# Activity Report 2017





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# Introduction







Luis M Liz-Marzán
Scientific Director

The Center for Cooperative Research in Biomaterials—CIC biomaGUNE, located in San Sebastián (Spain), was officially opened in December 2006. CIC biomaGUNE is a non-profit research organization created to promote scientific research and technological innovation at the highest levels in the Basque Country, following the BioBasque policy to create a new business sector based on biosciences. Established by the Government of the Basque Country, CIC biomaGUNE constitutes one of the Centers of the CIC network, the largest Basque Country research network on specific strategic areas, having the mission to contribute to the economical and social development of the country through the generation of knowledge and speeding up the process that leads to technological innovation.

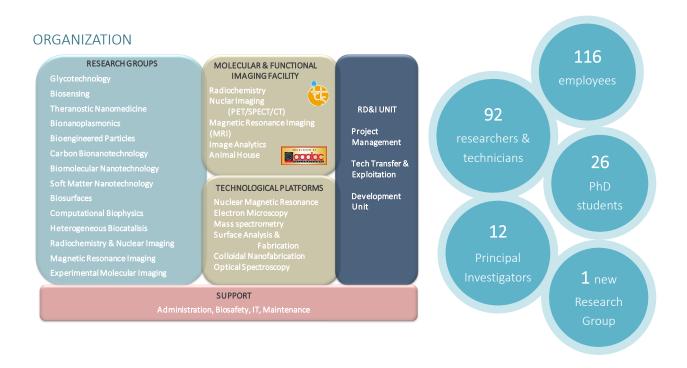
Prof. José M. Mato is the General Director of biomaGUNE since its definition in 2005. The scientific activity started in December 2006, under the direction of Prof. Manuel Martín-Lomas, who took the responsibility to shape the identity of the Center. After an initial phase where the first 8 research teams were selected from the international scientific community, the Molecular Imaging Facility was built and soon approved as a National Facility by the Spanish Government in 2010. The appointment in 2012 of the new Scientific Director, Prof. Luis Liz-Marzán, was considered a landmark that settled the maturity of the Center.

CIC biomaGUNE has established a state of the art research program at the interface between the chemical, biological and physical sciences, with a main emphasis on molecular scale properties and applications of biological nanostructures. The final aim of this programme is to contribute to understanding

the function of biological systems at the molecular and nanometer scale. The main research lines are within the field of design, preparation and characterization of biofunctional nanostructures, to be used in the study of biological processes and the development of biomedical tools.

These research lines include the synthesis and characterization of biofunctional nanoparticles, studies molecular self-assembly, nano-fabrication techniques toward nano-devices, bioconjugation of surfaces and study of interfacial processes, research on basic aspects of interface design and the production of biologically relevant patterns at the nanometer scale for protein-surface and cell-surface interaction studies. Another major area of research is molecular bioimaging, both related to development of contrast agents and to its application in nanomedicine. This basic knowledge may permit, in the long run, to improve the ability to intervene at different disease stages by developing diagnostic methods, "smart" treatments, and triggering self-healing mechanisms. CIC biomaGUNE celebrated its 10<sup>th</sup> anniversary in 2016.

In the course of these ten years, with an average critical mass of around 100 researchers, the Center has obtained national and international recognition as a scientific leader and knowledge builder in the field of biomaterials. Among other achievements, our activity has resulted in the generation of knowledge (publications, patents, PhD theses) the internationalization of research through collaboration with international bodies and institutions, as well as opening our facilities to the scientific community and the industrial sector.



### SCIENTIFIC OUTPUT

During 2017, 162 articles\* in high impact scientific journals have been published.



<sup>\*</sup> Information extracted from Web of Science. Only articles and reviews are considered.

# **FUNDING**

# Competitive public funding

**16** new projects have been launched with a total contribution of **2.9** M€.



# Private funding

Income from private sources amounted **0.5 M€**.



# **TECHNOLOGY TRANSFER**

During 2017, **1** new patent application has been filed, **1** patent has been granted and **8** new agreements have been established with companies.









### RESEARCH AWARDS AND DISTINCTIONS

# **Highly Cited Researchers**

Luis Liz-Marzán, Maurizio Prato and Wolfgang Parak have been included in the 2017 lists of Highly Cited Researchers (Clarivate Analytics), in the fields of Chemistry (Liz-Marzán, Prato) and Materials Science (Liz-Marzán and Parak).

#### JCIS Darsh Wasan Award

Luis Liz-Marzán received the 2017 JCIS Darsh Wasan Award. This annual award was given for the first time in 2007, for outstanding contributions within surface and colloid chemistry. Initially designated the "JCIS Award for Outstanding Life-time Achievements in Surface and Colloid Chemistry," the award has now been renamed the "JCIS - Darsh Wasan Award" in recognition of the achievements of the previous Editor-in-Chief of the Journal of Colloid and Interface Science, during his twenty-two years of service. In the words of the selection committee, Luis Liz-Marzán is "celebrated for his outstanding contributions to a range of topics in surface and colloid chemistry, notably nanoplasmonics".

### European Academy Membership

Luis Liz-Marzán has been elected as a new member of the European Academy of Sciences (EURASC). The European Academy of Sciences carries an important mission to promote excellence in science and technology and their essential roles in fostering social and economic development and progress.

## **IUPAC-Solvay International Award for Young Chemists**

Leonardo Scarabelli, former CIC biomaGUNE PhD student (Bionanoplasmonics Laboratory), has been awarded with the 2017 IUPAC-Solvay International Award for Young Chemists for the best PhD theses in chemical sciences. The award was presented at the 46th IUPAC World Chemistry Congress, Sao Paulo, Brazil, 9 - 14 July 2017.

#### Blaise Pascal Medal

Luis Liz-Marzán has been awarded the Blaise Pascal Medal in Materials Science from the European Academy of Sciences (EURASC), in recognition of his contributions to the understanding of nanocrystal growth and self-assembly, plasmonic properties and sensing applications. The European Academy of Sciences established the Blaise Pascal Medal in 2003 to recognise an outstanding and demonstrated personal contribution to science and technology and the promotion of excellence in research and education. Up to six medals may be awarded in any one year.

#### Young Researcher Award

Marek Grzelczak has been awarded with the 2017 Young Researchers Award from the Spanish Royal Society of Chemistry (RSEQ).

# Recognition to the professional career

The Gipuzkoa Science and Technology Park recognized the professional career of Manuel Martín Lomas, Founding Director of CIC biomaGUNE.

# Journal of Materials Chemistry B Emerging Investigators 2017

Mónica Carril and Fernando López-Gallego, Ikerbasque Fellows at CIC biomaGUNE, named Emerging Investigators in Materials Chemistry by the Royal Society of Chemistry and featured in the 2017 Themed Issue of Journal of Materials Chemistry B. This issue gathers the very best work from materials chemists in the early stages of their independent career. Each contributor was recommended by experts in their fields as carrying out work with the potential to influence future directions in materials chemistry.

# Best doctoral thesis Award of the Carbohydrate Group of the RSEQ

Katarzyna Brzezicka, former CIC biomaGUNE PhD student, awarded with the 2016 prize for the best doctoral thesis of the Carbohydrate Group of the Spanish Royal Society of Chemistry for the thesis entitled "Chemoenzymatic synthesis and immunological studies of xylosylated N-glycans" conducted under the direction of Niels Reichardt (Glycotechnology Laboratory).

The prize is endowed with 1000 euros and the awardee is invited to present its result in an oral communication at the next Scientific Meeting organized by the Specialized Group.

# Best doctoral thesis Award of the Specialized Group on Nanoscience and Molecular Materials of the RSEQ

Leonardo Scarabelli, former CIC biomaGUNE PhD student, awarded with the First prize for the best doctoral thesis of the Specialized Group on Nanoscience and Molecular Materials of the Spanish Royal Societies of Chemistry for the thesis entitled "Rational synthesis and self-assembly of anisotropic plasmonic nanoparticles" supervised by Luis Liz-Marzán (Bionanoplasmonics Laboratory).

The NANOMATMOL award to the best PhD thesis recognizes the best PhD thesis of the young researchers from the Specialized Group in Nanoscience and Molecular Materials (NANOMATMOL) from the RSEQ and RSEF. The aims of this award are to recongnize the creativity and the work done by these young researchers, and to encourage other researchers to become members of the group. The prize consists of 1000 € for the winner, and 250 € for the two runner-ups.

### **Best Presentation/ Poster Awards**

Luka Rejc (radiochemistry & nuclear imaging lab member) awarded for the Best Oral Presentation at the 2017 First young Spanish ESMI Group Meeting (ySMIN 2017) for the work entitled "Multidisciplinary approach towards the utilization of diphenylacetylene-based molecular probe for the detection of tau protein aggregates".

Best presentation prizes at the 31st Conference of the European Colloid and Interface Society (ECIS 2017) to Bionanoplasmonics lab members. Eric Hill awarded for the Best oral presentation of a young scientist for his talk entitled "Plasmonic Monitoring of Surface Topography Effects on Biofilm Growth". Christoph Hanske received a prize for his poster "Self-Assembly of Plasmonic Supercrystals and Metamolecules".

# **GENERAL ASSEMBLY**











# INTERNATIONAL SCIENTIFIC ADVISORY BOARD

The assessment of the scientific activity of CIC biomaGUNE is carried out by the International Scientific Advisory Board (ISAB), composed of internationally distinguished scientists active in CIC biomaGUNE's research fields. The ISAB is currently formed by the following members:

# Scientific Advisory Board



Peter Morris
Sir Peter Mansfield
Magnetic Resonance
Centre University of
Nottingham, UK



Monica Olvera de la Cruz

Department of
Chemistry
Northwestern
University, USA



Prof. Itamar Willner Institute of Chemistry The Hebrew University of Jerusalen, Israel



Prof. Helmuth Möhwald

Max Plank Institute of Colloids and interfaces, Germany



Prof. Peter Seeberger Max Plank Institute of Colloids and interfaces, Germany



Prof. Jon Dilworth
Depart. of Inorganic
Chemistry University
of Oxford. UK



Prof. Samuel I. Stupp

Institute for BioNanotechnology i Medicine Northweste University, USA

# **Group Leaders**

Glycotechnology

Niels Reichardt



Biomolecular Nanotechnology Aitziber L. Cortajarena



Biosensing

Valery Pavlov



Soft matter Nanotechnology Sergio E. Moya



Theranostic Nanomedicine Juan C. Mareque-Rivas



Biosurfaces Ralf Richter



Bionanoplasmonics

Luis Liz-Marzán Ikerbasque Professor



Computational Biophysics Ivan Coluzza Ikerbasque Professor



Bioengineered Particles Wolfgang Parak



Radiochemistry and Nuclear Imaging

Jordi Llop



Carbon Bionanotechnology Maurizio Prato



Magnetic Resonance Imaging Pedro Ramos Ikerbasque Professor



# Research Associates

Bionanoplasmonics Marek Grzelczak Ikerbasque Fellow



Mónica Carril Ikerbasque Fellow



Bioengineered Particles Heterogeneous Biocatalisis Fernando López Ikerbasque Fellow



Bionanoplasmonics Javier Reguera Ikerbasque Fellow



Bionanoplasmonics Isabel García-Martín CIBER-BBN



**Experimental Molecular Imaging** Abraham Martín Muñoz



# Molecular & Functional Imaging Facility

This integrated bioimaging structure offers state-of-the-art preclinical imaging instrumentation in positron emission tomography (PET), Single Photon Emission Computed Tomography (SPECT), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), optical/fluorescence imaging and ultrasound (US) imaging. It includes a fully equipped radiochemistry laboratory with a biomedical cyclotron, advanced microscopy equipment, a dedicated animal housing facility for rodents which holds AAALAC accreditation and complementary equipment including gamma spectrometry and autoradiography.

The Facility is currently integrated in the "Distributed Biomedical Imaging Network" (ReDIB, www.redib.net), recognized by the Spanish Government as a Singular Scientific and Technical Infrastructure (ICTS).

# Technological platforms

Each platform is managed by an expert platform manager, who provides technical and scientific support to the research activities at CIC biomaGUNE. The Platforms comprise the following state-of-the-art research infrastructures: Electron Microscopy, Nuclear Magnetic Resonance, Mass Spectrometry, Surface Analysis and Fabrication, Colloidal Nanofabrication and Optical Spectroscopy and Microscopy. All researchers have access to the platforms, upon training and supervision by the platform managers.

# **RD&I Unit**

A dedicated office dedicated to support and strengthen the capacities of the Center, in terms of attracting funding from various Research Programs, in particular Horizon 2020, strengthening links between academic and industrial environments, and promoting the transfer of research results to the society and industry, especially to the biotechnology sector.

# FINANCIAL AND ECONOMIC MANAGEMENT AREA

# Administration

This area is responsible for the management of finances, accounting, administration, and the human resources of the Center.

# Maintenance

Its main task is the preventive, predictive and corrective maintenance of all CIC biomaGUNE facilities.

# Computing & Communications

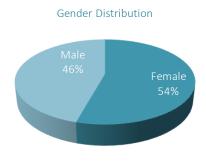
The IT service is in charge of supporting all the staff of the Center with setting up and maintaining computer-related equipment, data storage, e-mail servers, as well as the website and other social media.

# Biosafety & Radioprotection

This service is dedicated to establish safe working conditions of all CIC biomaGUNE's personnel by promoting good laboratory practices. Moreover, the service is in charge of the proper operation of the Center's Radioactive Facility.

The table below provides the distribution of CIC biomaGUNE's personnel as per December 2017

CIC biomaGUNE's Personnel	
Principal Investigators	12
Associate Researchers	4
Research Assistants	2
Platform Managers	8
Laboratory Technicians and Platform Specialists	22
Postdoctoral Researchers	18
PhD Students	26
Direction and Administration	15
IT and Maintenance	8
Biosafety and Radioprotection	1
Total	116





Argentina <b>1</b>	France <b>1</b>	Lithuania <b>1</b>	Tunisia <b>1</b>
China 1	Germany 9	Russia <b>1</b>	UK <b>1</b>
Colombia 1	India <b>2</b>	Slovenia <b>1</b>	Ukraine <b>1</b>
Denmark <b>1</b>	Italy <b>5</b>	Spain <b>65</b>	US <b>1</b>

Researchers from 16 countries

# **GROUP LEADER RECRUITMENTS**

**Dr. Ivan Coluzza** joined CIC biomaGUNE in June 2017 as Ikerbasque Associate Professor and head of the Computational Biophyiscs group.

Dr. Coluzza graduated in Physics at the University "La Sapienza" in Rome, obtained a PhD in Physics at the University of Amsterdam, and worked as a post-doctoral researcher at Cambridge University and at the National Institute for Medical Research in London. From April 2010 until April 2017 he held a University Assistant position at the University of Vienna. He has co-authored 30 publications in high-impact journals, such as Physical Review Letters (4). He has been invited to several international conferences, and with the support of CECAM organised 4 international workshops.

He has been awarded 12 research grants, 3 as co-principal and 9 as principal investigator for a total amount of more than 1.2 million euros. Overall he has supervised 4 PhD students (one graduated in 2017 and 2 are expected to graduate in 2018), 1 MPhil and 1 Bachelor student.

At CIC biomaGUNE he leads the Computational Biophysics group, which focuses on the application of statistical mechanics to soft matter and complex biological systems. The primary goal is to build simple models of natural complex systems, such as proteins, thereby learning their fundamental function and copying it into artificial systems. The knowledge gained hereby sheds light on critical problems of protein folding and design.

# **DEPARTURES**

- Dr. Luca Salassa, Ramón y Cajal fellow at CIC biomaGUNE (2012 January 2017) joined the Donostia International Physics Center (DIPC) as Ikerbasque Research Professor.
- **Dr. Torsten Reese** leader of the Magnetic Resonance Imaging group (2007 2009; 2011 June 2017) finalized his activity at CIC biomaGUNE in June 2017.
- **Dr. Marek Grzelczak**, Ikerbasque Fellow associated to the Bionanoplasmonics Laboratory (September 2012 August 2017) joined the Donostia International Physics Center (DIPC) as Ikerbasque Associate Researcher.
- **Dr. Fernando López-Gallego**, Ikerbasque Fellow and head of the Heterogeneous Biocatalysis Laboratory (February 2014 September 2017) joined the University of Zaragoza as Senior ARAID Fellow.

# Funding

# Funding

During 2017, **16** new projects (from competitive public funding sources) have been launched with a total contribution of € **2,970,983.77**.

# LIST OF FINANCED PROJECTS STARTING IN 2017



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Maurizio Prato	H2020-MSCA-RISE- 2016	108,000.00	2017 - 2021	CARBO-IMmap - Immune activity Mapping of Carbon Nanomaterials
Luis Liz-Marzán	H2020-INFRAIA- 2016-1	542,137.00	2017 - 2021	<b>EUSMI</b> - European infrastructure for spectroscopy, scattering and imaging of soft matter
Sergio Moya	NMBP-12-2017	220,042.00	2017 - 2021	BIORIMA - BIOmaterial RIsk MAnagement



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Aitziber L. Cortajarena	Retos de la Sociedad - proyectos I+D	157,300.00	2017-2019	FibroTOOLS - Designed modular nanobiotechnological tools to detect and interfere with the key signaling pathway of heart fibrosis in vivo
Maurizio Prato	Retos de la Sociedad - proyectos I+D	199,650.00	2017-2019	N3DSNEC - Novel 3D structures based on carbon materials nanocomposites for electroresponsive cell cultures
Luis Liz-Marzán (Jesús Mosquera)	Juan de la Cierva — Formación Fellowship	50,000.00	2017-2019	
Luis Liz-Marzán (Dorleta Jimenez de Aberasturi)	Juan de la Cierva – Incorporación Fellowship	64,000.00	2017-2019	



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Maurizio Prato	Adquisión de Equipamiento Científico	45,320.51	2017-2018	Analizador de Impedancia Celular en Tiempo Real
Jordi Llop	Organizacion de Congresos	10,000.00	2017	2 <sup>nd</sup> International Molecular Imaging Workshop
Aitziber L. Cortajarena	Elkartek 2017	120,8787.58	2017-2018	biomaGUNE 2017 - Bionanomateriales para aplicaciones biomédicas en diagnóstico y terapia
Aitziber L. Cortajarena	Elkartek 2017	80,669.14	2017-2018	FRONTIERS III - Superficies multifuncionales en la frontera del conocimiento
Luis Liz-Marzán	Dep. Salud- Potenciación de la invest. en salud	43,988.52	2017	INvitro Diagnostics for CAncer TEsting (INDICATE 2017) - Desarrollo de un biosensor económico, sensible y rápido para detectar mutaciones en sangre asociadas a medicina personalizada
Luis Liz-Marzán	Dep. Salud- Potenciación de la invest. en salud	43,589.02	2017	BACA 2017 - Bio-Reactor automatizado para células adherentes



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
CIC biomaGUNE	Programa RED- Infraestructura	100,000.00	2017-2018	RAMAN - Adquisición de un microscopio raman confocal de alta velocidad
Jordi Llop	Programa RED - Investigación	76,000.00	2017 - 2018	NANOBORON - Nanopartículas de oro como portadores de boro para su aplicación a la terapia del cáncer por captura de neutrones



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Luis Liz-Marzán	InterCiber PAI 2017	11,500.00	2017 - 2019	HyperNano - Nanotechnology-driven early diagnosis of pulmonary hypertension

# Technology Transfer

# **Technology Transfer**

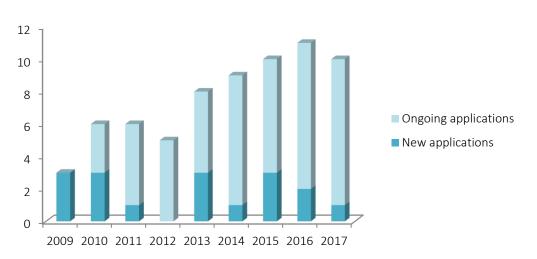
# Knowledge and Technology Transfer

CIC biomaGUNE is making a substantial effort to promote the transfer of research results produced at the Center to the market. In this respect, the Center has created an initiative to identify and continue the development of those technologies with a clear market potential, namely the Development Unit (DU) initiative within the RD&I Unit. The DU acts as an antenna and incubator of ideas, with the main objective of identifying and transferring research results from the Center into the market, by protecting the results, encouraging their exploitation and strengthening patent licensing. Projects to be matured within the DU are initially evaluated by the scientific direction of the Center, on the basis of criteria that include the consistency of the initiative with the Center's activity and the benefit that the initiative can obtain from the infrastructure/resources of the center for its maturation. In addition, the RD&I Unit works on establishing new contracts with companies, promoting cross-sectorial research and maximizing the transfer of knowledge and technology.

# **PATENTS**

The generation of patents is one of the instruments that indicate the transfer of knowledge from the Center to Society and to business development. The graph below shows the evolution over the years:

#### PATENT PORTFOLIO



#### 2017 Patent Applications

Metal Nanocluster Scaffold EP17382451.7 (11/07/17) A. L. Cortajarena, A. Aires-Trapote

#### 2017 Granted Patents\*

Synthesis and use of isotopically-labelled glycans EP2981541 (13/09/17)
N. Reichardt, B. Echeverria, J. Etxebarria, J.Calvo, N. Ruiz
Validated in DE, NL, FR, CH, DK, GB, BE, ES, SE, FI, LU

<sup>\*</sup> Only first granted application of a patent family is indicated.

#### SPIN-OFFs

# **Asparia Glycomics**

# www. aspariaglycomics.com



In 2016, CIC biomaGUNE staff researchers and private investors joined efforts to set up *Asparia Glycomics*, a spin-off company specialized in the production and marketing of reagents, reference standards, kits and software, intended for glycan analysis in clinical diagnosis and for quality control of biopharmaceuticals.

The business initiative markets the leading technology developed by CIC biomaGUNE's Glycotechnology Laboratory, directed by Dr. Niels Reichardt, to quantify and identify glycans more accurately and faster than existing solutions on the market. *Asparia Glycomics* offers unique, stable, isotope labeled glycans as internal standards, custom made quantification software and reagents for glycan analysis by mass spectrometry.

The company is led by Dr. Juan Echevarria, co-inventor of the technology, who moved to *Asparia Glyomics* from the Glycotechnology laboratory. The standards and kit solutions offered by *Asparia Glycomics* find multiple applications in clinical glycomics research, biopharmaceutical glycan analysis and glycobiology in general.

The company started operating in October 2016 and has currently obtained ca. 40 k€ from direct sells and signed a distribution agreement with the multinational company Sigma. The company also managed to obtain public funding in the form of 2 Torres Quevedo postdoctoral fellowships and 1 industrial PhD studentship (in collaboration with CIC biomaGUNE).

# RESEARCH AGREEMENTS WITH COMPANIES

CIC biomaGUNE develops joint research activities in collaboration with different types of organizations and companies, including spin-offs, SMEs, large companies and research organizations. This research activity has a sharp focus on innovation, to which CIC biomaGUNE contributes with scientific knowledge. Joint projects under development include privately funded research activities as well as research contracts and consultancy services.

During 2017 six new collaboration agreements with industrial partners were signed:

# Biokit research & development S.L.U.

Research contract

#### Progenika Biopharma, S.A.

Research contract

#### Quimatryx S.L.

Material transfer agreement

# AJL Ophthalmic, S.A.

Material transfer and technology application agreement

## Technoplastic Products, AG

Product development and joint venture agreement

#### IDOM Consulting, Engineering, architecture, S.A.U.

Consulting agreement

#### Asparia Glycomics

**R&D** Collaboration agreement

#### Midatech Pharma

Service provisiom agreement

# **INDEXED PUBLICATIONS**

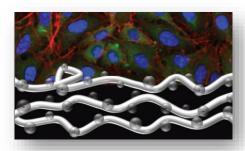


# ARTICLES PUBLISHED IN JOURNALS WITH IMPACT FACTORS ABOVE 9 (20%)

JOURNAL	IMPACT FACTOR	QUARTILE	DECILE	Nº OF ARTICLES
Chemical Society Reviews	38,618	Q1	D1	3
Science	37,205	Q1	D1	4
Nano Today	17,476	Q1	D1	1
Neuron	14,092	Q1	D1	1
ACS Nano	13,942	Q1	D1	3
Journal of the American Chemical Society	13,858	Q1	D1	3
Surface Science Reports	13,333	Q1	D1	1
Nano Letters	12,712	Q1	D1	1
Nature Communications	12,124	Q1	D1	3
Advanced Functional Materials	12,124	Q1	D1	2
Angewandte Chemie International Edition	11,994	Q1	D1	5
Chemistry of Materials	9,466	Q1	D1	3
Current Opinion in Biotechnology	9,294	Q1	D1	1
Green Chemistry	9,125	Q1	D1	1
TOTAL				32

## **RESEARCH HIGHLIGHTS**

Novel strategy for the enhancement of cell adhesion on Polyelectrolyte Multilayers



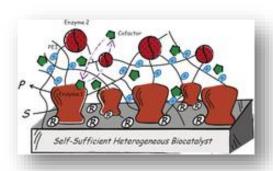
Thermal Annealing of Polyelectrolyte Multilayers: An Effective Approach for the Enhancement of Cell Adhesion

N.E. Muzzio, D. Gregurec, E. Diamanti, J. Irigoyen, M.A. Pasquale, O. Azzaroni, S.E. Moya

Adv. Mater. Interfaces 2017, 4, 1600126

Polyelectrolyte multilayers (PEMs) have many potential applications in tissue engineering and regenerative medicine. However, the softness of biocompatible PEMs results in limited cell adhesion. A novel strategy for the enhancement of cell adhesion on PEMs based on thermal annealing is presented here. The impact of thermal annealing at 37 °C of poly-l-lysine (PLL) and alginate (Alg) polyelectrolyte multilayers on the adhesion of human lung cancer A549 and myoblast C2C12 cell lines is studied. The properties of the PEMs after annealing are characterized by means of the quartz crystal microbalance with dissipation, atomic force microscopy, atomic force spectroscopy, zeta potential, and contact angle measurements. After annealing, PLL/Alg PEMs become smoother displaying an increase in stiffness. Furthermore, PEMs become more hydrophobic, with an increase in contact angle from 36° to 90°. Additionally, the surface charge decreases and protein deposition on PEMs significantly diminishes after annealing. Cell adhesion, measured by the projected average cell spreading and focal contact formation, is remarkably improved for the annealed PEMs.

# Self-sufficient heterogeneous biocatalysts

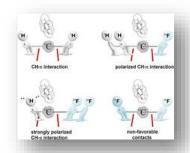


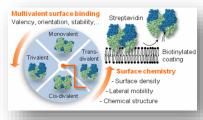
Co-immobilized Phosphorylated Cofactors and Enzymes as Self-Sufficient Heterogeneous Biocatalysts for Chemical Processes

S. Velasco-Lozano, A.I. Benítez-Mateos, F. López-Gallego *Angew. Chem. Int. Ed.* **2017**, *56*, 771-775

Enzyme cofactors play a major role in biocatalysis, as many enzymes require them to catalyze highly valuable reactions in organic synthesis. However, the cofactor recycling is often a hurdle to implement enzymes at the industrial level. The fabrication of heterogeneous biocatalysts co-immobilizing phosphorylated cofactors (PLP, FAD+, and NAD+) and enzymes onto the same solid material is reported to perform chemical reactions without exogeneous addition of cofactors in aqueous In these self-sufficient heterogeneous biocatalysts, the immobilized enzymes are catalytically active and the immobilized cofactors catalytically available and retained into the solid phase for several reaction cycles. Finally, we have applied a NAD+dependent heterogeneous biocatalyst to continuous flow asymmetric reduction of prochiral ketones, thus demonstrating the robustness of this approach for large scale biotransformations.

Fluoroacetamide moieties as sensitive tags for the Multivalent Binding Control through Surface Chemistry detection of sugar—protein interactions





Fluoroacetamide Moieties as NMR Spectroscopy Probes for the Molecular Recognition of GlcNAc-Containing Sugars: Modulation of the CH– $\pi$  Stacking Interactions by Different Fluorination Patterns

L. Unione, M. Alcalá, B. Echeverria, S. Serna, A. Ardá, A. Franconetti, J. Cañada, T. Diercks, N. Reichardt, J. Jimenez-Barbero

Chem. Eur. J. 2017, 23, 3957-3965

We herein propose the use of fluoroacetamide and difluoroacetamide moieties as sensitive tags for the detection of sugar-protein interactions by simple <sup>1</sup>H and/or <sup>19</sup>F NMR spectroscopy methods. In this process, we have chosen the binding of N,N'-diacetyl chitobiose, a ubiquitous disaccharide fragment in glycoproteins, by wheat-germ agglutinin (WGA), a model lectin. By using saturation-transfer difference (STD)-NMR spectroscopy, we experimentally demonstrate that, under solution conditions, the molecule that contained the CHF2CONH- moiety is the stronger aromatic binder, followed by the analogue with the CH<sub>2</sub>FCONH- group and the natural molecule (with the CH<sub>3</sub>CONHfragment). In contrast, the molecule with the CF<sub>3</sub>CONHdisplayed the weakest intermolecular interaction (one order of magnitude weaker). Because sugar-aromatic CH- $\pi$  interactions are at the origin of these observations, these results further contribute to the characterization and exploration of these forces and offer an opportunity to use them to unravel complex recognition processes.

Controlling Multivalent Binding through Surface Chemistry: Model Study on Streptavidin

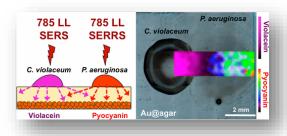
G.V. Dubacheva, C.Araya-Callis, A.G. Volbeda, M. Fairhead, J. Codée, M. Howarth, R. P. Richter

J. Am. Chem. Soc. 2017, 139, 4157–4167

Although multivalent binding to surfaces is an important tool in nanotechnology, quantitative information about the residual valency and orientation of surface-bound molecules is missing. To address these questions, we study streptavidin (SAv) binding to commonly used biotinylated surfaces such as supported lipid bilayers (SLBs) and self-assembled monolayers (SAMs). Purposedesigned SAv constructs having controlled valencies (mono-, di-, trivalent in terms of biotin-binding sites) are studied to rationalize the results obtained on regular (tetravalent) SAv. We find that divalent interaction of SAv with biotinylated surfaces is a strict requirement for stable immobilization, while monovalent attachment is reversible and, in the case of SLBs, leads to the extraction of biotinylated lipids from the bilayer. The surface density and lateral mobility of biotin, and the SAv surface coverage are all found to influence the average orientation and residual valency of SAv on a biotinylated surface. We demonstrate how the residual valency can be adjusted to one or two biotin binding sites per immobilized SAv by choosing appropriate surface chemistry. The obtained results provide means the rational design of surface-confined supramolecular architectures involving specific biointeractions at tunable valency.

Surface-enhanced Raman scattering spectroscopy for simultaneous detection of quorum-sensing-regulated bioactive chemical compounds produced by bacterial colonies

Flexible nanomaterials may recruit neurons or create artificial bridges to restore connectivity

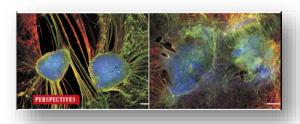


# Imaging Bacterial Interspecies Chemical Interactions by Surface-Enhanced Raman Scattering

G. Bodelón, V. Montes-García, C. Costas, I. Pérez-Juste, J. Pérez-Juste, I. Pastoriza-Santos, L M. Liz-Marzán

# ACS Nano 2017, 11, 4631-4640

Microbes produce bioactive chemical compounds to influence the physiology and growth of their neighbors, and our understanding of their biological activities may be enhanced by our ability to visualize such molecules in vivo. We demonstrate here the application of surface-enhanced Raman scattering spectroscopy for simultaneous detection of quorum-sensing-regulated pyocyanin and violacein, produced respectively by Pseudomonas aeruginosa and Chromobacterium violaceum bacterial colonies, grown as a coculture on agar-based plasmonic substrates. Our plasmonic approach allowed us to visualize the expression and spatial distribution of the microbial metabolites in the coculture taking place as a result of interspecies chemical interactions. By combining surface-enhanced Raman scattering spectroscopy with analysis of gene expression we provide insight into the chemical interplay occurring between the interacting bacterial species. This highly sensitive, cost-effective, and easy to implement approach allows spatiotemporal imaging of cellular metabolites in live microbial colonies grown on agar with no need for sample preparation, thereby providing a powerful tool for the analysis of microbial chemotypes.

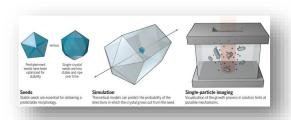


#### Nanomaterials for stimulating nerve growth

S. Marchesán, L. Ballerini, M. Prato *Science* **2017**, *356*, 1010-1011

Despite recent advances in supportive care for spinal cord injury (SCI), there is a great need for treatments that can improve the neurological outcome. After SCI, there is essentially no regrowth of axons beyond the point of the lesion, leaving intact, although nonfunctional, circuits below the site of injury. We discuss the potential for functional recovery from SCI by using nanomaterials to restore these dysfunctional circuits through a combination of artificial connections and devices to help stimulate motor and sensory recovery.

Single-nanoparticle imaging and theoretical modeling can guide synthesis strategies



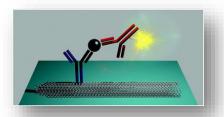
# Growing anisotropic crystals at the nanoscale

L.M. Liz-Marzán, M. Grzelczak

Science 2017, 356, 1120-1121.

Technological prospects of metal nanoparticles (NPs) have stimulated intense research activities into their growth mechanisms to predict shape, size, and crystallinity. Of high interest are low-symmetry nanocrystals (NCs), which exhibit high-energy facets that are relevant in catalysis or plasmonic properties that are attractive for applications in areas such as biomedicine. Rod-like shapes are in principle most challenging because the high-symmetry face-centered cubic (fcc) lattice of the metals of interest, such as gold, tends to form high-symmetry, compact NCs. To promote shape anisotropy, nucleation and growth are usually separated in the so-called seed-mediated growth, in which a metal precursor is reduced on preformed seeds in the presence of shape-directing additives. The growth of nanorods is a nonequilibrium process and remains poorly understood, which accounts for their limited reproducibility and yield. The required control over the crystal habit of the seeds and the effect of additives will necessitate insights from theoretical modeling as well as characterization, especially by state-of-the-art transmission electron microscopy (TEM).

Novel electrochemiluminescence ELISA-like immunosensor based on carbon nanotubes and a highly specific sandwich immunoassay for the Prostate-specific membrane antigen (PSMA) detection



# Highly sensitive electrochemiluminescence detection of a prostate cancer biomarker

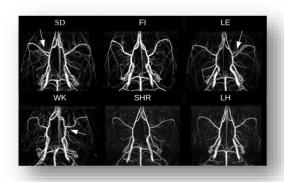
A. Juzgado, A. Soldà, A. Ostric, A. Criado, G. Valenti, S. Rapino, G. Conti, G. Fracasso, F. Paolucci, M. Prato

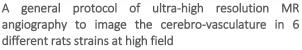
J. Mater. Chem. B, 2017, 5, 6681-6687

Prostate-specific membrane antigen (PSMA), a glycoprotein expressed in the prostatic epithelium endowed with enzymatic activity, is a very promising diagnostic marker for the early detection of prostate cancer. In this study, we report a novel electrochemiluminescence ELISA-like immunosensor based on carbon nanotubes and a highly specific sandwich immunoassay for the PSMA detection. To fabricate the device, an optically transparent electrode was modified with doubly functionalized multi-walled carbon nanotubes carrying amine groups and a monoclonal anti-PSMA antibody. Subsequently, to complete the sandwich immunosensing device. a second specific monoclonal anti-PSMA antibody was labelled with a electrochemiluminescent probe. Under optimized experimental conditions, the proposed sensing device exhibits a performance exceeding that of the state of-the-art in terms of the limit of detection (LOD) and limit of quantification (LOQ) as good as 0.88 ng mL<sup>-1</sup> and 2.60 ng mL<sup>-1</sup>, respectively, in real complex samples such as cell lysates. In addition, the unique role of carbon nanotubes is also discussed by comparison with an analogue sensor assembled without the nanocarbon-based material.

Ultra-high resolution MR angiography as method to study cerebro-vascular abnormalities in various animal models

Detection of  ${\rm Cu}^{2+}$  ions in real samples of mineral and tap water using the photocatalytic activity of cadmium sulfide nanoparticles

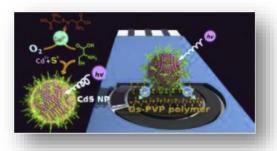




G. Pastor, M. Jiménez-González, S. Plaza-García, M. Beraza, D. Padro, P. Ramos-Cabrer, T. Reese

J. Neuroscience Methods 2017, 289, 75-84

Experimentally, we describe a new general protocol of three-dimensional time-of-flight magnetic resonance angiography to visualize non-invasively the cerebral vasculature in 6 different rat strains. Flow compensated angiograms of Sprague Dawley, Wistar Kyoto, Lister Hooded, Long Evans, Fisher 344 and Spontaneous Hypertensive Rat strains were obtained without the use of contrast agents. At 11.7 T using a repetition time of 60 ms, an isotropic resolution of up to 62  $\mu m$  was achieved; total imaging time was 98 min for a 3D data set.



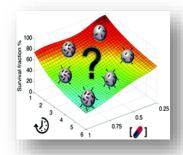
Photoelectrochemical detection of copper ions by modulating the growth of CdS quantum dots

R. Grinyte, J. Barroso, B. Diez-Buitrago, L. Saa, M. Moller, V. Pavlov

Anal. Chim. Acta 2017, 986, 42-47

We discovered that copper ions (Cu<sup>2+</sup>) catalyze the oxidation of cysteine (CSH) by oxygen (O2) to modulate the growth of CSH-capped cadmium sulfide (CdS) nanoparticles (NPs). This new chemical process was applied sensitive fluorogenic photoelectrochemical (PEC) detection of Cu<sup>2+</sup> ions in real samples of mineral and tap water using the photocatalytic activity of the resulting NPs. Disposable screen-printed electrodes (SPCEs) modified with electroactive polyvinylpyridine bearing osmium complex (Os-PVP) by cyclic voltammetry (CV) were employed for PEC analytical system. CdS NPs formed during the assay photocatalyze oxidation of 1-thioglycerol (TG) upon application of 0.3 V vs. Ag/AgCl to SPCEs. Os-PVP complex mediated the electron transfer between the electrode surface and CdS NPs. We proved that our assays did not suffer from interference from other ions accompanying Cu<sup>2+</sup> and the sensitivity of our assays covers the European Union standard limit of Cu<sup>2+</sup> ions in drinking water.

# Specific targeting of cancer cells can be achieved through the custom design of multivalent nanoparticles

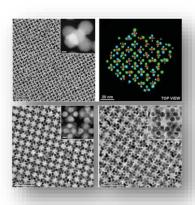


An experimental and computational framework for engineering multifunctional nanoparticles: designing selective anticancer therapies

A. Aires, J.F. Cadenas, R. Guantes, A.L. Cortajarena *Nanoscale*, **2017**, *9*, 13760-13771

A key challenge in the treatment of cancer with nanomedicine is to engineer and select nanoparticle formulations that lead to the desired selectivity between tumorigenic and non-tumorigenic cells. To this aim, novel designed nanomaterials, deep biochemical understanding of the mechanisms of interaction between nanomaterials and cells, and computational models are emerging as very useful tools to guide the design of efficient and selective nanotherapies. This works shows, using a combination of detailed experimental approaches and simulations, that the specific targeting of cancer cells in comparison to non-tumorigenic cells can be achieved through the custom design of multivalent nanoparticles. A theoretical model that provides simple yet quantitative predictions to tune the nanoparticles targeting and cytotoxic properties by their degree of functionalization is developed. As a case study, a system that included a targeting agent and a drug and is amenable to controlled experimental manipulation and theoretical analysis is used. This study shows how at defined functionalization levels multivalent nanoparticles can selectively kill tumor cells, while barely affecting nontumorigenic cells. This work opens a way to the rational design of multifunctionalized nanoparticles with defined targeting and cytotoxic properties for practical applications.

Non-close-packed nanoparticle arrays: porous materials with novel crystal structures assembled from nanoparticles



Tunable porous nanoallotropes prepared by postassembly etching of binary nanoparticle superlattices

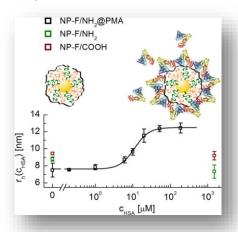
T. Udayabhaskararao, T. Altantzis, L. Houben, M. Coronado-Puchau, J. Langer, R. Popovitz-Biro, L.M. Liz-Marzán, L. Vuković, P. Král, S. Bals, R. Klajn

Science 2017, 358, 514-518

Self-assembly of inorganic nanoparticles has been used to prepare hundreds of different colloidal crystals, but almost invariably with the restriction that the particles must be densely packed. Here, we show that non-closepacked nanoparticle arrays can be fabricated through the selective removal of one of two components comprising binary nanoparticle superlattices. First, a variety of binary nanoparticle superlattices were prepared at the liquid-air interface, including several arrangements that were previously unknown. Molecular dynamics simulations revealed the particular role of the liquid in templating the formation of superlattices not achievable through self-assembly in bulk solution. Second, upon stabilization, all of these binary superlattices could be transformed into distinct "nanoallotropes"—nanoporous materials having the same chemical composition but differing in their nanoscale architectures.

## Laser-shaping of nanoparticles

## **Determining Protein Corona Formation**



# Femtosecond laser reshaping yields gold nanorods with ultranarrow surface plasmon resonances

G. González-Rubio, P. Díaz-Núñez, A. Rivera, A. Prada, G. Tardajos, J. González-Izquierdo, L. Bañares, P. Llombart, L. G. Macdowell, M. Alcolea Palafox, L. M. Liz-Marzán, O. Peña-Rodríguez, A. Guerrero-Martínez

Science 2017, 358, 640-644

The irradiation of gold nanorod colloids with a femtosecond laser can be tuned to induce controlled nanorod reshaping, yielding colloids with exceptionally narrow localized surface plasmon resonance bands. The process relies on a regime characterized by a gentle multishot reduction of the aspect ratio, whereas the rod shape and volume are barely affected. Successful reshaping can only occur within a narrow window of the heat dissipation rate: Low cooling rates lead to drastic morphological changes, and fast cooling has nearly no effect. Hence, a delicate balance must be achieved between irradiation fluence and surface density of the surfactant on the nanorods. This perfection process is appealing because it provides a simple, fast, reproducible, and scalable route toward gold nanorods with an optical response of exceptional quality, near the theoretical limit.

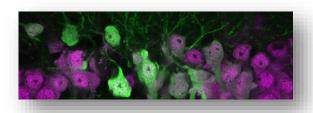
In situ detection of the protein corona in complex environments

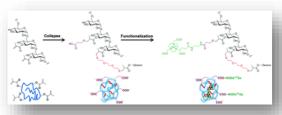
M. Carril, D. Padro, P. del Pino, C. Carrillo-Carrión, M. Gallego, W.J. Parak

Nature Commun. 2017, 8, 1542

Colloidal nanoparticles (NPs) are a versatile potential platform for in vivo nanomedicine. Inside blood circulation, NPs may undergo drastic changes, such as by formation of a protein corona. The in vivo corona cannot be completely emulated by the corona formed in blood. Thus, in situ detection in complex media, and ultimately in vivo, is required. Here we present a methodology for determining protein corona formation in complex media. NPs are labeled with <sup>19</sup>F and their diffusion coefficient measured using <sup>19</sup>F diffusion-ordered nuclear magnetic resonance (NMR) spectroscopy. <sup>19</sup>F diffusion NMR measurements of hydrodynamic radii allow for in situ characterization of NPs in complex environments by quantification of protein adsorption to the surface of NPs, as determined by increase in hydrodynamic radius. The methodology is not optics based, and thus can be used in turbid environments, as in the presence of cells.

PKD1 confers neuroprotection against the oxidative stress by triggering antioxidant defences and promoting neuronal survival in an excitotoxic environment Water-dispersible dextran-based single-chain polymer nanoparticles as imaging contrast agents for pulmonary diseases





Excitotoxic inactivation of constitutive oxidative stress detoxification pathway in neurons can be rescued by PKD1

J. Pose-Utrilla, L. García-Guerra, A. Del Puerto, A. Martín, J. Jurado-Arjona, N.S. De León-Reyes, A. Gamir-Morralla, A.S. Serrano, M. García-Gallo, L. Kremer, J. Fielitz, C. Ireson, M.J. Pérez-Álvarez, I. Ferrer, F. Hernández, J. Ávila, M. Lasa, M.R. Campanero, T. Iglesias

*Nature Commun.* **2017**, *8*, 2275

Excitotoxicity, a critical process in neurodegeneration, induces oxidative stress and neuronal death through mechanisms largely unknown. Since oxidative stress activates protein kinase D1 (PKD1) in tumor cells, we investigated the effect of excitotoxicity on neuronal PKD1 activity. Unexpectedly, we find that excitotoxicity provokes an early inactivation of PKD1 through a dephosphorylation-dependent mechanism mediated by protein phosphatase-1 (PP1) and dual specificity phosphatase-1 (DUSP1). This step turns off the IKK/NFκB/SOD2 antioxidant pathway. Neuronal PKD1 inactivation by pharmacological inhibition or lentiviral silencing in vitro, or by genetic inactivation in neurons in vivo, strongly enhances excitotoxic neuronal death. In contrast, expression of an active dephosphorylationresistant PKD1 mutant potentiates the IKK/NF-kB/SOD2 oxidative stress detoxification pathway and confers neuroprotection from in vitro and in vivo excitotoxicity. Our results indicate that PKD1 inactivation underlies excitotoxicity-induced neuronal death and suggest that PKD1 inactivation may be critical for the accumulation of oxidation-induced neuronal damage during aging and in neurodegenerative disorders.

Synthesis and functionalization of dextran-based singlechain nanoparticles in aqueous media

R. Gracia, M. Marradi, U. Cossío, A. Benito, A. Pérez-San Vicente, V. Gómez-Vallejo, H.-J. Grande, J. Llop, I. Loinaz *J. Mat. Chem. B* **2017**, *5*, 1143-1147

Water-dispersible dextran-based single-chain polymer nanoparticles (SCPNs) were prepared in aqueous media and under mild conditions. Radiolabeling of the resulting biocompatible materials allowed the study of lung deposition of aqueous aerosols after intratracheal nebulization by means of single-photon emission computed tomography (SPECT), demonstrating their potential use as imaging contrast agents.

# PhD THESES

During 2017, 13 students obtained their PhD at CIC biomaGUNE.



# Ruta Grynité

Analytical assays based on modulation of quantum dots in situ

Supervisor: Valery Pavlov

Date: 13/01/2017



# Emma Christelle Sery

Chemical biology tools for structurefunction studies on heparin sulphates: decoding specificity in FGF signalling

Supervisors: Niels Reichardt and

Jerry Turnbull

Date: 13/03/2017



#### Sameer Mahonar Joshi

Novel strategies for the preparation of <sup>13</sup>N-labelled compounds: Synthesis of <sup>13</sup>N-labelled aromatic azides, triazoles and tetrazoles

Supervisor: Jordi Llop

Date: 01/06/2017



## Guillermo González Rubio

Synthesis and assembly of uniform plasmonic gold nanostructures for biomedical applications

Supervisor: Luis Liz-Marzán

Date: 30/06/2017



## **Geraldine Pastor**

Optimisation of novel methods for pre-clinical imaging at 11.7T

Supervisor: Torsten Reese

Date: 08/09/2017



# Ane Ruiz de Angulo Dondorroso

Modular magnetite-filled nanomicelles for multimodal imaging-guided development of effective anticancer vaccines

Supervisor: Juan Mareque Rivas

Date: 08/09/2017



# Nerea Guedes Carrera

Solid phase synthesis of glycosaminoglycans

Supervisor: Niels Reichardt

Date: 15/09/2017



### **Eunice Da Silva Fernandes**

Application of enzymes in Nitrogen-13 radiochemistry; biocatalytic synthesis of PET radiotracers with biomedical interest Supervisors: Jordi Llop and Fernando López

Gallego

Date: 19/09/2017



### Amaia Garaikoetxea

Nanoparticle-based delivery and activation of platinum (IV) prodrugs and dsRNA for cancer chemotherapy

Supervisor: Juan Mareque Rivas

Date: 01/12/2017



# María San Román

Colorimetric assays for the detection of single nucleotide polymorphism based on plasmonic nanoparticles

Supervisors: Marek Grzelczak and Luis Liz-Marzán

Date: 01/12/2017



# Aiseta Baradji

Interactions of fibroblast growth factors with glycosaminoglycan brushes and the pericellular matrix

Supervisors: Ralf Richter and Dave Ferning

Date: 04/12/2017



# Malte Strozyk

Gold nanoparticles in polymeric matrices for biomedical applications

Supervisors: Luis Liz-Marzán and Mathias Brust

Date: 06/12/2017



# Ana Isabel Bocanegra

Biofunctional iron oxide nanoparticles as vaccine adjuvants for enhanced anti-cancer immunotherapy

Supervisor: Juan Mareque

Rivas

Date: 22/12/2017

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#### **COVER PAGES**



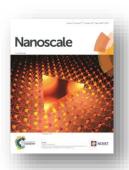
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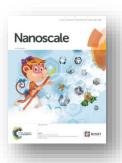
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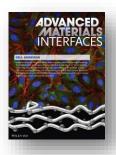
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Shape control in ZIF-8 nanocrystals and metal nanoparticles@ZIF-8 heterostructures

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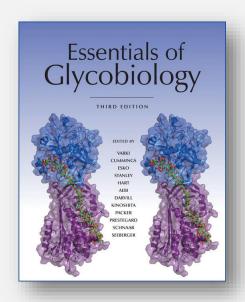


Optimization of Nanoparticle-Based SERS Substrates through Large-Scale Realistic Simulations

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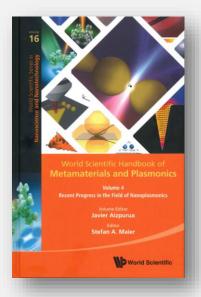
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#### **BOOK CHAPTERS**



#### Glycans in Nanotechnology

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#### **Chemical Synthesis of Plasmonic Nanoparticles**

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#### **EDITORIAL ACTIVITY**



#### Science

Board of Reviewing Editors – Luis Liz-Marzán



#### **ACS Omega**

Co-Editor-in-Chief — Luis Liz-Marzán

#### **ACS Nano**

Associate Editor – Wolfgang Parak Editorial Advisory Board – Luis Liz-Marzán, Maurizio Prato

#### **Accounts of Chemical Research**

Editorial Advisory Board – Luis Liz-Marzán

#### **Chemistry of Materials**

Editorial Advisory Board – Luis Liz-Marzán, Wolfgang Parak



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International Editorial Advisory Board – Maurizio Prato

#### **Faraday Discussions**

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#### Journal of Materials Chemistry B

International Editorial Advisory Board – Luis Liz-Marzán



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#### Journal of Colloid and Interface Science

Advisory Board – Wolfgang Parak

# Colloid and Interface Science Communications

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# Training

The training activities of CIC biomaGUNE during 2017 can be summarized as follows: **40** seminars, **92** research internships received, **42** guided tours and **2** scientific workshops/events organized.

#### PhD PROGRAMS

The objective of CIC biomaGUNE's PhD Program is to a provide PhD students with top quality multidisciplinary training at the interface between biology, chemistry, nanobiotechnology and materials science. The students benefit from international training and are exposed to different research areas. The training program offers weekly lectures by leading scientists, technical training courses on a broad range of scientific techniques and instrumentation, opportunities for short stays at renowned international research institutions, as well as complementary training in soft skills to prepare doctoral candidates to become highly qualified, autonomous and skilled professionals. The joint training of PhD candidates fosters closer ties and cooperation between research groups and researchers of the institutions involved.

During 2017, 13 students obtained their PhD at CIC biomaGUNE.

In partnership with the **University of the Basque Country (UPV/EHU)**, CIC biomaGUNE participates in the following Doctoral programs:

- Synthetic and Industrial Chemistry
- Applied Chemistry and Polymeric Materials
- Molecular Biology and Biomedicine
- Medicine and Surgery
- Biomedical Research

#### International Program

Since 2011, CIC biomaGUNE and CIC bioGUNE, together with the University of Liverpool (UoL), run the International joint graduate school program, aimed at implementing joint PhD degrees.

The objective of the joint PhD program is to a provide PhD students with top quality multidisciplinary training at the interface between the fields of biology, chemistry, nanobiotechnology and materials science. The students benefit from an international training and are exposed to different research areas. The joint training of PhD candidates fosters closer ties and cooperation between research groups and researchers of both CICs and UoL.

Additionally, a Joint PhD agreement between CIC biomaGUNE and the University of Manchester (UoM) was launched in 2016.

#### Co-supervised PhD Program

Since 2016, CIC biomaGUNE is running a program of cosupervised PhD theses, in collaboration with other research institutions, technology centers and enterprises in the Basque Country. Currently, 20 PhD theses are co-directed with the following institutions:

- POLYMAT
- DIPC
- CIC bioGUNE
- CIC nanoGUNE
- IIS BioCruces
- IIS BIODONOSTIA
- TECNALIA
- IK4-GAIKER
- IK4-CIDETEC
- ASPARIA GLYCOMICS

#### UNDERGRADUATE & VOCATIONAL TRAINING PROGRAMS

#### Undergraduate Students Program

In partnership with the University of the Basque Country (UPV/EHU), CIC biomaGUNE participates in the following MSc courses by providing lectures and direction of master thesis:

- Molecular Biology and Biomedicine
- Nanoscience
- Chemistry and Polymers

Since 2017, in partnership with the **University of Salamanca (USAL)**, CIC biomaGUNE participates in the Master in Supramolecular Chemistry by hosting Master students in our laboratories to perform their master thesis.

#### **Vocational Training Program**

CIC biomaGUNE has agreements with CPES CESA BHIP, Don Bosco and Colegio Inmakulada Ikastetxea, Centers for Intermediate and Superior level vocational training in the fields of Chemistry or Biosciences to host training internships of students.

Every year several training placements take place at different laboratories of the Center.

The selected undergraduates are mentored and supervised by postdoctoral researchers or PhD students and receive hands-on training.

#### **RESEARCH SECONDMENTS & SUMMER INTERNSHIPS**

In the framework of different national and international projects, CIC biomaGUNE has established collaborations with international institutions to **second** and **host research stays of PhD students and postdoctoral researchers**. During **2017**, our researchers performed **19** secondments at collaborating partners and we hosted **92** stays of visiting researchers.

During the summer period, **undergraduate students** with a background in Chemistry, Biology and Materials Science are hosted at CIC biomaGUNE's laboratories. The undergraduates work alongside pre- and post-doctoral researchers, and receive high level training while working on a research project, but also by attending weekly group meetings and seminars. At the end of the traineeship, the students are required to prepare a short report and a presentation summarizing their research and results. CIC biomaGUNE regularly hosts students from the University of the Basque Country, Autonomous University of Barcelona and University of Navarra.

	2013	2014	2015	2016	2017
Research stays <b>from</b> CIC biomaGUNE	14	47	30	30	19
Research stays <b>to</b> CIC biomaGUNE	45	67	59	105	92
<ul><li>Erasmus placements</li></ul>	1	0	1	7	7
<ul><li>Summer placements</li></ul>	1	2	2	5	6
<ul> <li>Vocational Training</li> </ul>	1	3	4	7	5

#### **SEMINARS**

CIC biomaGUNE runs an annual program of scientific seminars, which includes i) **international seminars** delivered by internationally recognized researchers of varying scientific backgrounds and fields, ii) **PhD seminars** delivered by PhD students of the Center, and iii) **Training seminars** delivered by CIC biomaGUNE's Pls or Platform Managers, aimed at strengthening the technical training program and soft skills training. During 2017, **40** seminars were delivered.

#### CIC biomaGUNE Seminars

#### 12/01/2017

A summary on phase transition dynamics of colloids in external fields

Raheema Muhammad Aslam - University of Navarra

#### 30/01/2017

Probing interactions between magneticnanoparticles and biological molecules/matricesby magnetic means

Francisco J. Terán - IMDEA Nanociencia

#### 09/02/2017

Multiscale modeling in mechanobiology:From computer simulations to microfluidics

José Manuel García-Aznar - University of Zaragoza

#### 16/02/2017

Photonic methods in medical diagnostics

Andreas Seifert - CIC nanoGUNE & Ikerbasque

#### 24/02/2017

Luminescent nanothermometers: What is next?

Luis D. Carlos - Universidade de Aveiro

#### 06/03/2017

Biomedical Applications of Nanoplasmonics

Romain Quidant - ICFO & ICREA

#### 16/03/2017

Multimodal brain imaging to characterize brain states in alcohol use disorders Santiago Canals Gamoneda - Instituto de Neurociencias de Alicante -CSIC

#### 17/03/2017

Nanoplatform-based molecular imaging; multimodal approaches with extremely small particles

Fernando Herranz Rabanal — National Center for Cardiovascular Research -CNIC

#### 23/03/2017

Close Encounters of the Virosphere: viruses, pathogens and miniaturised wonders

Nicola G. A. Abrescia - CIC bioGUNE

#### 27/03/2017

Additive manufacturing of biologically-inspired composites

André Studart - ETH Zurich, Switzerland

05/05/2017

Engineering Stimuli-Responsive Platforms for Cell Isolation and Neuron Stimulation

**Gabriela Romero** - Vindico Nanobiotechnologies

15/05/2017

The analytical biochemistry of single cells: recent progress and its impact on precision medicine Giacinto Scoles - Princeton University

26/05/2017

Role of lipids in cell autophagy

Alicia Alonso - Instituto Biofisika (CSIC, UPV/EHU)

09/06/2017

Chemical Challenges in Glycosyltransferase Modulation

**Pedro Merino** - University of Zaragoza

14/06/2017

Impact of the corona at the BioNano Interface

Marco Monopoli - Royal College of Surgeons

23/06/2017

Nanoparticles, SERS and Theory

George C. Schatz - Northwestern University

26/06/2017

Control of biological activity with light Pau Gorostiza – IBEC & ICREA

08/11/2017

Computational protein design: the computer as a virtual laboratory

Ivan Coluzza - CIC biomaGUNE

24/11/2017

Low-Dimensional Nano-Carbons: Form Doped Carbon Nanotubes and Doped Graphene to 3-D Hybrids and Biological Applications Mauricio Terrones - Penn State University

14/12/2017

Internet of functions in tailored-made 0D to 3D multicomponent nanostructures: from high-performance sensors to multiresponsive hybrid nanostructures

Paolo Samorí - Université de Strasbourg & CNRS

19/12/2017

Christmas Lecture: Retromer to the rescue

Dr. Aitor Hierro - CIC bioGUNE

#### CIC biomaGUNE PhD Seminars

11/01/2017

Analytical assays based on modulation of quantum dots in situ

Ruta Grinyté

12/06/2017

Novel strategies for the preparation of 13N-labelled compounds: Synthesis of 13N-labelled aromatic azides, triazoles and tetrazoles

Sameer Manohar Joshi

16/06/2017

Synthesis and Assembly of Uniform Plasmonic Gold Nanostructures for Biomedical Applications Guillermo González Rubio

04/09/2017

Modular magnetite-filled nanomicelles for multimodal imaging-guided development of effective anticancer vaccines Ane Ruiz de Angulo Dorronsoro

05/09/2017

Optimisation of novel methods for pre-clinical imaging at 11.7T

Geraldine Pastor

13/09/2017

Solid Phase Synthesis of Glycosaminoglycans
Nerea Guedes

27/11/2017

Colorimetric Assays for the Detection of Single Nucleotide Polymorphism based on Plasmonic Nanoparticles María Sanromán

28/11/2017

Nanoparticle-based delivery and activation of platinum (IV) prodrugs and dsRNA for cancer chemotherapy Amaia Garaikoetxea

18/12/2017

Gold Nanoparticles in Polymeric Matrices for Biomedical Applications Malte Strozyk

20/12/2017

Biofunctional iron oxide nanoparticles as vaccine adjuvants for enhanced anti-cancer immunotherapy Ana Isabel Bocanegra

#### CIC biomaGUNE PhD Training

04/10/2017

Tips for Giving a Scientific Presentation, 10 Tips for Preparing your Manuscript

Luis Liz-Marzán

06/11/2017

How does an MRI work?, Image contrast in MRI and Relaxivity and contrast agents

Pedro Ramos-Cabrer

13/12/2017

High Resolution NMR in real practice Daniel Padró

#### ORGANIZATION OF SCIENTIFIC WORKSHOPS/CONFERENCES

27-28 April 2017

2<sup>nd</sup> Young Researchers Workshop on Biomaterials and Bioapplications (biomapp17)



2<sup>nd</sup> Biennial Young Researchers Workshop on Biomaterials and Applications 27-28<sup>th</sup> April 2017

The Young Researchers Workshop is a scientific meeting focused on biomaterials and their applications in imaging, therapy and sensing, organized by and for doctoral students and young postdoctoral researchers. The workshop serves to present and discuss their work but also to strengthen internal collaboration and develop new ideas.

Running on a biannual basis, the first event took place at CIC biomaGUNE on October 2015 and was organized by our junior Research Associates. The second edition took place in Santiago de Compostela on April 2017, co-organized by CIC biomaGUNE Associate Researchers co-organized the bioMAPP17.

The workshop offers an excellent opportunity for young scholars to present their research and gain experience in academic conferencing, for networking and exchange of ideas.

The conference program included discussions on biofunctional materials, biosurfaces, molecular imaging, therapy and diagnostics, sensing and catalysis

CIC biomaGUNE Organizers: Mónica Carril, Isabel García-Martín, Marek Grzelczak, Fernando López-Gallego, Abraham Martin-Muñoz, Pedro Ramos-Cabrer, Javier Reguera.

20-23 November 2017

2<sup>nd</sup> International Workshop in Molecular Imaging



The International Workshop on Molecular Imaging is an international scientific meeting aimed at covering the most recent advances in the broad field of preclinical and clinical molecular imaging.

Running on a biannual basis, the 1<sup>st</sup> edition was held at CIC biomaGUNE on November 2015. A second edition was held on November 2017, with more than 120 participants.

The 2017 edition attracted world experts in molecular imaging and its applications in neurosciences, oncology, and cardiovascular and lung diseases both at the preclinical and clinical levels. Plenary lectures were complemented with poster sessions and flash presentations to promote fruitful interactions between world leaders and young emerging scientists. Scientific sessions were interspersed with technical sessions involving the sponsors and one industrial session, which gathered speakers from three different big pharmaceutical companies. The event attracted >100 researchers from 13 different countries.

CIC biomaGUNE Organizers: Jordi Llop (chair), Vanessa Gómez-Vallejo, Abraham Martin-Muñoz and the Radiochemistry & Nuclear Imaging group

Additionally, our researchers chaired or co-organized a number of international symposia as listed below:

Abraham Martín and Mónical Carril, organizers of the 1<sup>st</sup> young Spanish ESMI Group Meeting (ySMIN2017), Madrid, 30 Jan 2017.

Wolfwang Parak, organizers of the Symposia at SPIE Photonics West Meeting, San Francisco, 28 Jan -2 Feb 2017.

Luis Liz-Marzán, co-chair of the "Biohybrid, Biomaterials and Biological Materials" symposium at the 5<sup>th</sup> International Conference on Multifunctional, Hybrid and Nanomaterials (Hybrid Materials 2017), Lisbon, 6–10 Mar 2017.

**Luis Liz-Marzán** and **Wolfgang Parak**, co-chairs of the "Applied Biosensing Based on Functional Colloids" symposium at the **253<sup>rd</sup> ACS National Meeting**, San Francisco, 2–7 Abr 2017.

**Sergio Moya**, co-organizer of the "Design and hierarchical assemblies of nanomaterials towards energy, sensing, electronic, catalysis and detection applications" symposium at the **EMRS 2017** Strasbourg, 22–26 May 2017.

Luis Liz-Marzán and Wolfgang Parak, co-chairs of the "Multimodal Imaging with Colloids" symposium at the 254<sup>th</sup> ACS National Meeting, Washington D.C., 20–24 Ago 2017.

Luis Liz-Marzán, co-chair of the "Interactions of Nanoparticles with Biological Systems" symposium at the Mexican Materials Research Society Meeting, Cancún, 23–26 Ago 2017.

Maurizio Prato, organizer of the European Congress and Exhibition on Advanced Materials and Processes (EUROMAT '17), Thessaloniki, 17-22 Sep 2017.

Marta Quintanilla, organizer of the meeting Spectral shaping for biomedical and energy applications (SHIFT 2017), Tenerife, 13-17 Nov 2017.

One of the strategic objectives of CIC biomaGUNE is the communication and dissemination of knowledge within and beyond the academic community. During 2017 the following outreach events have been organized:

#### PINT OF SCIENCE

This initiative brings Science to local bars, thereby breaking down the barriers that separate science from society.

For the third consecutive year CIC biomaGUNE researchers take active part in the organization of the Pint of Science event in San Sebastián. The organizing team was led by Susana Carregal and Dorleta Jimenez de Aberasturi.

During the edition of this year, within the session entitled "Versatile Proteins", Aitziber López Cortajarena and Fernando López Gallego, Ikerbasque Professor amd Research Associate at CIC biomaGUNE jointly gave the following talk "Proteins beyond their nutritional role; From the washing machine to the spider web" explaining the role of proteins beyond nutrition.





#### OLATU TALKA – URBAN ZIENTZIA

Olatu Talka is a cultural festival organized by the citizens of San Sebastián. During a weekend, the streets, squares and parks of the city become the scene of multiple activities in which citizens are protagonists of cultural action. The Urban Science section aims bringing science closer to the citizens and, at the same time, making visible the work that is done in the research centers of the city. Monologues, talks, workshops and laboratories for small, small and major exhibitions and other activities are carried out throughout the day.

For the second consecutive year several PhDs and postdocs from CIC biomaGUNE (Susana Carregal, Patrizia Andreozzi, Ada Herrero, Dorleta Jimenez de Aberastauri) participated at the Olatu Talka Urban Zientzia (Urban Science) event by organizing a photo exhibition of food at the micro scale "Food & Science" and an experimental workshop entitled "GuessFood".





#### **INSPIRA**

The **INSPIRA project** is a pioneering project in Euskadi for the promotion of the scientific-technological vocation (STEAM - (Science, Technology, Engineering, Arts and Maths) among girls.

The mentors accompany students during a period of two months with the aim to:

- Provide new references of nearby women technologists.
- For boys and girls to discover the STEAM professions.
- Raise awareness of the need for the development of the country to occur between men and women.
- Sensitize and guide on the career in technology.
- Make visible and value women technologists.

The schools whose students receive mentoring from CIC biomaGUNE scientists are:

Deutsche Schule San Alberto Magno, where 5<sup>th</sup> elementary grade students receive mentoring from the hand of Irantzu Llarena and Susana Carregal, Axular Lizeoa, where girls of 6<sup>th</sup> elementary grade students receive mentoring from Ane Ruiz de Angulo, and IES Hirubide, where girls from the 1<sup>st</sup> year of ESO receive mentoring from Dorleta Jimenez de Aberasturi and Idoia Mikelez.

Also, on the 27<sup>th</sup> of November 2017, CIC biomaGUNE joined the **INSPIRA Manifesto** promoted by the University of Deusto to demand the opening of spaces for girls and women in science and technology.









#### **NANOPICCOLA**

The Piccola Accademia di Gagliato delle Nanoscienze is the junior arm of the Accademia di Gagliato. It is targeted for children between the ages of 5 and 14 and offers them opportunity to achieve an understanding and appreciation for nanotechnology and its applications. It is a central part of the mission of the Accademia di Gagliato of to help people understand how nanoscale science can change their world for the better.

Patrizia Andreozzi, Postdoctoral Fellow and Fernando López-Gallego, Ikerbasque Research Fellow at CIC biomaGUNE participated at the Nanopiccola school online by giving a master talk on Nanoscience to children between 4 and 18 years. The online school connected CIC biomaGUNE with a High school in Matera and Gagliato both in Italy.



#### "Donostia WeekINN" INNOVATION WEEK

For the second consecutive year CIC biomaGUNE has participated at the "Donostia WeekINN" Innovation Week from the 23<sup>rd</sup> until the 27<sup>th</sup> of October) with the following actions:

- 24 and 26 October: Guided school visits at CIC biomaGUNE: discussion with researchers about research techniques, future technologies, applications and visits to laboratories.
- October 26 at 18:30 at the Hotel Maria Cristina: "Topagunea Donostia-San Sebastián Strategy" Malou Henriksen-Lacey participates in a reflection forum where business and institutional representatives analyze the economic reality of the city of San Sebastián, from the view of public-private collaboration. On this occasion the speakers discussed about talent, its attraction, retention, recovery and linkage with the capital of Gipuzkoa.





#### MIKROFOOD - MICROSOPIC PHOTOGRAPHY EXHIBITION

What does milk or tomato look like on a small scale? Researchers from CIC biomaGUNE have tried to capture the complexity of each day's meals through photographs taken under a microscope.

The project "Mikro Food": food under the microscope, is born from an idea of Patrizia Andreozzi.

The Photography Exhibition run from 22/12/2017 until the 14/01/2018 in Vitoria-Gasteiz.



#### **CIC NETWORK**

CIC biomaGUNE is involved in the production of the CIC NETWORK magazine, the science magazine of the Cooperative Research Centers. To date 17 issues have been published, the most recent one in July 2017.



#### **OPEN DAYS & VISITS**

CIC biomaGUNE regularly receives visits from high-school and university students who come to have a closer look at our activity. These visits typically include a lecture about biomaterials in the context of life sciences, an open discussion with CIC biomaGUNE researchers, and a guided tour to six technical facilities/laboratories (Nanoparticle synthesis platform, Confocal Microscopy, Radiochemistry platform, Molecular Imaging Facility, Scanning Electron Microscopy, Atomic Force Microscopy). The program of visits is run by Ana Sánchez-Iglesias, Eneko San Sebastián, Daniel Padró and Vanessa Gómez with the support from other Platform Managers as well as PhDs, Postdocs and Principal Investigators.

#### January 2017

Visit from 2nd year Biosanitary Baccalaurate students from St. Patrick's English School.



#### February 2017

#### International Day of Women and Girls in Science

Aitziber L. Cortajarena took active part at the Women in Nanoscience event organized by CIC nanoGUNE presenting her scientific work and participating in a roundtable, where the specific challenges that women face over their scientific careers were discussed.



#### February 2017

Jon Darpón, Health Counselor together with Iñaki Berraondo, Health Vice-Counselor and María Aguirre, Director of health research and innovation from the Basque Government visit CIC biomaGUNE.



#### March 2017

Visit from high school students from Agrupamento de Escolas de Penacova, Coimbra (Portugal)



#### March 2017

Visit from Arantxa Tapia, Counselour of Economic Development and Infrastructures from the Basque Government, in the frame of the 10<sup>th</sup> Anniversary of CIC biomaGUNE.



#### April 2017

Luis Liz-Marzán participated at the Scientific Fridays (Viernes Científicos) from University of Almería. The Scientific Fridays is a series of conferences open to the society, media, industries and public authorities with the aim of disseminating various aspects of science in an entertaining way to the widest possible audience.



#### October 2017

Visit from 1<sup>st</sup> year Baccalaurate students from St. Teresa School from San Sebastián.



#### April 2017

Fernando López-Gallego visited Colegio Público Santo Domingo de Silos en Villaminaya, Toledo (Spain) to bring chemistry closer to the children. Students between 3 and 6 years played with scientific guessing games and enjoyed simple experiments, while students from 6 to 12 watched illustrative videos on biology and biochemistry and made a chemical reaction.



#### May 2017

Visit from high school students from "St Joseph Oloron Ste. Marie" high school from Pau (France).



#### October 2017

Visit from 1<sup>st</sup> year Baccalaurate students from Easo Instituto Politeknikoa from San Sebastián.



#### November 2017

Dorleta Jiménez mentored during 2 months 1<sup>st</sup> year ESO students from **IES Hirubide**, Irun, in the frame of the INSPIRA project for the promotion of STEAM among girls.



# October - November 2017

Idoia Mikelez mentored during 2 months (6 visits) 1<sup>st</sup> year ESO students from **IES Hirubide**, Irun, in the frame of the INSPIRA project for the promotion of STEAM among girls.



#### November 2017

Susana Carregal mentored during 2 months 5<sup>th</sup> elementary grade students **Deutsche Schule San Alberto Magno**, San Sebastián, in the frame of the INSPIRA project for the promotion of STEAM among girls.



#### November 2017

Irantzu Llarena mentored during 2 months 5<sup>th</sup> elementary grade students **Deutsche Schule San Alberto Magno**, San Sebastián, in the frame of the INSPIRA project for the promotion of STEAM among girls.



#### November 2017

Visit from 2<sup>nd</sup> year Baccalaurate students from Ikastola Laskorain from Tolosa.



#### December 2017

Visit from 4<sup>th</sup> ESO students from La Salle Beasain



#### **MEDIA**

CIC biomaGUNE is committed to disseminating research results and other news, not only to the scientific community but also to the general public. Such efforts are reflected in the table below.



Highlighted media appearances:

Date	Headline	Nº Impacts
1/18/2017	Luis Liz-Marzán, elected member of the European Academy of Sciences (EURASC)	7
2/8/2017	Jon Darpón, Health Counselour from the Basque Government visits CIC biomaGUNE	6
3/13/2017	10 <sup>th</sup> anniversary of the Center for Cooperative Research in Biomaterials - CIC biomaGUNE	14
3/31/2017	Fourth call for applications for access to the Singular Scientific and Technological Infrastructure (ICTS) ReDIB	2
6/6/2017	The Carbohydrate group of the Royal Society of Chemistry awards the best PhD prize to a CIC biomaGUNE researcher	6
6/16/2017	The prestigious journal Science, invites CIC biomaGUNE researchers to contribute with perspective articles on nanomaterials	6
6/27/2017	Carbon nanotubes show great potential to facilitate neuronal regeneration	12
9/13/2017	Ivan Coluzza joins CIC biomaGUNE as an Ikerbasque Research Professor	4
10/26/2017	The research paper, published in Science and involving CIC biomaGUNE researchers, reveals the potential to further expand the extensive family of nanostructured materials	25
10/30/2017	A research project on brain haemorrhage involving CIC biomaGUNE receives support from La Marató de TV3 telethon	3
11/2/2017	A Spanish research team involving CIC biomaGUNE succeeds in making gold nanoparticles behave as clones	16
12/12/2017	CIC biomaGUNE research enables the attachment of proteins to nanoparticles in the blood to be studied	10

The Twitter, Facebook and LinkedIn presence has remained with an increase of the number of followers/connections.

# Facilities

# Facilities

## Research Facilities

All the research lines, framed within the strategic research program of CIC biomaGUNE, are strongly supported by the Molecular & Functional Imaging Facility and the Technological Platforms, which constitute a major strength of the Center.

CIC biomaGUNE's state-of-the art facilities are depicted in the images below. In the first row the Technological Platforms are presented, whereas the second row shows the instruments of the Molecular Imaging Facility.



Electron Microscopy



Mass Spectrometry



Surface Analysis & Fabrication



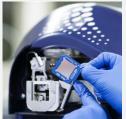
Colloidal Nanofabrication



Optical Spectroscopy















CIC biomaGUNE Technological Platforms & Molecular Imaging Facility



Nuclear Magnetic Resonance



Radiochemistry







Nuclear Imaging

















#### MOLECULAR & FUNCTIONAL IMAGING FACILITY

The Molecular and Functional Imaging Installation is a unique preclinical imaging facility in Spain, which was recognized as Singular Scientific and Technological Infrastructure (ICTS) by the Ministry of Science and Innovation in 2011, and has recently been integrated in the distributed ICTS ReDIB as a founding node, together with TRIMA-CNIC Advanced Image Installation, located at the National Center for Cardiovascular Research. The research-oriented preclinical imaging facility at CIC biomaGUNE offers state-of-the-art imaging resources in:

**Nuclear Imaging:** Equipped with a hybrid PET-CT (eXplore Vista-CT) and full ring SPECT-CT (eXplore speCZT CT 120), the latter offering the possibility of multi-isotope studies with energy discrimination.

Magnetic Resonance Imaging: Instrumentation to conduct advanced imaging and spectroscopic experiments applied to biological samples including small rodents, samples or tissue extracts and cell cultures is available. CIC biomaGUNE provides the instrumentation and the expertise to carry out a wide range of MRI and MRS experiments, and is equipped with surgery rooms for animal preparation and implementation of surgical models. Ancillary equipment is also available: anesthesia systems, MRI-compatible physiological monitoring systems, infusion pumps, and temperature regulation systems. Equipment available: MRI 7T/30 cm (70/30 USR), MRI 11.7T/16 cm (117/16 USR).

Radiochemistry Platform: The Radiochemistry platform is equipped with an IBA Cyclone 18/9 cyclotron able to accelerate protons (18 MeV) and deuterons (9 MeV) and is equipped with 7 targets for the routine production of [18F] F<sup>-</sup>, [18F] F<sub>2</sub>, [13N]-NH<sup>4+-</sup>, [15O]-O<sub>2</sub> [11C]-CO<sub>2</sub> and [11C]-CH<sub>4</sub>. It also has a solid target for the production of <sup>89</sup>Zr and <sup>64</sup>Cu.

The radiochemistry laboratory equipped with 5 shielded hot cells housing versatile automatic synthesis, suitable for the production (synthesis, purification and quality control) of PET and SPECT radiotracers. The facility has specially designed modules for:

- Synthesis of [<sup>11</sup>C] CH<sub>3</sub>I / [<sup>11</sup>C] CH<sub>3</sub>OTf from [<sup>11</sup>C] CO<sub>2</sub> / [<sup>11</sup>C] CH<sub>4</sub>, and subsequent methylation reaction
- <sup>18</sup>F-fluorination by nucleophilic and electrophilic substitution
- Radiotracer synthesis using microfluidics technology
- Chelation reactions using radiometals (<sup>68</sup>Ga, <sup>67</sup>Ga, <sup>64</sup>Cu, <sup>89</sup>Zr, etc.)

In addition, the laboratory has two shielded hot cells for manual handling of radioactive substances, suitable for the preparation of mono-doses or to perform syntheses with small amounts of radioactivity. The quality control lab, sited into the production lab, is equipped with state of art equipment to perform the complete quality control of the synthesized radiotracers, including adio-HPLC, radio-GC, radio-TLC, and gamma spectrometry.

Image Analytics: The platform of preclinical imaging analytics at CIC biomaGUNE provides the computational infrastructure required for the reconstruction, processing and imaging analysis. Working on different operating systems, the platform has 3 IMOD licenses for co-registration, segmentation, and quantification of multimodal

## **Facilities**

images. The platform also works with Matlab, FSL and IDL licenses in the development of analysis and processing algorithms.

The MRI unit and the Nuclear Imaging Unit sandwich a dedicated **animal housing area**, which holds accreditation of the **Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)**, and is prepared to house up to 800 mice and 400 rats in individually ventilated cages, with an experimental area specifically devoted to perform longitudinal studies.

The animal house is complemented with microsurgery areas for animal preparation. Four work stations and a data storage system in the Terabyte scale enable image reconstruction, processing, quantification and archiving.

Personnel with extensive scientific background and experience in handling and operating specific equipment, technologies, methodologies or experimental animals complete the scientific-technical staff.

#### TECHNOLOGICAL PLATFORMS

Managed by specialized platform managers, provide technical and scientific support to the research activities conducted at CIC biomaGUNE. They include the following state-of-the-art research infrastructures:

#### Nuclear Magnetic Resonance (NMR) – 500 MHz NMR:

Provides essential service for the characterization of molecules with biological activity, from complex glycans to molecules used in the design of nanostructures for biomedical applications.

Electron Microscopy – SEM-EDX, TEM – 120 keV and 200 keV: Offers techniques to study nanoparticles and biological or soft polymer materials (cryo-TEM) at the micrometer and nanometer scale to determine the materials dimensions, shape and composition.

Mass Spectrometry – MALDI-TOF, ICP-MS: Provides several high quality mass spectrometry techniques for the analysis of small molecules, complex biomolecules and nanomaterials. The platform is equipped with modern instrumentation and offers different ionization techniques.

#### Surface analysis and Fabrication - XPS, 3 x AFM:

Focuses on the analysis of materials at the surface level, including spectroscopic and microscopic techniques especially suited to surfaces. The platform offers also a deposition service of thin layers for controlled manufacture at the nanoscale.

Colloidal Nanofabrication: Within the priority area of biofunctional nanomaterials and nanomedicine, colloidal synthesis plays an essential role. This platform provides knowledge, training and service for the manufacture of nanoparticles with a wide variety of compositions and morphologies.

Optical Spectroscopy – 2 x Confocal, Raman, UV-VIS-NIR, Flow Cytometer, Cell Observer, CD, DLS, DCS, ITC, TGA, SPR: Offers a wide variety of techniques for the spectroscopic characterization of biomaterials and biosurfaces. Also included are optical microscopy techniques (confocal, Raman, etc.) that allow to investigate the interaction of nanomaterials with cellular systems of diverse complexity.



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