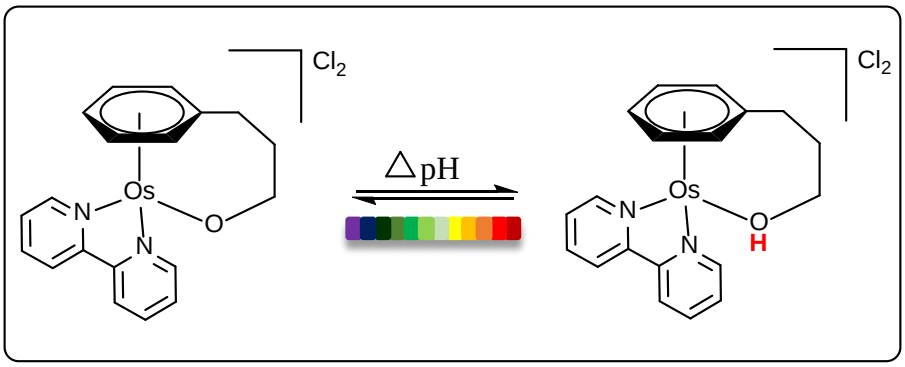
*E-mail: sonia.infante@imdea.org*

Osmium(II)-arene complexes have recently received attention as possible antitumor agents with novel mechanisms of action, such as triggering of metabolic shift and bio-catalysis.[1]

Cancer metabolism is characterized by a predilection for aerobic routes such as glycolysis, even in presence of oxygen, process known as the Warburg effect.[2] As a consequence, the intracellular accumulation of lactate and subsequent extrusion of lactic acid affect the acidity of the extracellular microenvironment ($pH_e$), which presents pH values as low as 6.5, instead of 7.4 in normal tissue, facilitating metastasis. Internal pH ($pH_i$) however, undergoes basification, which promotes proliferation.[3] One scarcely explored therapeutic strategy in cancer research consists in interfering with the finely controlled pH balance in tumours. Our approach intends to exploit the high potency of organometallic compounds in synergy with disrupting the pH gradient of tumour cells.

We have designed, synthesised and characterised two novel families of half-sandwich organometallic tether compounds, of ruthenium(II) and osmium(II). These complexes bear an alcohol-derivatised arene, $C_6H_5(CH_2)_nOH$ (n = 2, 3). The oxygen binds to the metal forming a coordination bond, which has the potential to capture a proton in the biologically relevant pH ($pK_a$ in the range 4.2–6.6). Additionally, the Ru(II) family can undergo Ru(II)-O cleavage upon protonation.

We believe that this type of compounds are able to highjack and release a proton in a biological context as a function of the pH, being capable of acting as proton shuttles that work against the pH gradient of the cancer cell. Additionally, as a consequence of the Warburg effect, this approach can achieve selectivity for the tumour cell. These complexes could have a key role in biological systems with a reversed pH gradient such as that found in tumour cells.

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# Evaluation of antibacterial activity of magnetite/Ag nanocomposites with different silver content synthesized by an aqueous route

**Y. Luengo*[a], B. Sot[a] and G. Salas[a]**

[a]*Imdea Nanoscience, C/Faraday 9, Ciudad Universitaria de Cantoblanco, 28049, Madrid, Spain. Tel: 91 299 87 00;*
*E-mail: yurena.luengo@imdea.org*

Nowadays, antimicrobial effects are intensively studied due to an enormously increasing bacterial resistance against excessively and repeatedly used classical antibiotics. Thus, day after day, the treatment of bacterial infections utilizing classical antibiotics is certainly becoming ore serious global problem (1). In order to overcome this problem, ther is an increase in need to design new antibacterial agents. Nanocrystalline silver has been proved to be a very effective antimicrobial agent since silver and its compuounds have powerful antimicrobial capatility and borad inhibitory biocidal spectra for microbes including bacteria, viruses and eukaryotic microorganisms (2). However, silver nanoparticles have some limitations: their low yield for penetrating bacterial biofilms and their concentration-dependent toxicity to human cells are the most serious drawbacks. The combination of magnetic nanoparticles with silver nanoparticles may enhance the depth of biofilm penetration and this binary system can be removed from the medium by an external magnet (3).

Thus, bifunctional γ-$Fe_2O_3$@Ag nanocomposites with both superparamagnetic and antibacterial properties were synthesized by an adaptation of Turkevich method. Different silver amount and reaction temperatures were studied to obtain samples with different Ag content and particle size. The antibacterial activity of the samples was tested against the bacterial pathogens E. Coli (Gram-negative) and S. Aureus (Gram-positive), by means of a standard dilution method. This method enables the substantiation of minimum inhibitory concentrations (MIC) of the magnetic silver nanocomposites, leading to a growth inhibition of the tested bacteria.

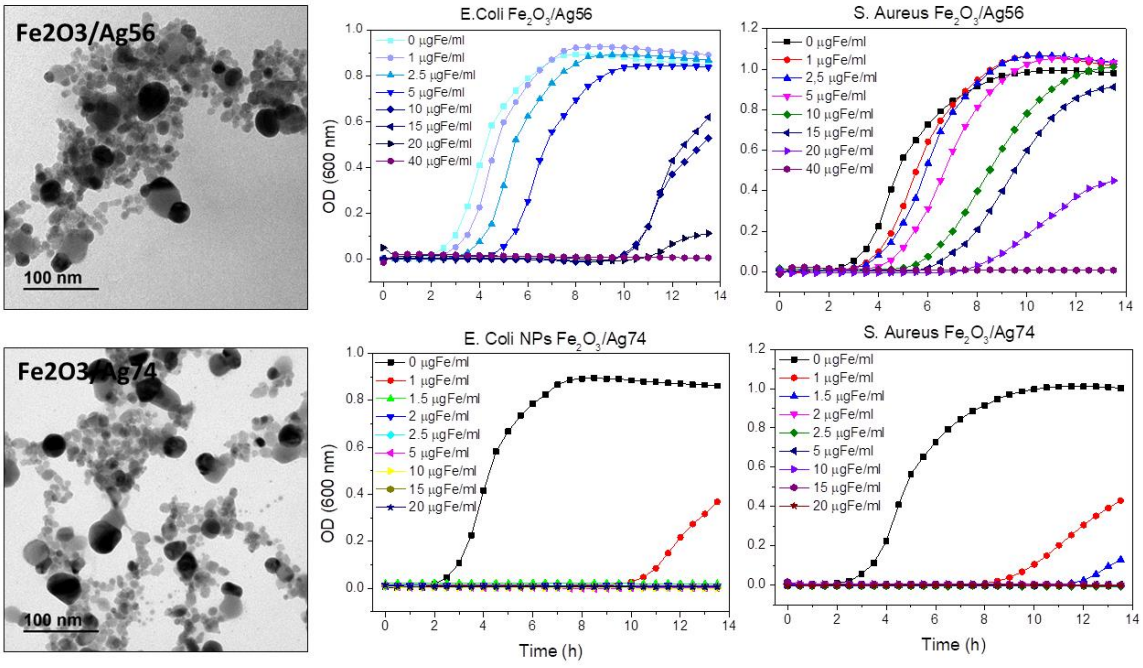


***Fig1.*** *TEM images and bacterial growth at different iron concentration for samples with 56% Ag (a) and with 74% Ag (b).*

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# Pyridine/Diazine derivatives to access a new lanthanide luminescent materials

**Paloma Martínez Martín* and Juan Carlos Rodríguez-Ubis**

*Departamento de Química Orgánica, Universidad Autónoma de Madrid, Spain.Tel: 914974496*

*E-mail: Paloma.martinezm@inv.uam.es*

Tris-N-heterocyclic ligands, such as 2,6-bis-(pyrazol-1-yl)pyridine derivatives, continue to be very widely used in lanthanide complexation chemistry[1] due to they provide a cavity for lanthanide chelation, optimal for the enhancement of the luminescent emission properties of the ion by antenna effect.

The family of luminescent MOFs based on lanthanide ions (LnMOFs) has a great impact within hybrid materials since they combine typical MOFs' properties such as porosity, with the good photophysical properties of lanthanide ions, greatly expanding the possible applications of these materials.

In this communication we will describe selected properties of new families of trisheterocyclic ligands based on pyridine and any of the three diazine rings, pyrazine, pyrazine and pyrimidine as central rings, flanked by two differently substituted pyrazol-1-yl rings. These polyheterocyclic frameworks give access to LnMOF's with different luminescent and crystallographic behavior. The crystallographic and photophysical data obtained from these LnMOF's let us to extract structure–property relationships.[2]

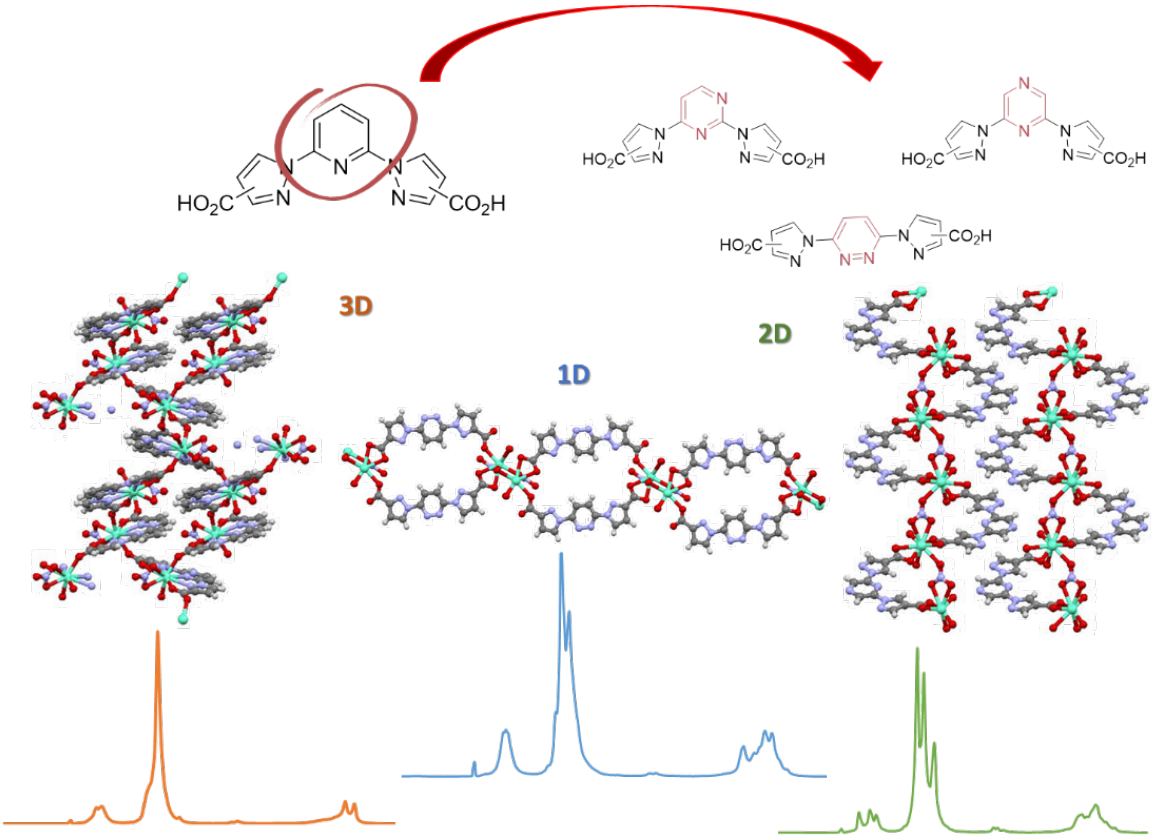


**Figure 1.** Crystallographic-photophysical relationships.

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# Synthesis of non-planar nanographenes

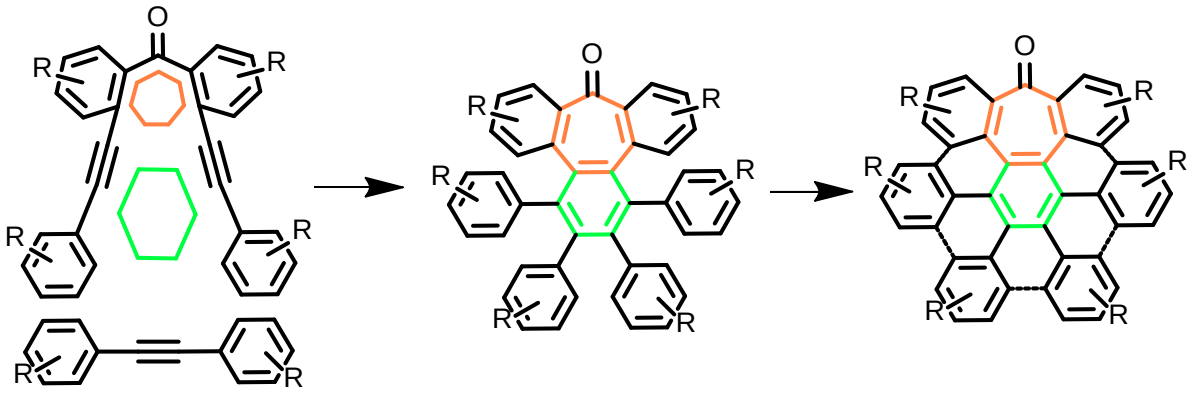
**Lucía Palomino-Ruiz[a,b], Vicente G. Jiménez [a], Carlos M. Cruz [a], Irene R. Márquez [a], Alba Millán [a], M. Teresa González [b], Araceli G. Campaña [a]**

[a]*Departamento Química Orgánica, Universidad de Granada (UGR), Granada, Spain. Tel: 958243320*
[b]*Fundación IMDEA Nanociencia, Ciudad Universitaria de Cantoblanco, Madrid, Spain. Tel: 912998700*

*lpruiz@ugr.es*

Nowadays graphene is one of the most outstanding topics in material science because its promising properties: lightness, flexibility and excellent electrical and thermal conductivity. It is known that the presence of structural defects promotes modifications in that properties [1], but an extensive understanding of the relationship defects-properties is still a challenge.

Graphene-like molecules or nanographenes have being extensively used as models for studying graphene [2] because its reduced size (ranging from 1 to 100 nm) facilitates their manipulation. These molecules can be obtained by synthetic strategies, which allow a total control of the structure in terms of shape and size, including the possibility to incorporate structural defects.
Within that context, we are interested in the synthesis of nanograpahenes containing diferent types of defects, and the subsequent evaluation of its properties. Recently, our group has presented a versatile synthetic route to rapidly prepare nanographenes incorporating seven-membered rings [3]. It is based on the sequence of Co-catalyzed cyclotrimerization and cyclodehydrogenation reactions (figure 1). That results in an extended aromatic structure containing an heptagon. A good selection of synthetic precursors allows the incorporation of certain groups in selected positions that colud be used for a subsequent elargements of the structure.
In this work, we present several distorted nanographenes incorporating seven-membered rings with diferent groups and shapes obtained from that innovative methodology.

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# Nanostructured graphene catalyzes the reaction between two organic molecules

**Michele Pisarra,*[a] Cristina Díaz,[b,c] Juan Jesús Navarro[a,d], Belén Nieto-Ortega[a], Julia Villalva[a], Fabián Calleja[a], Rodolfo Miranda[a,c,d], Emilio M. Pérez[a], Amadeo L. Vázquez de Parga[a,c,d] and Fernando Martín[a,b,c]**

[a] *Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nano), Campus de Cantoblanco, 28049 Madrid, Spain;*

[b] *Dep. de Química, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain;*

[c] *Condensed Matter Physics Center (IFIMAC), Universidad Autónoma de Madrid, 28049 Madrid, Spain;*

[d] *Dep. de Física de la Materia Condensada, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain;*

*E-mail: michele.pisarra@imdea.org*

The presence of the supporting substrate might strongly influence the physical properties of graphene. A paradigmatic example is the graphene/Ru(0001) interface, in which the lattice mismatch between the two systems gives rise to a strong corrugation in graphene, that exhibits a moiré pattern and dramatic variations of the graphene-metal interaction at the nanometer scale, as well as a strong modulation of its electronic properties. Besides, graphene has the capability to efficiently isolate further adsorbed molecules from the highly reactive metal surface, while allowing charge transfer from the metal to the adsorbates. This fact has been explored in the past, when the graphene/Ru(0001) interface has been used as an adsorption template for TCNQ molecules, which, due to charge transfer, have an unpaired electron when adsorbed on graphene/Ru(0001) and hence behave as magnetic impurities, displaying a Kondo effect [1]. The $CH_2$-CN· radical have also been employed to covalently pattern the graphene layer with high spatial selectivity [2]. A natural development is determining the role of supported graphene as a catalytic agent, studying the chemical reactions that may take place when multiple molecular species are adsorbed on the graphene/Ru(0001) surface.

In this work we try to get insight into this argument, studying the adsorption of a TCNQ molecule on a graphene/Ru(0001) surface, previously functionalized with $CH_2$-CN· radicals. By means of Density Functional Theory (DFT) calculations we determine the optimal geometric configuration of the two molecules on the surface and identify the new molecular species found in the scanning tunneling microscopy (STM) measurements. Our calculations suggest the formation of TCNQ-$CH_2$CN, in which the two molecules are bonded by means of a C-C covalent bond. The DFT calculations clarify that the catalytic role of graphene is multifaceted: it holds the reactants in place, it allows for an efficient charge transfer between the ruthenium substrate and the reactants thus favoring changes in carbon hybridization, and finally it adsorbs the reaction product. More interestingly, the reaction can be fully reversed by injecting electrons in the LUMO of the molecule by the STM tip. After this opeartion the reactants are recovered in their initial state, that is, the $CH_2$-CN- is again covalently bonded to graphene, while the TCNQ recovers its electronic configuration with one unpaired electron, therefore displaying a Kondo effect.

By a combined DFT-STM study we fully characterize the property of the newly formed molecule adsorbed on the graphene/Ru(0001) surface. We assign the scanning tunneling spectroscopy peaks to specific projected density of states features and molecular orbitals. The surface molecule charge transfer results in double occupation of all the molecular orbital, despite the fact that the TCNQ-$CH_2$CN has an odd number of electrons in gas phase. The molecule, hence, does not exhibit magnetic moment on the surface. Thanks to the reversibility of the reaction, the TCNQ-$CH_2$CN can be used as a reversible magnetic switch, controlled by a chemical reaction.

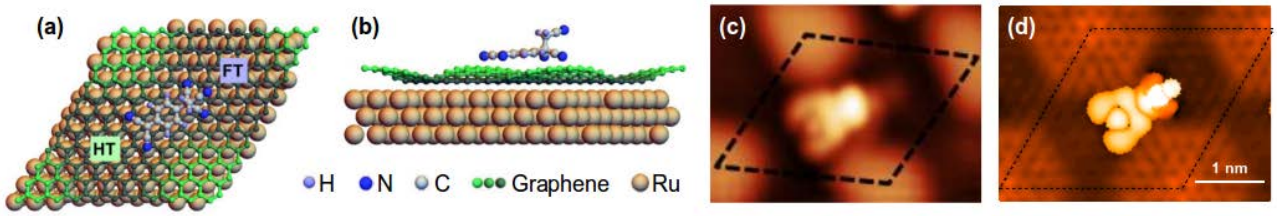


Figure 1. (a-b) Top view (a) and side view (b) of the unit cell including the ruthenium substrate, the corrugated graphene and the TCNQ-$CH_2$CN molecule as obtained in the DFT calculations. (c-d) STM images of the TCNQ-$CH_2$CN on the surface, as obtained in the STM measurements (c) and in the DFT calculations (d).

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# Oligonucleotide-Templated Stacking of Semiconductors

**Sonia Romero-Pérez,[a] Sara Sierra, [a] Manuel C. Martos-Maldonado,[a] David González-Rodríguez[a,b]**

[a] *Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, 28049 Madrid, Spain. Tel: 914972778*

[b] *Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, 28049 Madrid, Spain*

*E-mail: david.gonzalez.rodriguez@uam.es*

DNA has been widely used as a robust template because it is able to organise organic structures in programable architectures with high precision.[1] This fact is attributed to: **a)** an optimum distance between nucleobases, which favours π-π stacking interactions; **b)** a precisely defined sequence and length and **c)** high fidelity in terms of recognition.

In our proposal DNA would act as a building block for functional architectures taking advantage of H-bonding interactions between complementary nucleobases,[2] solvophobic forces and π-π interactions between extended polycyclic aromatic rings in aqueous media. Simple DNA oligonucleotide strands will guide the stacking of functional organic systems. The novelty here is the control and programmability over the sequence of modified π-conjugated electron donor/acceptor chromophores, a topic that had never been addressed in oligonucleotide-templated systems.

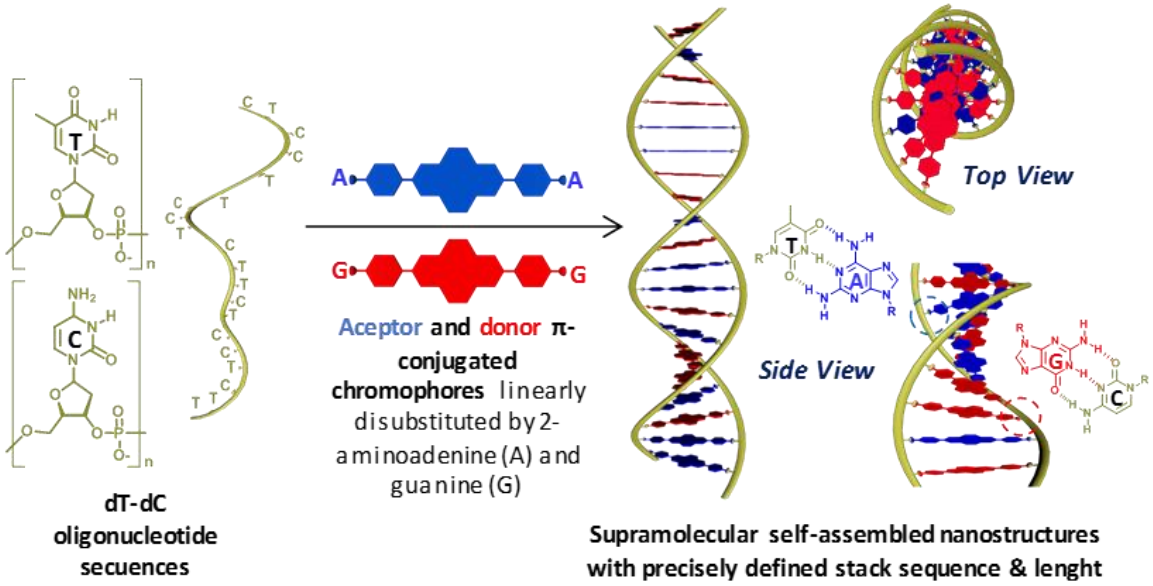


**Figure 1.** Schematic representation of the process in which two oligonucleotide chains guide the self-assembly of π-conjugated donor/acceptor systems attached to nucleobase directors.

We plan to demonstrate that simple DNA strands are an efficient template not only to guide the supramolecular self-assembly process that generates new aggregated double helix systems, but also that they provide a tool to control the stacking sequence of functional chromophores due to H-bonding patterns. Our research will be focused on double helix instead of simple one because this approach offers several advantages: **1)** the resulting nanofibers will be more stable; **2)** the control over the sequence could be reinforced by the summed action of a double template; **3)** the tendency to bind is reduced since the supramolecular structure is more rigid; **4)** we could achieve precise control over the length of the nanofiber as the combination of different nucleobases in the same strand would lead to complete parallel alignment of the two oligonucleotide-templates, while in literature the examples display polydispersity in this context.

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# Band gap opening in metallic single-walled carbon nanotubes by encapsulation of an organic salt

**Julia Villalva**[a], **Belén Nieto-Ortega, Mariano Vera-Hidalgo, Luisa Ruíz-González, Enrique Burzuri, Emilio M. Pérez**

[a]*IMDEA Nanoscience, Ciudad Universitaria de Cantoblanco, c/Faraday 9, 28049 Madrid, Spain*
*E-mail: julia.villalva@imdea.org*

Our group has recently described the synthesis of mechanically interlocked derivatives of single wall carbon nanotubes (MINTs). MINTs are rotaxane-type species where the single-wall nanotubes (SWNTs) act as threads, which are encapsulated by macrocycles formed around them through ring closing metathesis, following a "clipping" strategy.[1-4]

Since one of the most intriguing properties of mechanically interlocked molecules (MIMs) is the possibility of provoking controlled large-amplitude submolecular motion, our next objective is to investigate the controlled submolecular motion of the macrocycle(s) along the SWNT thread, making use of the dynamic nature of the mechanical bond. For this purpose, the SWNTs must be desymmetrized adding different “stations”. In this way, the macrocycle could be displaced altering its affinity for each of the stations by external stimuli. In a recent publication, Cambré *at al.*[5] have reported the possibility of generating assymetry in carbon nanotubes by the encapsulation of organic dyes. Following this metodology, in this communication we describe the encapsulation of a viologen salt into metallic SWNTs. Raman spectroscopy, thermogravimetric analysis and aberration corrected high resolution transmission electron microscopy confirm the encapsulation process (**Figure 1**).

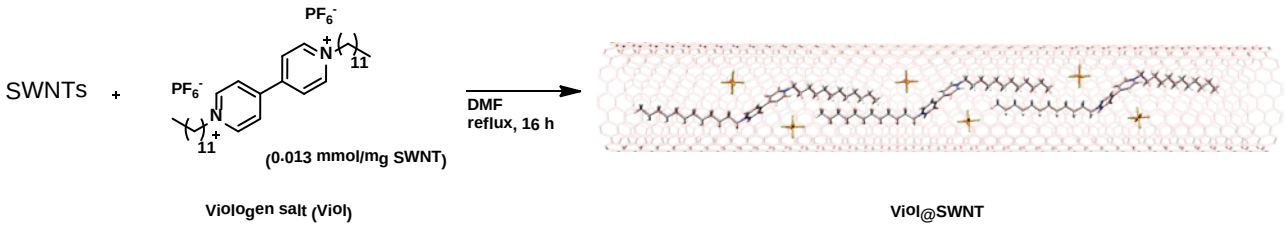


**Figure 1** Encapsulation of the viologen salt in opened SWNTs.

Serendipitously, these endohedral SWNTs have turned out to be very interesting by themselves. Their electrical properties have been measured in field-effect transistor (FET)-like devices revealing that the encapsulation of this kind of molecules opens a gap in the band structure of the tubes, changing its behaviour from metallic to semiconductor. Indeep, electrical measurements show that the metallic SWNTs become semiconducting with an on-off current ratio of around $I_{on}/I_{off} = 10^6$ and a FET mobility $\mu \approx 600$ cm$^2$/Vs. These values are better than most reported for semiconducting SWNTs functionalized with molecules.

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# POSTER COMMUNICATIONS

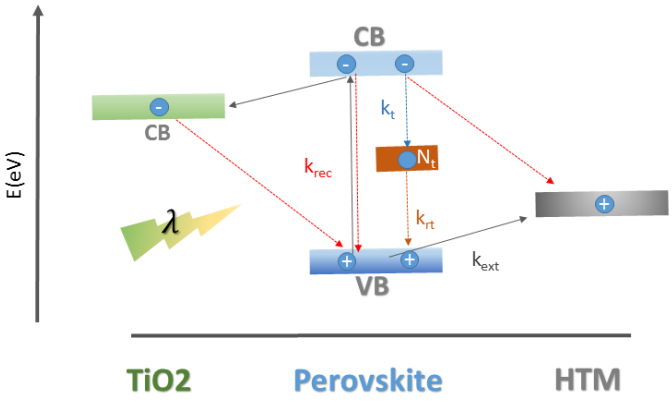
# New Hole Transporting Material for Perovskite Solar Cells

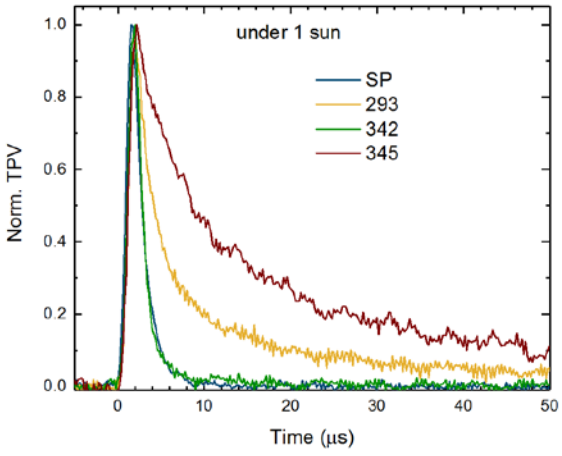
Abasi Abudulimu,[1] Rafael Sandoval-Torrientes,[1] Iwan Zimmermann,[2] José Santos,[1] Mohammad K. Nazeeruddin,[2] Nazario Martín,[1,3] Larry Lüer*[1]

*1IMDEA Nanociencia, Madrid, 28049, Spain*
*2EPFL VALAIS, Sion, 1951, Switzerland.*
*3Facultad de Ciencias Químicas, Universidad Complutense de Madrid, Madrid, 28040, Spain*
*E-mail: larry.luer@imdea.org*

Perovskite has become a hot research topic in the field of photovoltaics due to its broad optical absorption profile, high charge carrier generation yield, and fast charge carrier mobility. Power conversion efficiency (PCE) of 22 % has already been reached in a less than a decade [1]. The hole transporting material (HTM) is one of the essential ingredients in that, and Spiro-OMeTAD (SP) is the most common one found in the top performing devices [2]. However, it is expensive and needs to be doped by hygroscopic dopants, since it does not possess intrinsic high carrier mobility, which in turn decreases the stability of the device [3]. Thus, developing easy-to-produce, easy-to-process, scalable, environment and cost friendly new HTM material is an important milestone to reach.

Here we report three different HTMs (with representative name HTM342, HTM293 and HTM345) and their performances in the perovskite devices, in comparison with the SP. Without any systematic optimization, the HTM342 performed very well, delivering comparable PCEs to the that with SP. Current-Voltage measurements under one sun illumination showed that all the devices with the new HTMs produced significantly less short circuit current compared to the device with the SP. To better understand the effect of each HTM on the device performance, we studied the carrier extraction and recombination processes in the devices by transient photovoltage and photocurrent (TPV and TPC, respectively) methods with and without background illumination. The TPV measurements in the dark and under background illumination revealed that the trap induced recombination increases 40% and 50%, respectively, when SP is replaced with HTM293 and HTM345, and cannot completely be filled under one sun background illumination. Instead, it decreases 4% when HTM342 is used. However, the direct carrier recombination rises slightly, which can be due to the reduced energy gap between the conduction band of perovskite and HOMO of HTM342. The TPC measurements, on the other hand, disclosed that there are carrier extraction losses in the devices, especially with HTM293 and HTM345 due to charge accumulation. In the case of HTM342 we assume that the charge accumulation is caused by the energy barrier between HTM and Au electrode, while in the case of HTM293 and HTM345, it is caused from the reduced energy offset (carrier driving force) between perovskite and HTM. It is worthy to mention that conductivity and morphology of the HTM can also play an important role in the charge dynamics. Thus, by optimizing the HTMs and choosing a proper electrode, the device performance can be improved further, and the HTMs can be applied as alternatives for some of the expensive and difficult-to-produce HTMs.

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# Design of bactericidal surfaces by using micro-nano hierarchical topographies

**María Teresa Alameda, Manuel R. Osorio, Jaime Hernández, Daniel Granados, Isabel Rodríguez**

IMDEA Nanociencia, Faraday 9, Madrid, 28049, Spain;

*E-mail: mariateresa.alameda@imdea.org*

The vast utilization of antibiotics has provoked the appearance of super-resistant bacteria which has become a major public health threat. Nature inspired nanostructured surfaces have shown a potential to preclude bacteria implantation avoiding the use of chemical means which have proved to promote the development of resistant bacteria. For instance, biomimetic moth-eye topographies have demonstrated to reduce the adhesion and viability of bacteria on their surfaces [1].

From the point of view of clinical applications, it is also important not only to deter bacteria growth but to improve cell adhesion and proliferation for a more favourable host tissue response towards artificially implanted materials. Consequently, there is a need to better understand the interaction of both bacteria and mammalian cells with topographical features, to identify which ones produce among them a differential and opposed response.

With this aim, hierarchical micro and nano structures based on the moth-eye topography and micro pillars have been designed and fabricated. A novel fabrication process combining nanoimprinting and photolithography (CNP) has been developed. The method involves three steps including first nanoimprinting of moth-eye nanopatterns, secondly a deposition of a photoresist layer which is nanoimprinted and subsequently, optical lithography is performed by means of a maskless laser writer with an interferometer-controlled high precision stage to pattern the microfeatures. Implementing this process, a hierarchical topography is obtained comprising moth-eye patterns on two different levels.

Figure 1(a) shows a mold substrate produced consisting of a hexagonal pattern of 2 µm-diameter pores with 250 nm nanocone moth-eye patterns on the base and top layers. A replica via thermal nanoimprinting is displayed in Figure 1(b).

The response of bacteria to the topography is being studied. Preliminary results show a decrease in the number of bacteria attached to the surfaces with an increase in the number of non-viable bacteria.

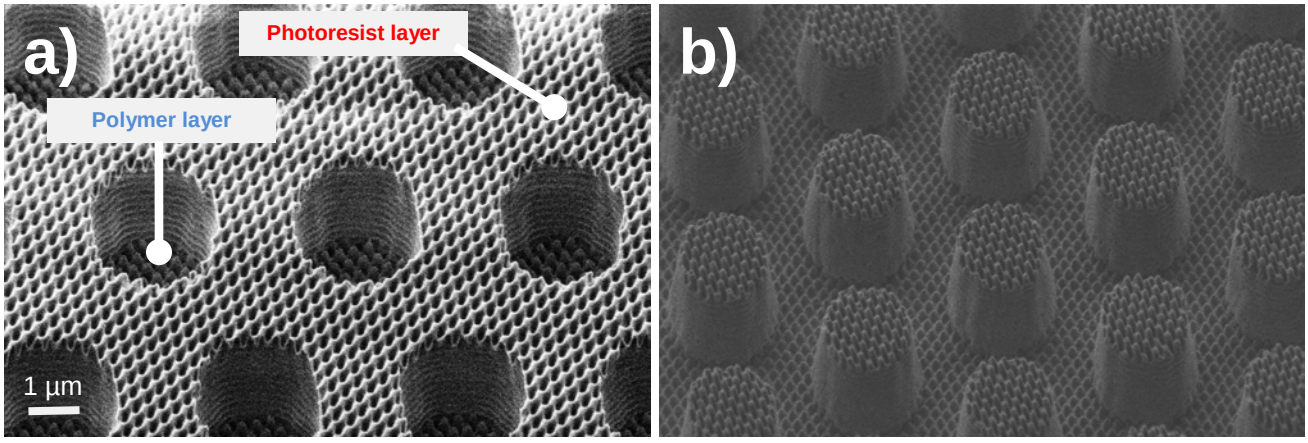


Figure 1. (a) Multiscaled structure fabricated by a three-step process involving nanoimprinting and photolithography . (b) Polymer replica obtained from (a).

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# Mechanical softening of lipid membranes by the rotating motor protein F1F0 ATP synthase

**V.G. Almendro-Vedia*[a,b], P. Natale[a,b], M. Mell[b], S. Bonneau[c], F. Monroy[b], F. Joubert[c] and I. López-Montero[a,b]**

[a]*Instituto de Investigación Hospital Doce de Octubre (i+12), Madrid, Spain ;*
[b]*Dpto. Química Física I, Universidad Complutense de Madrid, Madrid, Spain;*
[c]*Laboratoire Jean Perrin, CNRS- Université Pierre et Marie Curie, Paris, France;*
*E-mail: vgavedia@ucm.es*

ATP synthase is a rotating membrane protein that synthesizes adenosine triphosphate (ATP), the chemical energy source of the cell. To unveil the mechanical impact of this molecular motor protein on the bending properties of its lipid environment, we have functionally reconstituted the ATP synthase in giant unilamellar vesicles and tracked the membrane fluctuations by means of flickering spectroscopy. We find that ATP synthase rotates at a frequency of about 20 Hz, promoting large out-of-equilibrium deformations at discrete hot-spots in lipid vesicles and thus inducing an overall membrane softening. Therefore, the rotation of ATP synthases promote mechanically adapted membranes with a high bending compliance and able to support high local curvatures. Our results evidence a mechanical functionality of the ATP synthase for biomembrane re-structuring and shaping. The main text of the communication should appear here. Indenting of text is requiered all over the text including the first paragraph.

# Magnetic microwires for contact-less sensing application

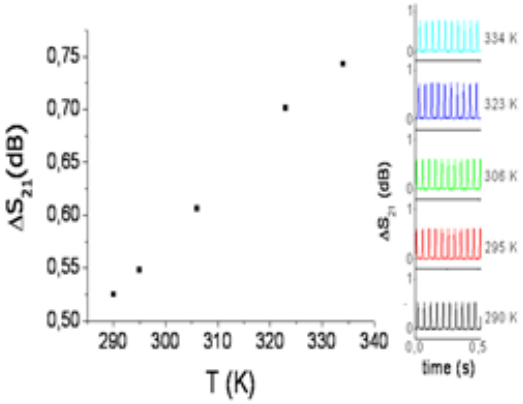
**Diego Archilla*[2] and Pilar Marín[1,2]**

[1] *Instituto de Magnetismo Aplicado, Universidad Complutense de Madrid-ADIF-CSIC, P.O. Box, 155, Las Rozas, Madrid 28230 Spain.*

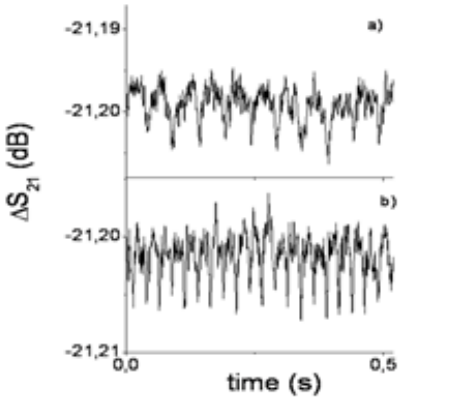
[2] *Departamento de Física de Materiales, Universidad Complutense de Madrid, 28224, SPAIN*

*E-mail: diegoarc@ucm.es*

Amorphous magnetic microwires presents unique magnetic properties, in particular, the giant magneto-impedance effect present in this type of microwires allows to detect the interaction of the sample with microwaves [1]. The changes of this interaction due to a variation of the physical properties of the microwire makes them useful as elements for contact-less sensing application [2, 3]. In this work microwires with composition $Fe_{2.25}Co_{72.75}B_{15}Si_{10}$ were used in order to measure changes in temperature and to detect AC current passing thought the microwire. Also the interaction with a Cu wire, acting as a dipolar antenna, has been measured.




Temperature dependence of the scattering parameter for AsCast microwire.




Scattering parameter caused by the presence of an AC of a) 10 Hz and b) 20 Hz current through the microwire.

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# Carbon nanodots for the oxygen reduction reaction electrocatalysis

**Emiliano Martínez-Periñán[a,b], Iria Bravo*[a,c], Samuel J. Rowley-Neale[b,d], Encarnación Lorenzo[a,c], Craig E. Banks[b,d]**

[a]*Departamento de Química Analítica y Análisis Instrumental, Universidad Autónoma de Madrid, 28049, Madrid, Spain. Tel: +34914972523;*

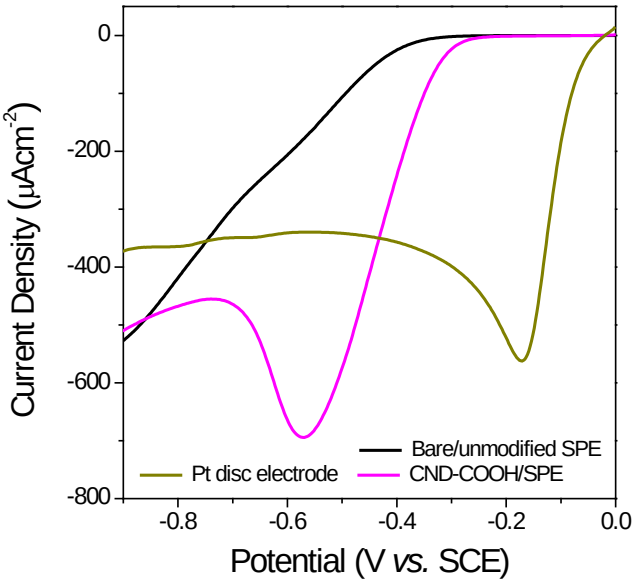
[b]*Faculty of Science and Engineering, Manchester Metropolitan University, Chester Street, Manchester M1 5GD, UK;*

[c]*IMDEA-Nanoscience, Faraday 9, Campus Cantoblanco-UAM, 28049 Madrid, Spain;*

[d]*Fuel Cell Innovation Center, Manchester Metropolitan University, Chester Street, Manchester M1 5GD, UK.*

*E-mail: iria.bravo@uam.es*

Carbon nanodots (CNDs) are a member of the carbon nanomaterials family, whose electrochemical properties are being currently studied. In this context, two types of carbon nanodots with different surface functional groups, amides (CNDs-CONH2) and carboxylic groups (CNDs-COOH), were synthesized. They were fully characterized by a variety of techniques, such as FTIR, XPS, DLS or TEM. After modification of screen printed carbon electrodes (SPCEs) with CNDs, their electrocatalytic activity towards the oxygen reduction reaction (ORR) was studied both in acidic (0.1 M H2SO4) and basic (0.1 M KOH) media. This reaction has a great importance for the development of proton exchange membrane fuel cells (PEMFCs). Due to the large kinetic barrier of this reaction [1] there is a great interest in the search for new electrocatalysts, which can not only reduce the overpotential and increase the achievable ORR peak current, but also allow the reaction to occur via the desirable 4 electron pathway [2]. In this sense, CNDs modified SPCEs show a higher ORR peak current and reduced overpotential when compared to unmodified SPCEs. Furthermore, CNDs-COOH are found to facilitate the ORR via a near optimal 4 electron pathway in oxygenated 0.1 M KOH. Therefore, CNDs-COOH modified SPCEs could be used as a cathodic electrode for PEMFCs as a cheaper alternative to the traditionally used platinum electrode.

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# Organometallic iridium(III) cyclopentadienyl complexes bearing a structural strain as potential anticancer pro-drugs

**Ana C. Carrasco,* Vanessa Rodríguez-Fanjul, Ana M. Pizarro**

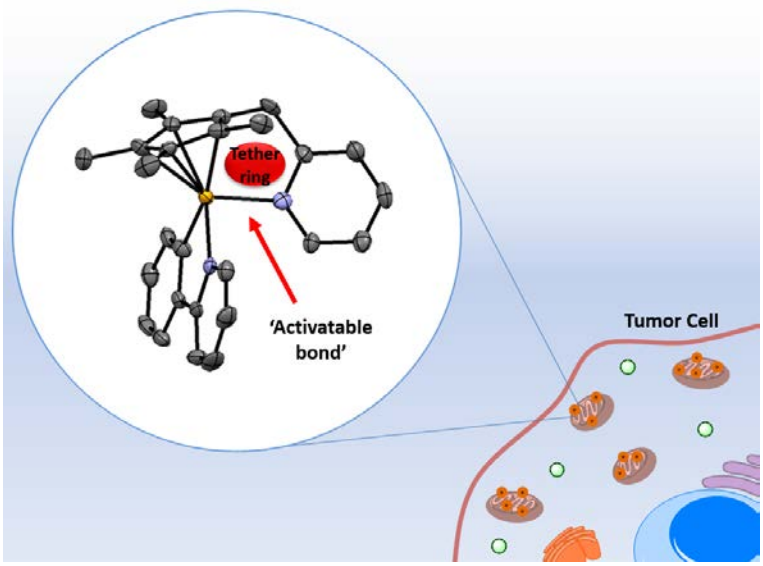
*IMDEA Nanociencia, C/ Faraday 9, Campus de Cantoblanco, 28049, Madrid. Tel: 912998700;*
*E-mail: ana.carrasco@imdea.org*

Novel metal-based anticancer drugs may be able to expand the range of treatable cancers. Iridium, as a member of the platinum-group, has recently produced organoiridium half-sandwich complexes that are emerging as excellent candidates with potential medical applications and exciting novel mechanisms of action, based on intracellular catalysis.[1] These organometallic complexes offer enormous scope for the desing of anticancer candidates due to their versatile structures. Varying the substituents in the cyclopentadienyl (Cp) ring, XY chelating, and Z monodentate ligands, in the general structure $[\eta^5\text{-}C_5Me_4R)Ir(XY)Z]^{0/+}$, can affect dramatically the reactivity and thus the cytotoxic effect of Cp complexes of iridium(III).[2] However, despite of recent advances, adverse side-effect are still a major problem, which a pro-drug approach can address.

We have designed a series of cyclopentadiendienyl Ir(III) complexes bearing a tethered pyridine that binds to the metal. Such a hemilabile ligand forms a strained chelate, which results in a $Ir–N_{py}$(tether) bond susceptible to break and be formed again in aqueous solution and in a biologically relevant time scale. The dissociation of the nitrogen renders the metal susceptible to macromolecule attack inside the cell, thereby activating the pro-drug.

Preliminary cell viability results of our Ir(III) complexes, activatable by dissociation of the Ir–N(tether) bond, show that the cytotoxic activity, as determined by the $IC_{50}$ value, can be finely modified by suttle modifications in the XY chelating ligand. Our data also show that the tether ring is a necessary feature of the Ir(III) organometallic structure to achieve sub-micromolar activity. Additional biological data tell us that the complexes accumulate favourably in the mitochondria, revealing that this organelle may be the potential target site of our complexes. Current work is directed towards understanding how the introduction of tether ring has a major effect on the deadly mechanism of action of this new family of iridium(III) metallodrugs.

Our data suggest that our Ir(III) tethered complexes could become a new family of mitochondria-targeting, potent activatable pro-drugs in cancer research.

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# The many faces of the topological insulator BiTeCl

(Poster contribution)

P. Casado Aguilar[a,b], A. Norris[a], C.G.Ayani[a], E.V. Chulkov[c], R. Miranda[a,b], A.L. Vázquez de Parga[a,b].

*aInstituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA-Nanociencia),Madrid, Spain*

*bDepartamento de Física de la Materia Condensada and IFIMAC, Universidad Autónoma de Madrid, Madrid, Spain.*

*cUnidad de Física de Materiales, Universidad del País Vasco, Donostia, San Sebastián.*

Owing to its inversion asymmetry, strong polarization and spin-orbit coupling (SOC), BiTeCl is a candidate spintronic compound [1-3] and a reported inversion asymmetric topological insulator (IATI) [4]. Furthermore, the accidental presence of a Bi2TeCl crystal structure, a predicted weak topological insulator (WTI) [5], and exposed quasi 2D Bi bi-layers [6], provide for a rich environment for studying exotic topological phenomena.

We investigate the surface terminations and electronic properties of BiTeCl, a tri-layered, non-centro symmetric, polar semi-conductor, who's band-gap width is being under discussion in the scientific community. We contest, by means of ScanningTunneling Microscopy/Spectroscopy (STM/S) experiments,several key points including,termination dependent electronic structures as the origin of the band gap inconsistencies and the highly contested issue of the presence or lack of a non-trivial topological state. We therefore discuss these aforementioned inconsistencies, alongside presenting entirely new structures, defects and evidence of sub-band structure.

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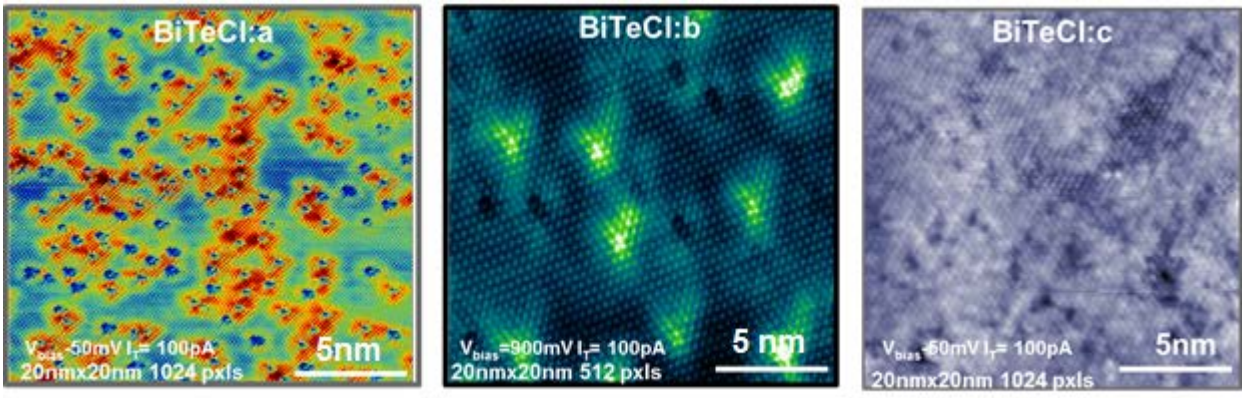


**Fig 1.**STM images of the three most common surface terminations of BiTeCl.

# Functionalized gold nanoparticles for the detection of uveal melanoma miRNAs

**Catarina Coutinho[a], Christian Duarte[a], Alfonso Latorre[a] and Álvaro Somoza*[a]**

[a]*Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia) & Nanobiotecnología (IMDEA Nanociencia), Unidad Asociada al Centro Nacional de Biotecnología (CSIC), 28049 Madrid, Spain*

*E-mail: catarina.coutinho@imdea.org*

Uveal melanoma (UM) is the most common form of ocular melanoma, which in turn is the second most common type of melanoma after the cutaneous.[1] There isn't yet an effective treatment for metastatic UM and "micrometastasis" are often formed several years before diagnosis, highlighting the need for earlier and more sensitive detection, as well as new effective therapies.[2]

One powerful tool for both treatment and early detection of uveal melanoma and other malignancies are microRNAs (miRNAs). Upon manifestation of metastasis, plasma levels of several miRNAs implicated in immune regulation have been shown to be increased in uveal melanoma patients. That is the case of the miRNAs 146a, 20a and 155. Interestingly, miRNAs are stable in blood due to their incorporation into microparticles and exosomes, allowing for detection and quantification in plasma/serum samples.[3]

Gold nanoparticles (AuNPs) possess several properties that make them excellent scaffolds for the design of chemical and biological sensors, such as their stability, biocompatibility and optoelectronic properties.[4] In this work, we propose the use of 10-13 nm AuNPs functionalized with oligonucleotides bearing a cholesterol moiety, for the detection of the miRNAs 146a, 20a and 155. In our system, a thiol or dithiolane group is placed at one end of the oligonucleotide, to ease the conjugation with AuNPs, and a cholesterol derivative is placed at the other, to modulate the colloidal stability of the nanostructure.[5]

Our system has shown good sensitivity (10-25 nM) and selectivity, allowing the detection of target sequences with the naked eye in few hours (2-4 h). We are currently exploring the possibility of using this promising system in the detection of overexpressed miRNAs in extracts from cancer cells.

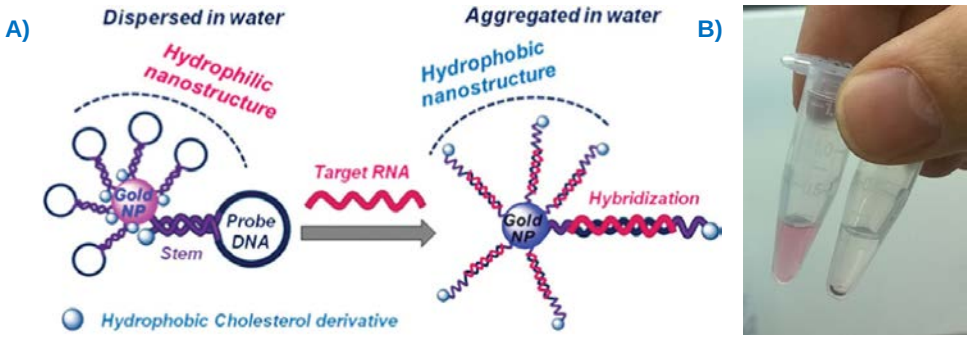


Figure 1 – A) Schematic representation of the miRNA sensor, composed of AuNPs functionalized with oligonucleotides. B) Left – sample with nanoparticles dispersed in water; right – aggregated nanoparticles in the presence of the target sequence.

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# Biomedical application of novel magnetic detection methodology based on AC magnetometry

**L. Cremades-Jimeno[a], E. Sanz[a], E. Artés-Ibañez [a], A. Aires[b], T. Pellegrino [c], A.L. Cortajarena[a,b,d], F.J. Teran[a,d]**

*[a]iMdea Nanociencia. Calle Faraday, 9. Ciudad Universitaria de Cantoblanco, 28049 Madrid. Spain. [b]CIC biomaGUNE, Paseo Miramón 182, 20014 Donjostia-San Sebastian. Spain. [c]Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genoa (Italia) [d]Nanobiotecnología (iMdea Nanociencia), Unidad Asociada al Centro Nacional de Biotecnología (CSIC), 28049 Madrid, Spain.*

*E-mail: lucia.cremades@imdea.org*

In the last years, importance of biomarkers in clinical practice is increasing, for their use in diagnosis, prognosis and therapy [1]. A biomarker is an objective and quantifiable biological parameter which serves as an index for health and physiological assessment [2]. However, routine detection methods such as ELISA or cytometry are not easy, fast and cheap as they should be. For this reason, many efforts are being made, in some cases taking advantage of nanotechnology, to develop new detection methodologies [3]. The current progress of material science supply novel materials with customized properties that enhance the performance of novel detection methods. Thus, the use of magnetic nanoparticles (MNP) is a very promising methodology,due to the huge progress in the syntesis and the different type of measurements leading to changes in electric, magnetic or magneto-optical signals [4, 5]. Nonetheless, current magnetic detection methodologies require exhaustive sample preparation and/or long (> 30 minutes) acquisition measurement times. Previous studies in our laboratory have shown that the magnetic signal of MNP varies after unspecific interaction with proteins [6]. Taking advantage of this fact, a novel magnetic detection method is being proposed based on the variation of the AC magnetization of MNP functionalised with recognition ligands after specifically interacting with a target analyte into biological fluids (e.g. blood, urine, cerebrospinal fluid). This magnetic signal variation provide a suitable fingerprint for biomarker sensing method with minimal sample preparation and instant (< 1 minute) acquisition times.

With this in mind, my thesis project will be focused on exploiting this magnetic detection for its application as diagnostic tool. This work will involve the selection of a biomarker - related to cancer or cardiovascular diseases - that suits the main features of this method, the preparation of the functionalized magnetic nanoparticles, access to an ideal set of patient samples and the validation of the proposed magnetic detection method by comparison with current detection methods used in clinical practice. A relevant aspect of my thesis project will rely on the capacity of this proposed methodology for quantifying the biomarker present in real samples, a key issue to test its potential to be transfer to clinics.

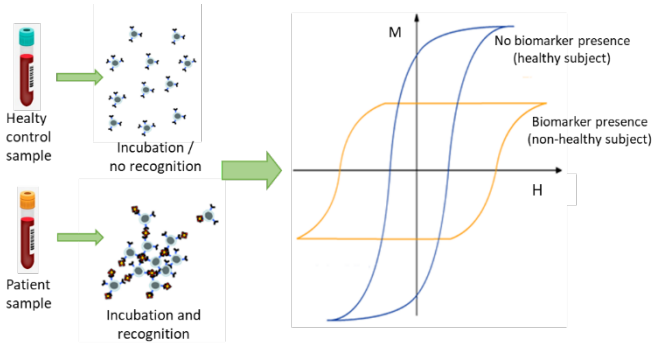


*Figure 1. Schematic representation of the proposed methodology*

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# Interfacing porphyrins and carbon nanotubes through mechanical links

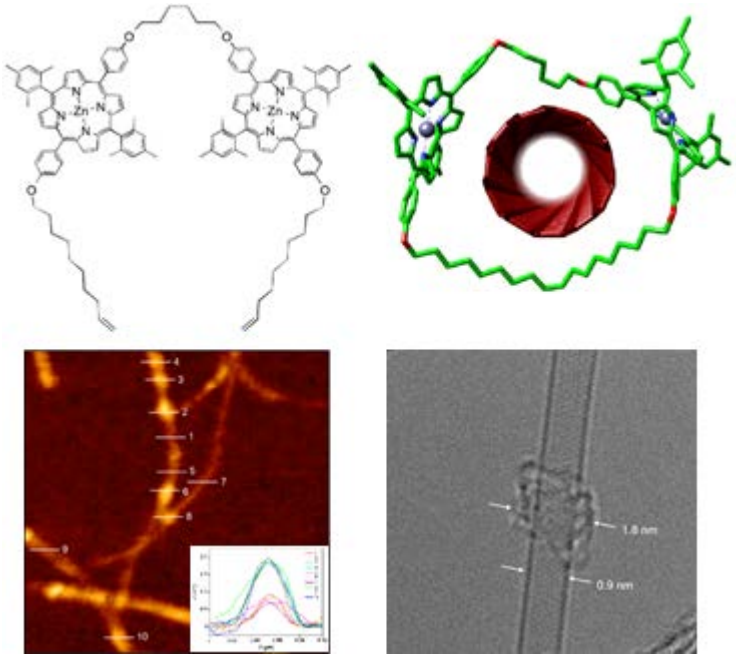
**Leire de Juan-Fernández,*[a] Peter Münich,[b] Arjun Puthiyedath,[b] Belén Nieto-Ortega,[a] Dirk M. Guldi[b] and Emilio M. Pérez[a]**

[a]*IMDEA Nanociencia, c/ Faraday 9, Campus de Cantoblanco, 28049, Madrid, Spain, Tel: 91 299 8838;*
[b]*Department of Chemistry and Pharmacy, Interdisciplinary Center for Molecular Materials, Friedrich-Alexander University of Erlangen-Nürnberg, Egerlandstr 3, 91058, Erlangen, Germany;*
*E-mail: leire.dejuan@imdea.org*

Porphyrins are very interesting molecules due to their unique electronic, magnetic and optical properties.[1] The supramolecular assembly of porphyrin-derived materials is subject to intense research efforts. They have been extensively studied as candidates for dyes sensitized solar cells,[2] organic photovoltaic cells, OLEDs and OFETs, and also they have numerous applications in nonlinear optics.[3]

In this work, we have used porphyrins to obtain mechanically interlocked derivatives of SWNTs (MINTs). MINTs are rotaxane-type molecules in which SWNTs are encapsulated by organic macrocycles. The mechanical bond combines the advantages of the covalent and the supramolecular approaches for the modification of SWNTs.[4-6]

In the key rotaxane-forming step, we have employed U-shaped macrocycle precursors equipped with two porphyrins recognition units and terminated with bisalkenes that are closed around the SWNTs through ring-closing metathesis. The mechanically interlocked nature of the derivatives is probed by analytical, spectroscopic and microscopic techniques. Individual macrocycles are observed by AFM and HR-TEM to circumscribe the nanotubes.

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# Simultaneous AFM nanoindentation and fluorescence microscopy of soft materials and individual bacteria.

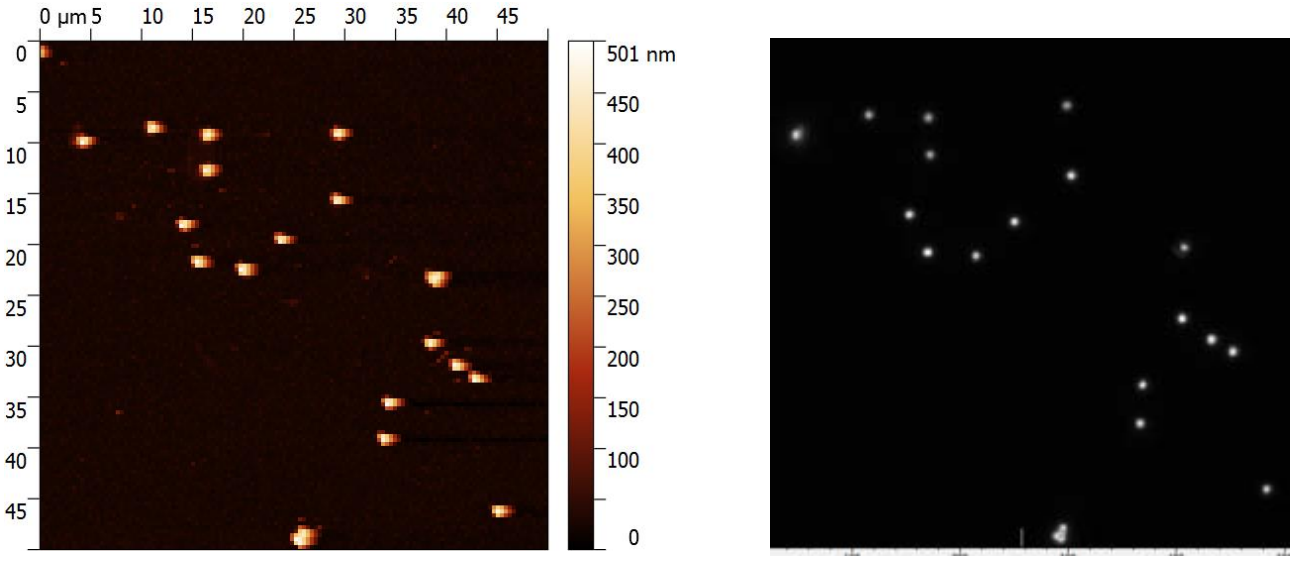
**Adrián Del Valle*[a], Patricia Bondia[a] and Cristina Flors[a]**

[a]*Madrid Institute for Advanced Studies in Nanoscience (IMDEA Nanoscience), Ciudad Universitaria de Cantoblanco. Faraday 9, 28049, Madrid, Spain.*

*adrian.valle@imdea.org*

Advances in microscopy have brought about important discoveries in biological systems and materials. Correlative microscopy, i.e. the combination of several techniques capable of providing complementary information, could be key to solving even more complex problems in a wide range of systems. In particular, correlative fluorescence and atomic force microscopy (AFM) has proven useful to combine chemical and topographical information [1]. In order to fully tap into the nanomanipulation potential of AFM, we have developed an experimental protocol to perform simultaneous AFM nanoindentation and fluorescence imaging. First, we have used fluorescent polymeric beads to test different AFM cantilevers, range of forces, nanoindentation times and fluorescence imaging configurations. These experiments have highlighted challenges such as reflections from the illuminating laser on the AFM cantilever [2].

We are now applying the above protocol on immobilized bacterial cells, with the goal of finding potential correlations between nanoindentation conditions (force, repetition pattern, tip shape…) and damage to the bacterial cell wall. While previous studies have shown that bacteria are rather resilient to nanoindentation [3], our experimental strategy using simultaneous fluorescence detection of propidium iodide as an active marker for bacterial cell wall damage, may allow refining previous observations.

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# Protein engineering for improved delivery in CRIPSR-based gene editing strategies

**Carmen Escalona Noguero[a], Rafael Soler[a] and Begoña Sot[a]**

[a]IMDEA Nanociencia, C/ Faraday 9, 28049 Madrid, Spain. *Tel: 91 299 87 00; E-mail: carmen.escalona@imdea.org*

The recently developed CRISPR/Cas-based strategies have meant a significant breakthrough in the field of genome edition, since they allow for a much more flexible and efficient manipulation of DNA sequences as compared to previous editing tools such[1,2]. The CRIPSR/Cas system basically consists of an endonuclease (e.g Cas9, Cpf1) in complex with a "guide" RNA whose sequence is complementary to that of the target DNA[3]. Following guide recognition, the endonuclease generates a double strand break on the DNA target site that can be repaired through two main pathways: non-homologous end joining and homology directed repair (HDR), which is typically less efficient but required for precise genome editing[1,2].

The correction of disease-causing mutations through CRISPR-mediated genome editing has a great therapeutic potential. However, safe and efficient delivery of the molecules involved in this edition still remains a major challenge. In this regard, nanotechnology constitutes a very promising tool. Nonetheless, the design of nanostructures to deliver CRISPR molecules must take into account the number of biological barriers that need to be overcome in order to reach the target. The aim of this research project is to generate nanostructures consisting of gold nanoparticles conjugated with ribonucleoproteins (endonuclease and guide RNA) that allow for a more efficient *in vivo* editing of oncogenic mutations. In order to achieve this, both Cas9 and Cpf1 are being engineered to carry modifications both for the conjugation with the nanoparticles and the evasion of different biological barriers. They will be subsequently purified and incorporated, together with the guide RNA, into gold nanoparticles. The nanostructures will also include the DNA template required for the correction of the mutation of interest through HDR and other molecules contributing to stability and efficient targeting.

Here, we present the devised cloning and protein expression strategies as well as the endonuclease purification tests results obtained thus far.

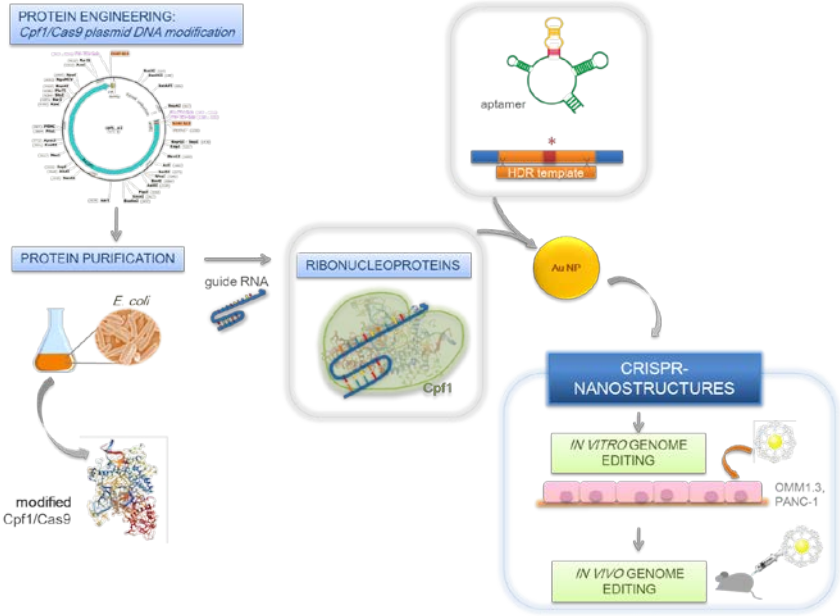


Figure 1. Schematic workflow of the project. Cpf1 and Cas9 will be engineered to enable their incorporation into gold nanoparticles. Furthermore, both endonucleases will carry modifications in order to overcome the different biological barriers (endosomal escape and immune evasion peptides, nuclear location signal, etc.) The engineered proteins will be expressed and purified from *Escherichia coli* and their cleavage activity will be tested *in vitro*. Ribonucleoproteins (RNP) will be generated via incubation of the endonuclease with the *in silico* designed guide RNAs.
Subsequently, these RNPs will be incorporated into gold nanoparticles together with the DNA template for HDR and aptamers for the target cell/tissue. Finally, the ability of these CRISPR-nanostructures to edit oncogenic mutations will be tested *in vitro* in tumour cell lines and *in vivo* in animal models.

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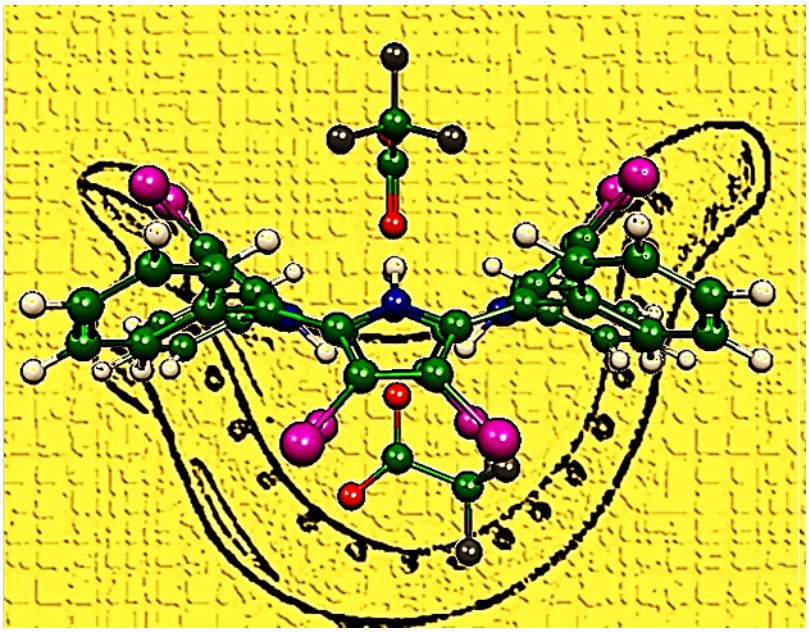
# Computational studies of core protonated and β-brominated of meso-tetraphenylporphyrin: High saddle shape structure properties

**Mortaza Eskandari,[a] Leila Alghooneh[a], Saeid Zakavi*[a] and Reza Omidyan[b]**

[a] *Department of Chemistry, Institute for Advanced Studies in Basic Sciences (IASBS), Zanjan, 45137-66731, Iran. Tel: +982833153202*
*E-mail: zakavi@iasbs.ac.ir*

[b] *Department of Chemistry, University of Isfahan, 81746-73441 Isfahan, Iran.*

The prediction of properties of substituent porphyrins is of high importance when structure–property relationships are discussed. Herein, the β-bromination and core protonation of $H_2$TPP (meso-tetraphenylporphyrin) with $CF_3$COOH and HCOOH acids was systematically studied and the absorption and fluorescence properties of these high saddle-shape porphyrins examined and related to DFT data. We considered, in particular, the correlation between the DFT and TD-DFT calculation and the β-bromination and core protonation of $H_2$TPP. Our main findings are: (1) The red shifts of the absorption bands is due to the greater stabilization of the LUMO relative to the HOMO level there are small differences between the energy gap of the dications with 6 to 8 bromine atoms at the porphyrin periphery related to the experimental results. (2) TD-DFT calculations predict small differences between the Soret and Q(0,0) bands of the higher degrees (x = 6-8) of β bromination. (3) Excellent agreement between the TD-DFT spectra and experimental data is found for β-brominated porphyrin dications. It seems that the bulky β-bromine atoms prevent the phenyl group to decrease their dihedral angle with porphyrin mean plane. Furthermore, the study of the flourescence spectra showed significant increases in the wavelength of the emission bands with increasing the degree of bromination of the porphyrin core. Also, the intensity of the bands was greater for those of the dications with respect to the free base porphyrins [1]. In summary, the results of this study show that concomitant bromination and protonation of $H_2$TPP is an efficient approach to design novel porphyrinic photosensitizers with desired absorption and emission bands as well as the radiative and non-radiative deactivation rate constants.



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‡ This work was supported by the Institute for Advanced Studies in Basic Sciences (IASBS).

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# A Robust and Unique Iron (II) Mosaic-like MOF Architecture.

**Estefania Fernandez-Bartolome,[a] José Santos,[a] Saeed Khodabakhshia,[a] Laura J. Mc Cormick,[b] Simon J.Teat,[b] Cristina Saenz de Pipaon,[c] Jose R. Galan-Mascarós,[c] Nazario Martín,[a,d] Jose Sanchez Costa*[a]**

[a] *IMDEA Nanociencia, C/ Faraday 9, Ciudad Universitaria de Cantoblanco, 28049, Madrid, Spain. Tel: 34 912998700.*
[b] *Advanced Light Source, Berkeley Laboratory, 1 Cyclotron Road, Berkeley, CA 94720, US*
[c] *Institute of Chemical Research of Catalonia. The Barcelona Institute of Science and Technology, Avda Catalans, 16, Tarragona, Spain.*
[d] *Facultad de Ciencias Químicas, Universidad Complutense de Madrid, Madrid, 28040, Spain*

*E-mail: estefania.fernandez@imdea.org; jose.sanchezcosta@imdea.org*

Coordination polymers, or most often called metal-organic frameworks (MOF), are currently a hot topic in science.[1] As an illustrative example of their relevance, in 2017 it was estimated that 6000 novel MOFs are published each year.[2] This vast interest derives from the fact that MOFs show a wide variety of potential applications, which include gas uptake, catalysis, luminescence, electrical conductivity or biotechnology among many others. All these properties arising from their intrinsic porosity and the versatility.[3] In fact, MOFs are extended molecular materials formed by metal ions or metal ion clusters bridged by relatively long organic ligands, thus creating size-tunable structural voids to absorb guest molecules and act as highly specific molecular vessels with different absorption capabilities.[4,5]

At the Switchable Nanomaterials group placed at IMDEA Nanoscience Institute, we develop functional coordination polymers with advanced properties capable of obtaining functionality in a single molecule and so achieving a very high level of sensitivity and selectivity. In this presentation, we report the synthesis of an unprecedeted MOF 3D architecture formed by assembling iron (II) and a novel extended triazole-based ligand (PM-Tria). This MOF contains a perfectly linear one-dimensional {Fe(II)-F}$_n$ bridging chain that shows an antiferromagnetic behaviour. Furthermore, the structure is compared with a 14$^{th}$ century mosaic found in the Alhambra Palace in Granada showing a surprising symmetry resemblance.

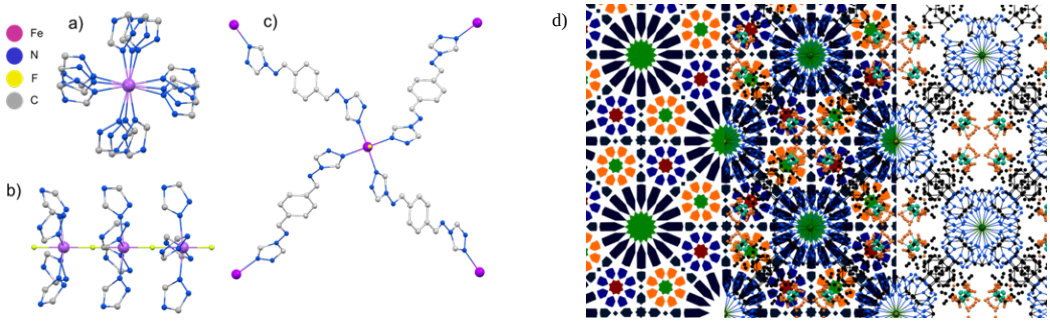


**Fig1. a)** *c view* of a trimeric unit. **b)** *b view* of a the Fe(II)··F··Fe(II) trimeric unit. **c)** A segment of **1** illustrating the metallic connection along the *c* axis *via* PM-Tria ligands **d)** On the left we see the Islamic mosaic found at the Alhambra Palace of Granada. On the right an illustration of Fe(II)-MOF along its *c* axis. On the middle, a superposition of the two pictures

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# Alveolar dynamics: implication on drug delivery assisted by pulmonary surfactant

**Cristina García-Mouton*[a], Alberto Hidalgo[a], Francesca Salis[b], Guillermo Orellana[b], Jesús Pérez-Gil[a] and Antonio Cruz[a].**

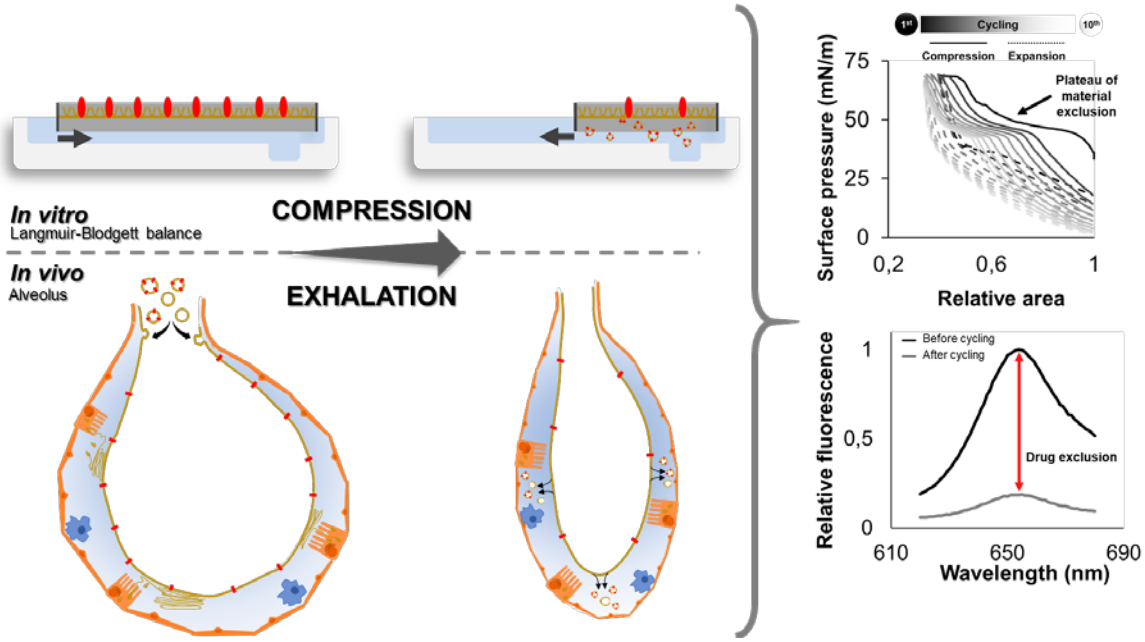
[a]*Departamento de Bioquímica y Biología Molecular, Facultad de Biología, e Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Universidad Complutense, Madrid, España. Tel: 91 394 5032*

[b]*Departamento de Química Orgánica, Facultad de Química, Universidad Complutense de Madrid, Madrid, España.*

*E-mail: crigar12@ucm.es*

Lungs are highly specialized organs responsible for ventilation and gas exchange in vertebrates with aerial respiration. These organs have the most extensive contact area with the environment (75-140m$^2$ in human adults), which is constituted by the respiratory epithelium and the thin aqueous layer that coats it. To reduce the surface tension generated at this air-liquid interface during breathing, type II pneumocytes synthetize, assemble and secrete the pulmonary surfactant (PS). PS is a complex mixture of lipids and proteins with unique biophysical properties to efficiently adsorb and rapidly spread along the air-liquid interface [1]. Using lungs as target and PS as vehicle for drugs and nanoparticles present numerous advantages, such as a large lung contact surface, thin alveolar epithelium, high permeability of their membranes and the efficiency of PS to solubilize and deliver different types of molecules, especially poorly water-soluble, along the air-liquid interface [2]. Consequently, nowadays, there is an increase in the interest on using inhalation as a pathway for drugs and nanoparticles administration.

Alveoli are very dynamic structures, constantly subjected to compression-expansion cycles, so the aim of this work was to evaluate how this dynamism could affect the diffusion of PS/drugs combinations along the surface and favour material exclusion from the air-liquid interface. Using Tacrolimus, a hydrophobic immunosuppressive drug, as a drug model, and a novel device that combines both a Wilhelmy balance as donor interface and a Langmuir-Blodgett trough to emulate the alveolar surface during respiratory mechanics, we can analyse the behaviour of an exogenous material once it is introduced at the donor balance and travels to the target interface to be subjected to compression-expansion cycles. According to our results, we propose a model in which PS vehiculization capabilities, as well as release of hydrophobic drugs at the alveolar spaces, could be enhanced by respiratory dynamics.




‡ **Figure**: Schematic representation of a Langmuir-Blodgett balance and an alveolus during compression (left). Graphs show surface pressure along different compression-expansion cycles measured at the Langmuir-Blodgett balance represented versus relative area (right, top) and Tacrolimus-NileBlue fluorescence before and after cycling (right, bottom).

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# Synthesis of ferrite nanoparticles for biomedical applications.

**David García [*1], Rebeca Amaro[1], Lucía Gutierrez[2], Fernando Herranz[3] and Gorka Salas[1]**

[1] *IMDEA Nanociencia, Campus Universitario de Cantoblanco, 28049 Madrid, Spain, Tel: 912998837;*

[2] *Department of Analytical Chemistry, Instituto Universitario de Nanociencia de Aragón (INA), Universidad de Zaragoza and CIBER-BBN, C/ Mariano Esquillor, s/n, 50018 Zaragoza, Spain;*

[3] *Nanobiotechnology and Molecular Imaging Lab, Fundación Centro Nacional de Investigaciones Cardiovasculares (CNIC) and CIBER Enfermedades Respiratorias (CIBERES), Melchor Fernández Almagro 3, 28029 Madrid, Spain;*

**Email: david.garcia.soriano@imdea.org*

Ferrite-based nanoparticles (NPs) for biomedical applications have been extensively studied mainly as contrast agents for magnetic resonance imaging (MRI) and as heating mediators for magnetic hyperthermia cancer treatment. In this work, we have evaluated the effect of doping iron oxide nanoparticles with different amounts of manganese on their properties, including those relevant for biomedical applications.

Synthesis of manganese ferrite nanoparticles ($Mn_xFe_{3-x}O_4$) has been carried out by thermal decomposition of [$Fe(acac)_3$] and [$Mn(acac)_2$] providing hydrophobic NPs with a narrow size distribution between 6 and 9 nm. The so-obtained hydrophobic nanoparticles have been then transferred to water by surface modification with dimercaptosuccinic acid (DMSA) and dopamine (DOPA).

We have studied the influence of changes in the composition and the surface coating on physico-chemical properties like the blocking temperature, (Fig. 1) heating properties and relaxivity values.

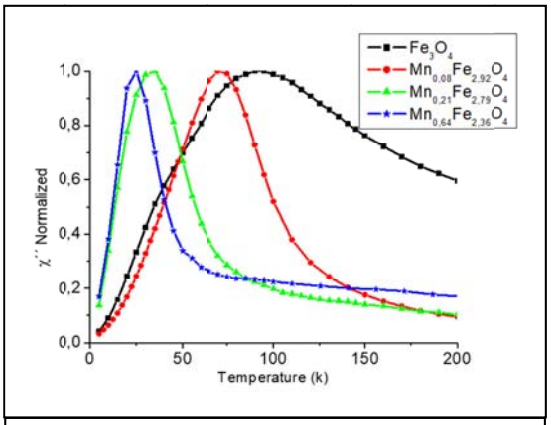


**Figure 1.** AC magnetic curves of manganese ferrites with different composition. Blocking temperature show a trend due to manganese ratio.

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# Smart self-immolative polymers as pH-responsive gatekeepers for mesoporous carbon nanoparticles

**M. Gisbert-Garzarán [a], D. Giasafaki [b], D. Lozano [a], G. Charalambopoulou [b], T. Steriotis [b], M. Manzano [a] and M. Vallet-Regí [a]***

[a] *Dpto. Química en Ciencias Farmacéuticas, Facultad de Farmacia, UCM, Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), 28040-Madrid, Spain, Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.*

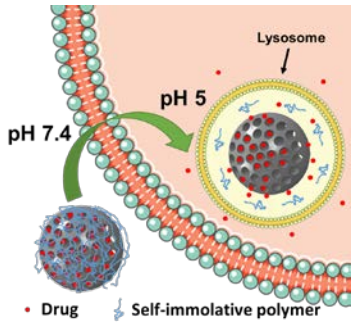
[b] *National Center for Scientific Research "Demokritos", Agia Paraskevi, Attikis 15341, Greece.*

*E-mail: vallet@ucm.es*

Despite chemotherapeutics have been shown to be effective against tumor growing, their lack of tumor tissue selectivity remains being one of their main drawbacks. In order to reduce the side effects owing to that nonspecific distribution many nanotechnological approaches have been developed, the so-called *nano-drug delivery systems* (nano-DDSs). Among all the nanocarriers proposed as nano-DDSs, mesoporous materials have attracted much attention due to their unique properties, including a network of cavities with excellent textural properties that allows the loading of large amounts of drugs. However, one of the main disadvantages of mesoporous nanoparticles is the premature release of the cargo before reaching the tumor. To address that, smart gatekeepers capable of preventing drug leakage until some stimulus is applied can be used to seal the mesopores. In particular, the subtle changes in pH between the blood and some cellular organelles can be used to engineer the gatekeeper.[1]

In the last few years there has been a growing interest regarding mesoporous carbon nanoparticles. Not only they show outstanding textural properties, but also present π-π interactions thanks to their aromatic structure that may facilitate the loading of aromatic cytotoxic compounds. In addition, carbon nanoparticles show excellent heat conversion capacity in the near-infrarred region which might be applied to photothermal therapy.[2] Regarding the smart coating, there is a class of polymers, the so-called Self-Immolative Polymers (SIPs), which possess a triggering moiety that can be removed upon some triggering events, thus leading to the dissasembly of the polymer into its building blocks.[3] In that sense, our group reported the use for the first time of pH-responsive SIPs as gatekeepers for mesoporous silica nanoparticles, showing promising results.[4]

In this work, two types of mesoporous carbons (CMK-1 and CMK-3) bearing pH-responsive SIPs have been used as nanocarriers. It has been shown that their impressive textural properties correlate with excellent loading capacities, compared to their silica counterparts. The pH sensitivity has been determined carrying out *in vial* release experiments at pH 7.4 and 5. Our results show that only small amounts of the cargo are released at physiological pH whereas at slightly acidic pH (*i.e.* that of lysosomes) the self-immolation takes place and a huge amount of the cargo is released. In order to test their cytotoxic capabilites the hybrids were loaded with doxorubicin and incubated with human osteosarcoma cells. The results show that the hybrid nanocarriers are not cytotoxic by themselves but induce significant cell growth inhibition when loaded with a chemotherapeutic. Furthermore, an additional group of nanocarriers functionalized with SIPs not bearing the triggering moiety was not able to induce any significant cytotoxicity, thus verifying the pH-responsive behavior of the hybrid carbon nanocarriers.

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# Superconductivity in tungsten carbide nanostructures and its importance in STM experiments performed on metal-supported graphene

**C.G. Ayani**[1], P. Casado[1], A. Norris[1], J.J. Navarro[1], J.G. Rodrigo[2], F. Calleja[1], R. Miranda[1,2] and A.L. Vázquez de Parga[1,2]

[a] Instituto Madrileño de Estudios Avanzados en Nanociencia, Cantoblanco 28049, Madrid, Spain

[b] Departamento de Física de la Materia Condensada and IFIMAC, Universidad Autónoma de Madrid, Cantoblanco 28049, Madrid, Spain.

*E-mail: cosme.gonzalez@imdea.org*

The study of superconductivity in graphene-based systems is a topic of great interest nowadays because it could shed some light in the general problem of 2D superconductivity [1]. In this context, STM is a great tool, since its ability to probe the local DOS close to the Fermi level can be exploited to explore the superconducting gap at the atomic level.

Back in the 60s it was shown that superconductivity can be present also in tungsten-based amorphous compounds and, in particular, in tungsten carbide alloys [2] and nanostructures [3]. This is of utmost importance in the present case because (i) tungsten is the most commonly employed material in the fabrication of STM tips and (ii) the presence of carbon is inherent to any graphene system.

In this work we present a systematic study of the functionalization of tungsten tips on Ir(111), gr/Ir(111), Pb/Ir(111) and gr/Pb/Ir(111). We show that, starting from Ar+ sputtered pristine tungsten tips, it is possible to build reproducibly a superconducting structure at the tip apex by means of voltage pulses only when done on graphene-covered surfaces (see Figure 1(a)). We have characterized the resulting superconducting gap as a function of temperature (see Figure 1(b)) and magnetic field, obtaining a transition temperature close to 3.7 K and a critical field well above 3T in all cases. We have further tested these superconducting tips on a Cu(111) surface, finding that the copper surface state and the tip superconducting gap can be resolved simultaneously in the STS spectra.

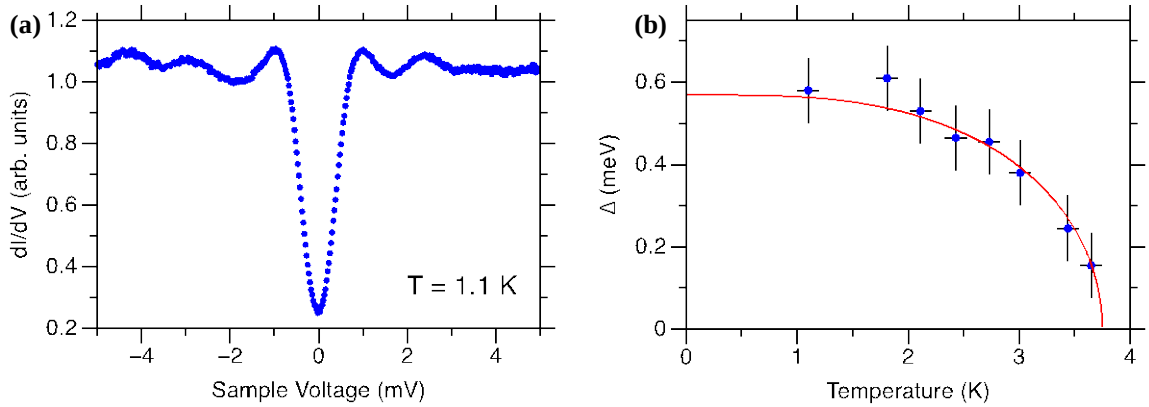


Figure 1: (a) STS spectrum recorded at 1.1 K on gr/Pb/Ir(111) with a functionalized superconducting tungsten carbide tip. (b) Temperature evolution of the superconducting gap.

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# Graphene/Ferromagnetic epitaxial stacks grown on oxides with tuned spin orbit coupling

**Adrián Gudín,*[a,b] Fernando Ajejas,[a,b] José Manuel Diez,[a,b] Pablo Olleros,[a] Alberto Anadon,[a] Leticia de Melo Costa,[a] Rubén Guerrero,[a] Julio Camarero,[a,b] Rodolfo Miranda,[a,b] and Paolo Perna[a]**

[a]*IMDEA Nanociencia, 28049 Madrid, Spain. Tel: 91 299 87 00;*
[b]*DFMC, Instituto "Nicolás Cabrera" & IFIMAC, Universidad Autónoma de Madrid, 28049 Madrid, Spain.*

*E-mail: adrian.gudin@imdea.org*

Graphene (gr) has a negligible intrinsic Spin-Orbit Coupling (SOC) in its pristine state. However, by intercalating adequate metals (such as Pb underneath gr/Ir(111)) it is possible to transfer to graphene a giant SOC [1]. The incorporation of active properties to gr can enable its use in spintronics technology, exploiting furthermore the long spin diffusion and lifetime [2].

Here, we report on the realization of high quality epitaxial stacks where a ferromagnetic (FM) material, as Co, and non-magnetic (NM) metals, as Pb and Bi, are successively intercalated and embedded between a 2D gr sheet and an heavy-metal (HM), as Pt or Ir [3]. The resulting stack gr/NM/FM/HM/oxide has been grown epitaxially in ultra-high-vacuum (UHV) condition on (111)-oriented oxide substrate. A careful investigation of the electronic and chemical properties of the systems at each stage of the growth, were performed by means of in-situ surface sensitive techniques, such as XPS-UPS and LEED, while their magnetic properties were investigated by Kerr magnetometry. The growth methodology employed here permits *i)* to achieve atomic control on interface/surface, *ii)* to avoid unwanted leakage current that enables their potential use in devices. The magnetic properties of the gr-based stacks, as the perpendicular magnetic anisotropy (PMA) and the interfacial Dzyaloshinskii–Moriya interaction (DMI), are tuned by varying the thickness of the FM layer, changing the bottom HM layer and modifying the electronic bands of gr through the insertion of an additional NM layer [3,4].

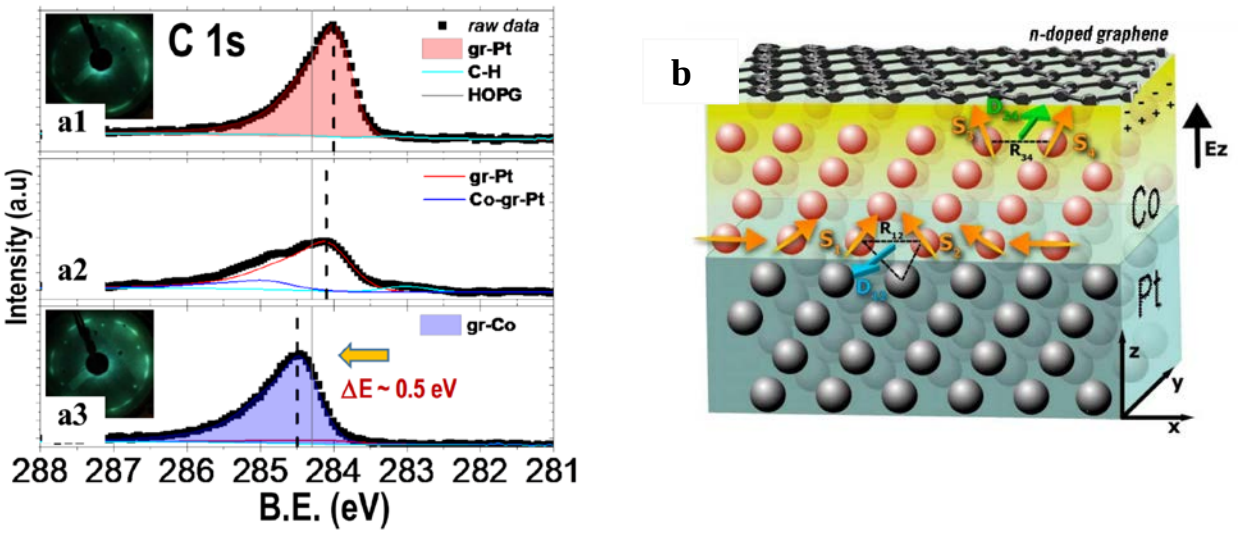


**Figure 1. (a)** XPS-LEED analysis at each stage of the growth process. **(b)** Sketch of the interplay between SOC-induced DMI at Co/Pt and opposite Rashba-type DMI at gr/Co interfaces.

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# Influence of ball milled pyrex free magnetic microwires on strontium ferrite, $BH_{max}$

**Papa Gorgui Birame Gueye,*Maria Pilar Marín Palacios [a,b] Miguel Angel Gonzales Barrio [b]**

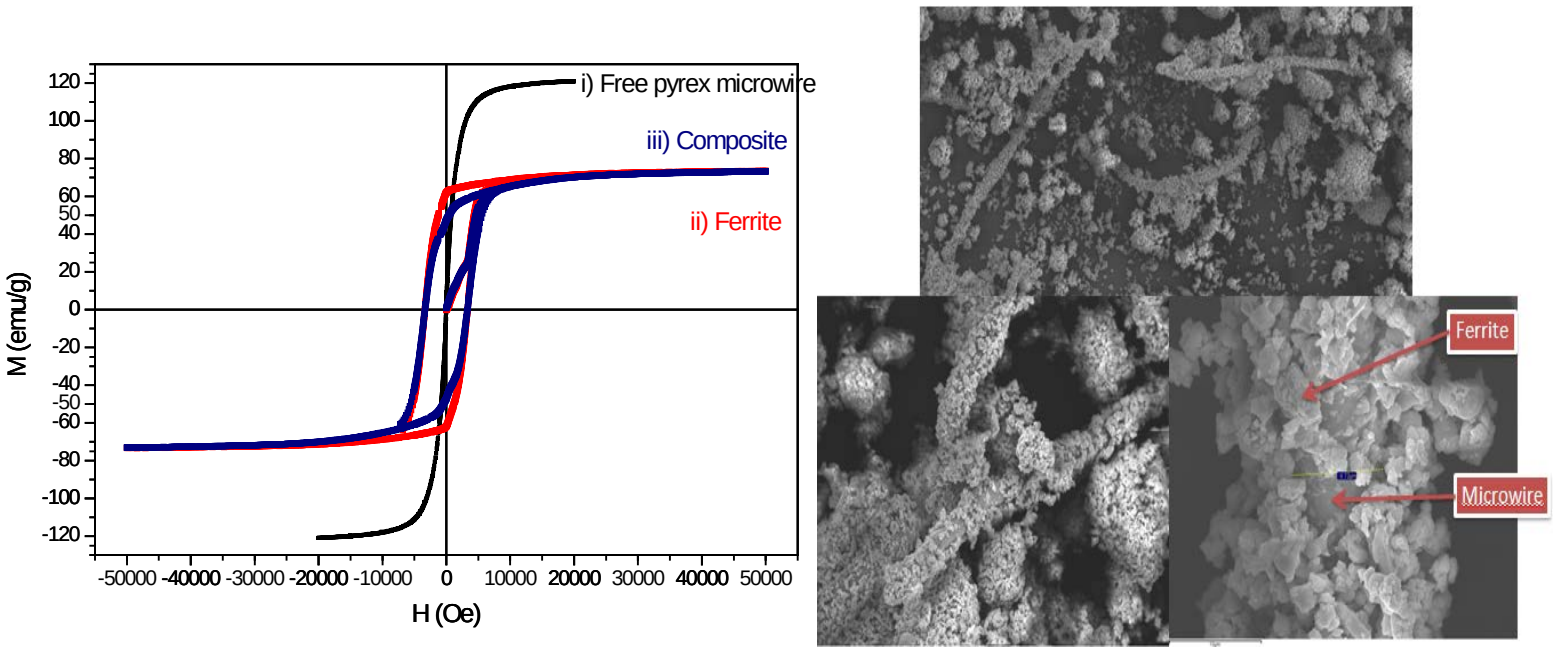
[a] *Instituto Magnetismo Aplicado IMA ,UCM, Las Rosas ( Madrid), Spain. Tel: 913007173;*

[b] *Departamento de Física de Materiales ,UCM, Madrid, Spain;*

*E-mail: pagueye@ucm.es*

- FeBSiCuNb amorphous magnetic microwire have been ball-milled for times between 6 and 30mn.Pyrex has been removed by meansof a magnetic method and pyrex free microwire with lenght of 10 um have been ball milled with ferrite. The influence on energy products $BH_{max}$ of the ferrite is studied by using SEM pictures and measuring their hysteresis loops.

FIGURE




**Left:** Hysteresis loops: (i) a hard phase, (ii) a soft phase and (iii) the exchange-coupled nanocomposites made of the soft and hard phases.

**Right:** SEM image of one exchange –coupled microcomposite.

## Notes and References

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# Moth-eye antireflective and self-cleaning surfaces with enhanced mechanical properties

**Alejandra Jacobo-Martín[*a], Iván Navarro-Baena[a], Jaime J. Hernández[a], Manuel R. Osorio[a], Miguel A. Monclús[b], Jon M. Molina-Aldarequia[b] and Isabel Rodríguez[a]**

[a] *Madrid Institute for Advanced Studies in Nanoscience (IMDEA Nanoscience), C/ Faraday 9, Ciudad Universitaria de Cantoblanco. 28049 Madrid, Spain. Tel: +34 912 99 87 00*
[b] *Madrid Institute for Advanced Studies in Materials (IMDEA Materials), C/ Eric Kandel 2, Tecnogetafe, Getafe. 28906 Madrid, Spain. Tel: +34 915 49 34 22*

**E-mail: alejandra.jacobo@imdea.org*

Antireflective transparent materials are essential for a multitude of applications in several fields, such as building, displays, light harvesting, and photovoltaic devices among others because they allow a clear vision and efficient light transmission [1]. Despite numerous advances in the development of these materials, efficient low cost solutions still remain elusive. Moreover, when exposure to the exterior environment is required, the optical quality is often reduced due to degradation and pollution. Therefore, the improvement of the weathering resistance and mecanical durability are crucial for their implementation in exterior settings. Adressing these challenges, we present a practical approach that enables the production of antireflective bio-inspired polymer surfaces based on moth-eye inspired features incorporating photoinduced self-cleaning properties and enhanced mechanical resistance [2]. The methodology involves the fabrication of sub-wavelength moth-eye nanocone features onto transparent composite films in a combined processing step of nanoparticle coating and surface nanoimprinting. Titania nanoparticles synthesized by a sol-gel hydrothermal process were used as reinforcement of the nanocones improving the film stiffnes and scratch resistance [3]. Concurrently, the nanoparticles induce self-cleaning properties due to photocatalytic reactions. The fabrication of the samples involves innitially producing a thin film of Poly(methyl methacrylate) (PMMA) on a Polyethylene terephthalate (PET) substrate. On this film, $TiO_2$ nanoparticles are deposited and the substrates are subsequentelly nanoimprinted. The resulting surfaces reduce the optical reflection loses from values of 9% of typical PMMA plastic films to an optimum value of 0.6 % in the case of double–sided nanoimprinted films.

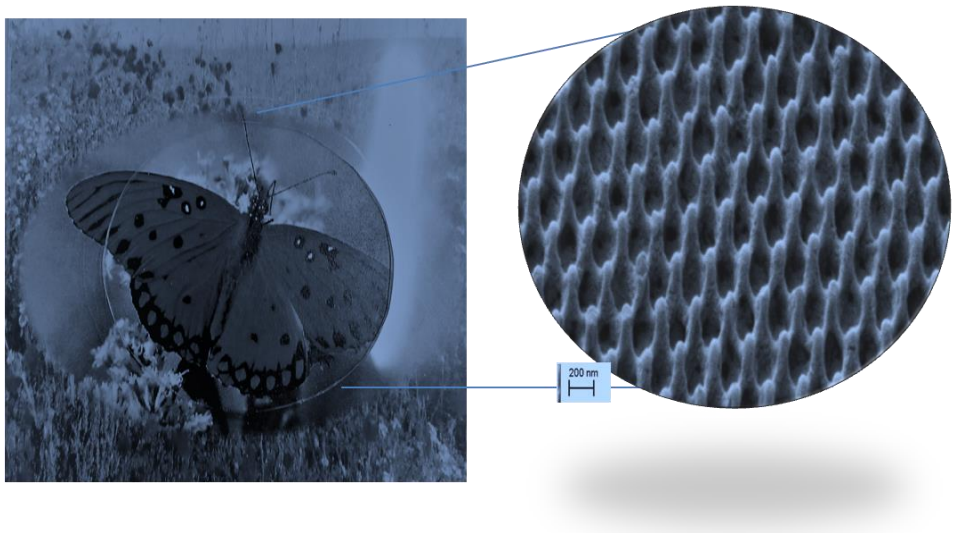


Figure 1: Photograph showing the reflection reduction caused by a film with moth-eye structures (centre circle) compared to the surrounding PMMA smooth film and a SEM image of the titania moth-eye nanocomposite surface fabricated.

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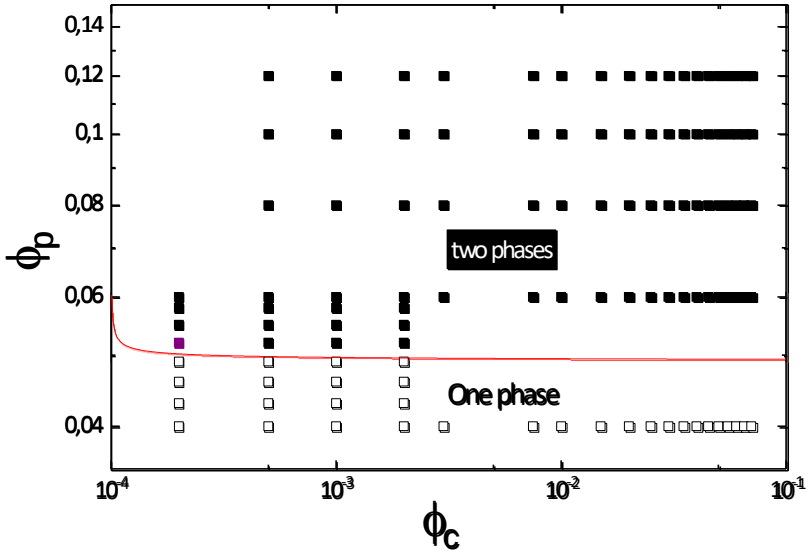
# Study of phase separation in a negatively charged colloid / polymer system

**Kharbedia, Mikheil*; Enciso, Eduaro; Monroy Muñoz, Francisco;**

*Universidad Complutense de Madrid, Facultad de CC Químicas, Departamento de Química Física I – Avenida Complutense s/n, Madrid - España*

**mikkharb@ucm.es*

Colloidal dispersions composed by mixtures of particles and non-adsorbent polymers separate into two distinct thermodynamic phases at certain particle-to-polymer ratios; this is due to a depletion force, generated by the polymer, which induces an attraction between colloidal particles, and thus their ultimate aggregation [1]. When both components are negatively charged, this phase separation occurs at lower concentrations of the components; this is likely due to the emergence of an ionic force that acts synergistically with the depletion force responsible for the phase separation observed in neutral dispersions. Nevertheless, the ionic force may lessen the depletion interaction due to a decrease of the ionic lenght of the particles [2]. To demonstrate this hypothesis, here we present data on the kinetics of the phase separation and on the mechanical properties of each thermodynamic phase. In particular, we show that the lower the concentration of polymer, the faster the phase separation. Moreover, the rheological study shows that the phase rich in particles has a high elasticity, and that the elasticity of this phase increases with polymer concentration, while the particle aggregates become more breakable. This study may help explain the posible consequences of overlapping depletion and ionic forces when designing coloidal systems for different applications.

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# Reaction of platinum(II) complexes with bismuth−halides: Pt−C($sp^3$) or Pt−C($sp^2$) bond cleavage‡

**Maedeh Koohi,[a] Hamid R. Shahsavari[a,]***

[a] *Department of Chemistry, Institute for Advanced Studies in Basic Sciences (IASBS), Zanjan 45137-66731, Iran. Tel : +982433153206*
*E-mail: shahsavari@iasbs.ac.ir*

Trivalent bismuth halides $BiX_3$ (X = Cl, Br, I) often display distinct Lewis acidic properties.[1] These compounds have also attracted significant interest because of their low cost, low toxicity and high abundance in comparison to other common Lewis acids.[2] In the present work, we have studied the reactions of platinum(II) complexes [PtR(κ$^1$C-C^N)(dppe)], **1**, in which C^N = deprotonated form of 2,2'-bipyridine *N*-oxide (Obpy), 2,2'-bipyridine (bpy), 2-phenylpyridine (ppy) ligands and dppe = 1,2-bis(diphenylphosphino)ethane, with bismuth trihalides, $BiX_3$ (X = Cl, Br, I; Figure1). These reactions were provided bismuth−halide oxidative addition to complexes **1** and bismuth−carbon reductive elimination from Pt(IV) complexes.

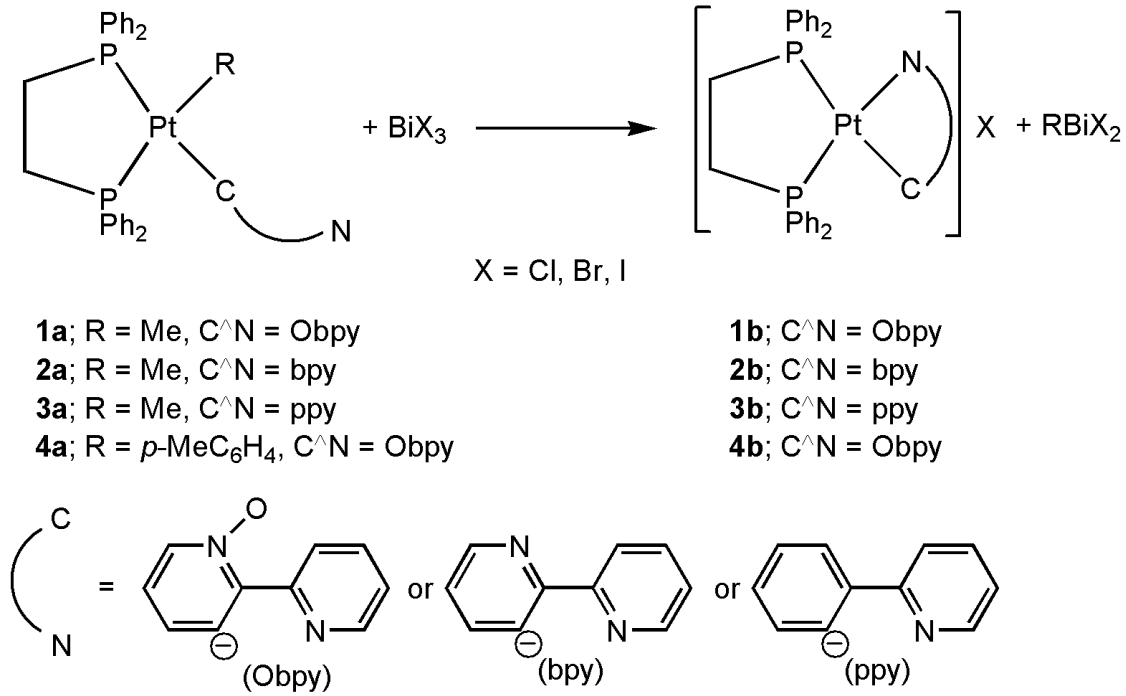


**Figure 1.** Reaction of $BiX_3$ with platinum(II) complexes.

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‡ This work was supported by the Institute for Advanced Studies in Basic Sciences (IASBS).

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# Functionalization of Magnetic Nanoparticles with Gemcitabine and Doxorubicin via disulfide bonds

**Nuria Lafuente Gomez *[a], Mercedes Lecea[a], Ciro Rodriguez Diaz[a], Yurena Luengo[a], Gorka Salas[a] and Alvaro Somoza[a]**

[a]*Institute for Advanced Studies in Nanoscience (IMDEA Nanociencia), Calle Faraday 9, Ciudad Universitaria de Cantoblanco, Madrid, Spain. Tel: +34 912998889.*

*E-mail: nuria.lafuente@imdea.org*

Nanotechnology has received tremendous attention, in particular from the field of medicine. Breakthroughs in nanomedicine have had a high impact on the development of more efficient drug delivery systems. Many scientists are focusing their research effort in the design of stimuli-responsive nanocarriers[1]. These devices may be sensitive to specific endogenous stimuli (we take advantage of specific microenvironmental changes associated with some diseases) or exogenous stimuli (we externally applied the stimuli)[2].

Differences between the extracellular and intracellular environments of cancerous and normal cells and the particular characteristics of tumors such as physicochemical properties, neovasculature, elasticity, surface electrical charge, and pH can be identified and it has motivated the design of smart nanoparticles[3].

In this work, we proposed a nanocarrier composed by dextran magnetic nanoparticles functionalized with two chemotherapy drugs: gemcitabine and doxorubicin (figure 1). The key to the successful treatment of tumors is to deliver as much drug as possible to the target tumor. In this case, we have selected a redox-sensitive system based on disulfide bonds. These bonds are prone to rapid cleavage by glutathione (GSH) which is in higher concentration in tumor tissues compared with healthy ones. It is well known that the intracellular level of GSH in cells is in the millimolar range (0,5-10 mM), whereas micromolar concentrations are found in the extracellular medium and blood plasma. This nanodevice is based on one previously described for DMSA magnetic nanoparticles. The linker design allows the release of the drugs with any chemical modification[4].

We have analyzed the quantity of drug loaded in Dextran magnetic nanoparticles with different concentrations of iron. Moreover, we have tested a scale-up process to produce this dextran magnetic nanoparticles loaded with drugs in larger quantities.

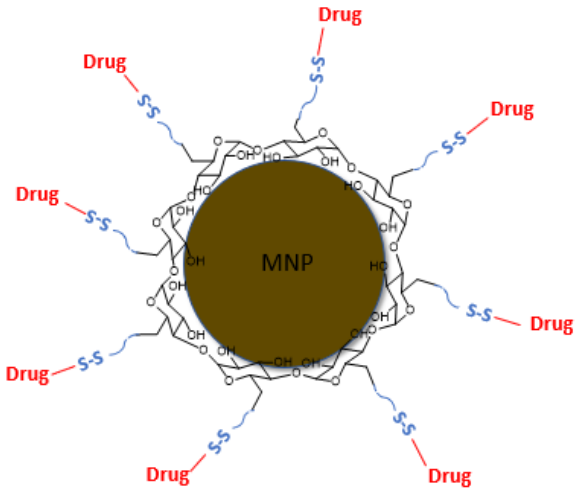


*Figure 1.-* Scheme of a Dextran magnetic nanoparticle functionalized with drugs

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# Advanced Therapies Based on Nanoparticles: efficient drug delivery and CRISPR/Cas9 gene editing

**Ana Latorre,[a] Alfonso Latorre,[a] Ana Lázaro,[b] Macarena Calero,[a,b] Alejandra Crespo,[c] Mercedes Lecea,[a] José Lombardía,[a] Pilar Martín-Duque,[c] Ángeles Villanueva,[a,b] and Álvaro Somoza*[a].**

[a]*Instituto Madrileño de Estudios Avanzados en Nanociencia, 28049, Madrid, Spain;*
[b]*Departamento de Biología, Universidad Autónoma de Madrid, Cantoblanco, 28049, Madrid, Spain;*
[c]*Universidad Francisco de Vitoria, 28223, Pozuelo de Alarcón, Madrid, Spain.*
*E-mail: anabelen.latorre@imdea.org*

The use of nanoparticles to treat diseases, such as cancer, has increased significantly in the last years, due to the advantages compared to conventional therapies. Particularly, the use of nanocarriers may have a profound effect on the solubility and biodistribution of drugs. Moreover, the nanoparticles accumulate preferable at the tumor are due to the well-known EPR effect, leading to a significant reduction of the side effects and increase in the effectiveness of the treatments.[1]

In this work, we report our progress on the development of an albumin-based nanostructure for the treatment of breast and pancreatic cancer and uveal melanoma. These kinds of nanostructures are biodegradables, non-toxic and easily modified with different molecules such as drugs or nucleic acid which will be released selectively and controlled inside the tumor cells. In particular, albumin gold nanoclusters (AuNCs) can be functionalized with drugs for breast cancer treatment such as Doxorubicin (DOX) and SN38, and AZD8055 for uveal melanoma. In both cases, we observed that the modified nanostructures can reduce the cell viability significantly. What is more, this system was able to reduce the tumor growth dramatically in *in vivo* studies.

On the other hand, we aim to treat different cancers, such as pancreatic cancer and uveal melanoma, by targeting key mutations using systems based on CRISPR/Cas9. Particularly, we tested both a functional CRISPR/Cas9 plasmid designed to specifically cleave the eGFP gene and the delivery ability of newly gold nanostructures. To assess the delivery ability of the nanostructures, we have used an eGFP reporter plasmid that allowed us to quantify their transfection capacity.[2]

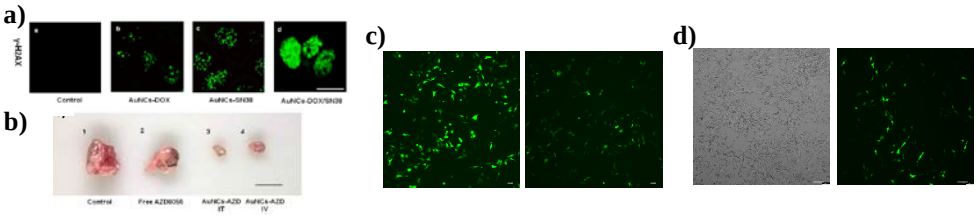


**Figure 1. A)** Analysis of DNA damage-induced H2AX phosphorylation (γ-H2AX) breast cancer cells. Scale bar: 10µm. **B)** Inhibition of uveal melanoma model tumor growth after treatment with AuNCs. Scale bar: 1cm. **C)** Fluorescence microscopy images of the CRISPR/Cas9 constructions against eGFP. Scale bar: 10µm. **D)** Transfection efficiency of gold nanostructures. Scale bar: 10µm.

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# Continuously modulate Förster energy transfer from fluorescein to rodamin 6G by electrical doping graphene

**Yansheng Liu,[a] Feng Luo*[a] and Reinhold Wannemacher [a]**

[a]*Calle Faraday, 9, 28049 Madrid. Tel: +34-655697188;*
*E-mail: YANSHNEG.LIU@IMDEA.ORG*

Resonant energy transfer (FRET) as a very important method has many applications especially in biological. Electrically controlling relative intensity of donor and acceptor in resonant energy transfer process provides a new way to to tune this process. Graphene as a zero band gape 2-dimension material makes it possible to modulate energy transfer from a variety of emitters at room temperature. In this research we demonstrate an electrically modulating resonant energy transfer (FRET) process between two kinds of molecules in which graphene as a quencher barrier and electrode. By shift Femi level of graphene using applied extra electrical field energy transfer process can be tuned. According to the result in this work ~10% of effected has been illustrated. This gate dependence of energy transfer modulation provides a potential application in optoelectronic domains.

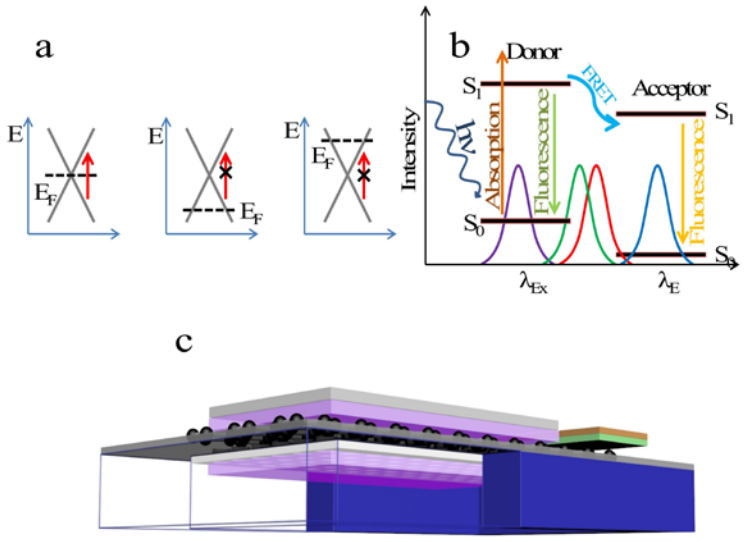


**Figure.** (a) Operation mechanism of electrically controllable energy transfer from molecular to graphene. (b) Schematic of the FRET process. (c) Device structure.

## Notes and References

‡ Footnotes should appear here.

1 Name, A.; Name, B.; Name, C. *Journal Title* **Year**, *Vol*, pp-pp

# *In vitro* study of the thermal stress mediated by iron oxide nanoparticles sujected to infrared irradiation and/or alternating magnetic fields

**Claudia Lozano,[a] Ana Espinosa[a], Begoña Sot[a,b] and Francisco J. Teran[a,b]**

[a] *iMdea Nanociencia. Calle Faraday, 9. Ciudad Universitaria de Cantoblanco, 28049 Madrid. Spain*
[b]*Nanobiotecnología (iMdea-Nanociencia), Unidad Asociada al Centro Nacional de Biotecnología (CSIC), 28049 Madrid,* Spain
*e-mail: claudia.lozano@imdea.org*

Cancer is one of the main cause of death in western countries. Then, the development of more efficient and specific cancer therapies is currently one of the main challenges in clinical research. In this context, the use of magnetic nanoparticles as heating mediators applying thermal stress to tumoral tissues has shown to successfully reduce cancer progress in clinical trials [1]. Among magnetic nanoparticles, iron oxide nanoparticles (IONPs) have been widely used as heating mediators due to their biocompatibility, and their duality to release heat by magnetic and optical activation means for killing cancer cells. Recent studies have shown that while dipolar magnetic interactions reduce the magnetic heat losses of MNPs inside cells [2], infrared irradiation induced MNP heat losses without being influenced by the intracellular environment. In addition, technical drawbacks have not yet allowed to clarify which molecular mechanisms are responsible of underlying cell death. However, unraveling these mechanisms is crucial to move from a preclinical to a clinical stage.
For these reason, we plan to study the effects of local heating on the cellular mechanisms related to cell viability, cell morphology and gene/protein expression, since recent studies have shown heterogeneous cellular response depending on the way the heat is applied [3,4]. In addition, my thesis work will perform a deep characterization of the parameters that influence heating losses mediated by MNPs while subjected to infrared irradiation, since little is known in this respect. In this context, special attention will be paid to determine a precise heat dose mediated by MNPs inside cells and the effect of the local heat in protein denaturalization, as well as the effects of the nanoparticle interactions with biological molecules, according to recent works [5]. As IONPs are biodegradable [6], we will study the dynamics of iron biodegradation, focusing on the degradation times, the pathways implicated and the formation of reactive oxide species (ROS). Finally, we are also interested in tracking this nanoparticle migration inside the cell in order to determine whether the intracellular location of IONPs influences the cell photothermal response.

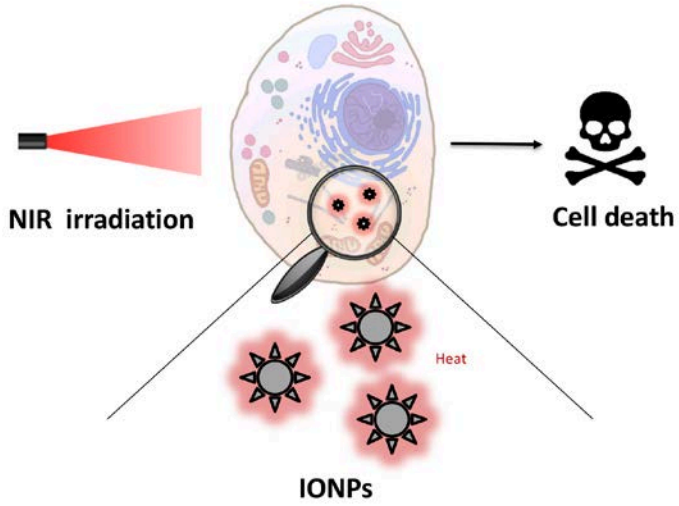


**Figure 1. Schematic representation of IONP-mediated heating losses inside cells when subjected to a NIR irradiation**. Local heat trigger cell death throught alteration of essential biomolecules, leading to the activation of intracellular death pathways.

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# Interaction of L-Alanine and L-Dialanine with Aluminium Oxide surfaces

**Juan Carlos Martín [a] , Andrés de la Escosura [b] , Oscar Rodríguez de la Fuente [c], Juan M. Rojo [a], Miguel Angel Niño* [a]**

[a] *IMDEA Nanociencia, C/Faraday, 9,28049 Madrid (SPAIN). Tel: +34.91.299.8769;*

[b] *Dpto. Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, 28049 Madrid (SPAIN). Tel: +34.91.497.2773;*

[c] *Dpto. Física de Materiales, Facultad de Ciencias, Universidad Complutense, Plaza de Ciencias, 28040 Madrid (SPAIN). Tel: +34.91.394.4495;*

*E-mail: juancarlos.martin@imdea.org; miguelangel.nino@imdea.org*

Aminoacids are one of the most important molecules for life as they are the building blocks of proteins, i.e., chains of aminoacids linked by a peptide bond. The basic processes at atomic level of aminoacid interaction and formation of peptides bonds are interesting for different disciplines like physical-chemistry, biochemistry or medicine. In particular, it has been suggested that polymerization of aminoacids through peptide bond formation might be mediated by a surface[1]. The same aminoacid-surface interaction is present in technological devices exploiting the chiral induced spin selectivity (CISS) effect, in which the interaction of films of chiral molecules, like polyalanine, with an aluminium oxide barrier is a key parameter for the spin injection[2]. From the point of view of prebiotic chemistry, the stabilization of a peptide bond on a surface can overcome the problems that the classical theory for the origin of life of a "primaeval soup" presents, i.e., the equilibrium displacement of the reaction of the peptide bond formation in acqueous solution makes hydrolization of dipeptides highly probable[3].

L-Alanine is one of the twenty $\alpha$-aminoacids encoded by RNA for the formation of proteins, and it is the simplest aminoacid that is chiral. We have studied the interaction of L-alanine, L-dialanine and cyclic alanine with a metallic copper Cu(100) surface and an aluminum oxide $Al_2O_3$ surface. We have grown thin films of these molecules by thermal sublimation on Ultra High Vacuum (UHV) and we have carried out a comparative study of the adsorption of L-Alaine and its L-Dialanine by means of x-ray photoemission spectroscopy (XPS) (ongoing measurement of infrared reflection absorption spectroscopy (IR-RAS) could be either considered). We discuss the dependence and stability of the zwitterionic character with film thickness, and the role of the the charge transfer processes in both surfaces in the possible polymerization reaction on these surfaces.

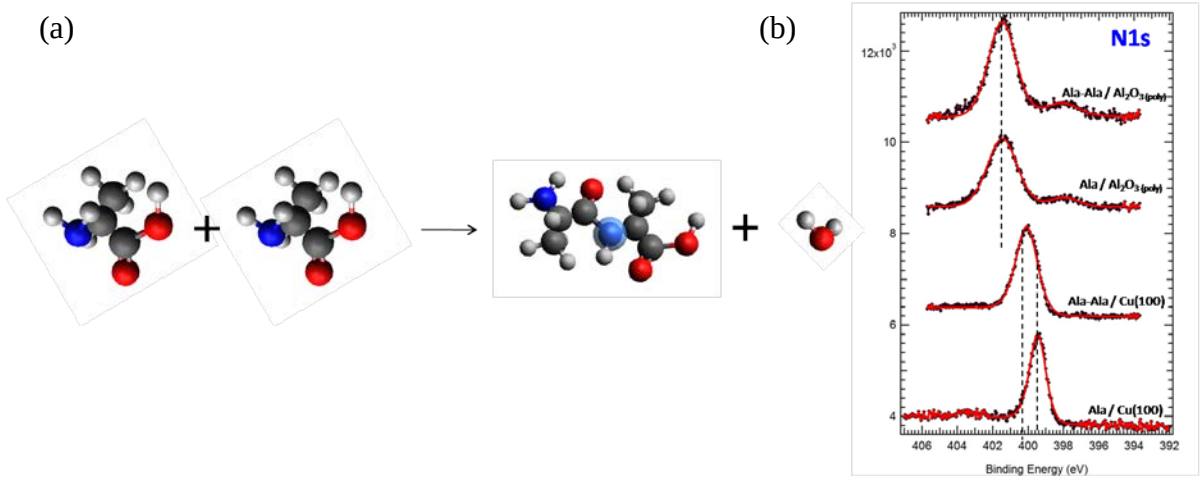


**Figure 1.** (a) Scheme of the dipeptide formation from L-Alanine monomers releasing a $H_2O$ molecule. (b) XPS spectra of the N1s core level for the aminoacid and its dipeptide in the two studied surfaces.

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# Antimonene 2D single layers as supercapacitors.

**Emiliano Martínez-Periñán[a,b], Michael P. Down[b], Carlos Gibaja[c], Encarnación Lorenzo[a,d], Félix Zamora[c,d], and Craig E. Banks[b].**

[a]*Departamento de Química Analítica y Análisis Instrumental Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, 28049, Madrid, Spain.*

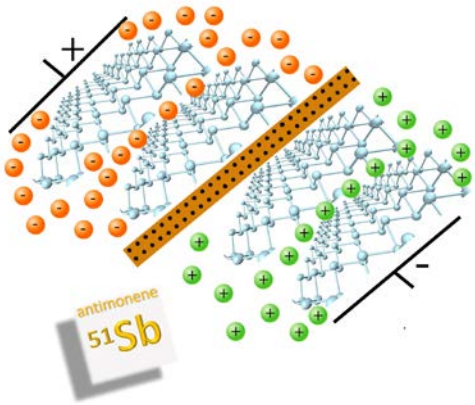
[b]*Faculty of Science and Engineering and Manchester Fuel Cell Innovation Centre, Manchester Metropolitan University, Chester Street, Manchester M1 5GD, UK.*

[c]*Departamento de Química Inorgánica, Institute for Advanced Research in Chemical Sciences (IAdChem) and Condensed Matter Physics Center (IFIMAC), Universidad Autónoma de Madrid, 28049 Madrid, Spain.*

[d]*Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA-Nanociencia) Cantoblanco, Madrid E-28049, Spain.*

*E-mail: emiliano.martinez@uam.es*

The increasing development of renewable energy sources, as solar and wind power harvesting devices, has required the development of sustainable energy storage technologies in order to satisficed the increasing energy demand. In energy storage devices, nanomaterials are playing a key role in bringing these devices toward practical applications. Therefore, much attention has recently been paid to the development of new nanomaterials, which are expected to allow electrode development with major storage capability. Among nanomaterials, 2D nanomaterials have a high specific surface area suitable for high double-layer capacitance1. Even so 2D nanomaterials have reactive basal planes and edges that can provide pseudocapacitance2. After graphene successful application in different energy storage devices, new 2D inorganic nanomaterial have been developed3, some of them following the graphene structure as a pattern. In recent years, a new family of compounds similar to graphene, base in anisotropic layered elemental materials is calling the attention of the scientific community. One of these new nnomaterials is Antimonene. It consist in one atom type two dimensions structure, each atom is covalently bonded with adjacent atoms to form a puckered honeycomb structure. In the present work, Antimonene is characterized for the first time as a material for applications in energy storage, being applied as an electrode material as the basis of a supercapacitor. Antimonene is shown to significantly improve the energy storage capabilities of a carbon electrode in both cyclic voltammetry and galvanostatic charging. It demonstrates remarkable performance with a capacitance of 1578 F g−1, with a high charging current density of 14 A g−1. The system also demonstrates a highly competitive energy and power densities of 20 mW h kg−1 and 4.8 kW kg−1 , respectively. In addition to the excellent charge storing abilities, antimonene shows good cycling capabilities over 10000 cycles until the drop-cast material is liberated from the substrate. Hence, this nanaomaterial is shown to be a highly promising for energy storage applications.

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‡ Schematic representation of two electrodes (anode and cathode) corresponding to a supercapacitor fabricated with antimonene 2D-layers

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# Towards graphene-based field effect transistors

**Víctor Marzoa,[a] Fernando Jiménez Urbanos,[a] Jorge Trasobares,[a] Rodolfo Miranda [a] and Daniel Granados[a,*]**

*a IMDEA Nanoscience, Calle Faraday, 9, 28049, Madrid, Spain.*
*E-mail: daniel.granados@imdea.org*

Graphene is a two-dimensional material with outstanding electrical properties, such as very high conductivity, which makes it an ideal candidate for some electronic applications.[1] In the last few years there has been an increased interest to develop graphene-based field effect transistors (GFETs) which could lay the foundation for the next generation of integrated circuits and radiofrequency electronics.[2] This project will cover the fabrication and characterization of back-gated GFETs from mechanically exfoliated graphite. Our objective is to obtain high mobility devices that could be used in future nanoelectronic applications. Different devices will be fabricated and compared employing HOPG, natural graphite and kish graphite as sources for the graphene.

The graphene flakes are transferred into a pre-pattern SiOx/Si (285nm of SiOx) P-doped substrate with aligning marks and number coding. This allows us to locate the absolute coordinates of the transferred flakes. The flakes are characterized employing Raman spectroscopy[4] (*Figure 1. a)*. If the flake is thin enough (ideally monolayer, bilayer or trilayer) it will be electrically wired. Metal connections are defined via optical laser beam lithography followed by a metal evaporation and a lift-off process to define the back-gated structure.

The fabricated devices are characterized using AFM, SEM, Raman, Optical microscopy. Electronic IV characteristics are measured in a probe station under atmospheric conditions and RT. The results– for a HOPG device are shown in *Figure 1 b)* where the drain-source current $I_{DS}$ is plotted as a function of the gate voltage $V_G$. Dirac Point voltage slightly below 0 V, indicating that the graphene is weakly N-doped. The electron mobility of the device at room temperature is very similar to the hole mobility ~200 $cm^2 \cdot V^{-1} \cdot s^{-1}$. Results from other devices will be presented.

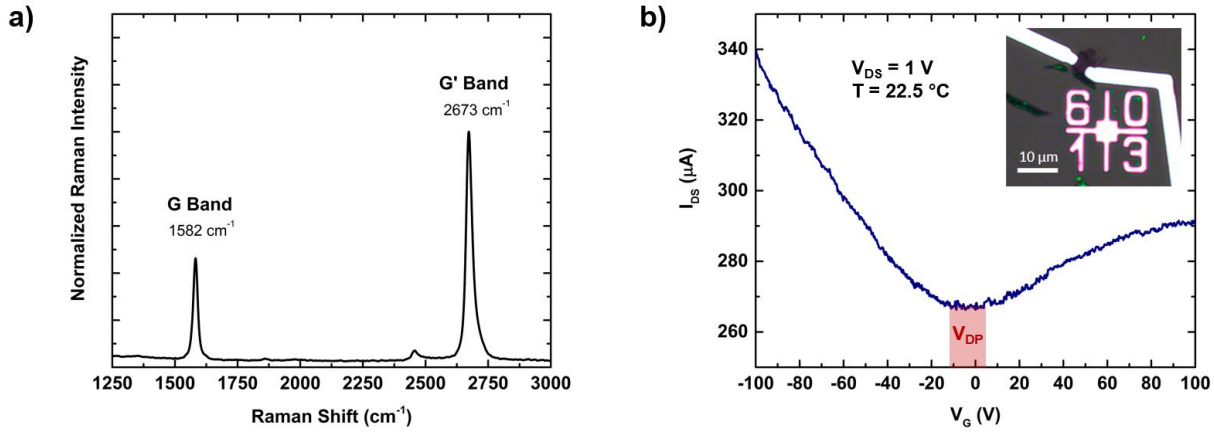


**Figure 1**. **a)** Raman spectrum of a typical single-layer graphene flake on a $SiO_x$/Si substrate ($\lambda_{exc}$= 532nm). **b)** Electrical measurement showing GFET drain-source current versus gate voltage at room temperature, when the applied voltage between drain and source is 1 V. The inset picture corresponds to the electrically contacted graphene flake (white lines are metallic contacts) laying on the substrate (pink numbers correspond to the substrate pattern).

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# CARBON DOTS MODIFIED ELECTRODES FOR CATALYSIS OF HYDRAZINE

**M. Mediavilla[1, 3], M. Revenga-Parra[1, 2,3], I. Bravo[1, 3], Félix Pariente[1, 2,3] and E. Lorenzo*[1, 2,3]**

[1] Departamento de Química Analítica y Análisis Instrumental, [2] Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain.
[3] Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA-Nanociencia), Campus UAM, Cantoblanco, 28049 Madrid, Spain.
***Email:*** encarnación.lorenzo@uam.es, Phone+34 91 497 4488

***Keywords:*** Carbon nanodots, hydrazine oxidation, electrocatalyst.

Electrocatalysis plays a key role in increasing efficiency of the interesting analytes such as hydrazine, and as a result, efforts have been made by the researchers to develop new materials easy to prepare and at low cost capable of reducing the hydrazine oxidation overpotential. In this context, a new nanomaterial of the carbon family, carbon nanodots with carboxylic surface groups (CDCOOH) have herein been fabricated and employed to modify screen-printed gold electrodes (AuSPEs). The resulting modified electrodes exhibit excellent electrocatalytic activity towards the oxidation of hydrazine. CDCOOH allow for a facile electrode modification. The oxidation of hydrazine takes place at 0.02 V. Therefore, modification of the electrode with carbon nanodots reduced the overpotential of hydrazine oxidation in 140 mV compared to bare AuSPE. The catalytic rate constant ($k_{cat}$) and the diffusion coefficient (D) was estimated by chronoamperometry and they were found to be $5.10x10^{6}M^{-1}s^{-1}$ and $8.42x10^{-6}cm^{2}s^{-1}$, respectively. The CDCOOH also exhibited excellent long-term stability, is very useful as hydrazine electrochemical sensor. The developed sensor responses linearly to hydrazine in the range of 1.0 to 100 µM with a detection limit of 0.8µM.

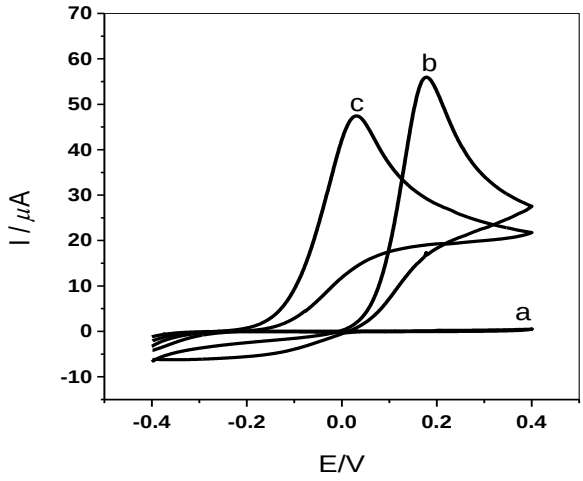


**Figure.1.** Cyclic voltammetric response for: Unmodified and Carbon nanodots modified AuSPE in presence (curve b y c respectively) and absence (curve a) of 1mM hydrazine in 0.1M pH 7.0 phosphate buffer solution. Scan rate: $0.010Vs^{-1}$

## Notes and References

‡ Departamento de Química Analítica y Análisis Instrumental, Facultad de Ciencias Módulo 16-203, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain

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# Towards the Synthesis of a Nanoswimmer

**Sofía Mena Hernando and Emilio M.Pérez**

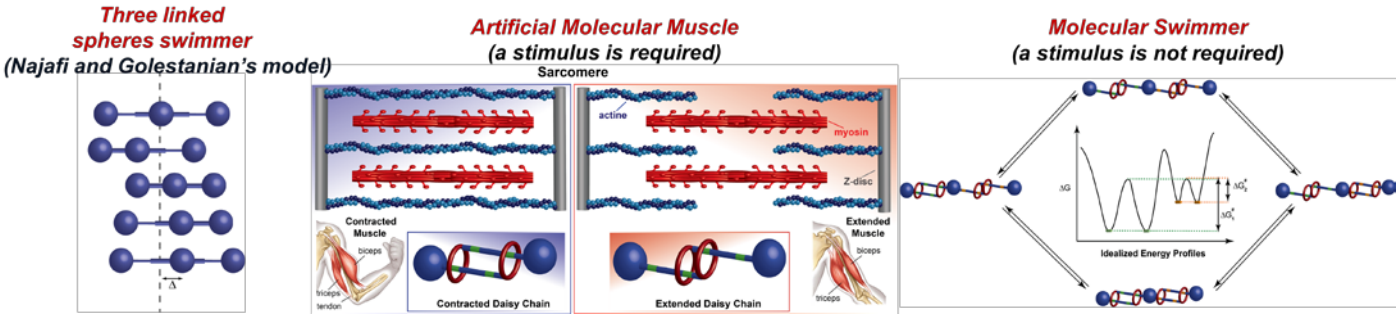
*IMDEA Nanociencia, C/Faraday, 9, Ciudad Universitaria de Cantoblanco, 28049, Madrid, España. Tel:+34912998852*

*E-mail: sofia.mena@imdea.org*

One of the main goals of nanotechnology is to make synthetic molecular devices that can propel themselves through fluidic environments. Ideally, they should also be capable of carrying out useful tasks such as performing mechanical work or acting as therapeutic agents. Therefore, the imitation of the macroscopic motions at the molecular level is a key step in the development of nanomachines, which represent small gadgets that perform computation, sensing or actuation.

The construction of artificial models in a simple manner could help to understand in depth the mechanism through which these molecular machines operate that, in turn, may help to make very useful devices. To achieve this target, it is essential to understand the differences between the physics of motion at macroscopic and molecular level.

For this purpose, this research is focused on the development of a molecular nanomachine called "*molecular swimmer*"[1] [1,2] following the three connected spheres model, proposed by Najafi and Golestanian in 2004.[3] Herein, we propose a model to synthesize it experimentally, at the molecular level, using a combination of covalent and non-covalent chemistry by the union of two mechanically interlocked molecules (MIMs),[4,5] called daisy chains.[6]

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# Uveal Melanoma Treatment Based on Gold Nanoparticles: Oligonucleotide Therapy Combined with Chemotherapy

**Paula Milán Rois[a*], Eduardo G. Garrido[a], Ana Latorre[a], Alfonso Latorre[a], Álvaro del Moral[a], Mercedes Lecea[a], Álvaro Somoza[a]**

[a] *C/Faraday nº 9, Madrid, Spain, Tel: 912998889;*

*E-mail: paula.milan@imdea.org*

Uveal melanoma (UM) is the most common primary intraocular malignant tumor in adults. Around half of the patients develop metastasis and die shortly after. This is due to the lack of effective therapies for metastatic UM. For this reason, new therapeutic approaches to this disease are welcome[1].

In this regard, microRNAs have shown to play a key role in neoplasia progression and might be used as therapeutic tools. It has been observed in different cancers, including UM, a particular microRNA's signature, which is different compared to the normal cells. Thus, restoring the normal levels of microRNAs can restore the normal behavior of cells[2]. In this study, four microRNAs downregulated in UM have been chosen to reprogram cancer cells. Through this approach, we expect to promote cell death or increase drug sensibility towards SN38 (Fig.1A). Furthermore, to improve the internalization and stability of the therapeutic molecules, gold nanoparticles (AuNPs) were used as carriers (Fig.1B). These nanoparticles are easy to prepare, modify, and present negligible toxicity.

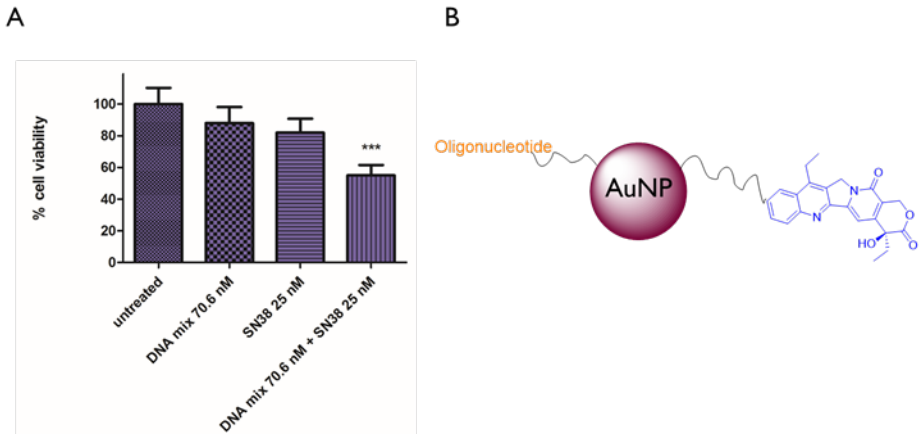


**Figure 1.** (A) Cytotoxicity assay of the individual chemotherapeutic, oligonucleotide therapy and combined therapy in MEL 202. (B) AuNP diagram of the combined therapy with oligonucleotides and SN38 drug.

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# Genetherapy for Osteoporosis using Mesoporous Silica Nanoparticles to Deliver sost siRNA and Osteostatin

**P. Mora-Raimundo,[1] D. Lozano,[1,2] M. Manzano,[1,2] and M. Vallet-Regí [*1,2]**

*[1]Departamento de Química en Ciencias Farmacéuticas, Facultad de Farmacia. Universidad Complutense de Madrid, Instituto de Investigación Sanitaria Hospital 12 de Octubre i + 12, Plaza de Ramón y Cajal s/n, E-28040 Madrid, Spain. E-mail: vallet@ucm.es*

*[2]Grupo de Investigación Biomateriales Inteligentes (CIBER-BBN), Madrid, Spain.*

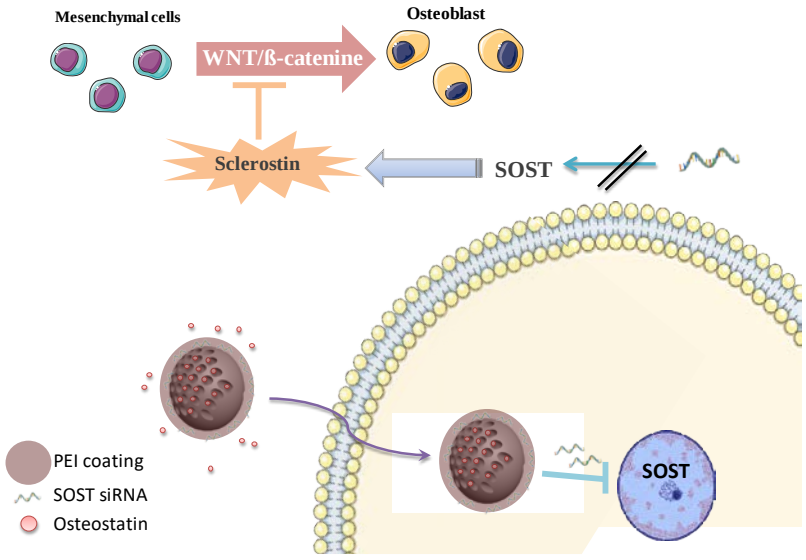
patmora@ucm.es

Osteoporosis is a progressive skeletal disease characterized by reduced bone mass and microarchitectural deterioration of bone tissue. The Wnt/β-catenin pathway is a major signaling pathway which regulates bone development and remodeling. This pathway migth be inhibited by the protein slerostin, encoded by SOST gene. This inhibition of the Wnt/β-catenin pathway decreases osteoblast differentiation and bone formation. For this reason, silencing SOST gene using small interference RNA (siRNA) could be an effective way to knock down the gene, reduce sclerostin expression and, therefore, treat osteoporosis. Generally, siRNAs have very short half-life, poor capacity of penetration through the cell membranes, and are immediately degraded by RNase, so an effective carrier of siRNA is needed.

Mesoporous silica nanoparticles (MSNs) could be used as an efficient and safe carrier for intracellular delivery of nucleic acids. Due to their mesoporous structure, we were able to load their pores with other molecules like osteostatin. It has been demostrated that osteostatin stimulates osteoblastic cell growth and. Attractive properties of osteostatin lie in the fact that it can affect bone cells at <nM concentrations and its structure is not likely to be degraded by proteolysis.

In this work we have modified the surface of the particles by a non-covalent attachment of polyethylenimine (PEI) which is known to increase cellular uptake and generate a cationic surface where siRNA constructs could be attached.[1] Osteostatin instead fits inside the nanoparticle pores due to its size, been able to load it and realease it from our MSNs. Here we have investigated the utility of these PEI coated MSNs (MSN@PEI) to overcome osteoporosis co-delivering SOST siRNA and osteostatin in primary mouse embryonic fibroblast (MEF). It is shown that MEF induce SOST gene expression,[2] providing a useful model to optimize SOST silencing by MSNs@PEI carrying a SOST siRNA.

The results demonstrated that it is possible to use the MSN@PEI system to successfully deliver SOSTsiRNA and knock down SOST expression in MEF cells, as well as, efficiently load and deliver osteostatin to accomplish osteoblasts differentiation in an additive or sinergistic fashion.

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# Nanocarrier for a controlled protein delivery to tumoral cells.

**V. Moreno-Zafra,[a,b] A. Baeza[a,b] and M. Vallet-Regí[*,a,b]**

[a] *Dpto. Química en Ciencias Farmaceúticas, Facultad de Farmacia, Universidad Complutense de Madrid, 28040, Madrid, Spain.*

[b] *Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain.*

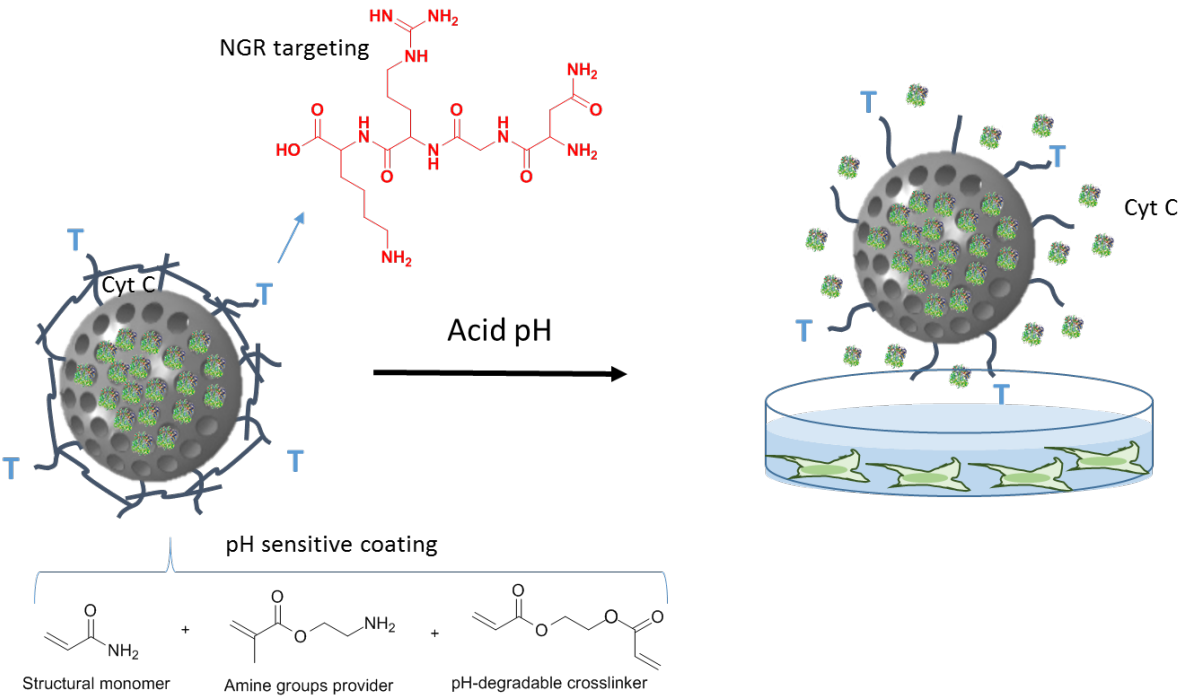
*E-mail: victomor@ucm.es, abaezaga@ucm.es, vallet@ucm.es*

One of the main problems in protein delivery for anticancer therapy is its low stability in the bloodstream and its inability to cross cellular membranes. Thereby, it is necessary to employ a nanocarrier in order to protect and transport the enzyme until being endocyted by the tumoral cells. Moreover, the poor tumor cell specificity of common chemotherapy agents makes necessary the design of new systems to overcome these problems.

We have designed a nanosystem for a controlled delivery of biomolecules. The employment of a Mesoporous Silica Nanoparticle (MSN) with large pore allows the entrapment of Cytochrome C in order to trigger apoptosis signals in tumoral cells. This MSN is coated with an acid-degradable polymer to avoid the premature release of the biomolecule at physiological pH and to degrade once the nanosystem reach the acidic tumoral microenvironment for the subsequent sustained release of the Cytochrome C into tumoral cells.

For a selective and effective endocytosis in tumoral cells overexpressing the CD13/aminopeptidase N (APN) receptor isoforms, we conjugated this nanosystem with a NGR peptide as a targeting element for these receptors widely present in tumor neovasculature. We test its efficacy "*in vitro*" with a HT1080 human fibrosarcoma cell line.

This nanocarrier is able to transport and to obtain a controlled release of therapeutic proteins to generate apoptosis signals once endocyted by the tumoral cells to provoke their destruction. This effect joined together with the targeting recognition is expected to enhance the efficacy and specificity against tumoral cells compared to traditional chemotherapy drugs.

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# Magnetic Composites: Strontium Ferrite with Magnetic Microwires and the dependence of its magnetic properties with the proportions

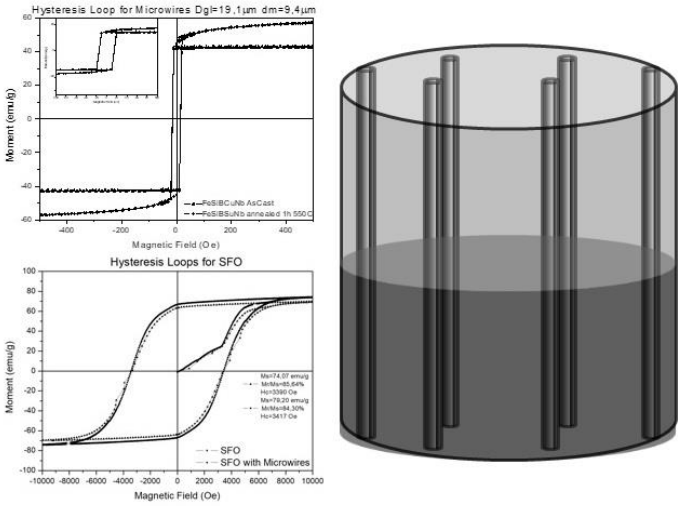
**Alberto Moya,*[a] and Pilar Marín[a]**

[a] *Instituto de Magnetismo Aplicado - Laboratorio Salvador Velayos, Nacional VI, Km. 22,500, Apartado de Correos, 28230 - LAS ROZAS (Madrid), Spain. Tel: 91 300 71 73;*

*E-mail: alberto.moya.senas@ucm.es*

Due to the low cost of Strontium Ferrites and its magnetics properties, the research for enhance these properties is an interesting way to expand its application range. A new structure, based on a combination of ferrites and microwires in adequate proportions, is proposed as an interesting way to enhance the energy product of these ferrites. Soft Magnetic Microwires, with length in the range of mm properly oriented are giving promising enhacement of BHmax. Samples have been characterized by means of Vibrating Sample Magnetometer (VSM).

FIGURE

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# Advantages of carbon-coated superparamagnetic nanoflowers for lateral flow immunoassays

**Amanda Moyano*[a,b], M. Salvador[b], J.C. Martínez-García[b], M. Rivas[b], M.C. Blanco-López[a], M. Gónzalez-Gómez[c], Z.Vargas Osorio[c], Y. Piñeiro[c], J. Rivas[c].**

[a] *Dpto. de Química Física y Analítica, Universidad de Oviedo, C/Julián Clavería, 8, 33006 Oviedo, Spain.*

[b] *Dpto. de Física, Universidad de Oviedo, Edificio Departamental Este, Campus de Viesques, 33204 Gijón, Spain.*

[c] *Dpto. Física Aplicada, Fac. Física, Universidad de Santiago de Compostela, Campus Vida, 15782 Santiago de Compostela, Spain.*

*uo210018@uniovi.es*

Lateral flow immunoassay is a rapid, simple and cost-effective test, which is used in fields such as diagnostics in medicine[1] or environmental control. Lateral flow immunoassay is a paper-based platform for detection and quantification of analytes which consists of three parts for a *dipstick format*: absorbent, nitrocellulose membrane and conjugate (Figure 1). Traditionally, this kind of immunoassays have been used only as qualitative tests, given that they rely on a visual signal (positive/negative test). Recently, we have shown that we can add to this the quantifying capacity by using superparamagnetic nanoparticles as labels.[2] Moreover, if the particles display a strong color intensity, we can profit from both, optical and magnetic measurement.

For this purpose, in this work we have used superparamagnetic iron oxide nanoflowers coated by a black carbon layer ($Fe_3O_4$@C). To test their performance as immunoassay we have chosen a model system by conjugating the particles to neutravidin and testing them against biotin printed across the membrane (Figure 1). For the bioconjugation of $Fe_3O_4$@C nanoparticles, the carbodiimide crosslinker chemistry was used. Some parameters were studied (reaction time and concentration of neutravidin) in order to optimize the immunoassay. Furthermore, the functionalization process was followed by dynamic light scattering measurements and it was demonstrated that the hydrodynamic diameter increases from 178 nm to 200 nm after the addition of neutravidin. The neutravidin coated superparamagnetic nanoparticles were allowed to flow through the nitrocellulose membrane. At the biotin line they were retained due to the strong, specific and non-covalent interaction between biotin and neutravidin, forming the test line. Finally, this line was quantified by an electromagnetic sensor based on the increase of the impedance induced by the varying magnetic moment of the particles on a RF current-carrying copper conductor.[2] As a result, we conclude that the carbon-coated superparamagnetic nanoflowers display a significant stronger signal compared to other kind of nanoflowers (see Figure 2).

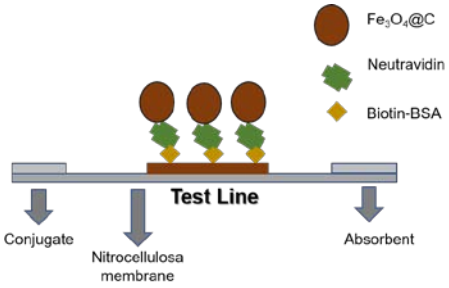


**Figure 1. Lateral flow immunoassay scheme**


**Figure 2. Immunoassay with citrate-coated nanoflowers (a) and carbon-coated nanoflowers (b).**

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# A neural bypass for sensing and stimulating at the spinal cord

**Vicente Muñoz Martínez[a], Beatriz L. Rodilla[a,b], Rubén Guerrero[a], Lucas Pérez[a,b], Julio Camarero[a,c], Rodolfo Miranda[a,c], María Teresa González[a]**

*[a]IMDEA Nanociencia, Campus Cantoblanco, 28049 Madrid, Spain, [b]Depto. Física de Materiales, Universidad Complutense de Madrid, 28040, Madrid, Spain, [c]Depto. Física de la Materia Condensada-IFIMAC, Universidad Autónoma de Madrid, 28049, Madrid, Spain*

*E-mail: vicente.munoz@imdea.org*

Spinal cord Injuries caused by trauma are usually irreversible and have devastating effects, including permanent or partial paralysis, due to the interruption of neural connections through the spinal cord. ByAxon propose a new generation of nanostructured sensors and electrodes that will bypass the existing injury with low tissue disturbance by sensing and stimulating. In that way, we aim to recover the sensitibity and restore the lost neural connection [1].

Byaxon proposal comprises the use of magnetic field sensors to detect the neural electrical signals without direct contact, and the use of metallic nanowired interfaces as nano-electrodes to stimulate.

To sense the neuronal magnetic signal, which has a magnitude of the order of nT, we use the anisotropic magnetoresistance (AMR) effect present in ferromagnetic materials. We are currently characterizing a new family of AMR sensors based on $La_{2/3}Sr_{1/3}MnO_3$ [2]. In these, we carry out the microfabrication using Wheatstone bridges (Figure 1.a) that yields a high sensitivity and high signal to noise ratio.

On the other hand, neural stimulation currently uses a large number of neural internal electrodes that face biocompatibility problems [3]. We have developed flexible nanostructured interfaces of metal nanowires grown by template-assisted electrodeposition (Figure 1.b and 1.c). We can vary the composition, arrangement and length of the nanowires in order to achieve the most optimal nanostructured configuration.

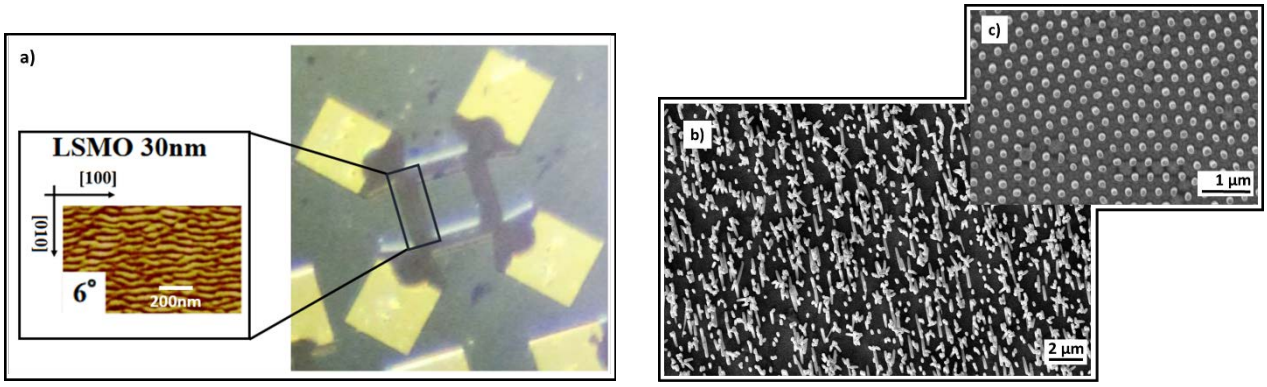


***Fig. 1**. a) AFM image of a LSMO sample and nanostructured Wheatstone bridge fabricated at IMDEA. Nanostructured electrodeposited interfaces of b) random and c) ordered nanowire arrangements.*

**FUNDING SOURCES:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 737116.

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# Efficient expression of OPA1 mitochondrial membrane fusion protein in *in vitro* and *in vivo* experiments by using Gemini/DOPE - based Lipoplexes

**Mónica Muñoz-Úbeda[a,b], Martina Semenzato[c], Anais Franco Romero,[c] Elena Junquera[b], Emilio Aicart[b], Luca Scorrano[c] and Iván López-Montero[a,b].**

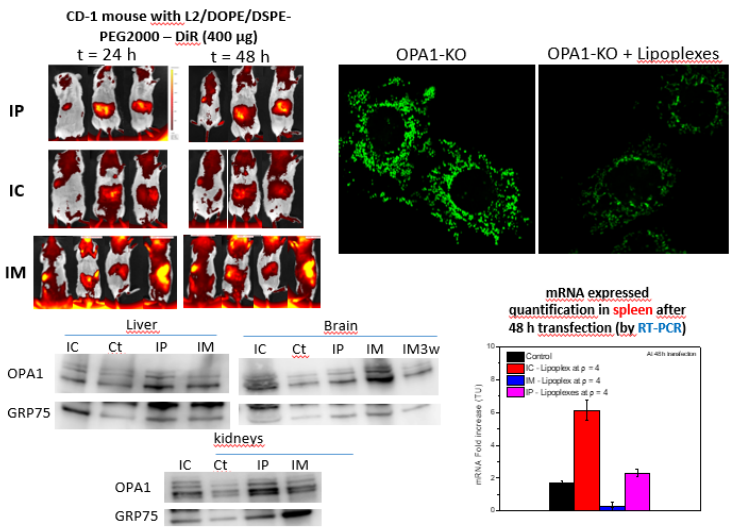
[a] Instituto de Investigación Biomédica Hospital 12 de Octubre (i+12), Avda. Córdoba s/n, Madrid, Spain

[b] Facultad C.C. Químicas, Dpto. Química Física, Avda. Complutense s/n, Madrid, Spain.

[c] *Fondazione per la Ricerca Biomèdica Avanzata, Venetian Institute of Molecular Medicine (VIMM), Via Giuseppe Orus 2, Padova, Italy.*

*E-mail: monicamubeda@gmail.com*

Recent advances on the mitochondrial morphology indicate that mitochondria are able to form a highly dynamic network that constantly fuse a divide. [1] Fusion and fission balances are very important for normal cellular function. [1,2] In mammalian cells, there are three main proteins involved in the mitochondrial fusion: Mfn1 and Mfn2 (OMM) and OPA1 (IMM). Deletion of any of them in mouse embryonic fibroblasts (MEFs) and CD-1 mouse models produces mitochondrial fragmentation, thus leading to mitochondrial diseases (MD), to which there is no cure yet. [3] In this work, lipoplexes have been conceived as efficient therapeutic agents against MD. Lipoplexes, lipid/DNA highly packed complex, are composed by Imidazol Gemini/DOPE mixed cationic liposomes[4] with a plasmid DNA coding on OPA1 protein. These lipoplexes are able to transport and efficiently delivery plasmid DNA into the cytoplasm thus inducing the recovering of normal mitochondrial phenotype in OPA1-Knockout MEFs. These lipoplexes show a good viability and high transfection efficiency as compared with other canonical transfer agents in *in vitro* experiments. Besides, these lipoplexes show a great bioaccumulation and transfection efficiency in different organs of CD-1 mouse model without any toxicity over time after intraperitoneal (IP), Intracardiac (IC) and intramuscular (IM) injection, as was confirmed by different techniques.

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# Loading capacity and stability of Gold Nanoparticles conjugated with oligonucleotides

**Demian Pardo[ab], Mercedes Lecea[a] and Alvaro Somoza*[a]**

[a]*Institute for Advanced Studies in Nanoscience (IMDEA Nanociencia), Calle Faraday 9, Ciudad Universitaria de Cantoblanco, Madrid, Spain. Tel: +34 912998889.*

[b] *Synthelia Organics, Calle Faraday 7, Ciudad Universitaria de Cantoblanco, Madrid, Spain. Telf: +34 910284729.*

*E-mail: demian.pardo@imdea.org*

Gold nanoparticles (AuNPs) have been used during the last years extensible for a variety of applications, including those dealing with biomedicine[1]. In this sense, gold nanoparticles have been proven very versatile, and their applications vary from nanocarriers of drugs to sensing systems or molecular diagnosis [2].

This type of nanomaterial can be functionalized with diverse molecules, such as polymers, sugars or proteins. Interestingly, oligonucleotides, when densely packed, have shown to provide to the nanostructures outstanding properties and for this reason are even considered a new family of nanostructures, Spherical Nucleic Acids[3]. Among the properties observed, is worth mentioning the high affinity for complementary sequences, great stability (thermal and enzymatic), negligible toxicity and great cell internalization capabilities [4].

Despite the great interest in this type of material it is difficult to define key parameters that will expand its application, such as loading capacity regarding the nature of the oligonucleotide and the final stability of the nanostructure.

In this work we have assessed the functionalization of AuNPs, using oligonucleotide with different size and sequences, at different loading concentrations (Fig 1). We have observed that the stability depends on the nature of the oligonucleotide as well as the loading obtained. This study provides useful insights for further developments of functionalized nanoparticles for biomedical applications.

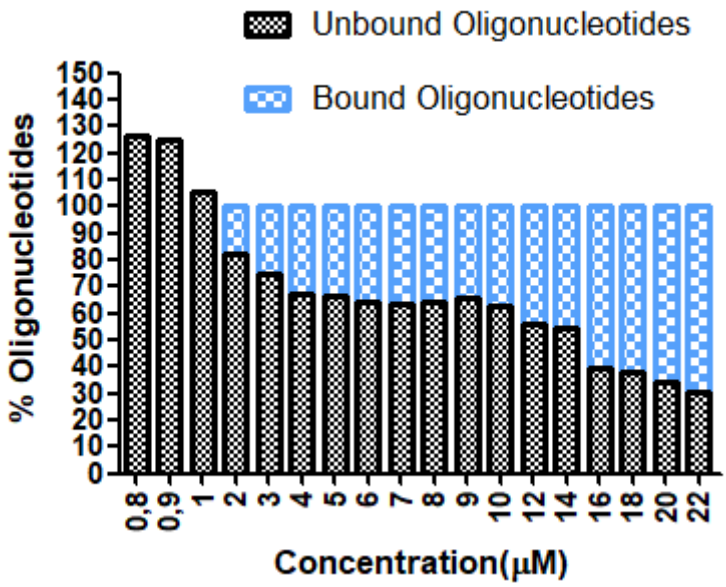


**Fig1.** Percentage of bounded and unbounded oligonucleotides during the functionalization of gold nanoparticles

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# In vitro Catalytic Transfer Hydrogenation Studies of Organoiridium Complexes

**Sonia Paz,*[a] Ana C. Carrasco[a] and Ana M. Pizarro[a]**

[a]*IMDEA Nanociencia, Faraday 9, Ciudad Universitaria de Cantoblanco, Madrid 28049, Spain.*

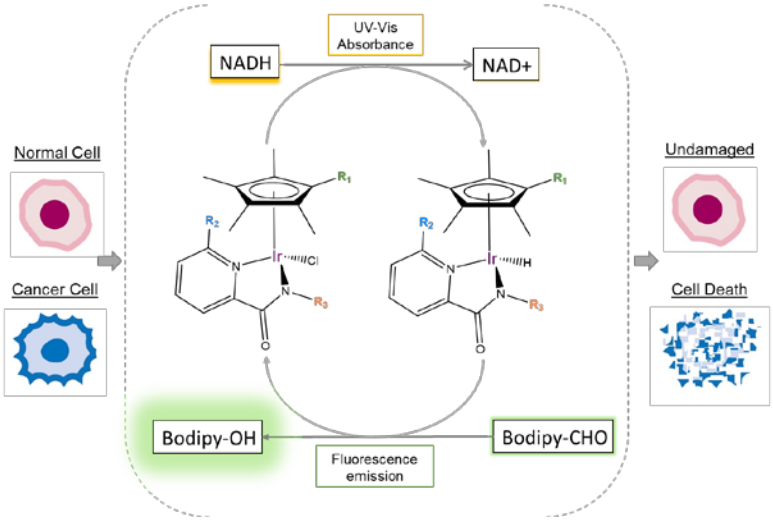
**E-mail: soniapazouteiral@gmail.com*

Since Cisplatin was approved by the FDA in 1978 as the first effective cancer treatment based on a metal, survival rates increased greatly in a number of cancers. However, its side effects are not negligible since it presents high toxicity to vital organs, such as the liver, mainly due to discriminated action in both cancer and healthy cells.

This scenario led to the creation of new compounds based on metals that are endowed with similar anticancer activity yet greater selectivity between tumor and healthy cells. Metallodrugs can present certain advantages over organic drugs, such as their structural diversity and high versatility in reactivity,[1] as well as novel mechanisms of action, which may reduce their side effects and expand the spectrum of treatable cancers.[2]

A new mechanism of action exploited by novel metallodrugs is metal bio-catalysis, which has a great potential value due to the low dose required by the drug, which would lead to less toxicity.[3]

In the present work we explore the catalytic transfer hydrogentation activity of piano-stool organoiridium complexes for the reduction of NADH to $NAD^+$. The $NADH/NAD^+$ ratio is a parameter of vital importance in cellular metabolism to regulate energy, DNA repair and transcription, immunological functions and cell death. Since cancer cells exhibit faster metabolic rates, they are also more sensitive to alterations between the proportions of these two molecules, resulting in selective antiproliferative activity comparable to that of cisplatin without affecting healthy cells.




The catalytic activity of a series of irganoiridium complexes is initially tested in *in vitro* studies in which a molecular probe is used. The proton of the iridium(III) complex, previously subtracted from NADH, reduces the probe resulting in a significant increase in its fluorescence emission. This catalytic process is carried out in aqueous solution at 37 °C, so that it can be compared to its potential activity in cells, and the conversion between the different species is followed by UV-Vis absorbance and fluorescence emission, as it has previously been done by Do and co-workers.[4] A family of similar compounds are synthesized using different ligands, which will potentially modify their catalytic activity and will allow to define the relationships between their activity and the chemical structure of their ligands.

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# Endosomal escape of plasmonic gold nanoparticles mediated and quantum dots by Listeria monocytogenes Listeriolysin O toxin LLO

**Ismael Plaza García-Abadillo [a,b], Vanessa Manzaneda González [a], Matic Kisove[c c], Diego de la Fuente Herruela[a,b], Gregor Anderluh[c], Andrés Guerrero Martínez [a], Paolo Natale [a, b] and Iván LópezMontero [a,b] ***

*[a] Dto. Química Física I, Universidad Complutense de Madrid, Avenida Complutense s/n, 28040 Madrid, Spain;*
*[b] Instituto de Investigación Hospital "12 de Octubre" (i+12), Avenida de Córdoba, s/n, 28041 Madrid, Spain.*
*[c] Department of Molecular Biology and Nanobiotechnology, National Institute of Chemistry, 1000 Ljubljana, Slovenia.*
**E-mail: ivanlopez@quim.ucm.es*

In the search of new alternatives for drug delivery systems, Listeriolysin O toxin (LLO) could be exploited for disrupting endosomal pathway. The pathogen Listeria monocytogenes produces LLO, which is a pore forming protein of the cholesterol-dependent cytolysin (CDC) family. During host infection the pH-dependent pore formation of the LLO toxin destabilizes the phagolysosome and this allows Listeria to escape form the endosomal system and to survive inside the host cells. In this work, we exploit the pH-dependent pore formation of the LLO toxin for endosomal escape during drug delivery. LLO wild-type and mutants, with a stronger pH-dependence, have been heterologously produced and purified in E. coli. The LLO WT and LLO H311A mutant were tested for functionality in vitro and then conjugated to functionalized gold nanoparticles (Au-NP) and quantum dots to probe the endosomal escape. This “proof-of-concept” will be further developed for further applications in plasmonic photothermal therapy of cancer cells (PPTT), the Au-NP convert non-harmful light into thermal energy through the interaction of laser radiation with the longitudinal localized surface plasmon resonance of the AU-NP. The resulting intracellular Au NP heating has demonstrated great potential for killing cancer cells by induced apoptosis or photothermolysis (Rubén Ahijado-Guzmán et al., ACS Omega 2016, 1, 388-395).

# Electrically conducting coordination polymer as an acetonitrile chemical sensor

**Esther Resines,[a] Enrique Burzurí,[a] Estefania Fernandez-Bartolome,[a] Miguel Ángel García García-Tuñón[b] and José Sánchez Costa[a]**

[a]*IMDEA Nanociencia, C/ Faraday, 9 , Ciudad Universitaria de Cantoblanco, 28049, Madrid, Spain, Tel: 34 912998700*
[b]*Instituto de Magnetismo Aplicado, Laboratorio "Salvador Velayos", A6 km 22.5, Apdo. correos 155, 28230, Las Rozas, Spain, Tel: 34 913007173*

*E-mail: esther.resines@imdea.org; jose.sanchezcosta@imdea.org*

Increased emissions of volatile organic compounds (VOCs) and their resulting impact on air quality is now considered of major environmental concern, as some VOCs are identified as highly toxic or carcinogenic.[1] Vapochromic materials, which show dramatic and reversible color changes upon exposure to vapors, have attracted much attention in terms of their potential application as chemical sensors of VOCs.[2] Nowadays, the design and synthesis of coordination polymers capable of selectively sensing specific guest molecules is a hot research topic.[3] This materials are good candidates for vapochromism since changes in the coordination sphere due to the inclusion of VOCs can lead to a change of color.[4,5] The use of coordination polymers offers solutions to the commonly encountered problems like sensitivity, selectivity, reproducibility, interference (from humidity), stability, or false responses due to sensor aging.[1]

In this communication, we present a novel non-porous crystalline one dimensional molecular-based Fe(II) coordination polymer acting as a porous material. The main interest of this coordination polymer is that the loss of the acetonitrile solvent as the temperature increases results in a change of color, from yellow to orange, and an abrupt increase of its electrical transport. These changes are a result of the transition from high spin to low spin state of the iron center. What is even more interesting, is that if the complex is exposed to acetonitrile after the spin transition, both the original color and the electrical properties are recovered. As a result, this easily synthetized complex can be used as a reversible acetonitrile sensing device at room temperature.

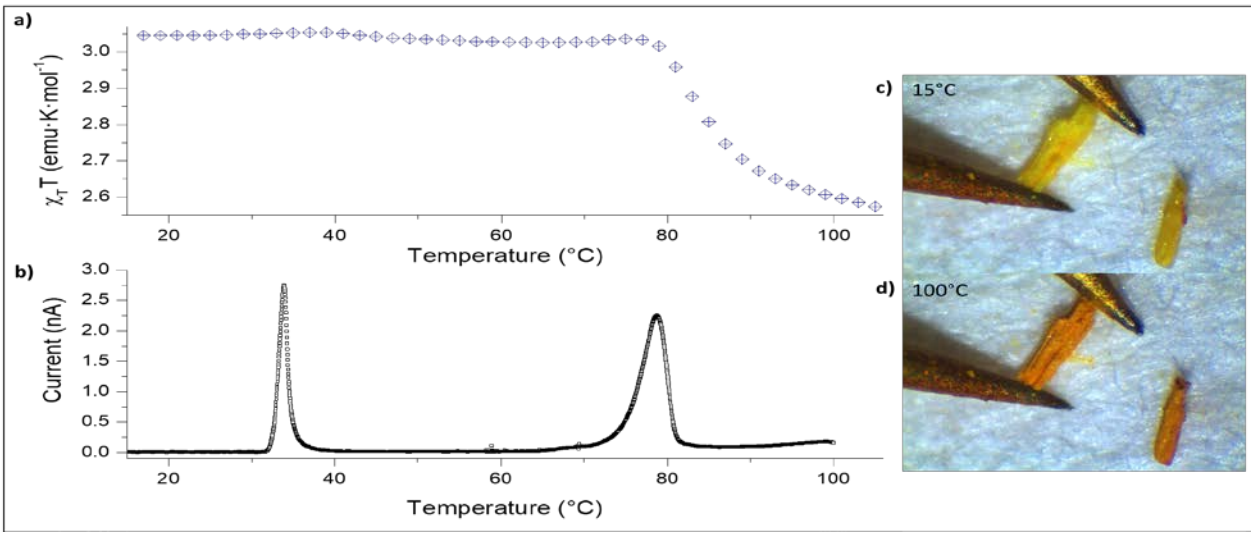


**Fig1. a)** χT vs temperature. **b)** Current vs. temperature graph. **c)** Image of the crystal at 15°C (yellow). **d)** Image of the crystal at 100°C (orange).

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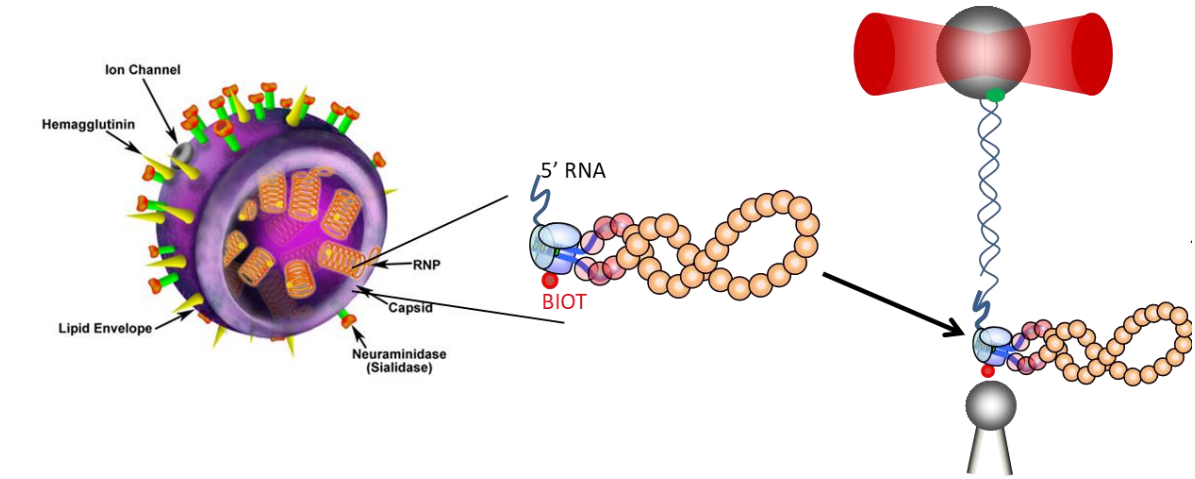
# A single-molecule manipulation assay to study the transcriptional dynamics of Influenza A virus

**Carlos R. Pulido[a], Rebeca Bocanegra[a], Rocío Coloma[b], Jaime Martín-Benito[b] and Borja Ibarra[b]**

[a]*Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia), C/ Faraday 9, 28049 Madrid, Spain*
[b]*Centro Nacional de Biotecnología (CNB), C/ Darwin 3, 28049 Madrid, Spain*
*E-mail: carlos.rodriguez@imdea.org*

Influenza A virus is an important human pathogen that causes yearly epidemics and occasional pandemics of flu. Because of its high mutation rate Influenza viruses evolve rapidly and are difficult to target with vaccines. On the molecular level, the dominant source of mutations is the error-prone RNA-dependent RNA polymerase, which is the protein complex responsible for replicating and transcribing the viral genome. We present an optical tweezers-based assay to establish the molecular and mechanistic processes that govern the real time kinetics of the viral transcription machinery at the single molecule level. This information is crucial to understand how the viral RNA polymerase influeces viral mutation rates. Our design will provide a new tool to test and understand the effect of drugs on the operation of the viral transcription machinery at the molecular level and therefore, may have direct implication in the development of alternative therapeutic strategies against Influenza viruses.



# In silico magnetic hypethermia: insights for a treatment planning platform

**Irene Rubia-Rodríguez[1], Helena Verdaguer[2], Teresa Macarulla[2] and Daniel Ortega[1]**

[1] *IMDEA Nanociencia, Campus Universitario de Cantoblanco, Madrid, Spain*

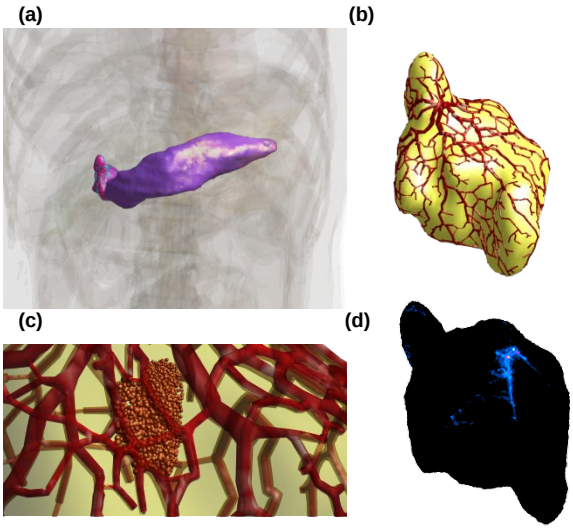
[2] *Vall d'Hebron University Hospital, Medical Oncology, Barcelona, Spain*

*E-mail: irene.rubia@imdea.org*

Computer simulations (in silico) have helped in vivo and in vitro experiments to develop new therapies in medicine, reducing time and costs to produce the tests. One of the treatments benefiting from in silico trials is magnetic hyperthermia, a nanotechnology-driven cancer therapy that has already been trialled in clinical settings as coadjuvant to chemotherapy and radiotherapy to succesfully treat several types of tumours [1-4]. When addressing localised tumours, magnetic hyperthermia relies on the intratumoral injection of magnetic nanoparticles that are excited by an external alternating magnetic field. The nanoparticles then release heat through hysteresis losses, eventually killing tumour cells [5].

The specialised instrumental development is moving forward, and some commercial systems are being deployed throughout Europe and USA [6]; nevertheless, research on safety, dosimetry, and treatment planning does not progress to the same pace. There are lots of variables to take into account to set up the therapy, and it has to be adapted to each patient and tumour as well as to the evolution of the tumour along the process. In silico trials can predict the effectiveness of a treatment and optimize it to get the best benefit/risk ratio.

Due to the complexity in designing the therapy plan, we are developing a software platform that provides clinicians with a semi-automatic treatment planning to work out and evaluate clinically relevant dosimetric parameters (like SAR and CEM43). The core element is a virtual 3D model of the tumour and its vascularization obtained from real diagnostic images, along with other devices that may guarantee a safer therapy. Previous works have shown the relevance of some of these gadgets to avoid skin overheating [7-8]. In this work we present the results obtained regarding SAR and CEM43 maps generated upon heating deep-seated tumors using different spatial distributions of nanoparticles. Also, we show the role of tumor vasculature and the use of external cooling devices.




**Figures: (a)** Human 3D model with pancreas and a pancreatic tumour highlighted. **(b)** 3D model of a pancreatic tumour with its vascularization. **(c)** 3D model of the magnetic nanoparticles injected inside the tumour model. **(d)** SAR distribution map over the tumour surface.

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# Enhancement of magnetic lateral flow immunoassays by means of a magnetic field gradient

**M. Salvador[a], A. Moyano[b], J.C. Martínez García[a], M.C. Blanco-López[b], M.P. Morales[c] and M. Rivas[a]**

[a]*Departamento de Física, Campus de Viesques – Universidad de Gijón, 33204 Gijón, Spain.*
[b]*Departamento de Química Física y Analítica, Universidad de Oviedo, 33006 Oviedo, Spain*
[c]*Instituto de Ciencia de Materiales de Madrid, CSIC, Cantoblanco, 28049, Madrid, Spain*
*E-mail: UO247670@uniovi.es*

Lateral Flow Inmunoassays (LFIs) have been widely used as *point-of-care* for bio-testing because of their good characteristics, such as quickness, portability, easy use and low cost. They are a paper-based technology, basically consisting of a nitrocellulose strip across which a reagent is immobilized to specifically capture the bio-analyte contained in the fluid sample (this constitutes the so-called test line); the latter flows along the strip by capillarity. The bio-analyte is labelled by some recognition probe. LFIs are often designed for applications in which a presence/absence response is desired. In this case, a naked-eye inspection of the test line is sufficient. For this purpose, gold or latex nanoparticles are used. For quantifying applications magnetic nanoparticles (NPs) have proved to be efficient [1]. They produce a magnetic perturbation that can be detected by a magnetic sensor. Besides this advantage, the possibility of pre-concetration (in the liquid sample) or post-concentration (in the test line) makes them even more attractive to increase the sensitivity of the technique.

In this work, we have used a magnetic field gradient applied to the sample after running and drying the immunoassay. For this we apply running buffer to the strip and place it on one of the poles of an electromagnet providing a magnetic field induction up to 200 mT. The particles, which had been immobilised across the thickness of the nitrocellulose membrane, are reaccomodated by the field gradient, and concentrated closer to the visible surface. To evaluate the magnetic signal of the LFIs a magnetic reader [2] has been used that profits from the superparamegntic character of the labels. It basically consists of an inductive sensor on which the magnetic moments of the particles produce an increase of impedance. The method has been tested with two different kind of particles (monodisperse iron oxide 8 nm nanoparticles [3], and 25 nm nanoflowers), both functionalised with neutravidin, on a lateral flow strip across which a biotin test line has been printed. A remarkable increase of the measured signal in the order of 30% was observed. The gradient amplitude and the effect of time have been analysed in order to optimise the procedure. The results lead to the conclusion that post-concentration of the magnetic labels of the LFI by a magnetic field gradient is an efficient approach to enhance their sensitivity.

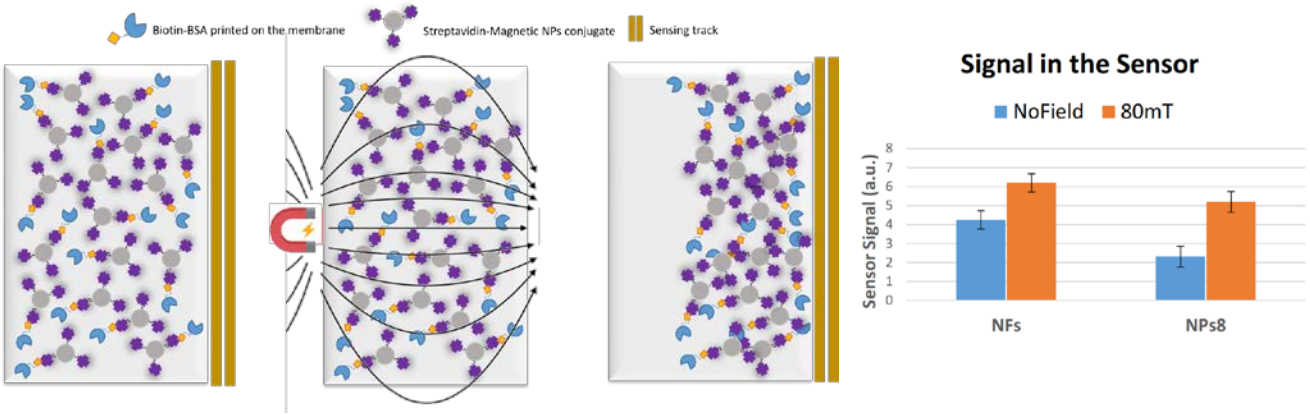


FIGURE. ***Left:*** A schematic view of a cross section of the membrane of the strip after the sample has been run. The magnetic NPs are caught by the interaction Biotin-Neutravidin and accommodate whithin all the section. After applying a magnetic field gradient, the NPs are move along the nitrocelulose fibers of the membrane towards the most external layer. ***Right:*** The bar graph shows the signal obtained in the sensor when no field and when a field of 80mT is applied into the strip for the two different kind of nanoparticles.

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# Fundamentals of detection methodology based on the AC magnetization signal of functionalized magnetic nanoparticles in biological fluids

**E. Sanz,*[a] L. Cremades[a] , N. Silvestri[b], T. Pellegrino[b], F.J. Teran[a,c] and A.L. Cortajarena[a,c,d]**

[a] *iMdea Nanociencia. Calle Faraday, 9. Ciudad Universitaria de Cantoblanco, 28049 Madrid. Spain*
[b] *Istituto Italiano di Tecnologia, Via Morego 132, Genoa, Italy*
[c] *Nanobiotecnología (iMdea-Nanociencia), Unidad Asociada al Centro Nacional de Biotecnología (CSIC), 28049 Madrid, Spain*
[d] *CIC biomaGUNE, Paseo Miramón 182, 20014 Donostia-San Sebastian. Spain*

*E-mail: elena.sanz@imdea.org*

The use of magnetic nanoparticles (MNPs) in biomedicine has been widely explored for diagnosis, therapeutic, and sensing purposes. Recent studies have proposed the use of MNPs functionalised with recognition ligands (F-MNPs) as transducer for magnetic detection of biomarkers related to diseases and/or pathologies. [1] The interaction of F-MNPs with biomolecules leads to variations of the MNP magnetic properties, which can be visualized by different magnetic measurements.[1,2] Among them, AC magnetometry provides a novel and suitable methodology (see Figure below) for which the proof of concept has been achieved but not yet published. Similarly to other magnetic detection methodologies[1], the suitable MNPs are those whose prevalent magnetic relaxation mechanism is the Brownian-one. Recent studies [3] have shown that CoxFe(3-x)O4 nanocubes are extremely sensitive to viscosity due to the prevalence of Brownian relaxation processes[4]. For this reason, these MPNs are adequate to be used as transducers for magnetic detection of biomolecules dispersed in aqueous fluids.

Based on it, my thesis work will deepen on different fundamental aspects related to this novel magnetic detection. First, learning the synthesis of CoxFe(3-x)O4 nanocubes of different sizes (10-20nm). Then, these magnetic nanocubes will be decorate with the suitable coated with a polymer such PMAO in order to provide MNPs outstanding colloidal stability in aqueous media and chemical groups for anchoring recognition ligands, allowing to interact with target biomolecules. The preparation of the transducer will rely on an exhaustive and careful characterization of physico-chemical properties of these nanomaterials. Then, my thesis work will study different fundamental aspects (field conditions, biomolecule and MNP concentrations, analyte multivalence) related to the effects of specific interaction between biomolecules and functionalized MNPs on their AC magnetization in presence and absence of analyte. These results will provide an extensive knowledge of the parameters that modulate the sensitivity of the proposed magnetic detection method. The collaboration with theoretical group to perform numerical simulations of the magnetic signal will offer the possibility of quantifying the biomolecule concentration. This will require a two-step process, first for modeling the averaged-hydrodynamic volume of the MNP-biomolecule assemblies after specific interactions, secondly, for modeling the AC hysteresis loop based on modified Landau-Liftshit-Gilbert equations which have been recently shown to successfully simulate this signal of similar nanocubes. [4] The modeling of the magnetic signal will allow then to determinate the amount of analyte present in the biological sample volume. Another relevant aspect related to this is the effect of unspecific interactions on the sensitivity of the proposed magnetic detection method. Experimental measurements on functionalised MNPs in serum plasma will allow to check the variation of AC magnetization signal due to serum absorption onto MNP surface, in order to determine the relevance of improving the MNP surface to decrease unspecific interactions between proteins and F-MNPs.

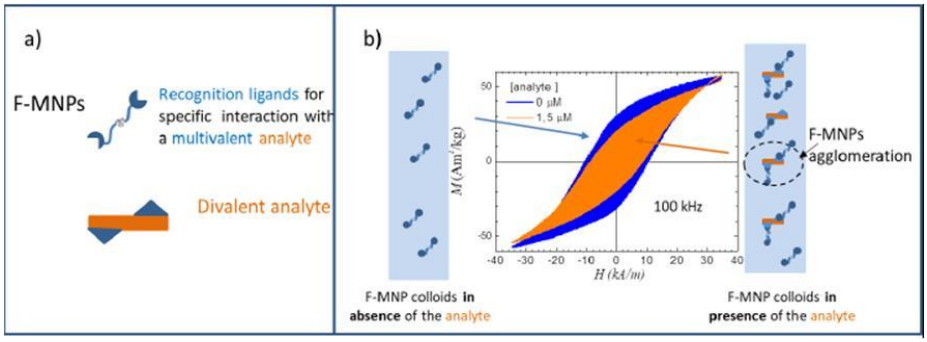


**Figure**: General scheme of the proposed detection method of biomolecules in biological fluids: a) F-MNPs and multivalente analyte; b) AC hysteresis loops in absence/presence of analyte in the magnetic colloidal dispersion.

The development of a low cost detection method with minimized sample manipulation, and high sensitivity will provide novel and efficient tools in clinical and biotechnological applications.

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# MOF:PDMS Composites as a Promising Luminescent Chemosensors: Photophysics and Sensing Characterization

**Ahmad Sousaraei,*[a] Jose M. Pedrosa[b], Ana M. G. Silva[c], Luis Cunha Silva[c], and Juan Cabanillas-Gonzalez [a]**

[a*] *IMDEA Nanociencia, Ciudad Universitaria De Cantoblanco 28049, Madrid, Spain. Tel: +34 655398281*

[b] *Departamento de Sistemas Físicos, Químicos y Naturales, Universidad Pablo de Olavide, Ctra. Utrera Km. 1, 41013 Sevilla, Spain.*

[c] *UCIBIO/REQUIMTE, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade do Porto, 4169-007 Porto, Portugal.*

E-mail: ahmad.sousaraei@imdea.org

Currently, metal-organic frameworks (MOFs) are being intensively studied as a novel class of hybrid inorganic–organic material with ultrahigh porosity, enormous internal surface areas, together with the extraordinary tailorability of structure, dimension, size, and shape [1]. Thanks to the inherent advantages of both organic links (easily modify, flexibility, versatility, etc.) and inorganic metal ions (unique electronic and optical nature), MOFs will open a territory of promising applications in photonics and sensing fields where conventional inorganic or organic materials might not be suitable [2]. [$Zn_2$(bpdc)$_2$(pbee)] are paddle-wheel 3D MOFs with large porosity and capability to host different small molecules. Owing to the large susceptibility of [$Zn_2$(bpdc)$_2$(pbee)] to moisture we have dispersed their crystals in free-standing PDMS films (70 μm thick), which is an ultra-hydrophobic, permeable, stretchable and green polymer matrix [3]. The composites were photophysically characterized and their sensing properties to a wide range of analytes were assessed. Composites have shown high sensitivity and reversibility to guest molecules (Figure 1(A)).

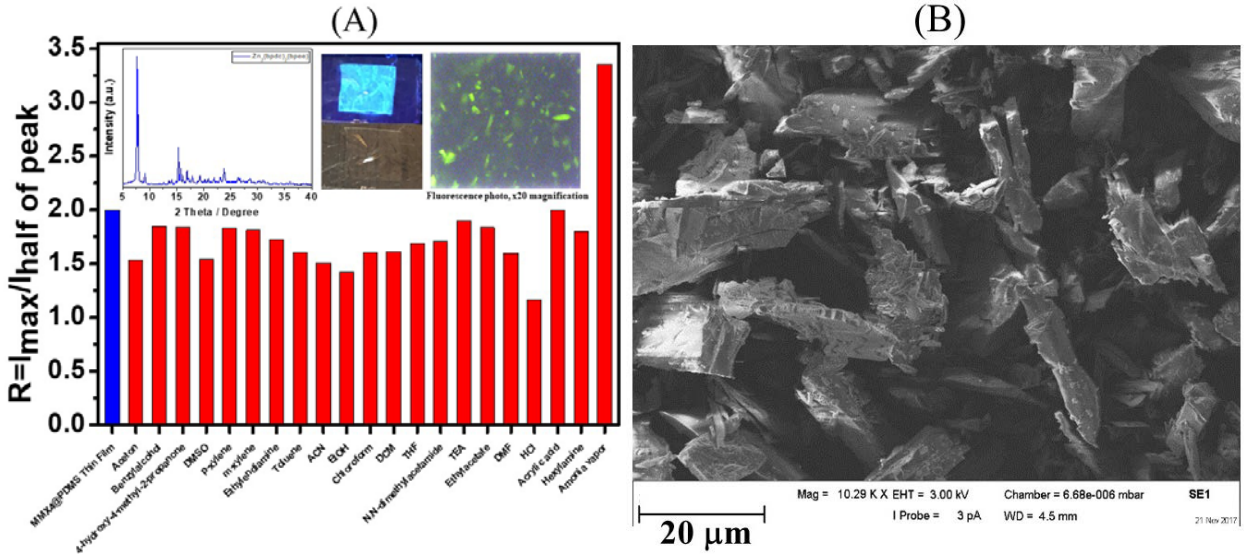


**Figure 1.** (A) Ratiometric photoluminescence intensity of [$Zn_2$(bpdc)$_2$(pbee)]:PDMS composites upon exposure to different analytes. (A inset shows XRD pattern, free-standing composite before and after exposuring UV lump and fluorescence photo of composite, respectively). (Fig. B) shows SEM image of [$Zn_2$(bpdc)$_2$(pbee)] microcrystals.

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# Preliminary study on a thermoresponsive drug delivery system based on the combination of magnetite NPs and liposomes

**Andrea Tabero,*[a] Maria Eugenia Fortes Brollo,[b] Puerto Morales[b] and Angeles Villanueva[a]**

[a] *Universidad Autónoma de Madrid, Madrid, Spain. Tel: 91 497 8235*

[b] *Instituto de Ciencias Materiales de Madrid (ICMM), CSIC, Madrid, Spain. Tel: 91 334 8995*

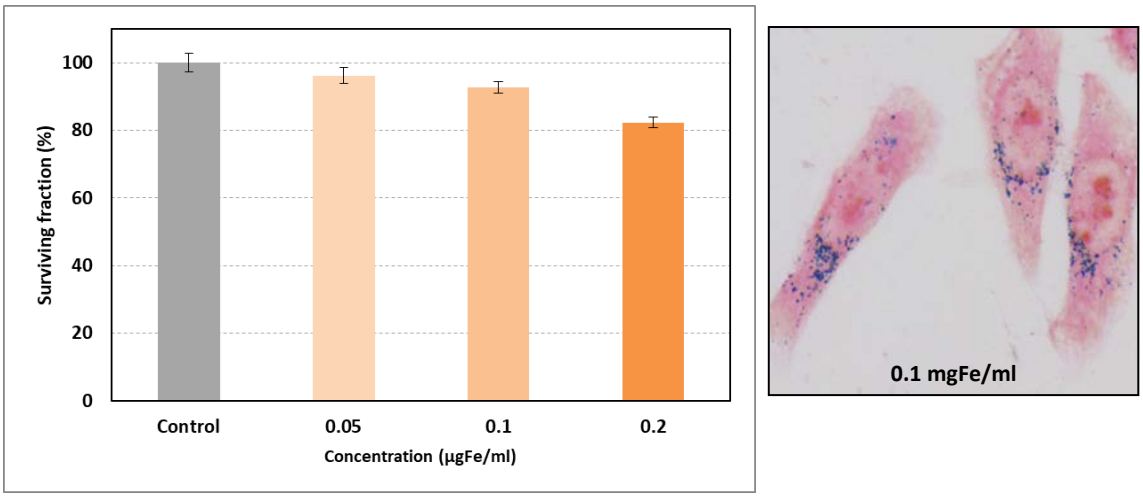
*E-mail: andrea.tabero@uam.es*

In the last decades, nanoparticles have been extensively investigated in the field of nanomedicine, especially as drug delivery systems, where they have already been proven as a powerful tool for overcome some limitations associated with conventional drug administration. Nanoparticles have been widely used in cancer research, to selectively target tumor cells, improve drug delivery and reduce systemic toxicity of drugs. In addition, a defined subgroup of nanoparticles, magnetic NPs (MNPs), can release heat during the exposure to an alternating magnetic field (AMF), triggering cell death on tumor cells due to hyperthermic temperatures. Moreover, MNPs are a promising tool for other biomedical applications, including diagnosis by magnetic resonance imaging (MRI) and/or delivery of anti-cancer molecules. In this sense, iron oxide NPs with magnetite or maghemite ($Fe_3O_4$ or $\gamma$-$Fe_2O_3$) core are the most commonly employed MNPs for biomedical applications due to its low toxicity. In recent years, with the rapid development of nanoscience, various sophisticated hybrid nanostructures are being designed for the augmentation and modulation of current therapeutic nanosystems.

The goal of this project is to develop a thermoresponsive drug delivery system based on the combination of magnetite NPs, liposomes and a chemotherapeutic agent (DOX). In this design, heat released by MNPs in the presence of an AMF could be used, not only for trigger tumor cell death with hyperthermic temperatures, but for the release of the chemotherapeutic agent into the tumor area.

In this preliminary study we analyze the biocompatibility and accumulation on HeLa cells of two magnetite nanoparticles obtained by microwave and thermal decomposition with a mean size of 7.3 nm and 14.8 nm, respectively and coated by dimercaptosuccinic acid (DMSA) and two hybrid systems containing each of these NPs incorporated into dipalmitoyl phosphatidylcholine (DPPC) liposomes.

Results confirm a low toxicity of the analyzed iron NPs and an increased accumulation of NPs due to its incorporation into DPPC liposomes.




MTT viability assay confirming low toxicity of analized NPs and Prussian Blue staining showing NPs accumulation into HeLa cells.

# Optimization of the resolution of pauses in biological motors

**Andrés Tejedor Reyes,*[a] Francisco J. Cao[a,b]**

[a]*Departamento de Estructura de la Materia, Física Térmica y Electrónica, Facultad de Ciencias Físicas, Universidad Complutense de Madrid, Plaza de Ciencias, 1. 28040 Madrid, Spain*

[b] *Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA-Nanociencia), Calle Faraday, 9. 28049 Madrid. Spain.*

*E-mail: andretej@ucm.es Tel: + 34 91 394 47 42*

Several single-molecule experiments studying molecular motors have been developed in recent years. One of the critical points of the data analysis is the identification, characterization and extraction of the effect of the pause states in the motor dynamics[1]. The theoretical model is well-known for several years, but in practice satisfactory results are dificult to attain. We simulate a molecular motor (DNA polymerase) moving with a displacement rate $k_p$ (replication rate), entering a pause state with rate $k_{a1}$ and exiting from it with rate $k_{1a}$. We mimic the experimental limitations by assuming the trajectories have a Gaussian random noise in position and measuring the process with time intervals of 0.001 *s*. The objective of this work is to measure the displacement rate by substracting the pause contributions. We have developed and optimized a criterion to separate the pause and displacement contributions to the velocity histograms. This has allowed us to measure the displacement rate of the motor quite precisely in spite of the experimental limitations simulated in our work.

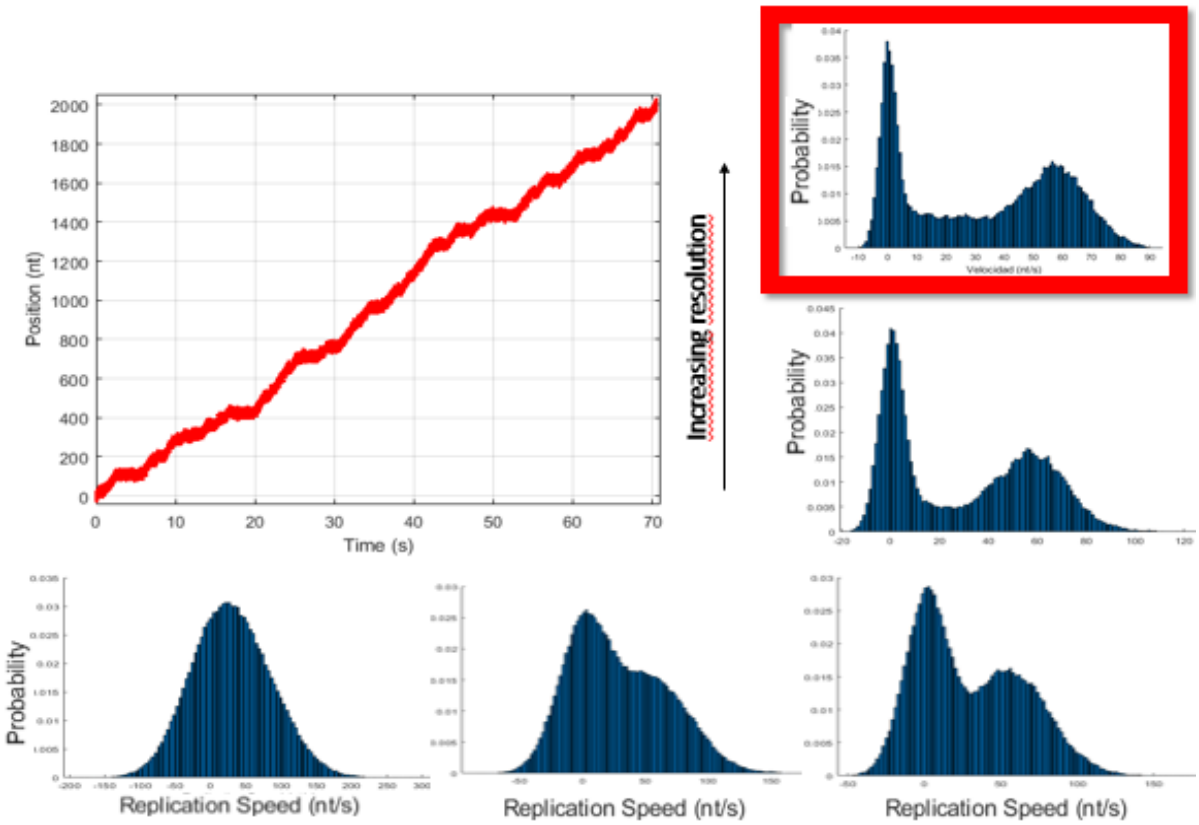



Figure 1: DNA-Polymerase trajectory during replication and typical replication speed histograms. Histogram for the optimal value indicated with a red box.

## Notes and References

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# Single Molecule Spectroscopy of Key Protein-Protein Interactions in the Pyruvate Dehydrogenase (PDH) Multienzyme complex

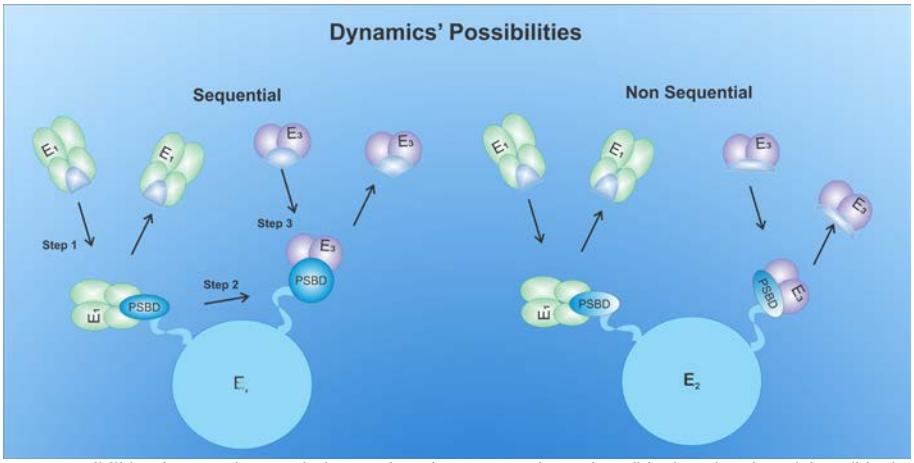
**Cintia C. Vequi-Suplicy[a], Mar Pulido-Cid[a,b], M. Pilar L. Navajas[a], Cristina Fernández[b], Luis A. Campos[a,b], Jose Requejo-Isidro[a,b], Victor Muñoz[a,c]**

*a - IMDEA Nanosciences, Faraday 9, Ciudad Universitaria Cantoblanco, 28049 Madrid, Spain. b – National Biotechnology Center, Consejo Superior de Investigaciones Científicas, Darwin 3, Campus de Cantoblanco, 28049 Madrid, Spain. c - Department of Bioengineering, University of California Merced, 95343 Merced, CA, USA.*

*E-mail: cintia.vequi@imdea.org*

The pyruvate dehydrogenase (PDH) multienzyme complex is composed of many copies of three different proteins: pyruvate decarboxylase (E1), dihydrolipoyl acetyltransferase (E2) and dihydrolipoyl dehydrogenase (E3)[1]. This enzymatic complex is essential to the oxidative metabolism of several organisms. The interactions between E1-E2 and E3-E2, which are key to coordinate the three-step reaction, happen with a subunit of E2 called peripheral subunit binding domain (PSBD). These two complexes have been investigated in bulk experiments using conventional binding techniques, which have shown that both are of very high affinity (sub-nM). However, the specific nature of the interactions of PSBD with E1 and E3, their stochastic dynamics and their interplay remain poorly understood.

To investigate the interplay between PSBD and E1/E3, and how it results in the coordination of binding events that is required for efficient multi-catalysis, we are applying single molecule tracking experiments on a microscope using Total Internal Reflection Fluorescence (TIRF)[2]. In these experiments, PSBD was labeled with Alexa 488 (green emission) and chemically immobilized on the coverslip surface whereas E1 and E3 labeled with mCherry are free in solution and available for binding. Two color detection allows to identify individual PSBD molecules on the surface, determine their interactions with each binding partner, and the lifetimes of the formed complexes. Key aspects of this experiment are: 1) achieving fine control of the number of PSBD molecules on the field of view; 2) maximizing the ratio between molecule brigthness and the fluorescence background of the system, so sample preparation is crucial. In addition, we have used Fluorescence Correlation Spectrocopy (FCS) to observe the interaction between PSBD and E1/E3 in quasi-single molecule conditions and in freely diffusing conditions that minimize any possible artifact potentially arising from interactions between the protein partners and the surface. One recurring challenge in this type of experiments is the presence of small protein aggregates in the samples, which could severely affect the observations. Here we discuss various sample preparation methods and how to best avoid protein aggregation in protein single-molecule experiments. As next step, we are developing computational routines for advanced statistical analyses of the TIRF images using hidden Markov model and from these data obtain the association and dissocation rates constants of the two complexes ($k_{on}$ and $k_{off}$).




Two possibilities for protein-protein interactions between E1(green)-E2(blue) and E3(purple)-E2(blue).

## Notes and References

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# High coercive MnBi magnets for high temperature applications, from quasi-isotropic particles to textured films

**Melek Villanueva,*[a] Eva Céspedes,[a] Cristina Navío,[a] Federico Mompeán,[b] Mar García-Hernández,[b] Almudena Inchausti,[a] Patricia Pedraz,[a] Manuel Rodriguez,[a] Julio Camarero[a,c] and Alberto Bollero[a]**

[a]*IMDEA Nanoscience, 28049 Madrid, Spain. Tel: 912 99 87 00;*

[b]*Instituto de Ciencia de Materiales de Madrid – ICMM-CSIC, 28049 Madrid, Spain. Tel: 913 34 90 00;*

[c]*Dpto. de Física de la Materia Condensada and Instituto "Nicolás Cabrera", Universidad Autónoma de Madrid, 28049 Madrid, Spain.*

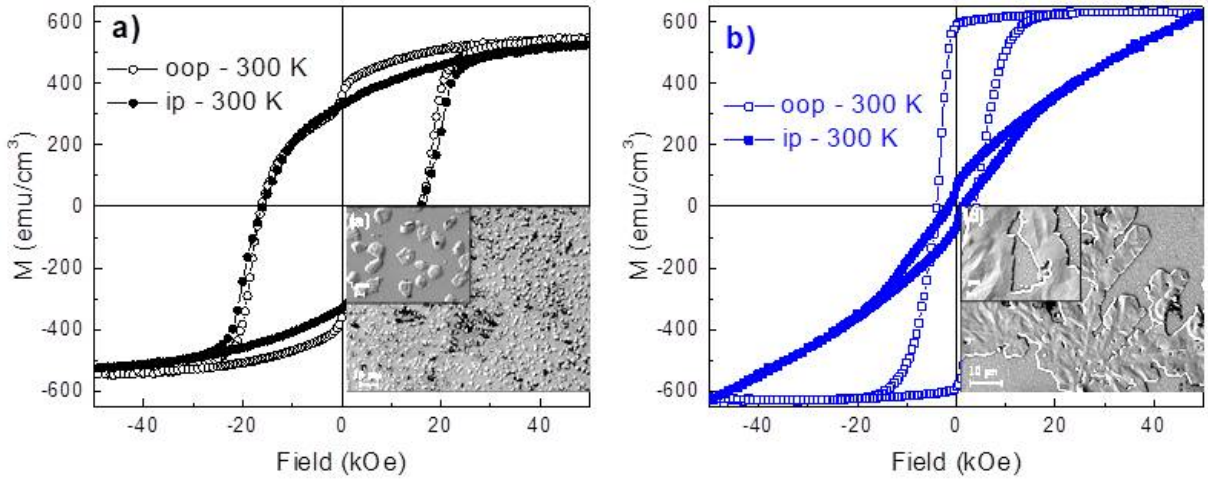
*E-mail: melek.villanueva@imdea.org*

Today's technological applications require a strong demand of permanent magnets (PMs). This increased demand combined with the strategically geographical situation of rare-earth (RE) materials has contributed to the search of new efficient PMs alternatives.

Mn-based ferromagnetic alloys, such as MnAl [1,2] and MnBi [3], show interesting PM properties. In particular, the LTP-MnBi is attracting increasing attention regarding its large uniaxial magnetocrystalline anisotropy about 1.6 MJ/m$^3$, a theoretical $(BH)_{max}$ of 17 MGOe, a Curie temperature of 711 K which is limited by its structural transformation temperature of 630 K (being still about 40 K larger than that the $Nd_2Fe_{14}B$ one), and its outstanding high coercivity with a positive temperature coefficient.

MnBi films, with nominal thickness between 60 and 120 nm, have been prepared by multilayer magnetron sputtering onto glass substrates. In-situ annealing was also performed in order to understand how deposition temperature and post-growth temperature affect depending on the thickness of the films. A wide range of coercive field has been obtained, from 4 to 16 kOe at room temperature. In addition, LTP-MnBi positive temperature coefficient makes coercivity increase up to 16 and 22 kOe at 300 and 350 K, respectively, reaching a maximum of 29 kOe at 500 K [3], being among the largest $H_C$ reported to date for MnBi films.

X-ray diffraction indicates highly pure LTP-MnBi in all samples. The choice of temperatures during deposition and post-growth annealing has a strong impact on the microstructure, i.e. the magnetic response. The sputtered MnBi gets into a homogeneous distribution of small islands, micro-platelets or coalesced film-like areas along all the substrate. Magneto-structural correlations in the MnBi system are of interest for practical applications at high temperatures.




Experimental out-of-plane (oop, open symbols) and in-plane (ip, filled) M-H curves for MnBi films under different conditions (substrate temperature, $T_S$, and post-annealing temperature, $T_A$): a) $T_S$=375 K and $T_A$=575 K b) $T_S$=450 K and $T_A$=575 K. Inset shows microstructure (SEM) of each one. Scale bar: 10μm.

## Notes and References

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# Entropy reduction by information in feedback flashing ratchets

**Daniel Villarrubia Moreno,*[a] Francisco J. Cao.*[b]**

[a] *Universidad Complutense de Madrid,Toledo, España.*

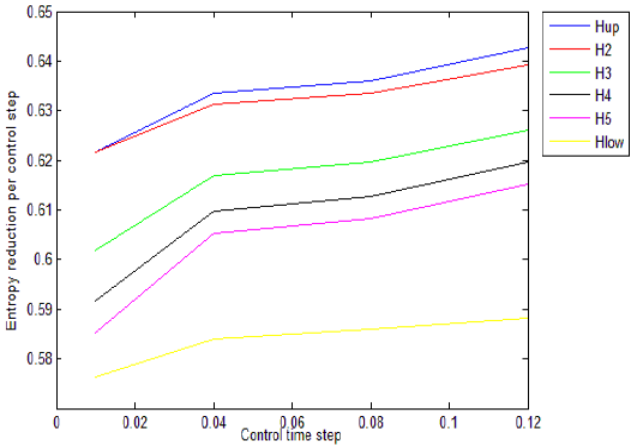
[b] *Universidad Complutense de Madrid,Madrid, España.*

*E-mail:* danvilla@ucm.es
francao@fis.ucm.es

Feedback flashing ratchets are nano-systems which can produce a certain amount of work, using the information gained by their control protocol to improve their efficiency. The knowledge of its thermodynamic is fundamental to understand how they work, and how much useful work we can obtain from them.

We have studied the entropy reduction rate of these systems, and how it depends on different parameters of the system, with the aim to obtain their efficiency curves and the optimal configuration.

Feedback flashing ratchets work moving a certain number of particles against a external force with higher efficiency than non feedback systems, and this is why they are interesting from the physical point of view, but also from the biological point of view; because they are used in the modelling of molecular and cellular motors.

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