
idm
X International
Workshop on
Sensors and
Molecular Recognition
7 y 8 de Julio de 2016
VNIVERSITAT
DE VALÈNCIA

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INDICE

PROGRAMA CIENTÍFICO

Jueves, 7 de Julio de 2016

SESIÓN DE MAÑANA

8.30 – 9.00h Entrega de Documentación

9.00 – 9.15h Apertura

Presidida por la Vicerrectora de Investigación de la Universitat de Valencia, doña Pilar Campins Falcó

9.15 – 10.15h Conferencia Plenaria

The Supramolecular Approach to
Enzyme and Membrane Transport Assays
Andreas Hennig

10.15 – 11.00h Primera Sesión de Comunicaciones Orales:

Moderador: Ana María Costero Nieto

O-01 Self-amplified photonic biosensing platform for microRNA-based early diagnosis of diseases
Daniel González-Lucas, M.J. Bañuls, J. García-Rupérez, A. Maquieira

O-02 Novel Peptide-Based Mechanized Nanoparticles for a Photocontrollable Delivery of Rhodamine B
Alberto Martinez-Cuezva, Silvia Valero-Moya, Mateo Alajarin, Jose Berna

O-03 PCB-based electrochemical detection of cancer biomarkers using MLPA-barcode
Josep Lluís. Acero Sánchez, O. Y. F. Henry, H. Joda, B. Werne Solnestam, L. Kvastad, E. Johansson, P. Akan, J. Lundeberg, N. Lladach, D. Ramakrishnan, I. Riley and C. K. O'Sullivan

11.00 – 11.30h *Pausa Café*

11.30 – 12.30h Segunda Sesión de Comunicaciones Orales:

Moderador: José Luís Vivancos

O-04 Fluorogenic sensing of low As(III) levels in aqueous media using aptamer-capped nanomaterials
Mar Oroval, Carmen Coll, Andrea Bernardos, M. Dolores Marcos, Ramón Martínez-Máñez and Dmitry G. Shchukin

O-05 Enzyme-Controlled Nanodevice for Acetylcholine-Triggered Cargo Delivery Based on Janus Au-Mesoporous Silica Nanoparticles
Antoni Llopis-Lorente, Paula Díez, Cristina de la Torre, Alfredo Sánchez, Félix Sancenón, Elena Aznar, Paloma Martínez-Ruíz, Ramón Martínez-Máñez, Reynaldo Villalonga

O-06 Sulfated γ-cyclodextrin enantiorecognition. Anticipation from visual inspection of 2D molecular structure
María José Medina-Hernández, Laura Escuder-Gilabert, Yolanda Martín-Biosca, Salvador Sagrado

O-07 Puertas moleculares con apertura en cascada a pH controlado
L. Alberto Juárez, Elena Añón, Cristina Giménez, Félix Sancenón, Ramón Martínez-Máñez, Ana M. Costero, Pablo Gaviña, Margarita Parra

12.30 – 13.30h Conferencia Plenaria

Low cost devices for improving screening analytical methods
Miguel de la Guardia Cirugera

13.30 – 15.00h *Comida*

SESIÓN DE TARDE

15.00 – 16.30h Sesión de Pósters

16.30 – 18.00h Tercera Sesión de Comunicaciones Orales

Moderador: Salvador Gil Grau

O-08 Pseudopeptidic and imidazolium derived amphiphilic systems for stimuli-dependent self-assembly
Adriana Valls, B. Altava, M.I. Burguete, L. Gorla, S.V. Luis

O-09 Azo.carbamate molecular gate in magnetic micro MCM-41 aiming colon epithelial delivery for Inflammatory Bowel Diseases treatment
Adrián Hernandez Teruel, C. Coll, F. Sancenón, M. González-Álvarez, V. Merino-Sanjuán and R. Martínez-Mañez

O-10 Derivados de tetrafeniletileno (TPE) para la detección óptica de NOx
Ana Mª Costero, Andrés Sala

O-11 Visible Light Induced Enantioselective [2+2] Photocycloaddition Reactions Employing a Chiral Catalyst based on the Thioxanthone Chromophore
Rafael Alonso, Thorsten Bach

O-12 TRIM21α Structure and its Mechanism Acting in Systemic Lupus Erythematosus Patients and Healthy Subjects
Noelle M. do Nascimento, Sergi Morais, Isidro Monzó, Roberto Tejero, Jesús V. de Julián–Ortiz, José L. Lopez–Paz, Elena Grau García, Jose A. Román–Ivorra, Rosa Puchades, Angel Maquieira & David Gimenez–Romero

O-13 Polymer-coated upconversion nanoparticles for pH-triggered drug delivery
Nestor Estebanez, Ileana Recalde, Laura Francés-Soriano, María González-Béjar and Julia Pérez-Prieto

Viernes, 8 de Julio de 2016

SESIÓN DE MAÑANA

9.15 – 10.15h Conferencia Plenaria

Química Supramolecular médica de poliaminas. Aplicaciones farmacológicas
Enrique García-España

10.15 – 11.00h Cuarta Sesión de Comunicaciones Orales:

Moderador: Virginia Merino Sanjuan

O-14 PPO-substrate interaction study in presence of silica nanomaterials
Sara Muñoz Pina, Carmen Coll, Ana María Andrés Grau, Ángel Luis Argüelles Foix, José Vicente Ros Lis

O-15 New nanoporous supports functionalized with molecular gates for the detection of *Mycoplasma Fermentans* genomic DNA
Luis Pla, Félix Sancenón, Ramón Martínez-Máñez

O-16 Diseño de materiales híbridos orgánico-inorgánicos para el reconocimiento de miARN-145
Vicente Candela Noguera, Àngela Ribes Momparler, Elena Aznar Gimeno, Ramón Martínez-Máñez

11.00 – 11.30h *Pausa Café*

11.30 – 12.30h Quinta Sesión de Comunicaciones Orales:

Moderador: Pablo Gaviña Costero

O-17 Nanotoxicology evaluation of functionalized and non-functionalized mesoporous silica particles on *caenorhabditis elegans*
Carolina Acosta, Patricia Martorell, Salvador Genovés, Daniel Ramón, Ramón Martinez-Máñez, José Manuel

O-18 The chemistry and antibody recognition of the TROVE2 superantigen
Augusto M. Juste, Noelle M. do Nascimento, I. Monzó, Sergi Morais, José L. Lopez-Paz, Elena Grau-García, Jose A. Román-Ivorra, Angel Maquieira, David Gimenez-Romero

O-19 Targeted delivery therapeutics to glioma cells by chlorotoxin conjugated mesoporous silica nanoparticles
Cristina de la Torre Paredes, Elena Aznar, Félix Sancenón, Ramón Martínez-Mañez, Eduardo Ruiz Hernandez, Garry P. Duffy

O-20 Evaluación del uso de acelerómetro triaxial como sistema de medida de distancia
Guillermo Puchalt Casáns, Miguel Alcañiz Fillol, Rafael Masot Peris

12.30 – 13.30h Conferencia Plenaria

A smart material for the in situ detection of mercury contamination in fish samples
Tomás Torroba

13.30 – 13.45h *Clausura*

SESIÓN DE PÓSTERS

Los pósters deberán estar colocados:

desde el Jueves 7 de Julio a las 9.30h hasta el Viernes 8 de Julio a las 13.45h.

LIBRO DE RESÚMENES

El plazo de presentación de los resúmenes de las comunicaciones para la edición del libro finalizará el próximo día **16 de Septiembre**.

El formato debe ser como los abstracts pero con una extensión de 4 o 5 hojas.

CONFERENCIAS PLENARIAS

The Supramolecular Approach to Enzyme and Membrane Transport Assays

Dr. Andreas Hennig

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Abstract

A keystone technology in the discovery of new drugs is high-throughput screening (HTS) for activators or inhibitors of target proteins, among which more than 50% are enzymes or membrane transporters.[1] This calls for enzyme and membrane transport assays that are compatible with existing HTS infrastructure, where fluorescence spectroscopy stands out owing to its favorable combination of information content, cost and the number of samples that can be measured per day.[2]

To address the lack of suitable HTS assays, we have initially used combinations of fluorescent dyes and macrocyclic receptors to develop "Supramolecular Tandem Enzyme Assays",[3-5] and we have also shown that artificial, supramolecular membrane transporters can be used for detecting enzyme activity as well.[5,6] In that line of research, we also realized that self-assembled, supramolecular systems can also be used to follow membrane transport by ion channels and cell-penetrating peptides,[7] which was subsequently also explored with macrocyclic receptors.[8]

In this presentation, we are going to summarize our previous efforts to develop supramolecular enzyme and membrane transport assays, and we present an outlook on the new concept of "Supramolecular Tandem Membrane Transport Assays".

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Low cost devices for improving screening analytical methods

Miguel de la Guardia

Departamento de Química Analítica, Universitat de València Dr. Moliner 50, 46100 Burjassot, Valencia, España

Some applications of the use of smart phones and low cost gas sensors will be presented to provide some ideas about the tremendous possibilities of the use of low cost devices to improve the analytical methods on both, qualitative and quantitative, perspectives to take in-field decissions and to move from the big facilities to easy available methodologies suitable to obtain fast information about analytical problems.
The use and treatment of photo images permits to evaluate global sample parameters, like the fish freshness (1) and thus, it is suitable to be applied on using phone cameras and in-cloud mathematical models. On the other hand, by using a little bit of chemometrics (as for example an image treatment by Partial Least Squares or Artificial Neuronal Networks) it could be possible to evaluate sample specific parameters, as it has been the case of banana maturity indexes obtained based on the banana skin color or fat content of meat products, based on simple photo images (2).
The aforementioned studies, made in our laboratory, are just examples that could contribute to open our mind to search for applications of our smart phones in order to democratize the analytical instrumentation and made it available for different purposes.
Another story is the appropriate use of commercially available sensors to evaluate new problems and risks and to do it , gas sensors have been evidenced a great applicability in subjects related to smoking practices or in-situ evaluation of engine motor uses and maintenance and, once again, the idea could be to try to solve our analytical problems with the faster and cheaper alternatives available (3).
To finish the presentation, our preliminary results on the use of a Nespresso coffee machine(4) for a fast and quantitative extraction of analytes from real samples will be discussed in order to evidence tha applicability in the analytical field of low cost tools.
In short, the idea is to put some simple ideas in the screen to dream on new and original applications that we could mede together Why not?

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Química Supramolecular médica de poliaminas. Aplicaciones farmacológicas.

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La química supramolecular, definida como "la química más allá de las moléculas" [1], se basa en la construcción de sistemas químicos formados por componentes moleculares que se asocian mediante interacciones no-covalentes [1,2,3]. Una ramificación lógica de la química supramolecular se extiende hacia la química médica [4].

En la presente contribución se discute una aproximación supramolecular, incluyendo conceptos de química coordinación, encaminada al diseño de sistemas con actividad antioxidante, antitumoral y/o antiparasitaria basados en compuestos poliamínicos. La elección de poliaminas como estructuras base no es sorprendente, teniendo en cuenta su presencia ubicua en los sistemas biológicos y la variedad de funciones bioquímicas que ejercen [5]. Dentro de esta aproximación supramolecular al desarrollo de fármacos, se discutirá la incorporación de las moléculas activas en la superficie de partículas, para aprovecharse así del efecto de la multivalencia [6] buscando incrementar la actividad, direccionar los fármacos a dianas específicas y explorar nuevos mecanismos de acción.

Agradecimientos. Ministerio de Economía y Competitividad (CONSOLIDER INGENIO CSD-2010-00065, CTQ2013-48917-C3-1-P) y Generalitat Valenciana (Project PROMETEO 2011/008).

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A SMART MATERIAL FOR THE IN SITU DETECTION OF MERCURY CONTAMINATION IN FISH SAMPLES.

Tomás Torroba, José García-Calvo, Patricia Calvo Gredilla, José M. García, Saúl Vallejos, Félix C. García, Mª José Rojo, Mª Teresa Rodríguez.

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Environmental contamination by mercury is a serious concern because of the large amounts of mercury released to the environment by human activities. Due to their inherent toxicity, Hg(II) species have to be continuously monitored, especially in fish samples. We have previously prepared new chromogenic[1] or fluorogenic[2] probes for the selective detection and speciation of Hg^{2+} and $MeHg^{+}$. Now, we have developed a new fluorogenic polymer capable to detect the presence of mercury contamination in fish samples. The modified polymer emits blue light when irradiated with UV proportionally to the quantity of mercury, as $MeHg^{+}$ or Hg^{2+} cations, present in fish. The quantitative relation between the concentration of mercury in fish and the increasing of fluorescence in the polymer, in contact with fish, was confirmed. The fluorescence increase of the polymer in contact with real fish samples resulted to be a complex process and many factors could interfere with the measurements. We have demonstrated that a careful experimental procedure by taking control of interferents gives rise to quick and reliable results in the measurements of the presence of mercury in fish by a portable fluorogenic polymeric probe (Figure 1).

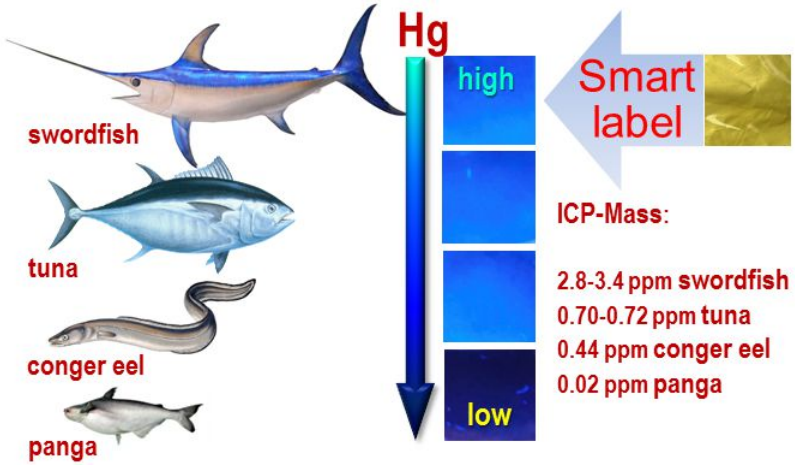

Figure 1: A representation of the fluorescent response and ICP values in fish samples.

Acknowledgments: We gratefully acknowledge financial support from the Ministerio de Economía y Competitividad, Spain (Projects CTQ2015-71353-R and MAT2014-54137-R), Dirección General de Tráfico, Spain (Project SPIP2015-01820), and the European Commission, Seventh Framework Programme (Project SNIFFER FP7-SEC-2012-312411).

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COMUNICACIONES ORALES

O-01

Self-amplified photonic biosensing platform for microRNA-based early diagnosis of diseases

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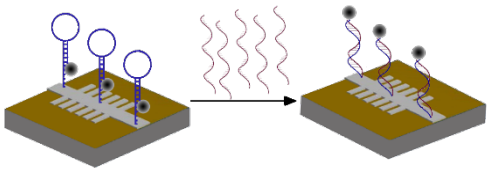
Keywords: Molecular beacons, nanophotonic biosensor, miRNA, cancer, thiol-ene click chemistry.

SAPHELY is a project funded by the Horizon 2020 European programme that aims at the development of a device for the ultra-sensitive detection of micro-RNAs which dysregulation have been associated with many diseases.[1] The detection is possible following a new approach based on photonic detection, resulting in a lightweight, cheap, small device that will provide the detection signal in real time.[2] High sensitivity will be obtained for the miRNA detection by using molecular beacons (MB). Molecular beacons having an attached nanoparticle (NP) will be selectively anchoraged to the sensing areas of the device using light induced coupling chemistries.[3] Each recognition event will therefore be transduced in a drastic change of the optical signal due to the displacement of the nanoparticle (NP) away from the surface (Fig. 1).

Fig. 1 – Designed Biosensor Device where the immobilized MB-NP probe (blue) recognizes the miRNAs (purple) leading to



a variation of the sensor response.

The first approach and optimization of MB probe attachment onto surfaces for the construction of the high performance nanophotonic biosensor was proved using fast and reliable thiol-ene chemistry under very mild conditions. Fast probe immobilization as well as specific detection of anti-probe is demonstrated in this work.

Acknowledgements: This research was funded by the European Union EU's Horizon 2020 ICT-26-2014-644242 programme, the MINECO project CTQ/2013/45875-R and GVA PROMETEO II 2014/40.

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O-02

Novel Peptide-Based Mechanized Nanoparticles for a Photocontrollable Delivery of Rhodamine B

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Since the beginning of this century the use of mesoporous materials for the smart delivery of analytes has been an attractive research area.[1] Mesoporous silica nanoparticles (MSNs) have become excellent materials for controlled delivery applications due to their exceptional features (high loading capacity, shape, pore diameter, easy functionalization or biocompatibility). Numerous stimuli-responsive methods have been established to govern the controlled delivery of small molecules from the pores of these materials functionalized by different organic or inorganic motifs behaving as gatekeepers.[2] One promising group of these tailor-made doors is based on interlocked structures, giving rise to the materials known as mechanized silica nanoparticles.[3]

Herein, we describe the synthesis of novel mechanized silica nanoparticles functionalized with peptide-based molecular shuttles.[4] These interlocked molecules act as photocontrollable gatekeepers. The loading and delivery of rhodamine B (RhB) as a model cargo in solution were also study.

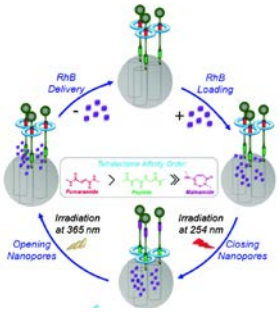

Figure 1. Uptake and release of RhB from the pores of a MCM-41 silica functionalized with a light-responsive peptide [2]rotaxane.

This work was supported by the MINECO (CTQ2014-56887-P) and Fundacion Seneca-CARM (19240/PI/14). A.M.-C. thanks the he MINECO (FPDI-2013-16623) for his postdoctoral contract.

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O-03

PCB-based electrochemical detection of cancer biomarkers using MLPA-barcode approach

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Asymmetric multiplex ligation-dependent probe amplification (MLPA) was developed for the amplification of seven breast cancer related mRNA markers and the MLPA products were electrochemically detected via hybridization. Seven breast cancer genetic markers were amplified by means of the MLPA reaction, which allows for multiplex amplification of multiple targets with a single primer pair. Novel synthetic MLPA probes were designed to include a unique barcode sequence in each amplified gene. Capture probes complementary to each of the barcode sequences were immobilized on each electrode of a low-cost electrode microarray manufactured on standard printed circuit board (PCB) substrates. The functionalised electrodes were exposed to the single-stranded MLPA products and following hybridization, a horseradish peroxidase (HRP)-labelled DNA secondary probe complementary to the amplified strand completed the genocomplex, which was electrochemically detected following substrate addition. The electrode arrays fabricated using PCB technology exhibited an excellent electrochemical performance, equivalent to planar photolithographically-fabricated gold electrodes, but at a vastly reduced cost (>50 times lower per array). The optimised system was demonstrated to be highly specific with negligible cross-reactivity allowing the simultaneous detection of the seven mRNA markers, with limits of detections as low as 25 pM. This approach provides a novel strategy for the genetic profiling of tumour cells via integrated "amplification-to-detection".

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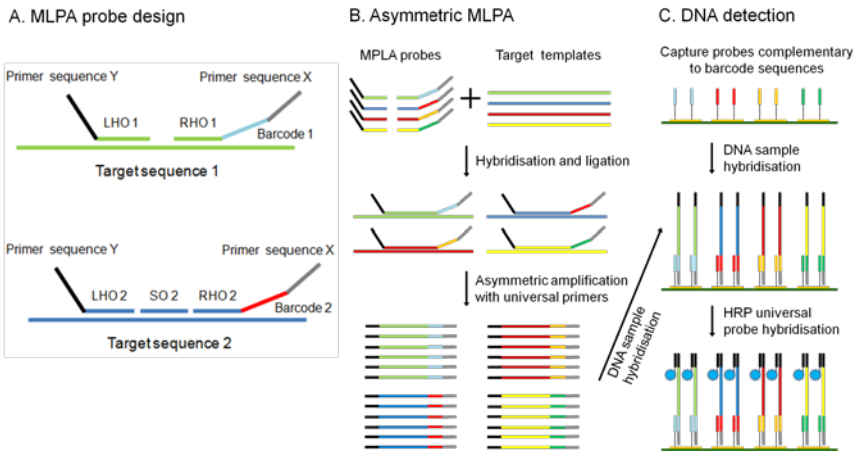

Figure 1. A) Design of the MLPA probes. The MLPA probe mix consists of either two or three oligonucleotides: a left hybridization oligonucleotide (LHO) consisting of a target-specific sequence and a universal primer sequence Y, a right hybridization oligonucleotide (RHO) consisting of a target-specific sequence, a unique barcode and a universal primer sequence X. Some of the probes also had a sequence-specific spanning oligonucleotide (SO) to increase specificity. B) Schematic representation of the asymmetric MLPA process showing the hydridization and ligation of the MLPA probes to the single strand MLPA samples and the asymmetric amplification with universal primers. C: Schematic layout of the electrochemical detection using unique barcodes and a universal reporter probe labelled with HRP enzyme.

O-04

FLUOROGENIC SENSING OF LOW As(III) LEVELS IN AQUEOUS MEDIA USING APTAMER-CAPPED NANOMATERIALS

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Arsenic pollution in aqueous media is a severe environmental and health concern due to its high toxicity to human health and other living organisms.[1] Among the predominant arsenic species in water, As(III) was identified as the most harmful substance because it is 100 times more toxic than As(V) and other organic arsenic compounds.[2] The current U.S. environmental Protection Agency (EPA) standard of 10 μg L^{-1} is an adjustment from 50 μg L^{-1} and such change motivated worldwide researchers to developing sensitive techniques for monitoring arsenic that can comply with the new standard.[3] In this context, the novel properties of gated nanostructured materials make them excellent components in such sensing protocols.[4]

Taking into account all the above mentioned, it is attractive and challenging to develop new capped nanomaterials for the selective detection of As(III). Therefore, we designed the preparation of an aptamer-gated silica mesoporous nanoplatform for the selective and sensitive fluorogenic signalling of As(III). In particular, the designed nanoprobe involves a MCM-41 type scaffold loaded with rhodamine B and grafted with 3-aminopropyltriethoxysilane on the external surface. Finally, the aptamer Ars-3 (with high binding affinity for As (III), K_d = 7.05 nM)[5] interacts electrostatically with the external moieties grafted onto the nanomaterial blocking the pores. The subsequent uncapping of the pores relies on the interaction of As(III) with Ars-3 aptamer. Pore opening leads to release of rhodamine B, thereby allowing the fluorogenic detection of As(III).

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O-05

Enzyme-Controlled Nanodevice for Acetylcholine-Triggered Cargo Delivery Based on Janus Au-Mesoporous Silica Nanoparticles

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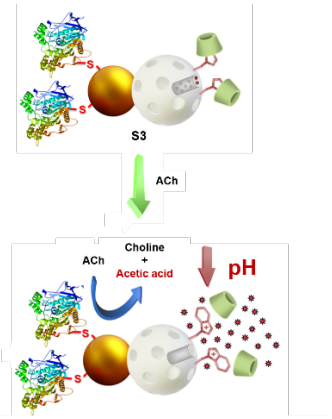
This work reports a new gated nanodevice for acetylcholine-triggered cargo delivery. We prepared and characterized Janus Au-mesoporous silica nanoparticles functionalized with acetylcholinesterase on the Au face and with supramolecular β-cyclodextrin:benzimidazole inclusion complexes as caps on the mesoporous silica face. The nanodevice is able to selectively deliver the cargo in the presence of acetylcholine via enzyme-mediated acetylcholine hydrolysis, locally lowering the pH and opening the supramolecular gate. Given the key role played by ACh and its relation with PD and other nervous system diseases, we believe that these findings could help design new therapeutic strategies.



O-06

SULFATED γ-CYCLODEXTRIN ENANTIORECOGNITION. ANTICIPATION FROM VISUAL INSPECTION OF 2D MOLECULAR STRUCTURE

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Few papers have tried to anticipate enantioresolution (*aRs*) of chiral compounds in capillary electrophoresis (CE) using chiral selectors[1]. In this work, the enantiorecognition ability of sulfated γ-cyclodextrin (S-γ-CD) is modelled for the first time, using novel topological parameters connected to the chiral carbon (*C**-parameters) and one from the whole molecule (aromatic atom count, *Aro*). A discriminant partial least squares-variable selection process suggests the preponderance of the topology adjacent to the chiral carbon for the enantiorecognition. A software-free anticipation protocol for new molecules is proposed (see Figure 1 as an example). 100% of correct anticipations (resolved and non-resolved compounds) are obtained. *Atom count* outside the 30-60 range *a priori* indicates 'influential' (out-of-the-model) structures.

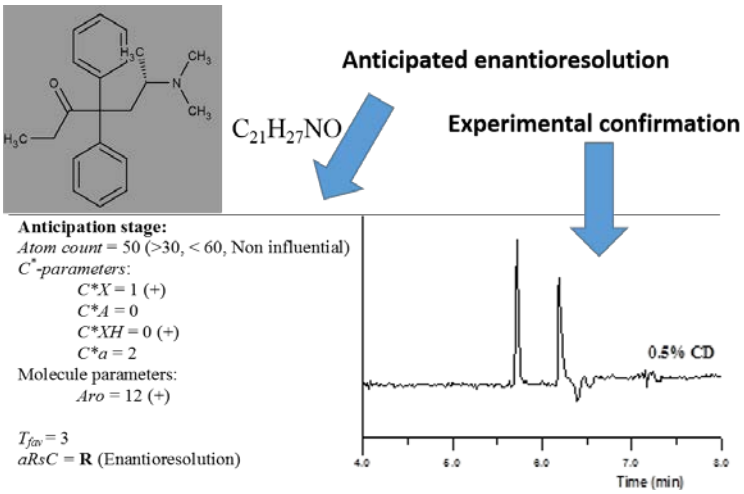

Figure 1. Favorable (T_{fav}>2 (+)) anticipated *aRsC* from methadone 2D-structure. *A posteriori* experimental enantioresolution confirmation.

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O-07

Puertas moleculares con apertura en cascada a pH controlado

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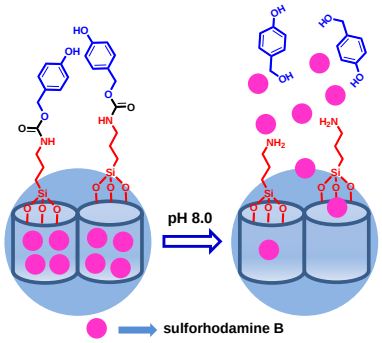
Debido al gran número de aplicaciones que presenta la liberación controlada de fármacos, tales como maximizar la eficacia terapéutica y minimizar los efectos adversos, se ha incrementado recientemente el desarrollo de técnicas con este fin[1]. Para ello se están empleando puertas moleculares ancladas a nanopartículas de sílice mesoporosa que permiten la liberación de su contenido únicamente en presencia de determinados estímulos externos, como pueden ser la luz, el cambio de pH, o la presencia de una enzima[2].
Las moléculas autoinmolantes son agregados covalentes que en presencia de un estímulo externo inician un proceso de desensamblaje a través de una cascada de reacciones. Recientemente se ha observado la amplia aplicación que presentan dichas moléculas en el campo de la liberación de compuestos activos[3].
Unificando estos conceptos, se ha diseñado y sintetizado una puerta molecular con propiedades autoinmolantes que anclada a un soporte de sílice mesoporosa cargado con sulforodamina B permite la liberación del colorante presente en su interior en un medio con pH básico como se muestra en la figura, debido a la desprotonación del grupo hidroxilo que da lugar a la rotura en cascada de la puerta y la consecuente liberación del contenido.



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O-08

PSEUDOPEPTIDIC AND IMIDAZOLIUM DERIVED AMPHIPHILIC SYSTEMS FOR STIMULI-DEPENDENT SELF-ASSEMBLY

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Nature uses different structural units for constructing complex systems which spontaneously arrange into functional forms or morphologies for specific biological functions. Self-assembly is mediated by intermolecular interactions through hydrogen bonding, electrostatic forces, hydrophobic interaction and π–π stacking interaction.[1] The resulted superstructures can exhibit distinct physicochemical properties from their single molecular components and extend their applications in many fields, especially for drug delivery and biomedical engineering.[2]

Our group have synthesized and study minimalistic pseudopeptidic and imidazolium amphiphilic systems shown in Figure 1. These compounds exhibit a high level of molecular diversity and sites for supramolecular interactions only by changing the nature of the spacer, the amino acid residue (R), and the length of the amphiphilic group.[3,4]

The different structural parameters of these systems, including the amino acid residue, the length and nature of the spacer and the N-substitution play a key and specific role in the self assembly of these systems in

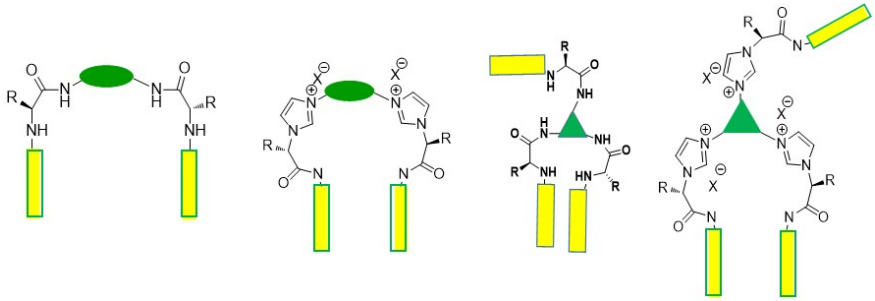

Figure 1. General structure of amphiphilic pseudopeptidic and imidazolium compounds.

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O-09

Azo.carbamate molecular gate in magnetic micro MCM-41 aiming colon epithelial delivery for Inflammatory Bowel Diseases treatment

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Even if great efforts have been made to develop tools to treat Inflammatory Bowel Diseases (IBD), there is no a definitive solution in the market to heal them. IBD is a group of autoimmune, chronic inflammatory conditions of the colon and small intestine, being ulcerative colitis and Crohn's disease the main manifestations of these diseases. One of the most important pitfalls is to target ileum and colon efficiently. That is, drug delivery only in the specific areas where wounds are present. Therefore, small amounts of drugs will be necessary to reach better results leading hardly any adverse effect.

Mesoporous silica supports are broadly accepted as advantageous drug delivery systems. Since they are able to encapsulate several molecules inside their pores as well as anchor (bio)molecules in its external surface, acting these lasts as molecular gates which respond to external stimulus, thus delivering their cargo under accurate conditions. These advanced devices can be used to carry drugs until their targets for smart or controlled release. This feature will be really profitable in situations where narrow therapeutic range are intrinsic.

Here, it is described once more, an innovative system combining an enzymatic responsive molecular gate with a magnetic mesoporous silica material MCM-41. The system should respond to azoreductor agents, since azoreductase enzymes are produced by colon-resident bacterial enzyme[1]. Magnetic nanoparticles (made with magnetite, Fe_3O_4)[2] was included within the scaffold of the micro MCM-41, that might increase the retention time of these particles in the desired area when applying a magnetic field. See Figure 1.

A new azo derivative was synthesized and bonded to an alkoxysilane by means of a carbamate link. This molecule was anchored into the surface of the support acting as molecular gate which controls the delivery of the cargo. In this job, our team used safranine O as cargo to study the correct running of the system.

These devices were later tested with in vitro release trials in pH conditions where the azoreductases enzymes (typically based in the colon as the colonic microbiota is it source) acts optimally.

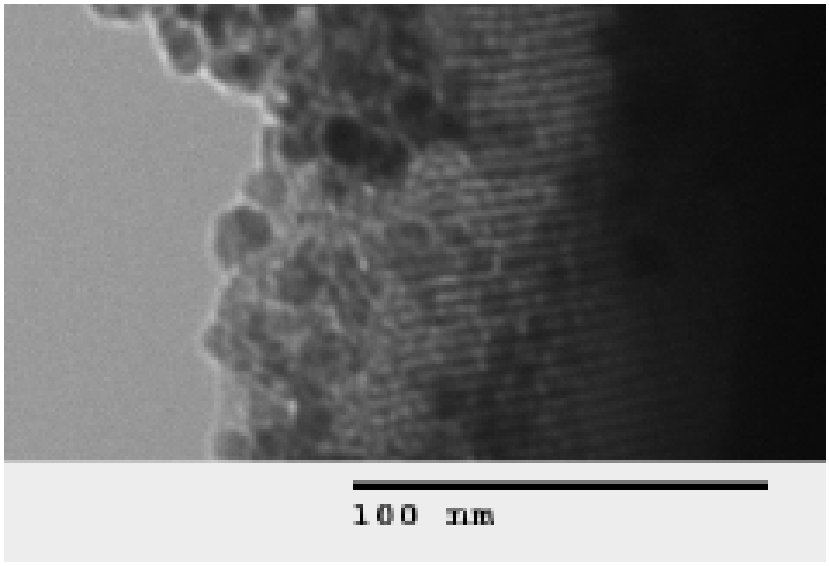

Fig. 1 – TEM image of micro MCM-41 containing magnetite nanoparticles.

In future works, our team plan to load the mesoporous frameworks with IBD drugs, thus a smart delivery system would be obtained to treat these diseases.

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O-10

DERIVADOS DE TETRAFENILETILENO (TPE) PARA LA DETECCIÓN ÓPTICA DE NOx

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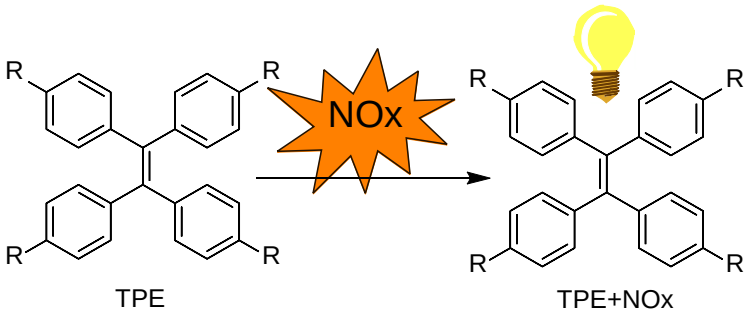
La investigación en el diseño, síntesis y evaluación de quimiosensores y dosímetros químicos colorimétricos y fluorescentes se ha consolidado en los últimos años como un área de trabajo de gran interés. Estos sistemas se han empleado tanto en la detección de especies cargadas (cationes y aniones)[1] si bien el desarrollo de sensores para moléculas neutras es todavía un desafío al que hay que hacer frente.[2] Particularmente los óxidos de nitrógeno (NOx) son uno de los casos que despiertan un fuerte interés.

El dióxido de nitrógeno (NO_2) se forma cuando los combustibles fósiles como el carbón, petróleo, gas o diesel se queman a altas temperaturas. Este gas provoca una serie de efectos nocivos sobre los pulmones, tales como aumento de la inflamación de las vías respiratorias, tos y sibilancias, función pulmonar reducida, aumento de los ataques de asma y el aumento de la susceptibilidad a las infecciones respiratorias[3]. Por su parte, el óxido nítrico (NO) es un importante neurotransmisor en los sistemas nerviosos central, periférico y entérico. Este compuesto es capaz de activar cadenas metabólicas intracelulares y, a diferencia de otros neurotransmisores, posee la capacidad de afectar células, procesos neuronales o efectores aunque éstos no se encuentren en contacto anatómico inmediato con el elemento celular que lo sinteriza[4]. Debido a todos estos efectos el diseño y preparación de sensores capaces de detectar NOx en distintos medios y concentraciones biológicas y ambientales es un campo de investigación en continuo desarrollo.



TPE TPE+NOx

Por otro lado, el tetrafeniletileno (TPE) presenta una unas aptitudes óptimas para ser un posible candidato para el diseño de sensores, debido a su elevada conjugación, a su alta densidad de grupos funcionales y especialmente a su fuerte capacidad emisiva bajo condiciones de agregación en mezclas de disolventes, lo que se conoce como *Emisión Inducida por Agregación* (AIE)[5]. En el marco de este contexto, se han diseñado derivados del TPE, di- y tetra- sustituidos con grupos funcionales adecuados para reaccionar con NOx bajo distintas condiciones, con el objetivo de obtener sensores ópticos capaces de cuantificar con precisión, concentraciones relativamente bajas de esta familia de analitos de gran importancia.

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O-11

Visible Light Induced Enantioselective [2+2] Photocycloaddition Reactions Employing a Chiral Catalyst based on the Thioxanthone Chromophore

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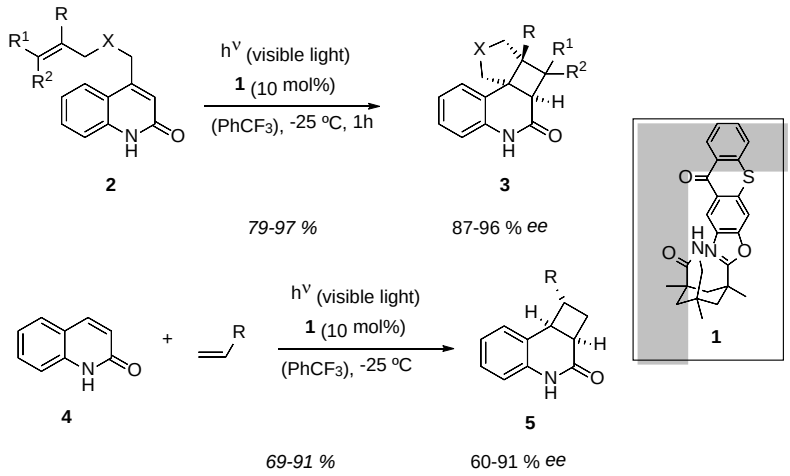
Triplet sensitization employing sensitizers that absorb visible light is an attractive strategy for carrying out photochemical reactions, since visible light is a very cheap and readily available energy that can induce photochemical reactions. The relatively low energy of this radiation, in many cases, reduces undesired side reactions which are often observed when the photoreactions are conducted employing higher energy UV light.

In the context of our studies on enantioselective [2+2] photocycloadditions employing a xanthone-based catalyst,[1] we decided to synthesize the thioxanthone catalyst (**1**) which is also able to bind prochiral lactams by means of two hydrogen bonds. The chiral catalyst **1**, which was prepared in a straightforward fashion from methyl thiosalicylate, shows a significant absorption in the visible light region. It allows for an efficient enantioselective catalysis of intramolecular [2+2] photocycloaddition reactions by triplet energy transfer due to its relatively high triplet energy. Good yields (79-97 %) and enantioselectivities (87-96 % *ee*) are obtained for the [2+2] photocycloaddition of 4-substituted quinolones (**2**) to their respective cylobutanes (**3**) in trifluorotoluene at -25 ºC.[2] The reaction remained highly enantioselective even if performed at room temperature, which allows highly enantioselective reactions to be carried out under ambient conditions using solar irradiation. High enantioselectivity was also achieved for intermolecular [2+2] photocycloaddition reactions between parent 2-quinolone (**4**) and olefins employing this methodology.



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O-12

TRIM21α Structure and its Mechanism Acting in Systemic Lupus Erythematosus Patients and Healthy Subjects

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Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease associated with a high morbi-mortality and affects to 5 million people worldwide. SLE is linked to a malfunction of the TRIM21α protein. Despite of that, the functional mechanism of this ligase has not been addressed yet. We found that the host-guest chemistry of this protein is strongly dependent on the serum origin (patients and healthy subjects). Additionally, the proposed TRIM21α three-dimensional structure allowed to establish the TRIM21α functional mechanism, which is related to the NF–κB signalling activity.[1,2] We show the key role of TRIM21α in regulating the immune response to infection, so that its malfunction may be significantly involved in the pathogenesis of SLE (Figure 1).

O-13

POLYMER-COATED UPCONVERSION NANOPARTICLES FOR PH-TRIGGERED DRUG DELIVERY

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Upconversion nanoparticles with an inorganic matrix doped with rare earths (e.g. $NaYF_4$: Er^{3+},Yb^{3+} ,UCNP) have unique photophysical features, such as a large anti-Stokes emission after near-infrared (NIR) excitation with a low-power continuous-wave diode laser. Due to these unique physical-chemical properties, the up-converting nanoparticles can be applied in many fields of biological sciences[1]. However, the periphery of the as-prepared nanoparticles is usually hydrophobic due to the nature of the capping ligand (oleate) and, therefore, it is necessary to make them water-dispersible soluble and biocompatible [2]. In addition, the organic coating is usually lost in a medium with a pH below 4, due to protonation of the anchoring group (carboxylate, amine, sulfides,) [3.4].

Recently, we have prepared functional water-dispersible UCNPs capped with a thin shell of a biocompatible copolymer HEMA-AMPS (Fig 1) via sulfonate-multigrafting to the UCNP surface[5]. Interestingly, these UCNP@COP nanohybrids proved to be considerable stable in acidic media (down to 2). The unusual stability of the UCNP organic capping in strong acid media makes UCNP@COP nanohybrids particularly suitable for many applications where the maintenance of the UCNP capping is crucial for their performance.

It was not expected that all the sulphonate groups would be involved in the COP binding to the UCNP surface, but rather that some would be at the nanohybrid periphery and consequently, it is possible to decorate them with various biomolecules. As a proof of concept we used methylene blue (MB), which is a water-soluble, positively charged cationic dye. The assembly of UCNP@COP and MB was successful and lead to UCNP@COP@MB nanohybrids. The UCNP@COP nanohybrid could be useful to build NIR-responsive nanosystems able to release progressively functional molecules *attached to their periphery via competitive binding of H^+ at decreasing pHs, i.e* via pH-stimulus (Fig 1).

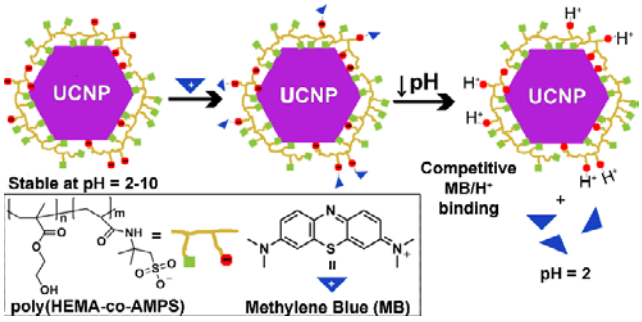

Fig 1. Electrostatic assembly of UCNP@COP and MB to lead to the UCNP@COP@MB nanohybrid, which releases drgerMB as the pH decreases.

Therefore, the dependence of the red/green emission ratio (R/G) on the pH in UCNP@COP@MB was evaluated. No changes were observed in the basic range. Remarkably, a good correlation between this R/G ratio and the pH was observed in the 2-7 pH range. The sample at the lowest pH was centrifuged to determine the degree of MB release at this pH, thus evidencing practically the complete release of MB

In summary, we report here the synthesis of a NIR-responsive nanohybrids consisting of $NaYF_4$: Er^{3+},Yb^{3+} UCNPs capped with a thin shell of a biocompatible HEMA-AMPS copolymer, which remains firmly anchored to the UCNP due to sulphonate-multigrafting to the UCNP surface. This capping not only remains stable in highly acidic media (as low as a pH of ca. 2), but also enables the UCNP@COP nanohybrid to bind electrostatically to cationic molecules, which can be progressively released when the pH decreases. Therefore, these nanohybrids can be used as functional molecule-release nanosystems.

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O-14

PPO-SUBSTRATE INTERACTION STUDY IN PRESENCE OF SILICA NANOMATERIALS

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Food industry has to face several problems such as changes on color, flavor and in nutritional values of some fruits, vegetables and their corresponding juices due to the activity of the polyphenol oxidase (PPO). This enzyme, also called tyrosinase, accelerates the phenolic's oxidation generating brown pigments.

Mesoporous silica nanoparticles have a large potential in several fields, including sensors, controlled release and interaction with biological systems.[1][2] For this reason, the researchers, but also the industry have been studying the properties and possible applications of such materials in the last decades.[3][4] Therefore, the application of those nanoparticles in the food industry to inhibit the activity of the PPO could be an alternative to the current treatments used to secure the good quality of food.

The objective of this work is to study the interaction between the enzyme PPO and the silica materials, to investigate whether the oxidation process could be stopped. Several materials with different characteristics in their structures, morphology and surface composition have been tested.

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O-15

New nanoporous supports functionalized with molecular gates for the detection of *Mycoplasma Fermentans* genomic DNA

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The implementation of molecular gates on nanostructured supports different from mesoporous silicia materials is practically anecdotic. Within this aim, this work presents the use of nanoporous anodic alumina (NAA) as suitable support. Furthermore, for the best of our knowledge, this nanoporous support has never been used beyond our research group.

Herein we describe a versatile nanoscopic detection system for *Mycoplasma Fermentans* genomic DNA based in a molecular gate previously described by our group.[1] Gate opening mechanism is based on the great affinity of complementary oligonucleotide chains, which only allow the cargo delivery in the presence of the corresponding DNA sequence (Figure 1). Thus, capped NAA support shows no significant delivery when *Mycoplasma Fermentans* is not present, showing great sensibility and selectivity.[1] Detection of *Mycoplasma* has interest in diverse areas because of their common presence in cell culture laboratories[2] and their relation with pathologies such as pneumonia, rheumatoid arthritis and non-gonococcal urogenital disseases among others[3].

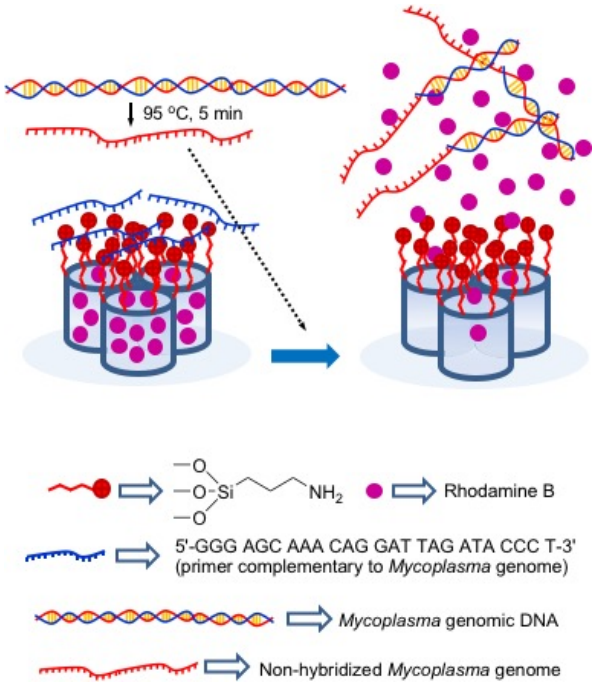

Figure 1. Scheme of the *Mycoplasma* genomic DNA detection mechanism.

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O-16

DISEÑO DE MATERIALES HÍBRIDOS ORGÁNICO-INORGÁNICOS PARA EL RECONOCIMIENTO DE miARN-145

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En los últimos años se han desarrollado sistemas supramoleculares que se inspiran en interacciones biológicas para una gran variedad de aplicaciones como la bioingeniería, el biosensado y la bionanotecnología. Una de estas técnicas se basa en el uso materiales híbridos en los que se combinan soportes mesoporosos inorgánicos, que pueden albergar moléculas, con puertas moleculares, que pueden cambiar su conformación espacial en presencia de estímulos concretos, para conseguir así un control sobre la salida de las moléculas que hay en el interior de los soportes mesoporosos.[1] Este tipo de nanodispositivo se han utilizado ampliamente para la liberación controlada o dirigida de fármacos, sin embargo, recientemente se ha explorado su uso como dispositivos de detección de moléculas.[2]

En este trabajo se he desarrollado un sistema sencillo, barato y rápido para la detección selectiva de miARN-145, cuya sobreexpresión en las placas arterioscleróticas se relaciona con la hipertensión. Éste se basa en la funcionalización de nanopartículas mesoporosas de sílice con puertas moleculares, cuya apertura se controlada mediante un reconocimiento de tipo ADN-miARN altamente específico, y en la encapsulación de una molécula señalizadora, que permite determinar la apertura de la puerta.

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O-17

NANOTOXICOLOGY EVALUATION OF FUNCTIONALIZED AND NON-FUNCTIONALIZED MESOPOROUS SILICA PARTICLES ON *CAENORHABDITIS ELEGANS*

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Nanomaterials have interesting features for application on life sciences, however a complete understanding of its risks and limitations is needed. In general, silica materials such as bulk silica or food-grade additive SiO_2 (E-551)[1,2] have few claims about safety considerations. However studies about reactivity, biocompatibility and toxicity of silica-based nanomaterial still on consideration.

This study evaluates the toxicity of mesoporous silica particle MCM-41 a well-known MSP used as scaffolds in controlled release applications. Microparticles and nanoparticles (M0 and N0 respectively) of MCM-41 were synthesized, and their outer surfaces were functionalized with a starch derivative (Glu-N) to obtain particles M1 and N1, respectively.

In order to carry out the toxicological evaluation, the nematode *Carnorhabditis elegans* was selected as *in vivo* screening model according to their properties, as a multicellular organism with a short lifespan, a well-studied biological system and simple maintaining[3]. Nematodes were fed with these particles and their lifespan and healthspan (monitoring of healthy aging through motor activity, response to oxidative stress and offspring) was assessed. In addition, particles monitoring was also done along the digestive tract of worms. Lifespan data was correlated with healthspan results so nematodes fed with smaller particles decreased their mean lifespan while large-sized particles and surface functionalized ones not only showed a recovering in mean lifespan but also recovers the nematode healthspan related to mobility, response to oxidative stress and its offspring.

Our results showed the potential of *C. elegans* as an *in vivo* model for nanotoxicology evaluation of silica particles, being possible to perform a pre-clinical screening before the studies in mammal models; while points toward the potential design of useful applications based on MSP suitable surface functionalization choice for minimizing risks.

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O-18

The chemistry and antibody recognition of the TROVE2 superantigen.

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ABSTRACT:

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune inflammatory disease characterized by the presence of B and T autoreactive cells[1]. This implies the antibody production towards the components of the Ro/SSA complex (TROVE2/TRIM21 and La proteins). These antibodies become the serological hallmark for the disease[2]. Particularly, specific antibodies to the TROVE2 protein are present in patients with SLE at high-levels. Nevertheless, the host-guest chemistry of the TROVE2 protein remains unknown. In this work, we found that the biorecognition mechanism of TROVE2 by autoantibodies is conserved regardless the serum origin but, the cell degradation pathways are different. Furthermore, we proposed a pathologic role for TROVE2 which involves the Ro/SSA complex formation by its interaction with TRIM21α. Knowledge about this synergy may contribute to design novel drugs, controlling the interactions that cause potential cellular damage.

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O-19

TARGETED DELIVERY THERAPEUTICS TO GLIOMA CELLS BY CHLOROTOXIN CONJUGATED MESOPOROUS SILICA NANOPARTICLES

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Primary brain tumors (gliomas) have the unusual ability to diffusely infiltrate the normal brain thereby evading surgical treatment. Chlorotoxin (Cltx) is a 36-amino acid peptide that was originally isolated from *Leiurus quinquestriatus* venom [(1)] that specifically binds to the surface of glioma cells and impairs their ability to invade. Studies show the principal Cltx receptor on the surface of glioma cells as matrix metalloproteinase-2 (MMP-2). Cltx exerts a dual effect on MMP-2: it inhibits the enzymatic activity of MMP-2 and causes a reduction in the surface expression of MMP-2. These findings suggest that Cltx is a specific MMP-2 inhibitor with significant therapeutic potential for gliomas.

We have designed a smart delivery system to develop a novel therapeutic option for glioblastoma multiforme (GBM) that overcomes the shortcomings of current treatments [(2,3)]. Mesoporous silica nanoparticles (MSNs) have been loaded with chemotherapy (temozolomide) and functionalised with chlorotoxin peptide that acts as a targeting ligand and also as a pore capping agent. The presence of intracellular proteolytic enzymes will induce the degradation of chlorotoxin, resulting in the release of temozolomide.

In conclusion, a novel delivery system that enables selective, triggered delivery of chemotherapy for local treatment of GBM recurrence has been developed.

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O-20

Evaluación del uso de acelerómetro triaxial como sistema de medida de distancia

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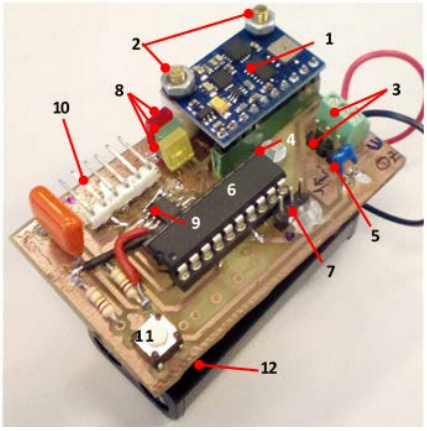
Resumen:

Los podómetros de hoy en día se basan en el contaje de los pasos que hace el usuario y la distancia promedio de su paso para saber la distancia aproximada que ha recorrido (a excepción de los podómetros con GPS). Dicho contaje de pasos se realiza por medio de un péndulo mecánico o de un acelerómetro triaxial pero siempre con la misma idea de contar pasos. Estos pasos pueden no ser uniformes, pueden no ser lo suficientemente fuertes como para detectarlos, pueden ser falsos si el usuario ha estado realizando algún movimiento que se asemeja a su caminar[1]. En resumen, que para medir con cierta exactitud la distancia que el usuario recorre, éste ha de realizar sus pasos lo más uniformemente posible a lo largo de todo el día.

En este proyecto se ha pretendido usar un acelerómetro triaxial no para contar pasos si no para, a través de medidas de aceleración del sujeto, medir la distancia recorrida por el usuario. De esta forma, la medida de distancias se independiza de la forma que el usuario camine o la situación en la que se encuentre. Se ha desarrollado un dispositivo (ver Figura 1) para ello y se ha comparado con otros podómetros recorriendo distancias entre 5 y 30 metros. De los datos recogidos se ha concluido que el sistema funciona para distancias cortas con un margen inferior al 5%.



Nº	Board Component
1	Accelerometer
2	Mechanical fixing of multi-sensor board to PCB
3	Power supply and selection jumper
4	Mechanical fixing of battery pack
5	Decoupling capacitor
6	Microcontroller
7	UART communication port
8	Status LEDs
9	Memory chip
10	Firmware download port
11	Mode selection push button
12	Battery pack (2xAA)

Figura 1: Dispositivo desarrollado y descripción de sus componentes

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POSTERS

P-01

CONTROLLED DELIVERY SYSTEM IN SMALL INTESTINE USING MESOPOROUS SILICA PARTICLES CAPPED WITH OLEIC ACID

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Mesoporous silica particles (MSPs) have constituted a promising research field last years for bioactive molecules controlled release, due to their versatile properties (low toxicity, high internal volume and easy chemical functionalization). The use of MSPs with the pores capped by 'molecular gates' that could be opened with different stimuli would guarantee the complete arrival of the cargo to the action point.[1] These systems have a great potential for applications in food, agricultural, cosmetic and pharmaceutical industries.[2]

The nutrients absorption and the production of bioactive compounds are activities achieved by the small intestine.[3] Also, in the small intestine there are different external triggers (pH changes, emulsifier molecules, presence of bio-molecules as enzymes...) that can open the 'molecular gates' of a MSPs system and could be employed to release a wide variety of guest molecules (vitamins, proteins, antioxidants, etc.).

Considering these facts, this work was focus on the design of new delivery systems in the small intestine and on the improvement of molecular absorption. Oleic acid was selected as a 'molecular gate' due to its natural presence in olive oil and its hydrophobic character. Oleic acid capped MSPs systems for the controlled release of a cargo and an antioxidant molecule were developed. PBS suspensions of oleic acid capped MSPs showed no cargo release, while a different behaviour of the carrier is observed in a bile salts suspension, where a marked release of the entrapped cargo is produced. Due to the strong hydrophobic character of the capping molecule (oleic acid), an impermeable layer is formed around the MSPs, and water molecules could not accede to the cargo until emulsifier molecules (bile salts) are present. This system can be employed as smart microdevice for the intelligent delivery of molecules which have to be absorbed along the first steps of the intestinal tract.

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P-02

ESTUDIO DE LA ABSORCIÓN INTESTINAL DEL GEFITINIB EN RATA

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Se ha evaluado el proceso de absorción intestinal mediante la perfusión intestinal *in situ* del gefitinib. La constante de velocidad de absorción (ka) del gefitinib se ha determinado tras la perfusión de una disolución de gefitinib a la concentración de 8 µg/mL, 40 µg/mL, o de 40 µg/mL adicionada de azida sódica 1 mM, en los tramos inicial y final del intestino delgado de rata. En todos los casos el volumen de perfusión ha sido de 5 mL. Las concentraciones remanentes en el lumen intestinal del animal se han determinado mediante cromatografía líquida de alta resolución (HPLC).

En la figura 1 se muestra la representación gráfica de las concentraciones medias de gefitinib remanente en lumen intestinal a los diferentes tiempos de muestreo.

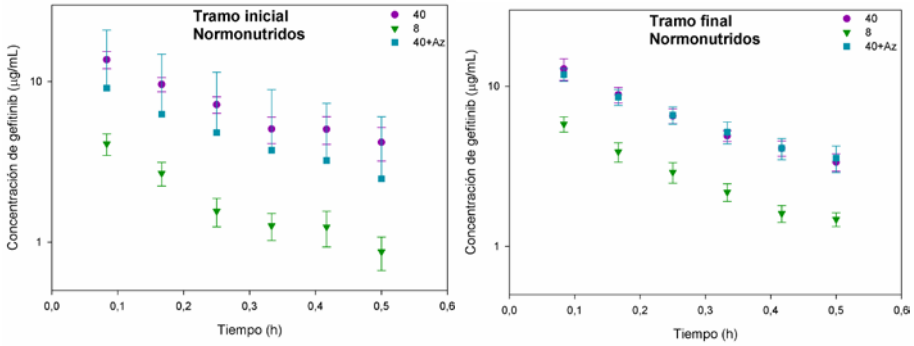

Figura 1. Representación gráfica de las concentraciones de gefitinib remanente en lumen intestinal (tramos inicial y distal de intestino delgado de rata (n=7-9)) obtenidas tras la perfusión de las disoluciones del fármaco a las concentraciones de 8 µg/mL, 40 µg/mL y 40 µg/mL en presencia de azida sódica.

En la figura 2, se muestra un resumen de los valores promedio de las constantes de velocidad de absorción aparente de gefitinib con su dispersión obtenidas en cada una de las condiciones indicadas.

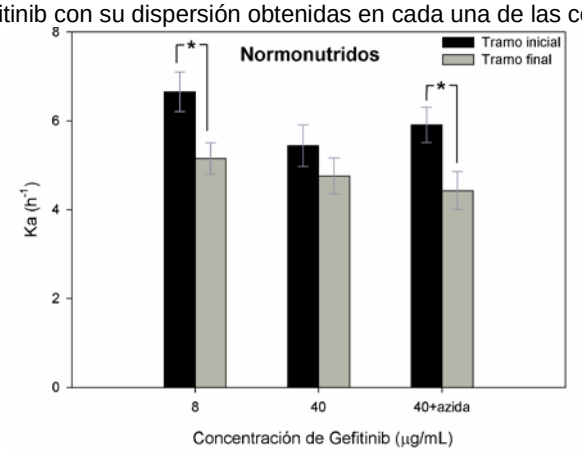

Figura 2. Representación gráfica de la constante de velocidad de absorción promedia de gefitinib junto a su error estándar obtenida tras la perfusión en los tramos inicial y final del intestino delgado de las soluciones ensayadas. (*): Diferencias estadísticamente significativas $p<0,05$.

El análisis estadístico realizado indica que la constante de velocidad de absorción del fármaco obtenida en tramo inicial y en tramo final de intestino delgado de rata es independiente de la concentración inicial de fármaco perfundida, por lo que en las condiciones ensayadas se podría afirmar que el proceso de absorción del gefitinib en los tramos inicial y final del intestino delgado de rata es lineal.

Por otra parte, la constante de velocidad de absorción del gefitinib tras la perfusión de la disolución de fármaco menos concentrada es mayor en el tramo inicial del intestino delgado. Este resultado también se ha observado tras la perfusión del fármaco adicionada del inhibidor metabólico azida sódica por lo que se puede concluir que el tramo inicial del intestino delgado es una zona de absorción preferente para el fármaco ensayado.

P-03

DETECCIÓN DE LA CALIDAD DEL PESCADO FRESCO Y DESCONGELADO CON LENGUA ELECTRÓNICA POTENCIOMÉTRICA

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En experiencias previas se comprobó la monitorización de la frescura del pescado por medio de un sistema de lengua electrónica potenciométrica formada por electrodos metálicos de distintos materiales[1] y su relación con diferentes parámetros bioquímicos y microbiológicos indicadores de la frescura del pescado[2]. En esta comunicación se presentan las conclusiones de experiencias realizadas con un sistema de medida similar a las experiencias anteriores y con la misma especie de pescado, dorada (Sparus aurata). Pero en lugar de utilizar siempre pescado fresco se ha utilizado pescado congelado para así comprobar si afecta los tiempos de congelación y de descongelación a las medidas realizadas con el sistema de lengua electrónica. Las medidas fueron las siguientes:

1) Tiempo de congelación del pescado. Se tomaron muestras de pescado fresco y se dividieron en cinco lotes para distinto tiempo de congelación (1 día, 1 semana, 2 semanas, 3 semanas y 4 semanas).

2) Tiempo después de la descongelación. Para cada una de esas muestras se realizaron medidas el primer día (fresco y la descongelación), últimos 3 días, 5 días o más de 5 días (hasta 14 días).

3) Parte del cuerpo del pescado. Los pescados fueron cortados en tres piezas, correspondiente a la parte cerca de la cabeza, para el centro del pescado y la parte de la cola, esta manera de comprobar si llegaron los resultados afectados por la zona del pescado donde se realiza la medida.

Una vez realizadas las medidas y utilizando los datos obtenidos por todos los electrodos se utilizaron técnicas de análisis multivariante para comprobar la posible relación entre los datos potenciométricos y los parámetros de interés. La técnica utilizada fueron las redes neuronales artificiales (ANN) de la Fuzzy-Artmap. Mediante este método se pretende conocer si el sistema es capaz de clasificar las medidas según categorías. Para ello se ha utilizado una validación cruzada de orden uno. En primer lugar se pretende saber si la lengua electrónica es capaz de determinar el número de días que ha estado el pescado congelado. En la tabla 1 se muestras los resultados donde se comprueba que sí es capaz de determinar los que no se han congelado pero en cambio es poco preciso a la hora de determinar el número de días congelados, dando a entender que el pescado no varía sus propiedades según los día de congelación. En la tabla 2 se muestran los resultados de la red según los días trascurridos desde la congelación, donde se puede comprobar que es más factible lograr la detección y clasificación de la muestras.

Tabla 1. Resultados red neuronal clasificación según días de congelación del pescado

Número de días congelado	Nº Medidas	Tasa de éxito
0	13/18	72.22%
1	5/15	33.33%
7	7/21	33.33%
14	3/15	20.0%
21	4/18	22.22%
28	2/15	13.33%
Total	**32/102**	**31.37%**

Tabla 2. Resultados red neuronal clasificación según los días transcurridos tras la congelación del pescado

Nº días	Resultados/	Tasa de
0	15/18	83.33%
2	12/18	66.66%
5	6/18	33.33%
+5	39/48	81.25%
Total	**72/102**	**70.58%**

Un caso particular es determinar si la detección donde la tasa de éxito es prácticamente es del 100%.

Congelado	Resultados/ Nº Medidas	Tasa de éxito
Fresco	18/18	100%
Descongelado	85/94	90.42%
Total	**93/102**	**91.17%**

Por último, se pretendió determinar la capacidad para detectar a que parte del cuerpo del pescado corresponde la muestra medidas. La tabla 3 indica que realmente es difícil detectar este parámetro, probablemente a la uniformidad del músculo del pescado a lo largo de todo su cuerpo.

Tabla 3. Resultados red neuronal clasificación según la parte del cuerpo del pescado

Parte del Cuerpo	Resultados/ Nº Medidas	Tasa de éxito
Cabeza	15/35	42.85%
Medio	15/32	46.87%
Cola	6/35	17.14%
Total	36/102	35.29%

Conclusión

Los resultados mostraron una capacidad para la detección entre las muestras de pescado congelado y descongelado, el número de días de congelación tuvo menor influencia de las señales, a excepción de no congelado. No se encontraron diferencias no significativas entre las mediciones en los tres diferentes partes del cuerpo del pescado.

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P-04

COMBINACIÓN DE MEDIDAS DE LENGUA ELECTRÓNICA Y DE IMAGEN SOBRE GRASAS DE CERDOS CON DIFERENTES TIPOS DE ALIMENTACIÓN

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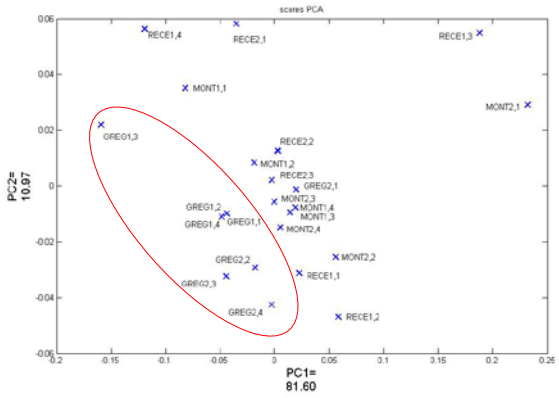
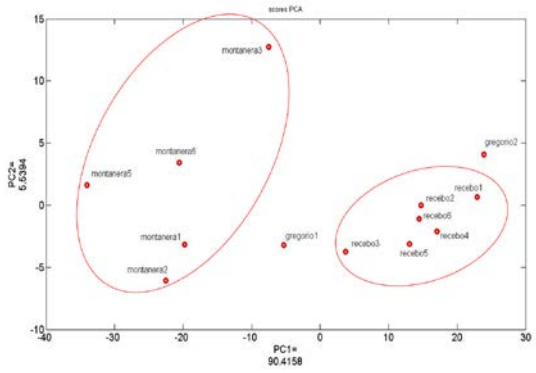
En esta comunicación se muestras los resultados de diferentes medidas realizadas sobre grasa de jamón de cerdo utilizando un sistema de lengua electrónica potenciométrica y medidas de imagen a distintas frecuencias. Los análisis pretendieron diferenciar muestras de tres tipos de jamón ibérico que se caracterizan por el tipo de alimentación de los cerdos. Las muestras analizadas fueron: Montanera (cerdos alimentados solo con bellota); Recebo: cerdos con alimentación mixta (bellota y pienso) y Gregorio: cerdos alimentados solo con pienso.

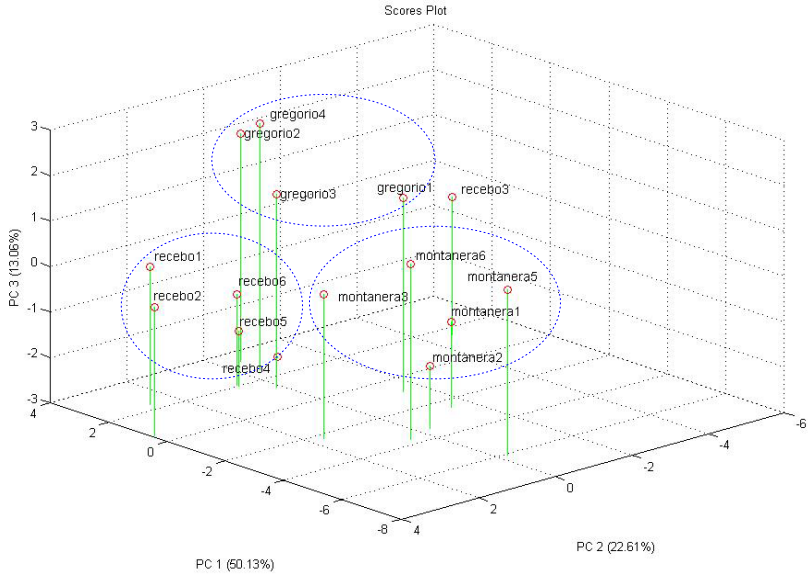
Para construir la lengua electrónica se utilizaron ocho electrodos potenciométricos de diferentes metales (tres de oro, tres de plata y dos de cobre). Este tipo de sistema de medida ya se había utilizado para el análisis de la frescura de la carne[1]. Se tomaron dos ejemplares de cada tipo de muestras. Con cada ejemplar se realizaron cuatro medidas. Con los resultados de estas medidas se realizaron análisis PCA logrando buena discriminación de las muestras de Gregorio. Con las muestras de Montanera aparecen cierta coherencia, pero Recebo muy disperso.



Por otro lado, se realizaron medidas de imagen con 60 longitudes de onda distinta (desde 430nm a 1020nm en saltos de 10nm). El análisis PCA de estas medidas mostraron una buena discriminación de las muestras de Recebo, también Montanera, en cambio de Gregorio solo hay dos muestras y muy diferentes entre sí.



Finalmente se realizaron con los resultados conjuntos de ambos tipos de medidas mediante un análisis PCA tridimensional donde se logra una buena discriminación de las diferentes muestras. Con lo cual se puede indicar que ambos tipos de medidas son complementarias para la diferenciación del jamón según el tipo de alimentación del cerdo.



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P-05

Gated mesoporous silica materials for the treatment of bone infection by *S. Aureus*.

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In recent years, bone diseases have gained importance due to the increase of the elderly population. Several materials and techniques have been designed for the treatment of these pathologies, and the implantation of prosthesis is a very common remedy. However, bone prosthesis get infected very frequently leading to a worsening of the patient's life quality and complications in the treatment.[1] One of the most common bacteria infecting bone prosthesis is *Staphyloccocus Aureus*[2], a microorganism able to create a biofilm on the prosthesis surface, improving the adhesion and proliferation of bacteria, and making them resistant to several antibiotics. The treatment of these infections often includes continuous drug administration or even prosthesis replacement, but these remedies are usually expensive and insuficient.

Apart from that, silica mesoporous nanomaterials have been proved to have meaningful applications in biotechnology and biomedicine. The mesoporous nature of these materials makes them suitable for drug delivery applications by means of the implementation of supramolecular-based nanoscopic gates, which are designed nanodevices using chemically modified mesopores, able to control mass transport by specific stimuli.[3]

In this work, we have designed a new gated-system which specifically recognizes the presence of an infection by *S. Aureus*. Thus, MCM-41 mesoporous nanoparticles were used as an inorganic scaffold, and its pores were loaded with a dye. Then, the solid was functionalized and capped with a designed peptide, cleavable by the specific activity of *S. Aureus* endoproteinase V8.[4] In this system, the molecular gate remains closed in the absence of an infection, while the presence of *S. Aureus* and the subsequent secretion of V8 causes the opening of the gate. V8 cleaves specifically peptide bonds on the carboxyl side of aspartic and glutamic acid residues,[5] hydrolysing the peptidic sequence and allowing the dye to be released in a local and specific way.

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P-06

LUMINESCENT PEROVSKITE NANOCRYSTALS: A NEW GENERATION OF FLUOROGENIC IMAGING LABELS

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Metal halide perovskites, where A=Cs^+, Rb^+, $CH_3NH_3^+$; B=Pb^{2+} or Sn^{2+} and X=Cl^-, Br^-, I^-), are currently the focus of a considerable research effort, owing to their important optoelectronic and photovoltaic propierties. These newcomer materials show unprecedent photoluminiscence (with quantum yields higher than 90%) and electroluminiscence propierties [1, 2]. The high emision quantum yields in the short life of this technology situate perovskite materials as a promising alternitive to conventional fluorogenic biomarkers for sensing, imaging and labeling.

Here we report a facile room temperature ligand mediated synthesis of $CH_3NH_3PbBr_3$ nanoparticles. The shape of the nanocrystals is tuned from spherical nanoparticles to nanowires by control of the reaction conditions. The colloidal spherical quantum dots of $CH_3NH_3PbBr_3$ exhibit 45% emision quantum yield. We also studied the effect of solvent and ligand in the crystallization rates, nanoparticle size and emission properties.

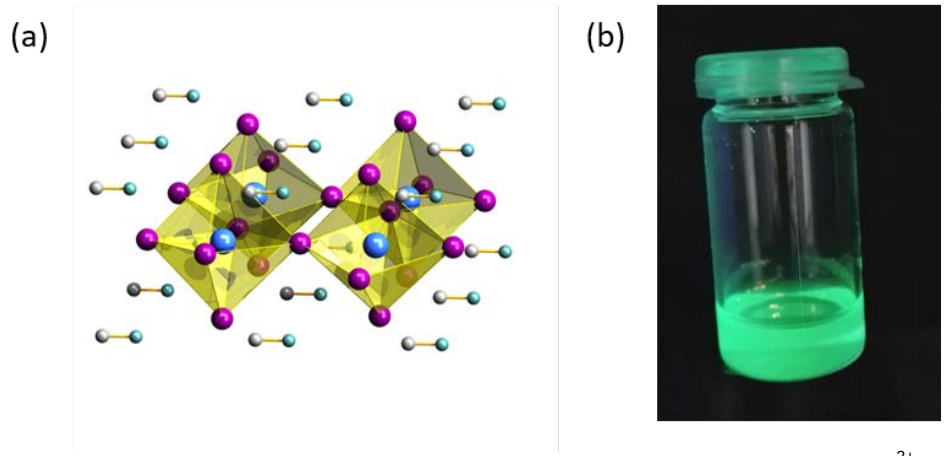

Figure 1. (a) Tetragonal perovskite, phase; the blue sphere is the B cation (Pb^{2+}), the purple spheres represent the X anion, and white and cyan spheres represent methylammonium. (b) Colloidal solution of $CH_3NH_3PbBr_3$ nanoparticles in toluene under UV lamp excitation.

Acknowledgments

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P-07

LABEL FREE INMUNOSENSOR BASED ON NANOPARTICLE 1D-PHOTONIC CRYSTALS

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1-D Photonic crystals, also known as Bragg mirrors, are based on dielectric periodical multilayer structure which produces Bragg diffraction of the incident light. The frequency and width of the reflection peak are determined by the refractive index and the thickness of the layers in the film. The molecular events occurring in the pore surfaces produce changes in the optical response of these structures modifying the intensity, the spectral position and the width of their characteristic Bragg reflections.[1] Therefore, biosensing applications of these structures have paid a great deal of attention and are being currently actively studied. In addition, these optically tunable structures are very appealing because further to the label free detection they are easy to integrate in optical platforms as they are prepared by wet deposition methods. [1]

Here we report a 1-D photonic crystal composed of dip-coated alternate mesoporous layers of TiO_2 and SiO_2 nanoparticles. As a proof of concept, biotin and streptavidin molecular binding events on the sensor surface are monitored by UV-Vis spectroscopy from a Bragg mirror constructed on a glass substrate. The inmunosensor presents a sensitivities of 1.7 ± 0.15 nm/(mgL^{-1}) (spectral shift) and 0.65 ± 0.2 (transmission increase at 780 nm) for the detection of streptavidin (Figure 1).

Despite there are still many efforts to do, these previous results pave the way towards the development of a new generation of solution processed cost-competitive and through-away label free biosensors.

P-08

Sistema de Monitorización y Control vía Wi-Fi

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Resumen:

Cada vez son más las necesidades de controlar de forma inalámbrica[1] [2] dispositivos electrónicos que monitoricen parámetros físico/químicos mediante sensores y que puedan actuar sobre el estado de un proceso industrial o doméstico. En este trabajo se desarrolla un equipo integrado de monitorización y control vía Wi-Fi. El sistema se compone de:

- Por un lado, un smartphone donde se desarrolla una interfaz/aplicación bajo el sistema operativo Android, en la que el usuario es capaz de visualizar los valores de los sensores monitorizados remotamente y además tiene la capacidad de tomar decisiones actuando sobre las características del proceso controlado.
- Y por otro lado, un microcontrolador de 8 bits que monitoriza el conjunto de sensores y tiene capacidad de actuación o control sobre cualquier carga. Además, está comunicado a un módulo Wi-Fi con el que establece la comunicación con el SmartPhone de forma inalámbrica.

Para hacerlo todavía más generalista, la idea es desarrollar el sistema que permita al smartphone controlar al microcontrolador, no solo desde su propia red Wi-Fi, sino desde cualquier otro punto de Internet. La comunicación entre estos dos bloques se realiza empleando protocolo TCP/IP.

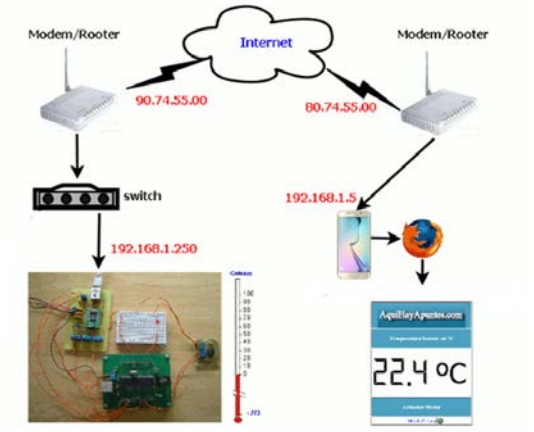

Figura 1: Esquema del sistema electrónico en el que se aprecia los dos bloques de los que se compone el proyecto.

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P-09

Ultra-high sensitive in vitro allergy diagnostic assays for β-Lactams

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This research is framed within the main activities of work package 3 (WP3) of COBIOPHAD project that was recently funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No. 688448. The project deals with the development of an integrated biophotonic device based on
compact disc technology to address the most prevalent drug hypersensitivity to β-lactams antibiotics (BLCs).

One of the main objective of WP3 is the preparation and evaluation of the antigenic determinants required for setting up high sensitive and selective in vitro allergy diagnostic test. The search for new antigenic determinants for allergy testing involves synthesis and screening of chemical entities to delineate the selectivity and the strength of interaction between the antigenic determinants and the IgE targets. In this context, we have been working in the preparation of new BLC-conjugates using human serum albumin, blue protein, and horse-radish peroxidase as carrier protein. The main tasks were initially the preparation of minor and major amoxicillin, penicillin G, penicillin V, and ampicillin determinants. In concrete, four haptenized conjugates were prepared for each BLC: a) BLC-lloyl, b) BLC-llanyl, c) Mannich derived and d) biotinylated BLC conjugates. All the conjugates were prepared at different molar ratios (50-300) by varying the concentration of BLC during the conjugation reaction. The evaluation of the as prepared BLC-conjugates was as follows: the haptenized conjugates were immobilized on a polymeric surface by physisorption. The reaction with specific anti-BLC IgEs, detection of the interaction with a labelled monoclonal anti-human IgE antibody and signal development are the steps to complete the assay. The selection criterion is based on the specific molecular recognition of specific IgEs. The assay format is schematized in Figure 1.

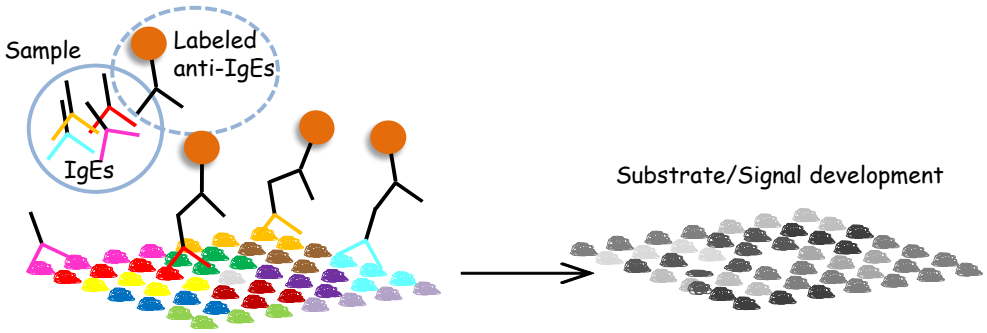

Figure 1. Scheme of the assay for testing the haptenized BLC-conjugates

P-10

BACTERIAL ENANTIORECOGNITION OF EMERGENT CONTAMINANTS: VERAPAMIL BIODEGRADATION EVALUATION

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Active pharmaceutical ingredients (APIs) are emerging contaminants in the natural environment. APIs reach the environment mainly due to inefficient removal by wastewater treatment plants (WWTPs) and by improper disposal of unused medicines[1]. Verapamil is a calcium channel blocker chiral drug widely used in the treatment of hypertension, angina and cardiac arrhythmia, which is employed as a racemate. So it could cause unpredictable enantioselective health and environmental problems, if it is not efficiently removed in (WWTPs). The present communication reports a biodegradability batch mode study of enantiomers of verapamil using minimal salts medium inoculated with activated sludge collected from a Valencian WWTP. In these in vitro simulation tests, the verapamil enantiomers concentrations have been monitored (e.g. Figure 1) by means of a capillary electrophoresis method using highly sulfated γ-cyclodextrin as chiral selector. Experiments are carried out with and without an extra carbon source. Abiotic degradation of verapamil enantiomers exposed to light and in the dark is also assessed.

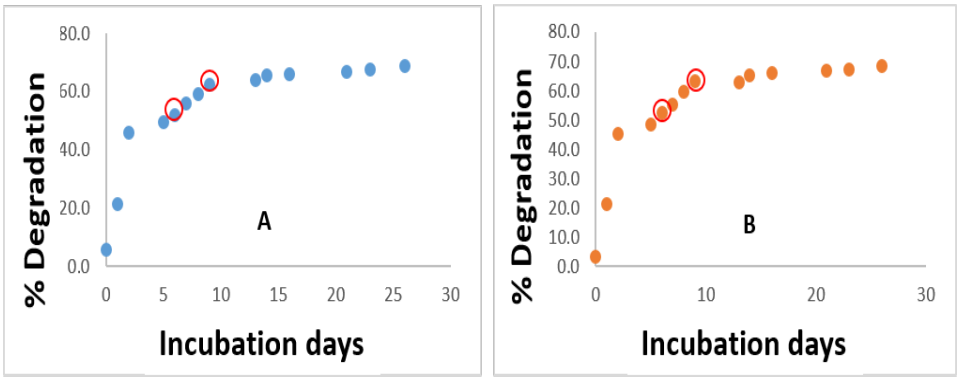

Figure 1. Bacterial enantiodegradation evaluation of verapamil enantiomers (A, B).

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This work has been supported by the Project CTQ2015-70904-R (MINECO/FEDER, UE).

P-11

BACTERIAL ENANTIORECOGNITION OF TOXIC CONTAMINANTS: METALAXYL BIODEGRADATION EVALUATION

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Metalaxyl is a widely used chiral pesticide that is employed as a racemate. So it could cause unpredictable enantioselective health and environmental problems due to its toxicity, if it is not efficiently removed in wastewater treatment plants (WWTPs). Since bacterial enantiorecognition can occurs, chiral analytical methods are crucial to assess the enantiomeric fractions[1]. The present communication reports a biodegradability batch mode study of enantiomers of metalaxyl using minimal salts medium inoculated with activated sludge collected from a Valencian WWTP. In these *in vitro* simulation tests, the metalaxyl enantiomers concentrations have been monitored (e.g. Figure 1) by means of a capillary electrophoresis method using highly sulfated γ-cyclodextrin as chiral selector.

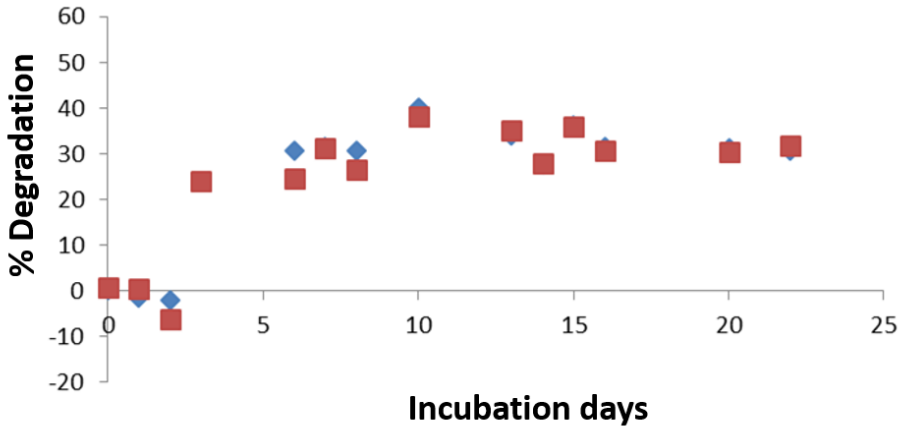

Figure 1. Bacterial enantiodegradation evaluation of metalaxyl enantiomers (◆ and ■).

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This work has been supported by the Project CTQ2015-70904-R (MINECO/FEDER, UE).

P-12

BACTERIAL ENANTIORECOGNITION OF TOXIC CONTAMINANTS: IMAZALIL BIODEGRADATION BY ACTIVATED SLUDGES

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Imazalil is a widely used chiral fungicide of the family of imidazole derivatives that is employed as a racemate. So it could cause unpredictable enantioselective health and environmental problems due to its cytotoxicity, if it is not efficiently removed in wastewater treatment plants (WWTPs). Since bacterial enantiorecognition can occurs, chiral analytical methods are crucial to assess the enantiomeric fractions. The present communication reports a biodegradability batch mode study of enantiomers of imazalil using minimal salts medium inoculated with activated sludge collected from a Valencian WWTP. In these *in vitro* simulation tests[1], the imazalil enantiomers concentrations have been monitored (e.g. Figure 1) by means of a capillary electrophoresis method using highly sulfated γ-cyclodextrin as chiral selector.

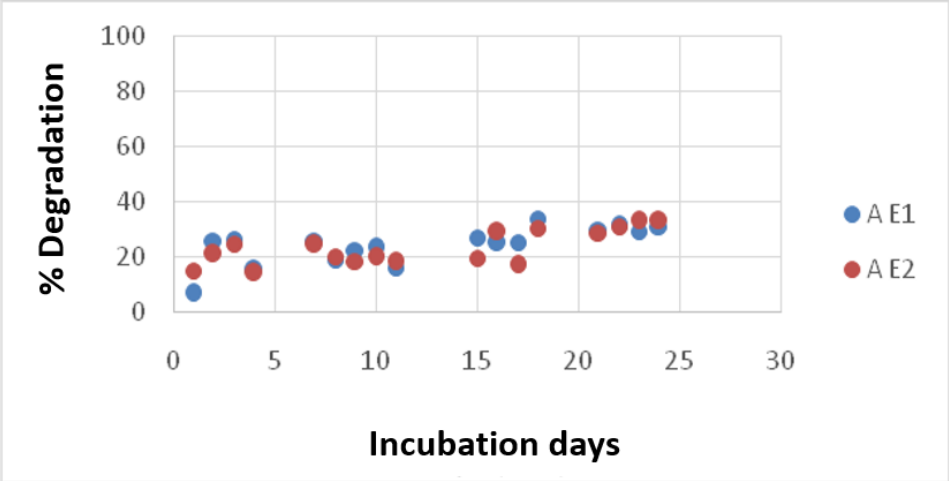

Figure 1. Bacterial enantiodegradation evaluation of imazalil enantiomers (**E1** and **E2**).

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P-13

MODELOS ANIMALES DE ARTRITIS EXPERIMENTAL

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La artritis reumatoide es una enfermedad autoinmune sistémica caracterizada por la presencia de inflamación crónica y la degradación articular. Provoca una disminución importante de la movilidad y diferentes alteraciones extraarticulares. Afecta al 1% de la población mundial y, al igual que para la mayoría de las enfermedades autoinmunes, no existe una cura definitiva, sólo tratamientos para los síntomas y en algunos casos, para retrasar el avance de la enfermedad, aunque no son efectivos en todos los pacientes. Como se trata de una enfermedad muy compleja, es imprescindible el uso de modelos animales para el estudio de posibles nuevos tratamientos más efectivos y seguros que los actuales, ya que intervienen numerosos tipos celulares y mediadores inflamatorios. Nuestro grupo de investigación tiene una amplia experiencia en modelos de artritis experimental y su aplicación en la evaluación de fármacos. En este estudio, se han comparado dos modelos animales de artritis: el CIA (*collagen induced arthritis)* y la artritis inducida por transferencia de suero de ratones K/BxN. El modelo CIA es un modelo muy completo en el que se reproducen fielmente todos las manifestaciones articulares, aunque tiene el inconveniente de que sólo unas pocas cepas de ratón son sensibles y desarrollan la enfermedad[1]. En este sentido, el modelo por transferencia de suero K/BxN no tiene ese problema ya que se induce el proceso artrítico en cualquier cepa de ratón, incluso en animales *knock out*. No obstante, este modelo tiene algunas diferencias en el proceso inmunológico de la enfermedad, así como en los tipos celulares que participan[2]. Ambos permiten seguir la evolución clínica de la artritis y determinar la participación de los diferentes tipos celulares, como neutrófilos, macrófagos, linfocitos, etc. y de mediadores inflamatorios como citocinas, quimiocinas, etc. Además, permiten evaluar la degradación articular y ósea. El modelo de CIA es imprescindible para estudiar la fase de inducción de la artritis, mientras que el modelo de transferencia de suero K/BxN es útil para estudiar la fase efectora de la enfermedad. En conclusión, se dispone de distintos modelos con los que estudiar los mecanismos implicados en la artritis reumatoide y los potenciales fármacos para su tratamiento. La importancia de su elección radica en las ventajas e inconvenientes de cada uno[3]. Se utilizará uno u otro modelo según la fase del proceso que se quiera estudiar, siendo conveniente la realización de ambos cuando se tenga que caracterizar el perfil antiartrítico de un nuevo principio activo.

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P-14

Sistema óptico de monitorización en tiempo real. Aplicación al seguimiento de la amplificación isotérmica de ADN

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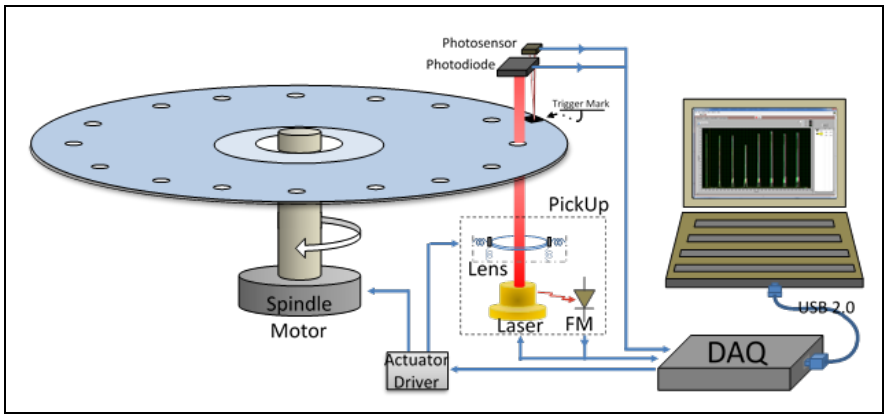
Los sistemas *point-of-care* presentan un elevado interés científico-tecnológico dada la necesidad de información de calidad. Esto implica el desarrollo de dispositivos/detectores de altas prestaciones, pero a un bajo coste. El presente estudio presenta un sistema óptico de detección basado en una unidad estándar de disco compacto para la monitorización y cuantificación en tiempo real de la señal transmitida a través del disco. Las principales características del sistema son: control de la velocidad radial del disco, fuente laser seleccionable de 780nm o 650nm, control de la potencia óptica del láser, ajuste de la lente de enfoque del cabezal y detector de fotodiodo de silicio. Además, dispone de un fotosensor para sincronizar el inicio de la captura con el giro del disco. La señal registrada por el fotodiodo es amplificada, filtrada y digitalizada por una tarjeta de adquisición de datos. Los datos capturados son enviados al ordenador personal para su procesado y análisis.

El prototipo desarrollado ha sido aplicado como herramienta analítica en seguridad alimentaria. Concretamente, se ha utilizado para la medida turbidimétrica y colorimétrica generada durante la amplificación isotérmica de ADN de patógenos alimentarios[1].



Esquema del sistema óptico de detección

Agradecimientos: PROMETEO II 2014/040, CTQ2013-45875-R

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P-15

Towards a new in vitro diagnostic tool for multiple determination of environmental allergen-specific IgEs

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Keywords: Environmental allergy, Microarray, Diagnostic, DVD.

Reliable methods for the determination of environmental allergen-specific IgEs are vital for the investigation and diagnosis of derived allergic diseases. The routine allergy diagnosis is performed by skin prick testing or using in vitro tests, such as RAST, ELISA, or fluorescent enzyme immunoassay (FEIA). Although skin testing is sensitive, in vitro testing has some advantages including precise quantitation, safety, lack of drug interference, and the possibility of long-term storage of specimens.[1]

The aim of this research work was to develop and validate a fully functional multi-analyte assay for the detection of IgE specific antibodies for 12 different environmental allergen proteins. The introducing of compact disc technology as platforms improves the in vitro diagnosis of IgE antibodies in human serum. The developed immunoassay is summarized as following; 25 µL of conditioned serum sample were incubated for 5 minutes with Au-labeled Anti-IgE at a concentration range of 1/100. The solution was dispensed on the DVD microarrays of 3 x 14 spots (12 specific allergen proteins, positive and negative controls) for 15 minutes. The immunoreaction was developed using silver enhancer solution (8 minutes). The results were measured using a DVD drive and analysed using a specific data analysis software. The total assay time was less than 30 minutes, reaching high sensitivity and selectivity. An entirely new, technologically advanced, effective, economically competitive and affordable allergy diagnostic tool is developed.

Acknowledgements
FEDER, MINECO (CTQ2013-45875-R), Generalitat Valenciana (PROMETEO II 2014/040 and Programa Santiago Grisolía; Grisolía/2013/040) are gratefully acknowledged.

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P-16

Isothermal bridge amplification and electrochemical detection for reliable and cost effective molecular diagnostics

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We aim to develop generic electrochemical platforms for rapid DNA amplification, detection, quantification and sequencing. The platforms will be based on 3 different technologies:

a) Recombinase polymerase amplification (RPA)
b) Electrochemical detection
c) Bridge amplification

In order to develop a thermocycler free DNA platform, the isothermal RPA technology has been chosen. It has been selected among other isothermal technologies because it is simpler, operates in a range of 37-41ºC, provides high sensitivity and selectivity, can incorporate modified nucleotides and it is the fastest amplification technology available.

We want to take advantage of RPA properties to incorporate electrochemically tagged dNTPs into the amplicons. With this strategy, the amplicons generated by RPA could be potentially measured after amplification without further steps. We also selected electrochemical detection as it allows miniaturization with the consequent reduction in cost, and also because the instrumentation required is less expensive, when compared to optical detection devices. Finally, we chose to develop amplification in a bridge amplification format to address problems with multiplexing. In bridge amplification, the primers for a certain target are immobilized onto a surface and no primers are found in solution. This strategy avoids primer-dimer problems and additionally can be designed to create spatially resolved primer spots for different targets, allowing then multiplexing.

P-17

Zeolites and MOFs: what they are and their use in sensing applications

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In this contribution we present selected materials in whose preparation we have a wide background; they are zeolites and Metal Organic Frameworks (MOFs). Their unique properties are highlighted and illustrative examples in sensing applications are given with the aim to awaken curiosity and collaboration with groups at our institutes.

Zeolites are a class of crystalline microporous materials whose basic building blocks are SiO_4 tetrahedra, although Si atoms can be substituted by other elements to affect the properties of the material. In its turn, MOFs are a class of crystalline hybrid materials composed of metal ions or clusters bridged by organic linkers. Both zeolites and Metal Organic Frameworks can be designed with pore apertures of molecular size, leading to materials with shape selectivity or molecular sieve properties that allow the design of novel sensors or the improvement of existing ones.[1]

Many MOFs have been used for sensor applications. For instance, Corma et al. reported the use of ITQMOF-2 (Figure 1) as a sensor for detection of ethanol.[2] Similarly, many zeolites have been proposed as sensors, even in heavy duty applications such as combustion processes, thanks to their remarkable thermal and hydrothermal stability. [3]

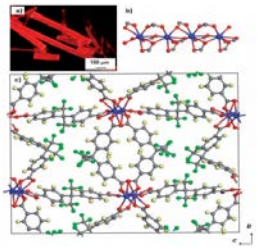

Figure 1. a) ITQMOF-2-Eu UV light optical microscopy image. b) and c) Solid structure solved by XRD.

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P-18

Desarrollo de un microarray de proteínas para la detección de *Campylobacter spp.*

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En la actualidad la campilobacteriosis es la toxiinfección alimentaria más frecuente en la Unión Europea, siendo su principal fuente de infección la carne de pollo y sus derivados[1]. Es por este motivo que las autoridades europeas han priorizado la reducción de *Campylobacter spp*.a nivel de producción primaria para evitar su paso a la cadena alimentaria. En la actualidad la identificación de la bacteria se lleva a cabo mediante métodos de cultivo tradicionales basados en la norma ISO 10272-1:2006[2]. Esta metodología resulta muy lenta y tediosa, ya que requiere 5 días para el aislamiento y caracterización del microorganismo. Por ello, el desarrollo de métodos más efectivos de detección y cuantificación de la bacteria resultan imprescindibles desde el punto de vista de la salud pública y la seguridad alimentaria. En este contexto, el objetivo de este estudio es el desarrollo de un inmunoensayo competitivo en formato de array sobre chips de policarbonato con detección colorimétrica para la cuantificación rápida de *Campylobacter spp*. Mediante esta tecnología se ha determinado cuantitativamente la bacteria a niveles de 10^3 UFC/mL, en cultivo puro. Esto conlleva una serie de ventajas respecto a los métodos tradicionales ya que permite disminuir el tiempo de análisis, y posibilita la automatización del ensayo y el análisis múltiple a escala de producción. Las prestaciones analíticas del ensayo desarrollado hacen de esta metodología una aproximación muy interesante para la detección de *Campylobacter spp. in situ* tanto a nivel de producción primaria, en matadero y en granja, lo que facilita la toma de decisiones y medidas de control.

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P-19

Synthesis of Novel Hydrogen-Bonded Rotaxanes *via* Suzuki-Miyaura Coupling Reactions

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Mechanically interlocked systems able to perform controllable motions are highly attractive for the design of a molecular devices.[1] The ability to reach a spatial organization of these compounds at the solid state and the exportation of their properties to the macroscopic world are vital for the fabrication of such devices. In this arena, [2]rotaxanes are considered one of the most appealing scaffolds for the construction of functional materials.[2]

Herein we present the synthesis of a hydrogen-bonded [2]rotaxane starting from a thread that acts as template, through a five-component clipping reaction. Using it as starting material, a wide range of functionalized interlocked derivatives can be obtained in a straightforward Suzuki-Miyaura cross-coupling protocol.[3] The dynamics of these interlocked compouns were studied in solution, obtaining the rotation energy barriers of the different macrocycles around the thread. Moreover several efforts are still going on in our laborarory to incorporate these molecules in different materials.

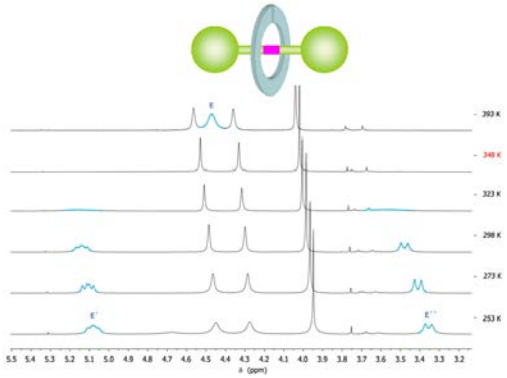

Figure 1. Variation Temperature ^{1}H NMR experiment to obtain rotation energy barrier of a functionalized hydrogen-bonding [2]rotaxane.

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P-20

BODIPY dyes functionalized with Benzylamine as a selective fluorogenic detection of serotonin

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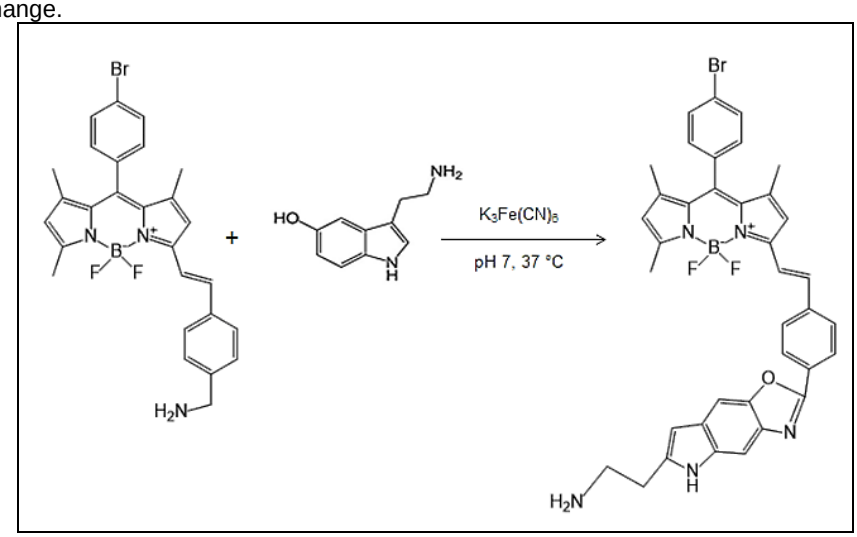
Serotonin (5-hydroxytryptamine, or 5-HT) is a biogenic amine that acts as a neurotransmitter in the central and peripheral nervous systems. It is present in a variety of organisms, ranging from humans to species such as worms that have primitive nervous systems, and mediates a variety of physiological responses in distinct cell types. It is believed to play a role in the regulation of various cognitive and behavioral functions, including sleep, mood, pain, depression, anxiety, aggression, and learning. Disruptions in serotonergic systems have been implicated as a critical factor in mental disorders such as schizophrenia, depression, infantile autism, and obsessive compulsive disorder. [1]

The detection of serotonin and other neurotransmitters from different biological samples (serum, plasma, platelets, urine, saliva, and cerebrospinal liquid) are very important in clinical diagnosis. [2] For this reason, several methods for detection of serotonin have been developed. Most of them electrochemical methods, so it is working on developing a molecular probe for the detection of serotonin, using Bodipy dyes, because are very attractive functional groups for construction of molecular sensors because of their advantageous characteristics, such as sharp absorption and fluorescence bands, high extinction coefficients, high fluorescence quantum yields, and high stability against light and chemical reactions[3]. Bodipy dyes is functionalized with a benzylamine, making detection of serotonin by reacting catechol group with benzylamine catalyzed by Potassium hexacyanoferrate (III) in dimethyl sulphoxide, at a temperature of 37 ° C[3] , causing a fluorescent change.



System of serotonin detection

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P-21

Design of Novel Nanodevices to Induce Exon Skipping for Duchenne Muscular Dystrophy

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Duchenne Muscular Dystrophy (DMD), a fatal degenerative disease, is the most common type of muscular dystrophy affecting 1 in 3500 male newborns.[1] Mutations in the gen that encodes dystrophin generate a lack of functional protein that results in muscle weakness and progressive loss of mobility. This gene is the largest in the human genome and it was found that exon skipping of certain exons could restore the production of partially functional dystrophin.[2] Antisense oligonucleotides (AONs) are currently being used to induce exon skipping and some of them have reached clinical trials. However, their biodistribution, biostability and efficacy remain still a major hurdle for future applications.[3]

Polypurine reverse-Hoogsteen hairpins (PPRHs) are a special type of oligonucleotides that have emerged as efficient gene-silencing tools.[4] Their stability and low toxicity makes them ideal candidates to induce exon skipping for the treatment of DMD. Additionally, they could be easily associated to mesoporous silica nanoparticles (MSNs), since these platforms have been reported to increase the biodistribution and internalization of oligonucleotides, acting as effective gene delivery vehicles.[5]

In this project, a new nanodevice based on the combination of PPRHs and MSNs is presented as an innovative alternative to induce exon skipping in primary cell lines from patients with DMD disorder. Two PPRHs that target regions around the exon 51 of DMD pre-mRNA were chosen and associated with MSNs. The internalization of the PPRHs-MSNs system in mybolasts from three DMD patients was evaluated and compared with other traditional transfection agents. Finally, the exon skipping efficiency of the internalized PPRHs was studied in order to assess the application of this technique to restore the production of dystrophin in cells from DMD patients.

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P-22

WETTABILITY PROPERTIES OF SILANIZED GLASS SURFACES. STUDY OF DIFFERENT SILANE TREATMENTS

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In this work surface free energy components of different derivatized glass surfaces are obtained. Glass surfaces were derivatized with different vinyl silanes (VTMS: Vinyltrimetoxysilane, ATMS: Allyl trimethoxy silane, BTES: 3-Butenyl triethoxy silane; OTMS: 7-oetenyl trimethoxy silane, DTES: Docosenyl triethoxy silane, HFMS: hexadecafluorododec-1-yl trimethoxy silane). Once total free energies were calculated also polar and apolar components were obtained.

For the probes liquids tested, HFMS and BTES showed, respectively, the largest and lowest contact angles (Figure 1). When calculating surface free energies, HFMS shows the highest value and the lowest polar contribution. Wettability data allows to have information about surface free energies and which components are prevalent (Lisfshitz-van der Waasls or Lewis acid-base)[1] this allows an in-depth knowledge of interactions of surfaces with different molecules, especially when studying bio-interactions and biosensing recognition.

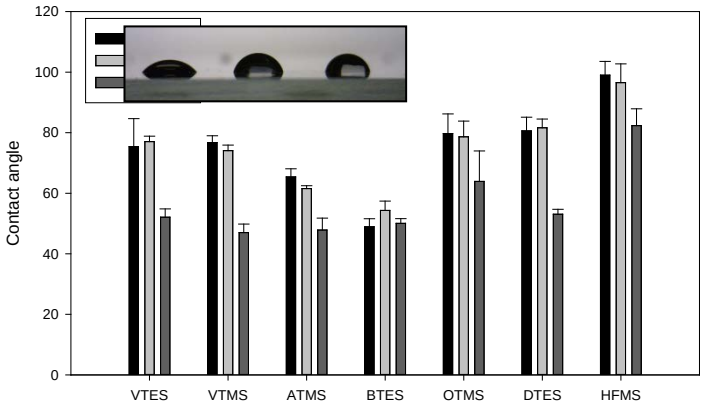

Figure 1. Contact angle of probe liquids on silanized surfaces.I

Acknowledgements
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P-23

RELATIOSHIP BETWEEN SURFACE DERIVATIZATION, WETTABILITY AND RECOGNITION IN BIOSENSING

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Biomolecular recognition events on surfaces are the basis of any biosensing device. The properties of these sensing systems are affected not only by the features of the recognition process used, but also by the physical properties of the surface itself, such as hydrophobicity and wettability. It is therefore interesting to learn how to modulate wettability of surfaces dedicated to biorecognition assays.

Our study uses biotin-streptavidin bonding as a model for biorecognition system.[1] In the applied scheme biotin is immobilized on a silanized silica surface and Cy5-labelled streptavidin is added in solution. Biotin immobilization is carried out by means of the click photochemical thiol-ene reaction between thiol-derivatized biotin[2] and an alkene-ended silica surface.[3] Surface wettability, estimated by measuring water contact angle (WCA), is set by derivatizing the surface with different alkene silanes, as well as with mixtures alkene-fluorinated silanes.

Results obtained by displaying Cy5 fluorescence in a CCD camera (Figure 1) show that thiolated biotin binds non-specifically on the hydrophilic native surface, but specific biointeraction is registered with alkene-derivatized glass such as vinyltrimethoxysilane (VTMS), better signals for hydrophobicity enhancing silanes docosenyltriethoxysilane and (DTES) hexadecafluorododec-11-en-1-yltrimethoxysilane (HFMS). However, mixtures of VTMS and 1H,1H,2H,2H-perfluorodecyltriethoxysilane (PFES), even 1/99, having the highest water contact angle led to very weak or no fluorescence signals, the fluorosilane hindering both the unspecific binding and thiol-ene reaction of biotin.

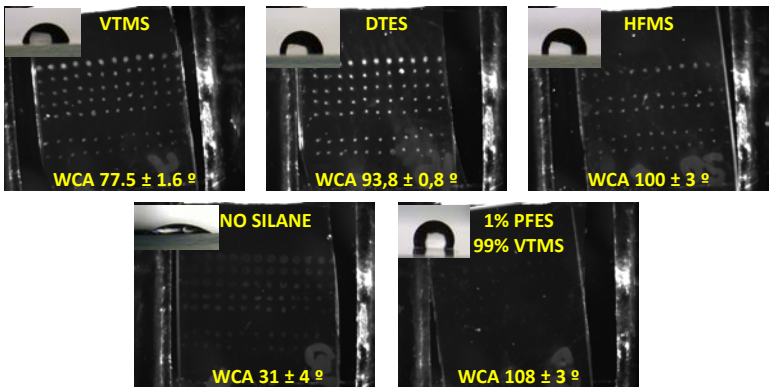

Figure 1. Comparison of the effectiveness in binding of Cy5-labelled streptavidin to immobilized biotin in diferent derivatized glass surfaces

Acknowledgements

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P-24

Molecular gate-like DNA as theranostic system for simultaneous drug delivery and radioimaging applications

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Development of nanobiomaterials for medical and biomedical applications has been increased day by day during the last decades. Among a great variety of nanobiomaterials, Mesoporous Silica Nanoparticles (MSN) arises as a great opportunity for medical and pharmaceutical sciences. Particularly molecular gate-like systems have excelled due to its capacity to prevent uncontrolled leakage of drugs before the application of the required stimulus for its action.[1] Commonly molecular-gate like MSNs were applied as drug delivery[2] and diagnostic systems.[3] Irruption of DNA nanotechnology in development of these systems promises a huge range of new possible applications.[4] Concretely, the application development of aptamers (oligonucleotides with a well-known conformation that allows them to bind specifically to target molecules)[5] highlighted because of its unique benefits as other targeting agents making them solid alternatives to antibodies and peptides in diagnostic assays. Combination of MSNs and aptamers have been successful for developing several recognition systems[6] and even they were applied for resonance imaging.[7] But as far we known the application of these systems for radioimaging diagnostic have not been explored. Combination of drug delivery systems with radiolabeling emerged as a powerful tool to develop nano-radiopharmaceuticals for theranostic (therapy + diagnostic) systems.

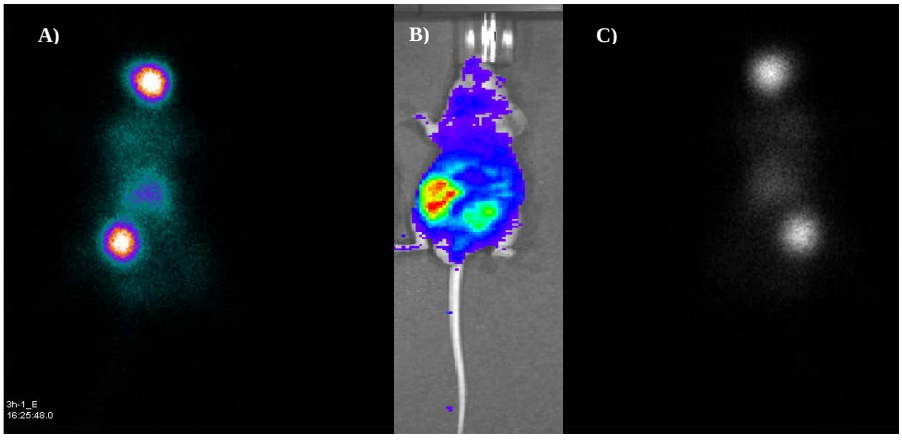

Figure 01. a) Planar imaging of inducted mouse with breast cancer after injection of loaded mesoporous silica capped with aptamer anti-MUC1. b) Bioluminescence images from nude mice on day 21 after intra-ventricular injection with $2x10^6$ Breast Cancer cells revealing tumoral lesions. c) Inverse Planar imaging of inducted mouse with breast cancer after injection of loaded mesoporous silica capped with aptamer anti-MUC1.

In this preliminar study we developed a new application of MSNs self-decorated with an antiMUC1 aptamer (responsive to the tumor marker mucine 1 glycoprotein)[8] as a nanoradiopharmaceutical for breast cancer

imaging. MSNs were firstly loaded with safranin O (a fluorogenic dye employed as model drug) and functionalized onto the surface with (3-aminopropyl)triethoxysilane. Finally antiMUC1 aptamer was immobilized electrostatically over the surface blocking the dye leakage from the pores. Characterization of the nanobiomaterial successfully confirmed the typical structural properties preserving its *on-command* drug delivery capability. For explore the nanoradiopharmeceutical applications nanobiomaterial was successfully labelled with 99mTc (over 98% of labelling) as quality controls confirmed. The behavior of the mesoporous silica self-decorated with antiMUC1 aptamer in inducted mice showed excellent results (high migration to tumor) as can be seen from planar imaging results (see **Fig.1**). Moreover biodistribution studies clearly confirmed also this uptake as can be seen on **Fig.2**.

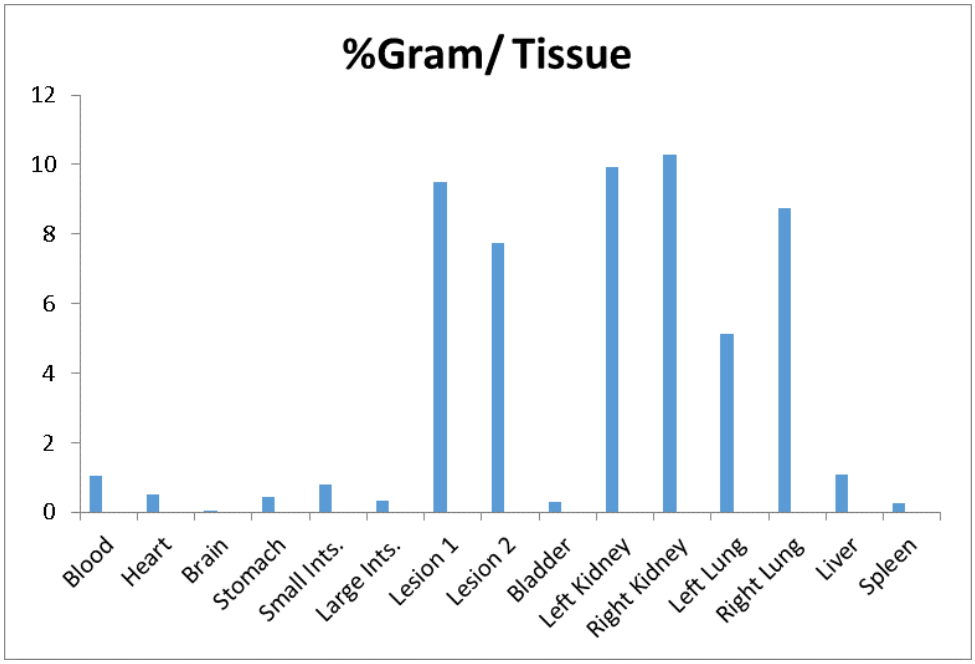

Figure 02. Biodistribution profile of S1-MUC1 in breast tumor inducted mouse expressed as percentage of radiation per gram of tissue

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P-25

TROVE2 superantigen in systemic lupus erythematosus patients. Chemistry and function.

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ABSTRACT:

INTRODUCTION

TROVE2/Ro60/SSA2 is a 60kDa protein which acts as an autoantigen in patients with rheumatic diseases such as Sjogren's syndrome (SS) or SLE. The TROVE2 protein acts as a quality control of non-coding RNA (5S-rRNA) and is also important for the survival of the cells towards the exposition to UV radiation.

PURPOSE

To study the TROVE2:hIgG antigenic recognition mechanism from SLE patients and healthy subjects using a TROVE2-based QCM-D biosensor.

METHODS

Cross-sectional prospective study of 20 SLE patients diagnosed according to the SLICC-ACR2012 criteria, from the Rheumatology Department of La Fe Hospital. All patients showed high anti-Ro Ab (SSA) concentrations (>200,0 U/mL). We have also taken 8 healthy individuals as negative controls, who had anti-Ro Ab concentrations <15 U/mL. A sensitive TROVE2-based QCM-D biosensor was developed.

RESULTS

Pre-steady-state analysis revealed an antibody bipolar bridging mechanism for SLE patients and healthy subjects. The major linear epitope recognized by anti-TROVE2 spanned GGMALALAVTKYKQRNGWSHKDLLRLSHLKPSSEGLAIVTKYITKGWKEVH sequence (aa 160-210) for healthy subjects. However, the major epitope in SLE serum is undiscovered. The difference between both epitopes corresponds to a majority necrosis-induced specificity in SLE patients, and an apoptotic pathway in healthy subjects. On the other hand, TROVE2 can be also used as a "*YES-logic gate"* capable of binding to Fcs, depending on alkaline earth cations in solution. Results suggest that the TROVE2-TRIM21α binding is a calcium-dependent protein interaction linked through the MIDAS-like motif in the vWFA-like domain (Figure 1).

CONCLUSIONS

A TROVE2-based QCM-D biosensor allows quantifying anti-TROVE2 antibodies in sera of SLE patients and healthy subjects at 0.05 U/mL level. The analysis of raw samples can be easily done since 40-fold dilution guarantees removing endogenous interactions due to the matrix effect.

The mechanism of hIgGs-TROVE2 interactions was defined as an antibody-bipolar bridging mechanism for SLE and healthy subjects. TROVE2 was also defined as a calcium-binding protein with a *YES-logic gate* involved in cell degradation processes which might be a crucial factor for development of SLE. Knowledge about this synergy may contribute to design novel metallodrugs, controlling the interaction that causes potential cellular damage.

ACKNOWLEDGMENT

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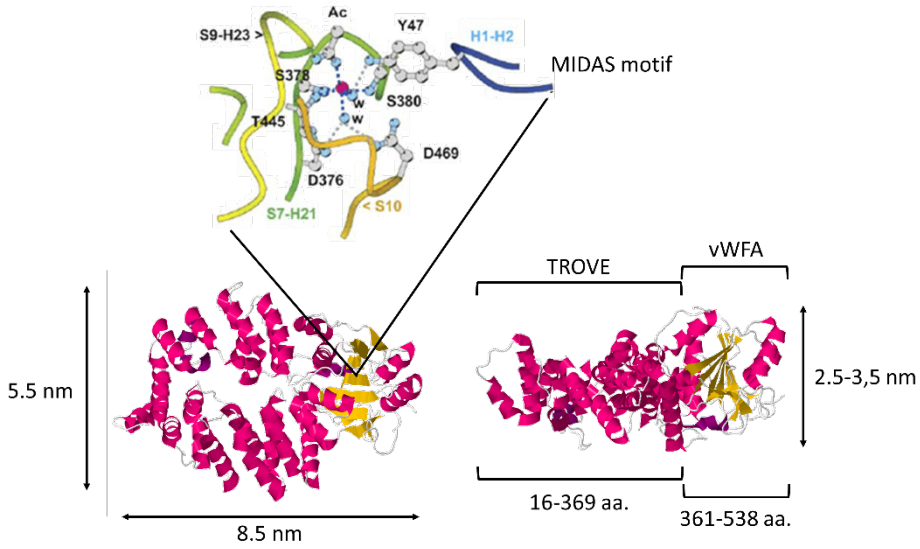

Figure 2.- Dimensions and domains of the TROVE2 protein.

P-26

SYNTHESIS AND CHARACTERIZATION OF IMIDAZOLIUM FUNCTIONALIZED SILICA BASED MESOPOROUS MATERIALS USING GLUTAMIC SURFACTANT WITH DIFFERENT LENGTH TAILS

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Mesoporous molecular materials attract Scientifics' interest due to many properties that confers to this material a huge field of applications. The applications of these materials fundamentally depends on the empty volume distribution, i.e. a pore size range from 2 to 50 nanometers, a regular spatial pore distribution, high specific area and pore volume, molecular polarity, size and the presence of boxes, canals.

The aim of this study is to synthesize other stable mesoporous materials with different porosity distribution. For this, we will use the co-structuring agent route, and anionic surfactants, which allows the exhaustive functionalization of the inner surface of the final porous material.

One manner to fine tune the applications of mesoporous materials based in silica is with the functionalization of the inner surface with an organic constituent with the goal of fine tune the interaction with specific samples or some polymeric matrix. In this case, the organic constituents used are imidazolium alkoxysilanes derivative groups as the co-structuring agent and glutamic surfactant with

different length tails. According to the g-Parameter model[1], porosities with different curvature are supposed to be obtained. Hence, size, charge and shape of surfactants are important structure-determining parameters. Larger head-group surfactants are used with the objective to generate maximum surface curvature.

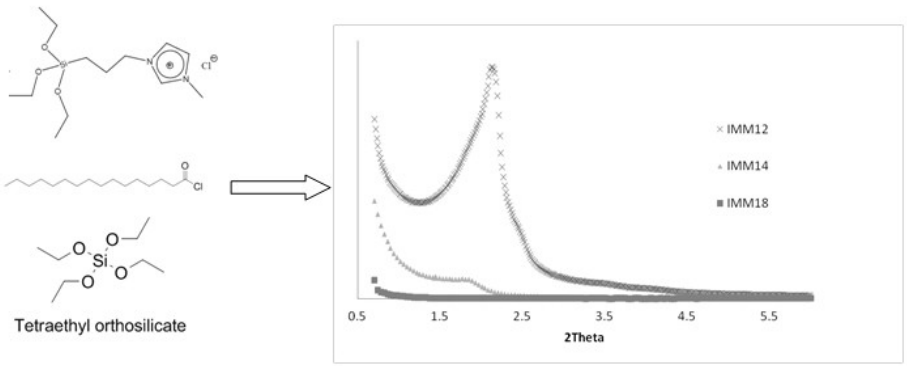

Fig.1- Synthesis of mesoporous materials with the co-structuring agent and glutamic surfactant and the obtained results.

Surface's functionalization using the co-condensation route permits the synthesis and polymerization of silica in a one stage reaction with organic groups uniformly distributed both inside the pores and over the surface[2]. On the contrary, grafting method only allows to organic group to be grafted in external surface and near pore entrance, involving problems as oligomerization at the pore entrance locking the pores[3].

The mesoporous material obtained with the co-condensation method will be characterized with a number of techniques such as X-Ray Diffraction, nuclear magnetic resonance, thermogravimetic analysis, N_2 adsorption and UV-vis spectroscopy.

Finally, we show the adsorption performance using several anionic dyes as adsorbates with different molecular size with a dual purpose, on one hand, to show their adsorption capacity, a useful parameter to decontaminate waste water from textile industry[4]. On the other, to characterize in a pretty realistic manner the window of access to the porous system loading the synthesized material with dyes and measuring the ability for different anions to displace the dye, which is then measured by UV-vis spectroscopy and representing an isothermal adsorption[5].

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P-27

INCREMENTO DE LA PERMEABILIDAD DE ATENOLOL MEDIANTE LA FORMACIÓN DE UN PAR-IÓNICO CON AZUL BRILLANTE

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El atenolol es un fármaco básico, con un pK_a de 9.6 y una amina secundaria en su estructura; se encuentra ionizado con carga positiva en el rango de pH fisiológico. Su carácter hidrófilo y elevada polaridad son los principales responsables de su baja permeabilidad intestinal, ya que las membranas biológicas que debe atravesar para alcanzar su lugar de acción son de naturaleza lipídica[1]. El desarrollo de un par-iónico es una estrategia útil para aumentar la lipofilia de compuestos ionizables. Consiste en la unión por atracción electrostática de dos moléculas de carga opuesta, formando un complejo de carga neta neutra y, por tanto, más lipófilo[2].

Por todo ello, el objetivo del presente trabajo es estudiar el incremento de permeabilidad del atenolol en colon de rata mediante la formación de un par-iónico y comprobar que dicho incremento se debe a la formación del par-iónico y no a un posible efecto del contra ion sobre la membrana del colon.

Tras una búsqueda bibliográfica se seleccionó el azul brillante como ion apropiado para formar el par-iónico con el atenolol. En primer lugar, se realizó un estudio *in vitro* en el que se evaluó el aumento de lipofilia del atenolol en presencia de azul brillante, mediante el cálculo del coeficiente de reparto. A continuación, se determinó la permeabilidad del atenolol en colon de rata utilizando disoluciones del fármaco en presencia y en ausencia de azul brillante mediante una técnica de perfusión *in situ*[3]. En último lugar, se perfundió el contra ion con rojo fenol, compuesto usado como marcador de posibles lesiones de la membrana intestinal por presentar una absorción despreciable siempre que la membrana intestinal no se encuentre alterada[4].

Los resultados obtenidos muestran que el aumento de permeabilidad observado en el atenolol en presencia de azul brillante es debido a la formación de un par-iónico. Por tanto, la permeabilidad del atenolol se podría incrementar coadministrándolo con azul brillante debido a la formación de un par-iónico entre los dos compuestos.

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P-28

A selective chemosensor for the chromo-fluorogenic detection of Cu^{2+}

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The development of chromo-fluorogenic probes for the sensitive and selective detection of transition metal cations has increased in interest in the last years.[1] The vast majority of the prepared sensors used the biding site-signaling subunit approach in which a coordinative unit and a dye/fluorophore are covalently linked. In these probes interaction of metal cations with the coordinative unit induced marked changes in UV-visible and emission features of the chemosensor. Detection and quantification of Cu^{2+} is of special interest because has several uses such as wires, electronic devices, architecture, antifouling applications, antimicrobial and folk medicine. Taking into account the above mentioned task, several chromo-fluorogenic probes for Cu^{2+} has been recently developed.[2]

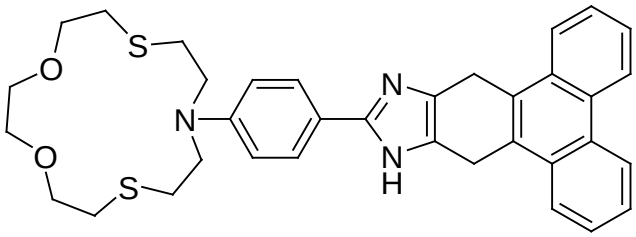

Figure 1. Chemical structure of the chromo-fluorogenic probe.

In this work we presented the synthesis and coordination behavior of a chromo-fluorogenic probe for the selective detection of Cu^{2+} cation (see Figure 1). Water-acetonitrile 1:1 v/v (pH 7.4) solutions of probe showed an UV band centered at 340 nm that suffers a selective bathochromic shift to 235 nm only in the presence of Cu^{2+} cation (with a color change from colorless to purple clearly visible with the naked eye). The induced bathochromic shift indicated that Cu^{2+} cation interacts with the acceptor part of the probe, namely, the nitrogen atoms of the imidazole heterocycle.

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P-29

NANOMINIATURIZATION AND QUANTUM COMPUTING

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Like a compass, an electron magnetic field (MF) dictates the binary code of either "0" or "1".[1–3] In a quantum system, particles can exist in two states simultaneously too (*superposition*). A two-quantum bit (*qubit*) system can perform simultaneous operations on four values, a three-qubit system, on eight values, *etc*. A quantum computer with 300 qubits could hold $2^{300} \sim 10^{90}$ values simultaneously (number of atoms in the universe) performing an incredible quantity of calculations at once. A quantum leap in processors? Beyond Si? Will such a technology really scale in the way it needs to? Provisional conclusions follow. (1) Main problem to design qubits is decoherence minimization, particularly from nuclear spins and dipolar interactions. The use of molecular spin qubits offers advantages (*i.e*., reduced decoherence, high reproducibility). Research is oriented to a better understanding of these basic yet extremely fragile building blocks. As the size of an object becomes increasingly smaller, quantum (entaglement) effects becomes increasingly important. (2) Something wrong exists in quantum mechanics. It predicts probabilities for experiments, not certainties. However, the formal mathematics of quantum mechanics predicts the quantum state with certainty. The mathematical conclusion is a Schrödinger's cat that is both alive and dead. Those people who observe Schrödinger's cat are also in a superposition of two states, but no way exists they can be aware of their other half. (3) Physics continues to make important contributions, which make a difference to everyone's life (*e.g*., new materials, progress in fluid dynamics, miniaturization techniques, quantum manipulations with applications to computing). The future will include better batteries and solar cells, which will make a big difference in people's energy usage. Future developments include chips directly interfacing with other components *via* light rather than electrical signals. However, the really exciting possibilities will be those people have not yet imagined.

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P-30

CLASIFICACIÓN DE DIFERENTES TIPOS DE CAFÉ MEDIANTE NARIZ ELECTRÓNICA

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En la actualidad el uso de equipos electrónicos está siendo aplicado en diferentes áreas de la industria alimentaria[1] cuyo propósito es lograr que mediante su uso se puedan establecer patrones característicos[2], que permitan garantizar la seguridad de los alimentos.

En el caso del café, una de las bebidas más extendidas en el mundo, se hace necesario realizar un control de calidad rápido, sencillo y objetivo. Es por ello por lo que el café es objeto de estudio y análisis[3,4] en todos sus estados de procesado. Cabe destacar quizás que el proceso más importante en la elaboración del café es el tostado[5,6] del cual dependerá el desarrollo de uno u otros componentes, no solo volátiles sino también sabor y color característico.

El aroma del café se forma durante el proceso de tostión, el cual se compone de una mezcla compleja de compuestos volátiles en la que se destacan los principales compuestos en el café tostado como compuestos de azufre, triazinas, pirroles, fenoles, furanos, entre otros[6].

Este estudio ha sido realizado por el Grupo de Investigación e Innovación Alimentaria, en él se ha utilizado la nariz electrónica desarrollada por el Group of Electronic Development and Printed Sensors (ged+ps) del IDM como sistema para clasificación de tres tipos de cafés (cafe1, cafe2 y cafe3). La nariz dispone de una matriz de 12 sensores que son capaces de obtener un patrón o huella característica de cada uno de los distintos tipos de café, para que más tarde mediante análisis posteriores de los datos obtenidos, el sistema sea capaz de clasificar los distintos tipos de café medidos en este estudio.

Para el proceso de medida se ha determinado una metodología adecuada al tipo de muestra a estudiar. Durante las medidas los sensores han mostrado una respuesta dinámica y otra estable, la cual se ha utilizado para el análisis de los datos.

En la figura 1 se puede observar tanto la respuesta de los sensores como un análisis por componentes principales (PCA) de las muestras medidas.

En la respuesta de los sensores se puede observar que sensores son los que aportan mayor información. Estos son los sensores que presentan mayor dispersión en las medidas.

Por otro lado, en la PCA se observan tres agrupaciones principales, las cuales corresponden a los tres tipos de cafés medidos, por lo que a priori podemos distinguir los tres tipos de cafés atendiendo a las muestras medidas. Se realizarán distintos análisis para corroborar estos resultados preliminares.

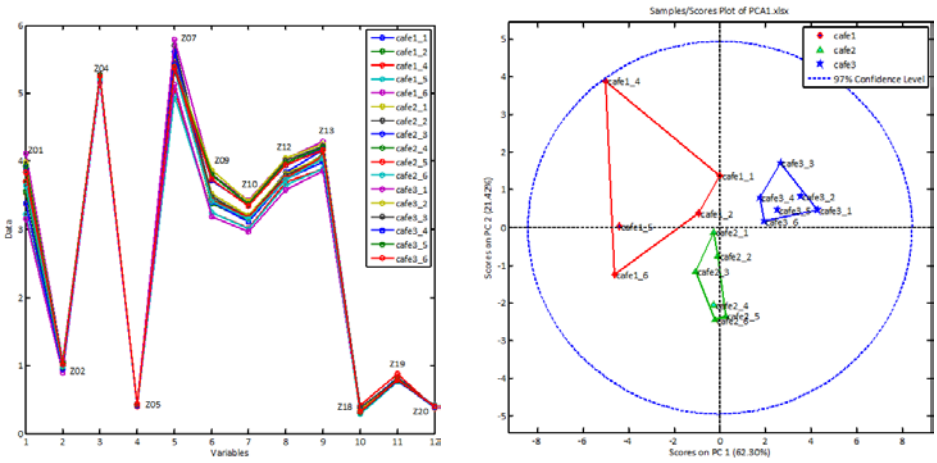

Figura 1: Respuesta de los sensores y PCA de los tres tipos de cafés.

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P-31

HACIA LA DETECCIÓN DE FORMALDEHÍDO EMPLEANDO COMPUESTOS CASSETTE

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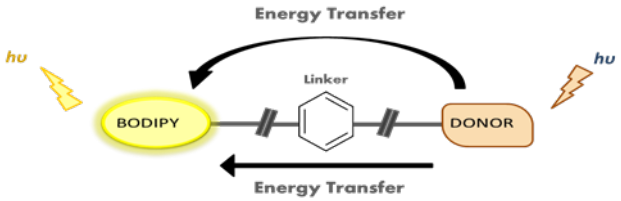
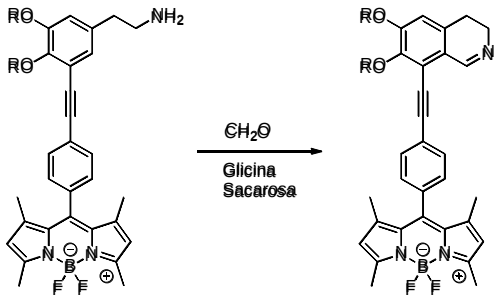
El formaldehído es uno de los compuestos orgánicos básicos más importantes de la industria química. Se encuentra principalmente junto con urea, melamina y fenol formando resinas destinadas a la industria de la madera y el mueble. Varias agencias dedicadas al estudio del cáncer, como la IARC o WHO, catalogan al formaldehido como irritante y carcinógeno. Los principales sistemas de detección para este compuesto tienen como inconveniente la baja sensibilidad y los falsos positivos en presencia de determinados interferentes. Estos hechos generan la necesidad de desarrollar sistemas capaces de detectar de forma fiable la presencia de formaldehido.

En los últimos años se ha llevado a cabo un gran desarrollo en la exploración de sistemas multifluoróforos con arquitecturas dador-aceptor o *cassettes*. Este tipo de sistemas están dominados por un mecanismo de transferencia de energía electrónica (EET), que consiste en la transferencia de energía entre dos cromóforos/fluoroforos.



En este trabajo, se combinará una feniletilamina como unidad coordinante o dadora y un núcleo de BODIPY como unidad señalizadora o aceptora. La molécula inicialmente propuesta es la mostrada a continuación, la cual reaccionará con formaldehído en presencia de una cantidad catalítica de glicina y sacarosa, dando lugar a la correspondiente dihidroisoquinolina.



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P-32

Drug photo-release system based on gold nanostars coated with mesoporous silica shell

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Currently, few drug photo-delivery systems based on plasmonic gold nanoparticles (AuNPs) and mesoporous gated materials that could be employed in cancer diagnosis and therapy have been developed. Gold nanostars (AuNSt) have not been used for this purpose in spite of their superior plasmonic properties and their increased uses in intracellular imaging applications. In this work, a novel drug photo-release system based on AuNSt coated with mesoporous silica shell (AuNSt@$mSiO_2$) was developed. AuNSt were directly coated with mesoporous silica shell using a surfactant-templated synthesis at 25 ^{o}C. Nanoparticles were characterized by Transmission Electron Microscopy, Field Emission Scanning Electron Microscopy, Energy Dispersive X-Ray Analysis and Visible-Near-Infrared (NIR) Spectroscopy. The hybrid nanoparticles contain a multi-branched gold core and mesoporous silica shell with pores extending radially. Mesoporous silica shell thickness was varied using different amount of silica precursor. Plasmonic properties of nanoparticles dramatically changed during silica coating process due to spatially-directed oxidation and reshaping of gold core. That's why, synthesis parameters were optimized for obtaining nanoparticles with suitable plasmonic properties for NIR laser induced drug delivery applications. AuNSt@$mSiO_2$ nanoparticles were loaded with rhodamine B (Rh) and the external surface was functionalized with octadecyltrimethoxysilane and heneicosane. The paraffin sets up a hydrophobic layer that blocks the pores and avoids dye release. AuNSt@mSiO2@Rh@paraffin nanoparticles aqueous suspension was irradiated using a laser at 808 nm to match the localized surface plasmon resonance (LSPR) band of nanoparticles. Cumulative release of rhodamine B was determined using fluorescence spectroscopy. NIR light induced heating of nanoparticles suspension was monitored using a fiber optic thermo-sensor. This hybrid nanosystem shows a good photo-delivery profile. Around 40 % of total released dye was delivered in the first 20 min NIR light irradiation at power density of 2 W/cm^2, whereas the control sample shows a negligible release; corroborating the gating efficacy of paraffin and the photothermal conversion efficiency of AuNSt. Dye photo-release and sample heating profile can be modulated using different nanoparticles concentrations and laser power densities. The system developed in this work is easier to synthesize than systems based on other types of AuNPs and thermosensible gatekeepers. That´s why, it could be employed in higher extension in nanomedicine, with potential applications in cancer diagnosis and therapy.

P-33

SYNTHESIS, CHARACTERISATION AND SENSING PERFORMANCE OF IMIDAZOLIUM FUNCTIONALISED MESOPOROUS MATERIALS USING ALANINE SURFACTANT DERIVATIVES WITH DIFFERENT TAIL LENGTHS

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Mesoporous molecular materials with a regular pore order were first noticed in 1992 by Mobil Oil Corporation investigators. These materials have a pore size range from 2 to 50 nanometers and have interesting properties like large surface area, uniform pore volume and pore size distribution, all of them very attractive properties for applications in catalysis, adsorption, pollution elimination and polymer-made matrix filler for gas separation[1].

The use of solid porous materials as active agents has received much attention in novel sensing protocols[2]. Silica-based MCM-41 type materials have been the most common solids used for these purposes.

Functionalization of silica materials with organic groups of these large surface solids is a common strategy in order to fine tune the interaction with specific samples or some polymeric matrices, as this property provides to this materials a wide range of applications[1].

The method used here to synthesize mesoporous materials is by the co-condensation route. Co-condensation allows the synthesis and polymerization of silica in a one-step reaction with organic groups uniformly distributed both inside the pores and over the surface.[3,4,5] Particularly, a method developed by Che et al.[6] based on the use of anionic surfactant and a positively charged silane derivative has been used.

In this work, we show our efforts to prepare and characterize stable ordered porous silica based solids using alanine surfactant derivatives and imidazolium silanes derivatives as CSDA. This method provides a high surface density of imidazolium pendant moieties, whose proximity and permanent electrostatic positive charge, independent of the pH value, provides a suitable host to carry out sensing activities for anions.

Several anionic surfactants were used in this work, all of them keeping the same small aminoacid as a headgroup (alanine) but we studied the variation of the length of the tails of surfactants from a hydrocarbon chain of 12 carbons into 14, 16 and 18 C. The reason for this variation lies in the subsequent variation of the ratio known as surfactant packing parameter or simply *g*-parameter[7].

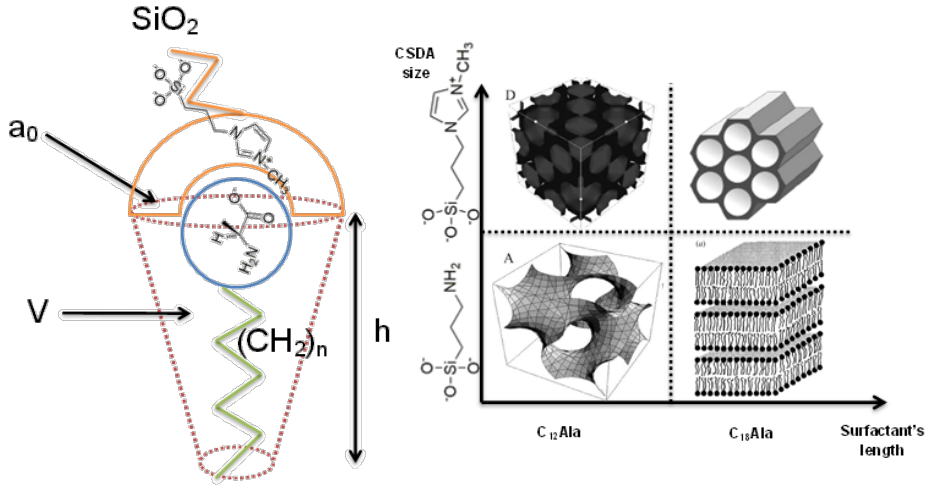

Figure 1. Definition of surfactant packing parameter *g* and structural variations.

The definition of this parameter is $g=V/a_0h$. By changing the g-parameter the geometry and topology of the mesopores is modified too according to Figure 1.

Stability of the structures will be examined with the extraction of the surfactants, and materials will be characterised with X-ray diffraction, nuclear magnetic resonance, thermogravimetric assays, IR spectroscopy and adsorption isotherms.

We assess the sensing performance by loading the solids with a dye and measuring the ability for different anions to displace the dye, which is then measured by UV-vis spectroscopy. Presumably, selectivity towards some analytes between different structures obtained with different surfactants will be variable as it depends on the pore size, distance between binding sites, analyte size and electrostatic affinity.

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P-34

NOU ECOSISTEMA PER AL DESENVOLUPAMENT DE XARXES DE SENSORS MÒBILS I ROBUSTES

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En l'última dècada tant les xarxes sense fils com els dispositius sensors han experimentat un enorme avanç quant a prestacions i noves tecnologies. Aquest avanç a portat al fet que aquest tipus de sistemes s'estiguen incorporant en entorns que fa uns anys la idea no era concebible [1].

En aquest treball es proposa un ecosistema complet per al disseny i avaluació de xarxes de sensors mòbils, que permeta el desenvolupament de xarxes de sensors amb mobilitat i garantía de funcionament que per tant poden aplicar-se a entorns crítics, seguiment i monitorització de matèries primeres o aliments, i un llarg etcètera.

Aquest ecosistema està format tant per programari con maquinari, permetent cobrir totes les etapes del anàlisi, disseny i implementació d'aquestes xarxes de sensors, i que permet proposar i avaluar noves millores del protocols implementats.

L'ecosistema proposat integra el simulador de mobilitat SUMO [2], que proporciona una sèrie de patrons de mobilitat, que prèviament han hagut de ser generats i analitzats, i permet generar comportaments similars al món real. La creació d'escenaris en SUMO es pot realitzar de dues formes, una mitjançant la descàrrega de mapes en format XML o mitjançant l'edició de fitxers XML. Si s'empra la primera opció, accedint previ registre a *OpenStreetMap* es pot descarregar la zona on es va a produir la mobilitat dels sensors, com pot observar-se en la figura 1.

Fig. 1- Exemple d'àrea de mobilitat en el simulador SUMO

Quan el mapa estiga descarregat cal convertir-ho a format XML, açò es realitza amb l'ajuda de la ordre *netconvert* de SUMO. Una vegada completat aquest pas s'obté el fitxer XML que conforma la xarxa dels nodes que formen els carrers, carreteres, etc.

Una vegada arribats fins a aquest punt, es procedeix a l'edició del fitxer de configuració de la simulació, per a açò, cal crear un fitxer amb extensió .cfg, on s'indicaran els fitxers que conformen la xarxa i les rutes, així com els paràmetres necessaris per a l'inici i finalització de la simulació de mobilitat, la grandària d'increment entre cada instant, entre uns altres.

Finalment, amb l'ajuda del script *traceExporter.py* que incorpora SUMO obtindrem el fitxer de configuració per al simulador de xarxes NS-3 [3], que constitueix la següent etapa en el dissseny de les xarxes de sensors mòbils com es pot apreciar en la figura 2, i el qual ens permetrà ajustar els paràmetres de funcionament de la xarxa de sensors i preveure el seu funcionament baix diferents models i condicions, estudiant l'evolució de les comunicacions i l'estat dels sensors. Finalment el maquinari integrat fins el

moment consisteix en la placa BeagleBone Black per a la implementació dels nodes de la xarxa de sensors amb el middleware ROS [4], però s'espera en el futur integrar més maquinari i dispositius que ens permeten ampliar les plataformes físiques per als sensors.

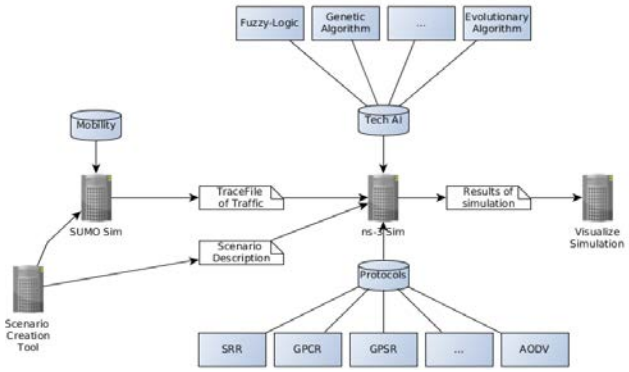

Fig. 2- Diagrama de blocs de l'ecosistema proposat

Amb les eines emprades s'ha obtingut un ecosistema maquinari/programari escalable i amb el qual poder dissenyar i implementar xarxes de sensors mòbils que permet guiar les decisions del dissenyador des de les primeres etapes i verificar el seu comportament en nodes sensors reals, d'aquesta forma s'obté a més un feedback entre l'avaluació per simulació i experimentació/validació en equips reals, millorant i optimitzant les etapes de re-disseny programari/maquinari i proporcionant una metodologia per implementar xarxes de sensors mòbils robustes.

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P-35

UN MODEL DE XARXA DE SENSORS INTEL·LIGENT PER A APLICACIONS CRÍTIQUES E-SALUT

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En aquest treball es presenta un estudi dels protocols per a xarxes de sensors proposant-se un nou model que incorpora tècniques intel·ligents ampliant les possibilitats reals d'aplicació de les xarxes de sensors a entorns de eSalut.

Els protocols d'encaminament per xarxes de sensors es divideixen en dos grans grups, els protocols basats per l'encaminament i els basats per localització geogràfica. El primer grup a més a més, es divideix en altres dos subgrups, els basats amb protocols reactius i amb els proactius. La diferència amb ambdós subtipus de protocols es que al cas dels reactius adquireixen la informació d'encaminament al moment exacte que es necessita, i en canvi estan constantment transmitent-la i sol□licitant-la. Els protocols m□es representatius d'estudi son AODV i DSR en quant al reactius, i OLSR i DSDV en quant als proactius. Pel que fa als protocols basats per geolocalització es caracteritzen per emprar dispositius GPS per al seu correcte funcionament. Als últims anys a aquest tipus de protocols se'ls ha anat afegint tècniques d'intel·ligència artificial per optimitzar i fer-los més robustos fiables.

S'ha desenvolupat un nou model de enrutament basat en el descrit en *Stability and Reliabilty Aware Routing* (SRR) [1], però sobre el qual s'han realitzat modificacions i incorporat certes millores, de cara a la seua aplicació en entorns crítics. El model s'ha desenvolupat per a ns-3 [2], mostrant-se el diagrama de flux en la figura 1.

Aquest protocol té dues maneres de funcionament: una mode connectivitat, en el qual existeix una xarxa ad-hoc que permet que els nodes sensors es comuniquen
entre ells sense la necessitat que existisca un infraestructura V2I i que estiguen sempre dins d'un radi de cobertura.

Quan s'envien els paquets cap al node destí es prenen una sèrie de decisions. Per al càlcul d'aquestes decisions es calcula la distància i adreça, a més de l'angle que existeix entre el node font i el node destí i l'orientació. Açò fa que l'enviament de paquets siga més directe per a aconseguir la destinació.

Els paràmetres de la distància, i orientació es calculen perquè el lliurament dels paquets siga més òptima i robusta, emprant-se un sistema basat en lògica difusa. Amb aquest sistema obté una funció de cost que serveix per a indicar què node sensors és el millor candidat per a aconseguir la destinació.

El segon mode de funcionament, s'activa quan el node transmissor ha perdut la connectivitat amb la resta de nodes sensors, açò es deu al fet que no existeix cap node sensor dins del radi d'abast, és el mateix que dir que la seua taula de veïns està buida. En aquesta manera els paquets es van guardant en una cua i periòdicament s'intenta enviar els paquets feia la destinació. En el cas de no tenir connectivitat durant un temps si la cua s'ha omplert s'empra un *buffer* temporal. Quan ambdues cues estan plenes el protocol descarta aqueix paquet i torna a intentar entrar en connectivitat.

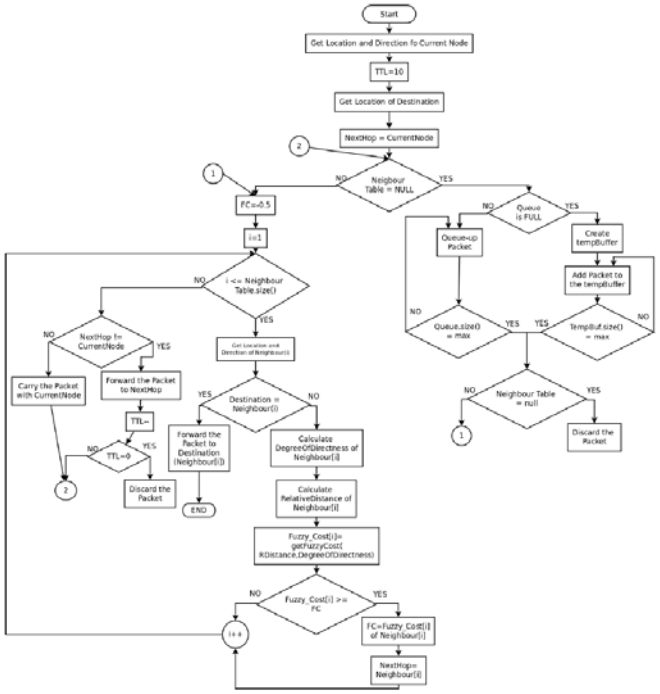

Fig. 1- Diagrama de flux del protocol proposat

S'ha dut a terme una completa avaluació del protocol proposat mitjançant simulació [3], utilitzant el simulador de xarxes ns-3 amb distints escenaris i condicions, obtenint-se en tots els casos resultats molt interessants respecte la taxa de paquets enviats, productivitat, taxa de paquets perduts, retard mitjà i sobrecàrrega del protocol, com pot observar-se en la figura 2.

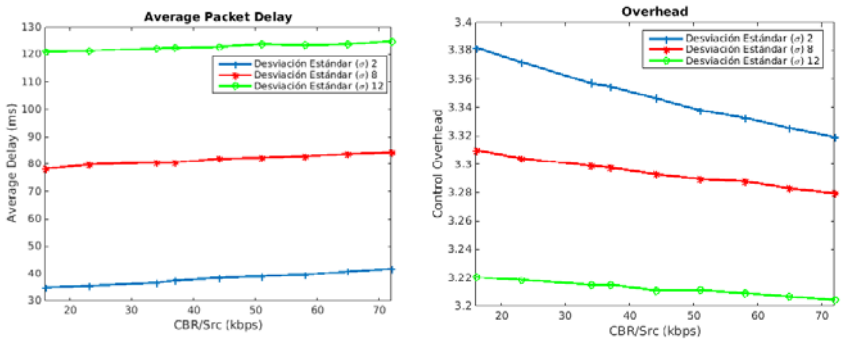

Fig. 2- Resultats obtinguts amb el nou model per xarxes de sensors en quant a retard mitjà (a) i sobrecàrrega del protocol (b)

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P-36

ACTIVITY OF ESSENTIAL OIL COMPONENTS AGAINST COLON CANCER IS ENHANCED THROUGH ENCASULATION INTO MESOPOROUS SILICA PARTICLES

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Plant secondary metabolites, such as essential oils and plant extracts have been widely studied for their antimicrobial, insecticidal, antifungal, acaricidal and antibacterial activities. Recently, activity against cancer of essential oil components (EOCs) has drawn much attention of researchers. In particular, some results suggest that EOCs may have therapeutic potential for the prevention and treatment of colon cancer[1]. Moreover the EOCs high volatility limits their application.

In contrast with traditional strategies for controlling the volatility of EOCs based on encapsulation into polymeric matrix, latest studies have shown the potential of mesoporous silica particles (MSP) as a suitable inorganic support for loading and release EOCs in a sustained manner [2].

This study evaluated the *in vitro* anticancer activity of selected EOCs (allyl-isothyocianate, carvacrol, cinnamaldehyde, diallyl disulfide, eugenol, and thymol) when loaded into mesoporous silica particles (MSP-EOCs) and when free. Microparticles and nanoparticles of MCM-41 were synthesized for the EOCs encapsulation. A controlled release evaluation of the MSP-EOCs in intracellular media was assessed and the cell viability of a colon carcinoma cell line (HCT-116) was evaluated after 24h and 48h of incubation.

It was found that the most EOCs encapsulated in the silica mesoporous material MCM-41 display remarkable inhibition of cell viability sustained in time when compared with free EOCs. These results pointed to the potential use of essential oil compounds encapsulated in mesoporous silica materials as an antitumor natural agent.

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P-37

Cámara termostática para experimentos de hipertermia y de liberación controlada

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Resumen:

La reproducibilidad es un aspecto crucial en la fase experimental, por ello es de suma importancia controlar el máximo número de variables de entorno en los factores variables en los ensayos. Los diferentes experimentos in vitro y ex vivo de hipertermia y liberación controlada requieren de unas condiciones térmicas determinadas, evitando las posibles fluctuaciones de temperatura del ambiente y a su vez, que ésta se adapte a las necesidades biológicas de los cultivos[1]. Así mismo, el correcto posicionamiento de los aplicadores y sensores también juega un papel muy importante en la optimización de los experimentos.

Con el ánimo de controlar la temperatura ambiental durante los ensayos en laboratorio, se presenta una cámara termostática aptada a experimentos de hipertermia y liberación controlada mediante aplicador láser y electromagnético, tanto en sistemas in vitro como para medios celulares. El equipo, además, sirve de base para el posicionamiento de los distintos elementos necesarios para los experimentos. En el caso de las aplicaciones fototérmicas, se dispone de unos accesorios para la fijación del cabezal láser y de la cámara CCD, que permiten el correcto centrado del spot láser en la muestra. Por otro lado su estructura es útil para el guiado de la sonda térmica de fibra óptica y para el soporte de la probeta o placa de cultivos (véase la figura 1).

Los experimentos realizados han verificado el excelente funcionamiento del equipo destacando la facilidad de uso y consiguiendo un ambiente con mínimas fluctuaciones.

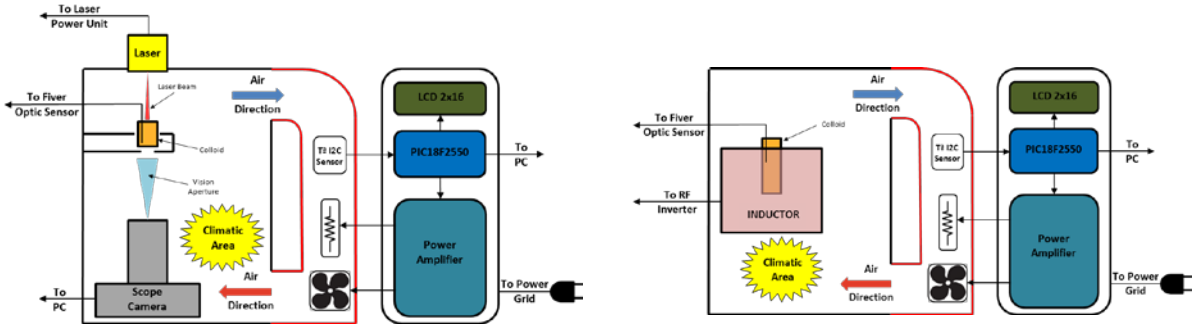

Figura 3: Esquema de la cámara termostática adaptada para experimentos láser (izquierda) y para experimentos electromagnéticos (derecha)

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P-38

Espectrofotómetro de bajo coste con Comunicación Inalámbrica

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Resumen:

La técnica de medida por espectrofotometría es una de las metodologías de análisis óptico más extendido en las áreas de química, biología, etc. Raro es no encontrarse con un espectrofotómetro en laboratorios de investigación donde su elevado coste hace que se consideren instrumentos delicados, manipulados habitualmente por personal cualificado. El principio básico de estos equipos consiste en la medición de la energía radiante que absorbe o transmite un sistema (químico, biológico, etc.) para una longitud de onda.

El proyecto consiste en el desarrollo de un espectrofotómetro de bajo coste[1] con componentes electrónicos económicos pero manteniendo la exactitud, calidad y sensibilidad de los equipos comerciales. Además, se ha incluido comunicación inalámbrica que permite la programación de una interfaz para que el usuario pueda recoger datos, graficarlos o incluso automatizar los ensayos.

El proyecto consta de las siguientes partes:

- El sistema electrónico basado en un microcontrolador de 8 bits donde se digitalizan las señales provenientes de los sensores que capturan la energía radiante y un módulo inalámbrico RF comunicado por protocolo USART. Todo el sistema electrónico se ha introducido en una caja con estanqueidad lumínica exterior.
- Interfaz gráfica de usuario programada en MATLAB donde el usuario podrá capturar los datos, visualizarlos y establecer temporizaciones para realizar ensayos.

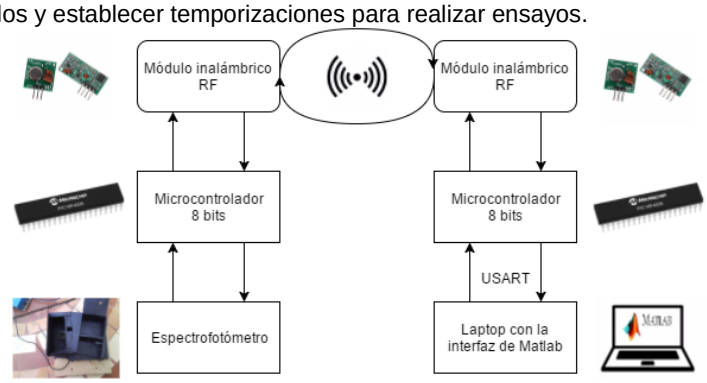

Figura 4: Esquema básico de un espectrofotómetro.

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P-39

Halogen-containing BODIPY derivatives for photodynamic therapy

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Photodynamic therapy (PDT) is a promising non-invasive technique for the treatment of a wide range of diseases including cancerous lesions through the selective destruction of the diseased tissue by light irradiation.[1] A photosensitizer (PS) molecule absorbs the energy of one photon becoming an excited state from which is able to react with dissolved molecular oxygen in the cellular environment, yielding singlet oxygen that induced oxidative stress, cell death and tissue destruction.[2] The use of BODIPY (boron dipyrromethene)-derivatives as PDT agents is an emerging and promising field for designing new PSs for improved PDT treatments. BODIPY is a family of molecules that present very suitable photophysical properties for its use as PDT agents. It is shown that including a heavy atom into the BODIPY core increase the quantum yield of singlet oxygen generation of BODIPY molecules by the heavy atom effect.[3]

In this work, it has been synthesized a panel of BODIPY-based photosynthesizers. Starting from a BODIPY core and adding one or two atoms of I or Br in one or both 2,6 positions in order to study how these substitutions are able to increase the properties as photosensitizer of these dyes. PDT behavior was further studied against four different cell lines: HeLa human cervix adenocarcinoma cells, MCF7 breast cancer cell line, SCC-13 squamous carcinoma cells and HaCaT immortal human keratinocyte with studies of *in vitro* phototoxicity, internalization and colocalization with organelle markers. Additionally, singlet oxygen quantum yield measurements and ROS generation measurement studies were performed.

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P-40

MODELO EXVIVO PARA EL ESTUDIO DE LA ACTIVIDAD CASPASA-1 EN MACRÓFAGOS PERITONEALES DE RATÓN

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El inflamasoma es un complejo multiprotéico que forma parte de la inmunidad innata. Actualmente se han descrito cuatro tipos de inflamasomas relacionados con procesos inflamatorios: NLRP1, NLRC4, NLRP3 y AIM-2. Estos complejos controlan y activan la caspasa-1, enzima responsable de la producción de las citocinas pro-inflamatorias como la interleucina-1β (IL-1β) e interleucina-18 (IL-18), aunque no es su única vía de producción.

La caspasa-1 se encuentra en la forma inactiva de procaspasa-1 localizada en el citosol de varias células como macrófagos, neuronas o células dendríticas. El inflamasoma se debe agrupar y ensamblar con el dominio de reclutamiento y la procaspasa-1 para lograr la formación de los dos hetereodímeros p20 (20kDa) y p10 (10kDa), correspondientes a la caspasa-1 activa 1. Este proceso se desencadena mediante distintos mecanismos como pueden ser cambios en la concentración de K+, aumento del ATP extracelular, generación de ROS intracelular o por estímulos inductores de inflamación como patrones moleculares asociados a patógenos y patrones moleculares asociados al peligro, característicos de un proceso inflamatorio.

En el presente estudio se lleva a cabo un modelo *ex-vivo* desarrollado en macrófagos peritoneales de ratón en los que se puede determinar la activación del tetrámero caspasa-1 ya que estas células son clave en la inmunidad innata. Para ello se inyecta al ratón tioglicolato vía intraperitoneal con el fin de estimular la presencia de macrófagos. Posteriormente se recogen las células del peritoneo y se siembran en placas de cultivo. Una vez adheridas son estimuladas con lipopolisacárido bacteriano (LPS) y ATP 2. Con ello se consigue modificar la conformación del inflamasoma y detectar la posible activación de la caspasa-1 por la liberación de la fracción p20. Esta fracción se detecta mediante Western Blot tras la purificación de las proteínas a partir de los sobrenadantes celulares. Paralelamente se determinan los niveles de las citocinas IL-1β e IL-18 resultantes de la actividad caspasa-1.

Estos modelo *ex-vivo* son idóneos para el estudio de nuevos fármacos antiinflamatorios que puedan actuar sobre el inflamasoma, posibilitando el conocimiento más detallado de los mecanismos de la activación de la caspasa-1. Además, son el paso previo para lograr estandarizar futuros modelos *in-vivo*, empleando incluso animales knockout condicionales, que nos ayuden a determinar la participación de estos complejos proteicos en patologías inflamatorias en las que se ven involucrados, como la artritis reumatoide, la enfermedad de Crohn, lupus eritematoso sistémico o la diabetes tipo II.

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P-41

CONTROLLED DELIVERY IN SENESCENT CELLS: GALACTOLIGOSACCHARIDE-CAPPED NANOPARTICLES AS SELECTIVE DRUG DELIVERY SYSTEM

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It is known that cellular senescence is a state of permanent cell-cycle arrest that proliferating cells can adopt in response to cellular stresses as a measure to avoid the replication and proliferation of damaged cells. Thus, like apoptosis, senescence can be considered as an emergency defence system for elimination of unwanted cells. Several events have been demonstrated to induce the senescent phenotype such as oncogene activation, telomere shortening, oxidative stress, DNA damage, and/or the action of cytotoxic drugs. In addition, senescent cells present several markers such as the absence of proliferative markers, senescence-associated β galactosidase (SA-β-Gal) activity, expression of tumour suppressors and cell cycle inhibitors and morphological changes.[1] It has been proposed that senescence is a key component of tissue remodelling both in normal development and physiology, and in multiple pathologies. An unified model must be considered, by which cellular senescence orchestrates tissue remodelling through three sequential processes: senescence induction, followed by senescent cells clearance and then tissue regeneration.[1,2] However, this sequence of events may not be efficiently completed upon persistent damage, in pathological contexts or ageing, thereby resulting in the accumulation of senescent cells. Therefore, strategies to detect or remove senescent cells are so of fundamental interest both for basic research and clinical applications.

In this context, a gated mesoporous silica nanodevice (MSN) capable to release its payload specifically in senescent cells with lack of toxicity has been recently published.[3] Following the same strategy, we have synthesized a set of three saccharide-capped mesoporous silica nanoparticles loaded with a cargo. GOS-MSN (formed with galacto-oligo-saccharide) and GAL-MSN (formed with the optimized galacto-hexa-saccharide) are able to release their cargo under the specific presence of SA-β-Gal enzyme in senescent cells. A third nanoparticle, GLU-MSN, capped with a gluco-oligo-saccharide, will be used as a control nanodevice. These nanoparticles can be opened by amylases present both in senescent and non-senescent cells. β-galactosidase responding nanoparticles have been loaded both with rhodamine B and doxorubicin, and several assays have been performed in different cell lines to test the specific senescence-selectivity of the proposed nanodevices, for detection and therapeutic applications.

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P-42

NANOCOMPOSITE POLYMERS ON MICRO INTERDIGITATED ELECTRODES FOR THE DETECTION OF VOLATILE ORGANIC COMPOUNDS

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Human breath analysis is an emerging field of medical diagnostics that promises rapid, non-invasive monitoring and even diagnosis of illnesses.[1] Among all kinds of volatile organic compounds (VOCs) found in human breath, acetone is of especial interest as it is a biomarker for diabetes.[2]

In this work, we report on the development of a highly sensitive chemo-capacitive sensor based on Micro Interdigitated Electrodes (M-IDE) for the detection of acetone. Preliminary acetone adsorption studies on M-IDE with different polymers, i.e. PS, PVDF, PVDF-PMMA, PMMA, PECH, PVPH, NIPAM, P2VP were developed. Emphasis is given on the development of these sensors based on the nanocomposite (NC) materials and amino-terminated silicon nanoparticles (Si-NPs). Sensor responses and selectivity studies showed excellent sensing performance of the NC towards the analytes under study with a high limit detection at room temperature.

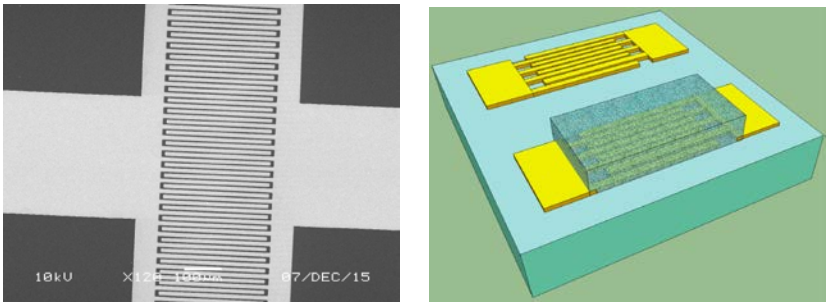

Figure 1. SEM image of Micro Interdigitated Electrodes (M-IDE) and schematic representation of polymer-coated M-IDE sensor device.

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P-43

SURFACE FUNCTIONALIZATION OF SILICON NANOWIRES BY SI–H ACTIVATION OF HYDROSILANES

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Silicon nanowires (SiNWs) are quasi one-dimensional (1D) structures with a diameter of less than 100 nm, which results in a high surface to volume ratio.[1] Due to the large surface to volume silicon ratio and unique quasi one-dimensional electronic structure, SiNW-based devices have properties that can outperform their traditional counterparts in many potential applications in the design of sensors, solar cells and Li-ion batteries. Most modification processes for oxidized SiNWs are based on silanization, esterification and phosphorization reactions, and hydrosilylation for oxide-free H-terminated SiNWs.

Here, we describe a fast methodology to modify SiNWs using hydrosilanes and $B(C_6F_5)_3$ as catalyst.[2] The successful modification of SiNWs was confirmed by X ray photoelectron spectroscopy (XPS) and static contact angle (SCA) measurements. This grafting protocol allows the formation of superhydrofobic surfaces in less than 10 min. This rapid functionalization may have potential applications in biomedicine due to its fast reaction time and the use of a nontoxic catalyst, as in case that boron-containing impurities remain they are expected to be nontoxic and/or biocompatible.

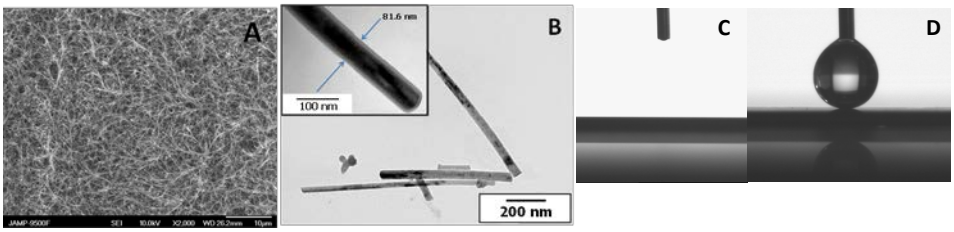

Figure 1. (A) SEM image of SiNWs forest with length of 45–50 µm, (B) TEM image of single SiNW with cross-diameter of about 80–100 nm, and SCA images before (C) and after (D) surface modification.

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P-44

COMPACT BIOPHOTONIC PLATFORM FOR DRUG ALLERGY DIAGNOSIS (COBIOPHAD)

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Drug hypersensitivity to antibiotics, mainly β-lactams (BLCs) affects more than 2.5 million European citizens. Moreover, preventable adverse drug reactions are estimated in additional hospitalization costs of 1750-4500 €/patient.

According to the European Network for Drug Allergy (ENDA), in vivo skin tests (prick and intradermal) and drug provocation tests are the gold standard methods in the detection of immediate BLCs allergy. However, although specificity (98-100%) is good, these tests are invasive, expensive and lack sensitivity (61-70%). Indeed, the high rate of false diagnosis has critical consequences, resulting in prolonged hospitalization and increased risk of mortality[2]. In daily practice, few in vitro diagnostic methods are available and only used at the tertiary health services. The use of in vitro diagnostic tests (IVD) for the detection of specific IgEs associated to BLC hypersensitivity is a highly demanded solution to substitute the invasive and risky in vivo tests (gold reference). The current IVD, developed with bulky autoanalyzers and based on classical technologies, show low sensitivity (lower than 40%; detection limits > 0.2 kU/L)[2], analyze only 5 BLCs and give false positive and negative results. The problems with existing tests are compounded by the fact that the costs of drug allergy diagnosis are high. The estimated amount is between 375 € and 525 € per studied drug. Besides this, erroneous allergy diagnosis causes additional costs, due to the critical patient condition and need for prolonged hospitalization.

COBIOPHAD consortium aims the development of an innovative in vitro diagnostic (IVD) device for diagnosis of IgE-mediated drug allergies by building an integrated biophotonic system based on compact disc technology. Mass consumer electronic technologies offer huge advantages to serve as basis of health devices. Between them, compact disc incorporates a potential analytical platform (disc) and a detector (disc player) with competitive performances and costs. Proofs demonstrating the viability of this concept have been shown[3]. For that, key enabling technologies, including photonics, use of advanced materials, opto-electronics, and bio-analytical tools, will be integrated in order to achieve a high sensitive (<0.1 kUA/L), selective (>98%), multiplexed (10 BLCs), rapid (30 min), and low-cost (2.4 €/allergen) drug allergy test.

The consortium comprises multidisciplinary knowledge on optics, electronics, advanced materials, biotechnology, smart microstructures, microfluidics, surface/organic chemistry, allergy, manufacturing systems, and telecom networking. Also, the key industrial actors, present in the consortium, will contribute to the manufacturing and placing the product on the IVD market.

The COBIOPHAD Project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 688448. It is an initiative of the Photonics Public Private Partnership (www.photonics21.org)

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P-45

Injectable chemotherapeutic hydrogels for the treatment of intracranial tumors

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We developed a novel delivery system that will be used to design and manufacture a therapy (Glio-Gel) for the treatment of glioblastoma multiforme (GBM), the most aggressive form of brain cancer [(1)]. Glio-Gel will comprise a unique combination of injectable matrices for local treatment of residual cancer after resection [(2,3)], and mesoporous silica nanoparticles (MSNs) with controlled release to treat infiltrative cancer migrations.

MSNs are biocompatible materials and there is evidence that they can cross the BBB [(4,5)]. We designed a GSHresponsive gated material, based on MSNs loaded with a cargo (a dye or drug) and functionalized with PEG chains in the pore outlets using a disulfide linkage. Then, we manufacture injectable polymeric matrices composed of hyaluronic acid or chitosan. Those gels were loaded with free dye or with the MSN synthetized. Therefore, we studied the kinetic release profile of the nanoparticles from the gel, the effect of the surface functionalization of the MSN to its release from the gel and the proper working of the molecular gate after the gelation process .

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P-46

Electrochemically stimulated molecules release from new hybrid MCM-41 materials.

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The use of mesoporous silica nanoparticles (MSNs) is particularly interesting for the development of hybrid materials with molecular gate nanoscopic functions.[1] Application of an external trigger (pH, redox reaction, light, enzymes, magnetic field, temperature) changed the chemical nature of the gating functionalities (anchored onto the external surface of the MSNs) allowing control of mass transport. Electrical signals are easy to generate and control. Electric stimuli have been successfully utilized to trigger the release of molecules via conducting polymeric bulk materials or implantable electronic delivery devices.[2,3]

We presented here new hybrid MCM-41 MSNs loaded with rhodamine B, functionalized with 1-methyl-4,4'-bipyridinium iodide and capped with heparin (**S1a**) and CB7 (**S2b**). Aqueous suspensions of both materials showed negligible dye release (due to the presence of strong electrostatic interactions between bipyridinium moieties and heparin in solid **S1a** and to the formation of bipyridinium-CB7 inclusion complexes in **S2b**). However, application of a -0.59 mV pulse in both materials induced pore opening and rhodamine B release. The mechanism of pore opening is related with bipyridinium moieties reduction with subsequent rupture of electrostatic interactions with heparin or the dethreading of the bipyridinium-CB7 inclusion complexes.

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P-47

Pseudo-rotaxane capped mesoporous silica nanoparticles for electron rich molecules detection.

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Mesoporous Silica Nanoparticles (MSNs) loaded with certain indicators (i.e dyes, redox-active species or fluorophores) have recently raised as a potential tool for sensing purposes.[1,2] Moreover, rotaxanes and pseudorotaxanes have been used as caps for the development of stimuli-responsive systems based on this support.[3,4] However most of these systems respond to redox species or enzyme activity while only few examples are described based on the displacement of a pseudorotaxane by species of interest.[5,6]

Taking these facts into account we designed a sensory solid using a pseudo-rotaxane of cyclobis(paraquat-*p*-phenylene) (generally known as “blue box” and which have a very high affinity for electron-rich compounds) as capping ensemble for the development of an organic-inorganic hybrid material for the detection of different electron rich molecules such as nucleotides (ATP, GTP, UTP, CTP, ADP, AMP), neurotransmitters (dopamine, adrenaline, noradrenaline, aspartic acid, glutamic acid, octopamine, GABA) and drugs (MDMA, amphetamines, cocaine, morphine).

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P-48

NOVEL CHIRAL IONIC LIQUIDS (CILs) AS ADDITIVES FOR *L*-PROLINE CATALYZED ASYMMETRIC ALDOL REACTIONS

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Catalytic applications represent a central subject in Green Chemistry. For the next future, research efforts need to be driven towards the development of practical catalytic processes for the preparation of Fine Chemicals and Pharmaceutical products, which are industrial areas with the highest waste factors. One of the more straightforward approaches to implement the potential for practical use and to implement the "Green character" of catalytic processes is the use of organocatalytic processes.[1,2] From the toolbox of small organocatalysts, proline is by far one of the most popular ones, as it is cheap, readily available in both enantiomeric forms and can be used for a wide range of synthetic transformations.[3,4] Among them the direct catalytic aldol reaction is a well-studied and broadly applicable C-C bond-forming reaction, which provides enantiomerically enriched β-hydroxy carbonyl compounds.[5]

On the other hand, since first CILs were used as catalysts in aldol reaction by Luo *et al*.[6] in 2007, many CILs were developed as catalysts for asymmetric reactions. However, in asymmetric reactions where CILs cannot be applied as catalysts, using CILs as the solvent to investigate their chiral inducing capabilities has rarely been reported. *L*-proline combined with ILs were also proved to be an efficient catalytic system for asymmetric aldol reactions.[7,8] ILs may interact with the organocatalyst through H-bonding interactions to form the supramolecular active catalyst.

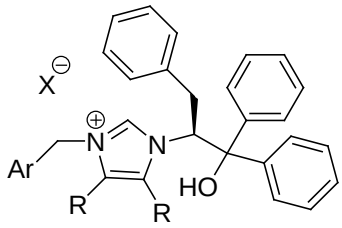

Figure 1. CILs derived from amino acids

Taking this into account and in connection with our ongoing interest in expanding the use of chiral imidazolium receptors derived from natural amino acids previously prepared by our research group,[9] herein we present our results on the use of new CILs derived from amino acids with the general structure shown in Figure 1 as additives for the (*L*)-proline catalyzed direct aldol reaction between ketones and aromatic aldehydes.

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P-49

Ultrasensitive β-conglutin detection by recombinase polymerase amplification-lateral flow competitive assay

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Food allergies is one of the most important health problems in developed countries[1,2], and to date no effective therapies have been developed, being the only prevention of an adverse allergic reaction the avoidance of the food allergen[3,4]. It is thus critical that food is correctly labelled an in order to have confidence in food labels, highly sensitive and specific assays for the detection of food allergens are essential. In the work reported here, we described a methodology for the lateral flow based detection of the anaphylactic β-conglutin allergen[5], in search of robust, simple, rapid, ultrasensitive and user-friendly assay. This approach is based on a competition off-strip between the target in the test sample and β-conglutin immobilised on magnetic beads. Following competition, aptamer bound to the immobilised β-conglutin is eluted and used as a template for isothermal recombinase polymerase amplification (RPA), which no requires initial denaturation step, and inherently overcomes all the drawbacks of the other isothermal approaches[6]. The RPA exploits the use of tailed primers, resulting in an amplicon of a duplex flanked by single stranded DNA tails, and the amplicon is rapidly and quantitatively detected using a nucleic acid lateral flow with immobilised capture probe and gold nanoparticle labelled reporter probe. The whole assay is just completed in 30 minutes with an impressive limit of detection of 9 fM (0.17 amol) and can be applied to any other target.

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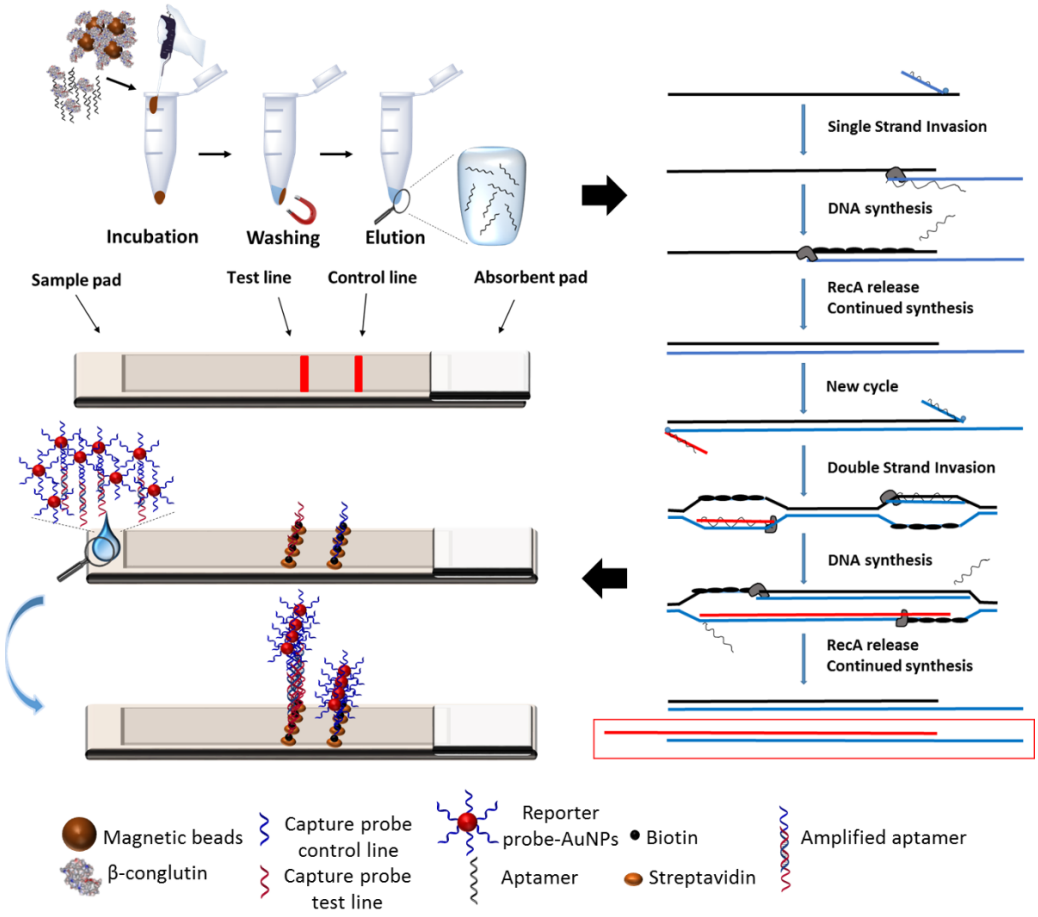
Incubation
Washing
Elution
Sample pad
Test line
Control line
Absorbent pad
Single Strand Invasion
DNA synthesis
RecA release
Continued synthesis
New cycle
Double Strand Invasion
DNA synthesis
RecA release
Continued synthesis
Magnetic beads
β-conglutin
Capture probe
control line
Capture probe
test line
Reporter
probe-AuNPs
Biotin
Aptamer
Streptavidin
Amplified aptamer

P-50

PROTEIN AND EXOSOME ANALYSIS WITH SERS-ACTIVE SUBSTRATES FROM CONSUMER ELECTRONICS

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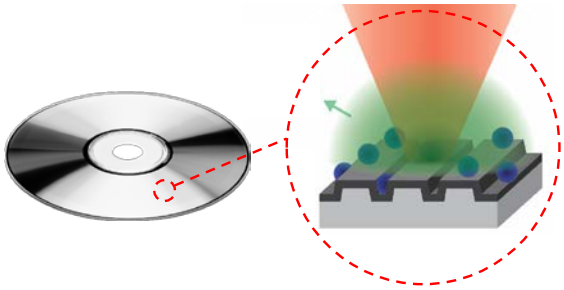
Surface enhanced Raman spectroscopy (SERS) entails appealing features to quantify and characterize biological samples in a sensitive, selective and label-free fashion. Within the framework of nanoscience and nanotechnology, many efforts are nowadays carried out towards the design and fabrication of SERS-active substrates applicable to biosensing.[1] Specialized nanofabrication techniques, materials, and benchtop spectrometers are typically involved in those advances, which restrict their potential to be disseminated in resource-scarce and non-specialized settings. Along these lines, to implement biosensing systems in mass-produced consumer electronics has demonstrated high potential for point-of-need analytical devices.[2, 3]

Herein we present preliminary results towards low-cost and mass-produced materials from consumer electronics to be used as SERS substrates for label-free biosensing. Protein and exosome samples were used to prove the concept for clinical analysis. These study suggest prospective inexpensive, compact and robust materials and devices to provide solutions in SERS analysis.

This work was supported by the Spanish Ministry of Economy and Competitiveness (CTQ2013-45875-R and FPI program), FEDER, and Generalitat Valenciana (PROMETEO II/2014/040).



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P-51

Polymixin B- gated mesoporous silica nanoparticles as a future nanosystem for efficient antimicrobial photodynamic therapy

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Antimicrobial photodynamic therapy (PDT) is a promising strategy to eradicate pathogenic microorganisms without inducing the appearance of undesired drug resistance and with broad spectrum of efficiency, which gives PDT advantages over traditional antibiotic therapy. PDT employs a non-toxic photosensitizer (PS) that when it is photo-stimulated generates reactive oxygen species (ROS) which cause toxicity through type I or II mechanisms. In this field, NIR bodipys are a promising PS. This class of molecules have the advantage of a deep penetration, low toxicity in dark and high singlet oxygen production. In the specific area of antimicrobial PDT, many studies have focused in achieving attraction between the negatively charged pathogen membrane and the used PS to be close or inside bacteria during PDT, either by using cationic PS or a combination of the PS with positive charged entities –like polypeptide, polymers and surfactants- which leads to effective destroy pathogens.[1]

Cationic polymer-capped silica mesoporous nanoparticles could be used to drive close to the pathogen membrane non cationic PS. In addition, the encapsulation of PS molecules leads to avoid their interaction with other species as environmental agents and PS leakage. Furthermore, it is reported that encapsulated PS enhances singlet oxygen generation, increasing efficiency of photo toxicity of the PS.[2]

Based on this background, in this work we have designed mesoporous silica nanoparticles (MSNs) loaded with a cargo (dye or bodipy) and capped with the cationic polymer polymixin B (PMB). The polymer will prevent the premature leakage of the cargo, promote the attraction of the system to the pathogen membrane and will act as membrane permeation agent to facilitate entrance of the nanoaprticle.[1, 2] We present herein our recent results of the preparation of a rhodamine B loaded PMB-capped nanosystem.

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P-52

LONG-TERM ANTIFUNGAL EFFECT OF ESSENTIAL OIL COMPONENTS WHEN LOADED INTO SILICA MESOPOROUS SUPPORTS

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The essential oils components have become known for their antibacterial and antifungal activity and can be use as suitable alternative to synthetic pesticides and food preservatives. But these compounds are very volatile, they often evaporate before they exhibit antimicrobial activity, for that reason it is very interesting to release them in a sustained manner to reduce their volatility and prolong their biological effect.

In this study, we tested the antifungal activity against *Aspergillus niger* of seven volatile essential oil components from plants – allyl isothiocyanate, carvacrol, cinnamaldehyde, diallyl disulfide, eugenol, thymol, and thymoquinone. To provide long-term effects by controlled release and ease of application, these substances were encapsulated into mesoporous silica material MCM-41 and then compared to the effects of pure substances.[1] Significant antifungal activity was verified in five out of the seven tested substances, which were able for more than 14 days to inhibit the growth of *Aspergillus niger*. The encapsulated substances showed significantly higher antifungal activity after 14 days than the same substance in a pure state.[2] The sulfur compounds diallyl disulfide and allyl isothiocyanate in our experiments appeared to be only slightly effective when encapsulated.

The encapsulation of essential oils compounds inside the MCM-41 may significantly facilitate the use of these compounds in medicine, the food industry, and in agriculture. These compounds, such as thymol, thymoquinone, and eugenol encapsulated in MCM-41 may find applications, such as in integrated pest management or organic agriculture, those are currently in high demand. Encapsulation of these substances is able to provide controlled release according to the needs of vegetation and, at the same time, thus contributes to the reduction of environmental pollution.

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P-53

Métodos de inmovilización de fragmentos de anticuerpos mediante reacciones inducidas con luz para su aplicación en nanobiosensado óptico integrado

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El proyecto PHOCNOSIS (H2020-PHC-634013) tiene como objetivo el desarrollo de un dispositivo de análisis *point-of-care* (POC), basado en diversos conceptos nanotecnológicos novedosos, para su aplicación en el diagnóstico precoz de enfermedades cardiovasculares. El diagnóstico pretende la detección rápida (<10 minutos), ultra-sensible (<1 ng/L), sin utilizar marcadores (*label-free*) y simultánea de diversos biomarcadores cardiacos de relevancia haciendo uso de una pequeña muestra de sangre del paciente (<100 µL). Para conseguir este objetivo, uno de los pasos claves es desarrollar métodos apropiados de inmovilización de los receptores específicos (anticuerpos) para los biomarcadores cardiacos seleccionados. Esta inmovilización ha de ser orientada, selectiva en las zonas sensoras del chip, y además permitir que el evento de bioreconocimiento se produzca lo más cerca posible de la superficie.

Este trabajo presenta la optimización de las metodologías de anclaje de los bioreceptores sobre el material (SOI) que constituirá el transductor en el dispositivo nanofotónico final. Estas estrategias están basadas en la fotoinmovilización mediante el uso de reacciones de *química click* (reacción de acoplamiento tiol-eno). Todo el trabajo de optimización se ha hecho empleando formato *microarray* de fluorescencia y usando un sistema modelo. Así, este primer biosensor utiliza el sistema BSA (*bovine serum albumin)*-αBSA como modelo de anticuerpo policlonal. Distintos parámetros como el tipo de funcionalización de superficie, el tipo de anticuerpo a inmovilizar, el tiempo de irradiación y, el método de detección han sido optimizados.

Después de realizar varios experimentos, se demostró que el fragmento $F(ab')_2$ es el que aportaba una mayor sensibilidad al ensayo, obteniéndose, además, los resultados más reproducibles y robustos, incluso mejorando al anticuerpo sin fragmentar.

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P-54

Cristales fotónicos basados en discos compactos

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El concepto de "cristal fotónico" engloba un amplio conjunto de estructuras periódicas[1] diferentes entre sí pero con un factor común: al incidir una onda electromagnética sobre él ciertos intervalos de frecuencia no pueden ser transmitidos. Ello se traduce en una disminución de la luz transmitida a ciertas longitudes de onda (depresión en el espectro de transmisión). Los cristales fotónicos pueden ser utilizados para el biosensado sin la necesidad de la utilización de marcadores, ya que la depresión en el espectro de transmisión es susceptible a la variación del índice de refracción sobre su superficie[2]. Una característica muy interesante de estos materiales es que el intervalo de frecuencia suprimido puede ser modulado para posicionarlo a la longitud de onda deseada variando el periodo, los materiales dieléctricos y/o su grosor[3]. Sin embargo, las dimensiones de las estructuras periódicas suelen ser nanométricas, por lo que hay que recurrir a métodos de fabricación costosos y tediosos.

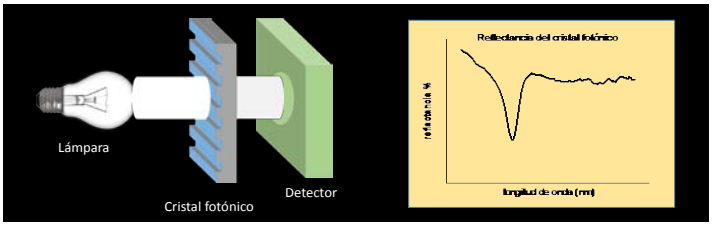

Imagen 1: Montaje del biosensor y el espectro de reflectancia obtenido con dicho montaje.

En este trabajo se ha utilizado la estructura que tienen los discos compactos para generar esa disposición periódica. Para la fabricación del cristal fotónico se han seleccionado 4 tipos de discos sobre los que se han depositado capas de TiO_2 de diferentes grosores. Los resultados obtenidos indican que ciertas estructuras combinadas con grosores óptimos de TiO_2 presentan depresiones en el espectro de transmisión que caen en el intervalo del visible. Los ensayos desarrollados muestran el potencial de estos materiales para leerse con un reproductor de discos de modo que se dispondrá de un nuevo tipo de biosensor óptico, label-free, de altas prestaciones y bajo coste.

Agradecimientos

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P-55

Evaluation of loop-mediated isothermal amplification as a tool for point-of-care diagnostics in the pharmacogenetic field

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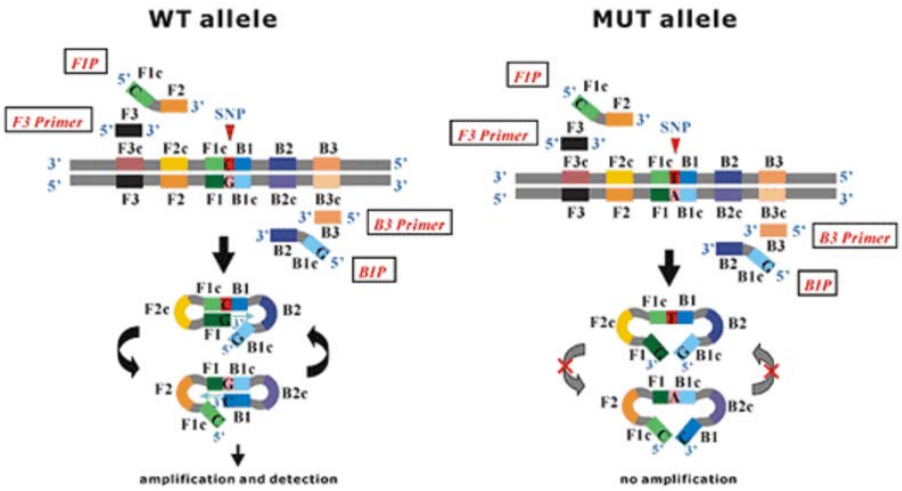
The genotyping of polymorphisms is particularly interesting for the field of personalized medicine, whether to diagnose certain genetic related diseases or to predict an individual's response to a therapy. Nevertheless, current methods turn out to be excessively expensive for clinical routine. A potential solution is the development of point-of-care genetic testing. To accompany this diagnostic goal, the nucleic acid detection procedure should be integrated in a small, low cost, disposable device with user-friendly operation. For that, the selection of genotyping approach and amplification technique is important.

This study analyses different approaches based on loop-mediated isothermal amplification (LAMP) and related to genotyping applications. Compared to other nucleic acid amplification methods, LAMP is isothermal (60 ºC) and highly sensitive, since the enzymatic activity of Bsu DNA Polymerase is capable of producing 10^9 copies of target DNA in 60 min. The described methods include allele specific amplification and allele specific hybridization. As a result, the processes lead to single-nucleotide polymorphism discrimination, by examining the individual's DNA sequence and categorizing each allele as wild-type or mutant.



Acknowledgement:

Projects MINECO CTQ2013-45875-R and GVA PROMETEOII/2014/040. Grisolía 2014/024 scholarship.

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P-56

Elastic nanovesicles of baicalin

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ABSTRACT

Baicalin, a natural flavonoid isolated from the dried roots of *Scutellaria baicalensis Georgi*, have shown various strong pharmacological properties[1-3], such as antioxidative, antiviral, anti-inflammatory, antitumor and antiproliferative. However, topical bioavailability is hindered by its poor solubility in aqueous media and low skin permeability[4]. Therefore, its incorporation into vesicles could be a useful tool to improve its performance.
The purpose of the present study was to formulate elastic vesicles of baicalin with different types and concentration of phospholipids (Phospholipon I and phospholipon II) to optimize the topical delivery of this anti-inflammatory drug. All systems were tested in vitro to study their ability to increase transdermal absorption of baicalin.
Elastic vesicles showed small size, low polydispersity index and high stability and negative Z-potential. The entrapment efficiency (EE%) was dependent of the phospholipon used. Permeation experiments were performed in vitro through human epidermis using Franz-type diffusion cells. Liposomal nanoformulations with phospholipon II improved baicalin entrapment and skin delivery.
Overall, results indicate elastic liposomes with phospholipon II as promising nanosystems for the improvement of cutaneous baicalin delivery in skin pathologies.

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P-57

Structured platforms for isothermal DNA quantification

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Different PCR-based devices have been developed for DNA sensing. However, some limitations hinder their integration into miniaturized systems, particularly related to thermal constrains and detection systems required [1,2]. Innovative platforms are presented for targeted DNA quantitation as an alternative to qPCR technique for decentralized laboratories. For that, the micro-reactors are embedded in the internal structure of plastic polymers using milling as manufacturing technique. The surfaces are exposed to oxygen plasma treatment in order to allow reagent dispensation and minimize unspecific interactions. The machined substrate can be laminated with a sealing adhesive layers for increasing lab-on-a-chip performances.

This approach has been tested performing real-time non-fluorescent DNA assays and optical read-out by a disc drive. For that, the micro-reactors are embedded in the internal structure of optical discs and their dimensions are suitable considering the tolerance of error correction system. Once the sample and reagents are dispensed, reactions take place into the microstructured platform under isothermal conditions and a cyclic scanning of disc surface is performed for 40 min. In presence of target, the turbidimetric or colorimetric properties of reaction solution change, modifying the transmitted intensity of disc drive laser as function of reaction yield at each time. So, the determination of targeted DNA can be achieved by kinetic monitoring. This economically affordable analytical system has been applied for pathogen detection; in-disc results being comparable to those obtained using conventional vial or qPCR approaches.

The next generation of microstructures have been designed for increasing assay automation. Therefore, the development will meet expected requirements of an effective, portable, low-energy consumption, low-cost and fast response device.

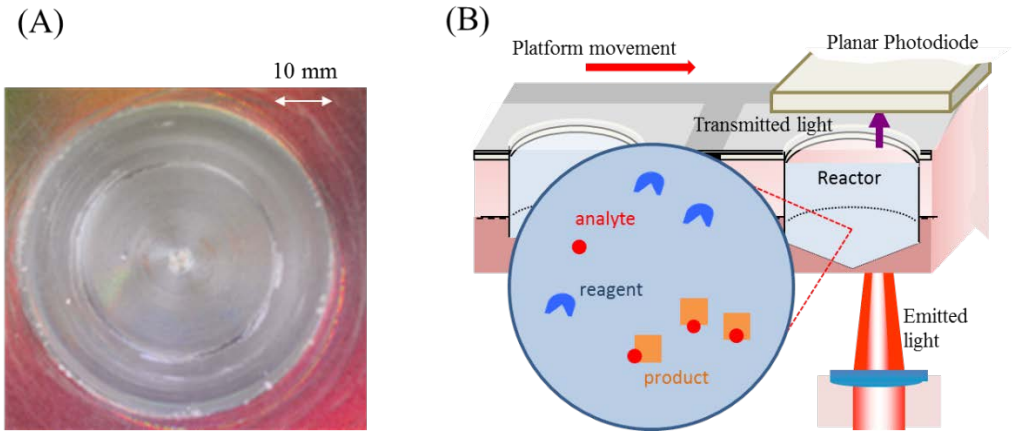

Figure: (A) Microscopy image of micro-reactor (reflexion mode), (B) Schematic diagram of detection system.

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P-58

A Novel Biosensor for Diagnostic and Monitoring of Systemic Lupus Erythematosus

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The anti-Ro/SSA autoantibodies are among the most commonly detected autoantibodies in the routine screening for Systemic Lupus Erythematosus (SLE). These antibodies are produced against Ro/SSA complex, composed by TRIM21, TROVE2 and La proteins.[1-4] While the common measurements to diagnose SLE considers the level of anti-Ro/SSA autoantibodies against the entire Ro complex, none of them takes into consideration the anti-TRIM21 and anti-TROVE2 autoantibodies independently. Thus, the clinical, prognostic and therapeutic utility of detecting anti-TRIM21/TROVE2 reactivity is yet to be established.

We developed a novel Ro-based QCM-D biosensor that was quantitatively correlated with clinical parameters, such as lupus disease activity index or the criteria for diagnosis of SLE (130 SLE patients and 35 healthy subjects). We have established a new quantitative screening method, based on the –df/dD function, for identification of SLE patients. Furthermore, the developed test for quantifying the disease activity index was performed on a standard CD/DVD surface. This technique is high-throughput and cheaper methodology current ones. Accordingly, we have developed a new diagnostic tests that enable easy transfer into clinical practice.

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P-59

DETERMINACIÓN DE POLIFENOLES TOTALES EN VINOS MEDIANTE UN SENSOR DE NANOPARTÍCULAS DE CERIO

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En la determinación de vinos, uno de los parámetros más importantes es el contenido en polifenoles porque estos constituyen un grupo esencial de las uvas y vinos. Para cuantificar los polifenoles en vino se emplea el método oficial[1,2], Folin Cicocalteu que se basa en la transferencia de electrones en un medio alcalino de los compuestos fenólicos a complejos de ácido fosfomolíbdico - fosfotúngstico que forman complejos azules que se determinan espectroscópicamente a 760 nm. Este método es laborioso, con múltiples pasos y tiempo de ensayo de más de una hora.

En este trabajo se evalúa el uso de nanopartículas de Cerio (NPCe) inmovilizadas sobre una superficie de celulosa[3] para la determinación de polifenoles. El Cerio IV (amarillo) inmovilizado sobre el soporte sólido se reduce a Cerio III (marrón) en presencia de polifenoles (**Figura 1**). Este cambio de color asociado al cambio de estado de oxidación permite determinar el contenido en polifenoles totales en vino tinto, blanco y rosado. Para ello es necesario la obtención de imagen (escaneo) y el análisis de la misma. La caracterización del método se ha llevado a cabo determinando parámetros de calidad como sensibilidad, límite de detección y cuantificación, precisión exactitud y selectividad, comparándolo con el método oficial.

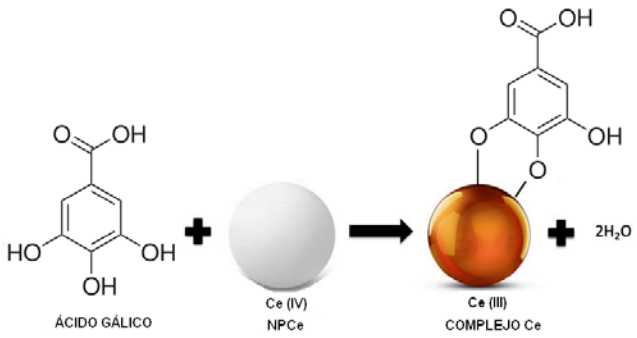
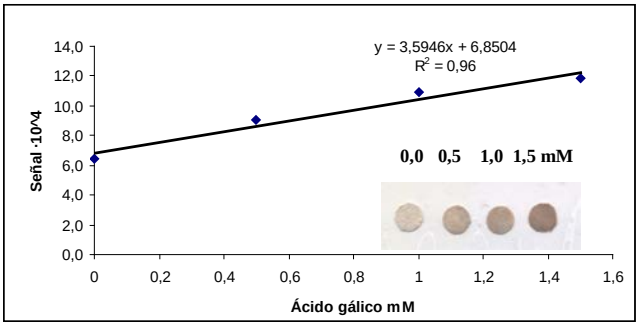


Figura 1: Reacción entre las NPCe y un polifenol (ácido gálico)

En la **Figura 2**, se comparan los resultados obtenidos con muestras de vino, tinto y blanco, expresando el resultado como equivalentes de ácido gálico.

(a)



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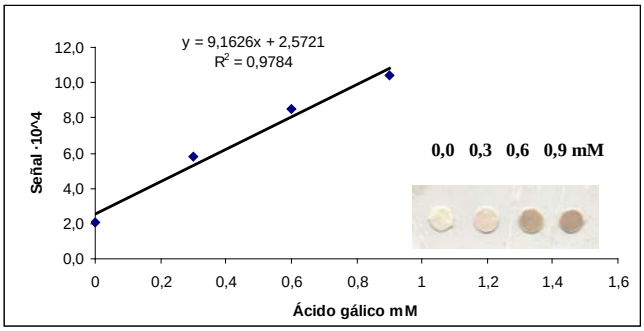

Figura 2. Recta de calibrado para vino tinto (a) y blanco (b). En detalle se muestra la intensidad de color en función de la concentración de antioxidantes.

El método desarrollado presenta buena exactitud y precisión, con una sensibilidad comparable a la del método oficial. El intervalo de trabajo para ácido gálico es de 0.5 -1.5 mM (100-280 mg/L AG).

A la vista de los resultados se observa que este método propuesto es rápido, sensible y no requiere entrenamiento ni instrumental especializado, pudiendose obtener los resultados con un ordenador y un escáner documental.

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P-60

Controlled hydrophobicity of surfaces for developing microarrays by covalent anchoring

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Microarray technology is an interesting tool to obtain massive analytical information, in short times and reduced costs. This can be applied to several fields such as the functional genomic analysis and forensic medicine.[1]

In their fabrication, activation of the probe and the surface present a big problem for production in full scale. The problem is due to the lack of control in the covalent anchoring and the ignorance in the liquid - solid interface processes. The aim is to modulate the hydrophobicity of the surface getting a smart surface, in which the analyte approaches only to the specific probe, avoiding the unspecificity and the high background.

Glass microscope slides were used as microarrays substrates because of their good optical properties, low cost, and easy functionalization by the organosilane chemistry.[2, 3] As the, unspecific adsorption is avoided on hydrophobic surfaces, we take the advantage to derivatize biochips with a perfluorinated silane hindering the adsorption of analytes or interferences over the surface, and allowing us a low background.

In this communication, we report for the first time a simple and rapid strategy to bind covalently DNA oligonucleotides on glass substrates using thiol-fluor click reaction, [4] without the use of intermediate reagents or cross linkers. However, the high hydrophobicity of perfluorinated surfaces and the low wettability hinder effective hybridization. For this, we have modulated the hydrophobicity of the surface by adding a hydropilic organosilane to reduce hydrophobicity and, at the same time, to avoid non-specific adsorption on the surface. Thus, we have achieved immobilization and hybridization of thiolated DNA probes on these hydrophobic surfaces in a fast, clean and effective way. Figure 1 shows a scheme of the different surfaces under study.

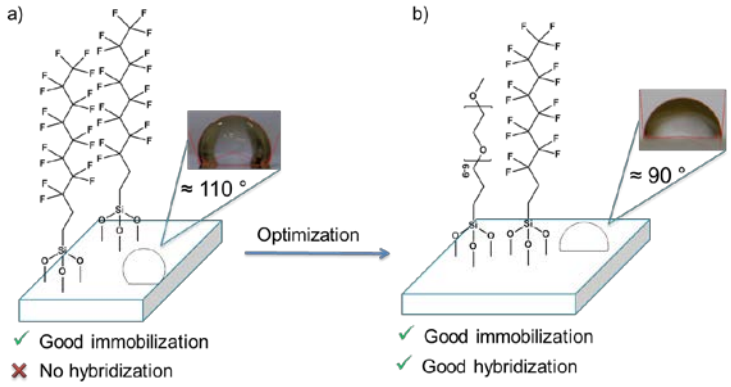

Figure 1. Optimization of the hydrophobicity and wettability of the surface. We can observe the schematic structure, and contact angle of the functionalized surfaces. a) Functionalization with 1H,1H,2H,2H-Perfluorodecyltriethoxisilane (PF) b) Functionalization with a mixture of PF and 2-[Methoxy(polyethyleneoxy)$_{6\text{-}9}$propyl]trimethoxysilane (PEG)

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P-61

Plastic substrates as platforms for mutational analysis of oncogenes

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The search of in genomic DNA alterations is important because specific genes, called oncogenes, of tumour cells are mutated causing activation of certain processes proliferation[1]. Currently, there are different technologies that are capable of performing mutational analysis detecting the replacement of a single base. However, its high cost, complexity, and low portability limit the implementation of these tools in the health system. Chips based sensors have a growing interest in this field of clinical analysis for its potential benefits in monitoring cancer patients.

The development of a microarray technology in a miniaturized and parallel format is proposed for the detection of point mutations. In the present study, synthetic polymers are evaluated as substrates of the analytical platform due to its low specific weight, high elasticity and low cost manufacturing[2]. The materials include polycarbonate (PC), olefin polymer cycle (COP), and polymethylmethacrylate (PMMA). The assay consists in immobilizing oligonucleotide probe on the polymeric material, performing the specific hybridization and subsequent detection. Particularly, the immobilization is based on the indirect adsorption via streptavidin / biotinylated probe and the covalent attachment by UV activation and acylation with the amino-probe.

As a model of oncogene determination, mutational analysis of phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), is performed. Specifically, histidine amino acid change in the 1047 position of p110α is studied[3]. These mutations cause greater enzyme activity significantly contribute to cellular transformation and development of human cancers, including ovarian, breast, lung, colon, brain, and stomach cancer.

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P-62

Preparation and characterization of colonic release systems

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ABSTRACT

Ulcerative colitis is a chronic inflammatory bowel disease and uncontrolled which causes with relapses and affects the colonic mucosa (1). The current treatments are based on the seriousness of the outbreak and to improve the symptomatology. A natural flavonoid can help to reduce symptoms of the disease and improve quality of life for patients. Baicalin, a bioflavonoid extracted from the root of Scutellaria baicalensis Georgi, presents several interesting pharmacological properties as an antioxidant, anti-inflammatory and antitumoral (2, 3).

In this work, several formulations for oral administration of Baicalin as polymer matrices and tablets, by means chitosan and hyaluronic acid, were developed. The tablets have been coated with an enteric acrylic polymer (Eudragit® S-100). The formulations were characterized by scanning electron microscopy and X ray diffraction. Moreover, the release profiles at different pH, simulating the gastrointestinal tract, have been determined. The profiles obtained indicate the formulations selected present gastrorresistant properties. Therefore, the baicalin could be released (> 40 %) in the colonic segment.

Key words: baicalin, ulcerative colitis, biodegradable polymers, controlled release.

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P-63

LIDOCAINE HYDROCHLORIDE BUCCAL BIOADHESIVE XEROGELS DESIGNED FOR ORAL ULCERS.

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Polymers as Chitosan (CH), Hydroxypropylmethylcellulose (HPMC), and Xanthan Gum (XG) have been used for the formation of polymeric matrices due to their pharmaceutical and biomedical relevant applications[1]. Their main properties such as biodegradability, erosion ability and biocompatibility, make them a desirable election for this type of formulation. The objective of this research is the development and characterization of a matrix system with different polymers added to lidocaine hydrochloride as an anesthetic drug for a possible buccal application. Initially, lidocaine hydrochloride (5%, w/w) was dissolved in water. Afterwards, the different polymers were joined at the same concentrations (2%, w/w) in this solution. The hydrogel was allowed to dry at room temperature for 48h. In this study release delivery, rheological and mucoadhesive properties of matrix systems, between each formulation and the buccal mucosa, were tested. The delivery profiles of the different polymers for the lidocaine do not present significant statistical differences ($P > 0,05$). The zero-shear viscosity (η_0) for XG is four orders of magnitude greater than for the other polymers. Oscillatory tests showed a viscous behaviour for formulations with HPMC and CH, as G”>G’, and moduli were strongly dependent on frequency. However, XG system showed an elastic behaviour, as G’>G” and a low dependence with frequency was observed. Finally, XG is the most elastic polymer and the adhesive properties of the formulations increased as a function of the viscoelasticity of matrix systems.

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P-64

ENZYME-CAPPED NANOMATERIAL FOR INSULIN CONTROLLED RELEASE

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In the last decades, many different types of nanomaterials have come to the forefront of research offering several advantages such as small amounts of analytes for diagnostic assays or release of active agents in a controlled manner for therapeutic applications.[1] In this context, bio-gated mesoporous silica nanoparticles have drawn great importance due to their outstanding characteristics such as biocompatibility, ease of functionalisation on the surface, high drug loading capacity and tunable pores size.[2] Between all the potential applications of nanomaterials, the development of a system which can detect fluctuations in blood glucose concentration and release insulin in a self-regulated manner is especially appealing.[3]

Bearing in mind the advantages of bio-gated silica nanoparticles as drug carriers and the importance to find new self-regulated controlled insulin release systems, we report herein the design of an insulin-loaded nanocarrier with glucose-sensitive properties in simulated human blood plasma. The developed nanocarrier consists of an expanded pore nanometric silica support loaded with fluorescein isothiocyanate-labeled insulin (FITC-Ins), functionalised with benzimidazole groups and capped with CD-modified-glucose oxidase (GOx-CD) by the formation of inclusion complexes with the grafted benzimidazole groups. The presence of glucose promotes the production of gluconic acid by GOx, inducing the dethreading of the inclusion complexes and the cargo release. Thus, we have developed a smart-nanomaterial that comprises both diagnostic and therapeutic functions integrated into a single agent.

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P-65

A NEW COLORIMETRIC AND FLUOROMETRIC PROBE BASED IN A BODIPY CORE DETECTING MERCURY ION IN WATER

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In the past several decades, the detection and quantification of transition metal cations has experienced a great interest in different areas, such as environmental chemistry and clinical toxicology, because of its polluting nature.[1-2] The design and construction of optical chemosensors for heavy metal cations (with high selectivity and sensitivity) has received considerable attention because they have caused severe risks for the environment and human health. Among them, mercury is one of the most toxic metal ions, even at slow concentrations.

We present here a new colorimetric and fluorometric probe able to detect Hg^{2+} in water (see Figure 1). We selected a BODIPY fluorophore because of its high quantum yields and its good solubility in water and organic solvents with medium-high polarity. This BOPIPY fluorophore was electronically connected with a crown ether containing nitrogen, oxygen and sulfur atoms.

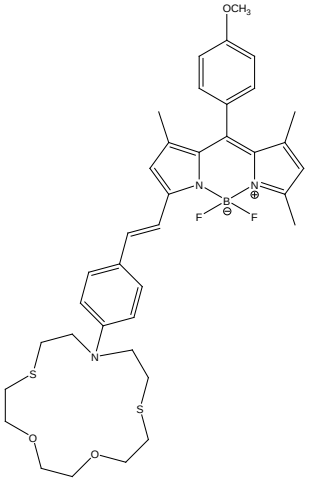

Figure 1

Solutions of receptor in water-acetonitrile 95:5 v/v at pH 7.0 present an absorption band centered at 614 nm, which gives an intense blue color. UV-visible and fluorescence spectra of probe were studied in the presence of 10 equivalents of several metal cations (Na^+, K^+, Li^+, Mg^{2+}, Ca^{2+}, Co^{2+}, Ba^{2+}, Cu^{2+}, Ni^{2+}, Zn^{2+}, Hg^{2+}, Al^{3+}, In^{3+}, Cr^{3+}, Ga^{3+}, Fe^{3+}, As^{3+}). Only Hg^{2+} is able to change the color of the solution (from blue to pink clearly discernible by the naked eye). These changes are reflected in the appearance of a new band in the visible region, centered at 561 nm. On the other hand, a significant increase in fluorescence upon addition of Hg^{2+} cation was also observed. The Job plot analysis indicated a stoichiometry 1:1. Finally, the detection limit (LOD) for Hg^{2+} was determined to be 99 ppm.

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P-66

Silica Mesoporous Supports Capped with an Azoaniline Derivative for *In vivo* Controlled Cargo Delivery in the Colonic Mucosa

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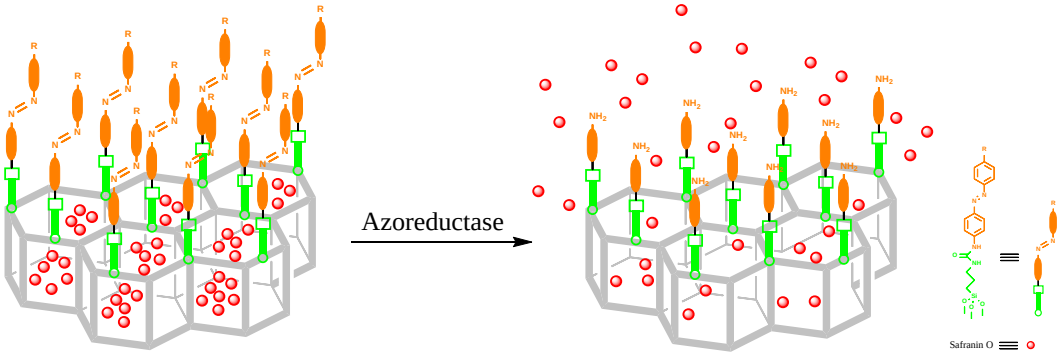
Mesoporous silica (MS) has proven to be an excellent solid support owing to its superior properties such as good biocompatibility, chemical stability, high surface areas and facile functionalization of the surfaces and pores.[1] Materials derived from the combination of MSs as solid supports and molecular gates as movable entities have emerged in the literature and play prominent roles in materials science nowadays.[2] In this work, we chose to synthesize an hybrid material, based on MSs microparticles whose surface is functionalized with an azoaniline derivative as a molecular gate. It is known that the azo bond is specifically cleaved by the action of the gut microbiota (azoreductases enzymes) in the large intestine. This, a molecular gate containing this functional group would be useful for controlled drug release in the colonic mucosa, for example in the treatment of Crohn's disease.[3] The mesoporous system has been loaded with a dye (safranin O) in order to study *in vivo* the release of the cargo under reducing conditions by UV-vis, fluorescence and HPLC.



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P-67

A nanoscopic hybrid gated material for CO cell signalling

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Carbon monoxide (CO) is widely known as a silent, invisible and odourless threat, but recently, therapeutic and cell-signaling role attributed to CO intensifying its interest and its use in biological systems.[1]

Thus, in order to develop a system capable of detecting CO in cells, we prepare a new nanoscopic CO probe based on a ruthenium (II) pyrenylvinyl complex[2] attached to MCM-41 mesoporous silica nanoparticles. The steric hindrance around the pore outlets imposed by the grafted complex avoids the uncontrolled delivery of the cargo (fluorescent dye hodamine B). However, in the presence of CO, the initial complex is converted in the corresponding pyrenylvinyl dicarbonyl compound via displacement of the BTD (2,1,3-benzothiadiazole) ligand (see Figure 1) allowing dye release.

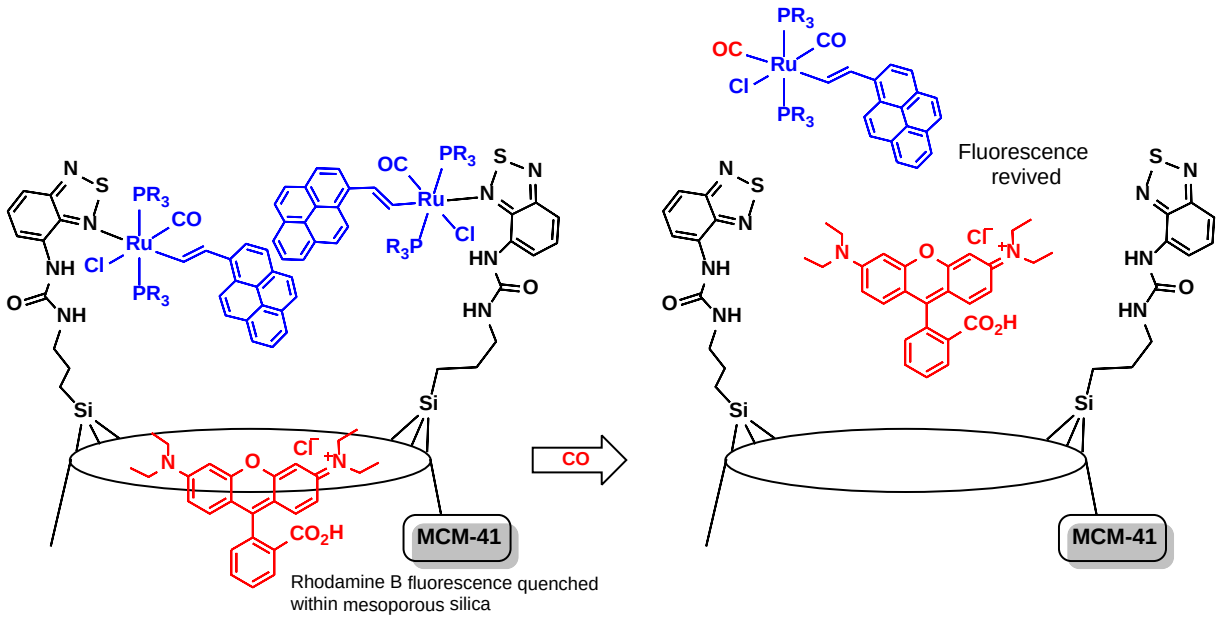

Figure 1. Scheme of the gate opening mechanism.

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P-68

Biosensing of mutations located in KRAS oncogene in colon cancer patients based on blocked amplification

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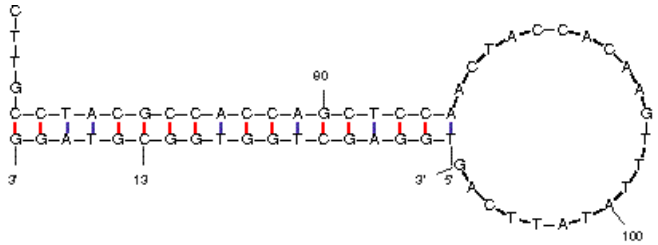
The research is focused on gen KRAS (Kirsten rat sarcoma viral oncogene homolog) which encodes a GTP union protein, involved in regulation of cellular division. Among 35 to 42 % of the adenomas have a mutation in the oncogene KRAS, activating tumour proliferation. The presence of these somatic mutations is linked with a resistance to monoclonal antibodies therapy targeting epidermal growth factor receptor (EGFR), involved in colon cancer development[1]. The mutational state analysis of KRAS gene is performed to select the therapy which best fit with the patient (personalized medicine) [2].

The goal of this project is to contribute in the development of mutational analysis methods based on biosensing technologies alternatives. Exon 2 codon 12 mutations have been selected: 34G>C (Gly12Arg), 34G>T (Gly12Cys) y 34G>A (Gly12Ser). The analysis is performed with genomic DNA from formalin-fixed, paraffin-embedded tissues. These samples obtained from biopsied tissue have generally normal cells and tumor cells, so it is studied the blocking during the amplification to enrich mutant alleles respect normal alleles[3]. To detect the product formed, different strategies are studied, including solution and hybridization assays. The methods proposed show high performance and are easy to be implemented in hospitals. Therefore, to increase the number of patients who could benefit of personalized therapy is expected as result of this study.



Scheme of wild-type template blocking (ΔG = -25.8 kcal/mol, Tm = 80.0°C)

Acknowledgement:

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P-69

CANDIDA ALBICANS GENOMIC DNA DETECTION BY USING GATED NANOPOROUS MATERIALS

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In the last decade, the cases for nosocomial fungal infections, as invasive candidiasis have increased in hospitalized patients.[1] There are several species of *Candida*, however the most common invasive fungal infections are caused by the species *Candida albicans*. Thus, it is relevant the development of new systems to rapidly detect this kind of infection. Also, it is important to discriminate between *Candida albicans* and other *Candida* species due to the different treatment by reason of the intrinsic resistance of *C. albicans* to the antifungal fluconazole.[2]

It is the aim of this work the design a new rapid and selective method for the detection of *Candida albicans* genomic DNA using gated materials. The developed system consists of a porous support loaded with a dye and with the pores blocked by a molecular gate.[3] As porous support, we tested mesoporous silica nanoparticles and nanoporous anodic alumina (NAA).[4] This second material is a merging support on the biosensing field.[5] As gating mechanism, oligonucleotides were selected for its affinity and specificity to recognize different molecules or biomolecules.
The prepared systems showed a good limit of detection and high selectivity to *Candida albicans* genomic DNA.

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P-70

VISUAL DETECTION OF ALUMINIUM ION USING A FLUORESCENT PROBE BASED ON A BODIPY CORE

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Al is the third most abundant element in the earth and its compounds was used in water purification, food additives and pharmaceuticals. Unfortunately, over dose of Al^{3+} in human tissues and cells can induce Parkinson's disease, osteoporosis, headache, gastrointestinal problems and Alzheimer's disease.[1-4] For this reason, a rapid and selective detection of Al^{3+} is very important.

We synthetized and studied a new probe able to detect selectively Al^{3+} in presence of different cations (Na^{+}, K^{+}, Li^{+}, Mg^{2+}, Ca^{2+}, Co^{2+}, Ba^{2+}, Cu^{2+}, Ni^{2+}, Zn^{2+}, Hg^{2+}, Al^{3+}, In^{3+}, Cr^{3+}, Ga^{3+}, Fe^{3+}, As^{3+}). We selected a BODIPY fluorophore because of its high quantum yields and its remarkable solubility in water and organic solvents (see Figure 1).

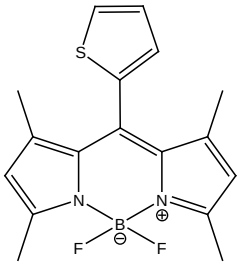

Figure 1

Solutions of probe in water-acetonitrile 2:8 are characterized by the presence of an absorption band centered at 509 nm, which gives a yellow color. Among all the tested cations, only Al^{3+} changes the color of the solution from yellow to orange. These changes are reflected in the appearance of a new band in the visible region, centered at 530 nm. The changes occur 10 minutes after the addiction of the cation Al^{3+} pointing toward a chemical reaction as a mechanism of the observed chromogenic response.

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P-71

Gated mesoporous silica nanoparticles functionalised PEDOT:PSS as a chemical bidirectional system of communication with neurons.

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Conducting polymers (CPs) are promising materials for use in the treatment of neurological lesions activating the molecular machinery necessary for cell adhesion and axonal elongation. In this field, scaffolds made of the conducting polymer PEDOT (poly (3,4-ethylenedioxythiophene)) combined with PSS (polyestyrene sulfonate) would provide a powerful tool to potentiate reparative responses by electrical stimuli, either by releasing growth factors or modifying the molecular interactions at the polymer/cell interface. However, these challenging technologies demand stable presentation of multiple biomolecules on the polymer surface and resisting detachment under electrostimulation.[1]

Due to the properties of mesoporous silica nanoparticles (MSNs) to regulate the release of encapsulated molecules in response a specific stimulus, the covalent attachment of gated MSNs on the PEDOT:PSS surface could be a promising tool to achieve a stable presentation of biomolecules needed in neural repair. In this case, in which electrostimulation is required, molecules that presented stable oxidation/reduction cycles could be use as organic electrodes as was described in a previous report.[2] The capped material remained closed, but if a potential was applied, the electrochemical oxidation/reduction of the molecule used as modifier organic electrode, induced the guest delivery.

Based on these premises, we design a system based on the use of PEDOT:PSS functionalized with MSNs capped with electro-responsive voltage-triggered organic molecules as substrates for promoting the reparative responses in neuronal applications. In our approach, we electrosynthesised a PEDOT:PSS scaffold on gold-coated surfaces which was functionalized by covalent immobilisation of MSNs loaded with the dye rhodamine B and with the external surface derivatized with (3-aminopropyl)triethoxysilane. Once MSNs assembled onto the polymer, we functionalized the unbonded surface with 4,4'-bipyridinium-1-(carboxymethyl)-1'-methyl diiodide. Finally, the pores of MSNs were capped with heparin (through electrostatic interactions with the positively grafted bipyridinium subunits). Preliminary in vitro release studies were performed by electrostimulation of the scaffold with a potential of -550 mV, with the consequent reduction of the 4'-bipyridiniun-1-(carboxymethyl)-1'-methyl di-iodide, resulted in heparin displacement which cause rhodamine B delivery.

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P-72

SILICA MESOPOROUS NANODEVICES TO OVERCOME DRUG RESISTANCE IN BREAST CANCER

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Important improvements have been achieved in recent years in chemotherapy and in patients' survival after cancer treatments; nevertheless, cancer cells resistance to drugs and anticancer agents side effects still remain crucial problems. Drug resistance, the phenomenon by which a drug is not able to inhibit cancer without producing high toxicity, is the first cause of failure of oncologic treatments and produces a significant decrease of chemotherapeutics efficacy, allowing resistant cells survival and consequent tumour recurrence, metastasis and poor prognosis. Over 50% of cancer relapses are caused by multidrug resistance, possibly due to a poor distribution of the drug to the targeted tissue.[1]

A key role in drug resistance is performed by cancer stem cells (CSCs), that are capable to survive and repopulate the tumour with self-renewing cells and variably differentiated offspring. To eradicate these CSCs with specific drugs is a crucial objective to prevent tumour repopulation and recurrence.[1]

In this work we present a new targeting delivery system, based on mesoporous silica nanoparticles, developed with the aim to treat a putative doxorubicin resistant breast carcinoma cell line. Doxorubicin represents the main chemotherapy choice in breast cancer treatment, especially for high-risk patients, however, is often associated with tumour cells acquired resistance. Our nanodevices are loaded with doxorubicin and the non-coding microRNA miRNA-200c, and decorated in their external surface with polyethylenimine and high molecular weight hyaluronic acid. Hyaluronic acid allows to direct our nanoparticles to CD44 receptor, a CSCs population marker in breast cancer, and at the same time has an effect in tumour inhibition,[2] while miRNA-200c has been shown to have a key role in monitoring chemotherapeutic drugs resistance and it seems to be downregulated in different human cancer types.[3]

Our first results demonstrate the supposed doxorubicin resistance in the investigated breast cancer cell line and cellular assays to study our nanodevices ability to revert such resistance are being performed.

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P-73

Determinación de parámetros de calidad en aguas de suministros potables mediante Lengua Electrónica Voltamétrica

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Las Lenguas Electrónicas son sistemas analíticos aplicados usualmente al análisis de muestras líquidas. La estrategia de Lenguas Electrónicas se basa en el uso de sensores semi-específicos que, aunque no respondan particularmente a ningún compuesto, permiten obtener una huella físico-química característica para cada tipo de muestra (Fig. 1). Normalmente se componen de varios sensores y generan información multidimensional. [1]

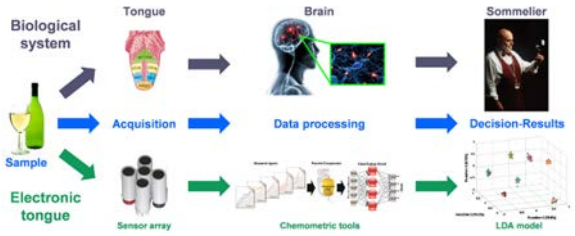

Fig. 1 – Representación esquemática de una lengua electrónica por analogía con un catador de vinos. Figura tomada de la referencia 8.

El uso e interés de las lenguas electrónicas ha crecido durante las dos últimas décadas. [2] Se han desarrollado varias técnicas tales como la potenciometría, la amperometría y la voltametría, y los datos obtenidos se analizan mediante técnicas de análisis multivariante. [2,3] Debido a la simplicidad y la versatilidad, las Lenguas Electrónicas, se han implementado para su aplicación al análisis de muestras complejas [4], en la industria de alimentos [5,6], en el análisis de vinos [7,8], el análisis medioambiental [9] y la monitorización de calidad del agua residual [10] y de consumo. [3]

Las Lenguas Electrónicas voltamétricas ofrecen medidas robustas e información versátil de los sistemas estudiados. En los experimentos de voltametría se aplican diferentes tipos de pulsos a los electrodos de trabajo, y la corriente resultante es una medida de las especies iónicas y los compuestos redox activos en la disolución. [4]

En este trabajo se presenta la aplicación de la lengua electrónica voltamétrica para el control de calidad de aguas de suministros potables mediante el análisis cuantitativo de diversos parámetros de calidad.

Se analizaron muestras de 9 suministros de aguas potables. De cada suministro se estudiaron 10 muestras (6 muestras en un caso). Dada la composición regular que suelen presentar los suministros de aguas potables, se realizó un análisis completo de los principales parámetros de calidad para cada uno de los suministros, y se asumió la composición invariable para las 10 muestras de cada uno de ellos.

Por otra parte, de cada muestra de cada suministro se analizaron 3 alícuotas de agua potable mediante lengua electrónica voltamétrica de metales nobles (Ir, Rh, Pt, Au). Para cada metal se programó un tren de 10 pulsos con diferentes potenciales, recogiendo 100 valores de corriente en µA (1 valor cada ms) para cada pulso. En total se recogieron 4000 datos (100 valores x 10 pulsos x 4 electrodos) para cada muestra.

Para evaluar la calidad de la voltametría en la predicción de diferentes parámetros analíticos, se realizó un análisis estadístico multivariante mediante Regresión de Mínimos Cuadrados Parciales (PLS). PLS se utiliza cuando el objetivo del análisis es la cuantificación de la concentración de alguna sustancia o alguna

característica de la muestra. [12,13] De todos los parámetros determinados para cada muestra se seleccionaron aquellos que presentaban un resultado numérico determinado (no <X o >X). De este modo, para cada uno de los suministros se estudiaron las predicciones para la conductividad y el contenido de nitrato, sulfato, fluoruro, cloruro y sodio.

Se construyeron modelos con un conjunto de muestras de entrenamiento, utilizando 7 de cada 10 muestras y se analizó la bondad del modelo para la predicción de los parámetros en las 3 muestras restantes para cada suministro.

De los análisis mediante PLS se obtuvieron los siguientes resultados:

Parámetro	Intervalo	R2 CV	R2 Pred.	RMSECV	RMSEP
Conductividad	0-1600	0.588	**0.856**	222.3212	**136.6133**
Nitratos	0-120	0.675	**0.804**	23.1263	**18.7902**
Sulfatos	0-500	0.814	**0.776**	51.3601	**52.7802**
Fluoruro	0.05-0.30	0.504	0.585	0.0411	0.378
Cloruro	10-200	0.823	**0.919**	19.7744	**13.7221**
Sodio	10-100	0.801	**0.898**	9.9611	**7.2328**

Los mejores resultados se obtuvieron para la predicción de la conductividad, y el contenido de nitratos, sulfatos, cloruro y sodio.

De acuerdo con estos resultados, las medidas con lengua electrónica sobre muestras con control de temperatura permitían establecer el contenido aproximado de Nitratos con un error relativo aproximado del 15%, y el contenido aproximado de Cloruros, Sulfatos, Calcio y Sodio así como de la Conductividad con un error relativo aproximado del 10% para muestras en el intervalo de parámetros de las muestras estudiadas.

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P-74

PARTIAL LEAST SQUARES APPLIED TO CORROSION STUDIES ON REINFORCED CONCRETE

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Keywords: Reinforcing steel, partial least squares, potentiostatic pulse.

Potentiostatic Pulse Testing (PPT) has been used to estimate i_{CORR} [1, 2].

A previous paper was submitted at IX International Workshop on Sensors and Molecular Recognition where reliable corrosion density values close to the Tafel ones were obtained by combining Partial Least Squares (PLS) with Linear Polarisation Resistance (LPR) raw data[3]. In this work, PLS statistical approach has been used to estimate the corrosion density and verify if by combining this technique with the data obtained through PPT is possible predict a reliable corrosion density value close to the values obtained directly with Tafel method (TP).

To study the corrosion process in concrete were made 50 concrete cylinder specimens, with a reinforced steel bar embedded in the center. After a curing period, all samples were immersed in aqueous solution 0.5M NaCl at laboratory conditions. A standard three-electrode cell was used to carry out the electrochemical experiments. PPT was implemented applying a short-potential pulse (OCP ±10mV). On the other hand, a voltammetric scan (OCP ±140 mV) was applied. By means TP, E_{CORR} and i_{CORR} were obtained.

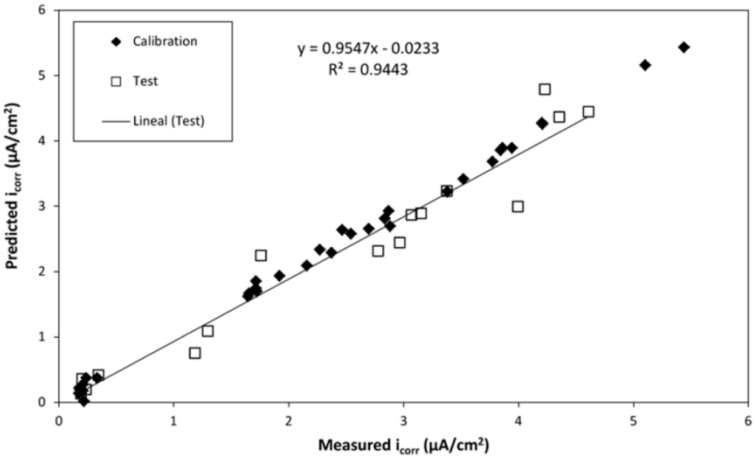

Figure 2. PPT-PLS model fit for calibration and validation samples.

X-matrix was built on current-time data obtained though PPT. The Y-matrix was built from the i_{CORR} value obtained with TP. Figure 1 shows the regression between measured and predicted i_{CORR}. Through R^2, line trend slope and RMSEP (0.40) obtained is possible to affirm that the combination of PLS and pulse is a reliable option for calculating i_{CORR} in solid specimens.

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P-75

ADENOSINE MONOPHOSPHATE-CAPPED GOLD(I) NANOCLUSTERS: SYNTHESIS AND LANTHANIDE ION-INDUCED ENHANCEMENT OF THEIR LUMINESCENCE.

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Fluorescent, water-dispersible gold nanoparticles of an extremely small size (with a diameter usually smaller than 2 nm) are currently being studied for chemical sensing and catalysis and also for biological applications (bioimaging and photodynamic therapy)[1-3] on account of their low toxicity, biocompatibility, chemical and photochemical stability, and easy surface functionalisation.

These gold nanoparticles present a considerable electronic energy quantisation and as a consequence they exhibit a discrete electronic structure and molecule-like properties. They are considered to be a new type of material and have been termed as ultra-small nanoparticles or nanoclusters (AuNCs) to differentiate them from plasmonic gold nanoparticle (AuNPs). For example, luminescent AuNCs capped with AMP have been prepared by reduction of $HAuCl_4$ using citrate and light exposure[4]; they exhibit considerably long-lived, blue-light luminescence (at ca. 470 nm, lifetime of ca. 1μs, quantum yield, Φ_f, of 1.6%). Polyadenosine-capped AuNCs obtained by the same strategy also show luminescence at ca. 470 nm.[5]

From the above-mentioned results it can be inferred that the presence of metal cations (either Au^+ or cations from other metals), could induce either enhancement or quenching of the charge-transfer luminescence in AuNCs. In line with this, we envisaged the interest of studying the effect of lanthanide ions, in particular, Yb^{3+} and Y^{3+} on the luminescence of AMP-capped AuNCs.

We report here the preparation of blue-luminescent AMP-capped Au^+ NCs by using HEPES, as the surfactant and reductant, and light exposure. The nanoclusters exhibit a quantum yield of 2.6%. The UV-Vis spectrum of the nanoclusters displayed a broad UV-band with two maxima at ca. 300 nm and 260 nm (Figure 1a). The AuNCs exhibited a blue luminescence with maximum at ca. 474 nm (Figure 1b, 1c). These nanoclusters proved to be considerably photostable in both nitrogen and oxygen atmosphere (Figure 1d shows the negligible variation of their emission after prolonged irradiation (up to 1h) under the fluorimeter lamp (λ_{exc} = 300 nm).

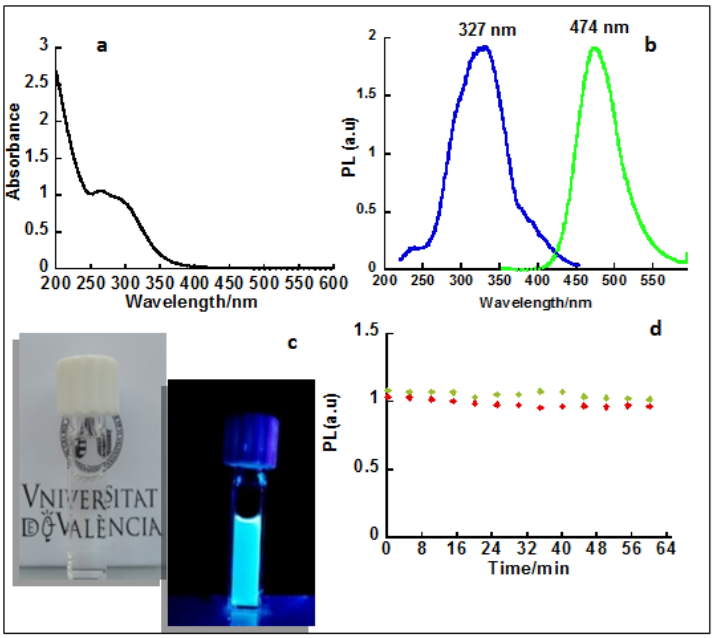

Figure 1: a) Absorption spectrum of Au^+ NCs in water; b) emission spectrum of Au^+ NCs in water recorded at λ_{exc}= 300 nm (green) and their excitation spectrum (blue) at λ_{em}= 474 nm; c) picture of Au^+ NCs under lab light and UVB light; d) room-temperature PL (λ_{em}= 474 nm) of Au^+ NCs in water as function of the irradiation time; (λ_{exc}= 300 nm).

The photoluminescence (PL) of the NCs was considerably enhanced after adding Y^{3+} and Yb^{3+}. The doped NCs exhibited a slightly red shifted PL peak (2 nm) compared to the undoped Au^+ NCs. The emission peak position and shape of the Au^+/Ln^{3+} NC PL did not exhibit dependence on the excitation wavelength (assayed wavelengths: 260, 300, and 350 nm) (Figure 2).

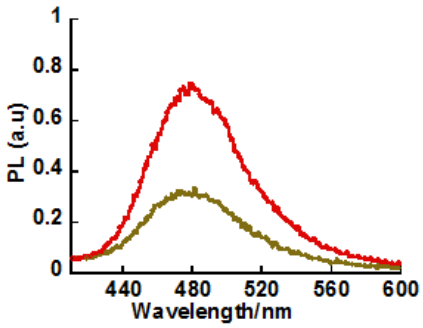

Figure 2: Comparison between the emission spectrum (λ_{exc} = 350 nm) of the Au^+ NCs and that of Au^+/Y^{3+} NCs at the same absorbance (0.016 at 350 nm).

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P-76

Integrated Electrochemical Microfluidic System for Molecular Diagnostics

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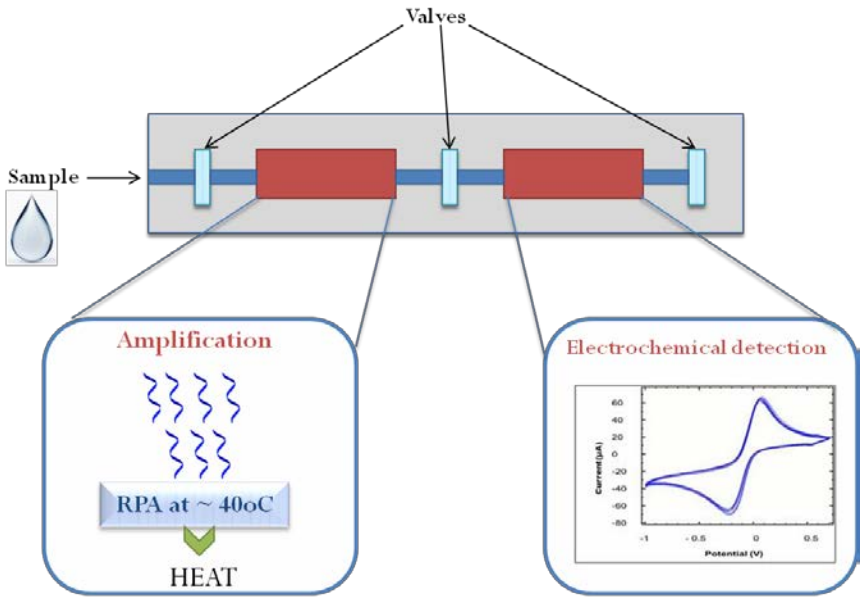
Abstract

We demonstrate a new electrochemical system for the rapid and inexpensive detection of nucleic acids with applications in molecular diagnostics. The objective is to achieve a low cost, integrated device for use at the point-of-need. The system should low cost (less than 1€ bill of materials) with the analysis being completed in less than 45 min with minimal user intervention, and total integration, truly achieving "sample in-result out". The power requirement should permit the system to operate with the battery of a mobile device such as a smartphone.

The availability of such a device can be transformational for health care not only in resource- limited environments but also for the rationalisation of health costs in advanced economies. Food safety and quality assurance from farm to fork and the disruptive innovation of HACCP implementation could be another beneficiary of the proposed technological innovation. Finally, environmental monitoring can be improved. The model system used for development is centred on the environmental monitoring field proposing the field detection of toxic algae.



Sketch for design and components of the proposed microfluidic system

This work has been carried out with the financial support from the Ministry of Economy and Competitiveness, (Seasensing Project, ref.BIO2014-56024-C2-1-R)):"Seasensing: Microsystems for rapid, reliable and cost effective detection of toxic microalgae on-site and in real-time"

P-77

Efecto de la polaridad del medio en la fluorescencia de TPEs con diferente cadena alquílica

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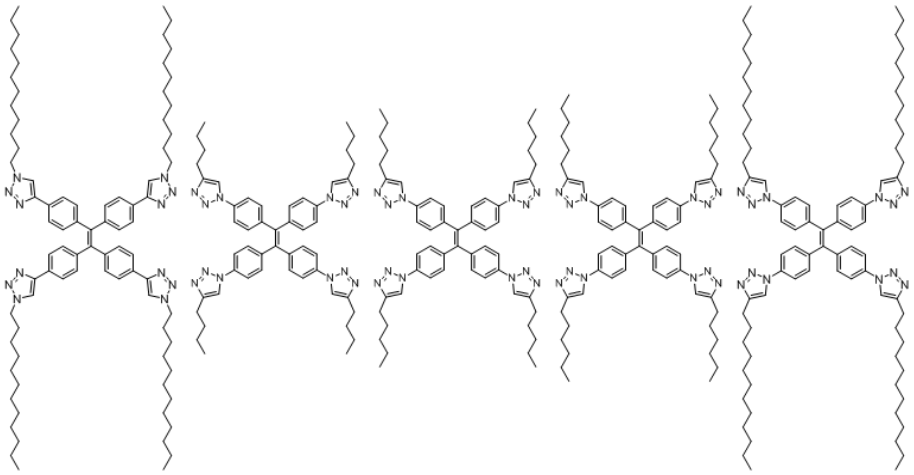
Los tetrafeniletilenos son una familia de compuestos que ha cobrado especial relevancia en los últimos años[1,2] debido a que presentan un fenómeno conocido como Emisión Inducida por Agregación (AIE). Éstos compuestos incrementan su emisión fluorescente de forma drástica cuando se favorece la agregación de las moléculas del mismo, a diferencia de lo que ocurre con luminóforos más comunes, que sufren el efecto contrario (ACQ). Por esto, se está explorando su uso en la creación de dispositivos electroluminiscentes, como quimiosensores fluorescentes, en "cell imaging" o para la obtención de agregados microestructurados con emisión configurable.[3]

De cara al posible uso de derivados de tetrakis(4-(triazolil)fenil)etileno aquilados como sensores, se ha realizado un estudio comparativo con el objetivo de caracterizar los efectos de la polaridad del medio en la emisión fluorescente en los **compuestos 1-5**.



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