Scientific Report
2015-2016

IQFR

Scientific Report 2015-2016

Physical Chemistry Institute

Rocasolano

Spanish National Research Council

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The editors would like to thank all the staff of the Institute who have contributed to the realization of this Scientific Report.

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Science vice-director

Juan Zenón Dávalos Prado
Technical vice-director

Presentation

Juan de la Figuera Bayón

The Institute of Physical Chemistry "Rocasolano" (*Instituto de Química Física "Rocasolano", IQFR*) continues the scientific tradition of the National Institute of Physics and Chemistry (*Instituto Nacional de Física y Química*), part of the Committee for Advanced Studies (*Junta de Ampliación de Estudios, JAE*), whose building it occupies presently. The building and the original institute were funded thanks to a generous grant from the International Education Board of the Rockefeller Foundation in the 1920s, with the condition that the building would be dedicated in perpetuity to research. It was designed to nurture and promote research in Spain after detecting a nucleus of competent investigators who realized their studies in precarious conditions. It was the first "modern" research center in Spain both in the design of the building and in terms of its operating standard, comparable to the best modern research centers. For example, the criterion for the formation of a section was: "A new section will not be created until a person qualified to direct it is found, whose abilities are demonstrated by the authority that their work enjoys among the specialists". It witnessed the work of researchers such as Blas Cabrera, Miguel Catalá, Enrique Moles or Julio Palacios, and their level of international connections is attested by distinguished visitors such as Arnold Sommerfeld, William Bragg and Marie Curie among others. This promising start was sadly cut off by the Spanish Civil War.

Later, in 1946, the Spanish National Research Council (*Consejo Superior de Investigaciones Científicas, CSIC*), who inherited the tasks and responsibilities of the JAE, created the IQFR, with its first director Antonio Ríus at its helm. Since then, the IQFR has become a national reference in research in Pure and Applied Physical Chemistry.

A proof of its relevance at the national scale is the many, more specialized Research Institutes within the CSIC have originated in our Institute. In addition, researchers from the IQFR contributed to the founding of several University Departments of Physical Chemistry throughout the Spain.

Since the 1930s, research lines have evolved and changed. Some have been extinguished or continued in other centers to which the IQFR has given birth. Other lines have become international references. At present, the Institute focuses its research in several areas within Physical Chemistry and Chemical Physics, emphasizing its strong multidisciplinary character in the boundary between Chemistry, Physics, Biology and Materials Science. It stands out for a set of outstanding experimental techniques that enhance the capabilities of the center and allow it to cover very diverse fields. In this time of ultra-specialized institutes, it is one of the few institutes that maintains a generalist approach that allows it to adopt new research directions that share the underlying physical-chemical orientation. Among these, we emphasize the research in Biological Chemistry and Atmospheric Chemistry. In the first case, the application of chemical-physical techniques to problems of biological interest has been quite successful, taking advantage of the top-level instrumentation of the Institute such as the "Manuel Rico" High Field Nuclear Magnetic Resonance Laboratory, which houses the CSIC's largest nuclear magnetic resonance spectrometer (one of the three available in Spain of its kind), fluorescence microscopy, high resolution mass spectrometry or the X-ray

Diffraction Laboratory for proteins. Furthermore, it is positioning itself at the forefront of the latest techniques such as the application of free electron lasers. In Atmospheric Chemistry, we highlight the construction of a spectrometer designed to orbit on the first Spanish Earth observation satellite, which will provide high-resolution maps of atmospheric concentrations of gases, taking advantage of tradition of the IQFR in photolytic studies, chemical reactivity and surface reactivity in their application in atmospheric studies. It is also noteworthy the continuous use that researchers of the institute, both on material science and biological chemistry, make of the Alba synchrotron at Barcelona.

The Institute also includes specialized support units in electronics and mechanics, that are a necessary complement and key part to the experimental work carried out at the IQFR. A serious accident in the machine shop, which has been successfully solved thanks to the prompt response of all involved, has reinforced the Institute's Health and Safety (H&S) culture, in which H&S and biosafety committees for have been set up. The library of the Institute, which is a direct descendant of the original library from the 1930's and is still a reference in Chemistry and Physics on the national level, with hundreds of journals and a good number of historical collections, has successfully made the transition to the digital age, being one of the main sources of loans to other institutions.

The excellent level of research, complemented by an outstanding technical capacity, positions the IQFR to take advantage of the still hoped for improvement of research in Spain. The scientific productivity per capita of the institute is the highest in its history as measured either by the number of papers or by the quality of the journals where the research is published, and it is receiving funding both from national and European agencies at a much higher level than during previous years. The recent award of a European Research Council grant is especially noteworthy. And yet, despite this excellent research, all its activity depends on a research administrative and technical staff which is increasingly aged and whose numbers dwindle due to retirement. There has been no new incorporation of staff researchers during this period, and each retirement represents an irreparable loss to the capacity of the center, and an irreversible loss of knowledge. In this subject, the draconian reductions in the number of fellowships for Ph.D students and postdocs as well as the severe dearth of faculty positions limits our research capacity and clouds our future. The Ramón and Cajal researchers of this Institute are especially affected as they see how, after a successful scientific career, their future becomes extremely uncertain. Finally, the institute has had to face the death of a collaborator of outstanding trajectory, Manuel Rico Sarompas, and one of its "young" investigators, Noe García Almarza. They remain in our memory.

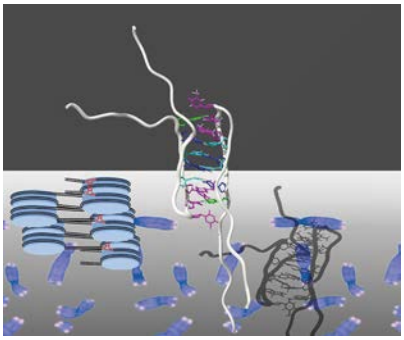
In summary, the IQFR covers topics related to Fundamental Physical Chemistry, such as the study of energetics and chemical reactivity (ion-molecule reactions, thermochemistry, computational chemistry, surface reactions), which complement interdisciplinary research with a strong implication in Science and Materials Technology and Nanotechnology, studies of the molecular basis of biological function in systems with increasing levels of organization, and the impact of chemical processes on climate change and pollution. Despite the difficulties encountered and thanks to its staff, it has not only maintained but improved its standing in these fields, and is ideally positioned to contribute to research in Spain.

Departments

Department of Crystallography and Structural Biology

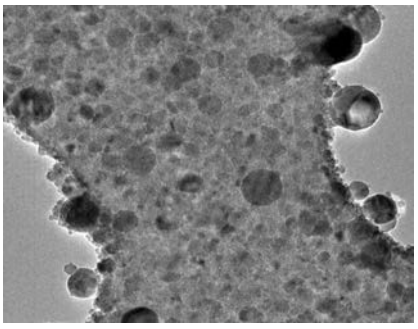
Department of Atmospheric Chemistry and Climate

- Energetics, Structure and Molecular Interactions Group
- Photolysis and Chromatography Group
- Atmospheric Chemistry and Climate Group



Department of Biological Physical Chemistry

- NMR of Protein Structure, Dynamics and Interactions Group
- Protein Bioconformatics and Assamblies Group
- Structural Bioinformatics Group
- Fluorescence and Molecular Biophysics Group
- Protein Structure and Thermodynamics Group
- NMR of Nucleic Acids Group



Department of Low Dimensional Systems, Surfaces and Condensed Matter

- Lasers, Nanostructures and Materials Processing Group
- Laser Materials and Laser-Materials Interaction Group
- Statistical Mechanics and Condensed Matter Group
- Surface Analysis and Mössbauer Spectroscopy Group


CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

Department of Crystallography and Structural Biology

Introduction

The members of the Department constitute the **Group of Protein crystallography and molecular recognition in biological processes** and focus their research to understand the biological functions of macromolecules in terms of their 3D structure at atomic, molecular and supramolecular levels. This provides information on their functionality and ability to recognize other molecular partners or a substrate, or to develop their activity in a particular environment. To achieve these objectives, we combine chemical, physical-chemical and biological techniques. Among them, crystallography occupies a preferential place since it is the most powerful technique to characterize single proteins or large stable macromolecular complexes at atomic level. Such knowledge provides the basis for new medical treatments and many biotechnological applications. In addition, our Department is also involved in the development of novel and efficient methods and strategies for phasing structures that make possible the solution of protein structures.

The Department is equipped with the state of the art technologies to develop our research. Our molecular biology laboratory is perfectly set up and equipped with all the modern technologies to produce recombinant proteins at milligram scale. The diffraction laboratory includes a new rotating anode generator equipped with two area detectors and a micro source generator for testing crystals. We also provide X-ray facilities for the crystallographic community through the RedLab network, which coordinates all the technological platforms of the Madrid Regional Government. In addition, we have established an automated crystallization platform which offers the newest and fastest tools for the screening of crystallization conditions using a minimum amount of protein sample. The platform includes two crystallization robots and a "crystal farm" for storage and analysis of the experiments. All these facilities are available for all CSIC researchers and for those coming from other institutions (http://www.xtal.iqfr.csic.es/DRXM/).

Group of Protein Crystallography and Molecular Recognition in Biological Processes

Tenured Staff Scientists

Armando Albert de la Cruz
(Associate Professor) ReID ORCID SCOPUS

Beatriz González Pérez
(Assistant Professor) ReID ORCID SCOPUS

Juan Antonio Hermoso Domínguez
(Professor) ReID

Lourdes Infantes San Mateo
(Assistant Professor) ReID ORCID SCOPUS

José Miguel Mancheño Gómez
(Assistant Professor) ReID ORCID SCOPUS

Martin Martínez Ripoll
(Professor Ad Honorem) ReID ORCID

María José Sánchez-Barrena
(Ramón y Cajal) ReID SCOPUS

Julia Sanz Aparicio
(Associate Professor) ReID ORCID SCOPUS

Non-tenured Scientists

Antonio Chaves Sanjuán
(Hired, 01/10/2014-31/08/2015)

Iván Acebrón (Contract, 1/12/2013-31/10/2015)

Martín Alcorlo Pagés (Contract, from 01/01/2015)

Rafael Molina Monterrubio
(Contract, from 01/10/2015)

Carol Siseth Martínez Caballero
(contract from 01/03/2016)

Ivanna Rivera Espinosa
(Estancia Post from 27/07/2015)

Concepción García Montañés
(Contract, from 01/12/2015)

Noelia Bernardo García
(Contract, 15/09/2015-17/02/2017)

Doctoral Students

Juan Luis Benavente Fernández
(Hired, 01/02/2016-31/12/2016)

Elsa Franco Echevarría
(Hired, 01/06/2013-31/12/2016)

Maria Moreno Alvero (Hired)

Mercedes Ramírez Escudero (Hired)

María Ángela Sainz Polo
(Hired, 01/01/2010-30/06/2015)

Noelia Bernardo García
(Contract, 01/12/2009-15/09/2015)

Alejandra Carriles Linares
(Fellowship, from 29/10/2015)

Teresa Domínguez Gil-Velasco
(Fellowship, 01/12/2012-31/12/2016)

María Teresa Batuecas Mordillo
(Fellowship, from 01/12/2015)

Rogeria Nunes Costa
(i-COOP, 02/04/2016–07/10/2016)

Technical Staff

Juana María González Rubio
(Titulado Grado Medio)

Rocío Benavente Rubio
(Contract, 01/02/2013-31/12/2014)

Pablo Fernández Cancelo
(Contract, from 01/05/2016)

José Miguel Moreno Verdejo
(Garantía Juvenil, 01/05/2016–30/04/2018)

Strategic Aims

- Structure and regulation of **large macromolecular machines** involved in bacterial division, bacterial and plant cell wall remodeling, ionic transport in plants and neuronal function.
- Lipid-protein interactions: Structure and function of **membrane proteins.**
- **Real time** structural characterization of enzymatic and **allosteric** processes.
- Multienzymatic cascades for the production of second-generation prebiotics and chitooligosaccharides from biomaterials.
- **In vivo labeling** of proteins and molecular machines on the cell surface.
- The generation **multienzymatic complexes** through the assembly of catalytic domains.
- "À la carte" production of novel high-valued **bioactive compounds** by means of enzymatic systems of *Lactobacillus plantarum* WCFS1.
- Application of magnetic nanoparticles for metastasis detection.
- Identification of **hot spots** in protein structures for the development of **new drugs** in the field of biomedicine and **agrochemicals**
- Development of a new tool for **multicomponent crystal formation prediction** for compounds with **pharmacological** interest.

Results

Structural biology of carbohydrate modifying enzymes

The plant cell wall is composed of an intricate net of interconnected polysaccharides of a dynamic structure that depends on the plant development and the environment. To cope with this complexity, nature has created a large variety of enzymes that act synergistically to deconstruct biomass. Our group has determined the molecular basis of the broad specificity of an enzyme isolated from the rumen microbiome that showed to constitute a novel family of proteins with permuted domains topology. Moreover, we have described that the tandem repeat of homologous ancillary domains in multimodular enzymes is not merely related to multivalency but, rather, represents a sophisticated mechanism of fine-tunning specificity (**Figure 1A**).

Our work has focussed also in the enzymatic production of bioactive compounds. Among them, prebiotics are functional ingredients stimulating selectively the growth of beneficial bacteria in the digestive tract, contributing to prevent cardiovascular disease, colon cancer and osteoporosis. These compounds show different functional profiles and, therefore, there is a growing interest in the design of new products to manipulate the individual microbiome. Thus, we have studied the molecular mechanisms of specificity of enzymes producing fructooligosaccharides (FOS, **Figure 1B**), isomaltoligosaccharides (IMOS) and xilooligosaccharides (XOS). The final goal is to get efficient biocatalysts.

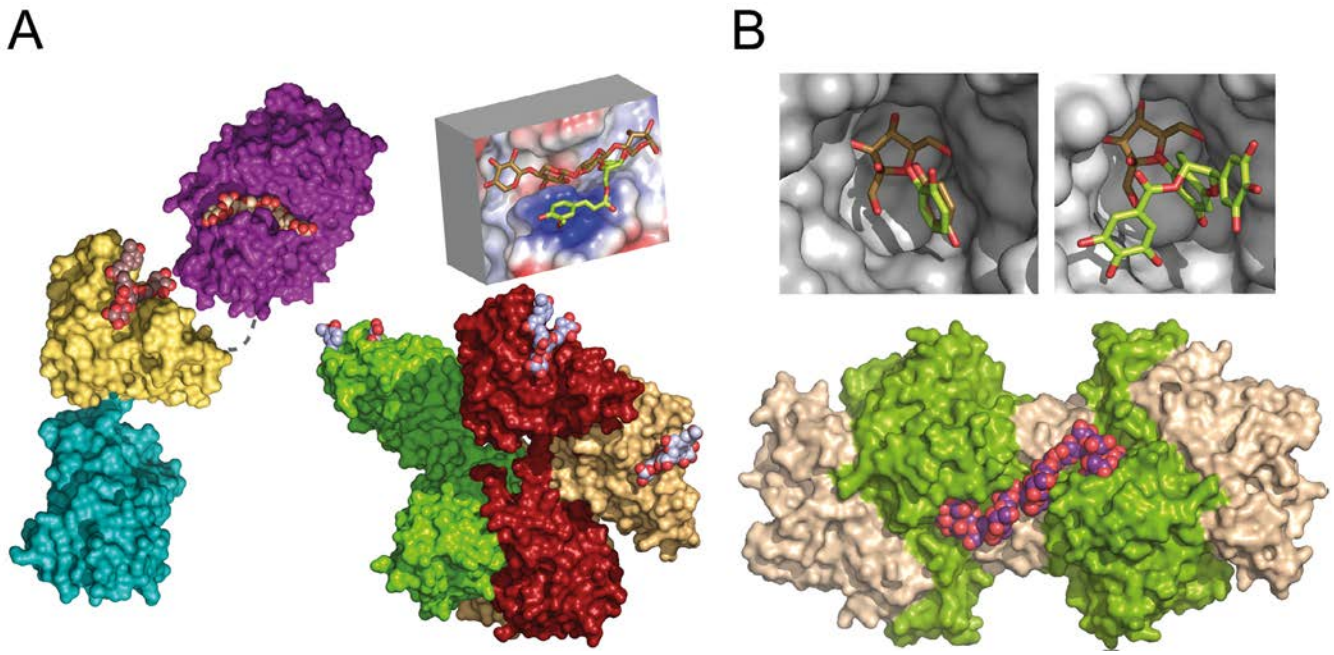


Figure 1: (**A**) Xyn10C is a multimodular xylanase with a N-terminal domain containing a XBD1-XBD2 tandem linked to the catalytic domain (magenta) by a flexible segment. Our results show that XBD2 (yellow) has affinity against specific sites at the polymeric substrate concerted with the catalytic domain, as it is shown in the inset; on the contrary, XBD1 (cyan) triggers the formation of a trimer (green, red and beige at the right.) (Sainz-Polo, J Biol Chem 2015). (**B**) Ffase is a dimeric enzyme from yeast that process FOS and presents a peculiar topology of its two binding sites. This topology is able to allocate branched fructans, which migth represent a molecular mechanism of adaptation to cope with extreme conditions. Ffase has a broad profile of acceptor substrates, what makes it a valuable biocatalyst (Ramírez-Escudero, J Biol Chem 2016).

Structural basis for the control of hydric stress in crop plants

Drought and salinity constitute the major limitation for crop productivity. Agriculture accounts for 70% of total water consumption and global water requirements are projected to be pushed beyond sustainable water supplies by 40% by 2030 Additionally, the global warming and climate change provoke that ordinary seasonal weather variations and other periodical atmospheric phenomena like El Niño have a major influence in crop production. Thus, it is required the development of strategies to improve the yield of crops under drought stress. A fundamental portion of the plant response to these environmental stresses occurs at the cell membrane, where the molecular machinery to preserve cell turgor and the appropriate balance of intracellular ions is found. The C2-domain ABA-related (CAR) family of proteins contributes to these processes by delivering the regulatory proteins controlling this machinery from other cell compartments to the cell membrane. In our recently published work "**Calcium-dependent oligomerization of CAR proteins at cell membrane modulates ABA signaling"** from the *Proceedings of the National Academy of Sciences* 2016, we provide an analysis that explains how CAR proteins specifically reach a particular membrane place to develop their function and trigger the plant defense mechanism against stress.

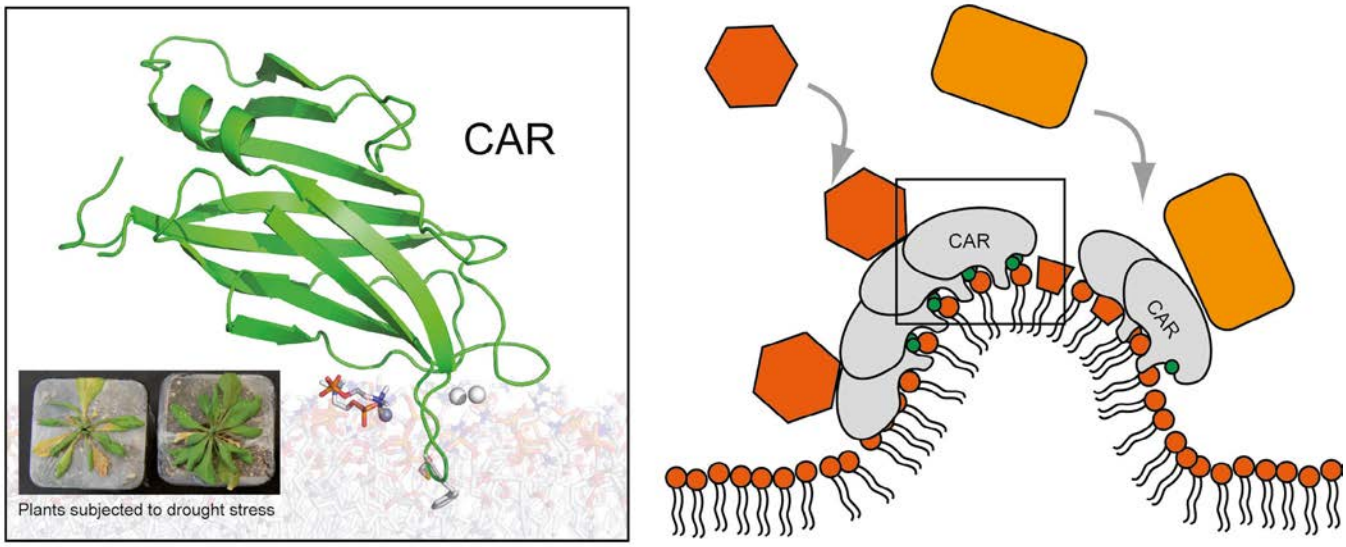


Figure 2. CAR proteins orchestrate at cell membrane the plant response to drought stress.

Enzymatic systems involved in the metabolism of phenolic compounds

The relevance of phenolic compounds (PhCs) in the diet and their potential role in disease prevention is progressively increasing these last years inasmuch as they are almost ubiquitous in our foods. One of the lactic acid bacterium present in the human gastrointestinal gut able to ferment PhCs-rich foods from vegetables is *Lactobacillus plantarum.* Our current interest is focused in the identification and further structural and functional characterization of the enzymatic systens involved in the reduction of hydroxycinnamic acids either directly, producing the corresponding phenyl-propionic acids, or indirectly acting on the vinyl derivatives that result from their previous decarboxylation catalysed by a decarboxylase. Nowadays, we have identified such enzymatic systems and also determined the crystal structure of one of the FMN-dependent reductases (**Figure 3A**).

Conversely, our group in collaboration with Prof. G. Köring and Prof. Federico Gago, has determined the structural basis of the Zn^{2+} and NAD^{+}-dependent stereoselective dehydrogenation of L-galactitol-1-phosphate to D-tagatose-6-phosphate (**Figure 3B**).

Biotechnological applications of β-trefoil lectin domains

Another research line is focused on biotechnological applications of β-trefoil lectin domains, particularly, in LSL_{150}. This small protein lectin has been used to devise a generic method aimed at the oriented attachment of recombinant proteins at the interface of agarose-coated magnetic nanoparticles (Ag-MNPs). In a joint collaboration with the research groups headed by Prof. Puerto Morales (ICMM, CSIC) and Prof. José M. Guisán (ICP, CSIC) we have designed such Ag-MNPs and also demonstrated that LSL_{150} acts as a molecular adaptor suitable for the oriented attachment of proteins. This is possible due to the particular topological features of LSL_{150} and its sugar-binding properties (Acebrón *et al*., 2016) (**Figure 3C**).

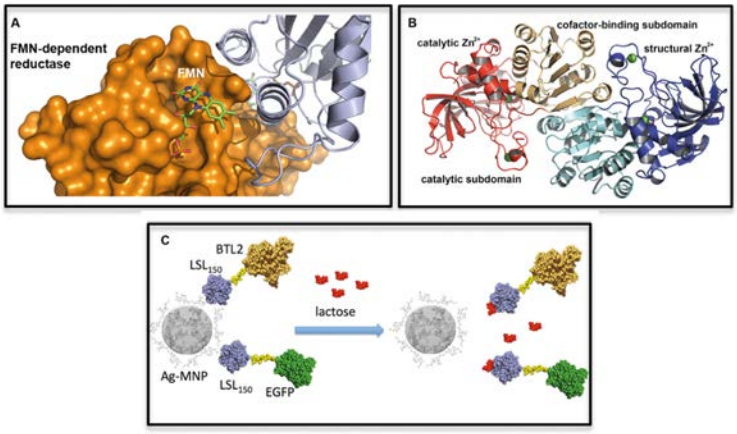


Figure 3. (**A**) Structure of one of the FMN-dependent reductases from *L. plantarum* involved in the reduction hydroxycinnamic acids. (**B**) Dimeric assembly of the galactitol-1-phosphate 5-dehydrogenase from E. coli. (**C**) Mechanism of the oriented attachment of proteins by the β-trefoil lectin domain LSL_{150} to Ag-MNPs.

The Ca^{2+} sensor NCS-1 as therapeutic target to regulate synapse function in neuronal disorders

In 2014 we showed that the complex formed by the Ca^{2+} sensor NCS-1 and the guanine exchange factor Ric8a regulates synapse number and probability of neurotransmitter release in neurons (Romero-Pozuelo et al., 2014; Baños-Mateos et al., 2014). Our results suggested that NCS-1 could be a potential target in diseases with altered synapse number. Therefore, the regulation of the interactions between NCS-1 and Ric8a with small molecules could be a new therapeutic strategy for synaptopathies such as Fragile X Syndrome. We are carrying out a multidisciplinar approach including structural studies, computational simulations to find active candidate molecules, and biochemical, cellular and behavioural studies with model animals to analyse the activity of the selected molecules.

Mechanistic study of the antibacterial activity of AS-48

AS-48 is a cyclic peptide with antimicrobial activity. Our crystallographic data, together with biochemical and biophysical studies on protein-protein and protein-membrane interactions shed light on the molecular mechanism of action of this bacteriocin (**Figure 4**). We have demonstrated that in a first step, the electrostatically driven approach of an inactive water-soluble dimer to the membrane takes place. At the bacterial membrane, the dimer dissociates and the protein inserts into the membrane. The presence of hydrophobic residues on the molecular surface of the protein strongly contributes to the overall affinity of this peptide to the membrane.

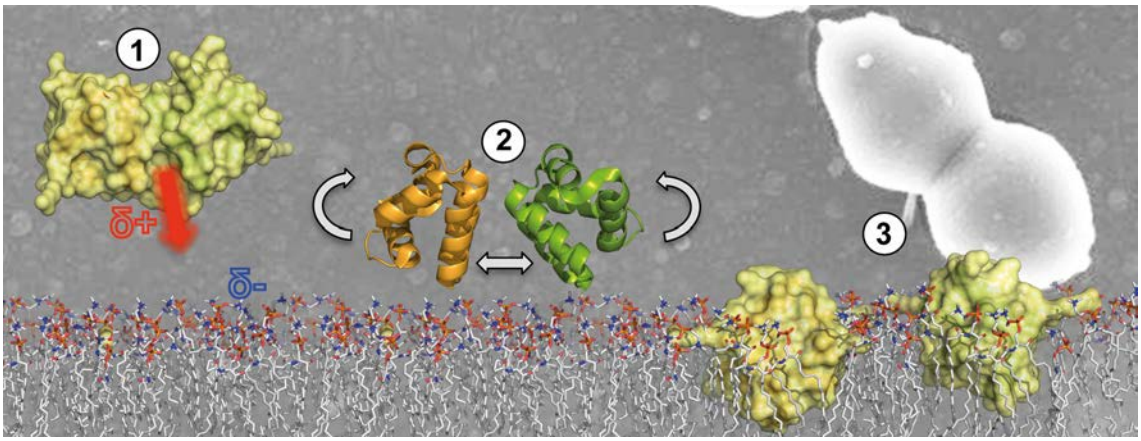


Figure 4. Molecular mechanism of action of the bacteriocin AS-48. (Cebrian et al, J Str Biol 2015)

Structure of inositol phosphate kinases and implications for health

The Inositol phosphates (IPs) kinases constitute a group of enzymes devoted to synthesize IPs, compounds with key roles in a variety of eukaryotic cell events. In particular, inositol 1,4,5-trisphosphate-3-kinase A (IP3K A) catalyses the synthesis of IP3, a well-known second messenger involved in calcium mobilization. In addition, this enzyme binds to and bundles actin filaments, regulating actin dynamics. IP3K increases the metastatic potential of lung tumour cells and both enzyme activities (catalytic and regulatory) are essential for it. These facts make IP3K as an attractive drug-target against cancer cells. A high through put screen allowed the identification of a specific and membrane-permeable inhibitor against IP3K activity (BIP4). We have already shown that this compound inhibits the adhesion and proliferation of lung cancer cells. A *docking* analysis (**Figure 5A**) guided by crystallographic partial results allowed us to propose a putative orientation of BIP4 in the active site of IP3K as well as its interacting groups (**Figure 5B**). This work (Schröder et al, Biochem. Pharmacol, 2015) represents the first approach to this enzyme inhibition combining *in vivo* and *in vitro* techniques with structural studies in order to give insights into a rational drug design.

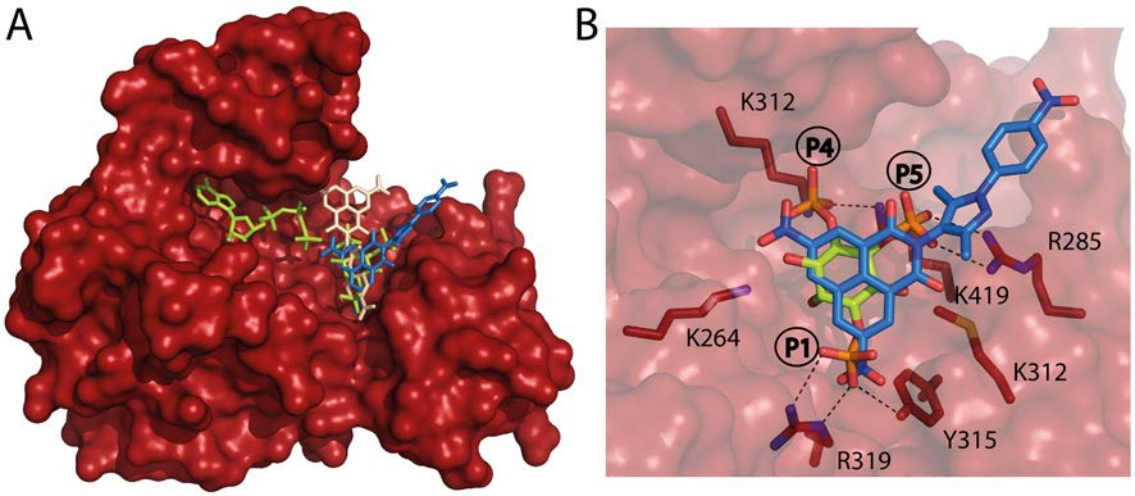


Figure 5. Prediction of BIP4 binding mode in IP3K by docking. (**A**) The structure of IP3K kinase domain (surface representation in red) in presence of an ATP analogue and the substrate IP3 (shown as green sticks). A representative for each BIP4 orientation obtained by docking is shown as sticks in a different colour (cream and blue). (**B**) A zoom showing the overlapping between IP3 (green) and the best BIP-4 orientation (blue) yielded by GOLD. The residues involved in IP3 phosphates recognition are represented in reddish colour. The colour code is as follows: orange (phosphates), yellow (sulphur), red (oxygen) blue (nitrogen).

Structural biology of bacterial pathogenesis

Antimicrobial resistance is one of the most serious health threats. The main goal of Hermoso's team is to generate the knowledge, based on an integrative study of some critical bacterial cell wall remodeling processes, to provide new pharmacological targets in the fight against some of the most dangerous multidrug-resistant pathogens. We focus on five main general objectives: (i) the study of the virulence mechanisms mediated by pneumococcal surface proteins, (ii) the molecular characterization of the pneumococcal divisome, (iii) Cell-wall recycling and antibiotics resistance in G(-) pathogens, (iv) The multidrug resistance mechanisms in MRSA, (v) Synthesis and regulation of cell wall mediated by non-canonical D-amino acids (NCDAA).

Inside these objectives, some of the main achievements during 2015-2016 were:

Methicillin-Resistant *Staphylococcus aureus* (MRSA): An essential protein in MRSA resistance is PBP2a. We have reported the crystal structure of PBP2a in complex with a ligand representing a new family of antibiotics against MRSA (**Figure 6B**). The antibiotics is located at the allosteric site—a remarkable 60 Å distant from the DD-transpeptidase active site— and opens a new way in treatment against MRSA (Bouley et al J. Am. Chem. Soc. (2015), Acebron et al Curr. Med. Chem. (2015)).

Cell-wall recycling and antibiotics resistance: *Pseudomonas aeruginosa* and members of Enterobacteriaceae have become very difficult Gram-negative bacterial pathogens. Of special interest is the relationship between cell-wall recycling and antibiotic resistance in these Gram(-) organisms (Domínguez-Gil et al Drug. Resistance Updates (2016), Rivera et al Microb. Drug Resist. (2015)). We have characterized two critical enzymes, SltB3 and MltF) involved in degradation of peptidoglycan (Lee et al ACS Chem. Biol. (2016), Domínguez-Gil et al Structure (2016)) (**Figure 6A**). These studies provided unprecedented regulatory mechanisms for the Lytic-transglycosilase family.

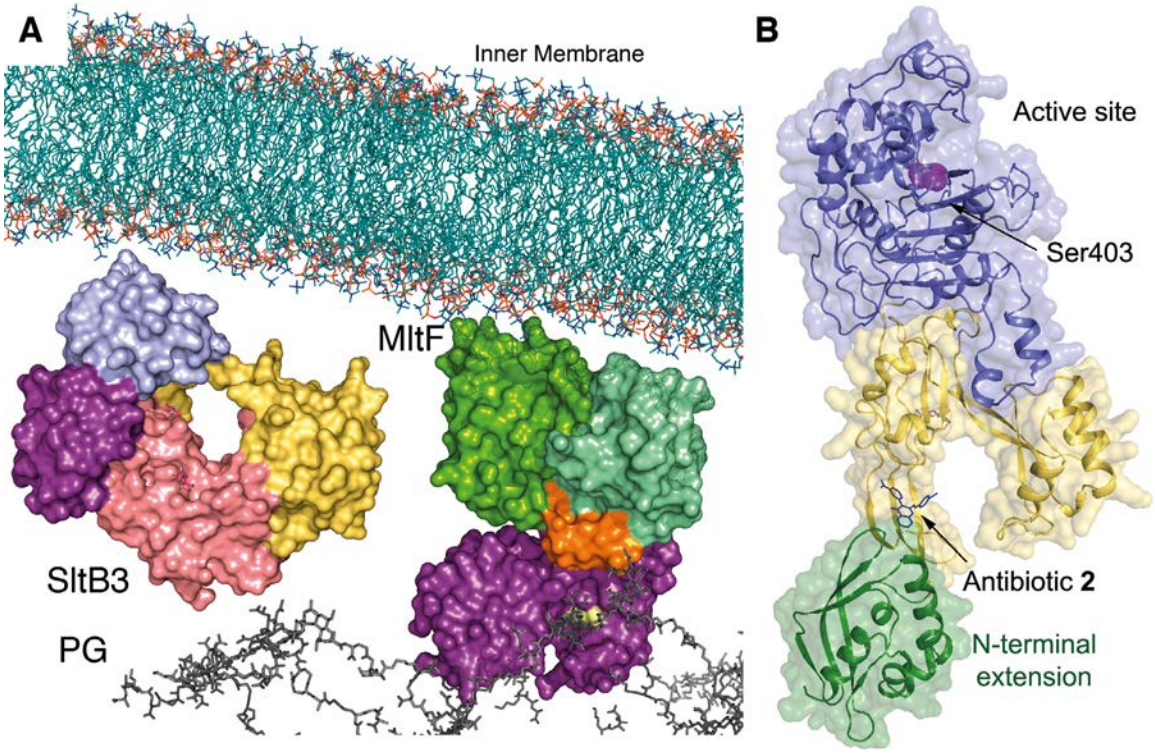


Figure 6. (**A**) crystal structures of SltB3 and MltF lytic transglycosilases involved in peptidoglycan recycling and antibiotics resistance in P. aeruginosa (Lee et al ACS Chem. Biol. (2016), Domínguez-Gil et al Structure (2016)). (**B**) Crystal structure of PBP2a of MRSA in complex with a new antibiotic bound at the allosteric site (60Å far from the active site) (Bouley et al J. Am. Chem. Soc. (2015)).

Drug design based on the complementarity between molecules to improve their physicochemical properties

Crystal composition and structure modify the performance of drug doses, "Active Pharmaceutical Ingredients" (APIs). Based on that, multi-component crystals have been considered as a possible solution for the improvement of their Bioavailability (Absorption, Distribution, Metabolism and Elimination, ADME)

Using concepts of probabilities of hydrogen bond formation, complementarity between the shape and size of the molecules and the ability to form intra- and inter-molecular interactions for different chemical groups; a tool is being developed to predict probabilities of co-crystalization between a drug and any possible human safe compound (coformer). In particular, nevirapine (NVP) is being used to improve its solubility. NVP is an antiretroviral drug and was the first non-nucleoside reverse transcriptase inhibitor.

Figure 7. *Left:* Full Interaction Maps (FIMs) calculated around NVP molecule with three specific probe types: Uncharged NH Nitrogen (blue), Carbonyl Oxygen (red) and Aromatic CH Carbon (yellow). *Right:* Repetitive packing motif of NVP showing the voids that are occupied for coformers.

Teaching and diffusion of Crystallography

The Department offers a fully-dedicated website for learning Crystallography (http://www.xtal.iqfr.csic.es/Cristalografia/) written in two languages (Spanish and English). It was announced by the International Union of Crystallography (http://bit.ly/dHj0Q0) and selected by this institution as one of the most interesting sites for learning crystallography (http://bit.ly/1zCsBOX). It was offered as such in the commemorative web for the International Year of Crystallography (http://bit.ly/1BYMGyd), and suggested as the educational website to learn about crystals, diffraction and crystal structure determination in the brochure (http://bit.ly/1DXoqxP) prepared by UNESCO. It is also offered as one of the best learning online tools by several USA universities (see for example: http://bit.ly/guMQax, http://bit.ly/gCLbYk). Google Analytics, and other web counters directly accessible through the web page menu (ie, http://bit.ly/2bz1qfx), show that this web gets over 1,500 different page visits a day (over 500,000 page visits/year), distributed over 190 countries, but especially from USA, Mexico, India, EU and Latin American countries.

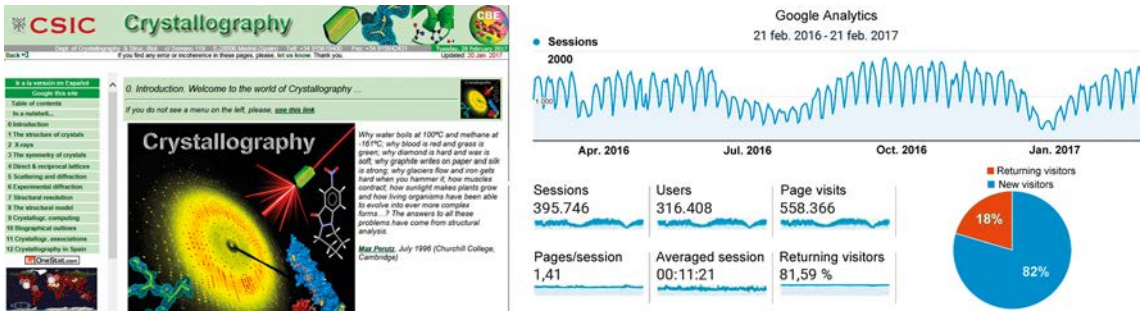


Figure 8. Website for learning Crystallography

Publications

Acebrón, I.; Chang, M.; Mobashery, M.; Hermoso, J.A. (2015). The Allosteric Site for the Nascent Cell Wall in Penicillin-Binding Protein 2a: an Achilles' Heel of Methicillin-Resistant Staphylococcus aureus. ***Curr. Med. Chem.*** *22,* 1678-1686.

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Benavente, R.; Esteban-Torres, M.; Kohring, G.W.; Cortés-Cabrera, Á.; Sánchez-Murcia, P.A.; Gago, F.; Acebrón, I.; de las Rivas, B.; Muñoz, R.; Mancheño, J.M. (2015). Enantioselective oxidation of galactitol 1-phosphate by galactitol-1-phosphate 5-dehydrogenase from *Escherichia coli.* ***Acta Crystallogr. D Biol. Crystallogr.*** *71,* 1540-1554.

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COMPETITIVE FUNDING

National Grants: individual

MINECO

Principal Investigator	Title	Reference
Armando Albert de la Cruz	Structural basis of the major determinants of plant ion homeostasis: Novel insights on the regulatory mechanism of ion transport and compartmentalization	BFU2014-59796-R
Rosario Muñoz Moreno	*Lactobacillus plantarum* as bacterial model system for the study of the interaction with phenolic compounds in food fermentation within the gastrointestinal gut	AGL2014-52911-R
María José Sánchez Barrena	Structural biology of SCF(SKP2A) E3 ligase complexes of the ubiquitin/ proteasome pathway in plants	BIO2011-28184-C02-02
Beatriz Gonzalez	Structural Biology of inositol phosphates signalling: Regulation by kinases and function in RNA export	BFU2011-24982
Beatriz Gonzalez	Structural and functional analysis of inositide signalling and its implication in health	BFU2014-53762-P
Juan A. Hermoso	Structural Biology of critical processes in bacterial cell-wall remodeling involved in antibiotics resistance	BFU2014-59389-P
Juan A. Hermoso	Nanodiscs: a promising alternative for membrane protein crystallization	BFU2014-61623-EXP

CSIC

Principal Investigator	Title	Reference
Juan A. Hermoso	Cell-wall remodelling Molecular Machines in multidrug-resistant pathogens: applications in developing new drugs	I-LINK0864

National Grants: coordinated

MINECO

Principal Investigator	Title	Reference
Juliana Sanz Aparicio	Crystallographic analysis of the molecular determinants of specificity in novel enzymes for biotechnology	BIO2013-48779-C4-2-R

Autonomous Government of Madrid

Principal Investigator	Title	Reference
Armando Albert (Coord. Federico Gago)	Integrated Bioinformatics platform for the discovery of the receptor structure based novel drugs	S2010/BMD-2457
Federico Gago Juan A. Hermoso (WP)	Bioinformatics Integrative Platform for structure-Based Drug Discovery	S2010/BMD-2457

International Grants: individual

INSTRUCT-European Comission

Principal Investigator	Title	Reference
María José Sánchez-Barrena	Structural biology of SCF(SKP2A) E3 ligase complexes of the ubiquitin/ proteasome pathway in plants: Auxin perception for cell division control	PID 388
María José Sánchez-Barrena	The development of new drugs against autism: The Ca^{2+} sensor NCS1 as a novel pharmacological target	2015 R&D Pilot Project Award. APPID 99
Beatriz Gonzalez	Structural biology of mammal inositide kinases	INSTRUCT (1303)

CSIC

Principal Investigator	Title	Reference
Lourdes Infantes	Drug design based on the complementarity between molecules to improve their physicochemical properties	COOPA20094

International Grants: coordinated

Organism NATIONAL INSTITUTES OF HEALTH (NIH)

Principal Investigator	Title	Reference
Mayland Chang Juan A. Hermoso (WP)	The Quinazolinone Class of Antibacterial Agents	1R01AI116548

Department of Atmospheric Chemistry and Climate

Introduction

The Department of Atmospheric Chemistry and Climate conforms eight staff scientsts in the period 2015-2016:

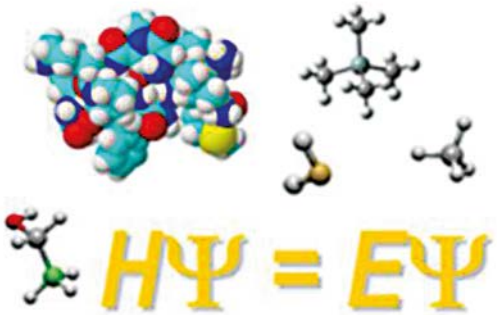
- Professors: Rafael Notario Bueno
- Associate Professors: Rosa Becerra Arias and Alfonso Saiz-López
- Assistant Professors: Juan Z. Dávalos Prado, Pablo Echenique Robba, Rosa Lebrón Aguilar, Josep Mª Oliva-Enrcih y José Mª Santiuste Bermejo

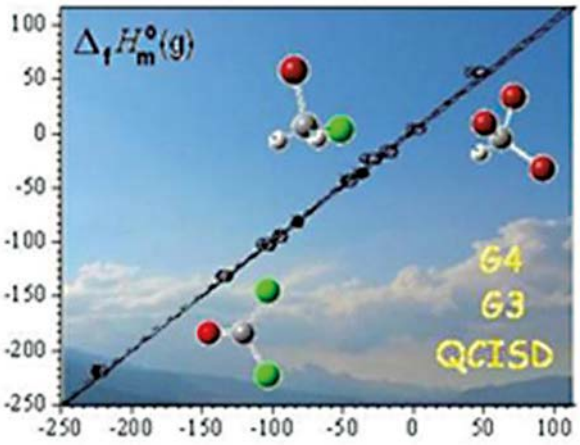
In the Department we follow different research lines, described in the report of the different groups. The main goals of the different lines are: the study of reactivity (by proton transfer), structural effects on the gas-phase acidity/basicity and the intrinsic thermodynamic stability of biological active species and/or environmental and technological interest; the study of the dynamics of photodissociation (UV and X-ray energy ranges) and energetics of organic species with N, Cl and S heteroatoms; development of methodologies, used the triple-quadrupole hybrid mass spectrometer and the high-resolution FT-ICR; study of heteroborane clusters, and their interactions with biomolecules; kinetic studies of new reactions of Si and Ge heavy carbenes of interest in the industry of materials; characterization and development of new stationary phases for gas chromatography based on ionic liquids; determination of chromatographic and thermodynamic parameters by gas chromatography, study of interactions between natural and anthropogenic emissions, chemical and physical climate system, the biosphere within the context of climate change; and the evaluation and improvement of molecular simulation methods.

In the Department we dispose of different experimental techniques, which are needed in order to carry ot the different research lines: combustion calorimetry with rotatory, static and semimicro pumps; combustion microcalorimetry (CMRT); scanning differential calorimetry (DSC), Knudsen effusion technique; FT-ICR high-resolution mass spectrometry (ion cyclotron resonance with Fourier-Transform) of 4.7T and 7.0T (with ESI and MALDI sources); photolysis with pulsed lasers; gas chromatographs for capillary and packed columns, with ionization flame detectors; gas chromatograph coupled to a quadrupolar mass sepctrometer, equipped with device for introdcuing gas-phase and liquid-phase samples; differential optical absorption spectroscopy (DOAS)/earth, ship, airplane, balloon, satellite; resonance and off resonance fluorescence by lamp excitation (ROFLEX)/earth, airplane; Incoherent Broadband Cavity Enhanced Absorption Spectroscopy (IBBCEAS); chemiluminiscence NO_x.

Groups Structure

Energetics, Structure and Molecular Interactions Group





Tenured Staff scientists

Juan Z. Dávalos Prado (Research Scientist)

Rafael Notario Bueno (Research Professor)

Josep M. Oliva Enrich (Research Scientist)

Summary

We study energetic, chemical reactivity, electronic and structural properties of neutral and ionic species – in the gas phase- of fundamental, technological and environmental relevance. For this purpose we use a variety of experimental (Linear Triple Quadrupole TQ /Fourier Transform Ion Cyclotron Resonance FT-ICR Mass Spectrometer with ESI/ MALDI sources; calorimetry of combustion; Knudsen's effusion; photoelectron-photoion coincidence spectroscopy PEPICO) and theoretical techniques. The combination of the experimental results with those obtained by means of quantum-mechanic calculations (ab-initio, DFT) allow us to: i) obtain quantitative information on thermodynamics and kinetics of a variety of chemical reactions in the phase gas, ii) determine interesting and novel relationship of reactivity-chemical structure, iii) determine the thermodynamic stability of neutral and ionic species.

Strategic Aims

Our research lines focus on the theoretical/experimental study of the energetics, chemical reactivity, structure, electronic properties and interactions of neutral and ionic species in the absence of the disturbing effect of the solvent.

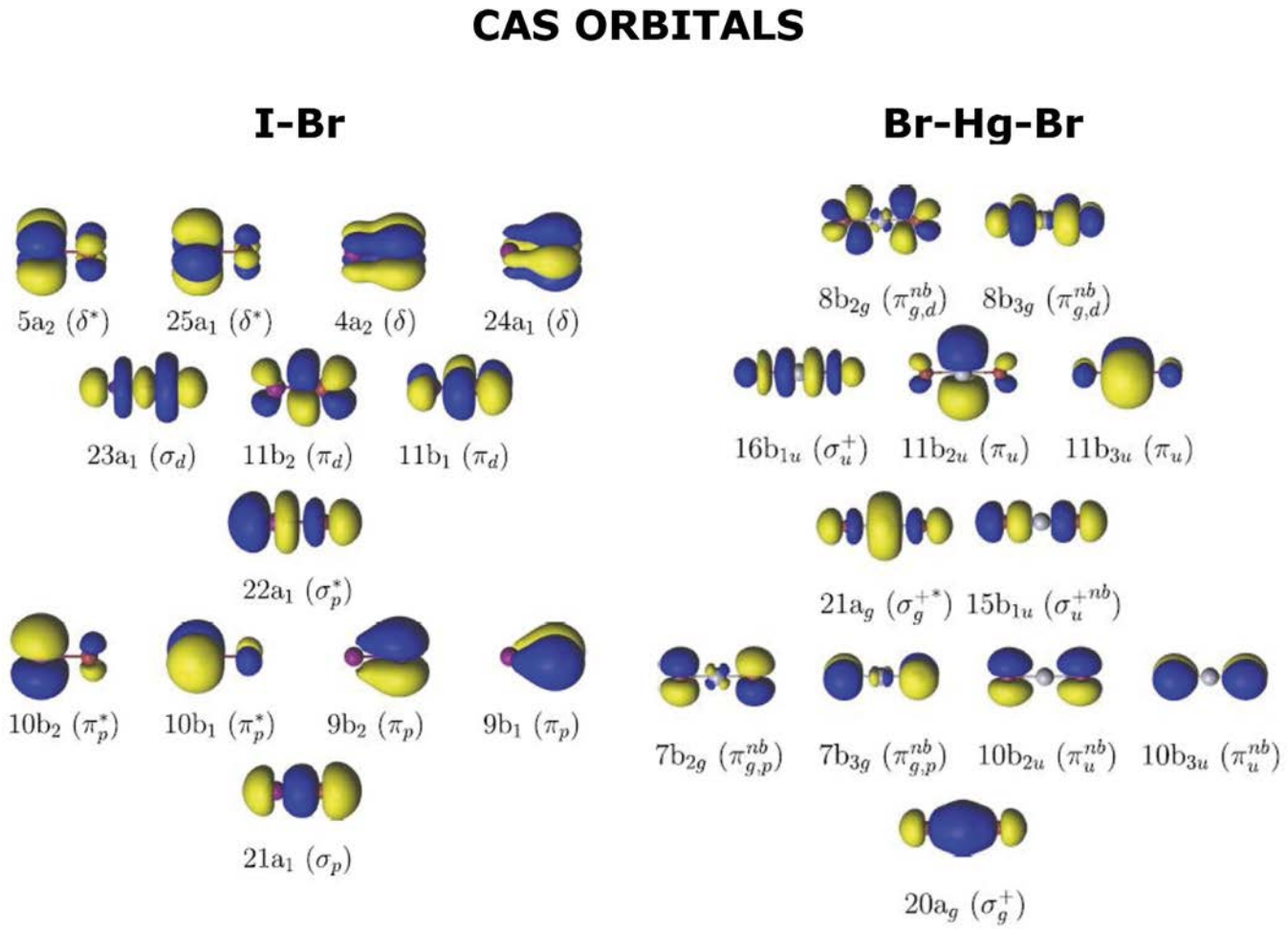
The specific goals pursued are:

- Thermodynamic stability, reactivity (by proton-interchange processes), structural effects and electronic properties of species with fundamental, technological and environmental relevance.
- Electronic structure of heteroborane clusters (HBC) in their ground and excited states.

Results

Computational Chemistry of electronic states of molecules with atmospheric relevance

We have studied electronic properties of representative species such as IBr o $HgBr_2$ which particular relevance on photochemical processes in the atmosphere. In this context, we show that the CASPT2 ("Complete Active Space Self Consistent Field Perturbation Theory") methodology allow us to determine confidence values of optical absorption parameters in the vis-UV range.

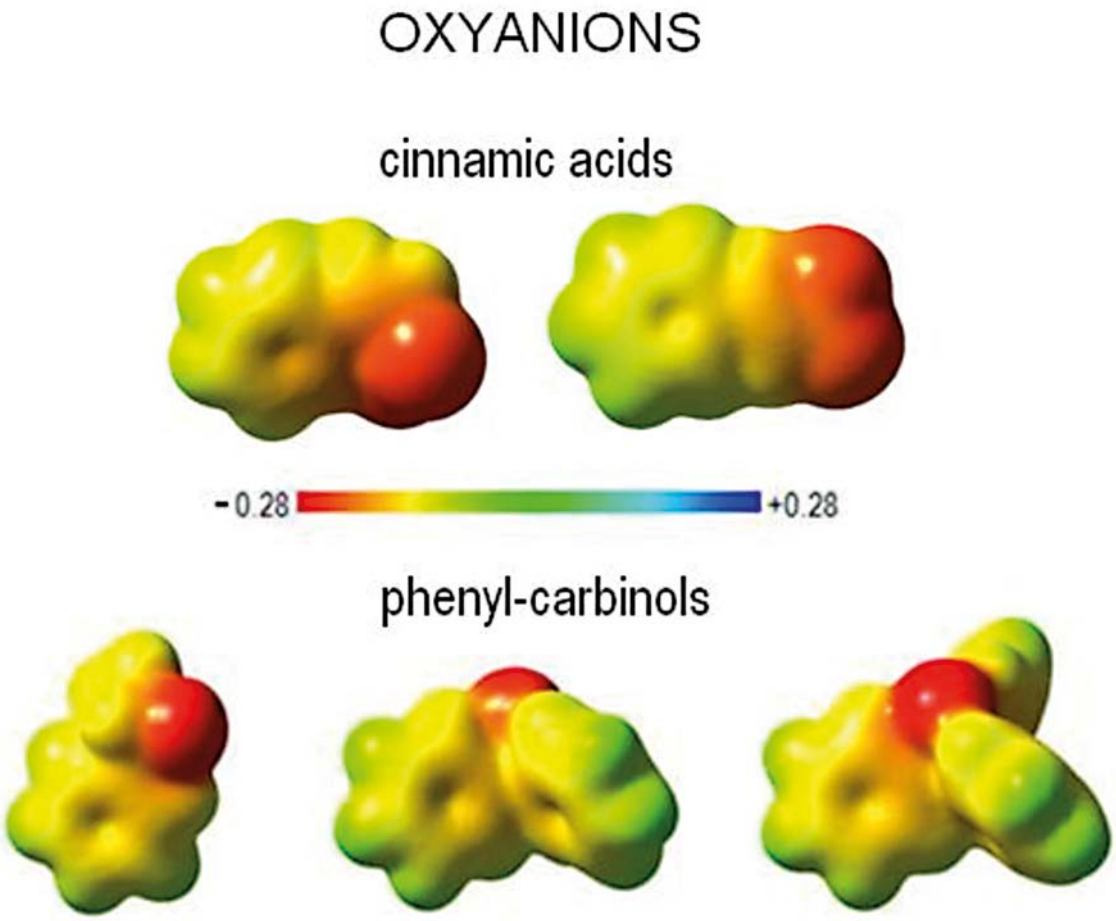


Energetic and structural properties, in the gas-phase, of neutral and deprotonated organic species

We have studied energetic and structural properties of (Z)-cinnamic acid and phenyl-carbinol compounds.

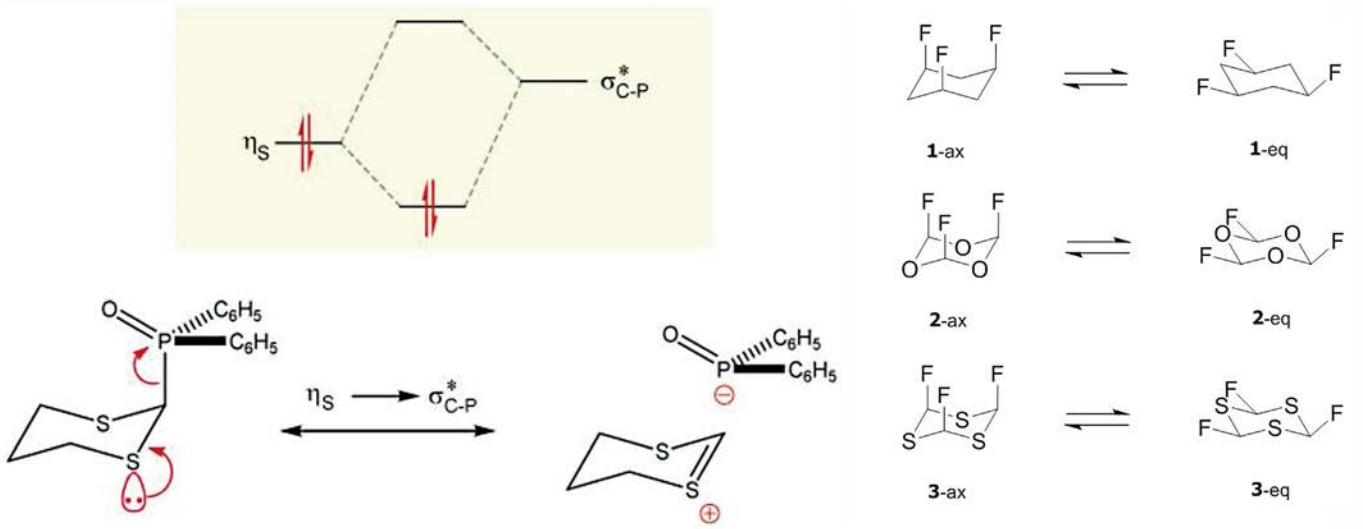
We have experimentally determined the, i) standard enthalpy of formation in the gas phase, $\Delta_f H_m^0(g)$ of phenyl-carbinols, using combustión calorimetry and Knudsen Efussion techniques, ii/ Acidity, in the gas phase of (Z)-cinnamic acid, applying the Extended Kinetic Cooks Method.

Our computational studies, using DFT (B3LYP and M05-2X) and ab-initio (G3, G4) theories have shown the good agreement with the experimental results for both, neutral and deprotonated species.



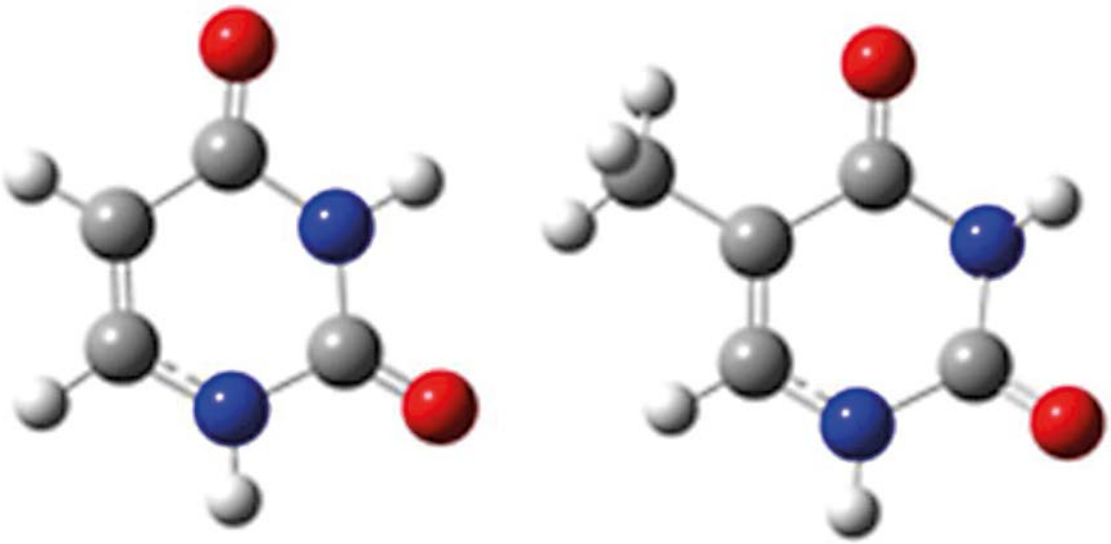
Study of electronic interactions

Theoretical studies on the electronic interactions in 2-diphenylphosphinoyl-1,3-dithiane and 2-trimethylphosphonium-1,3-dithiane have been carried out, reproducing the strong S-C-P anomeric effect previously observed. NBO calculations support the existence of dominant n(X) → σ*(C-Y) stereoelectronic interactions that stabilize the axial conformers. We have also studied the interactions in r-1,c-3,c-5-trifluorocyclohexane (1), r-2,c-4,c-6-trifluoro-1,3,5-trioxane (2) and r-2,c-4,c-6-trifluoro-1,3,5-trithiane (3), confirming the importance of n(F) → σ*(C-X) (X = H, C, O, S) hyperconjugative interactions. Contrary to the common wisdom, fluorine is a good lone pair electron donor toward geminal sigma bonds.



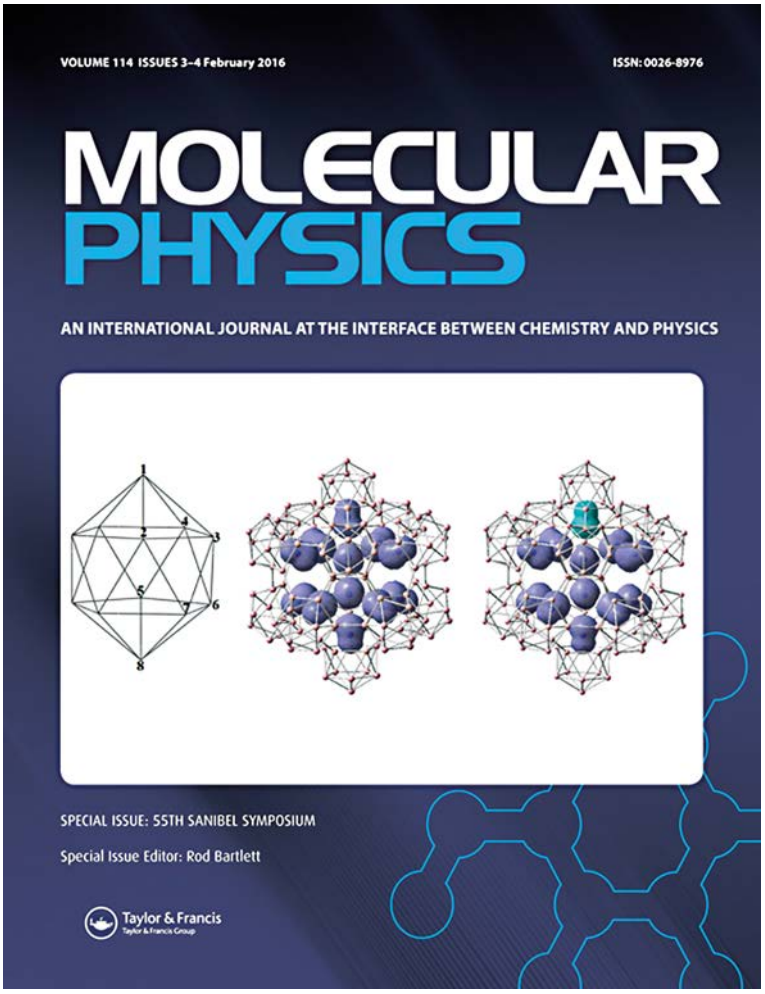
Thermochemistry of uracil and thymine

An experimental and theoretical study on the thermochemistry of uracil and thymine has been carried out. The enthalpies of formation of both compounds have been derived from energies of combustion measured by static bomb combustion calorimetry and molar enthalpies of sublimation determined using the transpiration method. High-level calculations at the G3 and G4 levels of theory have confirmed the quality of experimental results



Electronic structure of heteroborane clusters (HBC) with máximum spin S_{max}.

Molecular magnetism manisfests itself macroscopically through the magnetic moment (total spin S) of a molecule. We need unpaired electrons – (poly)radicals – in the ground state of the system for having S≠0. In a recent publication, chosen as cover of Molecular Physics, we designed a system with a maximum spin S_{max} = 6 in the ground state. This system is formed by twelve radical isocahedra of $NB_{11}H_{11}^{(\bullet)}$ (S = ½) interconnected and forming a supericosahedron (first iteration). This prediction opens the door to the design of molecular magnets based on HBC, since the system can be extended in the three dimensions, thus maximizing the total spin S_{max} in the succession $S_{max}(n) = \{ ½ , 6, 72, ..., ½\cdot 12^n\}$, being n the iteration order in three dimensions.



Publications

Sitkiewicz, S.P.; Dávalos, J.Z.; Notario, R.; Oliva-Enrich J.M., Saiz-Lopez A., Alcoba D.R.; Oña O.B.; Roca-Sanjuán D. (2016). Ab initio quantum-chemical computations of the electronic states in $HgBr_2$ and IBr: Molecules of interest on the Earth's atmosphere. ***J. Chem. Phys.*** *145*, 244304.

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Oliva-Enrich JM, Alcoba DR, Torre A, Lain L, Oña OB, Massaccesi GE (2016):A Local Spin Procedure to Determine Heisenberg Exchange Coupling Constants in Linear Polyradicals. Poster. X Congress on Electronic Structure: Principles and Applications - ESPA 2016. Castellón de la Plana (Valencia)-Spain, June 28– July 1.

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Santaballa López JA, Canle-López M, Oliva JM (eds) (2016) Book of Abstracts, I "Julio Palacios" International Symposium, A Coruña- Spain, July 20-22. Pages 1-55

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Romero V, Tirado A, Durán M, Dávalos JZ (2016) Propiedades energéticas de la harina de maca (Lepidium peruvianum Chacón o Lepidium meyenii Walpers). Rev Soc. Quim. Perú, 82 (1) 38-48. ISSN 1810-634X

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International Grants: individual

FINCyT-Perú

Principal Investigator	Title	Reference
J.Z. Dávalos P.	Energetics, structure and molecular reactivity: the last generation theoretical/experimental tools (2015)	ECIP-1-P-030-14

International Grants: coordinated

FINCyT-CONCyTEC, Perú

Principal Investigator	Title	Reference
H. Alarcón (UNI) J.Z. Dávalos (IQFR-CSIC) D. Oliveira Silva (USP)	Synthesis and characterization of new bio-polymeric materials for removal of toxic metals coming from mining industry (2013/2016)	PIBA-1-P-216-13

Group of Photolysis and Chromatography

Tenured Staff Scientists

María Rosa Becerra Arias (Associate Professor)

Rosa Lebrón Aguilar (Assistant Professor)

José María Santiuste Bermejo (Assistant Professor) (until 19/03/2015)

Doctoral Students

María Hernáiz Izquierdo (Master's student, from 15/02/2016)

Technical Staff

Plácido Galindo Iranzo (Specialized Technician)

Jesús Eduardo Quintanilla López (Superior Specialized Technician)

Summary

The main objectives of the Photolysis and Chromatography group are the study of chemical reactivity and molecular interactions. Specifically, we study the reactivity and reaction mechanisms of the intermediate species of Si, Ge, and Sn known as heavy carbenes. These heavy carbenes have high technological, industrial and theoretical interest. Absolute rates of the reactions of heavy carbenes are obtained by direct, time-resolved kinetic experiments using laser flash photolysis. The analysis of reaction products and stable intermediates is carried out by gas chromatography coupled to mass spectrometry (GC-MS).

In our studies of molecular interactions, we use the inverse gas chromatography (IGC) to characterize substances capable of being employed as GC stationary phases. This technique allows us to ascertain not only the type and intensity of the solute-stationary phase interactions, but also the solvation properties of the latter. We use this information both to improve the separation capacity of GC by the synthesis of stationary phases with new selectivities, and to develop methodologies suitable for solving complex analytical problems of interest in different areas (food, environment, etc.).

The Group manages the Mass Spectrometry laboratory of the IQFR (http://serviciomasas.iqfr.csic.es/), which has a MALDI-TOF mass spectrometer and an ion trap LC-MS system with electrospray and APCI sources. Since 2002, the laboratory provides research support for the different departments of the IQFR, as well as to external users of other Research Public Institutions, Universities and private companies.

Strategic Aims

- New reaction kinetic studies of silicon and germanium containing heavy carbenes of interest in the materials industry.
- Development and characterization of new stationary phases for gas chromatography (polysiloxanes and ionic liquids).
- Determination of chromatographic and thermodynamic parameters by inverse gas chromatography.
- Development and application of innovative methodologies for the analysis of environmental, food and biological compounds of relevance by chromatography and mass spectrometry.

Results

Gas phase kinetic studies of Silicon compounds. New reactions study of Si intermediates species known as "heavy carbenes" of interest in the materials industry

Studies of the Si "heavy carbene" SiH_2 (silylene) were carried out with oxygenated species: 2,5-dihydrofurane (2, 5-DHF). To create the transient intermediate species, SiX_2, laser flash photolysis technique is used, normally excimer lasers in combination with a suitable UV absorbing molecular heavy carbene precursors. The precursor molecules include commercial chemical compounds and compounds synthesized in our laboratories.

The reaction was studied in the gas phase over the pressure range 1100 Torr in SF_6 bath gas, at five temperatures in the range 296-598 K. End product analyses by gas chromatography at room temperature under these conditions no major product peak was observed.

Quantum chemical (ab initio) calculations indicate that reaction of SiH_2 with 2,5-DHF can occur at both the double bond (to form a silirane) and the O-atom (to form a donor acceptor, zwitterionic complex) via barrierless processes. Further possible reaction steps have been explored, of which the only viable one appears to be decomposition of the O-complex to give 1,3-butadiene + silanone (silicone monomer). RRKM calculations incorporating reaction at both π- and O-atom sites, can be made to fit the experimental rate coefficient pressure dependence curves at 296-476 K, giving values for $k^{\infty}(\pi)$ and $k^{\infty}(O)$ which indicate the latter is larger in magnitude at all temperatures.

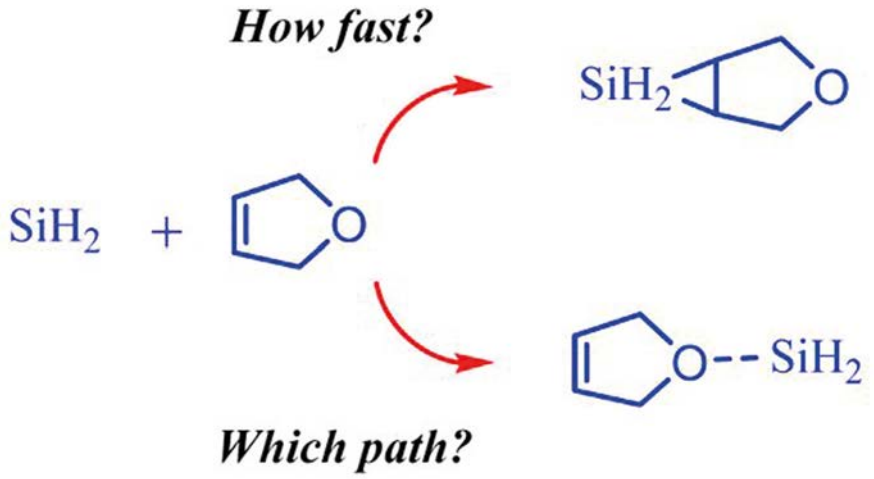

Figure 1. SiH_2 (silylene) reaction with 2,5-dihydrofurane

Kinetic studies of atmospheric interest: nitrate radical

Nitrate radicals, NO_3, are important initiators of atmospheric oxidation during night-time.

Nitrate radicals, NO_3, were produced for the first time by 193 nm laser flash photolysis of N_2O_5 and HNO_3. Detection was achieved due to NO_3's strong absorption at 622.7 nm confirmed by measurements of the absorption spectrum in the range of 617 to 625 nm using both NO_3 precursors.

Time-resolved kinetic studies allowed the determination of room-temperature rate coefficients for the reactions of NO_3 with 2methylbut-2-ene and NO_2. The rate coefficients compare well to previous measurements with alternative techniques suggesting that this method is valid and may be applied in follow-up studies.

Characterization of solute-stationary phase interactions

With the aim of getting further insight into the separation process in gas and liquid chromatography, we have continued our studies on the interactions between specific solutes and different stationary phases. In this biennium, the solutes studied were:

Phospho- and O-glycopeptides from bovine caseinomacropeptide

Post-translational modifications (PTMs) of proteins, as phosphorylation and glycosylation, are involved in key mechanisms that govern the regulation of cellular processes. Bearing in mind that PTMs are normally present in sub-stoichiometric amounts, their elucidation remains as a major analytical challenge. However, hydrophilic interaction liquid chromatography coupled to mass spectrometry (HILIC-MS) has evolved during the last decade as a powerful analytical tool in structural glycoproteomics.

Considering that there is a wide variety of HILIC stationary phases commercially available, and that the retention mechanism of HILIC is still under debate, we though that a comparison study of different HILIC columns addressed to the characterization of phosphopeptides and glycopeptides could contribute to gain a better understanding of the relationship between the separation mechanism of PTM peptides and the physicochemical characteristics of the used HILIC stationary phases. Therefore, we have tested three different HILIC stationary phases and a reverse phase stationary phase to the separation of phosphopeptides and *O*-glycopeptides derived from proteolytically digested bovine caseinomacropeptide (CMP).

We found that a zwitterionic sulfobetaine (ZIC) or an amide (BEH) stationary phases resulted to be the most efficient to separate and characterize post-translationally modified peptides derived from CMP hydrolysis without the need of any previous fractionation or derivatization step. The separation of phosphopeptides and differently sialylated *O*-glycopeptides in the ZIC column is dominated by an electrostatic repulsion interaction mechanism, whereas the separation of either non-modified peptides or neutral *O*-glycopeptides is based on a partitioning mechanism. In the BEH column, the separation is mainly dominated by hydrophilic partitioning.

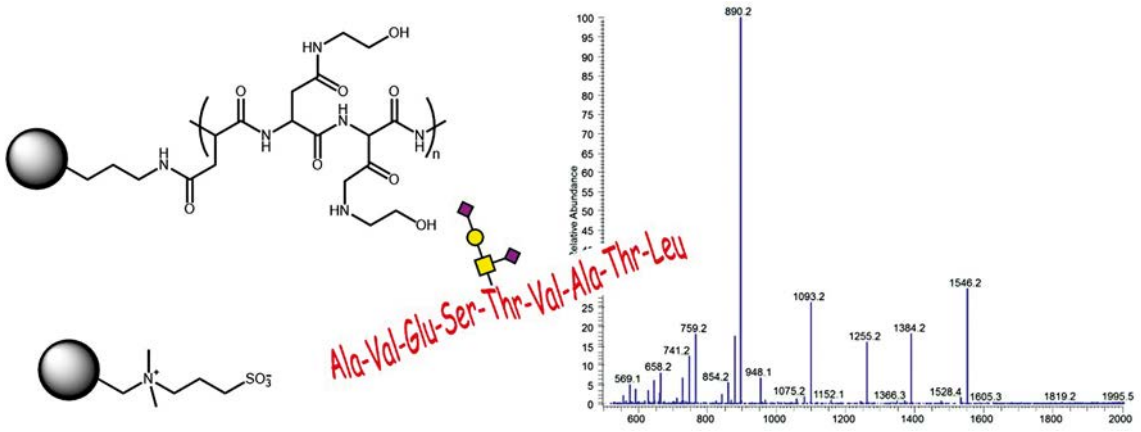

Figure 2. Characterization of phospho- and *O*-glycopeptides by HILIC-MS.

Phthalic acid esters metabolites

Nowadays there is an increased concern regarding endocrine disrupting compounds, capable of adversely affect the endocrine system of human. Among them, phthalic acid esters (PAEs) are a group of special interests since they have been used in the plastics industry from 1930s. Their metabolites (MPAEs) have been proposed as appropriate biomarkers to calculate human PAE intake. So, high-throughput analytical methods for screening of human exposure to these metabolites are mandatory.

Most analytical methods for MPAEs determination are carried out by LC-MS on phenyl-type (Phenyl) or octadecylsilane (ODS) stationary phases (SPs). The employ of other types of SPs, as polar-embedded SPs, with a more appropriate selectivity for MPAEs analysis has been rather limited. For that, we have studied in depth the retention mechanism of several MPAEs on three different stationary phases (ODS, Phenyl and Amide). We have found that the hydrophobic interactions are predominant in the Phenyl and ODS SPs, with a partial contribution of steric effects in the ODS SP. Conversely, the separation process of MPAEs in the polar embedded amide-type (Amide) SP is driven by a mixed hydrophobic/hydrophilic mechanism whose nature can be modulated modifying the eluent composition (pH and content of organic modifier). Therefore, it seems feasible to improve the separation of MPAEs using the Amide column.

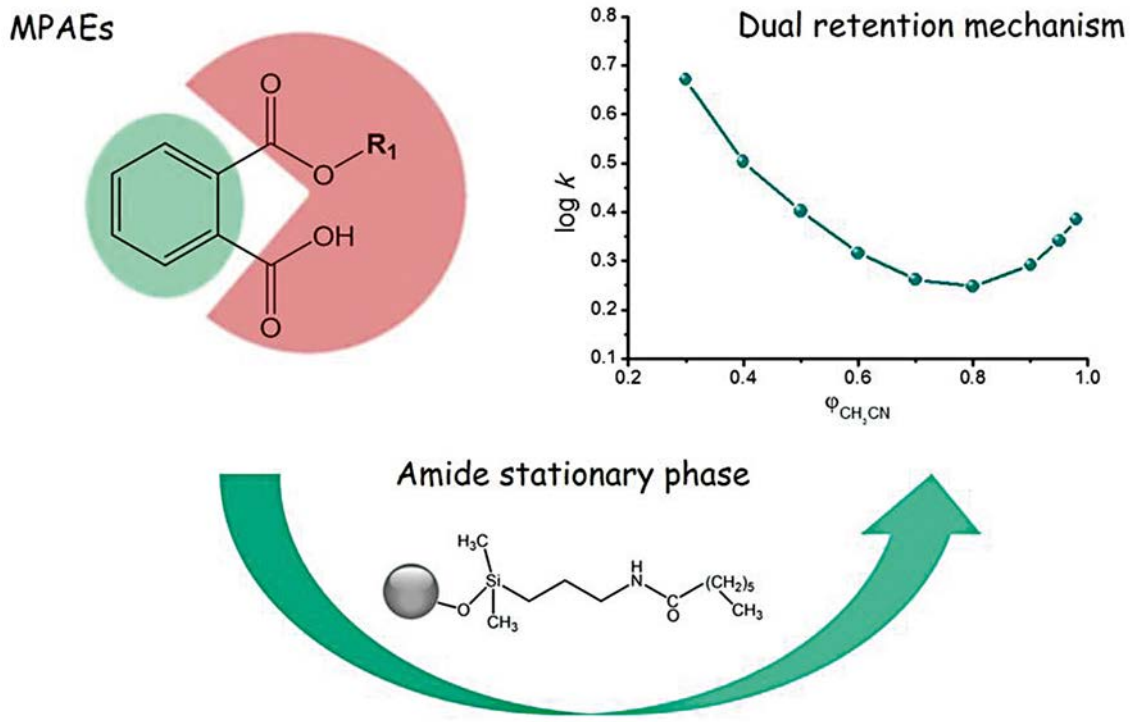

Figure 3. Dual retention process of MPAEs on amide-type stationary phases for liquid chromatography.

Compounds with varied functional groups

Isothermal Kováts retention indices (I) are essentially used in GC for identification purposes, but they are also useful in characterization of SPs and for studying structural and physicochemical properties of both the analyte and the SP. Thus, during this biennium, we have continued with the determination of retention indices of several classes of organic compounds on commercial SPs for contributing to the isothermal retention index library. Specifically, we have determined I values of more than fifty solutes at 333-413 K on twelve commercial columns covering a broad SP polarity spectrum.

Moreover, we have used a modification of the solvation parameter model (SPM) to investigate the interactions of those solutes on the above stationary phases. The modified SPM has proved to be helpful for estimating I values on SPs with McReynolds polarity lower than 3000 and for unraveling the influence of the polarity of stationary phase and solute on the retention indices. The information obtained in this way may help to decide what to do in a difficult chromatographic separation and in the selection of the most adequate combination of chromatographic columns in comprehensive two-dimensional gas chromatography (GCxGC).

Quantitative profiling of volatiles by DIMS in combination with multivariate regression methods

Sample characterization based on its volatile composition is a topic of high relevance in the food science and technology field for different purposes such as authentication of samples, quality control, etc. Gas chromatography coupled to mass spectrometry (GC-MS) has become the analytical technique of choice to carry out this sort of studies. However, it is usually a very time-consuming technique that has promoted the development of non-separative approaches based on direct injection MS (DIMS) for the high throughput and cost-effective characterization

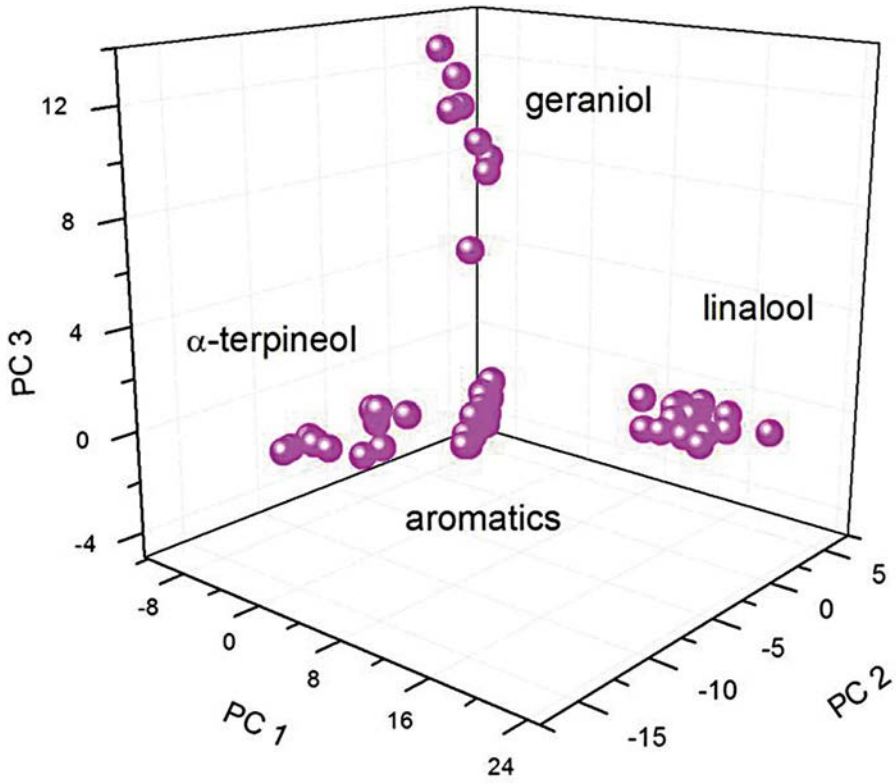

Figure 4. *Thymus zygis* subsp. *zygis* chemotypes found by principal component analysis.

of food samples. Despite these advantages, the number of contributions by DIMS aimed at quantitative analysis is still rather limited.

Thus, we have evaluated the applicability for quantification of different multivariate regression procedures to data collected by DIMS from simulated mixtures and from experimental mass spectral fingerprints of major volatiles in *Thymus zygis* subsp. *zygis* (Thyme) chemotypes. We chose *Thymus zygis* because is a widespread endemic plant in the Iberian Peninsula extensively used for culinary purposes and in popular medicine, which has three subspecies and four chemotypes with a different volatile profile. Therefore, to select the most appropriate chemotype for collection or cultivation, the rapid characterization of Thyme based on its content of volatile secondary metabolites would be of great interest.

We studied the effect of random noise, the number of calibration samples, type of validation, mixture complexity and similarity of mass spectra to ascertain the most relevant factors affecting quantitative response. The results obtained, validated with the conventional direct thermal desorption coupled to gas chromatography-mass spectrometry method (DTD-GC-MS), have shown the high potential of DIMS approaches for the fast and precise quantitative profiling of volatiles in foods.

Determination of endocrine disrupting compounds

The results obtained from the study of molecular interactions between MPAEs and different LC stationary phases have allowed us to develop and optimize an analytical method based on ultra-high performance liquid chromatography (UHPLC) coupled to MS. This method enables the simultaneous determination of nine primary and secondary phthalate metabolites in less than seven minutes, with detection limits as low as 60 ng μL^{-1}. It was applied to analyze twenty-one human urine samples from the general Spanish population. The content of MPAEs found in urine ranged from 2.55 mg L^{-1} (mono-benzyl phthalate) to 68.6 mg L^{-1} (mono-ethyl phthalate). These data are within the same order of magnitude as those found in other similar populations and can be applied to draw conclusions on the use of PAEs in the different countries.

Apart from PAEs, endocrine disrupting chemicals include a wide variety of substances found in several materials commonly used in daily life, such as pesticides, additives or contaminants in food and personal care products. Among them, parabens and bisphenol A have also received special attention in the last years due to their ubiquitous presence in the environment, the clear evidences of their reproductive toxicity, and their estrogenic activity.

In this field, we have contributed developing a fast and multicomponent analytical method, capable of quantifying thirteen endocrine disruptors (five phthalates, seven parabens, and bisphenol A) in a single chromatographic run. The UHPLC-MS method was optimized applying a Response Surface Methodology, and allowed us to separate all compounds (including isobaric pairs) in less than 4.1 min. The method is robust and its instrumental detection and quantitation limits are in the range of medium-high femtograms. The suitability of the method was demonstrated through its application to the analysis of commercial personal care products (shower gels) without any sample treatment, only a simple dilution, being possible to determine the simultaneous presence of phthalates, parabens, and bisphenol A in almost all the gels analyzed.

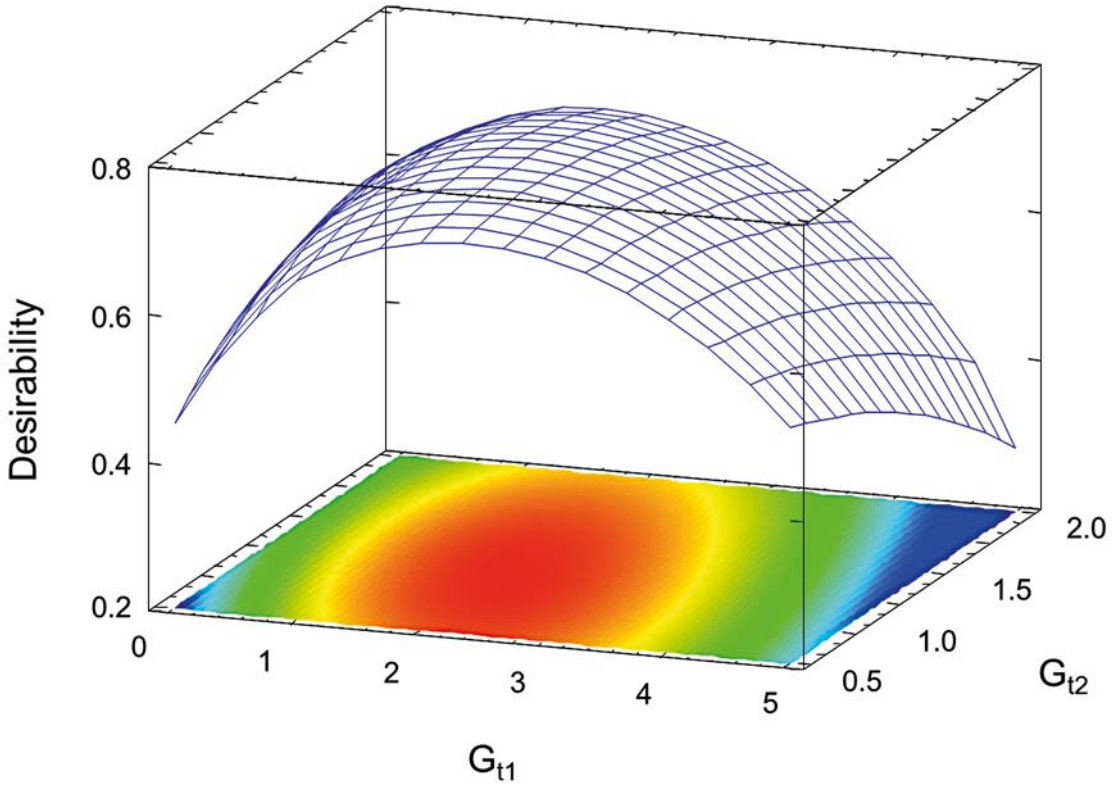

Figure 5. Response surface plot showing the behavior of the variables used in the optimization process.

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Herrero, L.; Calvarro, S.; Fernández, M.A.; Quintanilla-López, J.E.; González, M.J.; Gómara, B. (2015). Feasibility of ultra-high performance liquid and gas chromatography coupled to mass spectrometry for accurate determination of primary and secondary phthalate metabolites in urine sample. ***Anal. Chim. Acta*** *853*, 625-636.

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Hernández-Hernández, O.; Quintanilla-López, J.E.; Lebrón-Aguilar, R.; Sanz, M.L.; Moreno, F.J. (2016). Characterization of post-translationally modified peptides by hydrophilic interaction and reverse phase liquid chromatography coupled to quadrupole-time-of-flight mass spectrometry. ***J. Chromatogr. A*** *1428*, 202-211.

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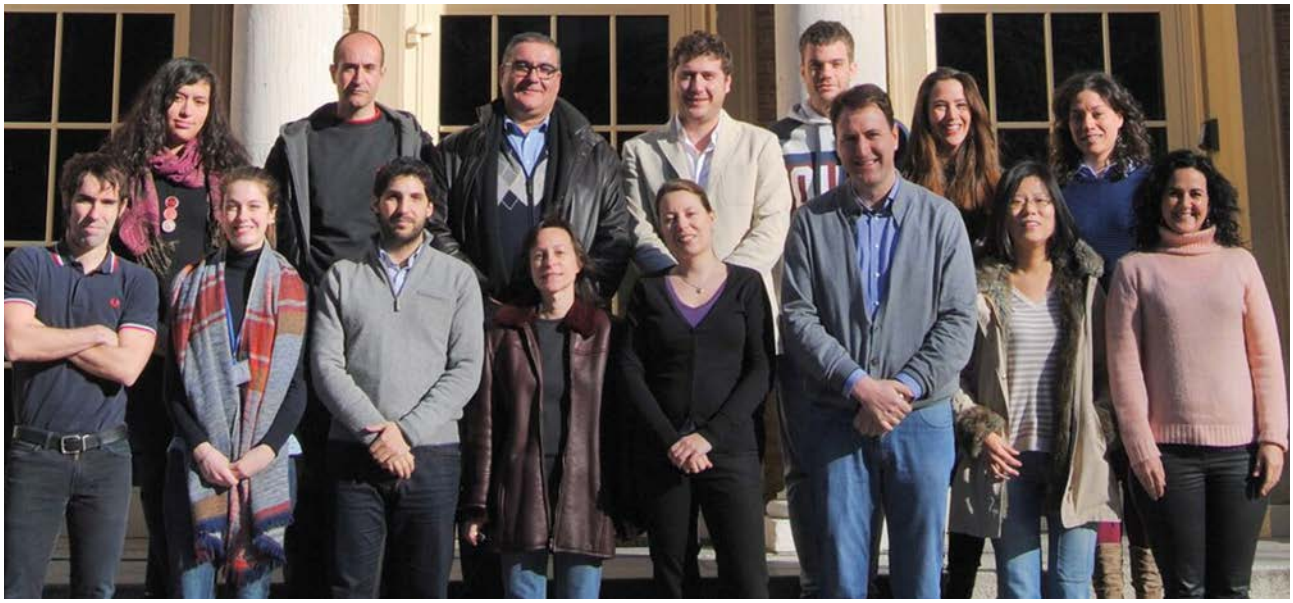
Becerra R.; Pfrang, C. (2016). Kinetic studies of nitrate radicals: flash photolysis at 193 nm. ***Int. J. Chem. Kin.*** *48*, 806-811.

National Grants: coordinated

Regional Government of Madrid

Principal Investigator	Title	Reference
Mª Luisa Marina Alegre	Estrategias avanzadas para la mejora y el control de la calidad y la seguridad de los alimentos	S2013/ABI-3028

Atmospheric Chemistry and Climate Group



Staff scientists

Alfonso Saiz-López (Scientific Researcher)

Investigadores Post-Doctorales (contrato)

Post-Doctoral researchers
Carlos Alberto Cuevas Rodríguez (desde III-2013)
Juan Pablo Corella Aznar (desde III-2015)
Shanshan Wang (II-2015-VII-2016)
Paul Smith (desde IX-2016)

Predoctoral researchers

Nuria Benavent Oltra (desde XI-2015)
David García Nieto (desde VI-2015)
Fernando Serranía Alarcón (desde XI-2015)
Antía Carmona Balea (desde XI-2015)
Caterina Juan Vicente (desde XI-2015)
María Muñiz Unamunzaga (XI-2015-XI-2016)

Technical

Arturo Alonso de León (desde IX-2016)
Noemí Hamer Heras (desde I-2016)
Leticia Roldán Montero (desde XI-2015)
Miguel Fernández Sánchez (desde III-2013 hasta X-2014)
Monica Anguas Ballesteros (desde XI-2014)
David Armenteros Escabias (desde IV-2015)
Manuel Pérez García (desde IX-2015)
Nani Martínez Calvo (desde IX-2016)

Summary

The Atmospheric Chemistry and Climate group (AC2) is a newly created research group within CSIC´s Institute of Physical Chemistry Rocasolano (IQFR). AC2 research efforts are directed at studying the role of atmospheric composition and chemistry in the climate system.

Within this scientific framework, AC2 provides an integrated research approach combining atmospheric measurements (satellite- and ground-based), modelling (microphysical to global chemistry-climate) and laboratory studies (photochemistry).

Strategic Aims

- The goals are to explore the interactions between anthropogenic and natural emissions, the chemical and physical climate system, and the biosphere, within a changing climate context.

Results

Atmospheric modelling of halogen chemistry at global level. Impact on climate

We have implemented a state-of-the-art scheme of the atmospheric chemistry of bromine and iodine in the 3D chemistry climate model CAM-CHEM (Community Atmospheric Model with Chemistry, version 4.0), included into the CESM framework (Community Earth System Model, version 1.1.1).

Using this model we have reported a new estimation of the injection of iodine into the stratosphere based on novel daytime (solar zenith angle < 45°) aircraft observations in the tropical tropopause layer and a global atmospheric model with the most recent knowledge about iodine photochemistry. The results indicate that significant levels of total reactive iodine (0.25–0.7 parts per trillion by volume), between 2 and 5 times larger than the accepted upper limits, can be injected into the stratosphere via tropical convective outflow. At these iodine levels, modeled iodine catalytic cycles account for up to 30% of the contemporary ozone loss in the tropical lower stratosphere and can exert a stratospheric ozone depletion potential equivalent to, or even larger than, that of very short-lived bromocarbons. Therefore, we suggest that iodine sources and chemistry need to be considered in assessments of the historical and future evolution of the stratospheric ozone layer. (*Geophys. Res. Lett., 42,doi:10.1002/2015GL064796*).

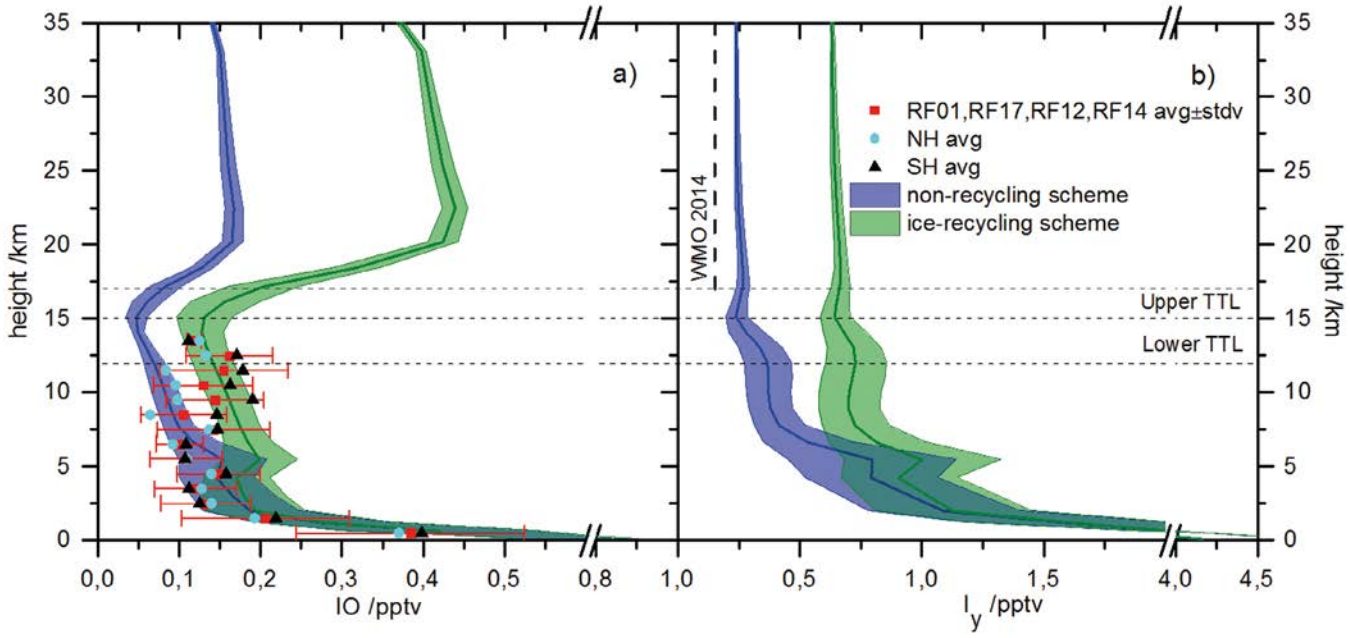


Figure 1. Vertical distribution of IO measured in the tropical troposphere and modelled daytime IO (a), and modelled I_y (b) concentrations for both ice-recycling (green) and non-recycling (blue) schemes. Red squares represent the average and standard deviation (±s) of the four flights, while cyan circles and black triangles account for the average of Northern (RF12 & RF17) and Southern (RF01 & RF14) Hemisphere flights. Shaded area represents the annual average with the standard deviation of modelled values (±s) within the tropics (20ºS-20ºN). I_y is defined as the sum of I + IO + HOI + $IONO_2$ + 2 x I_xO_y + I_{minor} + 2 ´ I_2 + IBr + ICl, where I_xO_y includes I_2O_2 + I_2O_3 + I_2O_4, and I_{minor} is defined as HI + OIO + INO_2 + INO. TTL is defined as the layer with a bottom boundary at the region of maximum convective outflow (~12 km) and an upper limit coincident with the tropical cold point tropopause at about 17 km.

Very short-lived brominated substances (VSLBr) are an important source of stratospheric bromine, an effective ozone destruction catalyst. However, the accurate estimation of the organic and inorganic partitioning of bromine and the input to the stratosphere remains uncertain. Here, we report near-tropopause measurements of organic brominated substances found over the tropical Pacific during the NASA Airborne Tropical Tropopause Experiment campaigns. We combine aircraft observations and a chemistry–climate model to quantify the total bromine loading injected to the stratosphere. Surprisingly, despite differences in vertical

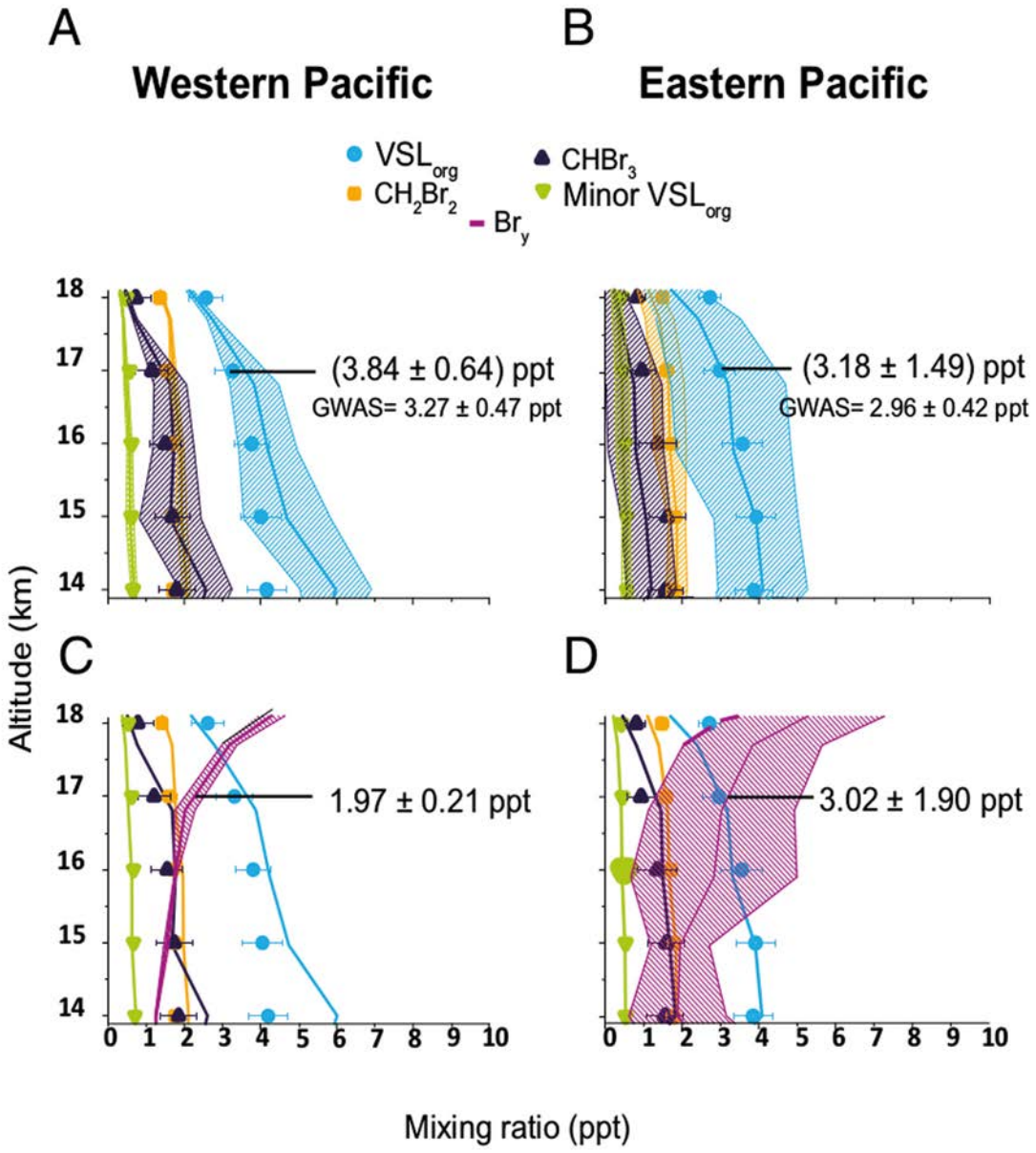


Figure 2: GWAS measurements and CAM-Chem simulations ±1 SD. Filled symbols are the 1 km average bins from GWAS measurements. Lines are the CAM-Chem simulation. Values from the arrows represent the mean mixing ratio (ppt) of VSLorg and Bry at the tropopause level (~17 km) derived from CAM-Chem simulations. (A and B) Organic brominated species multiplied by their atomicity for (A) estern Pacific and (B) Eastern Pacific. (C and D) CAMChem estimations of inorganic bromine (Bry) from measured brominated VSLS with shaded ±1 SD for (C) Western Pacific and (D) Eastern Pacific

transport between the Eastern and Western Pacific, VSLBr (organic + inorganic) contribute approximately similar amounts of bromine [□6 (4−9) parts per trillion] to the stratospheric input at the tropical tropopause. These levels of bromine cause substantial ozone depletion in the lower stratosphere, and any increases in future abundances (e.g., as a result of aquaculture) will lead to larger depletions. (*PNAS 10, 2015 vol. 112 no. 45 13789-13793,10.1073/ pnas.1522889113).*

Halogens produced by ocean biological and photochemical processes reach the tropical tropopause layer (TTL), where cold temperatures and the prevailing low ozone abundances favor the diurnal photochemical enhancement of halogen atoms. Under these conditions atomic bromine and iodine are modeled to be the dominant inorganic halogen species in the sunlit TTL, surpassing the abundance of the commonly targeted IO and BrO radicals. We suggest that due to the rapid photochemical equilibrium between halogen oxides and halogen atoms a natural atmospheric phenomenon evolves, which we have collectively termed "tropical rings of atomic halogens." We describe the main causes controlling the modeled appearance and variability of these superposed rings of bare bromine and iodine atoms that circle the tropics following the Sun. Some potential implications for atmospheric oxidizing capacity are also explored. Our model results suggest that if experimentally confirmed, the extent and intensity of the halogen rings would directly respond to changes

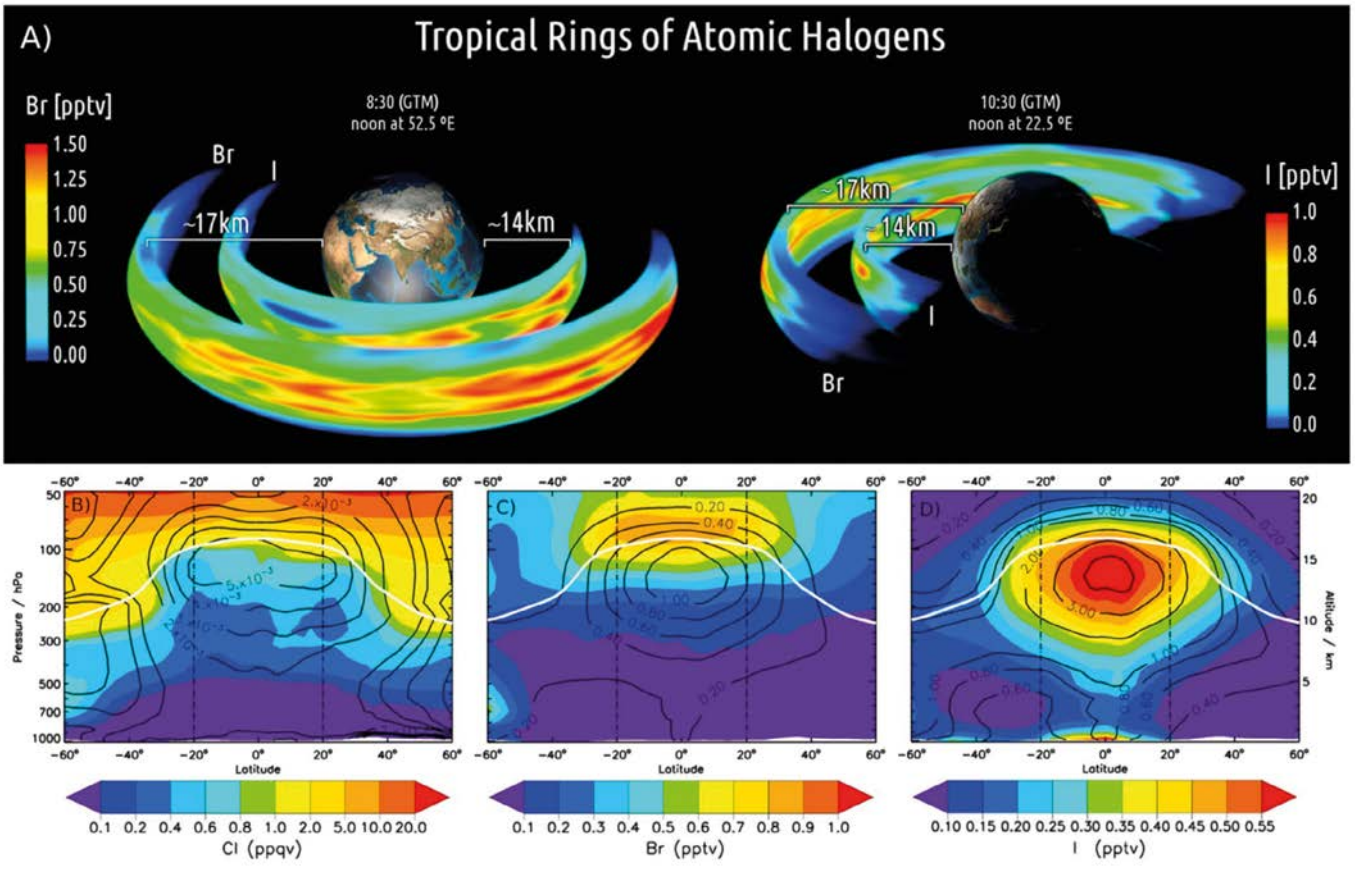


Figure 3. (a) Schematic representation of the "tropical rings of atomic halogens" at two different times of the day. Note that the Br and I rings should be superposed in height (11–17 km for iodine and 15–19 km for bromine) but have been intentionally separated to distinguish their different atomic vmr. (b–d) Annual daytime distributions of atomic halogens as a function of latitude and altitude for chlorine, bromine, and iodine, respectively. The black contour lines in the lower panels indicate the X/XO ratio for each family, while the white line shows the approximate location of the tropopause.

in oceanic halocarbon emissions, their atmospheric transport, and photochemistry. (*Geophys. Res. Lett, 43, DOI:10.1002 / 2015GL067608, 2016*).

Little attention has so far been paid to the nighttime atmospheric chemistry of iodine species. Current atmospheric models predict a buildup of HOI and I_2 during the night that leads to a spike of IO at sunrise, which is not observed by measurements. In this work, electronic structure calculations are used to survey possible reactions that HOI and I_2 could undergo at night in the lower troposphere, and hence reduce their nighttime accumulation. The new reaction NO_3+ HOI → IO + HNO_3 is proposed, with a rate coefficient calculated from statistical rate theory over the temperature range 260–300 K and at a pressure of 1000 hPa to be k (T) = 2.7 × 10^{-12}(300 K / T) 2.66 cm3 $molecule^{-1}$ s^{-1}. This reaction is included in two atmospheric models, along with the known reaction between I2 and NO_3, to explore a new nocturnal iodine radical activation mechanism. The results show that this iodine scheme leads to a considerable reduction of nighttime HOI and I_2, which results in the enhancement of more than 25 % of nighttime ocean emissions of HOI + I_2 and the removal of the anomalous spike of IO at sunrise. We suggest that active nighttime iodine can also have a considerable, so far unrecognized, impact on the reduction of the NO3 radical levels in the marine boundary layer (MBL) and hence upon the nocturnal oxidizing capacity of the marine atmosphere. The effect of this is exemplified by the indirect effect on dimethyl sulfide (DMS) oxidation. (Atmos. Chem. Phys., 16, 15593-15604, 2016)

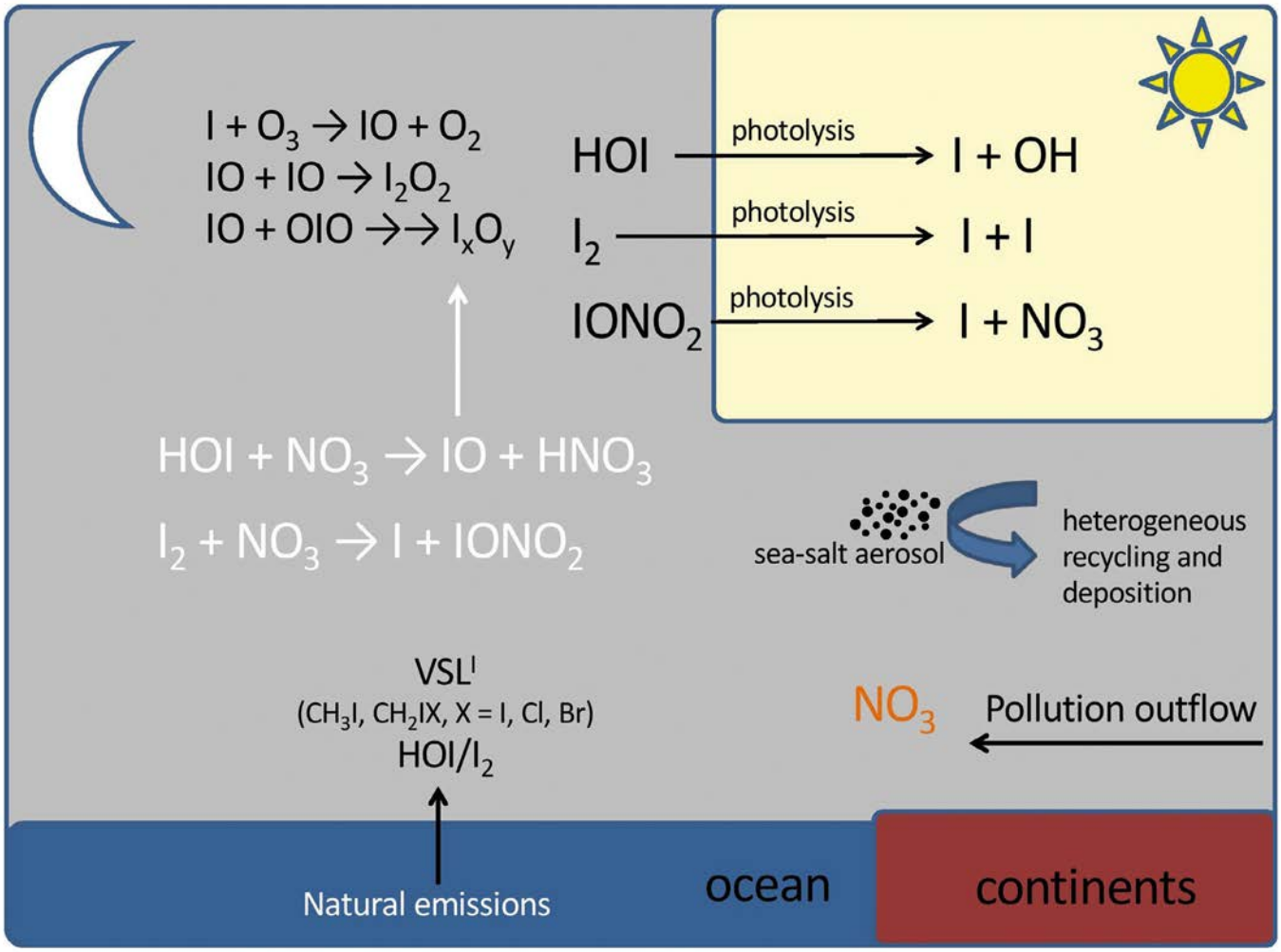


Figure 4. New nocturnal iodine chemistry (in white) implemented in the THAMO and CAM-Chem models.

Implementation of the polar module of emissions and iodine chemistry in CAM-Chem

The sources of the large iodine monoxide (IO) concentrations measured in coastal Antarctica remain unknown. We are also working in the implementation of polar iodine emissions in the global chemistry-climate model CAM-Chem. The implementation is based on three recent suggested mechanisms suggested by our group: i) release of iodine through the equilibrium HOI+I-↔I2+H2O from sea-ice algae and subsequent diffusion through brine channels to accumulate in the brine layer (Saiz-Lopez et al., 2015); ii) photolysis of iodate frozen salts (Galvez et al., 2015), and iii) emission of gaseous iodine from the production of triiodide (I3-) via iodide oxidation in frozen solution (Kim et al., 2016). The results will be compared to ground- ship- and satellite-based observations of IO in the Antarctic troposphere.

Atmospheric modeling of halogen chemistry at regional scale

The Community Multiscale Air quality (CMAQ) model has been used to assess the impact of ocean emissions and combined chemical processes of halogen (chlorine, bromine and iodine) and DMS on air quality.

Fate of ozone in marine environments has been receiving increased attention due to the tightening of ambient air quality standards. The role of deposition and halogen chemistry is examined through incorporation of an enhanced ozone deposition algorithm and inclusion of halogen chemistry in a comprehensive atmospheric modeling system. The enhanced ozone deposition treatment accounts for the interaction of iodide in seawater with ozone and increases deposition velocities by 1 order of magnitude. Halogen chemistry includes detailed chemical reactions of organic and inorganic bromine and iodine species. Two different

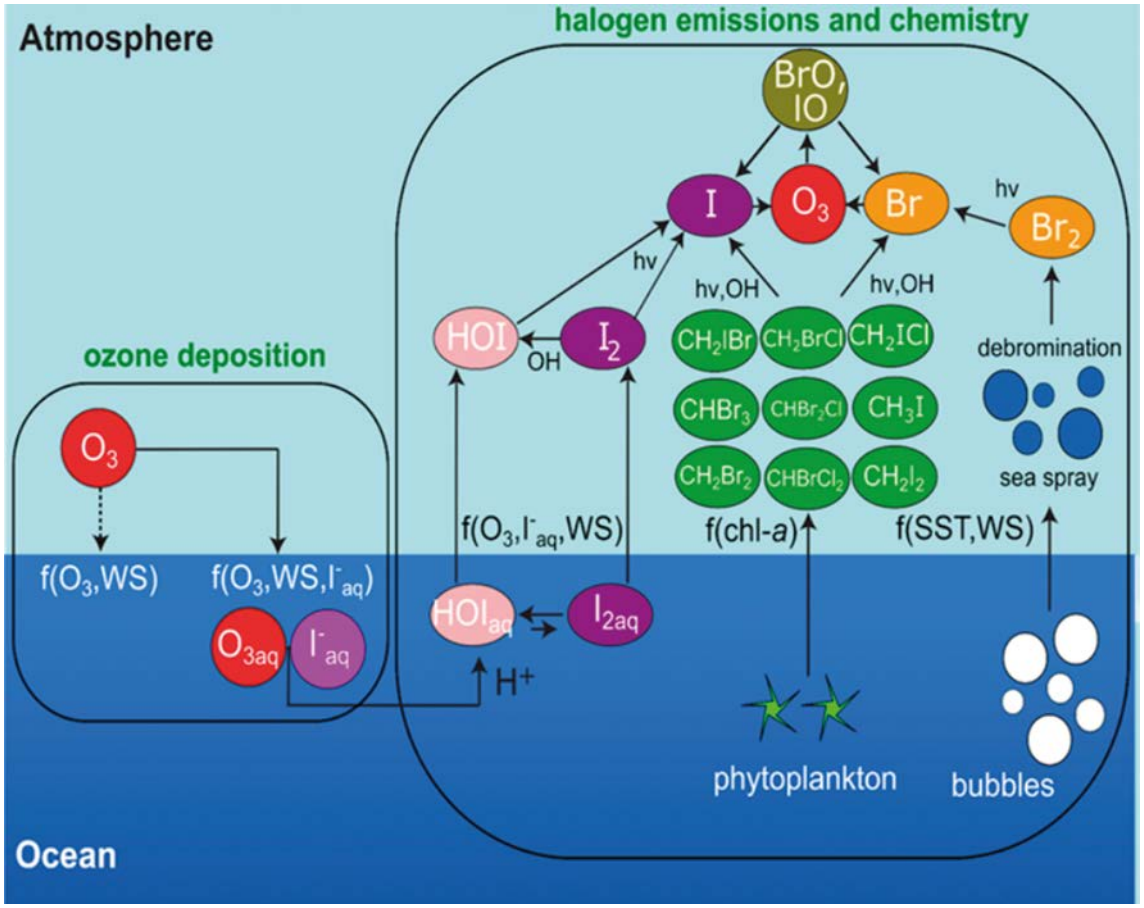


Figure 5. Bromine and iodine chemical scheme implemented in the CMAQ model.

simulations are completed with the halogen chemistry: without and with photochemical reactions of higher iodine oxides. Enhanced deposition reduces mean summer-time surface ozone by ~3% over marine regions in the Northern Hemisphere. Halogen chemistry without the photochemical reactions of higher iodine oxides reduces surface ozone by ~15% whereas simulations with the photochemical reactions of higher iodine oxides indicate ozone reductions of ~48%. The model without these processes overpredicts ozone compared to observations whereas the inclusion of these processes improves predictions. The inclusion of photochemical reactions for higher iodine oxides leads to ozone predictions that are lower than observations, underscoring the need for further refinement of the halogen emissions and chemistry scheme in the model (*Environ. Sci. Technol.*, 2015, 49 (15), pp 9203–9211).

Regional air quality modeling

Atmospheric oxidants such as ozone (O3), hydroxyl and nitrate radicals (OH and NO3) determine the ability of the urban atmosphere to process organic and inorganic pollutants, which have an impact on air quality, environmental health and climate. Madrid city has experienced an increase of 30–40% in ambient air O3 levels, along with a decrease of 20–40% in NO2, from 2007 to 2014. Using air pollution observations

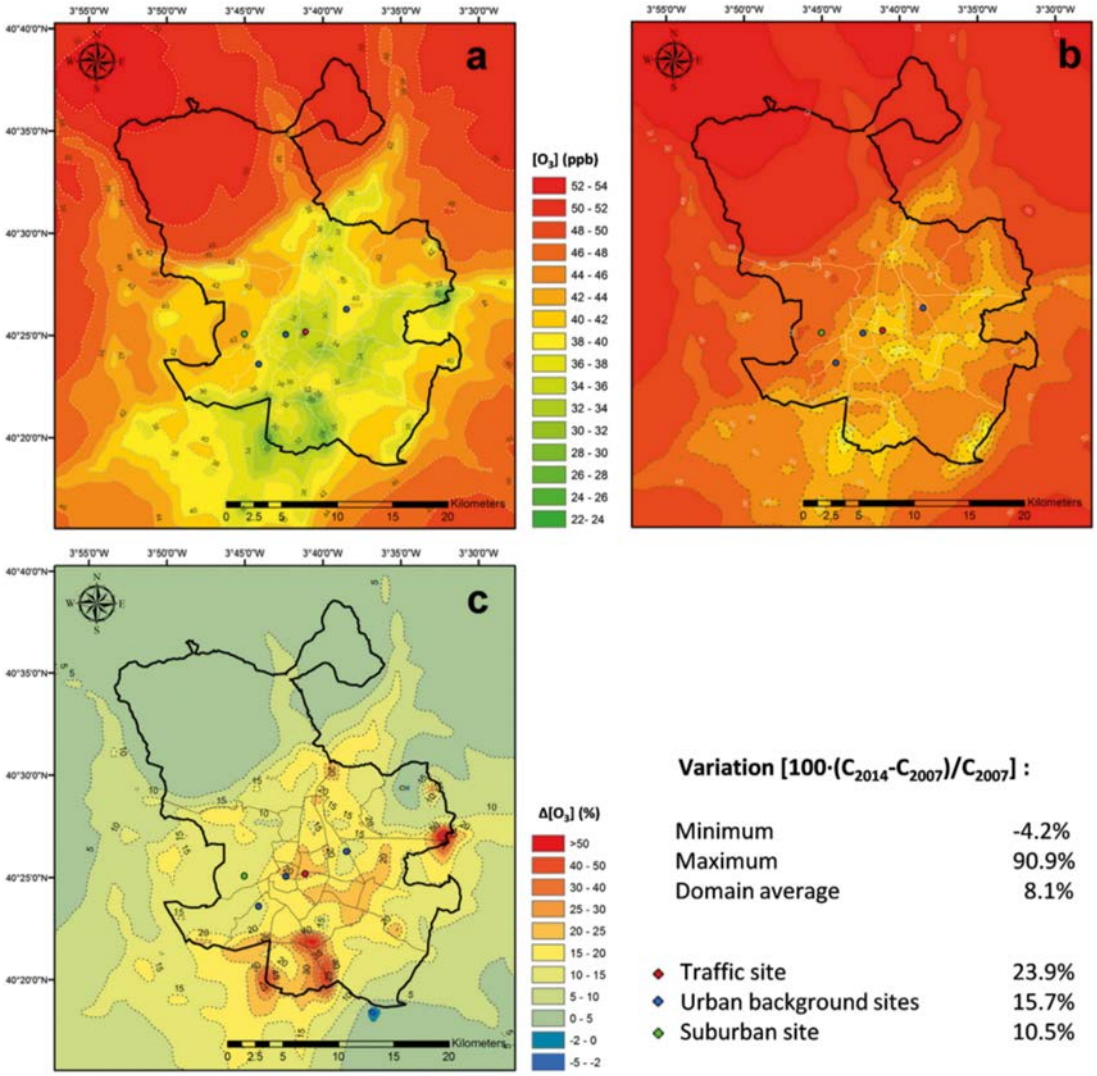


Figure 6. Modelled O3 annual mean concentration, (**a**) 2007; (**b**) 2014. (**c**) Variation of O3 annual mean concentration in 2014 with respect to 2007 and resulting statistics.

and a high-resolution air quality model, we find a large concentration increase of up to 70% and 90% in OH and NO3, respectively, in downtown Madrid (domain-wide average increase of 10% and 32% for OH and NO3, respectively). The results also show an 11% reduction in the nitric acid concentrations, leading to a remarkable denoxification of this urban atmosphere with implications for lower PM2.5 levels and nitrogen input into ecosystems. This study suggests that projected worldwide NOx emission reductions, following air quality standards, will lead to important changes in the oxidizing capacity of the atmosphere in and around large cities. (*Scientific Reports* ***7****, 45956 (2017)*).

Paleoclimate

The AC2 group has also recently developed a new research sub-discipline aimed to investigate past changes in the halogens atmospheric chemistry beyond the instrumental period. Geochemical elements such as bromine, iodine or mercury are deposited in natural archives (i.e. ice cores, peatbogs, lake and marine sediments). They provide us interesting information related to atmospheric processes occurring in the past at different time-scales. Our group has been actively working in close collaboration with researchers from the Niels Bohr Institute, University of Copenhagen in order to unravel the information provided by these paleoenvironmental proxies. So far, we have obtained significant achievements in the field of "paleo"sciencies:

Halogen enrichment in polar regions as a proxy to reconstruct sea-ice extent

We have investigated the depositional processes of halogens (i.e. bromine and iodine) and sea-salt (mainly sodium and potassium) in Polar regions (Both in the Artic and the Antarctic). Bromine and iodine concentrations in the Akademii Nauk ice core in Severnaya Zemlya (Russian Arctic, Fig. 7A) provided a reconstruction of sea ice variability in the Laptev Sea between 1950 and 1998 (Fig. 7B) (Spolaor et al., 2016a). This relation was established since the chemistry of halogens bromine and iodine is strongly active and influenced by sea ice dynamics, in terms of physical, chemical and biological process.

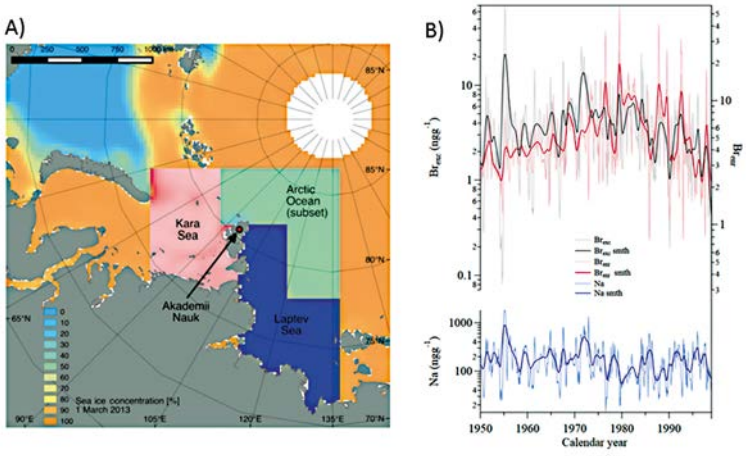


Figure 7. A) Arctic areas considered for sea ice calculations. The location of the Akademii Nauk ice core drillsite on Severnaya Zemlya also is shown. B) Brexc compared with sea ice area during spring and summer in the Laptev Sea region.

The same scientific approach was applied in Eastern Antarctica. An ice core drilled at the Law Dome (Fig. 8A) was investigated to evaluate the sea ice proxies variability during the 20th century (Vallelonga et al., 2017). In this follow-up study we compared bromine and iodine concentrations in the ice core record (and their enrichment beyond seawater compositions) with satellite observations of first-year sea ice area in the 90–130 E sector of the Wilkes coast. Our findings support the results of previous studies of sea ice variability in the Russian Artic but also agreed with other sea-ice proxies from Law Dome. This study highlighted that Wilkes coast sea ice area is currently at its lowest level since the start of the 20th century (Fig. 8b). We also suggested that sea-ice variability recorded in the halogens sequence could be related to the Interdecadal Pacific Oscillation (IPO) variability.

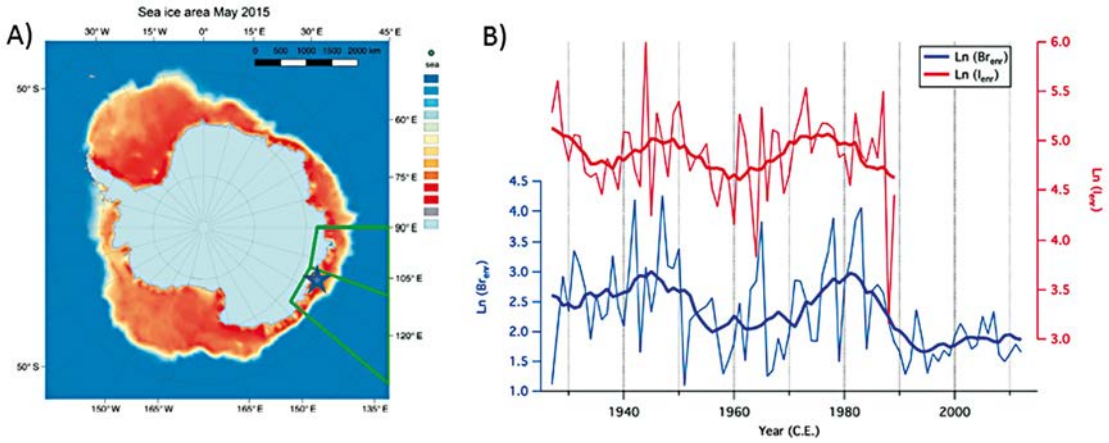


Figure 8. A) Antarctic sectors used for evaluating sea ice trends. The image shows an example of sea ice area for the month of May 2015 *B)* Time series of bromine and iodine enrichment. Bromine and iodine show similar trends, pointing to a common source of variability.

In Greenland, we used a 1-D chemistry transport model to quantify processes of bromine enrichment over first-year sea ice and depositional transport over multi-year sea ice and land ice (Fig. 9A). This modelling exercise contributed to the understanding and interpretation of halogen concentration variability in NEEM ice core record (Northwestern Greenland). The bromine enrichment indicates the photochemical recycling of bromine observed over first-year, or seasonal, sea ice in so-called "bromine explosions". In this particular study we showed the longest halogen sequence (i.e bromine enrichment) spanning the last 120,000 years as a proxy for sea ice extent in the Canadian Artic (Fig. 8b) (Spolaor et al., 2016b). We found the maximum extension of first-year sea ice occurred approximately 9,000 years ago during the Holocene Climate Optimum (9B), when Greenland temperatures were 2 to 3 °C above present values. Our study demonstrate a clear relationship between temperature and first-year sea ice extent in the Arctic and suggest multi-year sea ice will continue to decline as polar amplification drives Arctic temperatures beyond the 2 °C global average warming target of the recent COP21 Paris climate agreement.

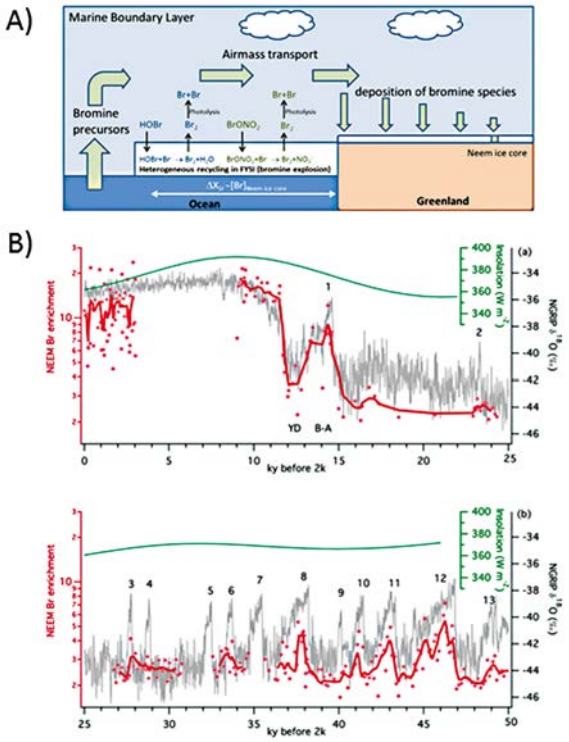


Figure 9. A) Schematic of chemical and physical processes in the THAMO chemical transport model scenarios. Bromine enrichment of an air mass occurs through heterogeneous recycling in first year sea ice (bromine explosion) which is then transported over the Greenland ice sheet. B) Variability in bromine enrichment occurs on stadial-interstadial scales

Reconstruction of atmospheric pollution beyond the Instrumental Period

We have reconstructed the mercury and lead atmospheric deposition in NE Spain during the last 700 years using the concentration of these pollutants in lake sediments from the Pyrenees (Lake Montcortès) (Corella et al., 2017) (Fig. 10). The main source of atmospheric mercury deposited in the lake is related to the mercury production in Almadén (the world´s largest mercury mine). Lead pollution is related to local mining activities in the Pyrenees and the use of leaded gasoline during the second half of the 20th century. This study highlights the sensitiveness of lake sediments to atmospheric pollution from a historical perspective.

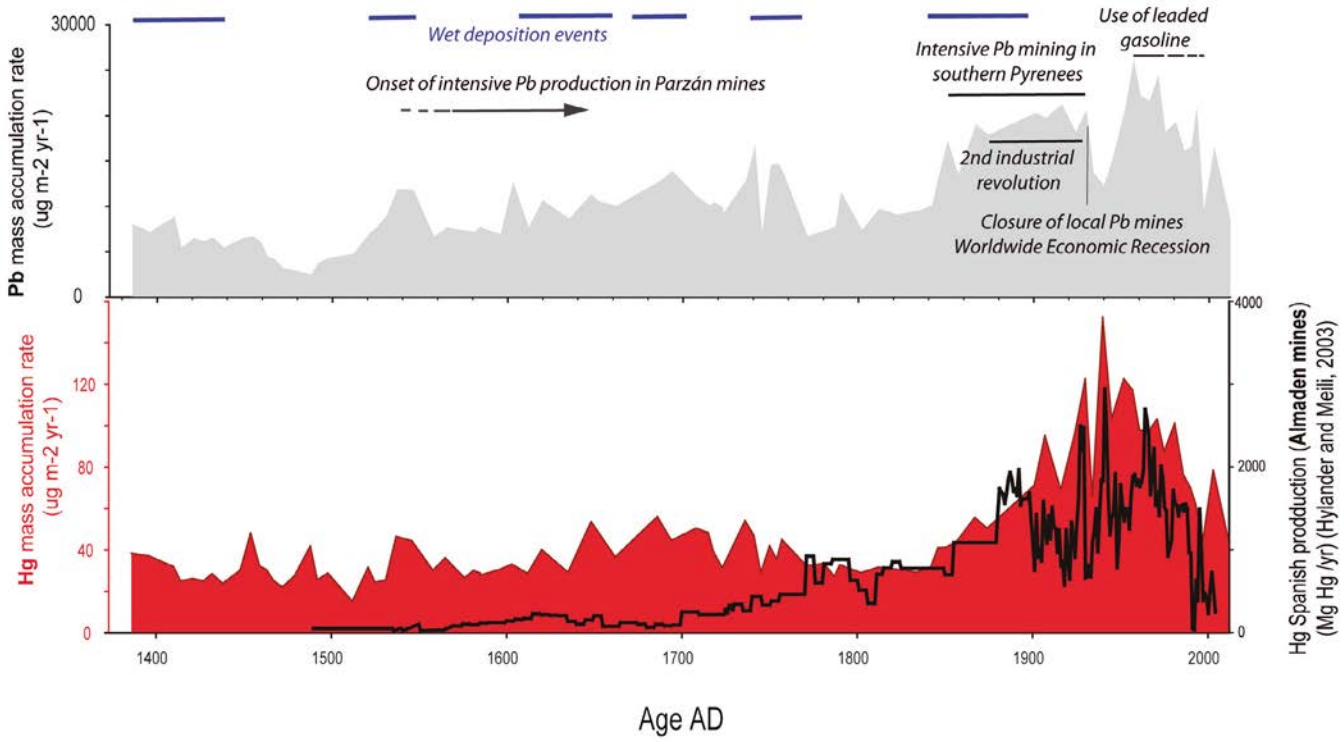


Figure 10. Accumulation rates of Mercury (Hg and Lead (PB) since XIVth century and its relation with i) Hg production in Almadén mines; ii) Local Pb mining in the Pyrenees and use of leaded gasoline in Europe (between 1950 and 1990)

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COMPETITIVE FUNDING

National Grants: individual

MINECO

Principal Investigator	Title	Reference
Alfonso Saiz López	Fases finales (C2/D/E1) del instrumento Ultraviolet and Visible Atmospheric Sounder (UVAS) en SEOSAT/INGENIO	ESP2014-60774-R

MINECO

Principal Investigator	Title	Reference
Alfonso Saiz López	Fases de desarrollo final y ensayos (C2/D) del instrumento Ultraviolet and Visible Atmospheric Sounder (UVAS) en SEOSAT/INGENIO	ESP2015-71299-R

National Grants: coordinated

Comunidad de Madrid

Principal Investigator	Title	Reference
Alfonso Saiz López	Tecnologías innovadoras para la evaluación y mejora de la calidad del aire urbano	TECNAIR

International Grants: coordinated

EU

Principal Investigator	Title	Reference
Alfonso Saiz López	QQuality Assurance for Essential Climate Variables	QA4ECV

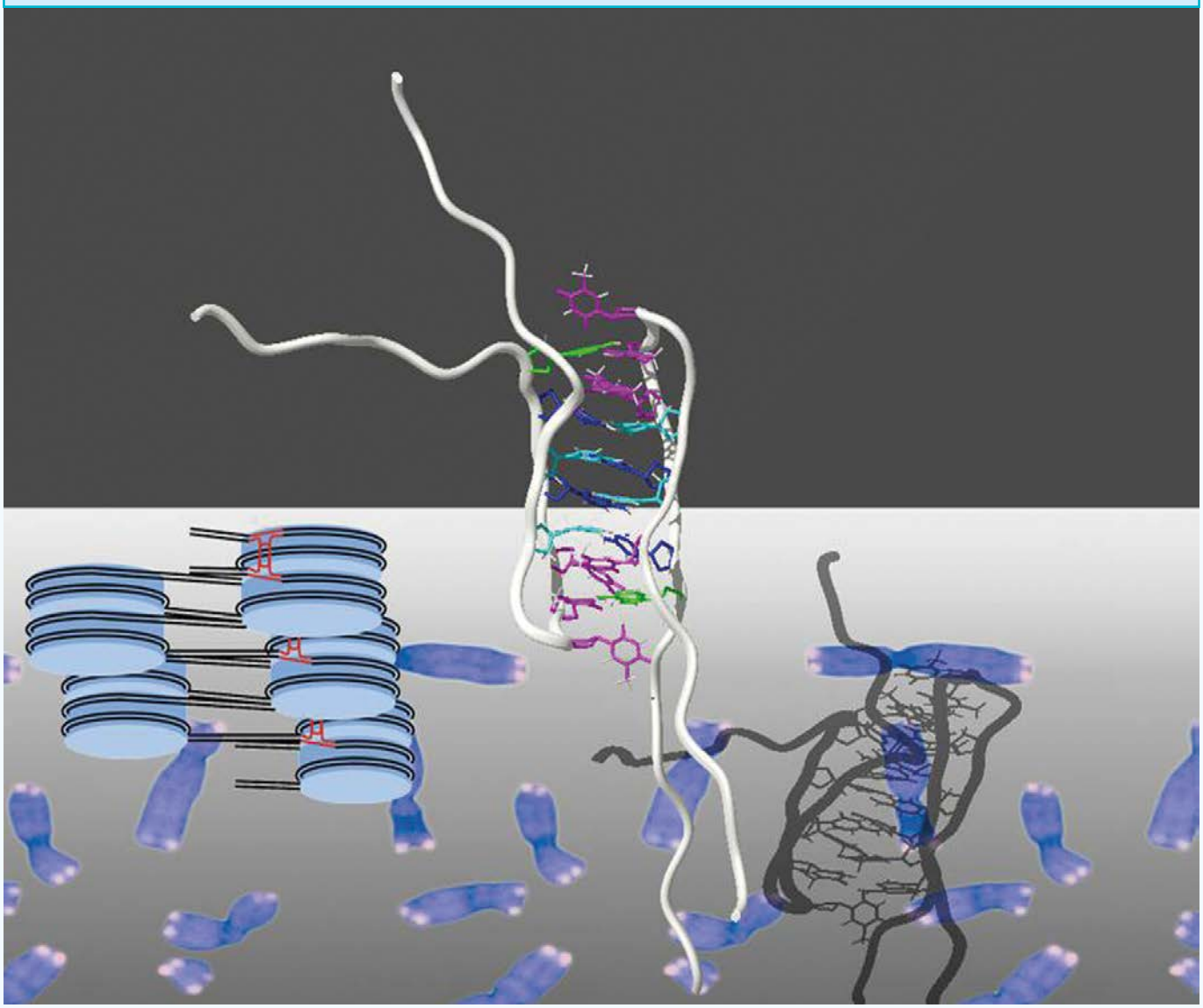
Aarhus University

Principal Investigator	Title	Reference
Alfonso Saiz López	DOAS measurements of halogen oxides at Station Nord (Greenland)	DOASGREEN

EU

Principal Investigator	Title	Reference
Alfonso Saiz López	Climate dimension of natural halogens in the earth system: past, present, future	726349 CLIMAHAL

Department of Biological Physical Chemistry



Introduction http://qfbio.iqfr.csic.es

The research experience in our Department covers the fields of Biochemistry, Molecular Biology, Structural Biology, Biophysics, Glycobiology, Bioinformatics and Biothermodynamics. The objective of our ongoing work is to understand the physical-chemical bases governing the structure, stability, dynamics and interactions of different biological molecules such as peptides, proteins, nucleic acids and carbohydrates. This investigation is conducted on systems with different levels of complexity, ranging from isolated molecules to macromolecular assemblies, membrane mimetics, cells and tissues. Many of these systems have biomedical, pharmacological or biotechnical importance.

We determine the structure and stability of nucleic acids and their complexes with proteins. The final aim is to characterise their relationship with the mechanisms of gene regulation at the transcriptional and post-transcriptional levels. We are also interested in the biophysical characterization of intrinsically disordered proteins, domains or protein fragments; and we are studying model systems in which this feature is essential for the biological function.

The Department also carries out research based on structural bioinformatics, and we are actively involved in the development of novel techniques for the simulation, analysis and modelling of large biomolecular systems.

We study processes involved in the assembly and functional properties amyloids, the broad aim of which is to understand pathologies related to aberrant conformations, neurodegenerative disease, and in general, the process of aging. We also study the role of carbohydrates as recognition signals, their binding to ligands, and the structural organization of protein receptors for carbohydrate recognition. Other systems that we study include choline receptors, murein hydrolases, pneumococcal virulence factors and various allergens and toxins.

We have extensive experience in studying the mechanisms of protein folding and the design of peptides with a defined structure. Our work has contributed towards establishing structure-function relationships in proteins and protein-inhibitor complexes implicated in, for example, angiogenesis, immune response, and antiviral and antimicrobial activity.

Moreover, our research efforts have also been directed towards the determination of the structural organization and stability of membrane protein complexes, how the associated interactions alter the physical properties of cell membranes, and the mechanisms of action of anesthetics, anticancer and antiparasite drugs.

Our Department is also actively involved in research aimed at developing methodology necessary for i) resolving problems related to molecular heterogeneity (isoforms, modifications and conformational heterogeneity), ii) enhancing the use and applicability of NMR Spectroscopy (development of new pulse sequences, reduced dimensionality and automatic assignment methods), iii) resolving molecular interactions in complex environments (fluorescence microspectroscopy or single cell spectroscopy), or whole-cell approaches (microarrays of design).

Experimental methods and equipment

The Department has all of the necessary instrumentation for in-depth experimental studies of biological samples. Laboratories are well-equipped to carry out the basic techniques employed in isolating, cloning, expressing, purifying and concentrating proteins and nucleic acids; and have instrumentation necessary for their biophysical characterisation: immunochemical analysis, high-performance liquid chromatography, analytical ultracentrigugation, light scattering (MALLS), spectropolarimetry (CD), UV-visible spectroscopy, fluorescence spectroscopy, differential scanning calorimetry (DSC), isothermal titration calorimetry (ITC). A departmental microarray scanner, a manual microarrayer and a scanner for microarrays are also available.

The Department is also well-equipped with instrumentation for advanced fluorescence methods required in high-resolution temporal (ps-ms) and spatial (mm-sub μm) studies of biological systems at different levels of organisation. We also have two high-field NMR spectrometers, a 600 MHz instrument and an 800 MHz one, each equipped with a gradient module and cryoprobe. All of the necessary software has been installed for processing and analyzing multidimensional NMR spectra, for calculations of macromolecular structures in solution, and for protein-protein and protein-ligand docking analyses.

Group Structure

NMR of Protein, Structure, Dynamics and Interactions Group

Tenured Staff scientists

Jorge Santoro Said
(Professor) (until 30/ 09/ 2015)

Marta Bruix Bayes (Professor)

ReID ORCID SCOPUS

ReID ORCID SCOPUS

María Ángeles Jiménez (Associate Professor)

ReID ORCID SCOPUS

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Subramanian Padmanabhan (Associate Professor)

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Jose Manuel Perez Cañadillas (Assistant Professor)

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Douglas Vinson Laurents (Assistant Professor)

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Non-tenured scientists

Aránzazu Gallego García
(Predoctoral 02/10/2014-21/12/2015;
Post-doctoral 21/12/ 2015-30/06/2016)

Soraya Serrano Serrano
(Post-doctoral 01/ 03/2015-31/08/2015)

Miguel Mompean García
(Predoctoral 01/ 12/ 2011-30/11/2015;
Post-doctoral 15/1/2016-31/08/2016)

Concepción Solanas Díaz
(Post-doctoral 15/ 12/2015-30/04/2016)

Doctoral students

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(Predoctoral 01/ 09/ 2015-30/11/2018)

Hector Zamora Carreras
(Predoctoral 01/ 12/ 2013-30/11/2016)

Jesus Fernández Zapata
(Predoctoral**,** 01/ 01/ 2014-31/12/2017)

Belen Chaves Agüero
(Predoctoral 01/ 01/ 2016-31/12/2019)

Technical Staff

David Pantoja-Uceda (TSE)

Miguel Angel Treviño Avellaneda (TSE)

Luis De La Vega Serrada (until 26/08/2016)

Sergio Camero Gigante
(TS 1/ 05/ 2016-30/ 04/2018)

Summary

The group has pioneered the application of NMR in Spain to the determination of the three-dimensional structure, dynamics and interactions of proteins and peptides (http://rmnpro.iqfr.csic.es). This knowledge is essential for understanding the physicochemical bases of their biological functions and the mechanisms which regulate their activities. Within this field, we are concerned with studies on the structure and dynamics of different biological systems while concurrently we implement and optimize NMR methods. The group shares with the Nucleic Acids NMR group the management and maintenance of the Manuel Rico NMR Laboratory (http://rmn.iqfr.csic.es). This laboratory has advanced instrumentation for the development of the projects and has been a reference of excellence at national and international level. Historically, studies have been developed related to the protein-lipid interactions responsible for the cytotoxicity of ribonucleases and actinoporines, the structural and dynamic characterization of allergenic and centrosome proteins, as well as those involved in the formation of ribonucleoparticles and post-transcriptional control, and interactions between regulatory proteins responsive to light in bacteria. Peptide design and protein folding-related issues, such as the structural characterization of non-native states and folding intermediates continue to be subjects of our interest.

Strategic Aims

- Development of new NMR methodology for fast and highly efficient determination of three-dimensional structures of biomacromolecules and their complexes.
- New methods to study IDPs (intrinsically disordered proteins) and detection of structural tendencies.
- Design of peptides with well-defined conformations.
- Structure-activity relationships.
- Structural study of proteins of biomedical relevance: applications in cancer, and allergy.
- Structural study of protein-nucleic acid complexes: applications in the control and regulation of gene expression.
- Description of the molecular mechanisms of light response in bacteria and use of these results in optogenetic applications.
- Characterization of the conformation and dynamics of amyloidogenic proteins.

Results

Implementation and optimization of NMR methods

Intrinsically disordered proteins (IDPs) have continued to focus our interest, since NMR spectroscopy is presented as one of the few techniques that can study from a structural point of view. We have continued to develop and implement new experiments that allow us to carry out not only their sequential assignment but also to obtain structural information. We have proposed new methods that correlate two consecutive CA-CO groups instead of the CO-N groups as previously proposed. This is because the chemical shift value of the CA is a better indicator of the secondary structure. On the other hand, once established the method called Iterative soft thresholding as the method for non-uniform sampling, this methodology has been standardized, and we have generated a series of tools based on Shell scripting that allow streamline the entire process. Finally, we have begun to implement this methodology in a ^{13}C detection experiment.

Design and structure-activity relationships in peptides

The determination of the structure of biologically active peptides contributes to our understanding of their biological function and paves the way towards the rational design of peptides with pharmaceutical applications. Among our recent studies, we highlight our results on peptides derived from the glycoprotein gp41 from the virus HIV, which are involved in membrane fusion and have inmunogenic capacity against HIV, and on bactericide and antitumoral peptides, such as crotalicidin. An interesting result is that a peptide encompassing the helical N-terminal region of crotalicidin is inactive, whereas that corresponding to the disordered C-terminal region of crotalicidin is active, but less toxic than the full-length peptide.

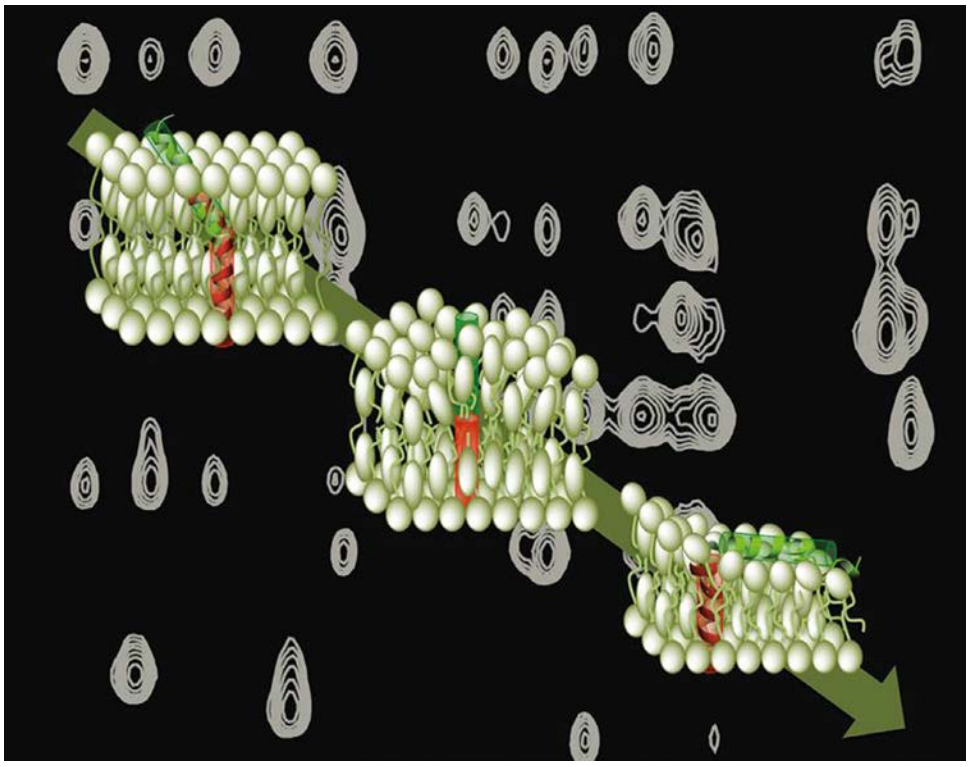

Figure 1. Scheme of the stages in the pathway of membrane fusion proposed on the basis of the helical structures determined by NMR for peptides derived from the MPER and TM regions of gp41 glycoprotein from HIV virus (*J. Biol. Chem.* 2015; doi:10.1074/jbc.M115.644351).

Structural transitions in peptides and proteins mediated by interactions

Autolysin LytA is a protein involved in the virulence of pneumococcus, a pathogenic microorganism in humans. Its C-terminal domain (CLytA) consists of six choline-binding repeats (CBR), arranged in the β-solenoid structure characteristic of choline-binding modules. We have characterised by NMR and CD a 14-residue peptide encompassing the sequence of the core β-hairpin from the third CBR repeat of CLytA. It has been found that this peptide conserves its native β-hairpin fold in aqueous solution, but forms a stable, amphipathic α-helix (i.e. with two faces, one hydrophobic and the other polar) in detergent micelles (with a hydrophilic surface and a hydrophobic core). These β-hairpin and α-helix structures differ greatly in the distribution of polar hydrophobic side chains. To our knowledge, this "chameleonic" behaviour of a micelle-induced structural transition between two ordered peptide structures has not been reported before, and shows the dramatic effect of hydrophobic-hydrophilic interactions. These results could not only be of relevance in the field of peptide design and biosensors, but may also help to understand the molecular basis for the peculiar mechanism of LytA translocation from the cytoplasm to the bacterial surface.

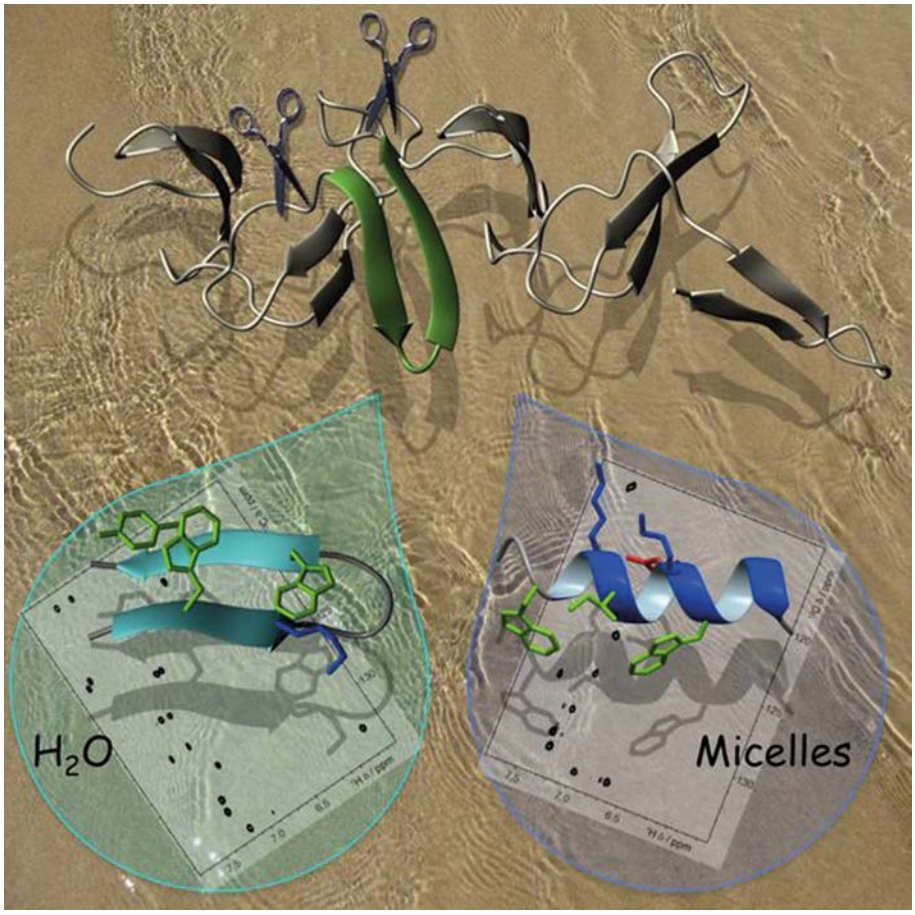

Figure 2. A peptide derived from a choline-binding repeat (CBR) of the pneumococcal LytA protein (top) conserves its native β-hairpin structure (left) in aqueous solution, but forms an amphipathic α-helix (right) in detergent micelles. This image was taken from Chem. Eur. J. 2015's frontispiesce (doi: 10.1002/chem.201582262).

Molecular Mechanisms of Light-Response in Bacteria

Our aim is to understand the molecular mechanisms in the detection and response to light in bacteria. We combine high resolution structural and biophysical studies with functional analysis (en collabaoration with the Genetics Group at the University of Murcia) of various protein factors that serve as sensors and transducers of the light signal, or are specific or regulators of gene expression in the model bacterium *Myxococcus xanthus*. Many of the factors we study have turned out be prototypes of new and widely distributed protein families. Our studies have led to the high-resolution structure-function description of transcription factors and light sensors that employ 5'-deoxyadenosylcobalamin (coenzyme B_{12}) as the chromophore and acts as a light-sensitive allosteric switch, how its activity can be counteracted by a protein with an SH3 domain-like topology that imitates DNA. We have also discovered a large family of RNA polymerase-binding proteins with crucial roles in the expression of essential genes, or of genes activated in response to specific signals such as light.

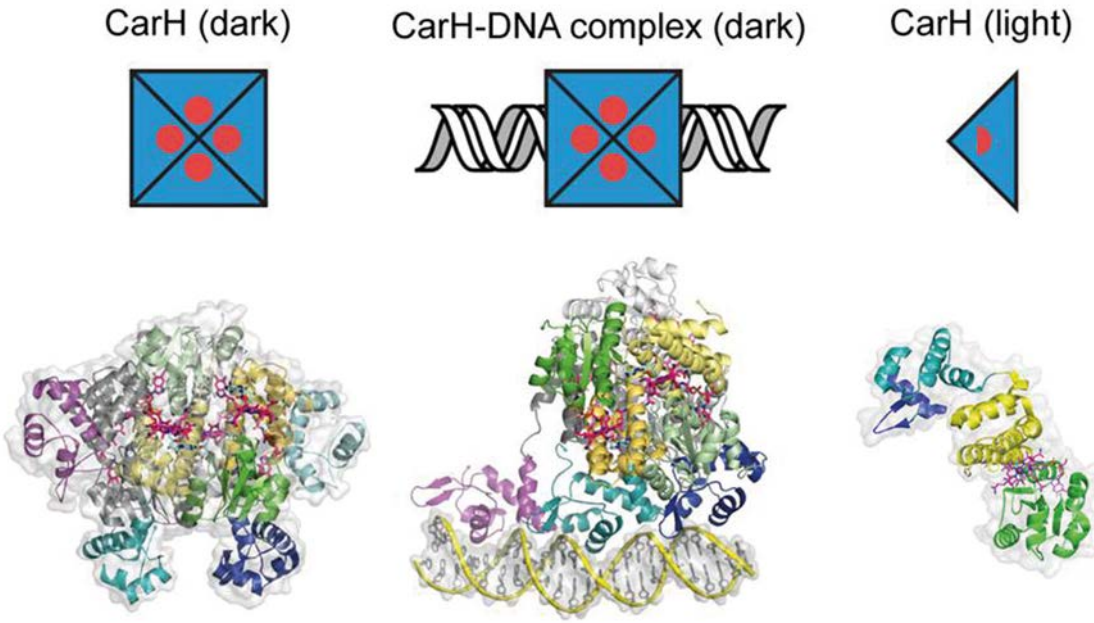

Figure 3. High-resolution structures of the B_{12}-dependent photoreceptor CarH tetramer in the dark free and DNA-bound states and in the light-exposed monomer form with a cartoon representation and labels on top.

Proteins involved in RNA metabolism

We have continued the study of several protein-RNA interactions on systems related to RNA metabolism. The study of Gbp2/Hrp1 proteins were completed and published during the period. These proteins contain several RRM domains, whose structures have been solved by NMR, that interact with RNA using a binding mode that mimics that of the SR proteins. Hrp1/Gbp2 RRM3 domains do not interact with RNA, instead they are involved in the specific interaction with the THO/TREX machinery. The study has been performed in collaboration with Prof. Betrand Seraphin (IGBMC-CNRS France). We have also studied the IDP domain of Tif4631 (eIF4G) by NMR and its interactions with Pab1 and Pub1 proteins. Finally we have studied the structure and binding mode of Nrd 1 RNA binding domain by NMR and X-ray crystallography in collaboration with Dr. Beatriz González-Pérez (IQFR-CSIC). Studies have been complemented with biophysical and cell biology data through collaborations with Dr. Silvia Zorrilla (CIB-CSIC) and Dr. Olga Calvo (IBFG-CSIC)

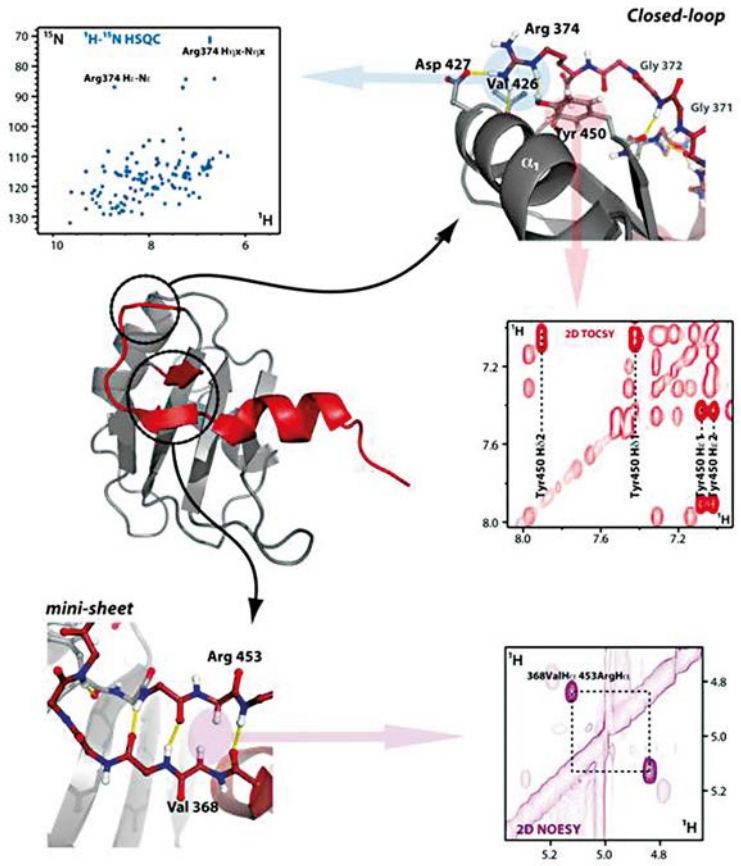

Figure 4. Structural detail of the novel element ("closed-loop") found in Hrb1 RRM3. Resonances of Arg374 guaninidium group NHs are downfield shifted (Hε) or exchange with the solvent slower than usual (Hhx) as an effect of a complex hydrogen bond network (Arg374, Asp427 and Tyr450). Tyr450 exhibit slowed down ring flipping dynamics. The C-terminal part of Hrb1 forms a small two-stranded antiparallel β-sheet wit characteristic Hα-Hα interstrand NOE

Structural bases of allergenicity

Understanding the role of biomolecules involved in allergy requires not only the knowledge of the isolated structure of each of them, but also the interactions with other biomolecules. In this field we have worked with the principal allergens of olive and ash pollen, important causes of respiratory allergies. The C-term domains of Ole e 9 and Fra e 9 have a β-glucanase activity. We have described the 3D structures of these domains from NMR data and the details at the atomic level of their interaction with laminarin. The results obtained explain how very subtle variations in the residues that are responsible for the interaction justify the different activity of these hololog ous domains.

Recognition events in the dynein motor

The protein recognition processes of the dynein system remain one of our working projects. We try to understand why these proteins interact with multiple cellular proteins unrelated to each other and with low sequence homology. Recently, we have used NMR spectroscopy to obtain the structure of the human DYNLT1 in solution by forming a complex with DIC1 (dynein intermediate chain). This is the first mammalian structure described so far and it should serve as a basis for future functional and structural studies on this system.

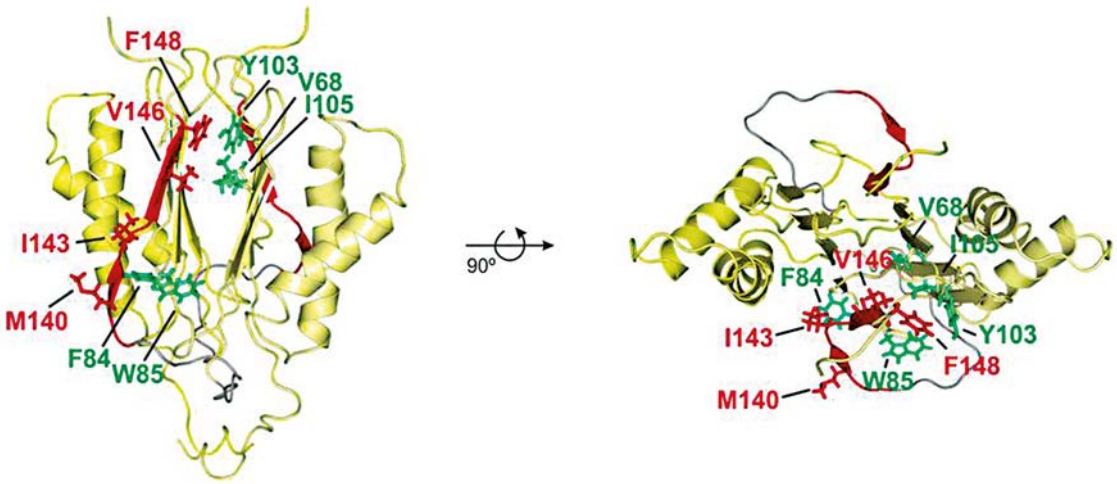

Figure 5. Solution structure of human DYNLT1 self-saturated with a DIC peptide. Two different views of the calculated 3D structure of DYNLT1-DIC2 in a ribbon representation. The two chains of each DYNLT1 monomer are coloured in yellow, and the DIC segment is highlighted in red. The hydrophobic contacts between the DIC segment and the DYNLT1 structure are also shown in a stick format. Interacting DYNLT1 hydrophobic residues are shown in green.

Structural aspects of protein-lipid recognition by ribonucleases

We have characterised at atomic level the interaction of some proteins with membrane mimetic systems or membrane components. Also, we have finished the work focussed in the interaction of ECP (from the ribonuclease family) with different lipopolysaccharides, from both the structural and functional point of view. Our results show for the first time that ECP is able to neutralize LPS and therefore opens a new route to develop new therapeutic agents based on the structural scaffolding of this protein.

Structure-activity relationships of a pheromone from *F. oxysporum*

The fungus *F. oxyporum* is a plant and human pathogen that has a small pheromone. By NMR methods, we have determined that α-pheromone adopts a defined secondary structure and, despite its small size, contains discrete regions involved in different biological processes such as polarization of the reorientation and control of the cell cycle. We consider it likely that these findings also apply to a-pheromones from other ascomycetic fungi and that the signaling functions of these pheromones may be more complex than anticipated. The work is now focused on understanding the role of the environment in the activation of the Ste2 membrane receptor.

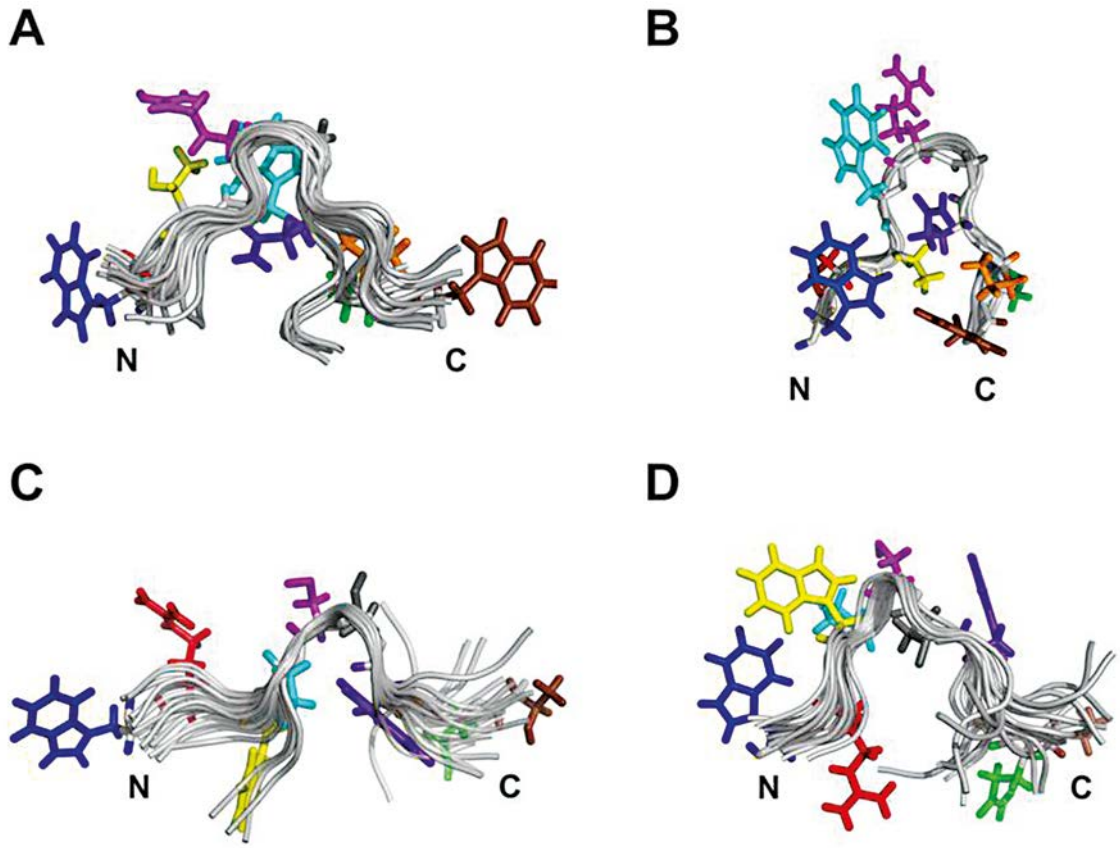

Figure 6. Solution structure of the preferred conformation of α-pheromone and a scrambled sequence in H_2O (A, C) and H_2O/TFE 7:3 mixture (B, D) calculated by NMR. The superposition of the backbone of the best 20 structures in each family is represented in grey. Side chains of the energetically best structure in solution are in different colors depending of the sequence position, 1: blue; 2: red; 3: yellow; 4: cyan; 5: magenta; 6: grey; 7: violet; 8: orange; 9: green and 10: brown. Peptide termini are indicated by N and C.

Conformation and dynamics of amyloidogenic proteins

In collaboration with the laboratories of C. Geraldes (Coim-bra) and E. Toth (Orleans), we have developed and tested new paramagnetic molecular probes for Abeta aggregates. The goal of this research is to develop safer and less expensive diagnostic tools for Alzheimer's disease.

TDP-43 is a important protein playing key roles in mRNA splicing, transport and translational regulation, but forms patho-logical aggregates tied to Amyotrophic Lateral Sclerosis (ALS), FrontoTemporal Lobar Degeneration (FTLD), and to a lesser extent Alzheimer's disease. Working with the groups of E. Buratti (Trieste), M. Carrión (I. Cajal), and A. McDermott (Columbia U., NY), we have proposed a structural model for the TDP-43 amyloid and explained how pH affects its formation.

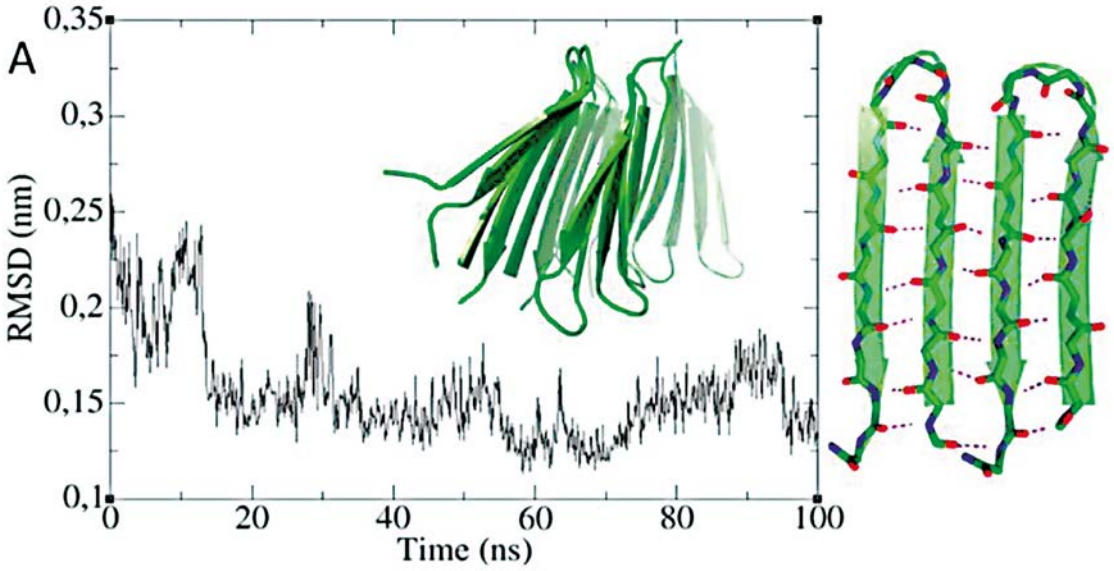

Figure 7. Structural model proposed for the nucleus of the TDP-43 amyloid (linked to ALS) formed by residues A341-SQQNQSGPSGNNQNQG357. The left panel shows the RMSD of 100 ns of molecular dynamics of ten beta hairpins of TDP-43341-357 (five hairpins in two facing beta sheets). The right panel represents the network of intra- and inter-hairpin backbone hydrogen bonds.

Moreover, we have determined the 3D structure, dynamics and stability of the N-terminal domain of TDP-43, and found that it adopts a novel fold. Finally, the side chains amide groups of Asn and Gln were found by us and the lab of T. Ezquerra (IEM, CSIC) to adopt a special class of exceptionally stable H-bonds in amyloids. All these findings advance our understanding of how TDP-43 ag-gregates form and could initiate and propagate in ALS and FTLD.

Apoptin is a small protein from chicken anemia virus that in-duces programmed cell death in over 80 cancer cell lines but does not harm healthy cells. In collaboration with A. Benito and M. Villanova (U. Gerona), we have characterized the confor-mation and dynamics of an active, soluble, monomeric variant of Apoptin and found that it is intrinsically unfolded. This variant does not fold when the pH, redox conditions, divalent cation concentration or phosphorylation state are varied. These results provide new insight into Apoptin's mechanism of action.

Figure 8. An apoptin variant, with an exquisitely selective cytotoxicity for cancer cells; is an intrinsically disordered protein

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COMPETITIVE FUNDING

National Grants: individual

MINECO

Principal Investigator	Title	Reference
M Ángeles Jiménez	Bases estructurales del reconocimiento entre biomoléculas mediante RMN: Proteínas y lípidos	CTQ2011-22514
Marta Bruix	Reconocimiento en sistemas complejos de biomoléculas mediante RMN: metodología, interacciones multimoleculares e IDPs	CTQ2014-52633-P

National Grants: coordinated

MINECO

Principal Investigator	Title	Reference
Douglas V. Laurents	QBP1 como agente profiláctico en TEPT: estudios estructurales y preclínicos	SAF2013-49179-C2-2-R
Subramanian Padmanabhan Iyer	Red reguladora de la respuesta a la luz y conexion con otras redes de regulacion en la bacteria *Myxococcus xanthus*: analisis estructurales	BFU2012-40184-C02-02
Subramanian Padmanabhan Iyer	Nuevos aspectos moleculares de la red fotorreguladora en la bacteria *Myxococcus xanthus* y su conservacion evolutiva: analisis estructurales	BFU2015-67968-C2-2-P
M Ángeles Jiménez (Coordinador: Allinky Biopharma SL)	Desarrollo preclínico de nuevos fármacos para el tratamiento personalizado del cáncer de pulmón	RTC-2014-1458-1

Comunidad de Madrid

Principal Investigator	Title	Reference
M Ángeles Jiménez (Coordinador: J.M. Carazo, CNB-CSIC)	PROFUN II: Interactómica del centrosoma	P2010/BMD-2305

International Grants: coordinated

European Union Joint Programme Neurodegenerative Diseases

Investigador Principal	Título del Proyecto	Referencia
Douglas V. Laurents	Identification and structural characterization of the primordial cytotoxic conformers of the amyloidogenic cascade: Ideal prevention/diagnostic/ therapeutic targets in neurodegeneration.	EU-JPND-AC14/00037

Group of Bioconformatics and protein assemblies

Staff

María Gasset Vega (*Investigador científico*)

ResearchID: I-2050-2014, ORCID: 0000-0001-6436-4055

Technical Staff

Javier A. Martínez Fernández (Titulado Superior Especialista G2, from 21/09/2015 to 09/03/2017)

Rosa Sánchez Herrero (Titulado Superior Especialista G2, from 21/09/2015, to 20/09/2017)

Laura Montoya González (Titulado Superior Especialista G1, from 15/11/2016 to 14/05/2017)

Summary

Our main goal is finding the basic codes ruling protein self-assembly in low to more complex systems for their biotechnological exploitation. The group is equipped with the instrumentation for molecular and cell biology, and for production, biophysical and functional characterization of recombinant proteins. Along these two years we have set collaborations with Drs A. Castro (IQM-CSIC), R. Rodríguez-Pérez (IdiPaz), M. Pedrosa (HULP-IdiPaz), S. Quirce (HULP-IdiPaz), V. Muñoz (IMDEA-CNB), F. Falcone (U. Nottingham, UK), P. Wittung-Stafshede (U.Chalmers, SE) and G. Meisl (U. Cambridge, UK).

Strategic Aims

- Identify protein self-assembly processes linked to food allergies and develop new tools for study them.
- Use protein self-assembly processes for diagnosis and therapy.
- Design peptide-based self-assembly elements.

Results

Identify protein self-assembly processes linked to food allergies and develop new tools for study them

Based on protease resistance and exposure to drastic pH changes, we selected as model of study type-I food allergy. Within this, we focused on fish allergy given the panallergenic features of fish β-parvalbumins. Using a recombinant chain of *G. morhua* β-parvalbumin (rGad m 1), gastric and instestinal-like conditions, a variety of biophysical characterizations and thioflavin T binding assays we found that the allergen assemblies into amyloids from its apo form both ant neutral and acid pHs (Figure 1a). These amyloid fibrils specifically bind the IgE from fish allergic patients. Furthermore, the development of methods using peptide arrays and the coupling of proteolytic digestions with mass spectrometry showed that amyloid forming regions overlap Gad m 1IgE epitopes (Figure 2b).

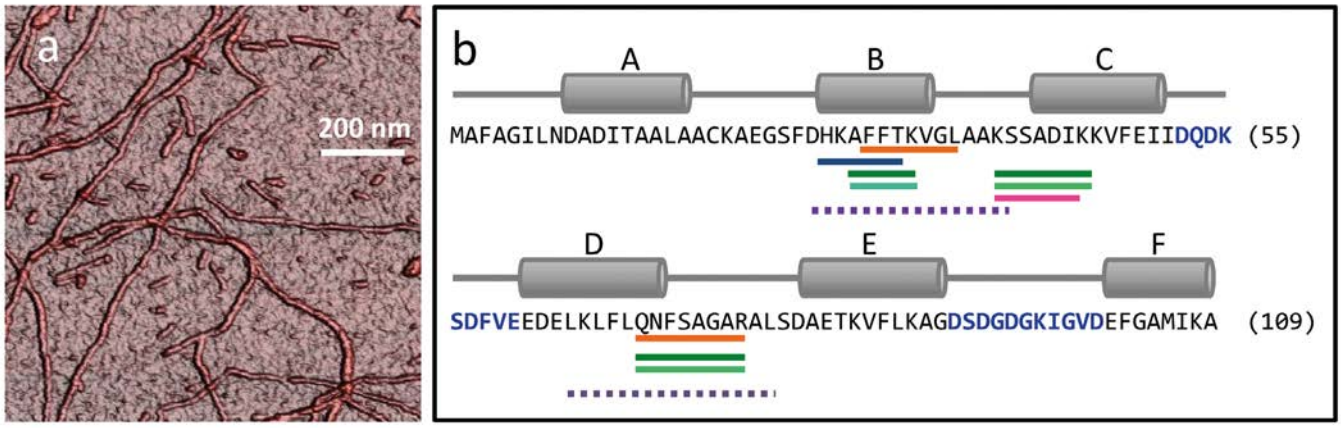

Figura 1. rGad m 1 self-assembly into amyloid fibrils. **(a)** Atomic force microscopy image of (**b**) Mapping amyloid forming sequences in Gad m 1 chain. Grey cylinders represent the helical segments of the globular fold and sequences in blue depict Ca^{2+}-binding sites. Lines correspond to binding regions of: OC (orange), A11 (dark blue), preformed fibrils (dark green), monomer (light green) and of a amyloid-prone mutant (pink). Dotted purple lines represent the protease-resistant cores identified by mass spectrometry.

Use protein self-assembly processes for diagnosis and therapy

To determine the value of amyloids for diagnosis, the interaction of IgE from fish allergic patient sera with rGad m 1 monomers and amyloids was characterized. After discarding SPR methodologies, an ELISA assay including allergen adsorption quantifications was designed. This assay showed 1000-fold differences in the affinity of IgE for the polymer and the monomer (Figure 2). These results were put together as basis for a European patent application. On the other hand, the identification of the motifs dictating self-assembly allowed us to design a collection of mutant chains with both impaired and prone aggregations. These chains exhibited a decreased IgE interaction then being Gad m 1 hypoallergenic forms with market added value.

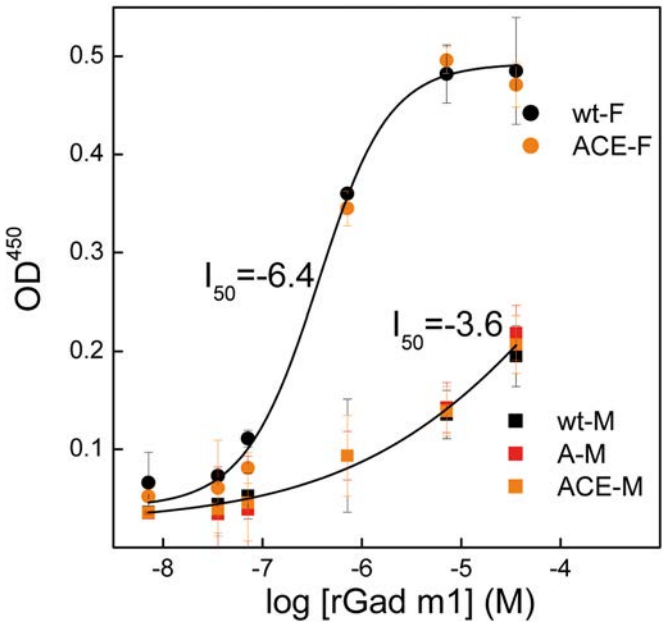

Figure 2. ELISA assay for the determination of the serum IgE relative affinity for rGad m 1 monomers (M) and amyloid fibrils (F). Symbols such as wt, A and ACE correspond to distinct Gad m 1 chains.

Design peptide elements for self-assembly

Analysis of both the sequences of β -parvalbumins of fishes with market value and of the aggregation processes of those corresponding to high and low allergenicity characterized yielded a collection of adhesive hexapeptides. Given their prebiotic features as judged by their composition, their study is expanding in functional terms.

Publications

Martínez, J.; Sánchez, R.; Castellanos, M.; Fernández-Escamilla, A.M.; Vázquez-Cortés, S.; Fernández-Rivas, M.; Gasset, M. (2015) Fish β-parvalbumin acquires allergenic properties by amyloid assembly. ***Swiss. Med. Wkly.*** *145,* w14128.

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National Grants: individual

Ministerio de Ciencia e Innovación (MICINN)

Principal Investigator	Title	Reference
María Gasset	Amyloid as targets for food allergy intervention	SAF2014-52661

Structural Bioinformatics Group

Tenured Staff Scientists

Pablo Chacon Montes (Assistant Professor)

Doctoral students

José Ramón López-Blanco

Erney Ramírez-Aportela

Summary

The Structural Bioinformatics Group (http://chaconlab.org) is focused on developing innovative techniques for the modeling, analysis and simulation of molecular structures in close contact with experimental labs. We are particularly interested in large macromolecules of dynamic composition and conformation whose actions and interactions are essential for cellular function. To better understand such systems, we work on new bioinformatics tools for bridging the resolution gap between atomic structures with low to medium resolution experimental data from different biophysical techniques (e.g. X-ray crystallography, Electron microscopy, SAXS, etc). Our research lines include efforts to deal with the analysis and prediction of molecular flexibility. We actively work to effectively address the study and simulation of the dynamics of large biomolecular systems with Normal-Mode Analysis (NMA), geometric algebra and other multiscale approximations. We also expand our interest to understand and forecast protein-protein and protein-ligand molecular interactions. Our group employs and develops computer-based methodologies (e.g. virtual screening) to aid the rational design of new compounds. The developed methodologies are available via software distributions and web servers.

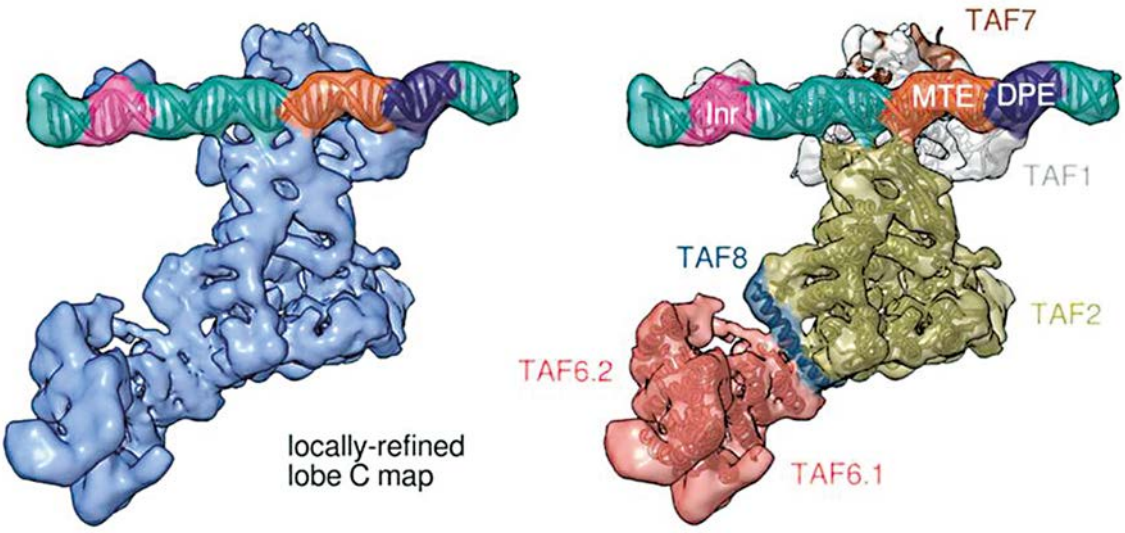
Strategic Aims

- **Bridging the resolution gap with hybrid methods**. We develop new hybrid methods for combining multiresolution structural information in collaboration with several experimental labs.
- **Multiscale dynamics of macromolecular biomachines**. We address the study and simulation of the dynamics of large biomolecular systems with NMA and other multiscale approximations.
- **Atomistic molecular simulations**. Our group employs molecular dynamic simulations to examine a variety of biological phenomena including protein interactions and macromolecular flexibility.
- **Protein modeling**. We develop tools for modeling protein structures and their interactions. This includes novel methods for protein-protein docking and loop modeling problems.
- **Exploring new strategies for structure-based rational design**. Our group employs and develops computer-based methodologies for drug discovery.

Results

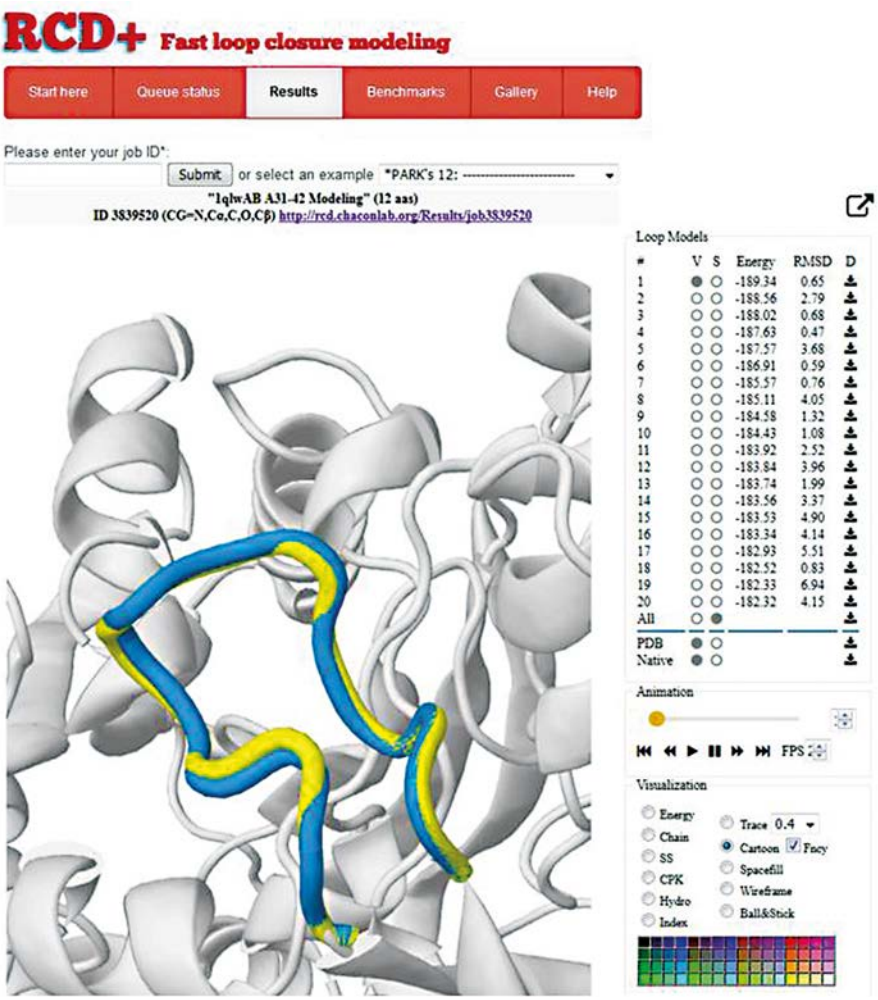
The structural characterization of large biomolecular complexes can be only tackled with coordinated application of complementary biophysical approaches. Computational hybrid methods bridge the gap between such experimental techniques (Lopez-Blanco et al. 2015). We develop several approaches to solve this problem that are accessible from our web. In collaboration with Prof. E. Nogales (U.C Berkeley) we have tested the usefulness of our developed methodology in the interpretation of different biologically relevant systems (Kellogg et. PNAS 2016, Louder Nature 2016).

Structure-based drug design and protein ligand docking are effective and low cost strategies for drug discovery. Our group employs and develops computational methodologies for the rational design of new active compounds. In collaboration with Prof. Andreu (CIB, CSIC) we have worked on the rational design of antibiotics with the target cell division bacteria FtsZ and advanced in the compression of the dynamics of its filaments. In this context, we have discovered new hits (Artola et al., 2015, 2017).



Modeling of the transcription factor IID (TFIID). Complete atomic model of the TAFIID through protein modelling and flexible fitting into a 8.7Å cryo-EM reconstruction density.

Finally, continuing our bioinformatics tools development, we have improved our server for protein-protein prediction (http://frodock.chaconlab.org, E. Ramirez-Aportela et al., 2016), for loop prediction (http://rcd.chaconlab.org, Lopez-Blanco et al., 2016), and for structural flexibility prediction (http://imods.chaconlab.org, JI Aliaga et al., 2016). In this context, we have also contributed with different reviews in the field (López-Blanco J.R. and Chacón P. 2015, 2016).



Loop prediction RCD+ server. Sample results page provided by the server for a bacterial hydrolase loop (PDB-ID 1qwl). In this case, for validation proposes only, the native loop (yellow) is displayed superimposed with the predicted lowest energy model. On the right, the 20 top-ranked loop models are sorted by energy and can be easily selected to activate visualization and customize representation.

Publications

López-Blanco J.R.; Chacón P. (2015) Structural modeling from electron microscopy data. ***WIREs Comput Mol Sci***, *5*, 62–81.

Kellogg, E.H.; Howes S.; Ti S.C.; Ramírez-Aportela E.; Kapoor T.M.; Chacón P., Nogales E. (2016) Near-atomic cryo-EM structure of PRC1 bound to the microtubule. ***PNAS***, *113*, 9430-9439.

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Artola M.; Ruíz-Avila L.B.; Ramírez-Aportela E.; Martínez RF; Oliva M.A.; J. Martín-Galiano; Chacón P.; M.L. López-Rodríguez; Andreu J.M.; S. Huecas (2017) The structural assembly switch of cell division protein FtsZ probed with fluorescent allosteric inhibitors. ***Chem. Sci.***, *8*, 1525-1534.

Ramirez-Aportela E.; Lopez-Blanco J.R.; Chacon P. (2016) FRODOCK 2.0: Fast Protein-Protein docking server. ***Bioinformatics***, *32*, 2386-2388.

Lopez-Blanco J.R.; Canosa-Valls A.J.; Y. Li; P. Chacon (2016) RCD+: Fast loop modeling server. ***Nucleic Acids Res.*** *44*, W395-400.

Aliaga J.I.; Alonso P.; Badía J.M.; Chacón P.; Davidović D.; López-Blanco J.R.; Quintana-Ortí E.S. (2016) A fast band–Krylov eigensolver for macromolecular functional motion simulation on multicore architectures and graphics processors. ***J. Comp. Phys.*** *309*, 314-323.

López-Blanco, J.R.; Chacón, P. (2016) New generation of elastic network models. ***Curr. Opin. Struct. Biol.*** *37*, 46–53.

National Grants: individual

Ministerio de Economía y Competitividad

Principal Investigator	Title	Reference
Pablo Chacon	Function and dynamics of macromolecular complexes explored by integrative structural and computational biology	BFU2016-76220-P

Fluorescence and Molecular Biophysics Group

Tenured Staff scientists

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A. Ulises Acuña Férnandez (Professor Ad honorem)

Technical Staff

Carolina García Rodríguez (TSE) ReID ORCID SCOPUS

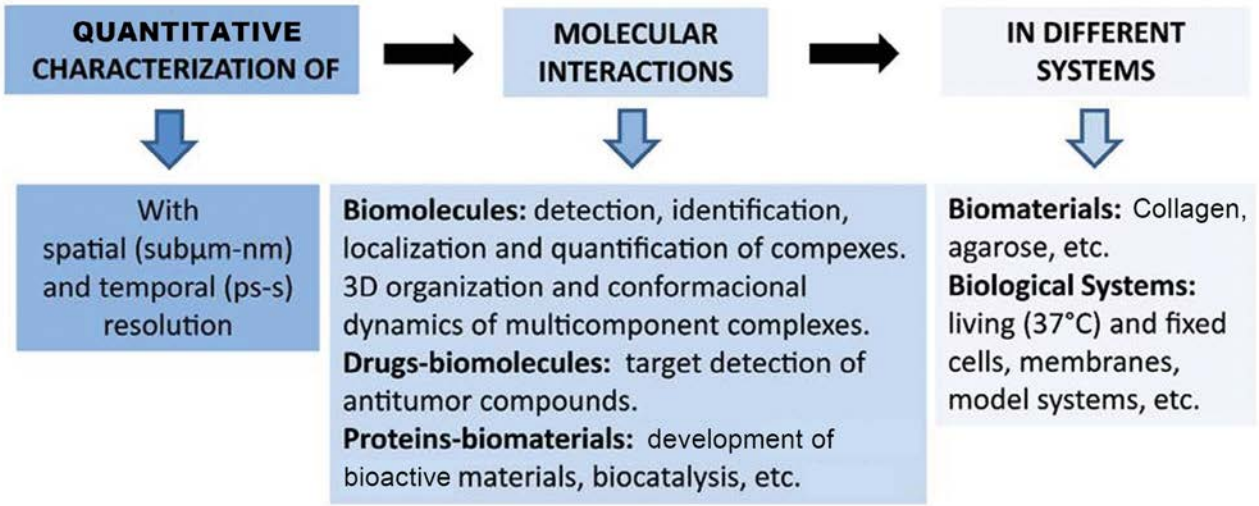
Miguel Ángel Sacristán Fernández (Titulado Superior de Actividades Técnicas y Profesionales, from 23/05/2016 to 22/08/2016)

Summary

The overall objective of the Group is to understand how biological systems work under physiological conditions. With this aim we develop and implement both theoretical and experimental methods based on ps-resolved fluorescence spectroscopy and two-photon laser excitation microscopy, to provide the required temporal (ps-s) and spatial (subμm-nm) resolution *in vitro*, in living cells and tissues.

We have developed theoretical and experimental protocols for simultaneous acquisition of fluorescence intensity, lifetimes (FLIM, FLIM-phasors), energy transfer (FLIM-FRET, FLIM-FRET-phasors) and polarization fluorescence (TRAIM and homo-FRET) XY, XZ and YZ sections, in different regions of the emission spectrum, with multi-photonic and 1 photon excitation. Now, we are setting up in the microspectrometer the second harmonic generation (SHG) imaging. These are non-invasive quantitative methods that discriminate and characterize supramolecular structures in different subcellular locations, in very heterogeneous media, with single molecule resolution, in time scales ranging from picoseconds to second-hours.

Strategic Aims



Results

Dynamics and stability of Immobilized Proteins on agarose beads

We have designed a methodology to correlate the dynamic aspects and function of immobilized proteins on agarose beads. Rotational mobility of immobilized proteins was quantified in any location of the agarose support, at different depths (0-100 microns; ~500-600 nm spatial resolution), from fluorescence anisotropy optical sections of the agarose beads.

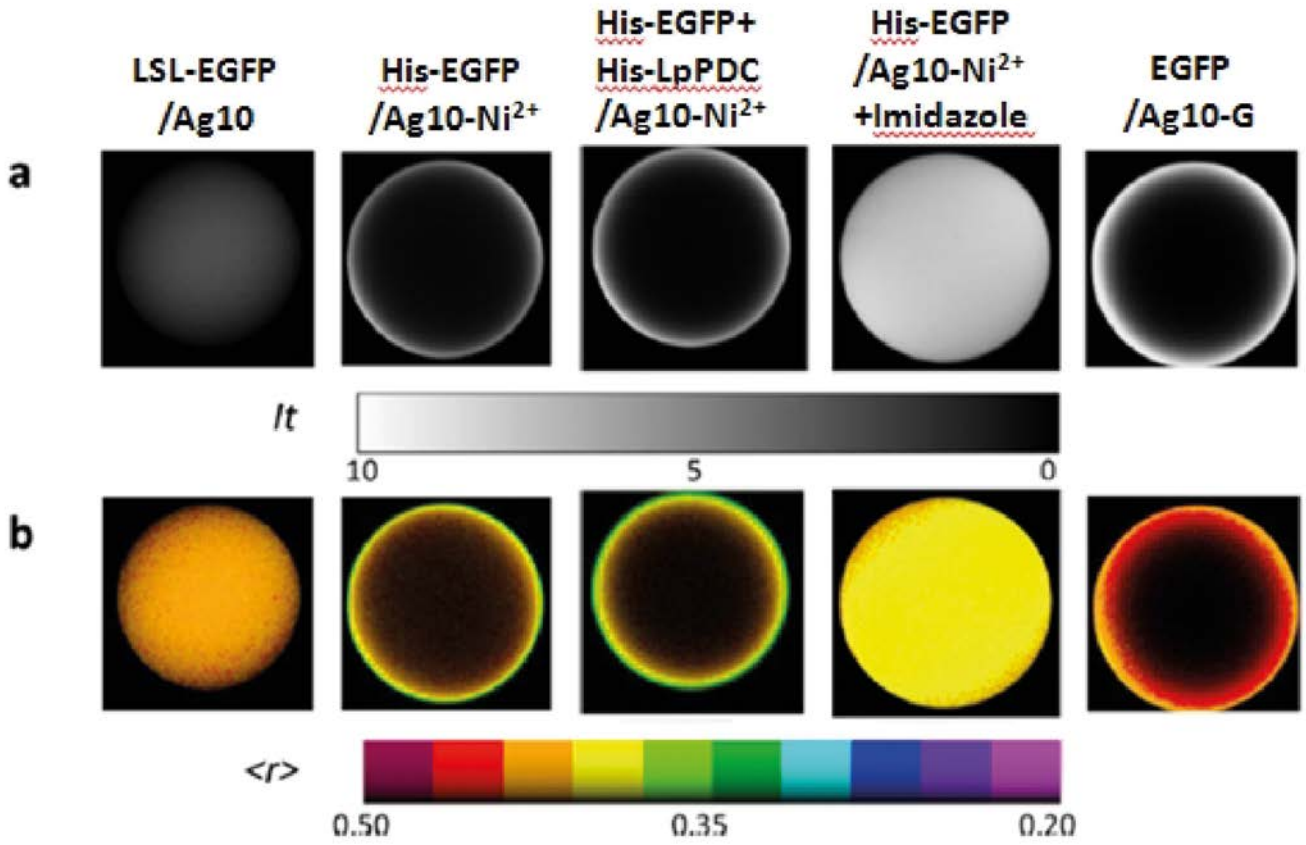


Figure 1. Fluorescence intensity (a) and fluorescence anisotropy (b) XY sections (80 × 80 μm) at the equator of representative microbeads, immobilizing different EGFP variants, through different chemistries. Adapted from Orrego et al. 2016.

Protein fluorescence anisotropy imaging informs about the degree of constraints to the global free rotation of the immobilized proteins onto a solid surface. We have defined a general protein mobility scale, independent of instrumental settings and fluorescent probes, quantified by the mobility factor, which is very sensitive to changes in the chemistry of immobilization used, the size and type of spacers, as well as changes in the hydrogel porous microstructure associated with immobilization chemistry itself (Orrego et al. 2016). This platform links conventional functional studies with advanced molecular characterization of immobilized proteins what may represent a guideline in the design of better immobilization strategies to achieve more stable heterogeneous biocatalysts with interest for the biodiesel and food industries.

Antitumor Irvalec® interactions in living cells. R & D Contract (CSIC-PharmaMar)

Plasma membrane integrity is essential for cell life. Any major break on it immediately induces the death of the affected cell. Different molecules were described as disrupting this cell structure and thus showing antitumor activity. We have previously described that elisidepsin (Irvalec®, PM02734), a synthetic cyclodepsipeptide closely related to the natural product Kahalalide F, inserts and self-organizes in the plasma membrane of tumor cells, inducing a rapid loss of membrane integrity, cell permeabilization and necrotic death ("Irvalec inserts into the plasma membrane causing rapid loss of integrity and necrotic cell death in tumor cells" (Molina-Guijarro et al. 2011).

Using FLIM-FRET fluorescence lifetime energy transfer imaging methods with FLIM-phasor analysis, we have studied the interaction of the antitumor compound Irvalec® with components of the plasma membrane of HCT-116 cells, wt and Irvalec® resistant, using the fluorescent Irvalec® analogs: Irv-OG488 (Oregon Green 488), as FRET donor, and Irv-A555 (Alexa 555) as FRET acceptor.

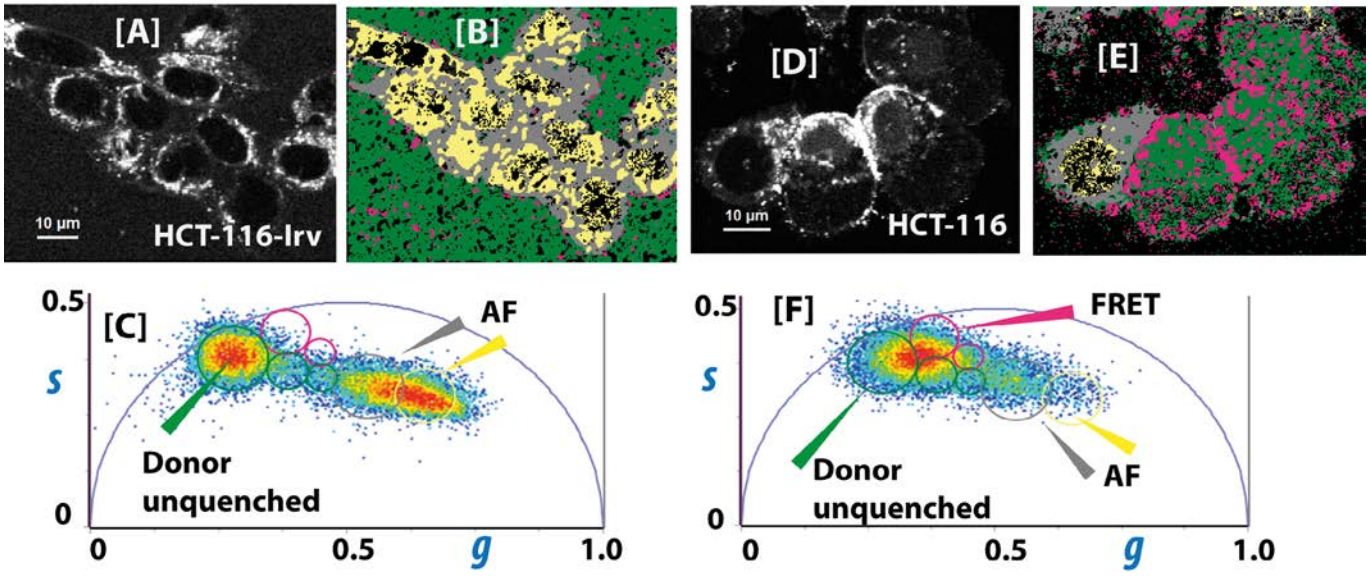


Figure 2. Interaction of Irvalec® with the plasma membrane of Irvalec® sensitive HCT-116 wt and resistant HCT-116-Irv cells. Fluorescence intensity representative images (**A, D**), FLIM-phasor (**B, E**) and phasor plot (**C**, **F**). Adapted from Molina-Guijarro et al. 2015.

Figure 2 shows the FLIM-FRET phasor analysis of Irvalec® interaction with the plasma membrane of Irvalec® sensitive HCT-116 wt and resistant HCT-116-Irv cells. This method provides a simple and quantitative graphical way of localization and quantification of the membrane active Irvalec® complexes comparison of the two types (FRET efficiency >0; pink color in the phasor diagram and FLIM-phasor images). It is important to note that we don't detect Irvalec® complexes in the plasma membrane of resistant HCT-116-Irv cells.

The ps-ns time-resolved fluorescence decay determined for each pixel of the image is represented as a point in the phasor plot. We label with color circular cursors the cluster of phasors corresponding to autofluorescence AF (gray and yellow cursors) and to the unquenched donor FRET (zero FRET efficiency; green cursor). In the presence of FRET, the corresponding phasor of the donor will appear on a circular trajectory towards the right with respect to the line linking the FRET donor and the AF species (pink cursor). In absence of FRET, the increase in the contribution of the AF signal (in this work, with a shorter lifetime) in any pixel, may also decrease in the average donor lifetime, but in this case the corresponding phasor will be located along the line FRET donor-AF. In resistant HCT-116-Irv cells (A-C) we don't observe Irvalec® inside the cell, and also we don't detect cluster of phasors outside the FRET donor-AF line, indicating that there is not self-assembly of Irvalec® at the plasma membrane of resistant cells.

Translation elongation factor eEF1A2 is a novel anticancer target for plitidepsin. R & D Contract (CSIC-PharmaMar)

eEF1A2 is one of the isoforms of the alpha subunit of the eukaryotic elongation factor 1. It is overexpressed in human tumors and it is endowed with oncogenic properties, favoring tumor cell proliferation while inhibiting apoptosis.

We have studied the interaction of plitidepsin, an antitumor agent of marine origin that has successfully completed a phase-III clinical trial for multiple myeloma, with eEF1A2 in living plitidepsin sensitive HeLa wt and resistant HeLa-APL-R cells, transfected with eEF1A2-GFP, using the coumarinated fluorescent analog plitidepsin-DMAC.

Figure 3 shows FLIM-FRET phasor experiments using plitidepsin-DMAC as FRET donor and eEF1A2-GFP as FRET acceptor. At time 0, each image contains a mix of expressing (green) and non-expressing eEF1A2-GFP (autofluorescence AF, gray) HeLa and HeLa-APL-R cells. After 30 minutes of treatment with 10 nM plitidepsin-DMAC, the images showed the formation of FRET plitidepsin-eEF1A2 complexes (pink or garnet color), both in HeLa and HeLa-APL-R cells expressing eEF1A2-GFP. The cyan/blue color in HeLa and HeLa-APL-R not expressing eEF1A2-GFP cells corresponds to the interaction of plitidesin-DMAC with wt cells (FRET donor only signal, Dn, in absence of FRET).

Plitidepsin localizes in tumor cells sufficiently close to eEF1A2 (d<50 Å) as to suggest the formation of drug-protein complexes in living cells. Our results strongly suggest that plitidepsin exerts its antitumor activity by targeting eEF1A2.

Other collaborations

Within our interest in plasma membrane and membrane model systems, we have established a new collaboration with the groups of Dr. F. Monroy and I. López Montero, experts in soft matter physics, hydrodynamics and cell mechanics. The publication "Thermomechanical transitions of egg ceramides monolayers" (Langmuir) has been a result of this collaboration: it is a study of the biophysical properties of the ceramides, lipids from the sphingolipid family.

Sphingolipids have attracted great interest in the last years because they are involved in important biological supramolecular structures as lipid domains. Recently, sphingolipids have been identified as active lipids, by their involvement in processes such as apoptosis. Because of their high melting transition temperature (~90°C), ceramides are considered to form solid-type layers and are able to modify the physical state of the cell membrane, including membrane fluidity and permeability, lateral domain segregation, and membrane stiffness.

Another result from this collaboration has been the coordinated project "LP-PHYS: Understanding active matter actuated by biological living polymers: from the microscopic stochasticity through hydrodynamics to macroscopic mechanics".

The objective of this project is to understand the physical principles that underlie the dynamics of hybrid material realizations of active soft matter built from a passive matrix of synthetic hydrogel that is made active with reversibly-polymerizing biological filaments (living polymers), the cytoskeleton. All cells, including bacteria, have a cytoskeleton that is a highly dynamic network of filamentous proteins that actively link all components of the cell. It is composed by passive

and active elements, living polymers (LPs), which are reversibly-polymerizing protein filaments fuelled by ATP (and GTP), and mechanoenzymes (motor proteins). The cytoskeleton can be seen as an active material that dynamically allows the cell to perform mechanical tasks at different functional scales.

The cytoskeleton differs from common polymer matter in the complexity of composition and in the fact that it is not at thermodynamic equilibrium, constituting a non-equilibrium composite soft material.

We are developing methodologies to characterize the physical behavior of the designed active hybrid materials, out of the equilibrium, internally activated by living polimers.

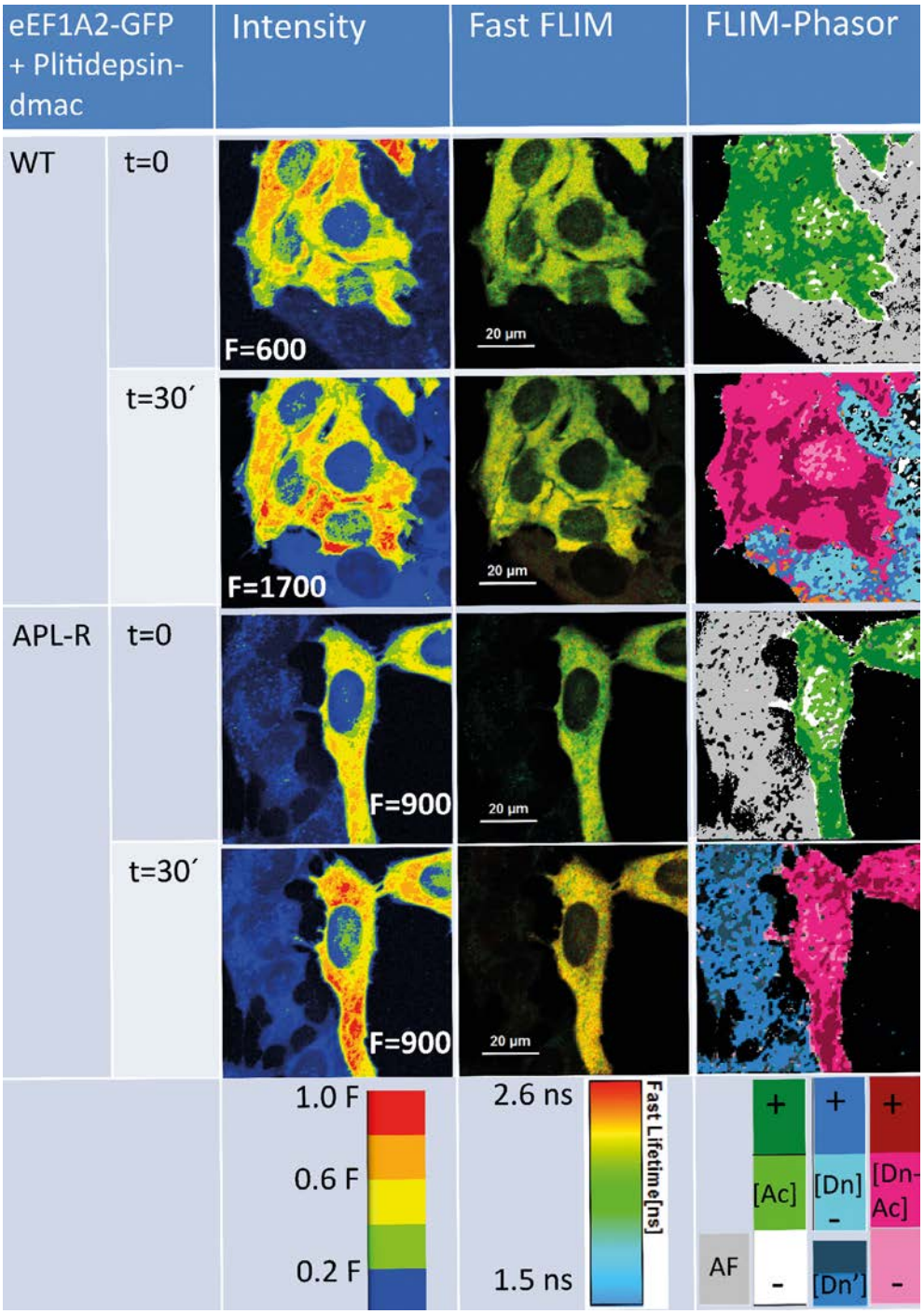


Figure 3. Cellular localization of plitidepsin-eEF1A2 complexes in living HeLa and HeLa-APL-R cells transfected with eEF1A2-GFP at time zero (t = 0) and after 30 minutes of treatment with 10 nM plitidepsin-DMAC. Adapted from Losada et al. 2016.

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COMPETITIVE FUNDING

National Grants: individual

Ministerio de Ciencia e Innovación (MICINN)

Principal Investigator	Title	Reference
Acuña, A.U. (Marcos, S.; I.P.)	Implante de lentes intraoculares mediante técnicas de "photobonding"	FIS2013-49544-EXPLORA

National Grants: coordinated

Ministerio de Economía, Industria y Competitividad (MINEICO)

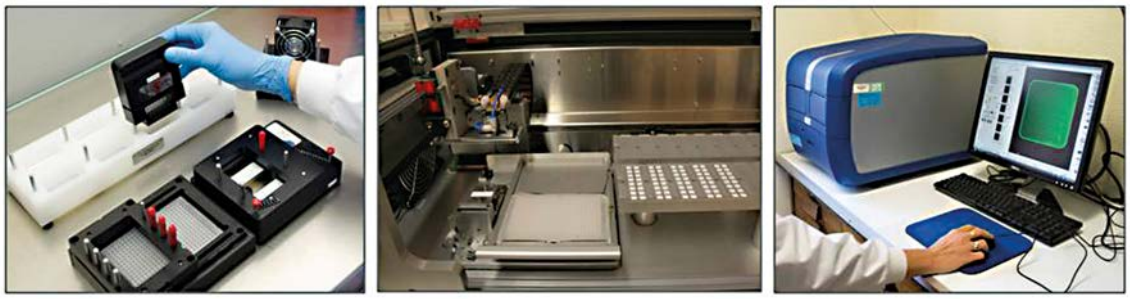
Principal Investigator	Title	Reference
Vélez, M. / Lillo, M.P.	Hidrogeles activos actuados por polímeros biológicos vivos: mecánica y dinámica de las proteínas fuera y dentro del hidrogel	FIS2015-70339-C2-2-R

Contracts and Agreements with Companies

Contrato I+D CSIC-PharmaMar S.A.

Principal Investigator	Title	Reference
Lillo, M.P.	Estudio de las interacciones de Aplidina e Irvalec con la membrana celular	

Protein Structure and Thermodynamics Group



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Mª Dolores Solís Sánchez (Associate Professor; Research ID: E-5992-2015; ORCID: 0000-0002-8148-1875)

Non-tenured scientists

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Noemí Bustamante Spuch (Post-doctoral)

Mª Asunción Campanero Rhodes (Post-doctoral)

Manuel Iglesias Bexiga (Post-doctoral)

Palma Rico Lastres
(Predoctoral, until 06/05/15) / (Post-doctoral, 07/ 01/2016-02/05/2016)

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Ioanna Kalograiaki
(Marie Curie fellowship, until 31/07/2015)

Lara López Merino
(EU projet contract, 16/02/2015- 15/02/2016)

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Mª Victoria López Moyano (Technician)

Noelia Hernández Ortiz
(TS, since 1/06/2016)

Begoña Morales Juanós
(TSE, until 31/10/2016)

Summary

Knowledge of the structure and energetics of proteins in solution provides information on the nature of forces governing structural stability or ligand recognition, among other properties. This information is particularly relevant for proteins of biomedical or technological interest, since it facilitates a rational design of ligands (drugs, vaccines, etc.), or the stabilization of proteins themselves. In our group we have recently studied, among other systems, different lectins, murein hydrolases with bactericidal capacity and other proteins of biomedical interest. In addition, we investigate the recognition of carbohydrates and other compounds by these and other proteins, with the final aim of elucidating their role in numerous processes of biomedical relevance, as host–pathogen interactions or virulence, and developing new diagnostic and/or therapeutic strategies.

Strategic Aims

- Bacteria glycophenotyping and identification of receptors involved in carbohydrate-mediated bacteria–host interactions.
- Characterization of the structural organization, stability and specificity in ligand recognition of different lectins and related proteins.
- Development, characterization and evaluation of new anti-infectives against *Streptococcus pneumoniae* and other relevant pathogens.
- Thermodynamic characterization of biomolecules and their complexes.

Results

Bacteria glycophenotyping

Bacterial surfaces are coated with carbohydrate-rich structures that usually correlate with virulence and serve to typify strains. Using a new application of the microarray technology, previously developed in our group, we have investigated the glycophenotype of different bacteria involved in infections of the respiratory tract. In collaboration with J. Garmendia (IdAB-CSIC-UPNA-Gobierno de Navarra), we have characterized 6 clinical isolates of nontypeable *Haemophilus influenzae* (NTHi), from asymptomatic carriers and otitis media and EPOC patients, along with different NTHi375 mutant strains expressing a lipooligosaccharide (LOS) truncated at selected positions or lacking specific proteins of the outer membrane, by examining the binding to microarrays of these strains of a collection of lectins with different binding specificities. In addition, in collaboration with T. Aastrup (Attana AB) we have developed a new application of the quartz crystal microbalance technology that has provided information on the kinetic parameters and affinity of the binding of three of these lectins to NTHi375 and its Δ*lgtF*Δ*lpsA* mutant, which lacks the LOS extensions at heptoses I and III. The role of the LOS as possible ligand of *Viscum album* and *Ricinus communis* agglutinins, two lectins frequently used for glycophenotyping, has been investigated in binding assays to LOS microarrays and by NMR-STD experiments, in collaboration with F.J. Cañada (CIB-CSIC).

We have also started the study of the glycosylation patterns of a collection of 24 clinical isolates of hypermucoviscous *Klebsiella pneumoniae* bearing or not the mucoviscosity associated genes *rmp*A and/or *mag*A, in collaboration with C. Ardanuy (Hospital Universitario Bellvitge). The results have revealed strain- and lectin-specific binding patterns, with weak or nonexistent recognition of *rmp*A+/*mag*A+ strains by most of the lectins tested, evidencing important changes associated to this genotype in the availability of carbohydrate structures on the bacterial surface.

Finally, in collaboration with E. García (CIB-CSIC) and J. Yuste (ISCIII), we have investigated the glycophenotype of *Streptococcus pneumoniae* (D39 strain, its P144 mutant lacking β-galactosidase A, TIGR4 and mutants of this strain lacking the surface proteins Diia or/ and PspA, and the non-capsulated strain R6,) and related bacteria *(S. mitis, S. mutans, S. oralis, S. pseudoneumoniae, S. pyogenes, and Staphylococcus aureus*). An interesting result is the clear preference of galactose-specific lectins for the non-capsulated strain over those capsulated, behaviour not observed for other lectins with different binding specificities. In contrast, the agglutinin from *Lycopersicon esculentum*, specific for N-acetylglucosamine, binds D39 with stronger intensity than the other strains.

Bacteria recognition by lectins of the innate immune system

The accessibility and density of glycans on bacterial surfaces make them key targets for recognition by host receptors, including endogenous lectins. NTHi glycophenotyping evidenced the availability of galactose, sialic acid and mannose/glucose residues on the bacterial surface that could serve as ligands for lectins of the innate immune system with the appropriate specificity. We have analyzed the binding of galectin-8, Siglec-14 and SP-D, to microarrays of different NTHi clinical isolates. The results have revealed recognition by the three lectins, providing the first experimental evidence of SP-D binding to NTHi.

We have also investigated the recognition of *S. pneumoniae* and related species by different galectins, in comparison with the non-lectin receptor TLR4, the results pointing to specific strain and lectin/receptor binding patterns. As observed for other galactose-specific lectins, there is a clear preference of some galectins for the noncapsulated (R6) strain over capsulated D39, while TLR4 binding patterns resemble those of other lectins with different specificity, also showing binding to *S. mitis, S. pseudopneumoniae* and *S. oralis*.

Study of bacterial adhesins

Binding of bacteria to host cells is often mediated by bacterial adhesins that recognize different structures, frequently carbohydrates, in the surface of those cells. Using binding assays to bacteria microarrays, we have detected the presence in *S. pneumoniae* D39 and P144, R6, and TIGR4, and in *S. aureus* of receptors for asialofetuin, lactoferrin, mucin and asialomucin. The influence on the receptor functionality of the method used for bacteria fixation/inactivation has also been examined. The binding of live and fixed noncapsulated *S. pneumoniae* to lactoferrin and asialofetuin has been confirmed by confocal microscopy.

In addition, we have developed novel designer microarrays for the study of adhesins in live bacteria, using as a model *E. coli* UTI89, whose adhesin FimH is the bacterial adhesin best characterized to date. We have proved the usefulness of these microarrays for assesing FimH functionality and evaluating different mannofullerenes, synthetized by S. Vincent group (Universidad de Namur), as inhibitors of bacterial adhesion. The results have been validated in a similar study carried out with the plant lectin concanavalin A, in parallel to the analysis of the concanavalin A-mannofullerene interaction by SPR and ITC.

Study of the structure-function relationships of galectins

Pursuing the systematic characterization of the complete set of galectins expressed in chicken, as important model organism, we have characterized the two CG-8 variants, which differ in the length of the linker connecting the two carbohydrate-recognition domains (CRDs), and the effects induced on these proteins by the binding of lactose and 3'-sialil-lactose. The binding of these two sugars to the isolated N-terminal CRD of CG-8 has also been examined, unveiling a higher affinity for the sialil derivative, and we have also initiated the study of the C-terminal CRD. Finally, we have characterized two chicken galectin-related proteins, GRIFIN and GRP, the results revealing important differences in quaternary structure, thermal stability, and binding ability of both proteins.

We have also approached the study of galectins from a different model organism, the lizard *Anolis carolinensis*, whose genome has been completely sequenced and unveils the presence of genes coding for 7 possible members of this lectin family. A galectin homologous to mammalian galectin-1, designated *Acar*G-1, has been recombinantly produced, and its structural organization, stability and ligand binding ability has been studied. The results demonstrate that this protein exhibits predominantly β structure, typical of galectins. Under reducing conditions *Acar*G-1 forms non-covalent dimers, as it is also the case for human galectin-1 and its chicken orthologues. However, non-reducing conditions induce dimer dissociation and affect the carbohydrate-binding properties, as observed in binding assays to glycoprotein microarrays. This behaviour can be explained by the formation of an intramolecular disulphide bridge that alters the dimer interface and the architecture of the binding site. This hypothesis is supported by molecular dynamics simulations using models built for reduced and oxidized *Acar*G-1, in collaboration with S. Martín-Santamaría (CIB-CSIC). Finally, two variants of a protein homologous to galectin-7 have been expressed. Their behaviour in affinity chromatography and microarray binding assays show that these proteins do not have carbohydrate-binding activity, indicating that they are galectin-related proteins and reducing to 5 the number of galectins potentially expressed in this organism.

Design, characterization and evaluation of new lytic enzymes built by domain shuffling or acquisition of additional domains

Aiming to develop new lysins with different range of susceptible bacteria, we have built chimeric lysins by domain shuffling or adding new domains to previously characterized lysins. PL3, comprising the choline-binding domain of LytA and the catalytic domain of Pal (pneumococcal Dp-1 phage endolysin), was active against choline-containing bacteria. Its lethality largely surpassed those of the parental enzymes (LytA and Pal). A single dose of 5 μg/ml fully sterilizes in 60 minutes the cultures of all pneumococcal strains tested (including multiresistant ones), as well as those of related opportunistic pathogens (*Streptococcus oralis, S. mitis* or *Streptococcus pseudoneumoniae* among others). Indeed, PL3 is the first lytic enzyme efficient as bacteriolytic agent against *S. oralis* so far described, and the best one with amidase activity against *S. pneumoniae*. Its capacity to protect against infections caused by *S. pneumoniae* was confirmed using zebra fish embryos as animal model of infection. Importantly, PL3 keeps 95% enzymatic activity after 4 weeks at 37°C and can be lyophilized without losing activity, demonstrating a remarkable robustness. Such stability, together with a prominent efficacy against a narrow spectrum of human pathogens, confers to PL3 the characteristic to be an effective therapeutic.

In addition, several chimeric lysins were generated using the scaffold of the choline-dependent pneumococcal CbpD murein hydrolase or the PlSs2 endolysin from a *Streptococcus suis* (strain 89/1591) pro-phage by substituting the catalytic domain by other potentially more active, using different SH3b cell wall-binding domains, or deleting the choline-binding repeats of CbpD. These lysins can kill a restricted range of pathogenic bacteria and do not require the presence of choline in the cell wall. Their structural and functional characterization is still

ongoing. All these activities were carried out in collaboration with P. Garcia (CIB-CSIC).

Overall, our studies have shown that, for Gram-positive, the narrow range of susceptible bacteria to the lethal action of a given lysin is modulated by other factors than the nature of the target recognized by the cell wall-binding domain of the lysin and its affinity of binding. When acting from without, their high specificity can be also modulated by *i*) the precise composition of the bacterial envelope (including the polysaccharide capsule), *ii*) lysin capacity to interact with the bacterial cell wall through regions that are distant from the catalytic site and from the specific binding sites used for its attachment to the cell wall, and *iii*) creation of multivalent interactions with the cell wall.

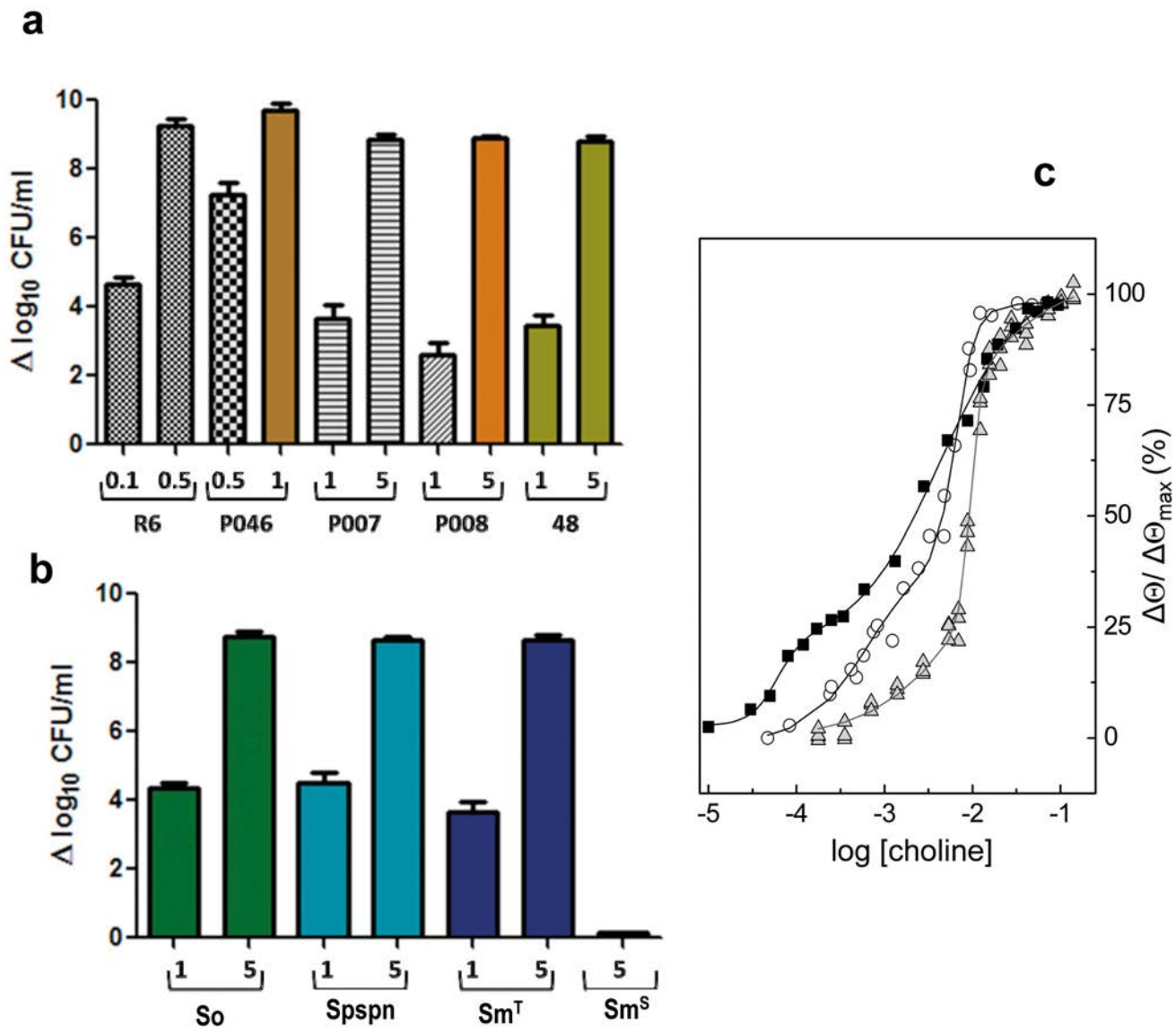

Figure 1. (a) Bactericidal activity of PL3 against the pneumococcal strains indicated on the X-axis: Decrease in the number of viable cells (CFU/ml) upon exposure to PL3 action for 60 min at indicated concentrations (μg/ml). (b) Decrease in the number of viable cells upon treatment of S. oralis (So), S. pseudopneumoniae (Spspn), S. mitisT (SmT) with PL3 for 60 min. (c) Comparison of choline titration curves obtained by circular dichorism fo PL3 (squares), LytA (circles) and Pal (triangles).

Screening and validation of pneumococcal LytA autolysin inhibitors

In the search of compounds that might help to decrease the incidence of pneumococcal diseases by inhibiting virulence factors, we have screened the Prestwick and Hitfinder libraries using the major pneumococcal autolysin LytA as target. A family of potential ligands of LytA was thus identified and their inhibitory activities established, in collaboration with J. Sancho (Universidad de Zaragoza-BIFI) and P. García (CIB-CSIC). Using different biophysical techniques we have shown that the inhibitors bind to the choline-binding domain, inducing the aggregation of LytA. Interestingly, they inhibited also *in vitro* pneumococcal growth, altering the bacterial morphology and reducing cell viability, a very different response than that observed upon addition of an excess of choline to the cultures. Figure 2 illustrates the results obtained for compound LH1. These results evidence that they have more than one target in the bacterium. The mechanism/s of action is under investigation.

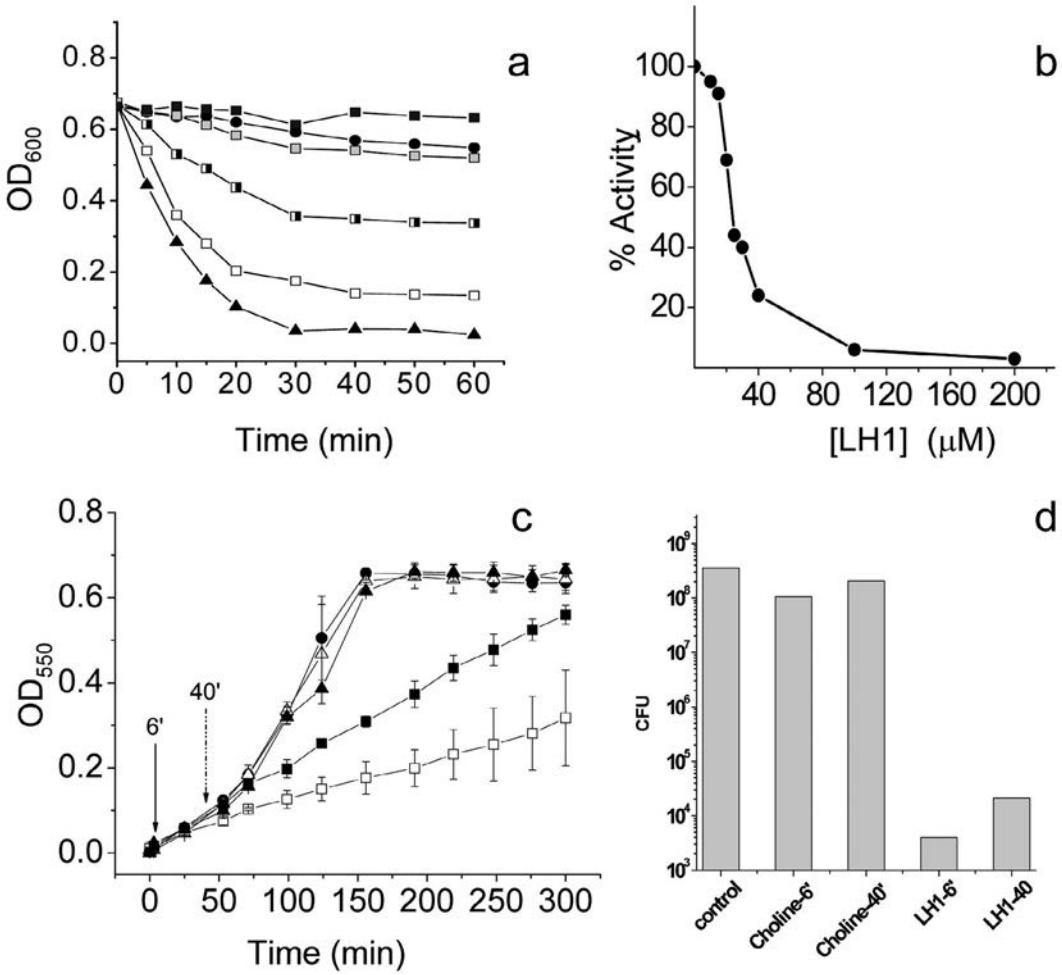

Figure 2. Effect of LH1 on LytA activity and S. pneumoniae growth. (a) Inhibition of LytA bacteriolytic activity. Decay of a bacterial suspension of S. pneumonaie (strain P046) after adding LytA (5 μg/ml) in the absence (black triangles) and in the presence of 100 μM (□), 200 μM (black and white squares), 300 μM (grey squares) and 400 μM (black squares) LH1. Black circles correspond to the control without LytA. **(b)** Inhibition of LytA activity on purified cell walls. Data correspond to the percentage of activity with respect to the value without LH1. **(c)** Pneumococcal growth kinetics (average of five experiments); no compound added (black circles; control); 50 mM choline added at the lag (4 min; white triangles) or the early exponential (40 min; black triangles) phases; 220 μM LH1 added at 4 min (white squares) or 40 min (black squares). **(d)** Cell viability at 5 h after compounds were added at the lag (6 min) or the early exponential (40 min) phases.

Other systems of interest

The group activities also included collaborations with different research groups aimed to the structural and / or thermodynamic characterization of biomolecules and their complexes. We can point out the thermodynamic characterization of the binding to concanavalin A of mannose derivatives used to generate glyconanoparticles, in collaboration with O. Ramström (KTH); the characterization of phospho-(tyrosine)-mimetic calmodulin mutants, in collaboration with A. Villalobo (IIBM-CSIC); the binding of the CAR4 protein, involved in plant defense mechanisms against stress, to Ca^{2+}, in collaboration with A. Albert; or the characterization of carbohydrates binding to the xylan-binding CBM22-1-CBM22-2 domains, in collaboration with J. Sanz (IQFR-CSIC).

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COMPETITIVE FUNDING

National Grants: individual

MINECO

Principal Investigator	Title	Reference
Margarita Menéndez	Exploring exogenous and endogenous factors as tools for the control of infectious and immune processes	BFU2012-36825
Margarita Menéndez and Dolores Solís	Search and development of new preventive and therapeutic approaches for fighting infections caused by *Streptococcus pneumoniae*	BFU2015-70052-R

National Grants: coordinated

CAM

Principal Investigator	Title	Reference
Federico Gago	Bioinformatics integrative platform for structure E-based drug discovery (BIPEDD2)	S2010/BMD-2457

International Grants: coordinated

UE

Principal Investigator	Title	Reference
Mihail Barboiu	Dynamic interactive nanosystems (DYNANO)	FP7-ITN-GA:289003
Dolores Solís	The Sugar Code: from (bio)chemical concept to clinics (GLYCOPHARM)	FP7-ITN-GA:317297

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Israel Serrano (FPI, desde 01/12/2015)

Summary

The chief objective of our group is to contribute to the understanding of molecular recognition events involving nucleic acids. These events are implicated in a myriad of processes of interest for Biology, Nanoscience and Macromolecular Chemistry. Understanding these processes has a direct impact on the development of new drugs.

One key approach to comprehend these molecular recognition processes is to know the 3D structure of nucleic acids (DNA, RNA and their derivatives). To this aim, our group is dedicated to the determination of oligonucleotide structures either alone or in complex with proteins and other ligands. We use a diverse set of spectroscopic techniques, principally Nuclear Magnetic Resonance (NMR) Spectroscopy.

Strategic Aims

- Structural studies of nucleic acid analogs with particular attention to non-canonical structures of relevance in Biology and Nanoscience.
- Structural studies of nucleic acids implicated in human diseases and their complexes with ligands.

Results

Molecular recognition: Complexes and conjugates between small ligands and nucleic acids

We have continued our studies on small ligand–nucleic acids interactions. On the one hand, we have completed a work on the interaction between ametrantone derivatives with mRNA stem-loop hairpins involved in splicing (Artigas et al., 2015). In addition, we have continued our studies on the effect of aromatic conjugates, in this case with interesting fluorescent properties, on DNA sequences able to form G-quadruplexes (Doluca et al, 2015). We have also made a notable progress on our research line on DNA-carbohydrate conjugates. In collaboration with Dr. Juan Carlos Morales, we have determined the solution structure of DNA monosaccharide conjugates able to form double helices with nucleobase-carbohydrate interactions that emulate natural base-pairs (Vengut-Clement et al, 2016).

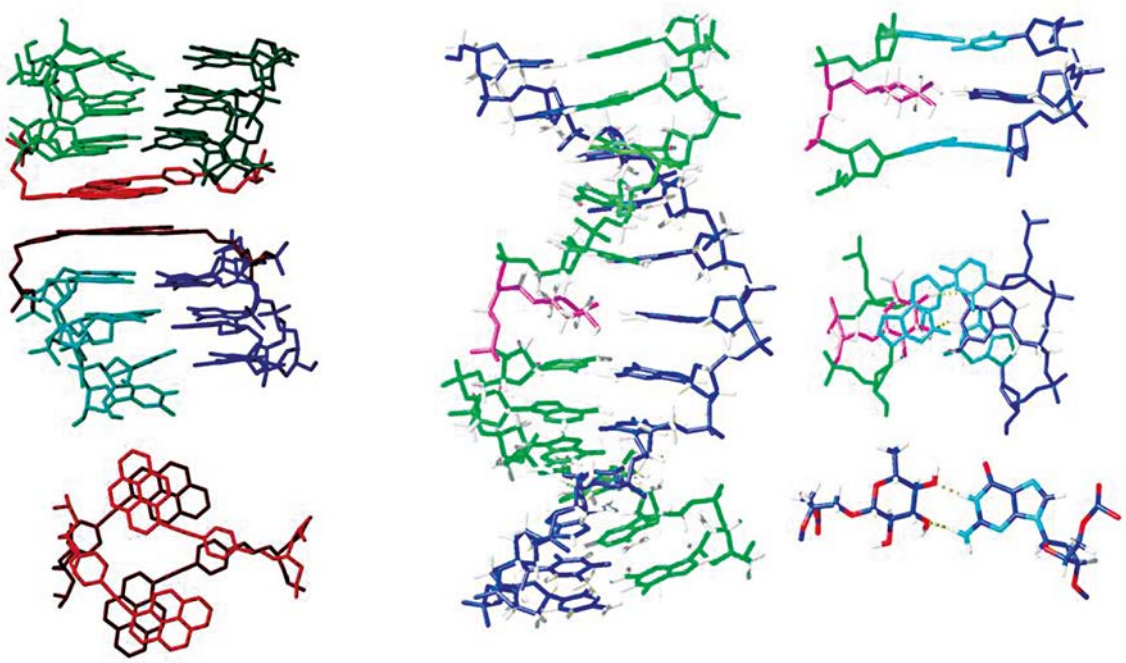

Figure 1: Left) Dimerization of two quadruplexes induced by the conjugation of the fluorescent conjugate TINA. Right) Duplex formed by oligonucleotides conjugated to carbohydrates and detail of the formation of a non-canonical DNA-monosaccharide base-pair.

New methodologies

From a methodological point of view, we have carried out a significant effort, in collaboration with an international consortium of theoretical chemistry groups led by Prof. Modesto Orozco, to improve the force fields used in molecular dynamics software packages. NMR can supply very useful experimental data to validate the results of this kind of computer calculations. The first results have been recently published in Nature Methods (Ivani et al, 2016). In addition, we have continued our long-standing collaboration with Dr. Juan Luis Asensio on the development of new strategies for identification and optimization of new ligands able to interact with RNA molecules more efficiently.

Non-canonical DNA structural studies

Within our research line on non-canonical DNA structures, in this biennial period we want to highlight our structural studies on i-motifs. Such structures result from the association of four cytosine-rich DNA strands, and consist of two intercalated parallel duplexes. The structure is stabilized by hemiprotonated C:C+ base-pairs. We have determined the solution structures of the main variants of the human A-box sequence, and we have found that *in vitro* this kind of structures occurs in centromeric sequences of evolutionarily very distant species, like the human being (Garavís, et al 2015a) or fruit fly (Garavís et al, 2015b). The presence of these structures in such distant organisms suggests that they may be involved in the structural organization of the centromere. If this were the case, the centromeric DNA could have been selected during evolution not for its primary sequence, but for its capability to form this non-canonical structure, the "i-motif".

I-motif like DNA structures may occur in contexts different than the centromere, such as telomeric and promoter regions. Moreover, these structures are very interesting for applications in nanotechnology. For this reason, in the coming years we will continue studying their structure, stability and folding.

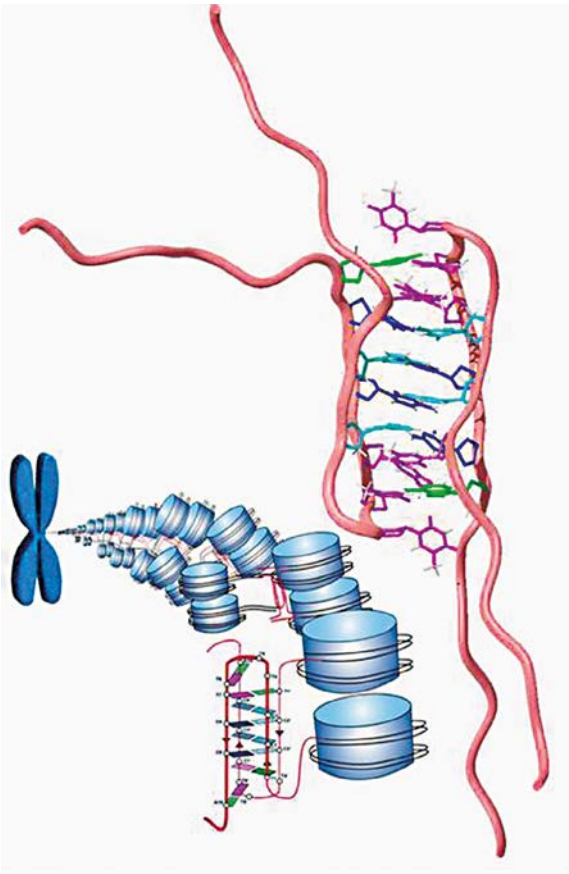

Figure 2: Structure of a dimeric i-motif formed by the A-box sequence in the human centromere.

Nucleic acids with chemical modifications

The effect of chemical modifications in i-motif structures has been a topic of particular interest for us during these years. With the aim of stabilize these structures in physiological conditions, we have studied several chemical modifications. First, we focused on the effect of introducing nucleotidic derivatives with acyclic backbones instead of deoxyriboses. We found that this modification destabilizes the structure.

In general, modifications in the sugar-phosphate backbone tend to provoke a destabilizing effect in i-motifs. However, we have observed that fluorine substitution in the 2' position of the pentose ring provokes the opposite effect. In particular, the incorporation of 2'-fluoroarabino-cytosine provokes a dramatic stabilization in different kind of i-motif structures, allowing their observation in physiological conditions. In collaboration with Prof. Damha group in Montreal, we have studied the structural bases of this stabilization (Abou-Assi, et al 2016).

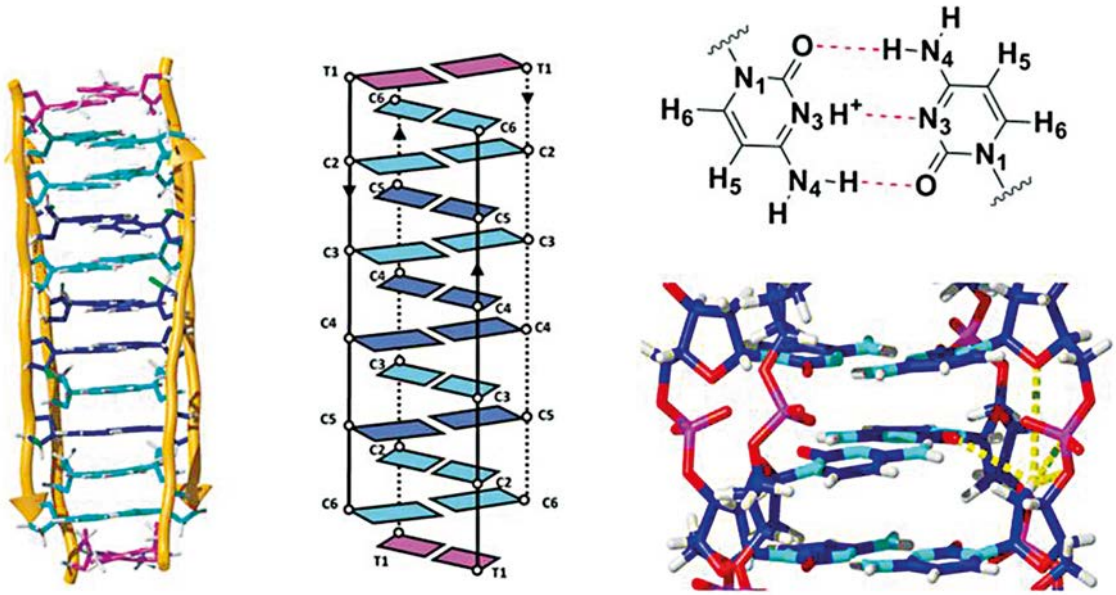

Figure 3: Structure and schematic view of a tetrameric i-motif modified with 2'-fluoroarabino-cytosines (cyan). The structure is stabilized by hemiprotonated C:C+ base pairs as shown in the figure. The fluorine in the 2'- position provokes favorable electrostatic interactions that stabilize the structure (yellow lines).

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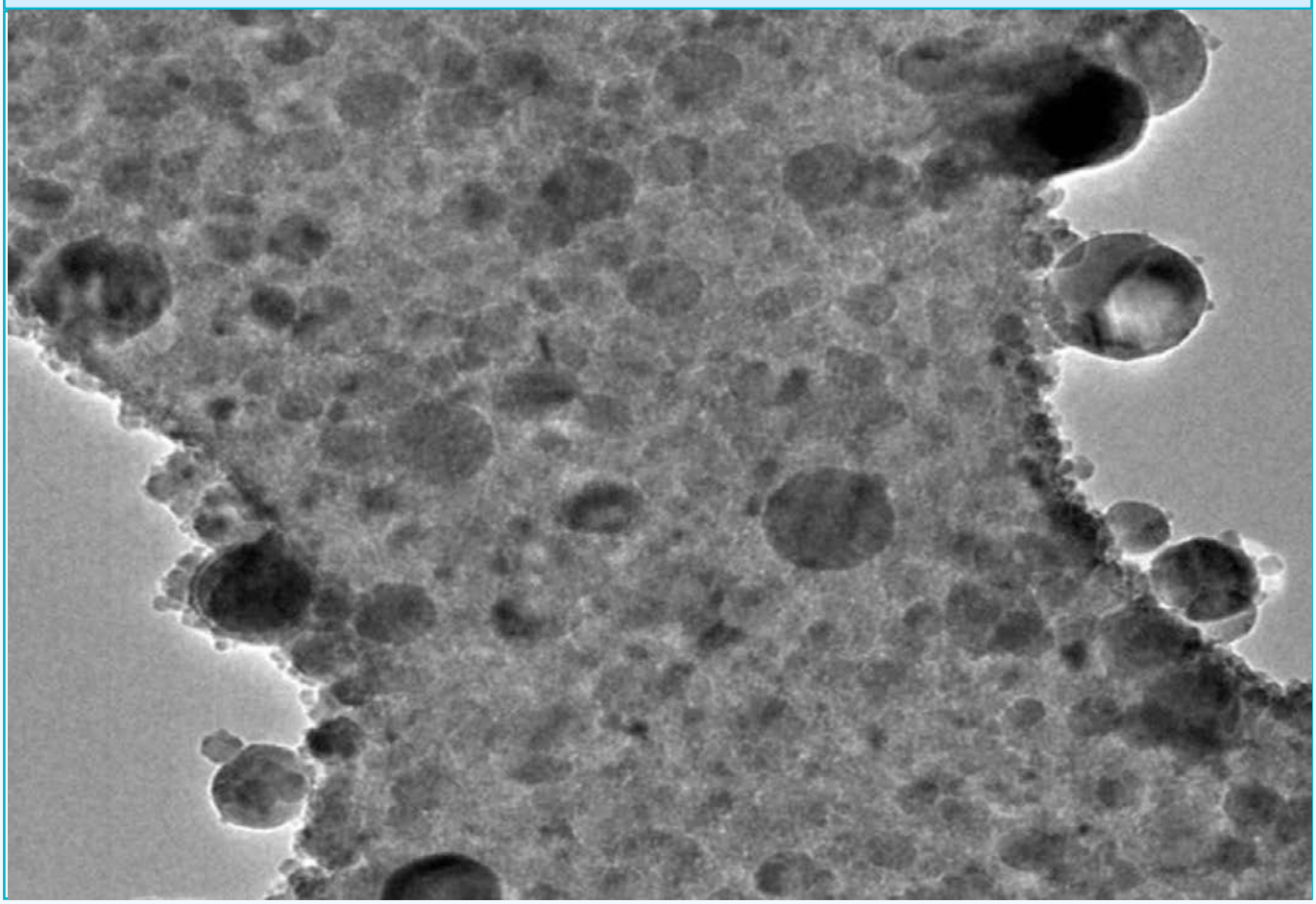
National Grants: individual

Ministerio de Economía y Competitividad

Principal Investigator	Title	Reference
Carlos González Ibáñez	Más allá de la doble hélice de Watson y Crick. Estructuras no-canónicas de ácidos nucleicos y sus posibles aplicaciones en biomedicina	BFU2014-52864-R


CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

Department of Low Dimensional Systems, Surfaces and Condensed Matter



Introduction

The Department of Low Dimensional Systems, Surfaces and Condensed Matter is constituted by four groups that develop their research activity in a multidisciplinar environment that covers physico-chemical aspects of Materials Science and Nanoscience. Research in the period of this Report include studies on micro- and nanofabrication of materials by laser irradiation and ablation, design and development of new photonic systems based on photosensitized and nanostructured materials, the study of the surface region of various materials by microscopy and spectroscopy techniques, including Mössbauer spectroscopy, and the application of statistical mechanics and condensed matter theory tools in conjunction with simulation approaches in order to analyse problems of physico-chemical interest.

The activity of the Groups pursues its practical application in areas of optoelectronics, biophotonics, biomedicine, magnetism, photovoltaic energy, and preservation and conservation of cultural heritage. Some of these applications are being developed in collaborations with industrial partners/ private companies.

In this Department, the scientific exchanges with other groups of CSIC, Universities and other international partners are frequent and provide the right framework for generating new knowledge and for training of young researchers. Sources of funding include the Plan Nacional (MINECO), Comunidad de Madrid and European Union.

In May 2016 we suffered the painful loss of our dear colleague, Dr. Noé García Almarza. At the beginning of 2016, Dr. Margarita Martín Muñoz, Director of our Institute during 2002-2005, went to retirement.

Group Structure

Lasers, Nanostructures and Materials Processing Group

Tenured Staff scientists

Marta Castillejo Striano (Investigador científico), ResearcherID: D-7448-2014, ORCID: http://orcid.org/0000-0002-5870-4380, Scopus ID: 7004342369

Margarita Martín Muñoz (Investigador científico, fecha jubilación 03/02/2016)

Rebeca de Nalda Mínguez (Científico titular) ResearcherID: E-9098-2015, ORCID: http://orcid.org/0000-0002-9720-6106.

Esther Rebollar González (Ramón y Cajal) http://www.researcherid.com/rid/ N-4065-2014, ORCID: http://orcid.org/0000-0002-1144-7102, SCOPUS ID: 15021220700, Researchgate: https://www.researchgate.net/profile/Esther_Rebollar

Non-tenured scientists

Esther Carrasco Burgos (Contrato Proyecto de Investigación, 01/11/2015 - 16/01/2017)

Margarita Hernández González (Contrato Proyecto de Investigación, 01/05/2016 - 31/12/2016)

Ignacio López Quintás (Contrato Proyecto de Investigación, 01/07/2016-01/01/2017)

Mohamed Oujja Ayoubi (Contrato Laboral Indefinido no fijo)

Mikel Sanz Monasterio (Contratos Proyectos de Investigación, 01/11/2015 - 31/12/2016), Scopus ID: 13004046000

Doctoral students

Ignacio López Quintás (Beca FPI, until 31/08/2015)

Technical Staff

Alejandro Martínez Hernández (Técnico de Garantía Juvenil, 01/05/2016-30/04/2018)

Summary

The activity of the Group Lasers, Nanostructures and Materials Processing (https://lanamap.iqfr.csic.es/) is focussed towards the investigation of physicochemical processes involved in the micro- and nanofabrication of materials by laser irradiation and ablation with pulses of nano- and femtosecond duration and wavelengths from the ultraviolet to the infrared. Our interest is the understanding and description of the mechanisms that govern the laser-material interaction from a fundamental perspective: electronic excitation, energy transfer and their temporal scales, heating of the solid lattice, plasma generation and expansion, etc. We tackle the study of ablative processes, that, in general, involve multiphoton absorption and ejection of aggregates or nanoparticles that constitute the building blocks in the synthesis of materials with laser. We also investigate characteristic interaction processes corresponding to the sub-ablative regime, where it is possible to generate superficial nanometre periodic structures by interaction of an incident laser beam with the surface scattered light.

In close relation with mechanisms, we search for control strategies of the laser-material interactions based in the following three fundamental approaches: the properties of laser light beams, the atmospheres where the processes take place and the temperature. Significantly, our work emphasizes the high degree of control derived from the use of controlled laser radiation in the temporal, spectral and spatial domains with selection of intensity, polarization or spectro-temporal map. These characteristics crucially influence the interaction with materials, thus the capabilities of laser control are based on the availability of laser sources with a wide range of properties and on the use of advanced methods of manipulation of laser light beams.

Although our activity is centred in the control of the properties and processes taking place in materials, the final applications are a source of inspiration and guidance. We pay special attention to the fabrication of low-cost, flexible electronic devices, information storage devices, sensor development and applications to the conservation of Cultural Heritage.

Strategic Aims

The general objective of the research carried out by the Group is to reach the understanding of the laser-material interaction processes to guide the selection of control strategies in the fabrication of nanomaterials by laser. The specific objectives are:

- Laser nanostructuring of soft matter and polymers applying advanced processing techniques, including LIPSS (laser induced periodic surface structuring), PLAL (pulsed laser ablation in liquids) and LIL (laser interference lithography).
- Laser synthesis of materials with specific properties in the form of thin or nanostructured films, with control of crystalline phase, composition and morphology, in the micro- and nanometre scales, using the technique of pulsed laser deposition (PLD) and implementing the control of spatial and spatio-temporal characteristics of the laser light source used.
- Development of new methodologies for the *in situ* determination of self-assembly and growth of nanomaterials generated in controlled PLD processes. We study ablation plasmas by combining nonlineal optical techniques, such as harmonic generation, optical emission spectroscopy (OES), and time-of-flight mass spectrometry (TOF-MS).
- Study and follow-up of ultrafast molecular dynamics, using femtosecond pulses, and exploration of the capacities of control over these dynamics using laser pulses intense enough to modify the system physicochemical properties.
- Development and application of advanced laser methodologies for analysis and conservation of substrates and objects of Cultural Heritage through the implementation of new techniques and instruments.

Results

In this period we have continued our studies on the generation of laser induced periodic surface structures (LIPSS) by irradiation with nanosecond pulses in thin films of semiconducting polymers, with application in organic solar cells, and ferroelectric polymers, with application in non-volatile organic memories.

First, we have investigated the formation of LIPSS in the semiconducting polymer poly(3-hexylthiophene) (P3HT). Near edge X-ray absorption fine structure (NEXAFS) and Raman spectroscopy techniques reveal a good chemical stability of P3HT during LIPSS formation while the measurement of the electrical properties with the atomic force microscope (C-AFM) shows an heterogeneous electrical conductivity alternating conducting and non-conducting regions. Resonance Raman and grazing incidence wide angle X-ray scattering (GIWAXS) results indicate a decrease in the crystallinity of P3HT upon LIPSS formation, which suggests a surface melting. Additionally, LIPSS have been formed on the blend of P3HT with the fullerene derivative [6,6]-phenyl-C71-butyric acid methyl ester (PCBM), which constitutes the active layer of an organic solar cell (Figure 1a).

LIPSS have been also created on the copolymer poly(vinylidenefluoride–trifluoroethylene), P(VDF-TrFE). Although this copolymer is transparent in all the UV-VIS range, LIPSS have been obtained in a bilayer of P(VDF-TrFE) with other polymer which absorbs at the irradiation laser wavelength. The ferroelectric nature of the bilayer was tested by measuring the piezoresponse with the AFM (PFM). Additionally, the bilayer presents an increase in the density of information stored of one order of magnitude in comparison to the non-structured bilayer (Figure 1b).

Finally, synchrotron radiation techniques have been applied to study the fundamentals and formation dynamics of LIPSS formation in polymers. A mapping of the structural order of LIPSS in polycarbonate has been performed by grazing incidence small angle X-ray scattering with a micrometric beam (μGISAXS) and formation of LIPSS has been in situ monitored by GISAXS by the acquisition of the scattering patterns simultaneously with laser irradiation. The samples were irradiated at different repetition rates (1-10 Hz) and the results support and give information on the existence of a feedback mechanism for LIPSS formation.

These studies were carried out in collaboration with the group of Prof. T. Ezquerra (Instituto de Estructura de la Materia del CSIC).

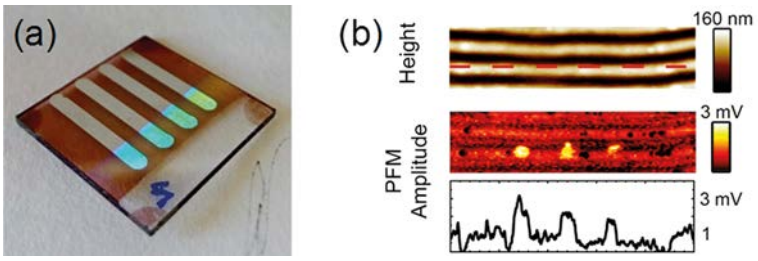


Figura 1. (a) Bulk heterojunction solar cell, which shows iridescence in the area nanostructured with LIPSS. (b) Topography and PFM amplitude images of LIPSS in a bilayer after applying a field of +12 V for 5 minutes in three different spots. Amplitude along the line drawn in the height image is shown below the PFM amplitude image.

Laser transfer of thin films and nanostructures

We have fabricated by nanosecond PLD, thin and nanostructured films with specific properties using solid targets of various materials. The morphology, structure, electric and magnetic properties have been characterized with a combination of techniques.

By ablating cobalt ferrite ($CoFe_2O_4$) targets at 1064 nm, and using $SrTiO_3$ (100) substrates heated at 748 K, we obtained epitaxial films with island structures of two different shapes: rectangular (~30 x 60 nm^2) with [100] or [010] orientation and squared of larger size and oriented according the [110] axis of the substrate. The analysis of results indicates that the composition of the former structures is cobalt ferrite and of the latter is magnetite. Upon laser irradiation at 1064 nm of haematite targets in ultrahigh vacuum and deposition on Ru (0001) substrates at 1573 K, we obtained stoichiometric FeO(111) deposits. XPS, LEED y ISS analyses indicate that deposits are monocrystalline with thicknesses between 1 and 8 nm. These studies have been carried out in collaboration with Drs. J. de la Figuera and F.J. Marco of IQFR and give evidence of the capabilities of the PLD technique for the growth of thin monocrystalline FeO (111) films.

We have also investigated the PLD process at 1064 of aluminium targets and have established the relation between the laser fluence and the characteristics of the deposited material. We have observed deposition of amorphous aluminium (dielectrics) at fluences below 7 J/cm^2 while at higher fluences, the deposits are constituted by metallic aluminium (conductor).

The effect of wavelength and deposition atmosphere in the PLD process was studied for the case of boron carbide, B_4C. In vacuum and by irradiation at 266 nm (Fig. 2a), deposits grow as amorphous material in columnar form, with sizes below one micron. At 1064 nm (Fig. 2b), crystalline micro columns are generated with section of 1-2 microns. In the presence of 1 mbar of Kr, the deposits present a dendritic structure (Fig. 2c).

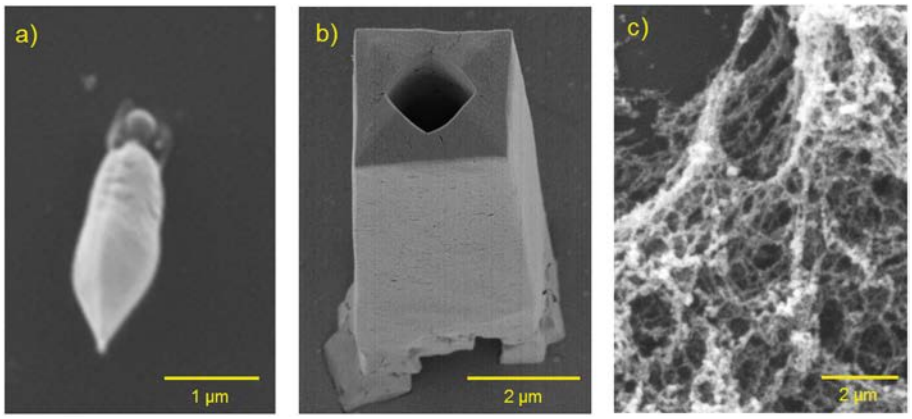


Figure 2. SEM images of PLD deposits from B_4C targets on Si (100): a) irradiating at 266 nm in vacuum, b) irradiating at 1064 nm in vacuum and c) irradiating at 1064 nm under 1 mbar of Kr. Adapted from Appl. Surf. Sci. 328 (2015) 170.

In this period we have also performed an experimental study designed to investigate the potential of PLD for the synthesis of semiconductor materials doped with magnetic atoms, or DMS (diluted magnetic semiconductors), which present interesting magneto-optical properties. We have performed a first investigation in this direction by studying the ablation plasma resulting from the irradiation of a mechanically mixed material (Co and ZnS) with ultrashort laser pulses. We have particularly explored the issue of the controllability of the ionic composition of this plasma by employing sequences of pairs of ultrashort pulses in the near infrared, whose delay and relative energy were controllable. The detection technique employed was time-of-flight mass spectrometry. The regime chosen was under ablation threshold for single pulses, which is a condition where the first pulse of the sequence merely causes modifications in a superficial layer of the material. The fluence of each pulse and the temporal delay then determine the mechanisms governing the interaction of this modified layer with the second pulse. Our work demonstrated that in the femto- and picosecond time scales it is possible to achieve a considerable degree of control on the composition of the plasma through the control of the laser irradiation characteristics. A planned second part of this work will tackle the fabrication of deposited material through PLD in these conditions.

Study of laser ablation plasmas

We have continued our previous studies on harmonic generation in laser ablation plumes, concentrating in materials such as B_4C and the semiconductor zinc sulphide, ZnS. In these experiments we use one or two pulsed probe lasers that propagate trough the plume induced by an ablating laser. This scheme allows the spatio-temporal diagnosis of the species present in the ablation plume.

We have studied even and odd harmonic generation of the fundamental probe laser (1064 nm) frequency in B_4C ablation plumes by frequency mixing of two nanosecond lasers in the infrared at 1064 nm and in the visible at 532 nm (Fig. 3). We characterized the dependence of fourth harmonic generation (at 266 nm) as a function of the intensity of the two probe lasers, indicating a nonlinear optical process of six-frequency mixing, highly favoured by considering parallel polarizations of the probe beams. The spatio-temporal characterization of the fourth harmonic emission shows a maximum efficiency at an ablation-probe delay of around 200 ns, without contributions at longer delays. This result indicates the generation by ablation of a highly atomized plasma with a low ionization degree.

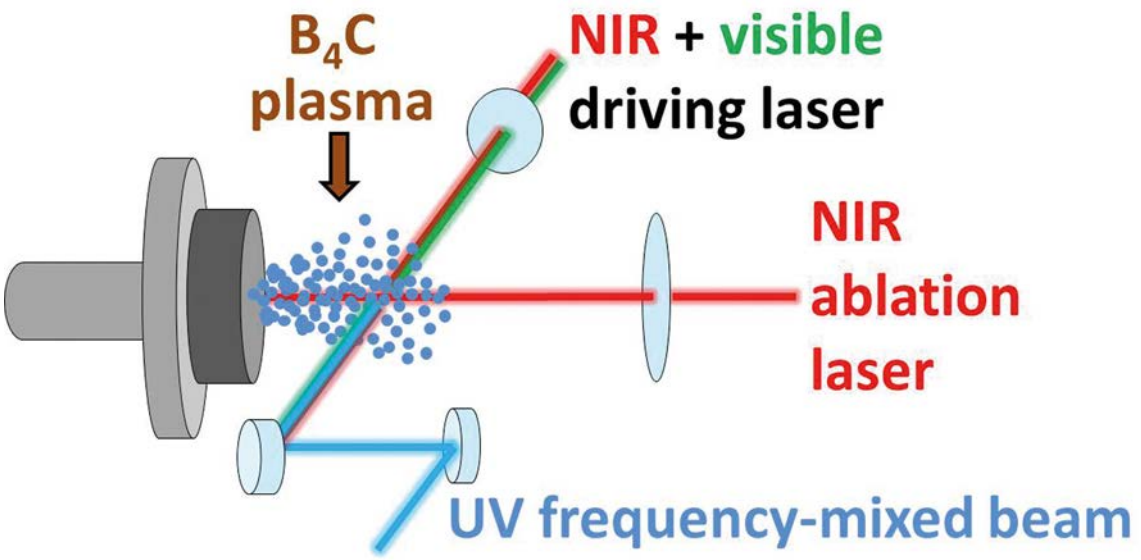


Figure 3. Experimental set-up for generation of even and odd harmonics in laser ablation plasmas. Adapted from Applied Surface Science 336 (2015) 53–58.

We have also undertaken the study of odd harmonic generation of the fundamental laser radiation at 1064 nm in laser ablation plasmas of ZnS. The harmonic spectrum contains nonlinear components up to the 9th order. The temporal evolution of the corresponding signals is characterized by the presence of two temporal components attributed to fast atomic species (Zn y Zn^+) and slow ZnS nanoparticles.

Ultrafast molecular dynamics

In these years we have continued our studies on dynamics and control of photodissociation processes in middle-size molecular systems. In one of these studies we have developed a novel methodology to measure predissociation lifetimes in radical species (CH_3 / CD_3). This has allowed obtaining new data on the lifetimes of vibrational levels of Rydberg states of these species. The procedure has consisted of employing three-pulse sequences of ultrashort pulses: the first pulse generates the radical from the photodissociation of a precursor, the second pulse resonantly excites vibrational levels of the Rydberg state under study, and the third pulse probes the presence of excited radicals through an ionization process (with velocity map imaging detection). This experimental study was completed with ab initio calculations, and globally has provided relevant information to understand the predissociation of this radical and the importance of the isotopic effect.

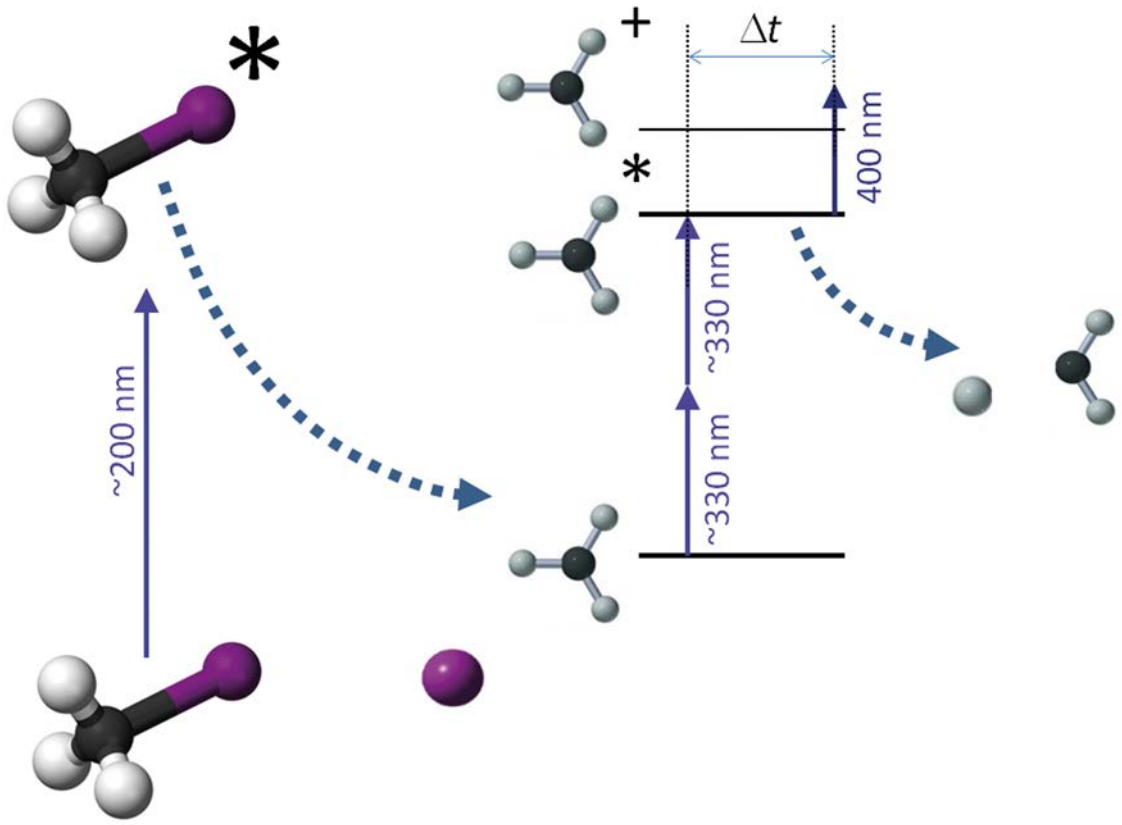


Figure 4. Schematic representation of the experimental concept that allows the measurement of excited state lifetimes of a radical species using a three-laser-pulse sequence.

In a different work, we have undertaken the study of the sterodynamics of a molecular predissociation process, with the novel ingredient that we have followed the angular character in a time-dependent scheme. For this aim, we have employed a pump-probe laser scheme, in combination with spatially resolved charged-particle detection that provides the angular information on the process. This method has been applied to the predissociation of the CH_3I molecule after excitation in its second absorption band in the UV region, and angular distributions of the CH_3 fragment appearing upon bond fission have been measured. The results have been analyzed by fitting the distributions using a quasiclassical model, and this has revealed the role played by factors like the lifetimes of excited states, the rotation of the parent and fragment species, and the angular momentum alignment of the fragment on these time-resolved angular distributions.

Finally, we have contributed with a Perspective paper in the PCCP journal where we describe the capabilities of strong laser field control for the manipulation of photochemical processes. This paper describes our own contributions to this field realized in the years 2013-2014, together with contributions by other groups.

Lasers in the conservation of Cultural Heritage

In the reporting period 2015-2016 we have continued our investigations on the laser treatment of contamination or unwanted layers over different substrates of interest in Cultural Heritage. In each specific case we aim at the formulation of optimized procedures to avoid damage to the substrate and to the design of strategies that mitigate deleterious physicochemical effects.

In what concerns inorganic substrates (stone, ceramics), we have developed new procedures for laser elimination of biodeterioration layers (lichens, cyanobacterias) based in the sequential irradiation with two wavelengths, in the infrared and the ultraviolet, and in the combination of laser irradiation ad the use of biocides (Fig. 5).

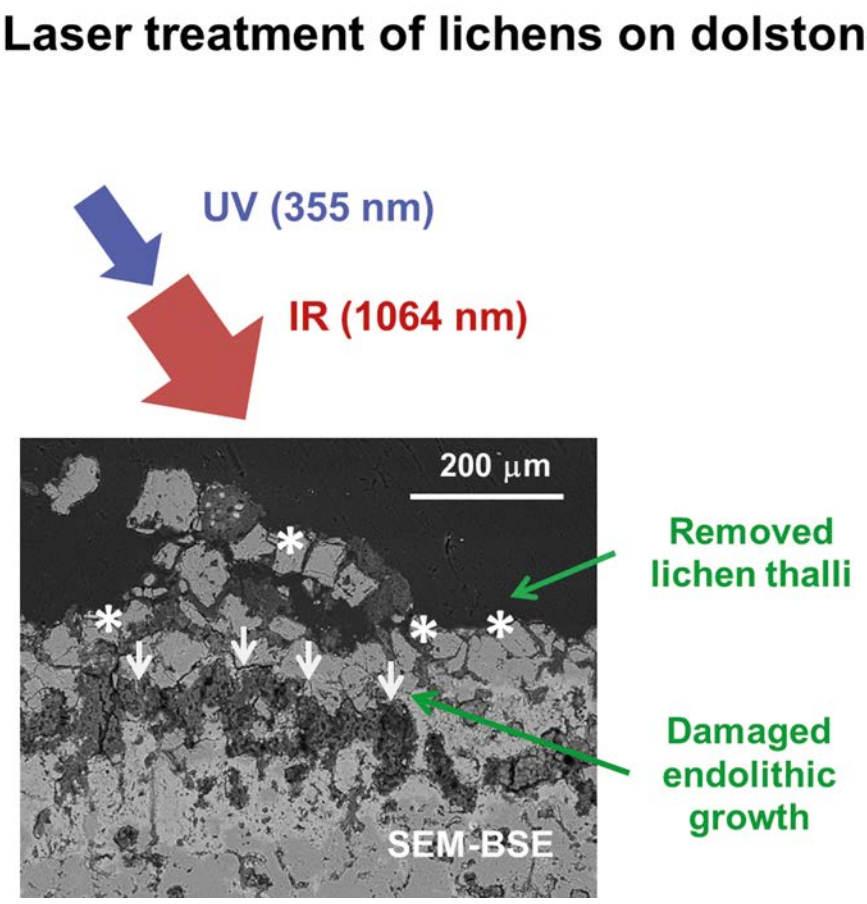


Figure 5. Sequential laser irradiation at 1064 and 355 nm for elimination of lichens on dolostones. Adapted from Appl. Surf. Sci. 346 (2015) 248.

During this period we have also investigated the laser cleaning of tarnished silver (pure and "sterling"), and we have concluded that irradiation at 1064 nm induces the loss of material and colour changes, while irradiation at 532 nm produces acceptable results in this type of metallic substrates.

In reference to molecular substrates, we have studied laser removal of varnishes, with different degrees of ageing and applied on pictorial layers based in egg tempera, using nanosecond pulses at different ultraviolet wavelengths. We have identified physicochemical modifications through a laser spectroscopy multianalytical approach including laser induced fluorescence (LIF) micro-Raman spectroscopy.

Together with our research on laser cleaning, we have applied the LIBS (laser-induced breakdown spectroscopy) technique for the compositional analysis of a set of historic glasses from the late Roman period comparing the application of the technique with nano- and femtosecond pulses.

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COMPETITIVE FUNDING

National Grants: individual

Subdirección General de Proyectos de Investigación (Mº de Economía y Competitividad)

Principal Investigator	Title	Reference
Marta Castillejo Striano	Control de Nanoestructuras Generadas por Láser: Interacción Láser-Material y Procesos en el Plasma	CTQ2013-43086-P
Esther Rebollar González	Microfabricación de palancas poliméricas mediante técnicas láser	MAT2014-61874-EXP
Rebeca de Nalda Mínguez y Esther Rebollar González	Procesado Avanzado por Láser para Síntesis y Modificacion de Materiales en la Micro- y Nanoescala	CTQ2016-75880-P
Francisco Javier Aoiz Moleres	Dinámica de procesos moleculares con láser y métodos teóricos	CTQ2012-37404-C02-01

National Grants: coordinated

Consejería de Educación – Comunidad Autónoma de Madrid

Principal Investigator	Title	Reference
Rafael Fort	Tecnologías y Conservación de Geomateriales del Patrimonio	S2013/MIT-2914
María Teresa Pérez-Prado	Diseño multiescala de materiales avanzados	DIMMAT, S2013/MIT-2775

International Grants: individual

European Synchrotron Radiation Facility ESRF

Principal Investigator	Title	Reference
Esther Rebollar González	Inner structure of Ferroelectric polymer/ Conducting polymer bilayers prepared by Laser Induced Periodic Surface Structures (LIPSS) method	SC-4204

International Grants: coordinated

European Union

Principal Investigator	Title	Reference
Luca Pezzati (INO-National Institute of Optics, Italia)	Integrated Platform for the European Research Infrastructure ON Cultural Heritage, IPERION CH	654028
Franco Niccoluchi (Universita di Firenze, Italia)	Pooling Activities, Resources and Tools for Heritage E-research Networking, Optimization and Synergies, PARTHENOS	654119

European Comission (COST Action)

Principal Investigator	Title	Reference
Manuel Alcamí (Universidad Autónoma, Madrid)	XLIC: XUV/X-ray light and fast ions for ultrafast chemistry	CM1204

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Tenured Staff scientists

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(Professor)

Inmaculada García-Moreno Gonzalo

Clara Gómez Hernández
(Assistant Professor)

Non-tenured scientists

Luis Cerdán Pedraza
Post-Doctoral Researcher with Project Contract from 16/07/2016

Doctoral students

Gonzalo Durán Sampedro
FPI Scholarship 01/08/2011 - 31/07/2015

Summary

The research of the group centers in the design and development of new photonic systems based on photosensitized and nanostructured materials for optoelectronic and biophotonic applications. For this, the processes that regulate their preparation, behavior and properties in relation to their structure and nanostructure are studied. We also study the modulation of the optical properties of materials based on dye-doped multifunctional photonic nanostructures, be they ordered or disordered, organic or inorganic, rigid or flexible, 1D or 3D as well as mono- or multi-chromophoric for photonic (laser and waveguides) and biophotonic (imaging) applications. In the field of biomedicine we continue our studies on the interaction of laser radiation with biological tissues and applications to Photodynamic Therapy.

Strategic Aims

- General objective: obtaining new advanced nanomaterials with defined optoelectronic and biophotonic applications.
- Design, synthesis and characterization of new molecular dyes, including chiral dyes, based on the BODIPY chromophore, with efficient and stable emission in the blue, red, and near infrared spectral regions, low synthetic cost, and with improved photonic and structural properties.
- Development of organic dyes in the red and near IR spectral regions for applications in photodynamic therapy.
- Functionalization of nanoscaffolds of different nature and geometries (organic and inorganic nanoparticles, fullerenes, nanocrystalline cellulose, and polyhedral oligosilsesquioxanes), with a variable number of dye molecules and chemically- and biologically-active groups.
- Encapsulation and anchorage of laser dyes in nanoparticles, polymers, and porous systems (hybrid and inorganic).
- Study of the photophysical properties of the new materials and their relationship to structure, microstructure and composition.
- Characterization of the new materials as laser systems, micro- and nano-lasers, photonic coatings, and saturable absorbers with improved laser action by non-resonant feedback lasing induced by nanometric sized scatters.
- Evaluation of the new photoactive materials in biophotonic applications allowing the development of easy-to-access, minimally invasive and cost-effective methods for improved diagnosis (bioimaging).
- Use of computational strategies for the design of new materials with optimized properties for application in the various proposed uses.
- Study of the laser radiation-biological tissue interaction to maximize the applications of the laser tool in Orthodontics.

Results

Photosensitized and nanostructured materials for optoelectronic and biophotonic applications

During the two years covered by this report, we have continued with the design, synthesis and characterization of new organic dyes with emission covering the spectral range from the blue to the near infrared, using BODIPYs as base chromophores. By covalent linkage of coumarins to BODIPYs to create hybrid compounds (Figure 6) or the incorporation of stabilized C nucleophiles to the *meso* position of BODIPYs, dyes are obtained with increased absorption in the UV region and tunable laser emission, highly efficient and stable, over the spectral region from the green to the red (Figure 7). The design and development asymmetric cassette triads based entirely on BODIPY chromophores (Figure 8) provides panchromatic absorption, with efficient light harvesting capacity over the UV-visible spectral region *via* very efficient energy-transfer processes. The programmed functionalization of polyfunctional BODIPY building blocks allows the versatile preparation of complex BODIPY derivatives, resulting in a new library of compounds with tailored photophysical properties for advanced photonic and biophotonic applications. In particular, it was possible to shift the BODIPY emission deep into the near-infrared spectral region (Figure 9) while retaining high fluorescence quantum yields as well as efficient and stable laser action. In a parallel development, we demonstrated for the first time red-shifted laser emission in J-aggregated dyes in common organic solvents without additives. These compounds are based in a new type of *O*-BODIPYs with a spiranic *B*-diacycloxy rigid structure.

We have continued the study of the emission properties of polymeric nanoparticles doped with organic dyes. In particular, we have studied in depth the photophysical and laser properties of cationic nanoparticles doped with rhodamine 6G in colloidal suspensions as well as the random laser emission properties in photonic materials based on self-assembled dye-doped cationic nanoparticles.

Blue-emitting lasers are tools of uppermost importance to many applications, ranging from spectroscopy and material processing to biotechnology and medicine. So far, blue-emitting laser materials are based on organic compounds or semiconductor nanocrystals that have significant limitations, such as low solubility in common solvents and polymers, low chemical- and/or photo-stability and/or lengthy and costly synthetic procedures which result in uncompetitive prices. We have demonstrated a novel and competitive alternative to these existing laser materials with emission in the blue that is based on boron hydrides (boranes), inorganic cluster compounds with a rich and diverse chemistry. In particular, we have demonstrated that solutions of the borane *anti*-$B_{18}H_{22}$ show, under pulsed excitation, blue laser emission at 406 nm (Figure 10) with an efficiency of 9.5% and a photostability superior to many of the commercially available state-of-the-art blue laser dyes.

Finally, we have recently started systematic studies on the generation of circularly polarized laser emission (CP), induced in achiral and isotropic dye laser systems without the use of extracavity polarizing elements. We demonstrated that it is possible to generate and modulate CP laser light from efficient and photostable conventional laser dyes (Figure 11).

Figure 6. Simple 7-hydroxycoumarin (blue) and BODIPY (red) chromophores, and a hybrid system based on them, indicating the absorption and emission regions of each compound.

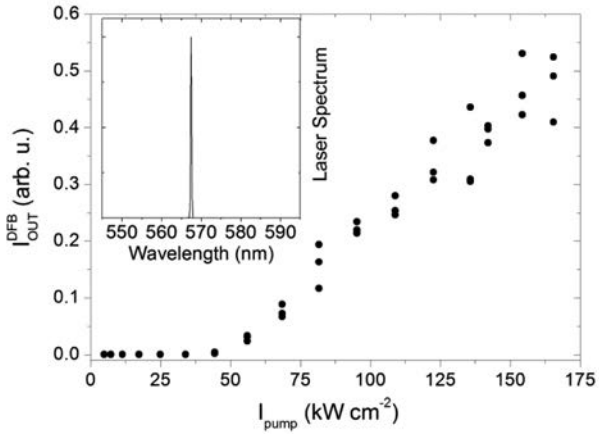

Figure 7. Distributed feedback laser emission from a thin film of PMMA incorporating a BODIPY with stabilized C nucleophile.

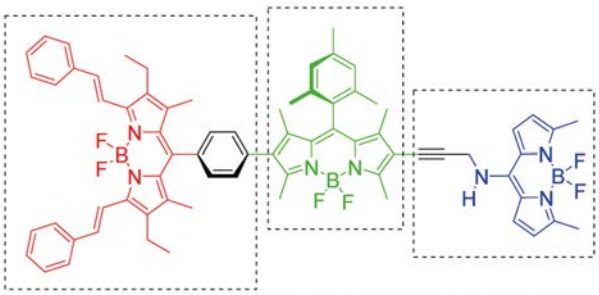

Figure 8. Cassette constituted by a triad of BODIPY compounds.

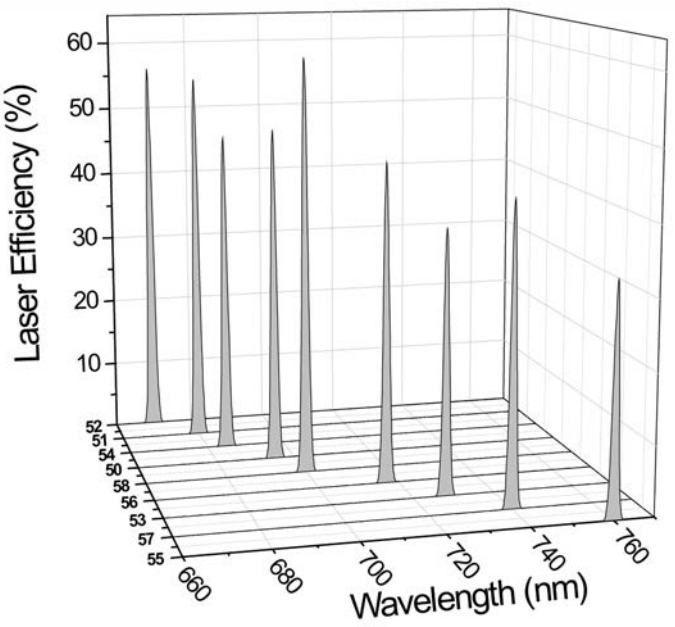

Figure 9. Red-shifted laser emission from specifically designed new BODIPY dyes in ethyl acetate

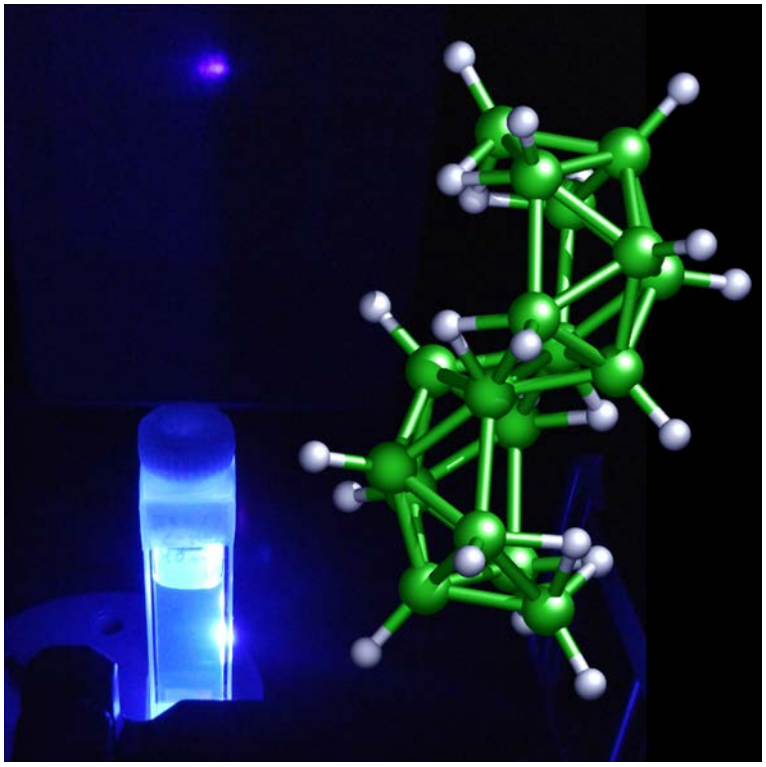

Figure 10. *Anti*-$B_{18}H_{22}$ borane structure and laser emission in cyclohexane solution.

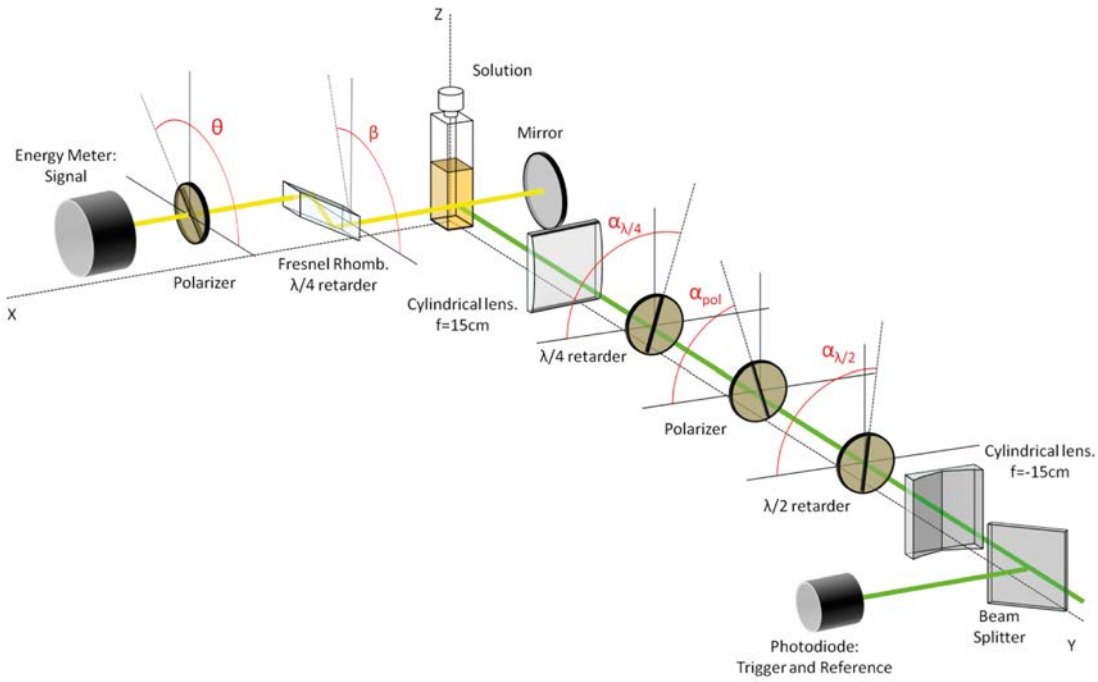

Figure 11. Generation of CP laser emission in achiral laser systems: experimental set-up used to determine the polarization state of a dye laser emission as a function of the pump polarization state.

Interaction of low energy laser radiation with periodontal tissue

Low energy laser therapy (or Laser Phototherapy LP), has a wide range of possibilities for application in the dental field. In co-operation with the Department of Stomatology IV of the Faculty of Dentistry of the UCM, we have evaluated possible applications for such therapy in Orthodontics.

A study was conducted with patients suffering from malocclusion due to severe dental crowding in the upper arch. The treatment involved extraction of the maxillary second premolars and placement of fixed multibrackets and Nance button as an anchorage to achieve distalization of the maxillary first premolars. Quadrant 1 received adjunctive treatment with LP applied in repeated doses. Differences in pain, speed of premolar distalation and RANKL and OPG concentrations in the gingival crevicular fluid (GCF) between orthodontic treatment and the same complemented by LP were evaluated. A decrease in the perception of pain, an increase in the speed of distalization movement and a slight increase in RANKL values as a consequence of high bone reabsorption due to a fast orthodontic movement in the early stages, were observed after the application of repeated doses of LP.

Lingual orthodontics treatment retains more plaque, generating more gingival inflammation than buccal orthodontic treatment (the lingual surface is smaller than the buccal one, so the bracket takes most of the space, remains closer to the gingiva and thus impedes plaque removal). In this context, a study was carried out evaluating short and medium-term application of LP in repeated doses in adults with a healthy periodontium treated by lingual orthodontics (Figure 12). Periodontal indices were recorded before and after 1, 2, 3 and 12 months, and levels of IL-1b and TNF-a in the GCF were assessed to determine differences between lingual orthodontic treatment and the same but complemented by LP. At short-term, LP prevented a substantial increase in the IL-1b levels. At medium-term, LP diminished periodontal scores allowing a faster recovery of the initial periodontal status.

Application of laser ablation to removal the adhesive resin

On-line controlled laser radiation was used for the selective removal of the adhesive on tooth after bracket debonding.

In this study, 10 brackets were bonded to 10 extracted human premolars from young patients and removed after a storage period of 2 months. The aim was to achieve a selective removal of the adhesive after bracket debonding without causing any iatrogenic damage to the enamel by using laser radiation at 355nm (third harmonic wavelength of a Q-switched Nd: YAG laser). As real-time diagnostic technique, the LIBS (laser-induced breakdown spectroscopy) technique was applied. This technique allows an elemental analysis "in situ" of the adhesive and enamel, and therefore allowed an on-line precise control in the adhesive removal process. SEM analysis revealed that with three pulses of the 355 nm UV laser radiation (0.8 J/cm^2; Ø = 1mm) a complete removal of the adhesive on the tooth without signs of damage on the enamel was achieved.

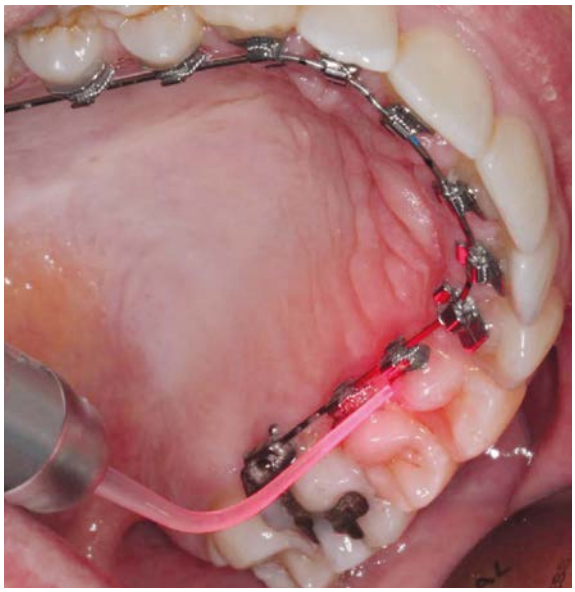

Figure 12. Low-level laser radiation applied on the lingual surface by a periodontal probe composed by a disposable light-diffusing tip covering a stainless steel autoclavable handpiece.

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Enciso, E., Cerdán, L., Gartzia-Rivero, L., Bañuelos, J., Costela, A., López-Arbeloa, I. and García-Moreno, I. (2015). Emission properties of dye-doped cationic nanoparticles: size, surfactant and monomeric composition effects. *RSC Adv. 5, 4454-4462.*

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Domínguez, A., Gómez, C., Palma J.C. (2015). Effects of low level laser therapy on orthodontics: rate of tooth movement, pain and release of RAKL and OPG in GCF. *Lasers Med. Sci. 30(2), 915-923.*

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Gómez-Durán, C.F.A., Esnal, I., Valois-Escamilla, I., Urías-Benavides, A., Bañuelos, J., López Arbeloa, I., García-Moreno, I. and M.A., Peña-Cabrera, E. (2016). Near-IR BODIPY Dyes à la Carte – Programmed Orthogonal Functionalization of Rationally Designed Building Blocks. *Chem. Eur. J. 22, 1048-1061.*

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Contribucions to books

Gómez, C. (2015). "Laser radiation as a therapeutic strategy in the treatment of periodontal disease. Photodynamic therapy as an adjunct to non-surgical periodontal treatment: clinical, microbiological and anti-inflammatory aspects." En Medical and Biological Papers 8. Tomo I. Fundación Eugenio Rodríguez Pascual (ed.) 109-130.

Costela, A., García-Moreno, I. and Sastre, R. (2016). "Solid-state organic dye lasers" in Tunable Laser Applications, Third Edition, Duarte, F.J. Ed (CRC Press, New York, USA), Chap 3, pp 141-174.

Costela, A., García-Moreno, I. and Gómez, C. (2016). "Medical applications of organic dye lasers" in Tunable Laser Applications, Third Edition, Duarte, F.J. Ed (CRC Press, New York, USA), Chap 8, pp 291-311.Edition, Duarte, F.J. Ed (CRC Press, New York, USA), Chap 8, pp 291-311.

COMPETITIVE FUNDING

National Grants: coordinated

Ministerio de Ciencia e Innovación (MICINN)

Principal Investigator	Title	Reference
Inmaculada García-Moreno Gonzalo	Organic and hybrid nanomaterials for optoelectronic and biophotonic aplications	MAT2014-51937-C3-1
Inmaculada García-Moreno Gonzalo	Photonic materials as bioimaging markers	MAT2015-68837-REDT

International Grants: coordinated

European Commission Framework Programmes

Principal Investigator	Title	Reference
M.H. Delville, Institut de Chimie de la Matière Condensée de Bordeaux, Université Bordeaux, Francia	Rational design of hybrid organic-inorganic interfaces: the next step towards advanced functional materials	COST Action MP1202

Statistical Mechanics and Condensed Matter Group

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Eva González Noya (Staff Scientist)

Enrique Lomba García (Professor)

Doctoral students

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Cecilia Bores Quijano (FPI, from 01/12/2011) / (FPI, until 30/11/2015)

Vicente Sánchez Gil (JAEpre, from 01/09/2011) / (JAEpre, until 30/08/2015)

Summary

The research carried out for the last two year focuses on the application of statistical mechanics and condensed matter theory tools in conjunction with simulation approaches in order to analyse problems of physico-chemical interest, basically in connection to phase transitions in bulk and under confinement, as well as adsorption processes in nanostructured porous materials, in this latter instance, including the structural elucidation at the atomic level of newly synthesized materials. Our main contributions can be cast into three main complementary lines: methodology, systems of fundamental interest, and systems of experimental interest.

Strategic Aims

- Development of new methodologies for the study of phase transitions.
- Study of phase transitions in complex fluids (water, liquid crystals, anomalous liquids)
- Self-assembly phenomena in simple models.
- Simulation and modelling of adsorption in disordered porous media (carbons, pillared interlayered clays) and ordered porous media (zeolites).

Results

Systems with competitive interactions

In collaboration with Prof. A. Ciach (PAN, Warsaw) we have studied simple lattice systems by means of theoretical approaches and computer simulation, for which it was analyzed the influence of confinement on the phase equilibria and the topology of the emerging phases. Also in collaboration with Dr. A. Perera (U. Pierre & Marie Curie, Paris), we have developed a simple mixture model with short range interactions able to exhibit microheterogenity. This model turned out to give rise to effective short-range attractive, long range repulsive interactions (competitive potential), by which a simple system without the presence of long range electrostatic interactions is shown to be able to be at the source of an effective SALR potential.

Microheterogeneity and self-assembling systems

In close connection with the previous line, we have here studied systems characterized by the presence of microheterogeneity and cluster formation. Very specially we have considered amphiphilic systems (polar heads with non-polar tails), focusing during this period on alcohol/water mixtures. Here we have analyzed how the disruption of the 3D H-bond network of water by the non-polar tails affects the singular behavior of water. To that aim we have used simple lattice models and continuum two-scale models -- in collaboration with the group of Prof. M. Barbosa (UFRGS, Porto Alegre, Brasil)—and all atom models developed to fit experimental excess properties of mixtures – in collaboration with Prof. D. González Salgado (U. Vigo).

Fluids under confinement: adsorption and phase transitions

In this line we have culminated a long term collaboration with Dr. J.M. Guil (IFR), Prof. J. Pires (U. Lisboa) and Dr. S. Valencia (ITQ). We have analyzed the influence of various adsorbates (noble gases, methane, toluene) on the structure of various pure silica zeolites (ZSM-11, ZSM-5), characterizing the different adsorption sites, as well as the phase transitions in the adsorbent induced by the adsorbate when approaching full loading. To that aim we have performed neutron and synchrotron X-ray experiments, in combination with extensive simulations and we developed a new Reverse Monte Carlo approach in order to invert experimental diffraction information to yield microscopic atomic configurations. Additionally, we have devised a new three dimensional integral equation approach that allows for a precise determination of the microscopic structure of adsorbed fluids, which has been put to successful test for Ar in zeolites and for hydrogen inclusions in short capped nanotubes. Finally, we have analyzed the influence of confinement in a regular slit pore geometry on the demixing transition of a simple symmetric mixture. For this system, we were able to show that the influence is non-monotonic and strongly depends on the commensurability of the length scales involved in the confinement and the volume effects that lead to demixing.

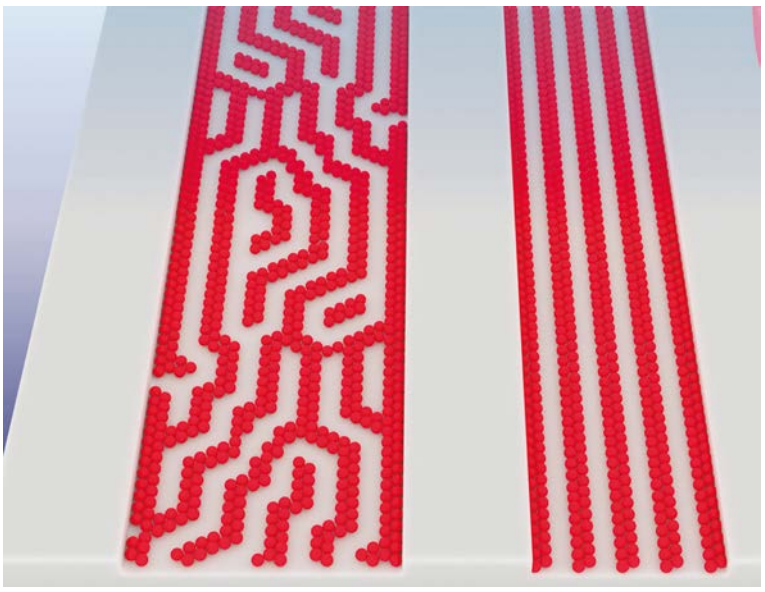

Figure 13. Pattern formation in a system with competitive interactions induced by confinement.

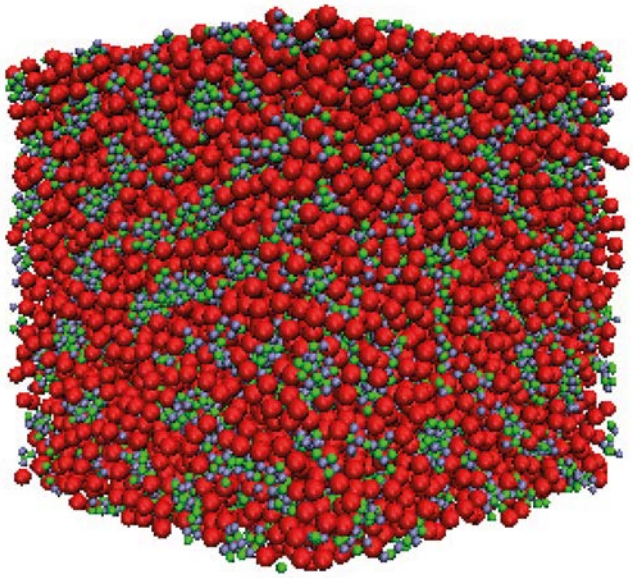

Figure 14. Microheterogenety induced by competition between short range interactions.

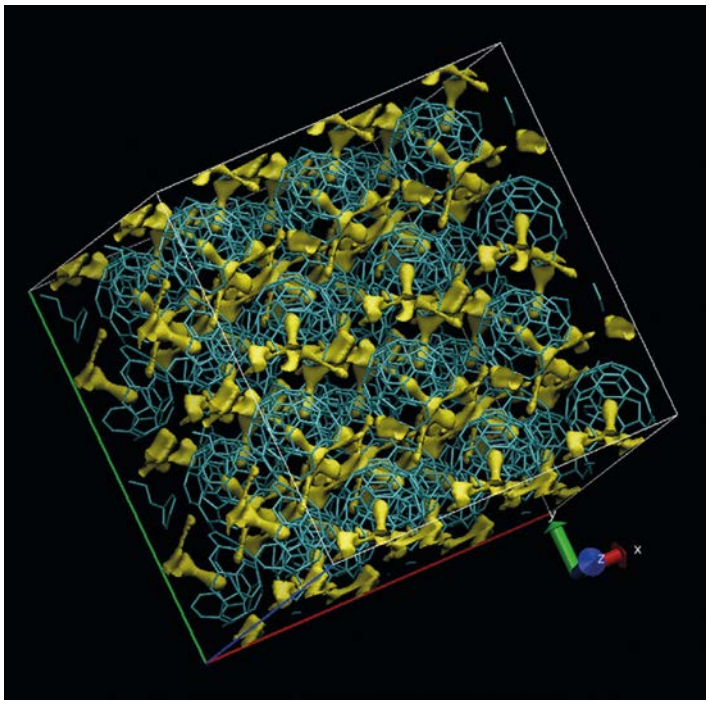

Figure 15. Three dimensional density distribution of H_2 inclusions in a cristal of short capped nanotubes as obtained from the 3DOZ-ROZ theory.

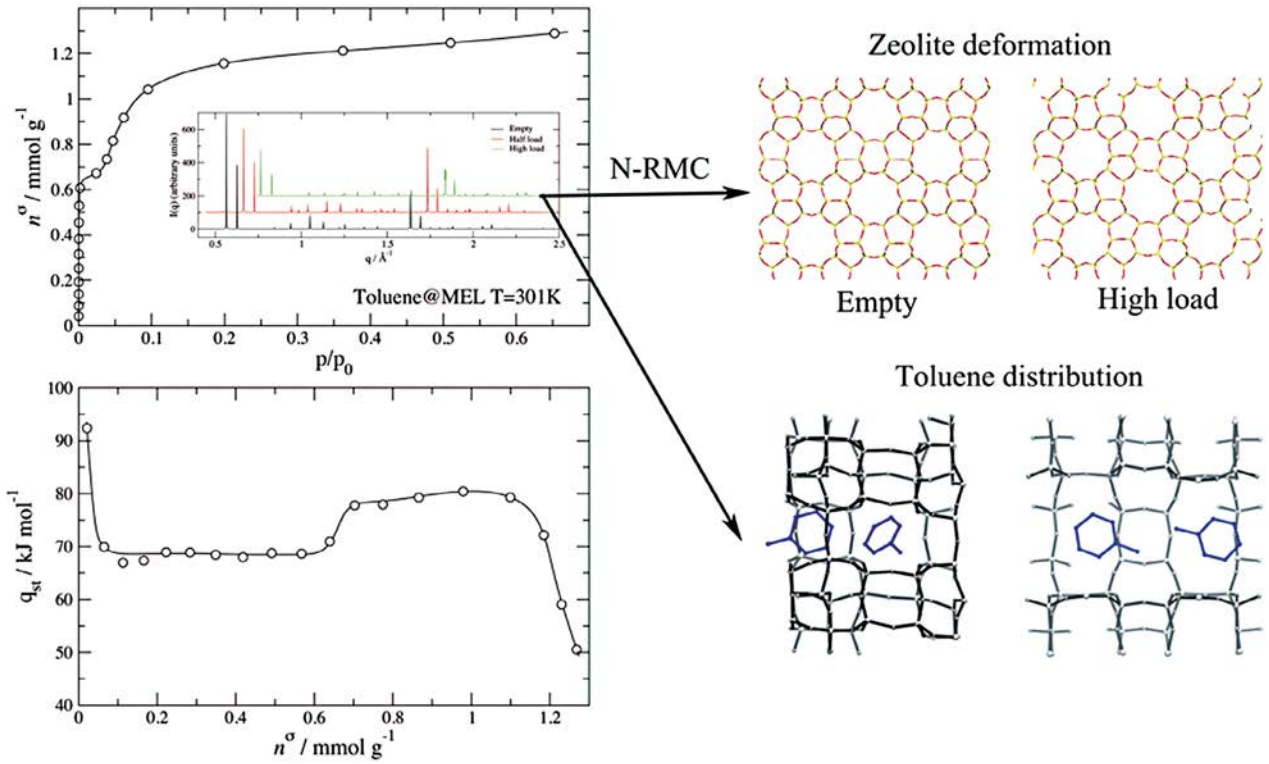

Figure 16. Calorimetric and volumetric adsorption curves in combination with computer simulation and X-ray diffraction make possible the elucidation of the microscopic structure of toluene adsorbed into ZSM-11 zeolites and the corresponding structural phase transitions induced in the adsorbent during the adsorption process.

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COMPETITIVE FUNDING

National Grants: individual

Ministerio de Economía y Competitividad

Principal Investigator	Title	Reference
Eva González Noya	Design of colloidal quasi-crystals from anisotropic particles	FIS2015-72946-EXP

National Grants: coordinated

Ministerio de Economía y Competitividad

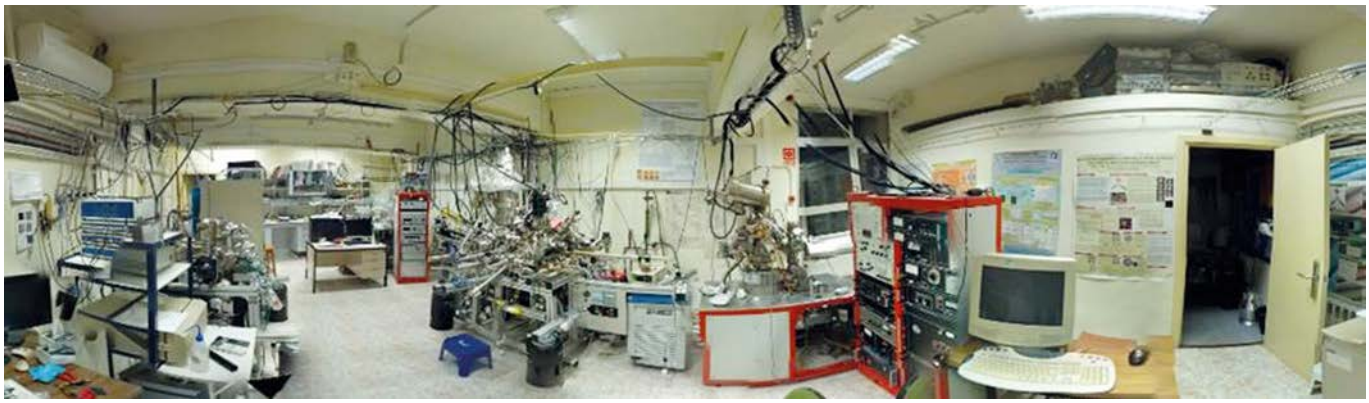
Principal Investigator	Title	Reference
Noé García Almarza/ Enrique Lomba García	Theory and simulation of complex fluids	FIS2013-47350-C5-4-R

International Grants: coordinated

Conselho Nacional de Desenvolvimento Científico e Tecnológico (Brasil)

Principal Investigator	Title	Reference
Marcia C.B. Barbosa	Modeling water/alcohol mixtures	PVE 401036/2014-6

Surface Analysis and Mossbauer Spectroscopy Group



Tenured Staff scientists

José Francisco Marco Sanz (Investigador Científico)

Juan de la Figuera Bayón (Investigador Científico)

Non-tenured scientists

Raquel Gargallo Caballero
(1/3/2015 a 31/8/16)

PhD students

Laura Martín García (FPI)

Technical Staff

Carlos Alonso González

Summary

The scientific activity of this research group focuses on the study of the surface region of various materials. To do this, we use microscopy and spectroscopy techniques, some of them in ultrahigh vacuum (including nanospectroscopy techniques based on synchrotron radiation), as well as Mössbauer spectroscopy.

In this period we have devoted most of our time to the study of oxides of transition metals, with special emphasis on oxides with the spinel structure. We have performed the chemical, structural and magnetic characterization of several such oxides, and we have studied the growth of oxide thin films on different substrates. An aspect of our activity that should be remarked is the construction of instrumentation for surface analysis. More information can be found on the website, http://surfmoss.iqfr.csic.es.

Strategic Aims

- To understand and control the thin film growth from a few atomic layers to hundreds of nanometers of oxides, both on metal substrates and oxide substrates.
- To determine the structural and magnetic properties of these films, taking advantage of the possibilities of specific techniques of growth to obtain new or improved properties.
- To determine the influence that stoichiometry and the preparation method exert on the cationic distribution in complex oxides of transition metals and through them in their properties.
- To build and implement new instrumentation for surface analysis and Mössbauer spectroscopy.
- To develop new characterization techniques, or to extend them, in the field of low-energy electron microscopy with special emphasis in the measurement of the vector magnetization on surfaces with nanometric resolution.

Results

Control of the growth of thin films and high quality heterostructures

In this area, we have always tried to take advantage of both the available equipment and collaborations in order to carry out research that represents an added value within the field. We highlight the following sections:

Growth of spinel free of anti-phase defects on metal substrates. One of the problems that have been found in spinel growth is the presence of anti-phase boundaries. The anti-phase boundaries appear when an spinel is grown on a substrate in which the spinel nuclei may be at non-integer distances of their lattice parameter. As they grow to give rise to a continuous film, these defects are formed between the initially nucleated grains. Anti-phase boundaries produce unexpected and sometimes unwanted magnetic behaviour. For this reason, it is relevant to study the effect of these defects on the properties of the films, and to the extent possible, to grow materials which are free of them. One possibility we have proposed is the use of high temperature growth conditions by molecular beam epitaxy under an oxygen atmosphere on metal substrates. In particular, during this period we have shown that this method allows to obtain islands several micrometers wide and with height in the range from a few nanometers to a few hundred nanometers. In order to be able to properly explore the growth conditions, it has been essential to use low-energy electron microscopy, which allows the real time observation with nanoscale resolution of the surface while the film growth is taking place. These experiments have been carried out on the microscopes at Sandia National Laboratories in collaboration with Dr. K.F. McCarty and at the Alba synchrotron in Barcelona in collaboration with Dr. L. Aballe.

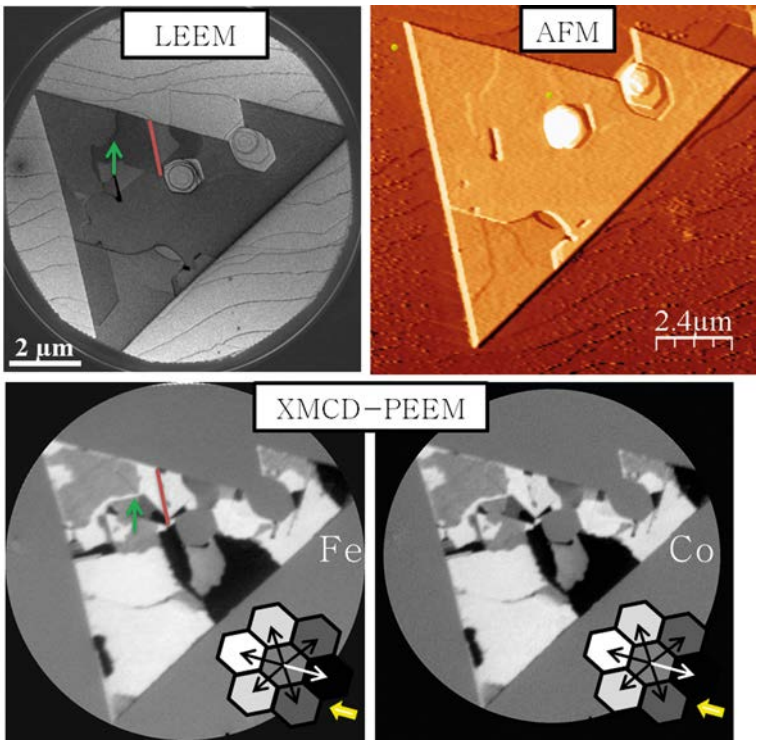


Figure 17. The figure shows a cobalt ferrite island grown by molecular beam epitaxy. The same island is observed by different tecniques: low-energy electron microscopy, atomic force microscopy and photoemission microscopy in circular dichroism.

Epitaxial growth of spinels on Si (100) through the use of intermediate layers of titanium nitride. Another problem for the use of oxide spinels in spintronic applications is its incompatibility with the fundamental material in microelectronics: silicon. This is due both to the difference in atomic structures between the transition metal oxides and silicon, and, crucially to the chemical differences between them. Therefore, it is necessary to use buffer layers that act as a diffusion barrier to prevent the oxidation of silicon and to adapt the lattice parameters of substrate and film. The collaboration of the research group with Prof. P. Prieto of the Universidad Autónoma de Madrid has focused on the use of titanium nitride films. Films a few nanometers thick of TiN on Si-(100) have been used to grow high quality magnetite films with an epitaxial relationship with the silicon substrate. This result opens the door to the integration of spinel oxides in silicon, and has been shown to work also for cobalt ferrite. The quality of the films is reflected in their strong biaxial magnetic anisotropy. The method of growth employed is sputtering assisted with a second ion beam.

Growth of FeO films on Ru. In collaboration with Dra. M. Castillejo's group of the IQFR, samples up to 20 nm thick of single crystal FeO on Ru (0001) have been grown. For this purpose, the growth has been carried out by pulsed laser deposition in the preparation chamber of the ultrahigh vacuum system available in the group. The growth in the preparation chamber allows to study the samples without exposure to the atmosphere. The specific case of FeO films shows the usefulness of this approach: FeO is rapidly oxidized in air, so it is essential to study in-situ the surfaces so grown.

Growth of cobalt ferrite by deposition of cobalt in a magnetite crystal. An alternative method that we have explored for the growth of cobalt ferrite is to deposit cobalt on a single crystal of magnetite (i.e., iron spinel). By successive annealing steps, cobalt is incorporated deeper into the magnetite crystal. By measuring the magnetic moment of the cobalt atoms and comparing them with first principles calculations, we can follow the location of the Co atoms in the different crystallographic sites available in the spinel structure.

Structural, electronic and magnetic properties of thin films and oxides surfaces

An important part of the group activity has been aimed at identifying the phases of Fe oxides obtained by the techniques described in the previous section. The application of Mössbauer spectroscopy, in its internal conversion electron mode (ICEMS), stands out in its application to thin films. This is the only group in Spain that uses this characterization technique on a regular basis. Mössbauer spectroscopy has also been used to characterize other complex oxides belonging to the perovskite family in collaboration with Prof. F.J. Berry at the Chemistry Department of the University of Birmingham, UK.

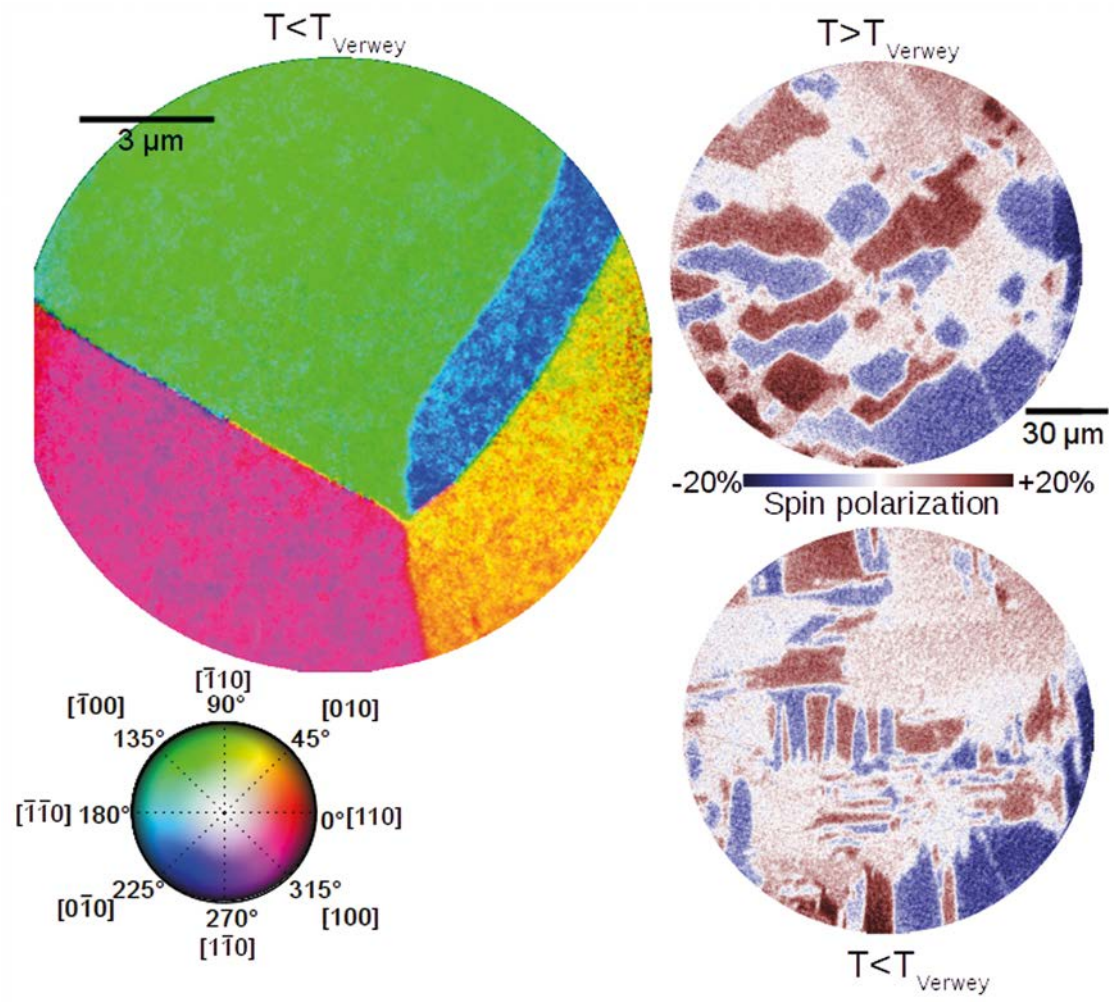


Figure 18. The upper left part of the figure shows an spin-polarized image of the magnetic domains on magnetite below the Verwey transition, where the colors indicate the direction following the color wheel shown below. The right part shows a spin-resolved photoemission image of the domains above (top) and below (bottom) the Verwey transition.

We also highlight in this section the work carried out to characterize the surface magnetization of both oxide (mainly magnetite) surfaces and the films grown in the previous section, using techniques related to the observation of low-energy electrons:

1. By electron microscopy of spin-polarized low-energy electrons (SPLEEM). In this technique, performed in collaboration with Dr. A. K. Schmid of Lawrence Berkeley National Laboratory, the sample to be observed is illuminated by a spin-polarized electron beam. This microscope is available in only a few laboratories around the world. Observation of the reflected beam allows the local component of the magnetization to be determined in the direction in which the incident beam is spin polarized. By changing the spin polarization of the electron beam, a map of the magnetization vector can be obtained with nanometre resolution. This technique has been used to observe the changes of magnetization in the magnetite surface (100) as a function of temperature, and in particular, when crossing the temperature of the metal-insulator transition known as the Verwey transition.
2. By means of photoemission electron microscopy combined with circular dichroism in x-ray absorption. The measurement of dichroism in x-ray absorption allows, taking advantage of the L absorption edges of the transition metals, to estimate the magnetic moment corresponding to a particular element. If a low-energy electron microscope is available, it can be used to perform the measurement with a resolution of ~ 30 nm using the secondary electrons emitted upon x-ray absorption. Thus it has been determined that the iron and cobalt spinel islands whose growth has been mentioned in the previous section have, in remanence, magnetic domains whose extension is up to four orders of magnitude larger than those typically observed in thin films. This technique has also allowed to determine experimentally the magnetic moment of the reconstructed magnetite (100) surface, whose value has been explained based on the detailed structure of this surface, according to the model proposed by the Prof G.S. Parkinson group in the Technical University of Vienna.
3. An additional method of observing magnetic domains is to measure the polarization of the photo-emitted electrons by a surface under illumination by ultraviolet light. This can be done in a photoemission microscope if a spin analyzer is available. There is only one instrument at this time in the world for this purpose. Through collaboration with Dr. Christian Tusche we performed measurements on the surface of magnetite by observing the magnetic domains through the Verwey transition.

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COMPETITIVE FUNDING

National Grants: individual

Ministerio de Economía y Competitividad

Principal Investigator	Title	Reference
Juan de la Figuera	Microscopio de electrones de baja energía para dinámica y crecimiento en superficies	CSIC15-EE-3056

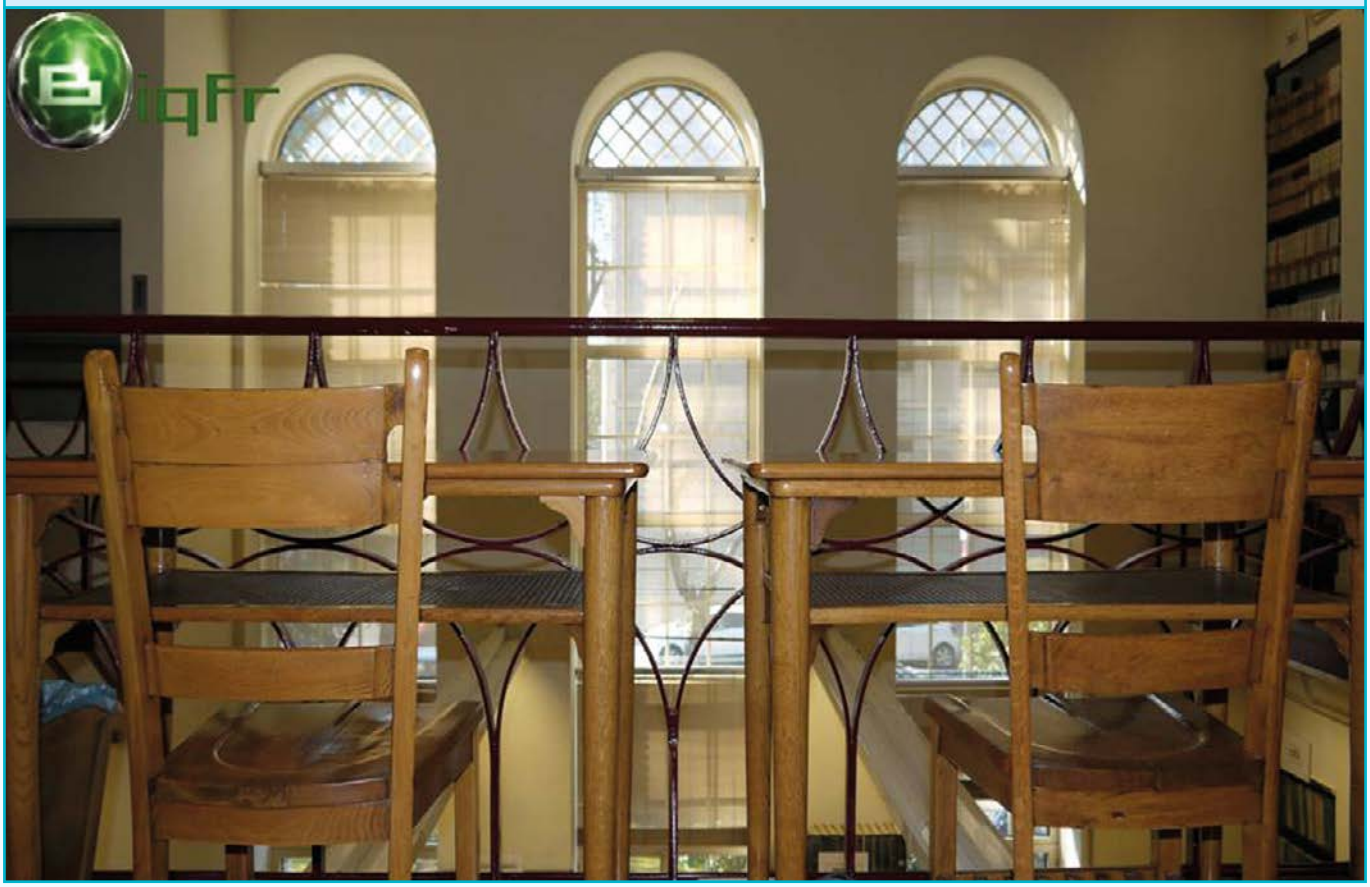
National Grants: coordinated

Ministerio de Economía y Competitividad

Principal Investigator	Title	Reference
Juan de la Figuera (coordinator)	Structural and chemical control at the atomic level of spinel oxide thin films and surfaces	MAT2015-64110-C2-1-P
Juan de la Figuera (coordinator)	Películas ultradelgadas para electrónica basada en óxidos. Crecimiento en tiempo real, efectos de intercara y magnetismo	MAT2012-38045-C04-01

Research Support Services

Library “BIQFR”



Introduction

The Rocasolano Institute of Physical Chemistry was set up in 1946 at same time as the Biqfr. Its holdings come from the "National Institute of Physics and Chemistry" created in 1932. Commonly known as the Rockefeller Institute, it was the cradle of all the research teams in the different disciplines of Chemistry, not only in Madrid, but throughout Spain. Three elements characterize the Biqfr: its Collection, Space and Management.

Collection: Among these old collections-unique in Spain-can be found famous titles such as: Annalen der Physik, Chemische Berichte, Annalen der Chemie. These are scientific journals in which the first advances in physics and chemistry are recorded. The Biqfr holds a valuable holding, mainly journals, of which 113 are complete starting from the first issue, 11 date from the 19th century to our days, and 16 start prior to 1920.

Space: Designed by the architects M. Sánchez Arcas and L. Lacasa (1932), innovators at the time, the library is arranged longitudinally with the rest of the building. It has an easy access from the main entrance and faces South with three large windows illuminating the two floors containing the reading room. This provides a silent and conducive reading environment, according to the architect Antonio Bonet Correa. The floors were communicated inside with original spiral staircase of the "flown boat" style, which was recently replaced by another wooden one. Subsequently, a basement has been added and their rooms refurbished, while retaining the original style. Because of its singular interest the library is the subject of visits by architects from various universities.

Management: At its genesis, the Biqfr was organized in a way that was revolutionary for those days, free access was permitted, and display stands facilitated access to the latest and the previous year's issues of the journals. The main goal has always been the satisfaction of its users. The Biqfr is considered by the scientific community as the Reference Scientific Periodical Library, a historical landmark in the service of innovation, and is obviously one of the most outstanding scientific libraries in Europe. It is a rare example of 80 years of continuous service to Spanish researchers.

Library "Biqfr"

Library Manager

Esperanza Iglesias Fernández

Assistant

Santiago del Olmo Rodríguez

Technicians

Jorge Pariente Moronta
(Until 30/01/2016)
Victoria Garrido Martínez
(from 17/09/2015)
Mª Felipa Arroyo Villa
(from 11/04/2016)

Strategic Aims

- New technologies.
- Visibility and Dissemination:The Blog & Social Networks
- Access to knowledge.
- The Historic Documents Collection of the Institute of Physical Chemitry "Rocasolano" and the Julio Palacios Chair (CSIC)
- Document supply.
- Economic implication.
- Standard management.
- Highlights

Results

New technologies

Since the beginning of technological age, in the 90s, the Biqfr has been aware that the technological changes, that were happening so quickly, provide an opportunity to the library to link it to the concept value. In recent years, this concept has been the mainstay of technical work to ensure that the library is competitive, proactive and even co-creative. By knowing the researchers' perception of the library in relation to the alternatives offered by its competitors (eg. Google), the Biqfr has developed links with scientists, to help researchers achieve their goals. Because of this, the Biqfr has an edge on its competitors.

Let's put it on a timeline!

1994	1995	1997	1998	1999	2001	2004
*eJournlas	*Launching Biqfr Website.	*Chemical Abstracts on CD in collaboration with CTI and Cindoc.	*Electronic documents supplied.	*Reconfiguration of space: 4 rooms.	*SciFinder in collaboration with The Cindoc.	*AtoZ a single portal to access Biqfr e_resources.

2007	2008	2009	2010	2011	2013	2016
*eBooks: acquisition 1371	*AtoZ for eBooks. *Creation of a logo, a brand and a slogan of the Biqfr. *Launch the Biqfr blog	*Brand recognition. *Web 2.0 tools for social networks. *Reward by UE as the best blog *Loan service of eBook readers.	*Organic positioning of the Biqfr brand. *Recognition for Biqfr on social networks. *Virilization of the web content into the blog.	*Insertion of the QR code in every post of the blog. *VPN as ubiquitous access.	*iLumina; Intregrates all Biqfr e_recursos.	*Compilation of the IQFR historical memory and dissemination on the Biqfr Web. *Julio Palacios Website.

Visibility and Dissemination: The Blog & Social Networks

The blog is the key tool for Biqfr dissemination and visibility. The Blog posts news from all areas of science and innovation. Always with the same purpose: trying to democratize "Science" and bring it to the public in a fun and an entertaining way. The interest of our blog's followers remains.

In 2015, due to lack of human resources, only 50 news items were posted on the blog. In addition, in 2016 the activity was resumed, publishing 143 news items. During this biennium, we achieved 46,390 visits to reach a total of 1,578,037 visits. The activity of our followers on the social networks Twitter and Facebook is constant and stable, as is the case with the Blog.

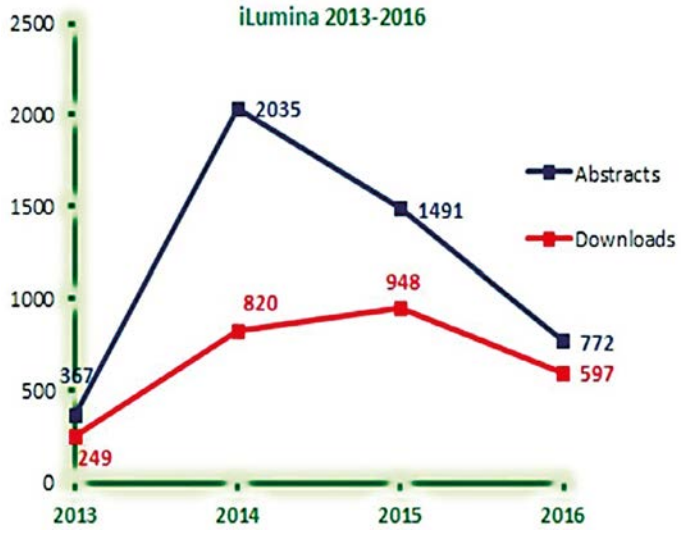
The Biqfr Blog is not only considered a scientific dissemination source in America (Mexico, Colombia, United States and Argentina, Peru, Chile) and Germany, but we have also detected that it begins to attract followers from other European countries (Russia).

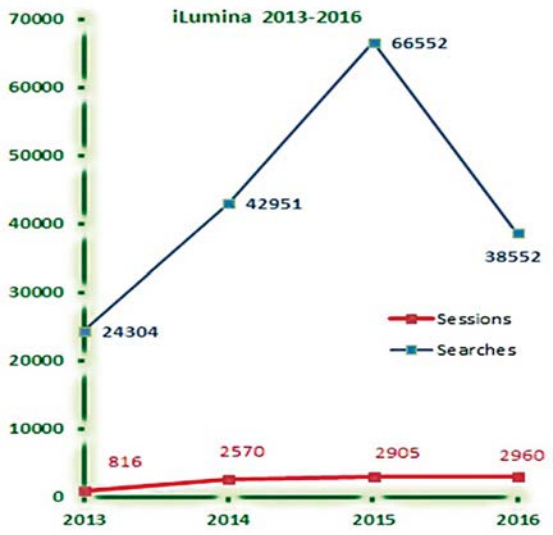
Access to knowledge: iLumina

iLumina is a smart tool to accelerate the search for scientific information, providing a competitive advantage to Biqfr over Google, while saving the user time and mouse clicks. All specialized databases in the fields of Chemistry, Physics and Biomedicine, to which users of the Biqfr have access, are brought together. Through a single search box, with one-click access to PDF or HTML, the user can access full-text content directly through the detailed record or from the result list preview pane. The AtoZ resource manager, can be utilized through the iLumina system, where it is now incorporated. So that "iLumina" was a single entry point to access to scientific information.

During 2015-2016, we were still customizing Ilumina. Observing the results of the statistics, we find that many searches have been made with few queries, in addition, the returned results were analyzed carefully by consulting the abstracts and then the most relevant and applicable search results were downloaded.

Years	Sessions	Searches	Abstracts	Downloads
2015	2.905	66.552	1.491	948
2016	2.960	38.136	772	597





In 2016, the online holds managed through iLunima were 73,853 journals & books, compared to 30,654 resources in 2014. The Biqfr current subscriptions are available online.

iLumina is available from the CSIC's site to the whole Institution, and ubiquitously through the VPN to Biqfr users. Technology for mobile devices is offered.

The Historic Documents Collection of the Institute of Physical Chemistry "Rocasolano"

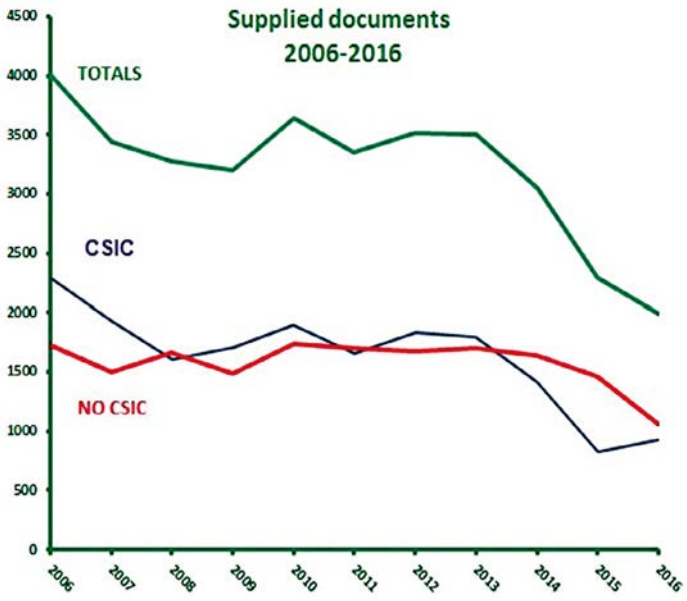
This Institute was created in 1946 and, at that time, the Library took responsibility for preserving the unique scientific documental legacy that was formerly assembled and curated by the Instituto Nacional de Física y Química, a research facility implemented in 1932 by the Junta para la Ampliación de Estudios (JAE). Although this legacy mainly consisted in a collection of Physics and Chemistry books and journals, there was also a large number of written documents, memories, photographs and even films which are of great historical interest. To better preserve and popularize this part of the BIQR funds the Library opened a new section at the web page of the Institute, named Colección de Documentación Histórica del IQFR, in which the digitized version of these written and graphic documents of historic interest would be made easily available to the interested reader.

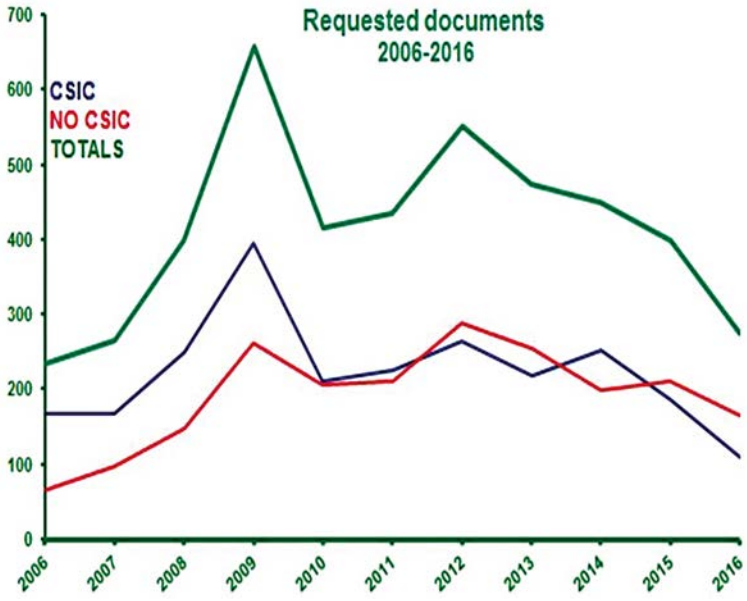
Historic documentation of the Julio Palacios Chair (CSIC)

In 2015 the CSIC funded the Julio Palacios Chair, from an initiative of Dr. J.M. Oliva-Enrich of this Institute, with the specific purpose of contributing to the general knowledge of the life and works of the Spanish scientist Prof. Julio Palacios Martínez (1891-1970). A large fraction of the research activity of Prof. Palacios on different fields of Physics and Mathematics was carried out at the Instituto Nacional de Física y Química (JAE). The BIQFR actively collaborated with this project in different ways from its inception. On one side the Library carried out an extensive compilation of scientific and historic documents relevant to the aims of the Chair. This search was performed in close connection with Prof. Palacios family, which provided a large number of very interesting manuscripts, press articles, photographs, etc. In addition, the Library designed a section on "Documentación" within the web page associated to Prof. Palacios Chair, www.jpalacios.iqfr.csic.es,that contains the digitized results of the compilation mentioned above. Later on, the Library also included within that web page an additional section, named "Galeria", specifically dedicated to graphic documents. More than 350 items were analyzed and digitized for both sections, that included journal papers, books, biographies, letters, press notes, etc.

Document supply: Inter librarian loan (ILL)

The wealth of the Biqfr's holdings satisfies the needs of its direct users, which is verified by the small number of documents requested to other centers and the significant number documents supplied to external centers such as universities, laboratories, and other CSIC centers. In 2015, as expected from modern science, 98% of document transactions were journal articles and only 2% were book loans. Otherwise, in 2016 these books loan declines to 0.48. Remarkably,





the Biqfr supplied 7% of all the shared journal articles within the whole CSIC Library Network.

Over the last 14 years, the average Biqfr ratio of the supplied documents to requested documents is nine. That is to say, the Biqfr supplied 9.3 times more documents than we requested from other centers. In the last years, this value decreased to 7, due to the insertion at the Institute of research lines in the areas of "Life Sciences" whose resources are not directly available to our library. In contrast, on the whole, the CSIC Library Network is slightly beneficiary as it shares 1.2 documents for every document that it requests.

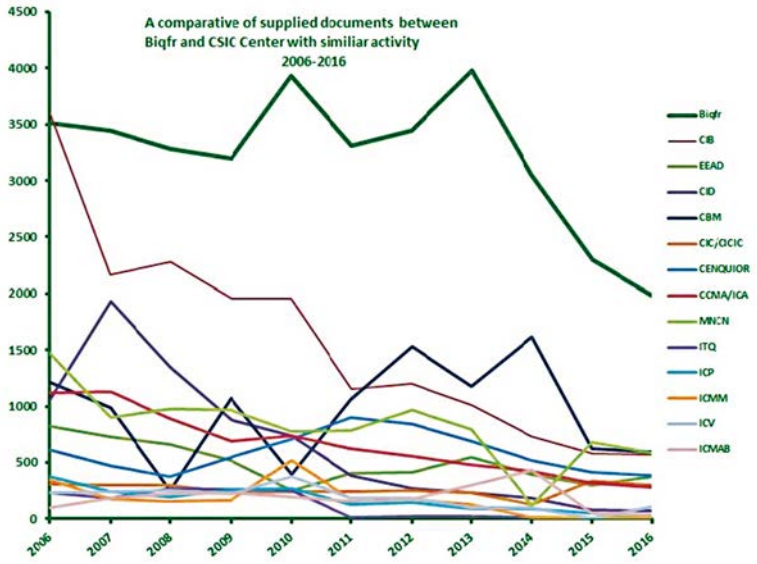
Over the last years, the flow of internal transactions among CSIC libraries has dropped, due to the advance of new technologies and the collective contracting by CSIC of the large packages of electronic resources, provided by the main publishers and other Institutions. 2001-2003 decreased 35%. Furthermore, we should remark that there was a 60% decline between 2006 and 2016. Increasingly, the electronic resources are extended to whole libraries of the Network, reason why the number of transactions decreased, and in their majority belong to the collection in print.

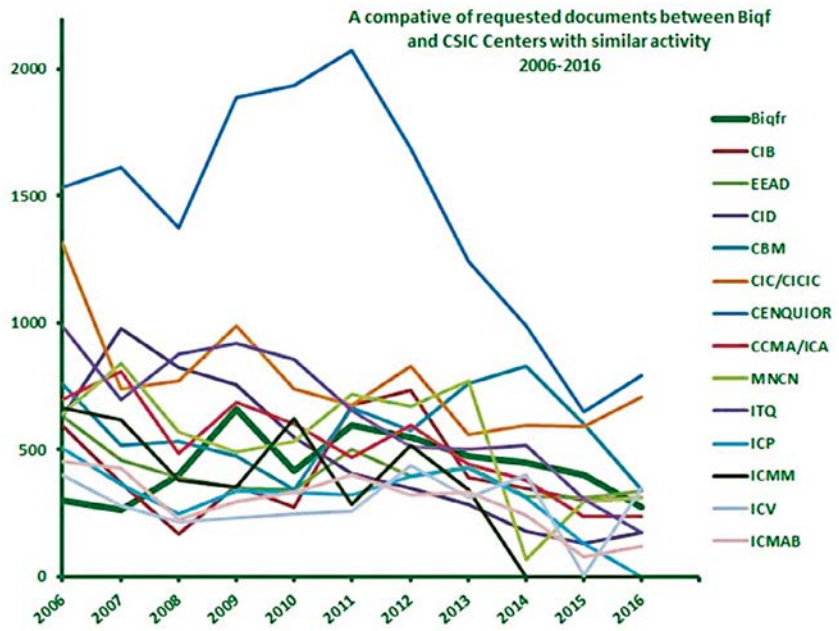
Nevertheless the number of documents supplied to CSIC and other institutions, has decreased with fluctuations.The level of total transactions decreased by 0.3 % in 2013, on the other hand, it decreased in 2014 by 12.8%. However, in 2015 the number of documents supplied to the CSIC centers fell a further 41.3%, which could be reasonably explained by a putative decrease of the CSIC's scientific activity and the closing of libraries at some CSIC centers.

During 2015, the total number of document transactions was 2,698 (both supplied and requested.) Of these, 2.299 documents were delivered (-24.73 % lower than 2014) with 833 being sent to the CSIC's library Network (-41.3% lower than 2014) and 1,466 to other institutions (1.6% higher than 2014). Regarding our requests, 399 documents (-11.3% lower than 2014); were obtained from other libraries, of which 187 (-25.4% lower than 2014) came from CSIC's network and 121 documents (6.5 higher than 2014) were sent by other institutions. 11% documents requested from other libraries were supplied by Subito. Of these 2,698 documents supplied, 2,646 came from journal articles and 52 were book loans.

During 2016 total number of items loaned or borrowed was 2,263, of which 1,989 documents were delivered (-13.5 % lower than 2015) with 925 being supplied to CSIC's library Network (11% higher than 2015) and 1,064 to other institutions (-27.4% lower than 2015). On the other hand, 274 documents (-12.3% lower than 2015) were requested from other libraries, of which 110 (-41.17% lower than 2015) came from CSIC's network and 164 (-22.6 % lower than 2015) were sent by other institutions, with 11.3 % of these documents coming from Surbiton. Of these 2,263 documents supplied, 2,263 came from journal articles, while 11 were book loans.

The number of book loaned to users was 35 in 2015 and 25 in 2016. It showed a decrease of 18.9% compared with 2013-2014.





Economic implications

Our staff has been reduced by one third with one technician retiring and a second on extended leave. The remainder of the staff has been forced to fill gaps while maintaining its activity. In many cases this has been a difficult and arduous task, surpassed only by the goodwill and enthusiasm its members. The situation is further aggravated if you consider that staff is aging and further retirements are planned. This situation can not be extended for much more time without risking a possible closing of the library.

In 2010, Biqfr had a book acquisition budget of 46.430 €. Afterwards, a centralized office, the URICI (Unit of Information Resources for Research) was placed in charge of the acquisition of books for the libraries of the network, and Biqfr has been uninvolved in the selection of books. Furthermore, since 2012 no funds have been allocated acquire new books or journal subscriptions. So, unfortunately, since 2013 no new books related to the IQFR's activity have been incorporated.

Furthermore, most journals are no longer subscribed to in paper, but only in the electronic format. Hence many are unavailable in the print edition, as is the case for the *International Journal of Chemical Kinetics, Chemistry Letters, Russian Chemical Reviews (*devoted to reviews, this is the English version of the legendary Uspekhi Khimii, the flagship of Russian Chemistry) etc. In 2013, due to economic cuts, many electronic resources were not subscribed to by the CSIC Library Network. In 2014 some subscriptions were renovated but all. This change represents an impoverishment of our cultural heritage, because some publishers (IOP, Wiley, Springer, etc.) cut electronic access when the subscription is dropped, even to the years that the journals were purchased in paper.

Currently only 44 journals are subscribed to in print, compared with 169 journals in 2012.

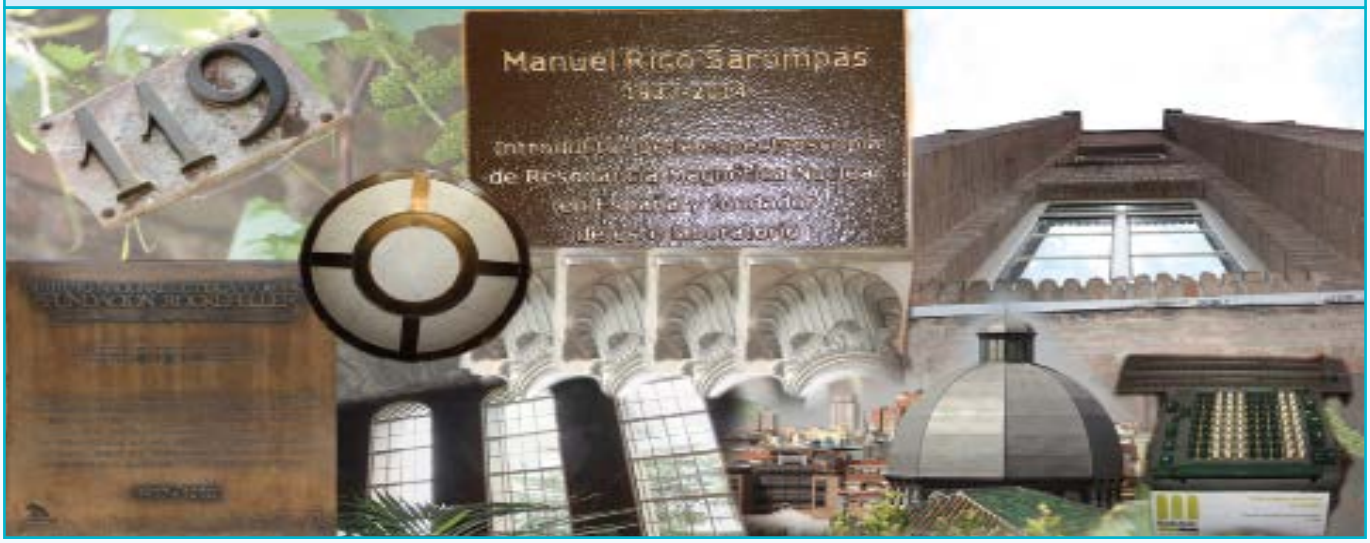
Standard management

The Biqfr has continued the work of technical process, collections control, organization of the holding and signaling, maintaining the reading room service, etc.

The Organization of Courses and Events

Organizer	Type	Title	Date	Place
Biqfr	Workshops	Presentation of ilumina	10/27/2016	IQFR

Administration-Stockroom-Reception



Management and Administration

Manager

Antonio Rubinos Pérez

Administration

Julia Cano García (Paymaster)

Sagrario Salado Rey

Jose Enrique García Ortega

Gloria Alonso Gómez

Pilar Ruiz Lafita

Mª Mar de la Torre Tante

Gloria Pinillos Pérez

Stockroom

Consuelo Martín de Loeches (Stockroom Manager)

Eva María Carpintero Vázquez

Reception

Jose Luis Rodríguez Garro

Mª Carmen González Liceras (from 04/ 08/ 2015 until 31/08/2015)

Esperanza Fiorito Martin-Consuegra (from 01/11/2015 until 31/03/2016)

Ana Mª Contreras Fernández (from 08/ 08/ 2016 until 02/09/2016)

Tomasa Grande Alonso (from 01/11/2016)


CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

Technical Support Units

Electronics Workshop

Pedro Durán Martín (Head until 29/06/2015)

Miguel Rodríguez Artigas(until 31/12/2015)

Pedro Navarrete Badorrey (until 26/ 04/ 2015)

Mechanics Workshop

José Antonio Serna Ferrero

Ignacio Sanz Gómez

Glassblowing Workshop

Nicomedes San Román (until 28/10/2015)

Computer Support

Antonio Diaz Pozuelo

David Armentero Escabias (until 01/ 04/ 2015)

Building Maintenance

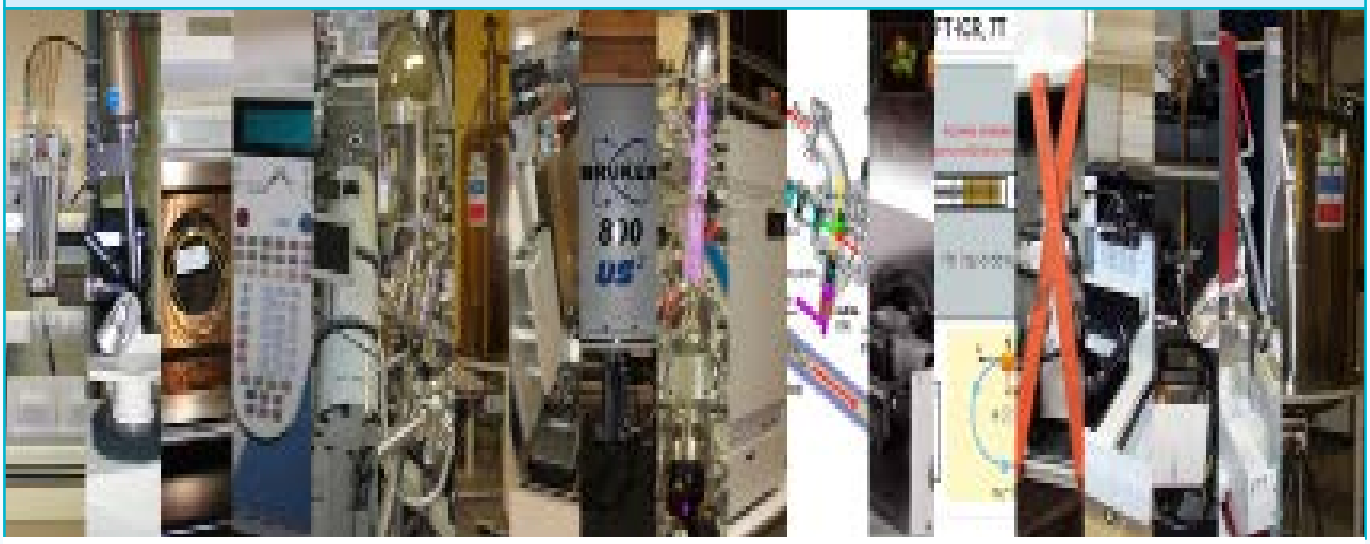
Jesús López Mascaraque (Head)

José Antonio Mulero Bravo

Juan Luis Martínez García


CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

Singular Instrumentation



X-Ray Diffraction Laboratory for Monocrystalline Samples (DRXM)

DRXM (http://www.xtal.iqfr.csic.es/DRXM/) forms part of the Network of Laboratories of Public Research Institutions and offers equipment for:

- crystallization,
- collecting diffraction spectra of monocrystalline samples, and
- if needed (through explicit agreement), structural resolution of the corresponding material.

The laboratory offers these possibilities to all researchers who may need its capabilities, for both small and complex biological crystalline samples (proteins, enzymes).

Head of the Lab:
Armando Albert de la Cruz

Technical Manager:
Juana M. González Rubio

Scientific Committee:
Armando Albert de la Cruz
Juan A. Hermoso Domínguez
Martin Martinez-Ripoll
Julia Sanz Aparicio
José M. Mancheño Gómez
Lourdes Infantes San Mateo

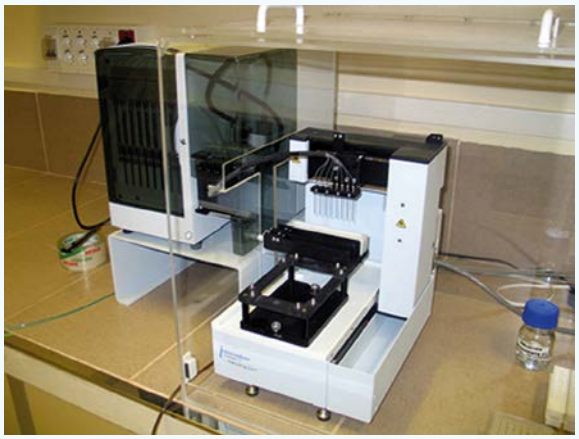
The lab is equipped to carry out diffraction experiments on monocrystalline samples of any origin, inorganic, organic, metal-organic and proteins. The available equipment and its characteristics are shown below:

1. Liquid Dispensers:

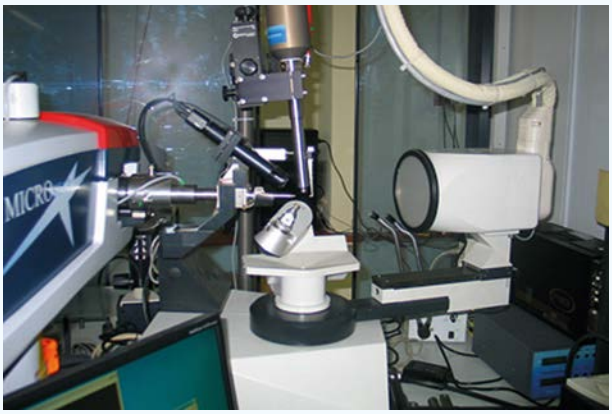
- Robot Liquid Handler Quad-Z 215, Gilson Inc., and
- Robot Nanodrop ExtY, Innovadine,

prepared to scale from milliliters to nanoliters, to perform 96 (or 192) crystallization experiments per plate, minimizing the time of evaporation.

Liquid handler robot Quad-Z 215, Gilson Inc.

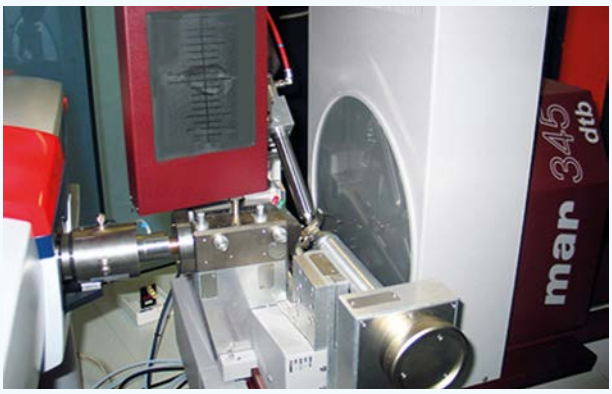


Nanodrop robot ExtY, Innovadine



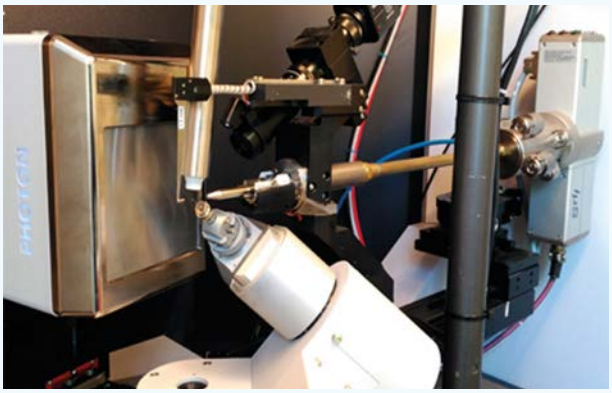
X-ray diffractometer #1

- X-ray source with rotating anode (2.7 kW, MicroStar, Bruker), 100 μ microfocus three times brighter than conventional rotating anodes. CuKα radiation, filtered by Helios (Bruker) mirrors.
- 4-circle goniometer with Kappa geometry and CCD detector (Bruker).
- Cryoprotection system (Oxford Cryosystems) using N_2 stream in the range 350-100 K.



X-ray diffractometer #2

- This equipment shares the X-ray source described in the diffractometer #1.
- Goniometer and detector of type Imaging Plate Mar345dtb (MarResearch).
- Cryoprotection system (Oxford Cryosystems) using N_2 stream in the range 350-100 K.



X-ray diffractometer #3

- X-ray microsource IμS (Bruker) for CuKα radiation, with multilayer optics Elm3 (Bruker).
- 4-circle goniometer with Photon detector (Bruker).
- Cryoprotection system (Oxford Cryosystems) using N_2 stream in the range 350-100 K.

GC-MS system

- Gas chromatograph coupled to a quadrupolar mass spectrometer, fitted with sample introduction systems for liquids and gases.

(Responsible: Rosa Becerra Arias)

Gas chromatographs

- Gas chromatographs for capillary and packed columns, with flame ionization detectors

(Responsible: Rosa Lebrón Aguilar)

MALDI-TOF mass spectrometer

- Matrix assisted laser desorption/ionization-time of flight mass spectrometer,with a mass range in low resolution up to 300.000 u (linear mode) and in high resolution up to 10.000 u (reflector mode).

(Responsible: Rosa Lebrón Aguilar)

LC-MS system

- Liquid chromatograph with a quaternary gradient pump coupled to an ion trap mass spectrometer, with electrospray (ESI) and atmospheric pressure chemical ionization (APCI) interfaces, and with the possibility of tandem mass experiments (MSn).

(Responsible: Rosa Lebrón Aguilar)

Manuel Rico high field NMR laboratory (LMR)

The LMR lab (http://rmn.iqfr.csic.es) has the most advanced techniques in the field of NMR spectroscopy required to address problems involving macromolecular structures and interactions. Our high field spectrometers are the main research tools utilized by the groups of Structure, Dynamics and Interactions of Proteins by NMR (http://rmnpro.iqfr.csic.es) and NMR Spectroscopy of Nucleic acids (http://rmnac.iqfr.csic.es/index.php/es/) to address the questions posed by their research projects. Moreover, the lab operates as a service to external users, from both Spain and Europe, providing the instrumentation, support and the expertise of the specialized staff to resolve their problems in the most efficient manner.

Laboratory director:
Marta Bruix

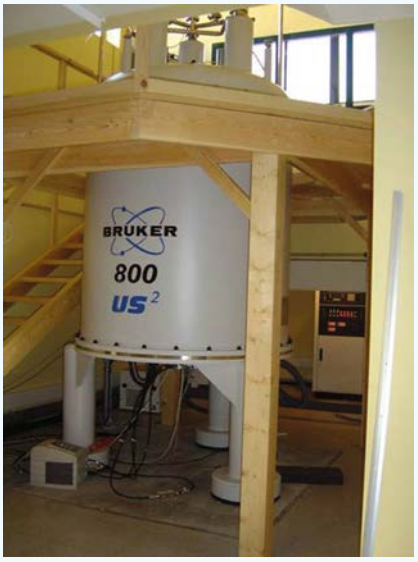
Technical director:
David Pantoja Uceda

Technical staff:
Miguel Treviño, Irene Gómez Pinto, Sergio Camero

Scientific committee:
Carlos González, M. Angeles Jiménez, Douglas V. Laurents, José M. Pérez, S. Padmanabhan.

Spectrometer Bruker AV-600

- Cryoprobe TXI (1H,13C,15N)/Z gradients
- Probe TXI (1H,13C,15N)/5 mm
- Probe TBI (1H,13C, BB)/5 mm/gradient
- Probe TXI (1H,13C,15N)/8 mm/Z gradients
- Probe (1H-BB reverse)/10 mm



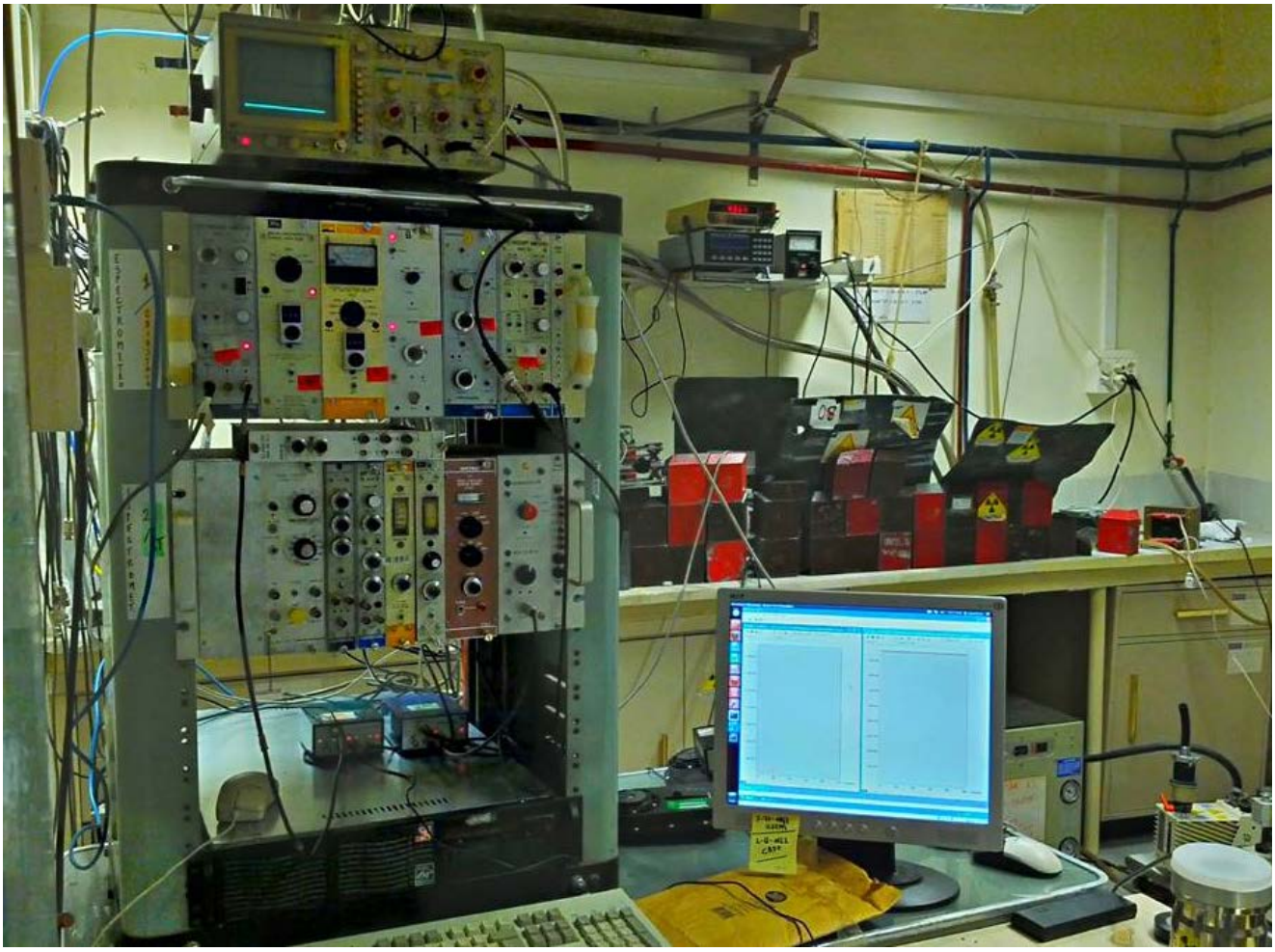
Spectrometer Bruker AV-800 US2

- Cryoprobe TCI (1H,13C,15N)/ Z gradients
- Probe TXI (1H,13C,15N)/5mm/ Z gradients
- Probe QXI (1H, 13C, 15N, 31P)/5mm/ Z gradients

Mössbauer spectrometers

Mössbauer spectroscopy is based on the Mössbauer effect, that is, the emission and resonant absorption of gamma rays by nuclei without loss of energy due to nuclear retreat. Using the spectroscopy Mössbauer spectroscopy can quantify the magnitude of hyperfine interactions. From the quantification of these interactions, which depend on the medium in which the Mössbauer atom is located, one can obtain chemical, structural and magnetic information. For example, the oxidation state, the coordination type or the magnitude of the hyperfine field can be easily determined if there is any type of magnetic arrangement.

Contact: José F. Marco




CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

IQFR Facts and Figures

Formación Académica:

Technology Transfer and Socio-Economic Impact:

Academic Training

PhD awardees

Name	Department	Date	University	Thesis title
María Ángela Sainz Polo	Cristalografía y Biología Estructural (Juliana Sanz Aparicio)	16/11/2015	Complutense de Madrid	Molecular mechanisms of enzymes that process the plant cell wall
Teresa Domínguez Gil-Velasco	Crystallography J.A. Hermoso	02/12/2016	Complutense de Madrid	Antibiotics resistance mechanisms: structural biology of proteins involved in bacterial cell-wall recycling of P. aeruginosa
Noelia Bernardo García	Crystallography J.A. Hermoso	14/09/2015	Complutense de Madrid	Structural biology of two new families of bacterial surface proteins involved in infection and bacterial cell-wall regulation
Javier Gutiérrez Fernández	Crystallography J.A. Hermoso	25/03/2015	Complutense de Madrid	Characterization of proteins involved in synthesis, degradation and binding of bacterial peptidoglycan. Implications in virulence and antibiotics resistance in S. pneumoniae.
Fco. Javier González Alonso	Structure, Energy and Chemical Reactivity	24/11/2015	Universidad Complutense de Madrid	Energetics and interactions of simple and macromolecular species with fundamental, biological and technological relevance
Héctor Zamora Carreras	M.A. Jiménez M. Bruix	16/12/2016	UCM	Investigaciones sobre reconocimiento molecular mediante RMN: estructura e interacciones de péptidos y proteínas
Miguel Mompeán	D. V. Laurents	20/11/2015	UAM	Structural and computational studies of amyloids and noxious folds in biomolecules
Aránzazu Gallego García	S. Padmanabhan	21/12/2015	UMU	Función de la proteína CdnL en las bacterias *Myxococcus xanthus* y *Caulobacter crescentus*

Name	Department	Date	University	Thesis title
Javier A. Martínez Fernández	María Gasset Vega	18/12/2015	Complutense of Madrid	Modulators of amyloid formation and structural diversity
Santiago García Sánchez	Departamento de Ciencias de la Computación, Arquitectura de la Computación, Lenguajes y Sistemas Informáticos y Estadística e Investigación Operativa (Pablo Chacon Montes y Raul Cabido Valladolid)	01/06/2015	Universidad Rey Juan Carlos	Optimización de procesos de ajuste en microscopía electrónica y cribado virtual de proteínas mediante arquitecturas gráficas
Erney Ramirez-Aportela	Departamento de Física de Materia condensada	12/12/2016	Universidad Autónoma de Madrid	Dinámica de los Filamentos de FtsZ y Búsqueda Racional de Inhibidores Sintéticos con Actividad Antibacteriana
Palma Rico Lastres	Margarita Menéndez	05/11/2015	Complutense de Madrid	Structural and functional characterization of *Streptococcus pneumoniae* glucosaminidase LytB
Dr. Miguel Garavís	Carlos González Alfredo Villasante	18/02/2015	Universidad Autónoma de Madrid	Estructuras no canónicas de ácidos nucleicos en telómeros y centrómeros
Dr. Miguel A. Mompeán	Douglas V. Laurents Carlos González	20/11/2015	Universidad Autónoma de Madrid	Structural and computational studies of amyloids and noxious folds in biomolecules
Gonzalo Durán Sampedro	/Department of Organic Chemistry 1, Faculty of Chemistry, Univ. Complutense Madrid (Inmaculada García-Moreno Gonzalo; Mª Josefa Ortiz García; Antonia Rodríguez Agarrabeitia)	14/07/2015	Complutense de Madrid	Organic dyes for laser and biophotonic applications

Name	Department	Date	University	Thesis title
Susana Pérez Fernández	Marta Castillejo Striano	29/01/2016	Universidad internacional Menéndez Pelayo-CSIC.	Nanoprocesado láser de polímeros y biopolímeros
Jing Cui	Esther Rebollar González and Aurora Nogales Ruiz	21/11/2016	Universidad Complutense de Madrid. Facultad de Ciencias Físicas.	Nanoestructuración y propiedades de superficies de polímeros con aplicaciones en energía
María Eugenia Corrales	Rebeca de Nalda Mínguez and Luis Bañares Morcillo	22/01/2016	Universidad Complutense de Madrid. Facultad de Ciencias Químicas.	Efectos estructurales y control láser de dinámicas moleculares ultrarrápidas
Ignacio López Quintás	Marta Castillejo Striano and Margarita Martin Muñoz	24/10/2016	Universidad Complutense de Madrid. Facultad de Ciencias Químicas.	Caracterización y control de plasmas de ablación láser para la síntesis de nuevos materiales y como medios ópticos no lineales
Alberto Gallardo Sanz	Noé García Almarza	19/02/2015	UNED	Study of inhomogeneous fluids in slit-like systems and disordered porous media
Jakub Pekalski	Noé García Almarza	15/12/2015	Polish Academy of Sciences	Effect of boundary conditions on self-assembly
Vicente Sánchez Gil	Eva González Noya	25/01/2016	UAM	Reverse Monte Carlo modeling and Monte Carlo simulations of adsorption processes on zeolites
Cecilia Bores Quijano	Enrique Lomba García	17/03/2016	UAM	Modeling Simple and Complex Fluids Under Confinement

PhD fellowship/contract holders

Department of Crystallography and Structural Biology

Name	Funding body	Starting date	Supervisor
María Ángela Sainz Polo	CSIC	01/01/2010-30/06/2015	Juliana Sanz Aparicio
Mercedes Ramírez Escudero	MINECO	01/01/2012-Actualidad	Juliana Sanz Aparicio
Juan Luis Benavente Fernández	MINECO	01/02/2016-31/12/2016	Armando Albert de la Cruz
María Moreno Alvero	MINECO	01/01/2016-31/12/2016	Armando Albert de la Cruz
Elsa Franco-Echevarria	MINECO	01/07/2013-31/12/2016	Beatriz González
Noelia Bernardo García	MINECO	01/12/2009-15/09/2015	J.A. Hermoso
Alejandra Carriles Linares	MINECO	29/10/2015-presente	J.A. Hermoso
Teresa Domínguez Gil-Velasco	MINECO	01/12/2012-31/12/2016	J.A. Hermoso
María Teresa Batuecas Mordillo	MINECO	01/12/2015- presente	J.A. Hermoso
Jesús Fernández Zapata	FPI, MINECO	01/01/2014-31/12/2017	S. Padmanabhan
Belén Chaves	MINECO 31/12/2019	Inicio-Fin 01/01/2016- J.M. Pérez	M.A. Jiménez
Aránzazu Gallego García	MINECO	02/10/2014-30/06/2016	S. Padmanabhan
Angélica Inés Partida Hanon	CONACYT	01/09/2015-30/11/2018 M. Bruix	M.A. Jiménez
Erney Ramirez-Aportela BFU2016-76220-P	Contrato Proyecto	01/01/2015 -31/12/2016	P. Chacon
Miguel Ángel Sacristán Fernández		23/05/2016-22/08/2016	M.P. Lillo
Radoslaw Borowski	UE, Marie Curie Actions	01/09/2013-31/08/2016	Dolores Solís
Cristina Gallego Páramo			Margarita Menéndez
Ioanna Kalograiaki	UE, Marie Curie Actions	01/08/2012-31/07/2015	Dolores Solís
Lara López Merino	UE, Marie Curie Actioes	16/02/2015-15/02/2016	Dolores Solís
Israel Serrano	FPI- MINECO	Inicio-01/12/2015	Carlos González
Miguel Garavís	FPI- MINECO	Final-01/06/2015	Carlos González

Department of Low Dimensional Systems, Surfaces and Condensed Matter

Name	Funding body	Date	Supervisor
Ignacio López Quintás	Subdirección General de Proyectos de Investigación (Mº de Economía y Competitividad), FPI	01/09/2012- 31/08/2015	Marta Castillejo Striano y Margarita Martin Muñoz
Gonzalo Durán Sampedro	FPI	1/08/2011-31/07/2015	Inmaculada García-Moreno y Mª José Ortiz
Laura Martín-García	FPI (MINECO)	01/01/2014-31/06/2017	Juan de la Figuera y Jose F. Marco

Post-doctoral fellowship/contract holders

Department of Crystallography and Structural Biology

Name	Funding body	Starting date	Supervisor
Antonio Chaves Sanjuán	Ministerio de Economía y Competitividad	1/10/2014-31/08/2015	María José Sánchez-Barrena
Ivan Acebrón	MINECO	1/12//2013-31/10/2015	J.A. Hermoso
Martín Alcorlo Pagés	MINECO	01/01/2015-presente	J.A. Hermoso
Rafael Molina Monterrubio	NIH	01/10/2015-presente	J.A. Hermoso
Carol Siseth Martínez Caballero	MINECO	01/03/2016-presente	J.A. Hermoso
Ivanna Rivera Espinosa	CIATEJ	27/07/2015-presente	J.A. Hermoso
Concepción García Montañés	MINECO	01/12/2015-presente	J.A. Hermoso
Noelia Bernardo García	MINECO	15/09/2015-17/02/2017	J.A. Hermoso

Department of atmospheric chemistry and climate

Name	Funding body	Starting date	Supervisor
Carlos Alberto Cuevas Rodríguez	MINECO	III-2013	Alfonso Saiz López
Pablo Corella Aznar	MINECO	III-2015	Alfonso Saiz López
Shanshan Wang	EU	II-2015	Alfonso Saiz López
Paul Smith	MINECO	IX-2016	Alfonso Saiz López
Nuria Benavent Oltra	AARHUS UNIVERSITY	XI-2015	Alfonso Saiz López
David García Nieto	Comunidad de Madrid	VI-2015	Alfonso Saiz López
Fernando Serranía Alarcón	MINECO	XI-2015	Alfonso Saiz López
Antía Carmona Balea	MINECO	XI-2015	Alfonso Saiz López
Caterina Juan Vicente	MINECO	XI-2015	Alfonso Saiz López
María Muñiz Unamunzaga	MINECO	XI-2015	Alfonso Saiz López

Department of biological physical chemistry

Name	Funding body	Starting date	Supervisor
Soraya Serrano	Proyecto RTC-2014-1458-1	01/03/2015 31/08/2015	M. A. Jiménez
Concepción Solanas	Proyecto RTC-2014-1458-1	15/12/2015 30/04/2016	M. A. Jiménez
Aránzazu Gallego	Proyecto BFU2012-40184-C02-02	2/10/2014 30/06/2016	S. Padmanabhan
Miguel Mompeán	Proyecto SAF2013-49179-C2-2-R	15/01/2016 31/08/2016	D.V. Laurents
J.R. Lopéz-Blanco	Contrato Proyecto BFU2016-76220-P	01/01/2015 - 31/12/2016	P. Chacon
Mónica Álvarez Pérez	MINECO	Until 26/04/15	Dolores Solís
Noemí Bustamante Spuch	CIBERES		Margarita Menéndez
Mª Asunción Campanero Rhodes	UE MINECO	Until 29/02/2016 Since 01/07/2016	Dolores Solís Dolores Solís
Manuel Iglesias Bexiga	CIBERES		Margarita Menéndez
Begoña Morales Juanós	UE	Until 31/10/2016	Dolores Solís
Palma Rico Lastres	MINECO UE	Until 06/05/15 07/01/2016-02/05/2016	Margarita Menéndez Dolores Solís
Irene Gómez-Pinto	MINCEO	01/02/2015	Carlos González 30/06/2016

Department of Low Dimensional Systems, Surfaces and Condensed Matter

Name	Funding body	Starting date	Supervisor
Ignacio López Quintás	Subdirección General de Proyectos de Investigación (Mº de Economía y Competitividad)	01/07/2016-01/01/2017	Marta Castillejo Striano
Esther Carrasco Burgos	European Union, Project: Integrated Platform for the European Research Infrastructure ON Cultural Heritage, IPERION CH	01/11/2015 - 16/01/2017	Marta Castillejo Striano
Mikel Sanz Monasterio	Subdirección General de Proyectos de Investigación (Mº de Economía y Competitividad) y Consejería de Educación – Comunidad Autónoma de Madrid	01/11/2015 - 31/12/2016	Marta Castillejo Striano
Margarita Hernández González	Project Contract MINECO	01/05/2016 - 31/12/2016	Esther Rebollar González
Luis Cerdán Pedraza	Project Contract	Inicio: 16/07/2016	Inmaculada García-Moreno Gonzalo
Raquel Gargallo Caballero	Project MAT2015-38045-C04-01	1/3/2015-31/8/2016	Juan de la Figuera
Vicente Sánchez Gil	CSIC	01/09/2011-30/09/2015	Eva González Noya
Cecilia Bores Quijano	MINECO	01/12/2011-30/11/2015	Enrique Lomba García

Scientist exchange

Name	Home institution	Destination institution	Dates	Department
Loreto Martínez González	CIB, CSIC	IQFR, CSIC	01/12/2015-actualidad	DCyBE
Rogeria Nunes Costa	Univ. Federal de São Paulo (Brasil)	IQFR/CSIC	02/04/2016–07/10/2016	DCyBE
Lourdes Infantes	IQFR/CSIC	CCDC Cambridge, UK	31/07/2015–14/08/2015 08/08/2016–19/08/2016	DCyBE
Pablo Corella Aznar	CSIC	University of Manchester	From X-2016 to II-2017	Química Atmosférica y Clima

Departament of Structure, Energy and Chemical Reactivity/ Atmospheric chemistry and climate

Name	Home institution	Destination institution	Dates
Ana Valderrama-Negrón	Univ. Nac. Ingeniería (Perú)	IQFR/CSIC	19/01/2015-13/02/2015
Juan Z. Dávalos	IQFR/CSIC	Univ. Nac. Ingeniería (Perú)	14/02/2015-14/03/2015
Juan Z. Dávalos	IQFR/CSIC	Sincrotrón LNLS (Brasil)	14/06/2015-19/06/2015
Juan Z. Dávalos	IQFR/CSIC	Univ. Nac. Ingeniería (Perú)	12/09/2015-16/10/2015
Julio Barrios	Univ. Nac. Ingeniería (Perú)	IQFR/CSIC	02/11/2015-29/12/2015
Gastón Perdomo	Univ. Puebla (México)	IQFR/CSIC	15/06/2015-15/09/2016
Franco Centurión	Pontificia Univ. Católica (Perú)	IQFR/CSIC	01/03/2016-07/05/2016
Juan Z. Dávalos	IQFR/CSIC	Univ. Nac. San Cristóbal de Huamanga (Perú)	18/04/2016- 22/04/2016
Juan Z. Dávalos	IQFR/CSIC	Univ. Nac. Ingeniería (Perú)	14/11/2016- 02/12/2016
Joel Fallaque	Univ. Nac. Ingeniería (Perú)	IQFR/CSIC	06/09/2016- 09/01/2017

Department of biological physical chemistry

Name	Home institution	Destination institution	Dates	Departmentt
Joana Dantas	U. Nova de Lisboa	IQFR	1/05/2016-8/05/2016	QFB
Hector Zamora	IQFR	IBG-KIT center	1/09/2015-5/11/2015	QFB
Sezgin Kara	IBG-KIT center	IQFR	04/05/2015-08/05/2015	QFB
Mar Forner	Universidad Pompeu-Fabra	IQFR	09/05/2016-13/05/2016	QFB
Roberto Silva Rojas	UCM	IQFR	01/2015-06/2015	QFB
Jesús Fernández Zapata	IQFR-CSIC	Centro Andaluz de Biología del Desarrollo (CABD)-CSIC, Sevilla	03/05/2016-02/08/2016	QFB
Federica Dommarumma	U. de Napoli	IQFR	7/09/2016-21/12/2016	QFB
Carlos A. Salgueiro	U. Nova de Lisboa	IQFR	14/12/2016-18/12/2016	QFB
P. Chacon	IQFR	U.C. Berkeley	01/05/2015-25/09/205	QB3 Berkeley
Radoslaw Borowski	Instituto de Química Física Rocasolano	Centro de Investigaciones Biológicas	25/11/2015-18/12/2015	Biología Química y Física
Giulia Cazzanelli	Centro de Biologia Molecular e Ambiental, Universidade do Minho	Instituto de Química Física Rocasolano	04/04/2016-08/04/2016 13/07/2016-27/07/2016	Química Física Biológica
María de la Soledad Escolano Martínez	Centro Nacional de Microbiología, Instituto de Salud Carlos III	Instituto de Química Física Rocasolano	21/11/2016 -22/12/2016	Química Física Biológica
Bartomeu MIR	UB	IQFR	02/11/2016-11/11/2016	QFB
Bartomeu MIR	UB	IQFR	10/04/2016-15/04/2016	QFB

Department of low dimensional systems, surfaces and condensed matter

Nombre	Institución Origen	Institución Destino	Fechas
René Israel Rodríguez Beltrán	Universidad de Salamanca	IQFR/CSIC	05/10/2016-18/12/2016, 24/02/2016-04/03/2016, 18/04/2016-03/06/2016, 16/08/2016-26/08/2016, 05/09/2016-04/11/2016
Juan de la Figuera	IQFR	Lawrence Berkeley Nat. Lab.	24/7/2015-28/8/2015

Nombre	Institución Origen	Institución Destino	Fechas
Juan de la Figuera	IQFR	Sincrotrón Alba	10/3/2015-15/3/2015, 4/5/2015-8/5/2015, 18/5/2015-22/5/2015, 8/9/2015-17/9/2015, 5/11/2015-8/11/2015, 23/12/2015-25/12/2015 28/3/2016-1/4/2016, 27/6/2016-1/7/2016, 7/8/2016-24/8/2016, 17/10/2016-21/10/2016, 1/6/2015-6/6/2015 2/11/2016-6/11/2016,
Juan de la Figuera	IQFR	Max Planck Institute for Microstructure Physics, Alemania	
Jose F. Marco Sanz	IQFR	Universidad de Chile y USACH, Chile	3/10/2015-24/10/2015, 28/3/2016-11/4/2016, 27/6/2016-18/72016, 27/9/2016-12/10/2016
Laura Martín-García	IQFR	Lawrence Berkeley Nat. Lab.	23/5/2015-25/7/2015
Laura Martín-García	IQFR	Marie Curie-Sklodowska University, Polonia	23/5/2016-23/6/2016
Laura Martín-García	IQFR	Sincrotrón Alba	8/9/2015-17/9/2015
Raquel Gargallo Caballero	IQFR	Sincrotrón Alba	18/5/2015-22/5/2015
Claudia Andrea Yañez Soto	Universidad de Chile, Chile	IQFR	18/1/2015-19/2/2015, 29/8/2016-4/9/2016
Juan Luis Gauthier	U. de Santiago (USACH), Chile	IQFR	13/9/2016-26/9/2016
Alexandre P. Furlan	UFRGS (Brasil)	IQFR	01/01/2016-30/07/2016

Courses and scientific meeting organization

Organizer	Class	Title	Date	Place
María José Sanchez-Barrena	Congreso Bienal de la RSEQ	Simposio S16 "Chemistry and Crystallography: Matter and Life with Atomic Precision"	23/07/2015	La Coruña, España
J.A. Hermoso A. Albert	Workshop	Macromolecular Crystallography School	25/05/2016-29/05/2016	IQFR, Madrid
J.A. Hermoso A. Albert	Workshop	Macromolecular Crystallography School	18/05/2016-23/05/2016	IQFR, Madrid
M. Martínez-Ripoll L. Infantes	Workshop	Cambridge Structural Database, CSD	21-23/09/2016	URICI, Madrid
Rosa Lebrón Aguilar	Specialization course	Cromatografía de Líquidos acoplada a la Espectrometría de Masas. 2015	5-8/10/ 2015	Instituto de Química-Física "Rocasolano" (Madrid)
Rosa Lebrón Aguilar	Specialization course	Cromatografía de Líquidos acoplada a la Espectrometría de Masas. 2016	14-17/11 /2016	Instituto de Química-Física "Rocasolano" (Madrid)
Josep M. Oliva		Cátedra "Julio Palacios"	01/03/2015 31/05/2015	IQFR/CSIC
Juan Z. Dávalos P.	Specialization course	Energética, estructura y reactividad molecular: Herramientas teórico/ experimentales de última generación	14/02/2015 14/03/2015	Fac. Ciencias, Univ. Nac. Ingeniería (Perú)
Juan Z. Dávalos P.	Specialization course	Energética y reactividad molecular: un enfoque teórico/ experimental	08-12/06/2015	Fac. Ciencias Univ. Nac. Ingeniería (Perú)
Juan Z. Dávalos P.	Specialization course	Métodos computacionales específicos utilizando funcionales DFT (M05, M06) para el estudio de especies orgánicas y organometálicas	12/09/2015 16/10/2015	Fac. Ciencias, Univ. Nac. Ingeniería (Perú)
Juan Z. Dávalos P.	Specialization course	Curso Internacional Teórico-Práctico "Química Computacional Básica"	18-22/04/2016	Fac. Ing. Química y Metalurgia, UNSCH (Perú)
Juan Z. Dávalos P.	Workshop	Trabajos de Investigación sobre la Aplicación de la Química Computaciona	02/05/2016	Univ. Nac. Ingeniería (Perú)
Juan Z. Dávalos P.	Pos-graduate course	Métodos teóricos y experimentales de última generación para el estudio de especies con interés tecnológico y medio ambiental	14/11/2016-02/12/2016	Fac. Ciencias, Univ. Nac. Ingeniería (Perú)

Department of biological physical chemistry

Organizer	Class	Title	Date	Place
M. Bruix	Organising Committee	Congreso GERMN	27/06/2016 29/06/2016	Valencia
M. Bruix	Organising Committee	Congreso SBE	10/06/2015 12/06/2015	Granada
M. Bruix	Organising Committee	Congreso SBE	15/06/2016 17/06/2016	Oporto
D.V. Laurents	Coordinator	Semana de la Ciencia en el IQFR CSIC	3/11/2015 13/11/2015	Madrid
D.V. Laurents	Coordinator	Semana de la Ciencia en el IQFR CSIC	8/11/2016 18/11/2016	Madrid
D.V. Laurents	Coordinator	II Simposio de Investigadores Jóvenes del IQFR CSIC	26/02/2015	Madrid
D.V. Laurents	Coordinator	III Simposio de Investigadores Jóvenes del IQFR CSIC	29/02/2016	Madrid
D.V. Laurents	Coordinator	II Encuentro Científico IQFR CSIC	25/11/2015	Madrid
Dolores Solís	Course	Chemical Glycobiology & Biomedicine. Module III: Lectins	04/02/2015	CIC bioGUNE
Dolores Solís	Scientific Conference	GLYCOPHARM Final Conference	27-29/07/2016	Instituto de Química Física Rocasolano
RANN	Comité organizador	10ª reunión de nucleótidos y nucleósidos	29/06/2015	Barcelona

Department of Low Dimensional Systems, Surfaces and Condensed Matter

Organizador	Tipo	Título	Fecha	Lugar
Blanca Ramirez Barat, Marta Castillejo Striano, Mohamed Oujja Ayoubi, Emilio Cano Diaz, Mikel Sanz Monasterio, David Martinez Bastidas	Doctoral School	1st Iperion-CH Doctoral Summer School. "Advanced Chracterization Techniques, Diagnostic Tools and Evaluation Methods in Heritage Science".	15/07/2016	Instituto de Química Física Rocasolano
Jing Cui, Amelia Linares, Daniel Martínez-Tong, Belén Maté, Esther Rebollar, Álvaro Rodríguez, Igors Sics, Jaime J, Hernández	Scientific Conference	Synchrotron Radiation in Polymer Science 6	7-10/09/2016	CSIC, Madrid
Felipe J. Blas/ Enrique Lomba	Summer School	II Escuela de Simulación Molecular	27/07/2015	UNIA, La Rábida
Manuel M. Piñeiro/ E. Lomba	Workshop	II Wokshop on Molecular Simulation	26/06/2016	Baiona
Rebeca de Nalda Mínguez y Javier Solís Céspedes	National Scientific Conference	USTS2015 – Ultrafast Science and Technology - Spain	24-25 Nov. 2015	Instituto de Química Física Rocasolano
Rebeca De Nalda y José Miguel Mancheño	IQFR Seminars, I 2016-2017		Oct.- Dic. 2016	Instituto de Química Física Rocasolano

IQFR seminars cycles

Speaker	Title	Date
María José Sánchez Barrena	Frequenin/NCS-1 as a pharmacological target for synapse regulation in X-linked mental retardation and autism	17/12/2014
Elsa Franco-Echevarría	Estudios cristalográficos de una IPK de mamífero	29/02/2016
Ioanna Kalograiaki	II Young Investigator Symposium of IQFR: Exploring glycosignatures of pathogenic bacteria: the "sweet" side of biological recognition	26/02/2015
María Asunción Campanero Rhodes	IQFR Seminar Cycle: Bacteria microarrays for exploring pathogen-host interactions	08/04/2015

Speaker	Title	Date
Ioanna Kalograiaki	IQFR Seminar Cycle: Functional glycomics: towards biomedical application	03/06/2015
Ioanna Kalograiaki	IQFR Seminar Cycle: Design microarrays for the screen and evaluation of anti-adhesive agents	15/12/2015
Esther Rebollar González	Estructuras periódicas inducidas por láser en polímeros. Fundamentos y aplicaciones	09/12/2015
Luis Cerdán	Anti-B18H22, a borane shining again	12/11/2015
Juan de la Figuera	Towards antiphase-boundary free spinel-based oxides	2/12/2015

Tecnology Transfer And Socio-Economic Impact

Patents

Authors	Title	Year	Code
Martínez A, Gil C, Campillo NE, Sánchez-Barrena MJ, Mansilla A, Ferrús, A	Aminofenotiazinas para la modulación del número de sinápsis	2015	P201531358
Martínez A, Gil C, Campillo NE, Sánchez-Barrena MJ, Mansilla A, Ferrús, A	Aminofenotiazinas para la modulación del número de sinápsis	2016	PCT/ES2016070649
María Monagas Juan, Fernando Sánchez-Patán, Jesús Eduardo Quintanilla López, Rosa Lebrón Aguilar, Begoña Bartolomé Sualdea, Mirtha Navarro-Hoyos	Extractos fenólicos de uncaria tomentosa L. (uña de gato) que contienen procianidinas, propelargonidinas y flavanolignanos, procedimiento de obtención y sus aplicaciones	2015	ES2478690 B1
Sánchez R, Martínez J, Castro A, Pedrosa M, Quirce S, Rodríguez-Pérez R, Gasset M	Food allergen extracts and methods of producing and using the same	2016	EP1641.1256
Esther Rebollar González, Álvaro Rodríguez Rodríguez, Tiberio Ezquerra Sanz, Mari Cruz García Gutiérrez	Material semiconductor micro- y nano-estructurado, procedimiento de obtención y uso como patrón de calibración	2016	P201630556

Awards and distinctions

Name	Title	Date and place
Antonio Chaves Sanjuán	Xavier Solans award from the RSEQ to the best crystallographic work	2015
J.A. Hermoso	"Manuel Rico- Bruker" Award of the Spanish Society of Biophysics	2015
Juan Z. Dávalos	Medal distinction to scientific merits. Universidad Nacional San Cristóbal de Huamanga	03/10/2015 Ayacucho-Perú
Juan Z. Dávalos	CSIC-award for the scientific merits during the academic 2015/2016 year	30/06/2015 Madrid

Editorial and scientific committees

Participant	Committee/Journal	Role
Juliana Sanz Aparicio	Comission of Biological Macromolecules (CBM) – International Union of Crystallography (IUCr)	Vocal
Armando Albert de la Cruz	Grupo Especializado de Cristalografía y Crecimiento Cristalino-RSEQ y RSEF	Treasurer
J.A. Hermoso	Scientific Committee of the 20th Meeting of the European Biophysical Societies' Association (EBSA)	Vocal
Alfonso Saiz López	Mission Advisory Group of the European Space Agency's Earth Observation Satellite Sentinel-5 Precursor, TROPOMI.	Mission and scientific requirements
Alfonso Saiz López	Scientific Steering Committee of the international Surface Ocean-Lower Atmosphere Study (SOLAS)	Definition of strategic goals: atmospheric chemistry
Alfonso Saiz López	Scientific Report	Editorial Board Member
Alfonso Saiz López	Science, Nature, PNAS, JGR, Geophysical Research Letters, Atmos. Chem. Phys., Environmental Chemistry, NASA, NSF, NRC, DFG, NERC	Reviewer
Alfonso Saiz López	Sesión de halógenos troposféricos en las conferencias AGU 2014 y EGU 2013 y 2014	Coordinador
Juan Z. Dávalos	Revista de la Sociedad Química del Perú	Consulting Commitee Member
Juan Z. Dávalos	REVCIUNI (Fac. Ciencias, UNI-Perú)	Editorial Board Member

Participant	Committee/Journal	Role
Juan Z. Dávalos	J Phys Chem, J Chem Thermodyn, J Phys Org Chem, J Therm Anal Calorim, React Kinet, Mech Cat, J Colloid Interf Sci, Heterocyclic Comm, J Fluorine Chem	Reviewer
M. A. Jiménez	NMR Group (GERMN) of the RSEQ	Treasurer
María Gasset	PLoSOne	Editor
María Gasset	American Alzheimer Association	External evaluator (calls 2015, 2016)
María Gasset	Research Council of Norway	FRIMEDBIO panel 3
María Gasset	Research Council of Austria	External reviewer
María Gasset	Fund for Scientific Research – FNRS	External evaluator
Lillo, M.P.	ISRN Biophysics	Editor
Acuña, A.U.	IUPAC Photochemistry Group	Project member

Media coverage

Nombre	Medio y fecha
Átomos y moléculas de cristal	conCIENCIAS.digital (10/11/2016) http://bit.ly/2eW9sF7
Human centromeric DNA is able to form quadruplex hélices	Atlas of Science (23/12/2015) *http://atlasofscience.org/human-centromeric-dna/*
M. Bruix	Radio Nacional de España interview in the program "A Hombros de Gigantes" (national program) presented and directed by Manuel Seara Valero, with the title: "Resonancia Magnética Nuclear para estudiar biomoléculas sin destruirlas". 14/04/2015
D.V. Laurents	Press Release, CSIC: "Solo un aspecto clave distingue las proteínas que desatan el Alzheimer de las implicadas en consolidar la memoria"
Human centromeric DNA is able to form quadruplex hélices	Atlas of Science (23/12/2015) *http://atlasofscience.org/human-centromeric-dna/*

Scientific Cloister

President: Juan de la Figuera Bayón (Director), Associate Professor

Secretary: Armando Albert de la Cruz (until 24/05/2015) , Professor
Beatriz González Pérez (from 25/05/2015), Assistant Professor

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Claudio Gutiérrez de la Fé,	Professor Ad Honorem (until 03/06/2015)
Martín Martínez Ripoll,	Professor Ad Honorem
Armando Albert de la Cruz,	Professor
Marta Bruix Bayés,	Professor
Angel Costela González,	Professor
Inmaculada García-Moreno Gonzalo,	Professor
Carlos González Ibáñez,	Professor
Juan Antonio Hermoso Domínguez,	Professor
Enrique Lomba García,	Professor
Rafael Notario Bueno,	Professor
Jorge Santoro Said,	Professor (until 30/09/2015)
Rosa Becerra Arias, Associate	Professor
Marta Castillejo Striano, Associate	Professor
Juan de la Figuera Bayón, Associate	Professor
Maria A. Gasset Vega, Associate	Professor
Mª Angeles Jiménez López, Associate	Professor
Jose Francisco Marco Sanz, Associate	Professor
Margarita Martín Muñoz, Associate	Professor (until 31/01/2016)
Subramanian Padmanabhan, Associate	Professor
Alfonso Saiz-López, Associate	Professor
Juliana Sanz Aparicio, Associate	Professor
Mª Dolores Solís Sánchez, Associate	Professor
Pablo Chacón Montes, Assistant	Professor
Juan Z. Dávalos Prado,Assistant	Professor
Pablo Echenique Robba, Assistant	Professor (until 18/06/2015)
Noé García Almarza, Assistant	Professor (+ 05/05/2016)
Clara Gómez Hernández, Assistant	Professor
Eva González Noya, Assistant	Professor
Beatriz González Pérez, Assistant	Professor
Lourdes Infantes San Mateo, Assistant	Professor

Douglas V. Laurents, Assistant	Professor
Rosa Lebrón Aguilar, Assistant	Professor
Mª Pilar Lillo Villalobos, Assistant	Professor
Jose Miguel Mancheno Gómez,	Assistant Professor
Rebeca de Nalda Mínguez,	Assistant Professor
Jose María Oliva Enrich,	Assistant Professor
Jose Manuel Pérez Cañadillas,	Assistant Professor
Jose María Santiuste Bermejo,	Assistant Professor (until 19/03/2015)
Esther Rebollar González, Ramon y Cajal	Contract
Mª José Sánchez Barrera, Ramon y Cajal	Contract (until 11/10/2016)

Board of Institute

President: **Juan de la Figuera Bayón**
Director

Secretary: **Antonio Rubinos Pérez**
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Vice Director

Douglas V. Laurents
Vice Director

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Head of Department of Crystallography and Structural Biology

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Head of Department of Structure, Energy and Chemical Reactivity (until 17/12/2015)

Alfonso Saíz-López
Head of Department of Structure, Energy and Chemical Reactivity (from 18/12/2015)

Marta Bruix Bayés
Head of Department of Biological Physical Chemistry (until 25/05/2016)

Carlos González Ibáñez
Head of Department of Biological Physical Chemistry (from 26/05/2016)

Jose Francisco Marco Sanz
Head of Department of Low Dimensional Systems, Surfaces and Condensed Matter (until 11/05/2015)

Marta Castillejo Striano
Head of Department of Low Dimensional Systems, Surfaces and condensed Matter (from 12/05/2015)

Maria Dolores Solís Sanchez
Personnel Representative (until 05/03/2015)

Jesús López Mascaraque
Personnel Representative (until 05/03/2015)

Plácido Galindo Iranzo
Personnel Representative (from 06/03/2015)

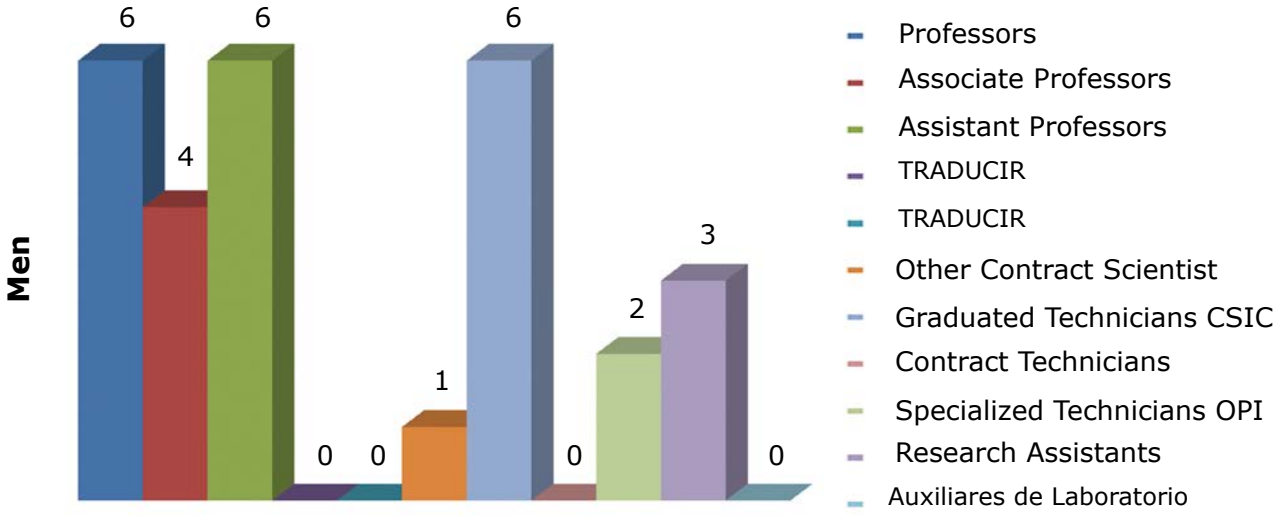
Eva González Noya
Personnel Representative (from 06/03/2015)

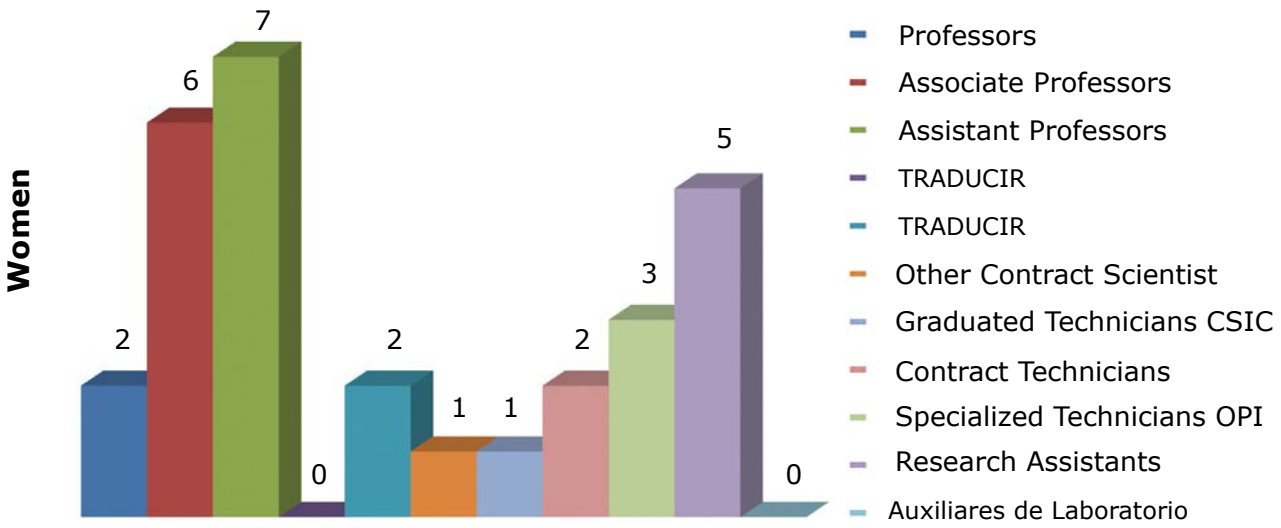
Rebeca de Nalda Mínguez
Personnel Representative (from 06/03/2015)

Sagrario Salado Rey
Personnel Representative (from 06/03/2015)

Gender distribution of scientific staff according to professional category

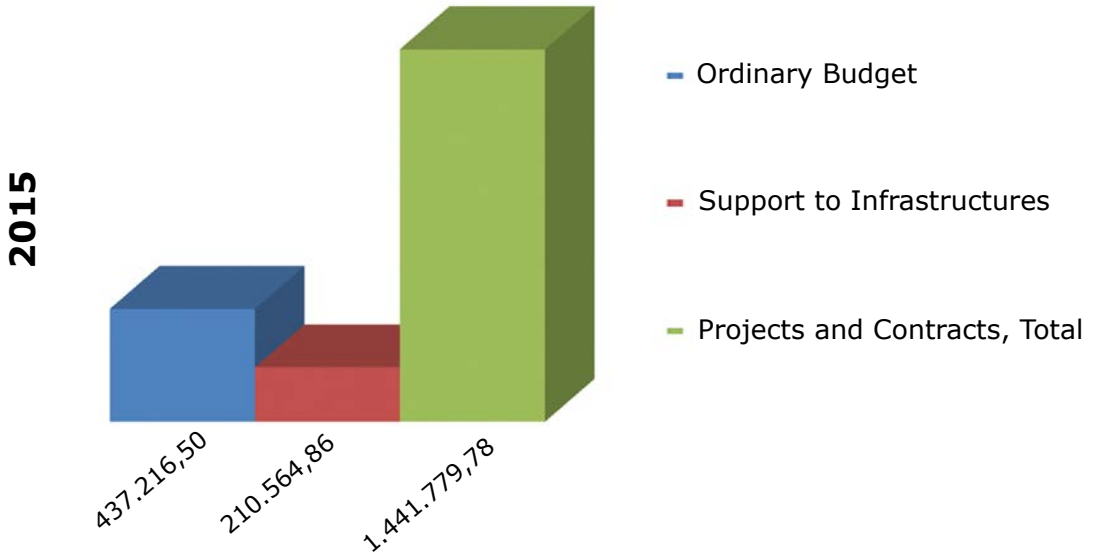
Category	Women	Men
Professors	2	6
Associate Professors	6	4
Assistant Professors	7	6
Scientific Investigators OPI	0	0
Contract Investigators "Ramón y Cajal" programme	2	0
Other Contract Scientists	1	1
Graduated Technicians CSIC	1	6
Contract Technicians	2	0
Specialized Technicians OPI	3	2
Research Assistants	5	3
Laboratory Assistants	0	0
Total	**29**	**28**

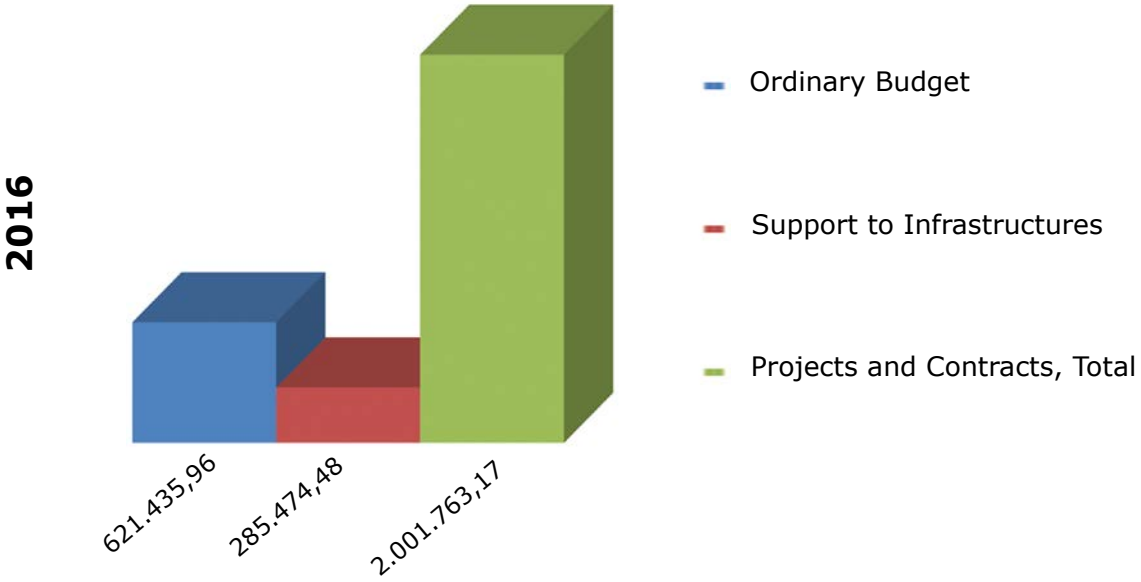




Summary of economic data

Concept	2015	2016
Ordinary Budget	437.216,50	621.435,96
Support to Infrastructures	210.564,86	285.474,48
Projects and Contracts, Total	1.441.779,78	2.001.763,17
Total	**2.089.561,14**	**2.908.673,61**





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