
IBEC
Institute for Bioengineering of Catalonia
IBEC
Annual Report
2014

IBEC

Institute for Bioengineering of Catalonia

IBEC Annual Report 2014

Introduction

2014 has been my first full year as director of IBEC. It was also the year that the first class of students from the University of Barcelona's degree programme in Biomedical Engineering, which I founded together with IBEC group leader Daniel Navajas, graduated. In this way, while my efforts at the university have come full circle, IBEC's triumphant year marked an exciting new beginning.

A large part of 2014 was dedicated to the close analysis of the institute's activities in order to draw up our Strategic Plan for the period 2014-2017. This exercise took into account the recommendations of the CERCA and ISC reviews, which took place in 2013, as well as the opinions and insights of IBEC's external stakeholders and its internal staff. IBEC's plan aims to increase the institute's visibility, its ability to attract talent, and its internationalization and training capacities, with the ultimate goal that the centre grow both in size and in results by recruiting new professionals and scientists, as well as renewing groups that perform at the highest standard in terms of both scientific quality and transfer and innovation. More information about the IBEC Strategic Plan 2014-2017 can be found in this report.

One of the challenges of our strategic plan is to consolidate our top-class research. Our scientific output during 2014 has given us much cause to feel proud. We celebrated six *Nature* group papers, including a *Nature Materials* cover; 98 indexed journal papers in total, 77% of them in the first quartile; 2 new patents; 12 PhD theses; two more ERC grants; and private funding successes from sources such as RecerCaixa and La Marató de TV3. Research highlights during the year included the study featured on the cover of *Nature Materials*, which demonstrated how the molecules that cells use to attach to their environment, integrins, allow cells to detect and adapt to tissue rigidity, one of the first signs of tumor development in breast cancer; the design of the first-ever functional 3D splenon capable of reproducing the function of the spleen, which is to filter red blood cells; and the discovery of a way to directly measure DNA's electric polarizability for the first time ever.

Another challenge is to develop a culture of excellence in management and self-sustainability. In this way, we have been very successful this year in generating alternative sources of support for the institute. We renewed our collaboration with La Caixa, having come to the end in 2014 of a successful two years as one of only five centres to be selected to take part in their pilot initiative to fund research evaluation and technology transfer. Thanks to the efforts of the Research Affairs Unit, IBEC was one of 34 organisations in the country to be awarded funding for the growth of its Project Management Office under a scheme launched by Spanish Ministry of Economy and Competitiveness, achieving top ranking among the applicants. The Communications and Outreach Unit also secured funding from FECYT, as well as being accepted into it's Red de Unidades de Cultura Científica y de la Innovación (UCC+i), a network of centres which have been accredited for their contribution to scientific culture.

A third important area of the strategic plan is to develop technology that helps to improve business competitiveness and the quality of hospital services. As far as our industry relations are concerned, 2014 saw the launch of our first IBEC/industry joint unit with Genomica S.A., which will be based at IBEC and aims to develop and bring to market point-of-care diagnostic products and other medical devices and technologies. Spin-off company Rob Surgical Systems celebrated the first validations of its Bitrack Surgical Robot System for minimally invasive laparoscopic surgery; and we continue to collaborate with the major hospitals in Barcelona and beyond on concrete health applications such as Dermoglass.

The Strategic Plan considers the attraction and retention of international talent as a crucial part of IBEC's success. For this reason, a great effort has been put into the development of our Human Resources Strategy for Researchers, fully aligned with our Plan and according to the principles of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, during 2014. Part of this has been the IBEC Equal Opportunities and Diversity Management Plan, and we're delighted that IBEC's female researchers are really making waves, with two of our existing junior group leaders and our new tenure track candidate recruited for 2015 – all women – in the running for ERC grants. 2014 also saw the recruitment as ICREA Professor of a new group leader who will join IBEC from Germany's MPI for Intelligent Systems, boosting our activity in the areas of miniaturized devices such as integrated biosensors in microfluidic chips and self-propelled nanorobots.

As far as our visibility and international status is concerned, there were several reasons to celebrate in 2014. We've seen our media appearances in the general press make a fourfold leap. In May I was one of four delegates for Spain nominated to take part in the new Working Party on Biotechnology, Nanotechnology and Converging Technologies of the Organisation for Economic Co-operation and Development (OECD). Even more excitingly, we learnt at the end of 2014 that our consortium of 144 European companies, research institutes and universities was chosen to be the Knowledge and Innovation Community (KIC) on healthy living and active ageing, EIT Health, of the European Institute of Innovation and Technology (EIT). The Spanish node will be based right here at IBEC's headquarters, the Barcelona Science Park.

Which such strong global positioning, and thanks to such fantastic efforts being put in year after year by each and every one of IBEC's researchers and staff, we can overcome such obstacles as the continued shortfall in resources and other external impedance to the fast growth we originally envisaged, and look forward unabated to another successful year in 2015.

Josep Samitier
Director of IBEC


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Endowing surgical robots with cognitive capabilities

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Unlike in industrial scenarios, surgical procedures are not predictable in most ca
Robots cannot develop autonomous tasks, unless they are fully preprogrammed
the environment's sensing allows planning the action in real time. Current surg
robots provide certain level of assistance, which is expected to increase in the
by being endowed with cognitive capabilities. In this abstract, a cognitive sys
is presented for telesurgery. Robots recognize the environment and evaluate
surgical task in real time. The system knowledge increases by experience a
a confidence level is reached, the surgeon is assisted by force feedback to
suturing task. Cognitive algorithms involved are:

Subtasks automatic identification: in order to recognize the surgeon's
suturing task is divided into minimal subtasks. Each subtask is charac
trajectories of the robots, the force sensors expected values and the p
clamps (open/closed). Theoretical and captured data are compared
distances among values and the probability of changing from one st
(Hidden Markov Model), so that each action is associated to a pre

2014 in review

News Highlights

January 2014

Double dose of ERC success

At the start of the year Xavier Trepat of the Integrative Cell and Tissue Dynamics group (page 112) was awarded both a new Consolidator Grant and a Proof of Concept award from the European Research Council (ERC).

The project "TensionControl: Multiscale regulation of epithelial tension" will receive funding over five years under the ERC's new Consolidator Grant scheme, which issued its first call in 2013 and constitutes a third core funding arm of the independent funding body, alongside their Starting and Advanced grants. The highly-competitive ERC grants are considered Europe's most prestigious research awards.

Group leader and ICREA professor Xavier, who already has an ERC Starting Grant, also received funds from the ERC for his project "Micro Gradient Polyacrylamide Gels for High Throughput Electrophoresis Analysis (MICROGRADIENTPAGE)" under their 2013 Proof of Concept funding call. It makes him one of the very few researchers in Europe to have received back-to-back ERC grants.

IBEC group leader to head CMRB

Ángel Raya, ICREA professor and head of IBEC's Control of Stem Cell Potency group (page 92), took up the role of director of Barcelona's Center of Regenerative Medicine in Barcelona (CMRB). With the resignation of director Prof. Juan Carlos Izpisua from the nine-year-old centre, Ángel will combine his new executive role there with his ongoing research activities at IBEC. CMRB scientists have made important contributions in the field of induced pluripotent stem cells (iPS cells) – which are just as versatile as embryonic cells but which can be obtained from adult cells such as stomach, liver or skin cells – and only a few months ago created human kidney cells from iPS cells. This breakthrough was heralded by the journal *Science* as one of the top ten scientific achievements of 2013.

RecerCaixa funding for IBEC projects

Two research projects were awarded funding under the 2013 RecerCaixa programme, among just 26 successful proposals chosen from a total 362 applications submitted.

Alícia Casals' (page 42) "Desenvolupament d'un sistema robòtic de baix cost d'ajut a la rehabilitació de la marxa per a nens amb transtorns motors greus" and Elisabeth Engel's (page 47) "Tendon Tissue Engineering: A Helping Hand for Rotator Cuff Tears (BIOTENDON)" received funds under the scheme, which is a joint initiative by the Associació Catalana d'Universitats Públiques (ACUP) and Obra Social la Caixa launched in 2010.

Right: Eli Engel gives a speech at the RecerCaixa awards ceremony.

Below: CosmoCaixa's Top Ciencia exhibition, featuring six IBEC researchers.

The chosen projects, which will be developed over the next two years, aim to respond to specific problems and challenges of today's society. IBEC already has two other ongoing projects with funds from the scheme: InHands (Joan Aranda, Robotics group, page 42) and 'Development of light-modulated ligands for remote, non-invasive regulation of neuropathic pain' (Pau Gorostiza, ICREA professor and head of IBEC's Nanoprobes and Nanoswitches group, page 60).

In March's official ceremony, IBEC junior group leader Elisabeth Engel represented all the winners and centres as the investigator chosen to speak at the event.

April 2014

Generalitat's education event held at IBEC

IBEC welcomed members of the Generalitat's Department of Education and about 150 teachers through its doors in April, when the Department held its event 'Presentació del Programa de Competències Científiques' in a research institute for the first time.

The visitors, who included the Consellera d'Ensenyament Irene Rigau, enjoyed demonstrations and explanations about IBEC's research in biomaterials and robotics and the Nanotechnology Platform at a 'mini-fair' of stands manned by IBEC researchers, as well as visits to the labs in the Helix.

IBEC advisor to EC and Horizon 2020 under RO-cKETs study

On 2nd April the European Commission's RO-cKETs study rounded up its activities with a high-level conference led by the EC in Brussels. IBEC's Head of Knowledge Exchange Arantxa Sanz presented the health and healthcare findings of the study in at the two-day event, which welcomed 180 stakeholders from every industrial sector, from energy to environment and agriculture.

The RO-cKETs study's findings will provide fundamental input to the EC's new funding instrument Horizon 2020 – the successor to FP7 – by developing the methodology, work plan and road map for a seven-year cross-cutting Key Enabling Technologies (KETs) work programme. This will help determine which products should be manufactured by European industry in the coming decades under three or more technology enablers (photonics, biotechnology and nanotechnology, for example).

IBEC's leading role in the project follows on from former director Josep A. Planell's role as Sherpa in the KET High Level Group on nanotechnology in 2012. The institute has helped identify innovative products in the pharmaceutical and medical technology sectors, as well as livestock and agriculture, that may be supported by the integration of nano-bio-info-cogno techniques or methods.

May 2014

IBEC researchers share their stories in CosmoCaixa exhibition

Six IBEC researchers featured in CosmoCaixa museum's new exhibition, Top Ciencia, that promotes scientific careers in a range of disciplines and gives visitors a glimpse into what it's like to be a researcher today.

Juan Crespo, Jérôme Noailly, Oscar Castaño, Rosa Letizia Zaffino, Ester Rodríguez and Isabel Oliveira all appeared in videos in the hands-on exhibition, explaining what motivated them to chose their careers in science, and describing the various fields they're working in. With these testimonials from 'real' researchers, which also featured people working at several of the other institutions in Barcelona and around, budding scientists can learn about the various fields of science, see what sort of different career paths it's possible to take, and hear about the rewards – as well as the difficulties – of a career as a researcher.

Building bridges with business

Together with the IRB, IBEC representatives took part in the inaugural event of the Catalan Foundation for Research and Innovation (FCRI)'s 'Café amb la Recerca' initiative, which was held at IBEC.

Josep Samitier, director of IBEC, and Joan Guinovart, director of the Institute for Research in Biomedicine (IRB Barcelona), presented their research at the pilot episode of the scheme, which aims to provide a

friendly meeting point for research organizations, businesses and investors to get together and identify ways to collaborate. The presentations led to lively and informative discussions about what industry and research can offer each other and what they need to work together. The business people in attendance came from companies such as AXA, Reig-Jofre, Nature Bisse, Semillas Fitó, Damm, Lipotec, Lucta and AB Médica Grup, among others.

IBEC receives national stamp for diffusion of science

IBEC was accepted into FECYT's Red de Unidades de Cultura Científica y de la Innovación (UCC+i), a network of centres which have been accredited for their contribution to scientific culture. The institute received this accreditation because of its record of outreach and scientific diffusion activities and the actions it takes to spread its research results to the media.

MINECO's FECYT (Fundación Española para la Ciencia y la Tecnología) established the UCC+i system to promote the popularization of science in universities, research centres and other public institutions in Spain. There are only seven other centres in the Barcelona area which have this accreditation – UB, UAB, PCB, CRESA, CRG, ACCC and the Fundacio Universitaria Balmes – with two more in Tarrogona (Rovira i Virgili university) and Girona (University of Girona), totalling ten in Catalonia.

Josep Samitier selected as Spanish expert in bio- and nanotechnology for OECD

IBEC Director Josep Samitier was one of four delegates for Spain nominated to take part in the new Working Party on Biotechnology, Nanotechnology and Converging Technologies (BNCT) of the OECD, which will start work in January 2015.

The Working Party for BNCT will be a body of representatives from all over the world combining to provide expert input on technical areas such nanoengineering and on issues related to the convergence of technologies. They will guide the development and implementation of global BNCT-related projects, identify funding sources, and provide a voice for BNCT matters to the different national systems.

Selected by the Secretary General for Science, Technology and Innovation of the Spanish Ministry for MINECO, the other members for Spain are Zuleika Saz Parkinson of the Fundación Investigación Biomédica del Hospital Clínico San Carlos, Madrid; Paula Queipo Rodríguez of PRODINTEC technology centre, Madrid; and Luis Miralles de Imperial of the Deputy Directorate-General for Europe and International Relations at MINECO.

June 2014

Marie Curie IOF for IBEC researcher

Andrea Malandrino, a postdoc in IBEC's Biomechanics and Mechanobiology group (page 88), will spend two years at the Massachusetts Institute of Technology (MIT) with a Marie Curie International Outgoing Fellowship. Andrea will work in new ISC member Roger Kamm's Mechanobiology lab developing the "Coordination And Migration of Cells during 3D vasculogenesis" (CAMVAS) project, in which existing 3D microfluidic techniques are combined with a computational model of vasculogenesis.

Marie Curie IOFs, which help experienced European scientists to gain new skills and expertise while conducting high-level research in a country outside Europe, require that the researcher go through a training process based on a topic which is complementary to his or her research career path.

IBEC and Sant Feliu de Guíxols join forces to create health exhibition

On Monday 16th June IBEC signed an agreement with the council of Sant Feliu de Guíxols to work together on a new museum exhibit on the history of health and medicine in Catalunya, "Curar-se en salut".

Sant Feliu de Guíxols' Museu d'Història hosts the exhibition, which opened in November 2014. It begins with a journey through the past to the present and future of medicine. The exhibition has six major thematic areas starting with the birth of a person and

tracking them throughout their life as their health gradually starts to fail. The exhibition's entertaining and educational format includes audiovisual displays, visual metaphors, historical material and other artefacts to show the long fight that medicine has taken to reach present-day standards.

IBEC's part of the exhibition focuses on the present day situation of medicine as well as reflecting on the future. The institute developed the exhibition's content with its scientific expertise, and both sides are working together to conduct educational workshops related to research in bioengineering and nanomedicine.

July 2014

IBEC and Israeli Ministry of Health join forces to promote nanomedicine

IBEC's Xavier Fernández-Busquets (page 52) appeared in a video produced by the EU-funded ERA-NET project EuroNanoMed on "Drug Delivery: The Use of Nanoparticles in Medicine".

It was the second in a series of videos featuring scientists working in the field of nanomedicine which were being produced for EuroNanoMed by its Israeli partner, the Chief Scientist Office of the country's Ministry of Health (CSO-MOH). They aimed to introduce the subject and its potential contribution to human health to the general public by describing some current areas of research.

Xavier, who is head of the IBEC/CRESIB Joint Unit on Nanomalaria, talked about the bottlenecks still found in malaria treatment and described his lab's development of liposomal and polymeric nanovectors for the targeted delivery of antimalarial drugs to cells infected by the parasite. The clip was filmed at IBEC and then produced in Israel.

The collaboration with the CSO-MOH came about following IBEC Director Josep Samitier's fact-finding visit to Israel with President of Catalonia Artur Mas in November 2013. Other scientists featured in the clip were Prof. Simon Benita, Director of the Institute for Drug Research at The Hebrew University of Jerusalem, and Dr Kaspar Tars of the Latvian Biomedical Research and Study Center.

October 2014

IBEC awarded funds to help researchers towards H2020 success

IBEC was one of 34 organisations in the entire country to be awarded funding under the 2013 'Acciones de Dinamización Europa Redes y Gestores' programme of MINECO, Spain's Ministry of Economy and Competitiveness, to increase the capabilities of its Project Management Office (PMO).

Not only that, but the institute was ranked top among the applicants, meaning it received one of the two largest portions of the total grant money, the other going to the ISCIII.

The programme has earmarked €5.3m to finance actions aimed at establishing or strengthening management structures that

Right: the 'Café amb la Recerca' meeting in May.

Below: the exhbition at Sant Feliu de Guíxols' Museu d'Història

promote and facilitate the participation of Spanish research groups in international R&D projects. IBEC's proposal, 'Internationalization strategy of the Institute for Bioengineering of Catalonia: Towards better health through Bioengineering and Nanomedicine', will aim, at an institutional level, to increase the support it offers to researchers in applying to European competitive projects under Horizon 2020, the EC's successor to FP7.

To do this, the PMO, which belongs to the Research Affairs Unit, recruited a further project manager, with the result that all of IBEC's project managers will have more time to devote to each of their groups. As well as providing guidance and support with H2020 applications, they'll try to help to increase the number of coordinated projects at IBEC, as well as exploring other funding avenues such as NIH calls.

IBEC group to receive Marató funding for Parkinson's research

IBEC's Molecular and Cellular Neurobiotechnology group (page 98) received funding from 2013's La Marató de TV3 for their project "Role of the cellular prion protein as "cross-talk" protein between α-syn/ LRRK2 and p-Tau in sporadic and familiar Parkinson's disease."

The group's proposal was one of 44 selected for funding under the annual award, which in its 2013 call focused on neurodegenerative diseases. Group leader José Antonio del Rio attended the official award ceremony in l'Auditori de l'Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i Balears yesterday.

The project, which is a collaboration between researchers at IBEC, the University of Barcelona and Vall d'Hebron Research Institute (VHIR), will study the relationship between Parkinson's with dementia and Alzheimer's diseases. Specifically, it will focus on the cellular prion protein (PrP^C) as a "cross-talk" protein between amyloid-beta and p-Tau, which contribute to Alzheimer's by forming plaques or creating tangles inside affected neurons respectively, to try to determine the role it plays in Parkinson's disease.

November 2014

IBEC wins funding from FECYT for outreach activities

IBEC's Communications and Outreach Unit won funding for a year of outreach activities under FECYT's call "Convocatoria de Ayudas para el fomento de la cultura científica, tecnológica y de la innovación 2014".

The Fundación Española para la Ciencia y la Tecnología (FECYT) received 881 proposals from 383 public and private organisations for the call, which offers a total funding pot of €3,25 million for ideas and activities aimed at the promotion of scientific culture, technology and innovation. IBEC's project, which received a total mark of 86 out of 100 in the scoring process, was one of 41 to be funded under the call's subsection on 'Networks for dissemination and communication'.

The project will consolidate and develop some of the institute's existing outreach activities, such as increasing the range of demonstrations and hands-on experiments available for the group visits from schools. It also proposes some new ones, such as an outreach blog and a calendar of dates related to IBEC's research areas, such as the International Day of Biotechnology. All the activities will be aimed at the general public or secondary school and undergraduate students.

CIBER-BBN YSF in Biomaterials Award goes to IBEC researcher

Oscar Castaño, a senior researcher in IBEC's Biomaterials for Regenerative Therapies group (page 47), was awarded the CIBER-BBN YSF in Biomaterials prize for 2012-2014.

Awarded biennially by the CIBER-BBN-Young Scientist Forum in Biomaterials, the prize recognizes, encourages and stimulates outstanding research contributions to the field of biomaterials by young scientists working in Spanish institutions who incorporate an international dimension and perspective into their research. The prize is in its second edition, the 2010-2012 edition having been won by Prof. Manuel Salmerón Sánchez (CBM-UPV, Valencia).

Oscar accepted the award at the 8th CIBER-BBN Annual Conference in Girona, which two-day event also featured contributions by several IBEC researchers including group leaders Raimon Jané, Pau Gorostiza, Ángel Raya, Elisabeth Engel and Josep Samitier.

December 2014

Ramon Margalef Prize for former IBEC PhD student

Xavier Serra, formerly a PhD student in IBEC's Integrative Cell and Tissue Dynamics group (page 112), was awarded a prestigious Ramon Margalef Prize for the best paper derived from a doctoral thesis at a ceremony at the UB.

Xavier received the prize for a 2012 *Nature Physics* paper, "Mechanical Waves during tissue expansion", which describes a new type of mechanical waves in living matter.

There were 82 candidates for the prize, now in its 10th edition, which is conferred by the UB's Board of Trustees and the Bosch i Gimpera Foundation and which is named after of Spain's first professor of ecology.

Since completing his PhD at IBEC in 2013, Xavier has moved away from the bench, and is currently involved in the scientific evaluation of the research projects of La Marató de TV3, the telethon that raises money every year for research into different diseases.

EIT selects IBEC consortium for new KIC on health

It was announced at the end of the year that a consortium involving IBEC was the winning proposal for the EIT's Knowledge and Innovation Community (KIC) on healthy living and active ageing.

The partnership of 144 European companies, research institutes and universities was selected by the European Institute of Innovation and Technology (EIT) as the EIT Health KIC.

With a total of €2.1 billion it is one of the largest public funded initiatives for health worldwide. For the next seven years, the partners – which also include INSERM (France), Imperial College (UK), Roche, Siemens and Philips – will develop innovative products, education and services addressing the challenge of demographic change in Europe.

IBEC will play a key role in the project, as Barcelona has been selected as one of Innolife's six co-location centres, serving as a regional cluster to bring together the partners of the KIC and ensure that its innovation potential is fully realised.

The EIT's first three KICs on climate change, ICT and sustainable energy – Climate-KIC, EIT ICT Labs and KIC InnoEnergy – were selected in 2009. The new KICs announced in 2014, EIT-Health and EIT-RawMaterials, are expected to become fully operational after signing a seven-year Framework Partnership Agreement with the EIT in 2015. They will each receive a start-up grant of up to €4m.

Right: José Antonio del Rio (left) receives his certificate at the awards ceremony of La Marató de TV3

Below: Xavi Serra, winner of the Ramon Margalef Prize for the best paper derived from a doctoral thesis, explains his research

Scientific Highlights

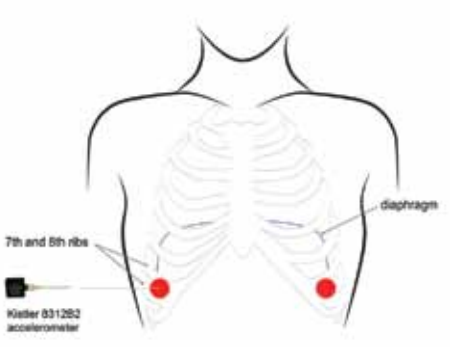
February 2014

Every breath you take

The Biomedical Signal Processing and Interpretation group (page 64) described in *PlosOne* a new method to evaluate the signals produced by the activity of the respiratory muscles. These signals enable the detection and quantification of the level of muscular weakness caused by pathologies such as chronic obstructive pulmonary disease, a common cause of death in the USA.

The mechanical activity of the respiratory muscles is measured by accelerometers placed in the chest surface at the level of the diaphragm. Traditionally, the method used to diagnose and evaluate patients is based on pressure and measuring respiratory flow. Among the drawbacks of this are that as well as being intrusive and uncomfortable and requiring effort on the part of the patient, it delivers a result based only on the activity at the moment of testing. In their paper, the team proposed a non-invasive method based on a new algorithm that will improve monitoring of patients.

This new method, based on the signal sample entropy estimation (fSampEn), is more reliable in estimating the muscle effort than existing ones, even at low levels of flow.

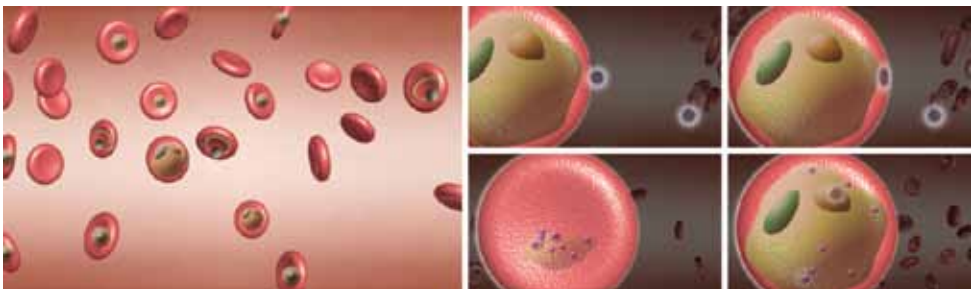


Right: The Biomedical Signal Processing and Interpretation group and their collaborators developed a new non-invasive method to monitor patients with respiratory diseases.

Nanoparticles as drug carriers for malaria

A study by researchers from Nanomalaria (page 52), the joint unit with the Barcelona Centre for International Health Research (CRESIB), demonstrated that an antimalarial drug encapsulated in nanoparticles—chloroquine salts in polyamidoamine polymers—is significantly more effective when delivered *in vivo* than free (unencapsulated) drugs and may help to curb drug resistance. The study, published in the *Journal of Controlled Release*, indicated that the nanoparticles are capable of recognising different *Plasmodium* species, making their potential as carriers for malarial drugs broader than that of other options.

The researchers explored the usefulness of two polymeric nanosystems as carriers for antimalarial drugs that selectively target the pathogen. The first, AGMA1, also has antimalarial activity, which is demonstrated by its inhibition of the growth of *Plasmodium falciparum in vitro*. The study showed that both polymers bind preferentially to *Plasmodium*-infected red blood cells compared to uninfected cells, as well as being able to recognise divergent species.



Below: When added to *Plasmodium*-infected blood (left panel), drug-conjugated polymers (small panels, clockwise from upper left) (i) bind and (ii) enter parasitized erythrocytes, (iii) releasing a drug that (iv) eliminates the pathogen. culture containing both infected and non-infected cells.

March 2014

First functional human 'splenon-on-a-chip'

Scientists from Nanobioengineering (page 103) and ISGlobal's research centre CRESIB designed the first-ever functional 3D splenon capable of reproducing the function of the spleen – filtering red blood cells. They created a microscale platform that reproduces the physical and hydrodynamic properties of the functional unit of the splenon, or splenic red pulp, including two flow-division channels to recreate the closed-fast and open-slow microcirculations of the blood in the spleen. In the slow channel, the blood flows through a pillar matrix that resembles the actual environment where the hematocrit is increased and unhealthy blood is destroyed. The device has been tested with healthy and malaria-infected human red blood cells, and may serve to investigate potential drugs for malaria and other blood disorders. The study was published in *Lab on a Chip*.

Research into organs on chips integrating microfluidics and cell systems is still in its early phases, but it offers holds enormous promise for testing drugs for different diseases in the future. These 3D devices, by mimicking the tissue–tissue interfaces and unique microenvironments seen in whole living organs, allow new insights into diseases that cannot easily be obtained with conventional animal studies, which are costly and time-consuming. They may also yield results related to humans that animal models cannot predict.

Helping the brain rebuild itself

Tissue regeneration researchers in IBEC's Biomaterials for Regenerative Therapies group (page 47) and their collaborators at the UB and the UPC developed an implant that could aid the regeneration of brain tissue, particularly in cases of injury at birth.

In the study, headed by Dr. Soledad Alcántara from the Neural Development Group at the University of Barcelona, the scientists found that implants made of biodegradable polylactic acid nanofibers reproduce some aspects of the natural embryonic brain environment and encourage tissue to regrow. These implants, known in tissue engineering as scaffolds, release L-lactate, a common cellular cue that induces angiogenesis; and they also mimic the neurogenic niche – the environment in which the brain develops – allowing neural progenitors to generate new neurons and glial cells that migrate in the same way as during brain development.

April 2014

More accurate testing for lower respiratory tract infections

A study involving researchers from Nanobioengineering (page 103), the University of Barcelona and the Catalan company Biokit SA described the development of a device 'on-a-chip' able to carry out automated extraction and testing for bacterial or viral DNA or RNA directly from human samples. Focused specifically on lower respiratory tract infections (CA-LRTI) such as pneumonia and bronchitis, the miniaturized device carries out the entire sample preparation procedure, extracting purified DNA or RNA from real samples of CA-LRTI pathogens more effectively than in existing experiments. It also offers hands-free operation, self-explanatory data and reliable results, even if used by a non-expert. Since respiratory tract infections are the most common reason for prescribing antibiotics, improving diagnostics in this field could also help curb antibiotic resistance.

May 2014

Uncovering a basic mechanism in breast cancer

In a study published in and featured on the cover of *Nature Materials*, researchers in IBEC's Cellular and Respiratory Biomechanics group (page 82) and London's Barts Cancer Institute demonstrated how the molecules that cells use to attach to their environment, integrins, allow cells to detect and adapt to tissue rigidity, one of the first signs of tumor development.

In healthy breast cells, the adhesive properties of integrins lead cells to reduce the force they apply to their environment if the tissue is stiffer than normal. Because reducing force also reduces tissue stiffness, this mechanism can prevent tissue stiffening.However, cancer cells in the breast express a different type of integrin with different adhesive properties,

which leads cells to apply higher forces as tissue stiffness increases, creating a feedback mechanism that can eventually lead to the hard lumps characteristic of breast tumors.

The study is the first time that a molecular mechanism of rigidity sensing by cells has been described, and it's been demonstrated in healthy and unhealthy human breast cells. Abnormally rigid tissues are found not only in breast tumors but in several other types of cancer that express many different types of integrins, so mechanical changes induced by altered integrin expression could be a key aspect behind the onset of several diseases.

June 2014

What regulates the migration of Cajal-Retzius cells?

Researchers from Molecular and cellular neurobiotechnology (page 82) and the UB, in collaboration with scientists in France and the USA, identified a new molecular mechanism regulating the migration of Cajal-Retzius cells in the early stages of development of the cerebral cortex, the outermost layer of the brain.

The correct distribution of Cajal-Retzius cells in the cortex is essential because, in humans, if there are alterations in distribution or no expression of some of the molecules produced by these cells, lissencephaly will develop, a disease in which the cortex is smooth, leading to mental retardation and impaired control of movements. In the study, published in *Nature Communications*, the researchers demonstrated the functions of a signaling molecule, Semaphorin 3E (Sema3E), which, by joining PlexinD1 (its specific receptor present in Cajal-Retzius cells) is able to modulate the action of the CXCL12 / CXCR4 system, indicating when the Cajal-Retzius cells have to stop migrating.

July 2014

Why Alzheimer's patients have no memory loss when the disease starts

There are two stages of Alzheimer's disease: the initial one, where symptoms aren't clear, and a second phase with well-defined symptoms. In a paper published in *Molecular Neurobiology*, IBEC researchers from Molecular and cellular neurobiotechnology (page 82) revealed that our nervous system's naturally protective response to the onset of Alzheimer's may contribute to the fact that patients do not suffer memory loss until the disease has progressed further.

Alzheimer's can be attributed to two major events in the brain; the presence of extracellular aggregates, mostly a compound known as beta-amyloid peptide, which forms plaques; and the accumulation of a very phosphorylated form of the protein tau, which forms small tangles inside affected neurons. Until now, it was known that the formation of these tau tangles in neurons depends on the toxicity of the beta-amyloid peptide, but it the mechanisms of this interaction between the two wasn't understood.

The researchers – who worked in collaboration with members of CIBERNED, the Centre for Molecular Biology in Madrid, and the Institute of Neuropathology IDIBELL-Bellvitge University Hospital – described the relationship between beta-amyloid peptide oligomers and tau phosphorylation and the presence of another protein, the cellular prion protein (PrP^c), during the early, asymptomatic stages of the disease. The results show that when the levels of PrP^c are high, the levels of phosphorylated tau protein inside the cell are lower, even if the beta-amyloid peptide oligomers are present. When PrP^c levels are low, however, the amount of tau – as well as its phosphorylated form that makes the tangles inside the cell – increases, contributing to the brain deterioration observed in Alzheimer's. They conclude that the overexpression of PrP^c seen at the beginning of the disease is part of the protective response of the nervous system in an attempt to suppress its progress.

Heparin exhibits dual activity against malaria

A study published in *Nanomedicine* by researchers from Nanomalaria (page 52) and the University of Barcelona opened the door to improved treatment of malaria with heparin, which has been shown to have antimalarial activity and specific binding affinity for red blood cells infected with *Plasmodium falciparum* versus non-infected blood cells. The study explored whether these properties could be exploited in a strategy based on the targeted delivery of antimalarial agents.

Using confocal fluorescence and transmission electron microscopy, the researchers observed that heparin adsorbed onto positively charged liposomes loaded with the antimalarial drug primaquine achieved three times the activity of the encapsulated drug alone in *P. falciparum* cultures. At heparin concentrations lower than those inducing anticoagulation of mouse blood *in vivo*, the improved parasiticidal activity was found to be the combined result of two distinct activities: that of free heparin as an antimalarial, and that of liposome-bound heparin as a targeting element for the encapsulated drug primaquine. The results open the door to improving antimalarials with heparin both a drug and as a specific targeting element for other antimalarial agents.

Delving deeper into the inner workings of cells

IBEC's Nanoprobes and Nanoswitches group (page 60) and their collaborators published a paper in *JACS* outlining a new way to use light-regulated proteins – protein 'switches' which, controlled remotely, can turn specific biochemical functions in living cells on or off, thus enabling researchers to set up and test a multitude of scenarios within the cell – to activate or deactivate processes at a much deeper level in tissue, and with higher 3D resolution.

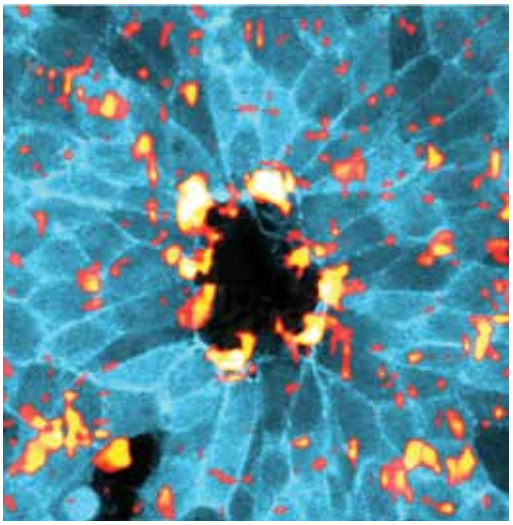
Photoswitchable biomolecules are used to precisely manipulate cellular biochemical processes, but nobody had explored a microscopy method known as two-photon excitation – which offers deeper tissue penetration, smaller excitation volume, and reduced phototoxicity and photobleaching – in relation to these switches. Now, existing protein switches can be also used with multi-photon excitation with near-infrared light, providing subcellular resolution. The discovery also constitutes an important advance in optogenetics and optopharmacology to control and monitor the activities of individual light-sensitized neurons in order to be able to map neural circuits.

August 2014

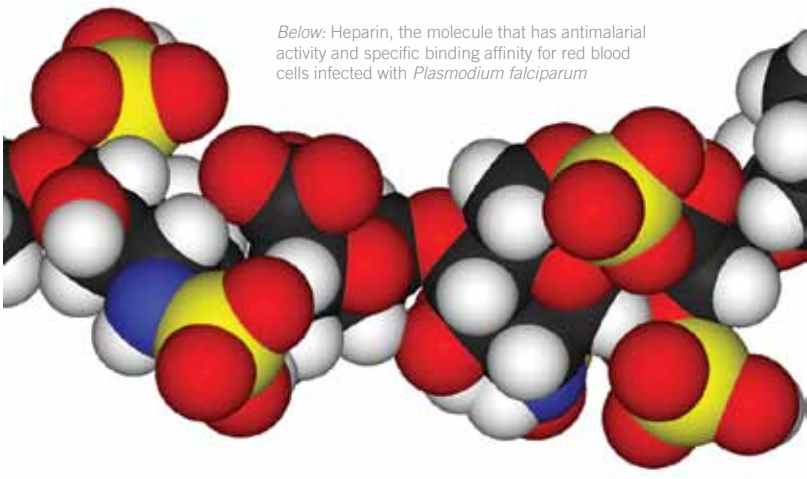
New mechanism for wound healing

IBEC's Integrative Cell and Tissue Dynamics group (page 112) found a new way to decipher the mechanisms of wound healing, and by doing so uncovered a new understanding of how cells move and work together to close gaps in tissue. The work, published in *Nature Physics*, signified a big step forward in unravelling the mystery of how wounds are repaired and could eventually help with the development of drugs to accelerate healing.

It's been known for a while that two different mechanisms contribute to wound healing. One is the 'purse-string' method, where a ring of contractile proteins forms at the edges of the wound and tightens like the strings of a purse; and the other is 'cell crawling', when cells themselves throw out 'arms' called lamellipodia to drag themselves along to close the gap. The IBEC group, together with their collaborators at the IRB, UPC and UB in Barcelona, the University



Left: Map of the physical forces exerted by cells during wound healing. Cells are labelled in blue, forces are shown in red and yellow, and the wound is the central black region.



Below: Heparin, the molecule that has antimalarial activity and specific binding affinity for red blood cells infected with *Plasmodium falciparum*

Paris-Diderot, the Mechanobiology Institute of Singapore and the University of Waterloo in Canada, pioneered a technique to measure the nanoscale forces behind wound healing and, in doing so, they discovered that the two currently accepted mechanisms are not sufficient to fully explain the phenomenon. Instead, they showed that a new mechanism applies, in which cells assemble supracellular-contractile arcs that compress the tissue under the wound, and that contractions arising from these arcs make the wound heal in a quicker and more robust way.

Being able to optimize tissue repair is a major need for the treatment of acute and chronic diseases. The discovery of the basic mechanism reported in the study is a major step in the quest to achieve effective organ regeneration.

Researchers measure a property of DNA for the first time

In a study published in *PNAS*, researchers from the Nanoscale Bioelectrical Characterization (page 56) and their collaborators at the Institute for Research in Biomedicine (IRB), the Barcelona Supercomputing Center (BSC), the Centro Nacional de Biotecnologia (CNB-CSIC) and IMDEA Nanociencia in Madrid described how they have found a way to directly measure DNA electric polarizability – represented by its dielectric constant, which indicates how a material reacts to an applied electric field – for the first time.

The researchers used their own technique, recently developed at IBEC, based on electrostatic force microscopy (EFM). This type of atomic force microscopy allows researchers to explore not only the morphology of single biological complexes in their natural environment, but also to measure the electrostatic properties that make each object unique. They quantified DNA's dielectric constant – a fundamental property that directly influences its biological functions – in a non-invasive way by measuring the DNA in its native condensed state inside a single bacteriophage (a virus that infects and replicates within a bacterium). The special nature of these viruses means that they carry genetic information condensed into a small shell, thus having their DNA in an almost crystalline structure which the researchers were able to dissect to determine the dielectric constants of the main components, the protein shell and tail.

Their experiments and calculations revealed an inherent property of DNA that will allow the realistic prediction of its conformation and functions based on computational tools and help us better understand the essential roles tht DNA plays in our bodies.

September 2014

Scientists develop first light-operated drug for most common target proteins

Researchers in IBEC's Nanoprobes and Nanoswitches group (page 60) and their collaborators announced the development of the first ever light-controlled therapeutic agent whose effects focus specifically on the largest, most important class of drug target proteins – G protein-coupled receptors.

In the journal *Nature Chemical Biology*, the scientists revealed Alloswitch-1, the latest advance in their research into photoswitchable (or light-operated) drugs. Controlling drug activity with light means that the therapeutic effects can be accurately delivered locally, thus reducing their effect on other areas and the resultant side effects, and helps reduce the dosage required.

The colleagues, from IBEC, IQAC-CSIC, UAB and IDIBELL in Barcelona and the IGF-CNRS in Montpellier in France, developed the small molecule therapeutic agent that modulates drug target protein receptors specifically at the allosteric, or non-active, site of the protein. Allosteric modulators have a number of advantages over traditional drugs, offering higher selectivity of target receptors, tunable release according to whether the undesirable protein receptor activity is present, and lower potential for toxicity. The effects of this 'optopharmacological' compound can be remotely controlled in space and time in living, wild-type organisms. This is an advantage over optogenetic manipulations, which require gene overexpression using viruses, for example.

Small molecule therapeutic agents such as Alloswitch-1, if they can be made available orally, could offer a competitive advantage over traditional drugs, which often affect off-target tissues and organs, leading to unwanted consequences and compromising their beneficial effects.

IBEC collaboration succeeds in measuring bacterial cell response to electrical fields

Gabriel Gomila's Nanoscale Bioelectrical Characterization group (page 56) and that of Antonio Juárez, Microbial Biotechnology and Host-pathogen Interaction (page 70), combined their expertise on microscopic electrical measurements and bacteria respectively to come up with a way to study the response to external electrical fields of just a single bacterial cell.

Being able to measure the electric polarizability – which indicates how it reacts to an external electric field – of a single bacterial cell can shed light on the biochemical constituents of the bacterium, as well as on their internal structure, thus opening new possibilities for analytical studies and new explorations to evaluate their critical biological properties, such as adhesion, virulence or viability.

The researchers quantified the electric polarization response of four bacterial types – *Lactobacilus sakei, Salmonella Typhimurium, Escherchia coli* and *Listeria innocua*, all of which are of either clinical or industrial relevance – and revealed important differences between Gram-negative and Gram-positive bacteria.

Previous electrical studies – which until now have only been able to be done on bacterial populations involving millions of bacterial cells, and not on single cells – have allowed researchers to detect bacteria in an environment, count and differentiate them, determine their viability, distinguish mutants even among highly similar genotypes, and separate them from other cells.

November 2014

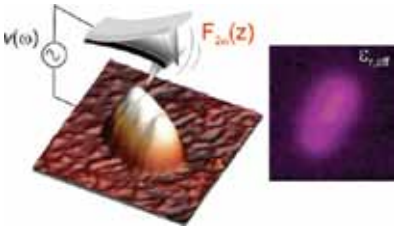
Olfactory system segregates odour data at moment of input

IBEC's Signal and Information Processing for Sensing Systems group (page 74) uncovered how we immediately identify smells even when their concentrations are very low, essentially segregating information about identification and concentration in order to recognise the odour. They did this by looking at the first stage of the olfactory bulb – the glomerular layer, which is the 'input' stage for smells – to see whether this segregation of information is performed there. The group built a computational neural model of the area based on its known anatomical connections and tested it with two simulations. In the first, the model was exposed to six different smells at different concentrations; the second was an 'odour morphing' experiment, where one odour becomes a distinctly different one in stages.

They found that the glomerular layer, where the identity and concentration information of an odour is mixed up when it enters, is indeed the origin of the olfactory system's ability to quickly identify smells while preserving information about their concentration. It does this using two different types of neurons – the mitral cells (MCs) and the external tufted cells (ETs). The MCs are in charge of encoding the odour's identity, while the ETs focus on its concentration – not because of their morphological differences, but because the two types of neurons have contrasting ways of interacting within the glomerular network. It's the first time that this important segregation of information in odour processing has been attributed to the glomerular layer, which was already known for other tasks such as contrast enhancement.

Right: Mitral and tufted cells. © Brain Institute and Department of Physiology, University of Utah School of Medicine

Below: The Nanoscale Bioelectrical Characterization group used electrostatic force microscopy to study the response to external electrical fields of a single bacterial cell.



About IBEC

IBEC Strategy 2014-2017

After IBEC's new Director was appointed in 2013, one of the first actions was to push forward a collaborative exercise to define IBEC's Strategic Plan for the period 2014-2017.

This plan identified the following four areas in which to concentrate efforts:

- To expand the centre both in size and in results by recruiting new professionals and scientists, as well as renewing groups that perform at the highest standard in terms of both scientific quality, and transfer and innovation.
- To focus its scientific work on the areas where it can stand out most distinctively and compete internationally, with an orientation towards scientific and technological challenges with a high impact on people's health and quality of life.
- To forge alliances with organisations of recognised international standing to consolidate the institute's path of specialisation, differentiation and internationalisation.
- To improve the way the institute is managed by implementing tools such as an integrated management system and management by results, in order to make the best use of resources and align management with its strategy.

In this way, IBEC's Strategic Plan for 2014-2017 is structured in terms of four strategic goals:

- **SG1.** To consolidate top-class science which enables IBEC to strengthen its international position, by focusing its core activity on three areas of application: "Bioengineering for Regenerative Therapies", "Bioengineering for Future Medicine" and "Bioengineering for Active Ageing" (see opposite).
- **SG2.** To develop technology and applications thereof that help to improve business competitiveness and the quality of hospital services.
- **SG3.** To run a distinctive specialist training programme to attract international talent.
- **SG4.** To develop a culture of excellence in management, self-sustainability and management by objectives.

Each of these strategic goals is pursued in the following areas of action: Research, Technology transfer and translation, Training development, Human resources (see box opposite), Management, Alliances, and Communication (below).

IBEC's Communications Plan

The IBEC Communications Plan forms an important part of the IBEC Strategy 2014-2017. As well as directly addressing its own five objectives, the plan will contribute to the rest of the strategy's goals by strengthening the messages conveyed by IBEC and its positioning. It proposes a new communications structure and strategy for IBEC, based on clear mission statements for the organization and a derived communications architecture. It sets out a resourcing plan for the Communications Unit for the period 2014-2017 and proposes tactics to address five institutional objectives to which communications can contribute:

- To demonstrate that IBEC is an attractive destination for the best researchers at all stages from all over the world;
- To communicate the services and products IBEC has to offer to industry and hospitals;
- To achieve more visibility in the media to contribute to establishing IBEC as a strong bioengineering brand;
- To identify collaboration opportunities with foundations with shared interests as alternative sources of support;
- To improve internal communication at a scientific and social level.

The plan was approved by IBEC's Board of Trustees in 2014.

Human Resources Strategy

An important part of IBEC's Strategic Plan 2014-2017 has been the design and implementation of a new Human Resources Strategy for Researchers (HRS4R) according to the principles of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers. During the second half of the year, a working group conducted an internal analysis to identify improvement areas. As a result, an Action Plan for the next four years has been created.

One of the first measures of the HRS4R's Action Plan was to set up a Gender and Diversity Committee comprising researchers at all career stages which is committed to analysing equal opportunities and diversity topics. This committee produced the 'IBEC Equal Opportunities and Diversity Management Plan' which includes 17 actions to be implemented from mid-2014 to end 2016.

The main action implemented in 2014 was an "Internal procedures guide" which contains useful information about different aspects of IBEC's internal operations that can be quickly consulted by staff. The guide covers a number of measures related to balancing work and family life for IBEC employees, such as telecommuting, paid leaves or part time work to mention just a few. Its aim is to improve labour conditions in order to achieve an optimal balance and better compatibility between work responsibilities and personal lives for all IBEC staff.

Both documents have been approved by the Board of Trustees.

Three areas of application

On the basis of the generating knowledge in bioengineering and nanomedicine, IBEC focuses its scientific and technological work – which can be grouped into the three flagships of Nanomedicine, Cell Engineering and ICT for Health – around three core areas of application:

■ Bioengineering for Future medicine

Developing technology that goes beyond the existing paradigm of medical care in hospital to incorporate new areas like photopharmacology, organs on chips and diagnosis based on the mechanical behaviour of cells and tissues.

IBEC researchers use their bioengineering tools, technology and techniques to better understand the behaviour of proteins, cells, tissue and organs in the body, or develop solutions such as nanocapsules for targeted drug delivery, nanoscale tools to study biological systems, molecular actuators that can be switched on with light, and *in vitro* organs 'on-a-chip'.

■ Bioengineering for active ageing

Developing care and telemonitoring technology to meet the needsn of an increasingly ageing population and make it possible to enhance the quality of life and independence of elderly people.

Biomedical engineering can contribute greatly to improving the quality of life of older people. Assisted living technologies such as telecare, home-based devices and services that support daily life with a remote link to a call-centre, and telehealth can help support independent living at home, keeping patients out of hospital and residential care for longer.

■ Bioengineering for regenerative therapies

Developing regeneration technology to allow the creation of implants able to bring about the regeneration of damaged tissues or organs and to develop cell therapies.

Combining new tailored nanobiomaterials with cell engineering drives advances in tissue engineering for the repair and replacement of human tissues damaged by injury, illness and ageing. Biomaterials engineering involves the synthesis, processing and characterization of new materials, including polymers, proteins, glasses, cements, composites and hybrids, to make materials that can act as physical supports for engineered tissues, as well as providing the crucial topographical and chemical cues to guide cells in regeneration.

The IBEC foundation

IBEC is a non-profit foundation established at the end of 2005 by the Generalitat de Catalunya (Autonomous Government of Catalonia), the University of Barcelona (UB) and the Technical University of Catalonia (UPC).

The main governing body of IBEC is its Board of Trustees with representatives from the Catalan ministries of Health and Research, the UB and UPC. The Board of Trustees meets twice a year to approve IBEC's annual budget and monitor its activity to ensure that it pursues scientific excellence with societal impact. For executive purposes, a Management Committee (chosen from the Board) monitors IBEC's activities through *ad hoc* meetings with the Director and Managing Director.

The Board's decisions are guided by an independent International Scientific Committee (ISC). This committee ensures practices and criteria are implemented in accordance with international standards of excellence in research.

IBEC's relationship with the universities

IBEC's forerunner, the Centre of Research for Bioengineering (CREB) of the Technical University of Catalonia (UPC), was founded in 1992 by six research groups from five different departments with the aim of collaborating in research and industrial projects in the broader area of bioengineering. IBEC's first director, Prof. Josep A. Planell, was director of CREB from 1997 and led the process that resulted in the creation in 2003 of the Catalan Reference Centre for Bioengineering (CREBEC), composed of different divisions from the above-mentioned CREB and the Research Centre on Bioelectronics and Nanobioscience (CBEN) of the University of Barcelona (UB). CREBEC, which aimed to coordinate the multidisciplinary research activities in biomedical engineering carried out in Catalonia, was transformed at the end of December 2005 into the Institute for Bioengineering of Catalonia (IBEC).

Today, two thirds of IBEC group leaders are faculty members at either UB or UPC. IBEC's PhD students are able to follow their doctoral courses at the universities, which offer degrees in physics, chemistry, biology, materials science and engineering, among others, and masters courses related to bioengineering and nanomedicine, attracting students from all over the world.

Several others of IBEC's research staff are also involved in the doctoral programmes, particularly in the joint Biomedical Engineering Programme. Moreover, being located on the same campus, the relationship with both universities and the access to their facilities – library, scientific services, etc – is very fruitful.

IBEC's current director, Josep Samitier, was Vicerector of Research and Innovation and Acting Rector of the University of Barcelona (UB) from 2005 to 2008. He remains Full Professor of Electronics in the university's Physics Faculty.

The research groups affiliated with the two universities which are seconded at IBEC are listed on page 126.

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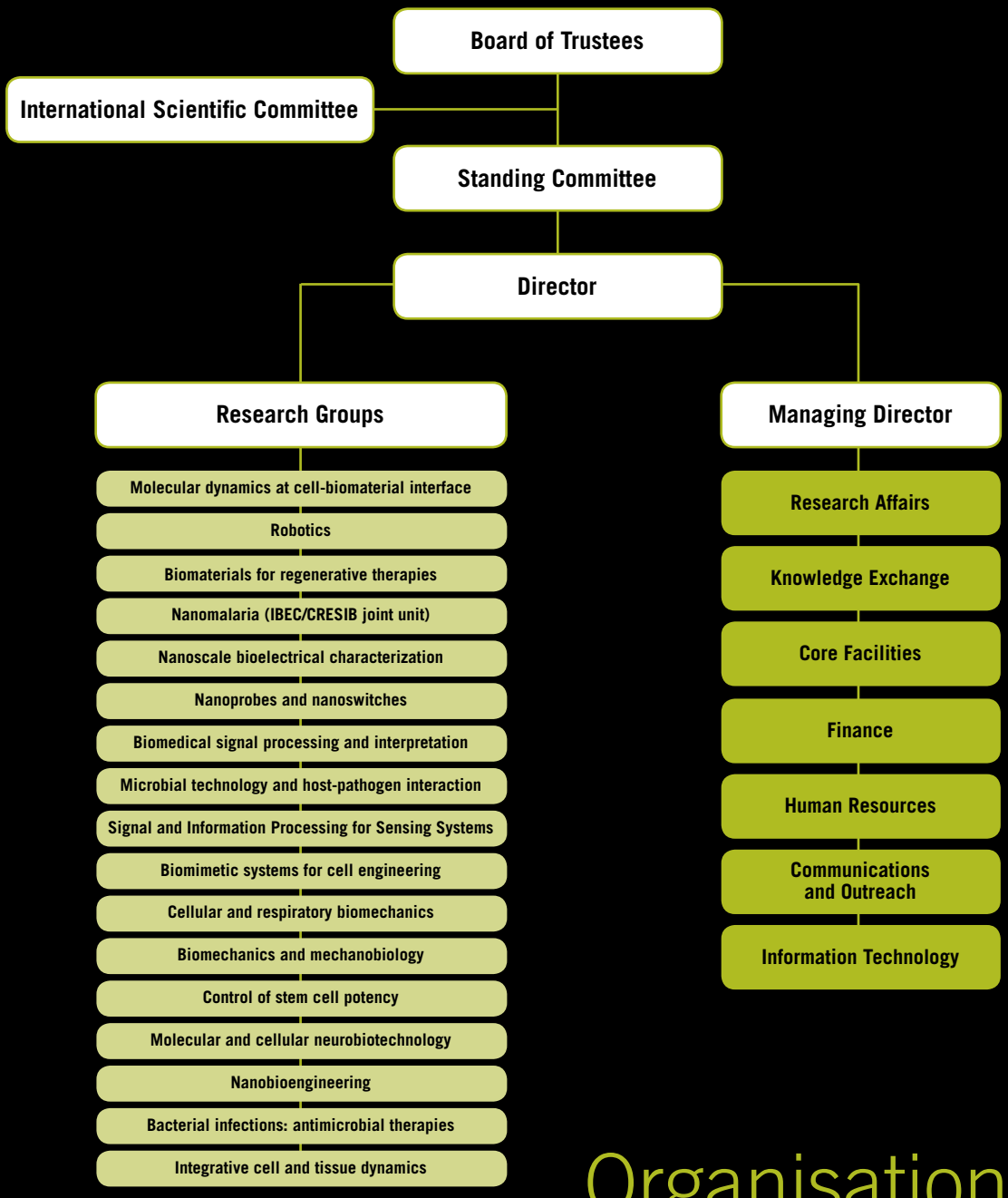
Prof. Bernat Soria
Director Departamento de Células Troncales, Centro Andaluz de Biología Molecular (CABIMER), Seville, Spain

Prof. Molly Stevens Professor of Biomedical Materials and Regenerative Medicine / Research Director for Biomedical Material Sciences, Institute of Biomedical Engineering Imperial College, London, UK

Jocelyne Troccaz, PhD
Director de Recherche, CNRS Equipe Gestes Médico-Chirurgicaux Assistés par Ordinateur (GMCAO), Laboratoire TIMC-IMAG, Université Joseph Fourier-CNRS, France



Organisational chart

RESEARCH AFFAIRS

Head of Research Affairs Teresa Sanchis

Coordinator of Project Management Office Javier Adrián

Project Managers Ester Rodríguez, Javier Selva, Guillermo Talavera

Funding Managers Esther Gallardo, Rosa Bonet

Research Affairs Assistant Judith Forné

Managing Director
David Badia

HUMAN RESOURCES

Head of Human Resources Carol Marí

HR Technician Ricard Rius

HR Junior Technician Ciara Boter

Occupational Hazards Prevention Technician Raquel Guillén

IT

IT Manager Juli Bafaluy

IT Technician Francisco Contreras

KNOWLEDGE EXCHANGE

Head of Knowledge Exchange Arantxa Sanz

Project Managers Marta Soler, Miroslava Ogorelkova

COMMUNICATIONS AND OUTREACH

Head of Communications and Outreach Vienna Leigh

Coordinator of Media Relations and Branding Àngels López

Coordinator of Events Pilar Jiménez

Communications and Outreach Assistant Carolina Llorente

FINANCE

Head of Finance Ana González

Purchasing Technician Mayte Muñoz

Accounting Technician Francisco Buenestado

Finance Assistant Victoria López

Junior Accounting Technician Laia González

Support Services (Administration)

For the staff list for Core Facilities, see page 118.

Statistics

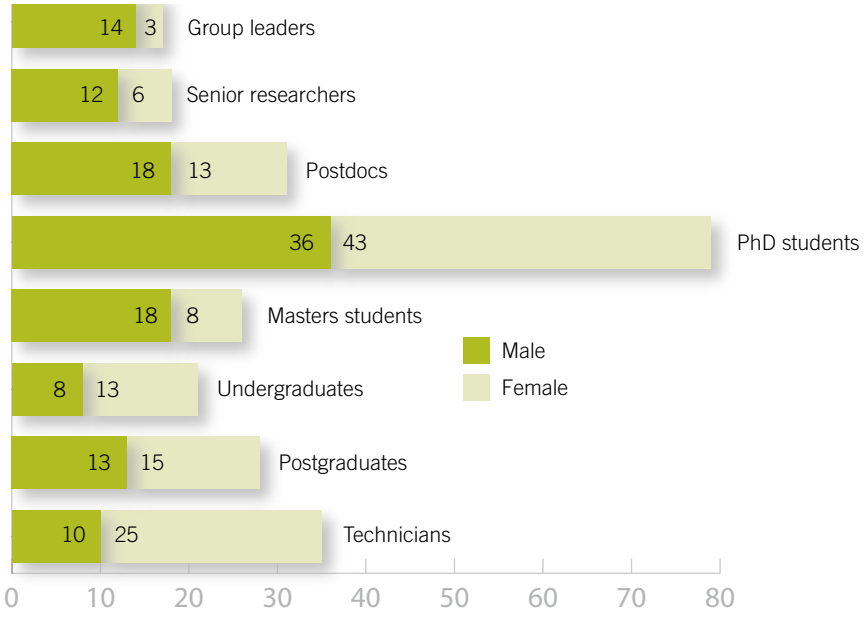
In 2014 IBEC's total staff, including administration staff as well as researchers, students and technicians, numbered 255. Of the researchers, some work on an in-house basis, some come from the University of Barcelona or the Technical University of Catalonia, and some are funded through programmes that support the recruitment of research staff such as the Bosch i Gimpera Foundation, ICREA and the Ramón y Cajal programme (MEC).

The following statistics reflect the state of affairs on 31st December 2014.

1. Age of all IBEC staff (researchers, technicians and administration)

2. Gender of all staff

3. All staff by gender and job category



The 255 personnel at IBEC in 2014 (including administration staff) represented

27 countries

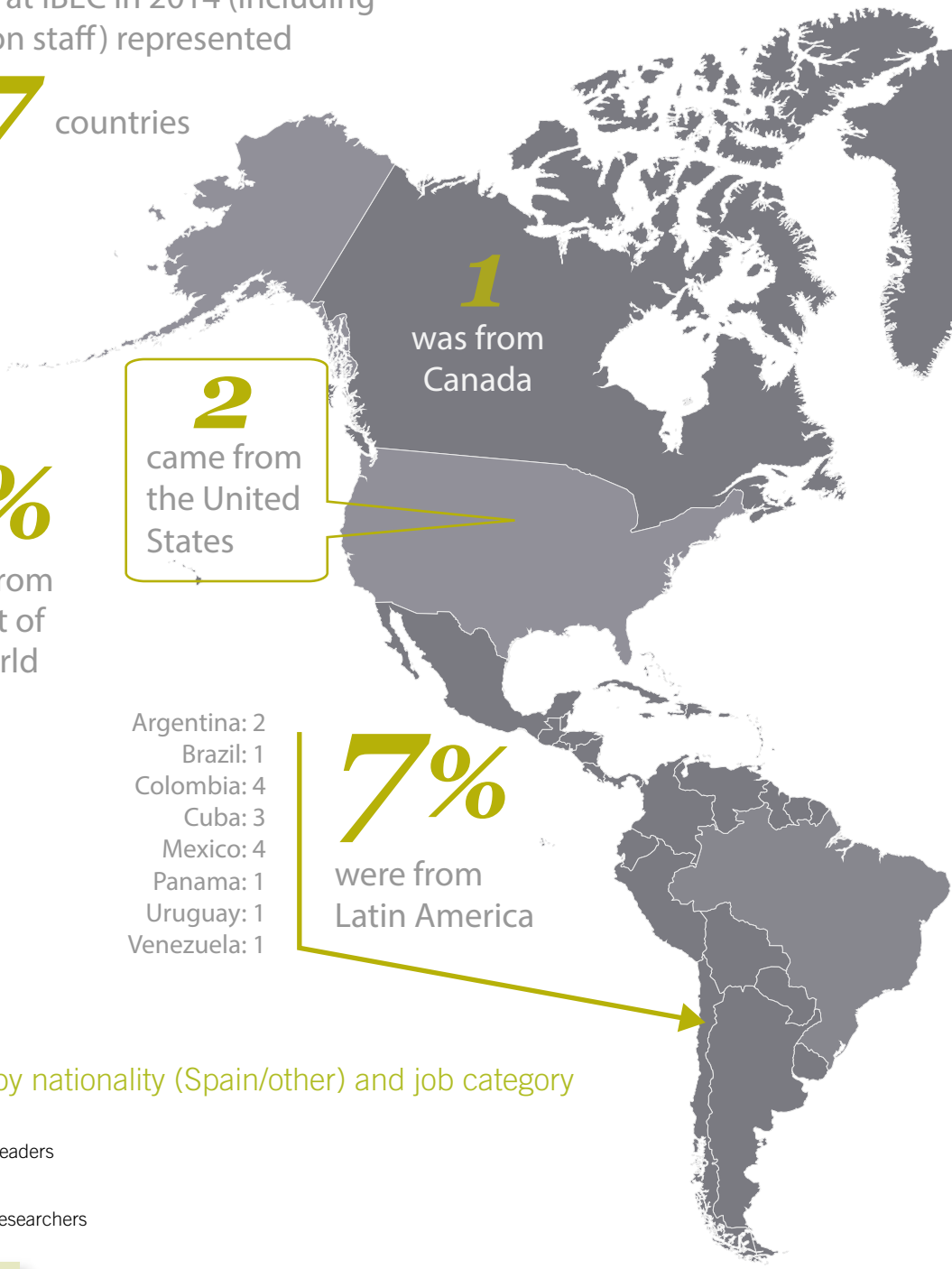
1 was from Canada

2 came from the United States

1% came from the rest of the world

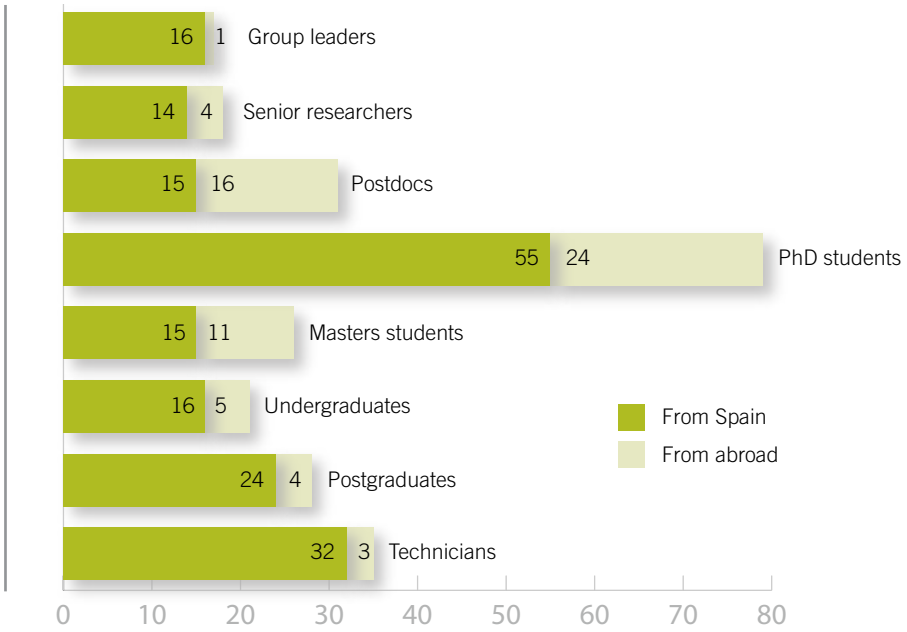
7% were from Latin America

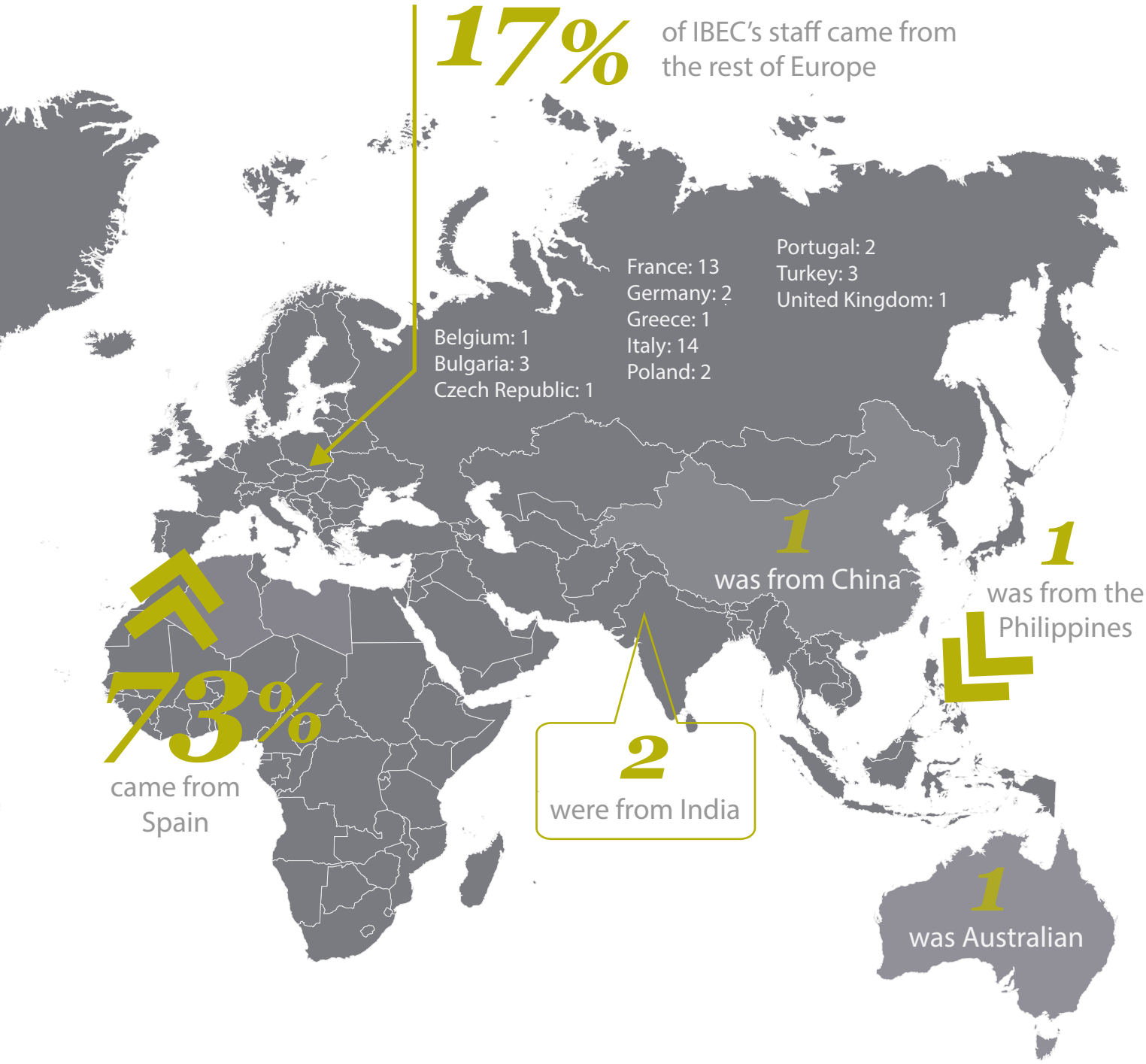
Argentina: 2
Brazil: 1
Colombia: 4
Cuba: 3
Mexico: 4
Panama: 1
Uruguay: 1
Venezuela: 1



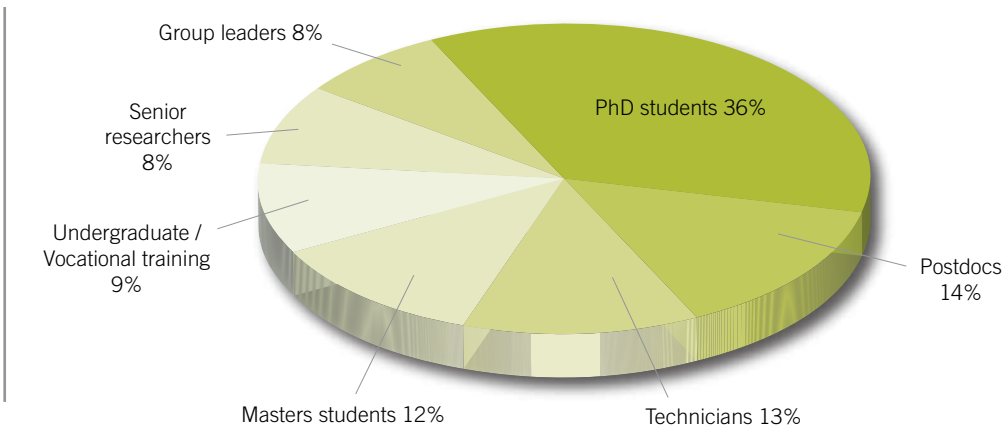
4. IBEC staff by nationality (map)

5. IBEC researchers by nationality (Spain/other) and job category





6. IBEC researchers and technicians by job category

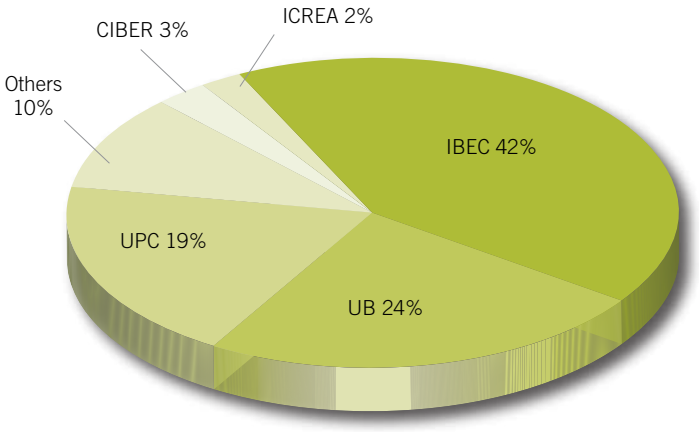


7. Mobility during 2014

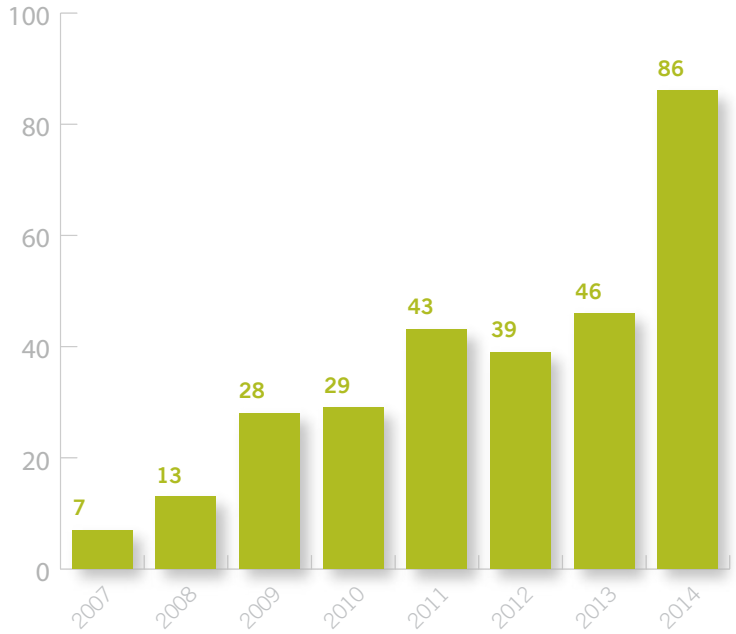
Data refers to researchers only.
Average length of stay in host institutions: 3-6 months.

Percentage of researchers who spent time in labs elsewhere	8%
In Spain	8
In the rest of Europe	6
In the rest of the world	3

8. IBEC staff by contracting institution

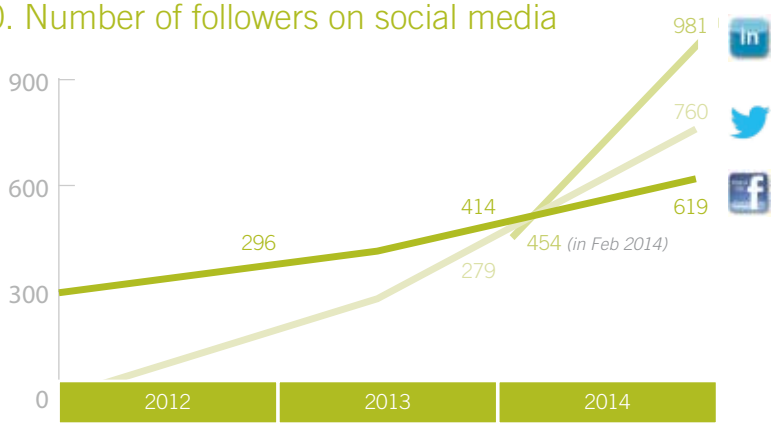


9. Media appearances 2007-2014



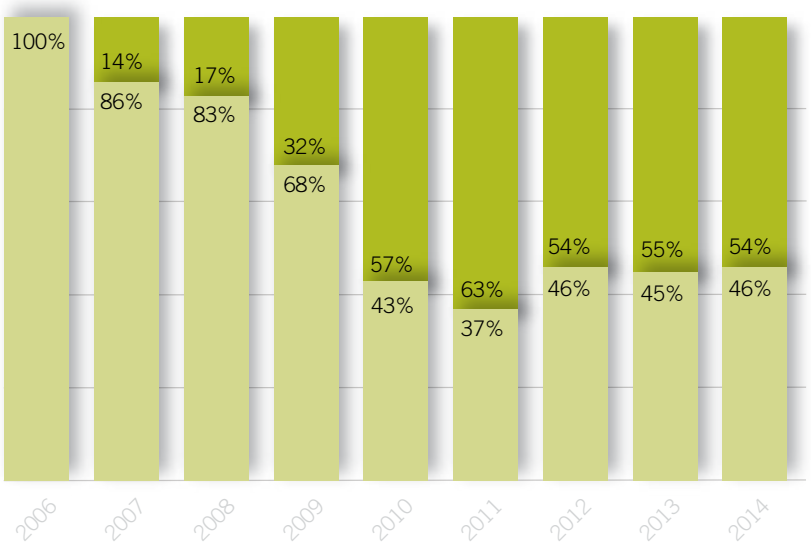
Data counts appearances in general media (such as national daily newspapers, national or regional TV, etc) or established specialist media (eg. Diario Medico, The Lancet)

10. Number of followers on social media



Figures from 31 December of each relevant year, unless indicated

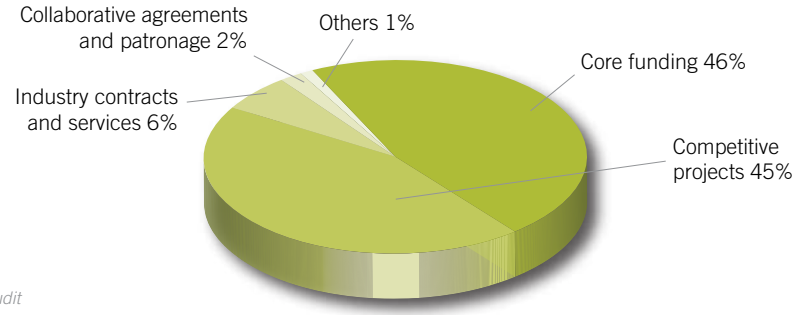
11. Funding sources in 2014*



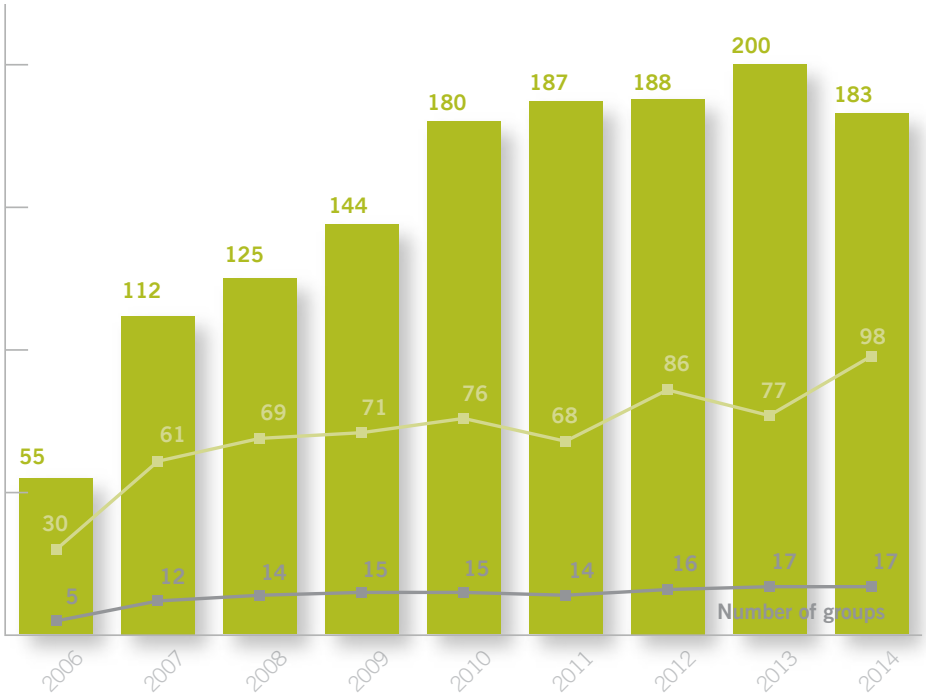
Graph: Percentage of funding from core v. competitive sources. Core funding is funding from trustees. Soft funding includes competitive projects (funded by sources such as the EU's FP7 programme, the Spanish Ministry of Science or the Catalan Ministry of Research), Industry contracts, funding from private institutions.

Pie chart: Different sources of funding in 2014, broken down into types.

** Figures for 2014 are provisional, pending audit*



12. 2006-2014: Evolution of IBEC (groups, publications, researchers)

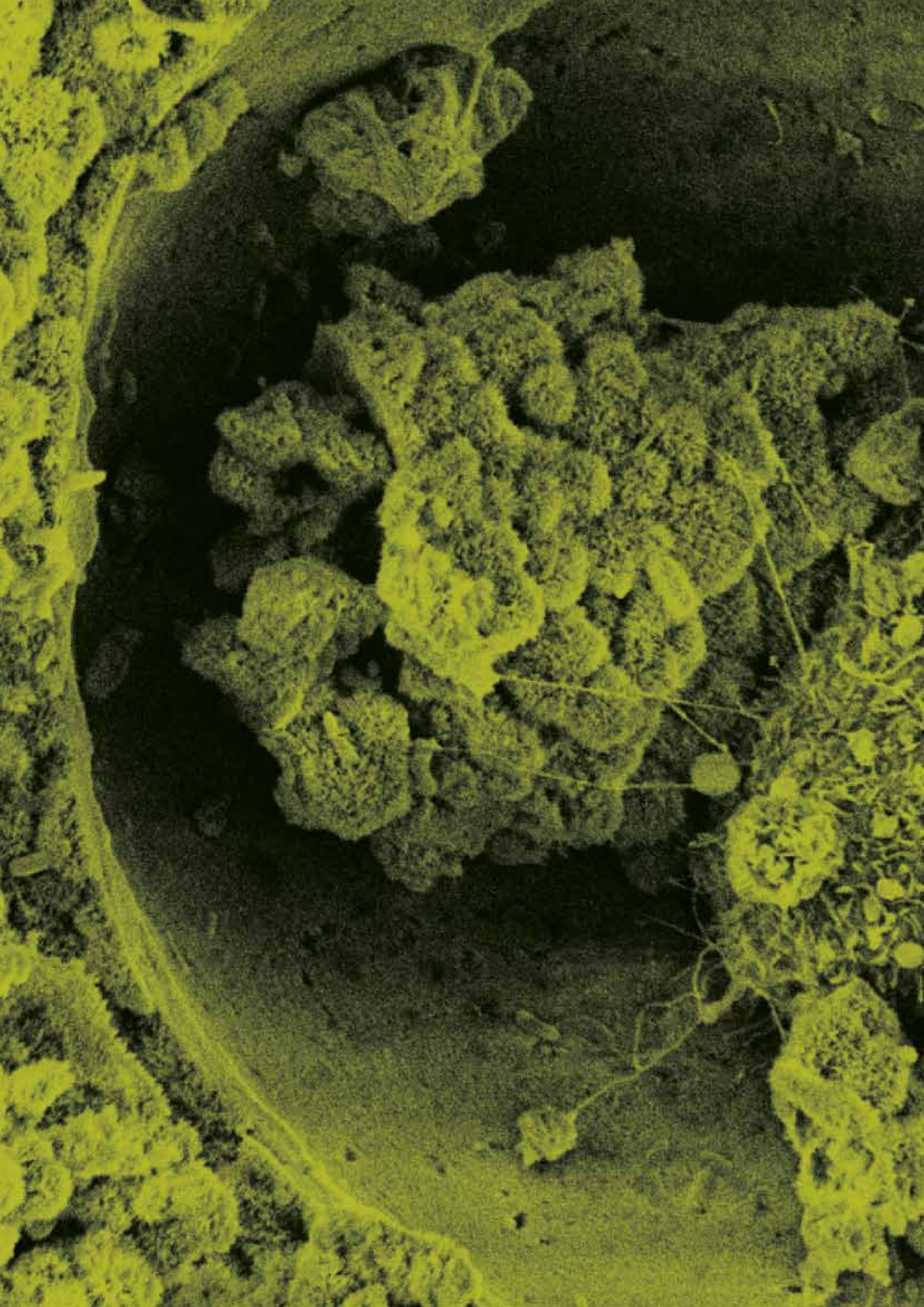


Researchers

Not including under- and postgraduates, vocational students or laboratory and research technicians

Publications

Indexed journal articles only, not including conference proceedings, etc



Research

Molecular Dynamics at Cell-Biomaterial Interface

Group leader/ICREA research professor: George Altankov
Postdoctoral researchers: Johan Gustavson, Tatiana Coelho
PhD student: Dencho Gugutkov
Undergraduate student: Ana Giordani

We are interested in cell–biomaterials interaction, and more specifically, on the dynamic formation of the provisional extracellular matrix (ECM) – the thin protein layer that cells recognize, produce, and remodel at the materials interface.

We aim to learn how this process affects the biocompatibility of materials, and if it can be controlled by engineering the surface properties of materials.

For this purpose, we perform systematic studies in the following directions:

Remodeling of ECM proteins at cell-biomaterials interface

ECM remodeling occurs in various physiological and pathological processes, such as normal development, wound healing and angiogenesis, but also in atherosclerosis, fibrosis, ischemic injury and cancer. It consists of two fundamental processes: assembly and degradation. The organization of ECM is fundamental for biology and medicine, and it proteolytic degradation is a physiological mechanism for the removal of excess ECM. Although matrix remodeling is a subject of extensive biomedical research, the way it is related to the biocompatibility of materials is poorly understood and is therefore a hot topic of our research.

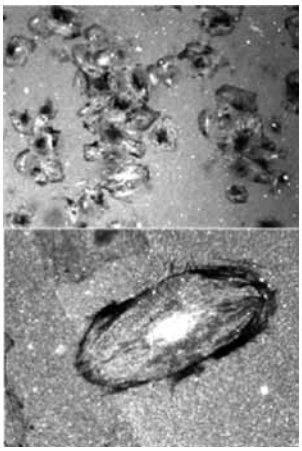
ECM organization at the biomaterial interface depends on the allowance of cells to rearrange adsorbed matrix proteins. We anticipate that materials that bind proteins loosely will support the arrangement of a provisional ECM, while stronger binding provokes its degradation.

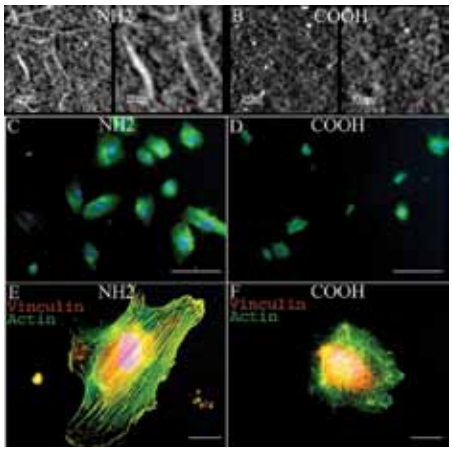
Materials surface-driven assembly of ECM proteins at the nanoscale

Upon adsorption at material interfaces, proteins may assemble spontaneously and this interaction has significant consequences for their biological response. Recently we have employed distinct silane-inspired chemistries and polymer compositions to create model substrates with tailored densities of -OH, -COOH, $-NH_2$ and $-CH_3$ groups, thus varying the chemistry, charge and hydrophilic/hydrophobic balance.

In a series of communications combining AFM and other nanoindentation techniques, we have described a novel phenomenon of substratum-driven protein assembly depicting the fate of various matrix proteins such as fibronectin, collagen IV, vitronectin and fibrinogen at the above model biomaterials interfaces. Specifically, we show that by varying the density of chemical functions one can tailor both the assembly and degradation of proteins. Following those findings we aim to control ECM remodeling by engineering specific material properties. Understanding the behavior of ECM proteins on flat biomaterials interface further boosts an important bioengineering target – the biohybrid organ technologies based on two-dimensional protein layers that mimic the arrangement of the natural basement membrane.

Below left: Pericellular proteolysis of adsorbed vitronectin by HUVECs adhering for five hours on CH_3 chemistry.





Left: AFM images of adsorbed native collagen type IV (50 mg/ml for 30 minutes) on NH_2 (A) and COOH (B) functionalized surfaces, showing network-like protrusions on the NH_2 versus aggregated morphology on COOH. It results in a distinct difference in the efficiency of cellular interaction: endothelial cells are better spread on NH_2 (C, E) while rounded on COOH (D, F).

Electrospinning of nanofibers from natural and synthetic polymers for guiding cellular behavior

In solution, proteins can form structures of various shapes, including fibers with a diameter of only a few nanometers and with lengths up to centimeters. A fascinating possibility to mimic similar ECM structures is to engineer protein-like or matrix protein-containing nanofibers via electrospinning technology. For this purpose we are developing electrospun nanofibers from natural (e.g., fibrinogen) and synthetic polymers (e.g. PLA, PEA) in order to direct the desired cellular response via spatially organized cues (e.g. fiber size and geometrical organization) as well as by tailoring their chemical and mechanical properties.

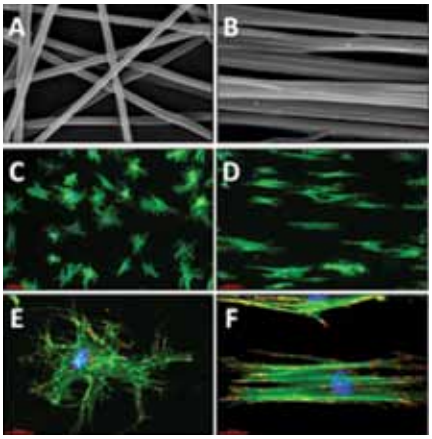
Nanofibers-based 3D constructs to provide cells with spatially organized stimuli

Examining hierarchical biology in only two dimensions (i.e., cells confined to a monolayer) is in most cases insufficient as cells typically exhibit unnatural behavior if excised from native three-dimensional (3D) tissues. Therefore, within the European STRUCTGEL project (under our coordination) we are developing 3D biohybrid constructs that combine the structural and biological properties of electrospun nanofibers with the optimized mechanical properties of specific hydrogels in order to provide stem cells with relevant spatial orientation in three dimensions.

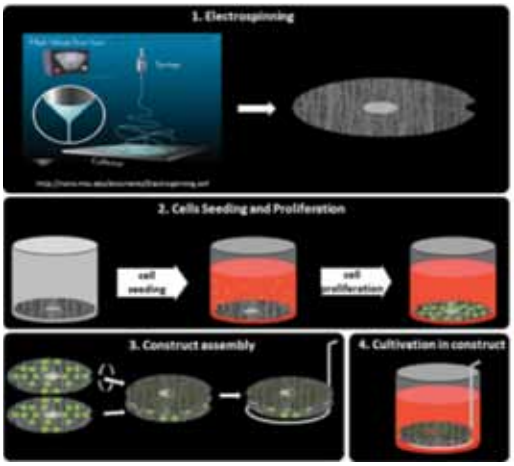
Creating dynamic stem cell niches using stimuli-responsive biomaterials

In addition to engineering the spatial configuration of cellular microenvironments, we are also interested in addressing the dynamic (i.e., temporal) aspects of the stem cell niche. To do that we take advantage of stimuli-responsive polymers to obtain control over an artificial cell-adhesive environment via dynamically altering either cell-cell (using cadherin-like ligands) or cell-matrix (using ECM proteins) interactions. By modulating the strength of adhesive protein-to-substratum interactions we aim to control the stem cell adhesive machinery, and which allows us to mimic the dynamic conditions of the stem cell niche.

Hybrid PLA/fibrinogen nanofibers deposited in random (A) and aligned (B) configurations. Human mesenchymal stem cells adhere to the fibers and acquire a stellate-like (C & E) or elongated (D & F) morphology, depending on the fiber orientations (staining: vinculin in red and actin in green).



Schematic illustration of the STRUCTGEL concept.



Research projects

- **STRUCTGEL** Nanostructured gel for cellular therapy of degenerative skeletal disorders (2012-2014).
PI: **George Altankov** (coordinator)
EU - EuroNanoMed

- **FIBROGELNET** Network for development of soft nanofibrous construct for cellular therapy of degenerative skeletal disorders (2013-2016).
PI: **George Altankov** (coordinator)
EU - FP7-PEOPLE-2012-IAPP

- **HEALINSYNERGY** Material-driven Fibronectin Fibrillogenesis to Engineer Synergistic Growth Factor Microenvironments (2012-2014).
PI: **George Altankov**
MINECO, MAT359-2012-P4-L02-AC

Collaborations with other research centres

Center for Biomaterials, Technical University of Valencia, Spain

Institute of Pharmacy, Martin Luther University, Halle, Germany

National University of la Plata, Argentina

Institute of Biomedical Science, Federal University of Rio de Janeiro, Brazil

Institute for Biophysics and Institute of Solid State Physics, Bulgarian Academy of Sciences, Sofia, Bulgaria

Institute of Cytology of the Russian Academy of Science and Institute of Neurology named after Prof. A.L.Polenov, St. Petersburg, Russia

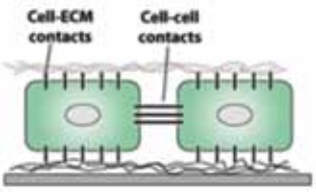
Industrial collaborations:

Bio-Elpida, France

Genekam Biotechnology A.G, Germany

Scientific equipment and techniques

- Universal fluorescent microscope for performing dynamic studies with living cells
- Full facilities for cell culturing
- Electrospinning device designed for the production of nanofibers from natural and synthetic polymers
- Laboratory freeze-dryer (Telstar Cryodos)
- Spectrofluorometer Fluormax 4 (Horiba, Jobin Yvon)
- Complete chromatographic and electrophoretic equipment
- Flow chamber setup for measuring the strength of cell adhesion
- Equipment for photo-polymerization processes
- Programmable compact spin coater



Stimuli-responsive polymers are used to spatio-temporally control cell-cell and cell-ECM interactions in the microenvironment.

Publications

- Perez, R. A., Riccardi, K., Altankov, G. and Ginebra, M.-P. (2014). Dynamic cell culture on calcium phosphate microcarriers for bone tissue engineering applications, *Journal of Tissue Engineering*, 5: 1–10

Robotics

Group leader: Alícia Casals

Senior researchers: Joan Aranda, Manel Frigola

PhD students: Eduard Bergés, Xavier Giralt, Albert Hernansanz, Olga Mur, Vijaykumar Rajasekaran

Masters students: Enrique Javier Ajenjo, Jordi Magdaleno

Undergraduate students: Adrià Giner, Guillem Güell

Research Technician: Manuel Vinagre

Research Assistants: Emili Boronat, Roger Comas

Publications

- Badesa, F. J., Morales, R., Garcia-Aracil, N., Sabater, J. M., Casals, A. and Zollo, L. (2014). Auto-adaptive robot-aided therapy using machine learning techniques. *Computer Methods and Programs in Biomedicine,* 116 (2): 123-130
- Aviles, A. I., Sobrevilla, P. and Casals, A. (2014). An approach for physiological motion compensation in robotic-assisted cardiac surgery. *Experimental & Clinical Cardiology*, 20 (11): 6713-6724
- Rajasekaran, V., Aranda, J. and Casals, A. (2014). Recovering planned trajectories in robotic rehabilitation therapies under the effect of disturbances. *International Journal of System Dynamics Applications*, 3 (2): 34-49 (2014).

Book chapters:

- Marbán, A., Casals, A., Fernández, J. and Amat, J. (2014). Haptic feedback in surgical robotics: Still a challenge. In: *ROBOT2013: First Iberian Robotics Conference* (ed. Armada, M. A., Sanfeliu, A. and Ferre, M.), Springer International Publishing. 252: 245-253
- Aviles, A. and Casals, A. (2014). On genetic algorithms optimization for heart motion compensation. *ibid*, 237-244
- Aviles, A. I. and Casals, A. (2014). Interpolation based deformation model for minimally invasive beating heart surgery. In: *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013* (ed. Roa Romero, L. M.). London, Springer International Publishing. 41: 372-375
- Berges, E. and Casals, A. (2014). Considering civil liability as a safety criteria for cognitive surgical robots. *ibid*, 113-116.
- Campos, J., Laporte, E., Gili, G., Peñas, C., Casals, A. and Amat, J. (2014). Characterization of anastomosis techniques for robot assisted surgery. *ibid*, 109-112.

The growing potential of robotics in the medical field leads to face challenging problems, but at the same time creates great expectancies to the society, as new devices and equipment are envisioned as killing solutions with respect to current technology.

The IBEC's Robotics group research aims to contribute to the slow but continuous advances in the medical field, in the areas of assistance to disabled, in rehabilitation and assistance in surgery. A common factor in these three areas is the need of adaptation to the user's needs, what implies perceiving not only the user's will and status, but also the environment conditions and the evolution of the ongoing activity.

Our current research within the HYPER project (Hybrid Neuroprosthetic and Neurorobotic Devices for Functional Compensation and Rehabilitation of Motor Disorders) is to search for new adaptive control algorithms focusing on specific actions, as the transition from sit to stand or keeping the walking pattern under internal or external perturbations. This control has to deal with disturbances caused by muscle synergies, taking into account unpredictable effects of artificial stimulation in muscles during rehabilitation therapies or other effects as fatigue or the own user's attention to the therapy. In this field, the work carried out has been focused on developing a control system with variable hierarchy and a status evaluator that allows adapting the control variables, mainly the variable stiffness at each joint, to reach the desired response and stability.

Being human-robot interaction a key factor in medical robotics, our research in assistive robotics is devoted to interpret human activity and the operation context so as to be able to program robots to cooperate proactively in assisting disabled in their daily tasks. This implies the extraction of relevant image features to recognize human posture and actions and relate them to the context environment and the evolution of tasks and activities, using recognition and learning techniques. The challenge is finding adequate algorithms that are reliable enough and can reduce the amount of data to process so as to be able to operate in real time. Figure 1 shows the original data, the human joints, and the reduction of triangles, trisarea feature, that define each posture in a sequence of poses corresponding to the human movement. For the adequate robot control this information has to be compatible with the environment status, thus perception and context interpretation is necessary. Further work has been done on the integration of multiple robot arms to deal with tasks that need cooperative actuation.

The research in surgical robots has progressed going deeper in the development of robot aids, as the analysis of tissues deformation aiming to solve problems as physiological movement detection for robot motion compensation or for estimation of the force applied on the tissues due to the lack of sensors to be integrated on the surgical tools. Figure 2 shows a sequence of images of the heart and the changes produced on the heart surface by the forces applied. The image processing operates from the minimization of an energy functional using the l_1–regularized optimization class in which cubic b-splines are used to represent the changes produced on the heart surface.

In technology transfer, much progress has been done in the spin-off, Rob Surgical Systems S.L, having already started the experimentation with models in an experimental operating room and advancing in the regulatory process. We have also advanced in the Surgitrainer project, a training simulator for minimally invasive surgery and a new specific robotic trainer has been designed, built and evaluated in Hospital de Sant Pau and in the Leuven premises of our partner, as part of the European Society for Gynaecological Endoscopy. We are now in the process of creating a company with the aim of progressively advancing in new robot surgical techniques that assist surgeons from the training phase to their assistance in clinical interventions.

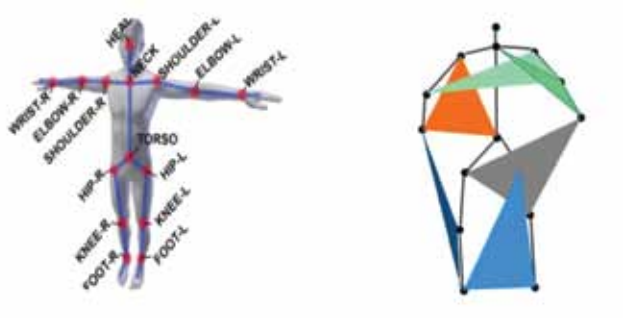


Figure 1: Pose descriptor and trisarea as new geometric pose-based feature for human motion recognition

Research projects

- **EuRoSurge** European Robotic Surgery.
PI: **Alícia Casals**
Coordination Action FP7-ICT-2011-7

- **HYPER** Hybrid NeuroProsthetic and NeuroRobotic Devices for Functional Compensation and Rehabilitation of Motor Disorders (2009-2014).
PI: **Alícia Casals**
MINECO, Actividad Investigadora CONSOLIDER – INGENIO 2010

- **IPRES** Interacción persona robot en entornos semiestructurados bajo criterios de permitividad.
PI: **Alícia Casals** (project coordinator)
MINECO

- **InHANDS** Interactive robotics for Human Assistance iN Domestic Scenarios (2013-2014).
PI: **Joan Aranda**
RecerCaixa

- **ATRIO** Control para el guiado de un robot de radioterapia intraoperativa (2013-2014).
PI: **Alícia Casals**
FIBHGM, industrial contract

- **CAMPE** Desenvolupament d'un sistema robòtic de baix cost d'ajut de la marxaper a nens amb transtorns motors greus (2014-2016).
PI: **Alícia Casals**
Recercaixa

Collaborations with other research centres

Dr. Ramon Rovira and Gabriel Gili Hospital de Sant Pau, Barcelona, Spain

Dr. Enric Laporte Corporació Sanitària Parc Taulí, Sabadell, Spain

Dr. Oriol Puig Hospital de la Vall d'Hebrón, Barcelona, Spain

Dr. Carlos Torrens Hospital del Mar, Barcelona, Spain

Dr. Javier Magriñá Mayo Clinic, Scottsdale, Arizona, USA

Dr. Rudi Campo President of ESGE, European Society for Gynaecological Endoscopy

Prof Paolo Fiorini Università degli Studi di Verona, Verona, Italy

Prof Nicolás García Universidad Miguel Hernández de Elche, Alicante, Spain

- Rajasekaran, V., Aranda, J. and Casals, A. (2014). Handling disturbances on planned trajectories in robotic rehabilitation therapies. *ibid*, 85-88
- Urra, O., Casals, A. and Jané, R. (2014). Evaluating spatial characteristics of upper-limb movements from EMG signals. *ibid*, 1795-1798
- Casals, A., Fedele, P., Marek, T., Molfino, R., Muscolo, G. and Recchiuto, C. (2014). A robotic suit controlled by the human brain for people suffering from quadriplegia. In: *Towards Autonomous Robotic Systems* (ed. Natraj, A., Cameron, S., Melhuish, C. and Witkowski, M.), Springer Berlin Heidelberg: 294-295
- Vinagre, M., Aranda, J. and Casals, A. (2014). An interactive robotic system for human assistance in domestic environments. In: *Computers Helping People with Special Needs* (ed. Miesenberger, K., Fels, D., Archambault, D., Peňáz, P. and Zagler, W.), Springer International Publishing. 8548: 152-155

Conference proceedings:

- Vaca, R. and Aranda, J. (2014). Approximating coupler curves using strip trees. *11th World Congress on Computational Mechanics (WCCM XI); 5th European Conference on Computational Mechanics (ECCM V); 6th European Conference on Computational Fluid Dynamics (ECFD VI); Advanced Numerical Methods* II, 1-2. Published by CIMNE
- Vaca, R. and Aranda, J. (2014). Triangular-fan-based algorithm for computing the closure conditions of planar linkages. *ibid*
- Urra, O., Casals, A. and Jané, R. Study of synergy patterns during the execution of stroke rehabilitation exercises (2014). *CASEIB 2014*, Barcelona, Spain, Published by Sociedad Española de Ingeniería Biomédica

- Urra, O., Casals, A. and Jané, R. Synergy analysis as a tool to design and assess an effective stroke rehabilitation. (2014). *36th Annual International Conference of the IEEE Chicago,* USA, Engineering in Medicine and Biology Society (EMBC), 3550-3553
- Berges, E. and Casals, A. (2014). Identification of non-technical roadblocks in cognitive robotic surgery. *The Hamlyn Symposium on Medical Robotics. London, UK. From Exo-Skeletons to Surgical Robots*, 3-4. Published by The Royal Geographical Society and Imperial College London
- Aviles, A. I., Sobrevilla, P. and Casals, A. (2014). In search of robustness and efficiency via l1– and l2– regularized optimization for physiological motion compensation. *XII International Conference on Agricultural, Biological and Ecosystems Sciences (ICABES 2014),* Geneva, Switzerland *International Journal of Medical, Health, Pharmaceutical and Biomedical Engineering*, 501-506. Published by World Academy of Science, Engineering and Technology
- Aviles, A. I., Sobrevilla, P. and Casals, A. (2014). Unconstrained ℓ1 — regularized minimization with interpolated transformations for heart motion compensation. *36th Annual International Conference of the IEEE* Chicago, USA (2014). *Engineering in Medicine and Biology Society (EMBC)*, 5109-5112. Published by IEEE
- Aviles, A. I., Marban, A., Sobrevilla, P., Fernandez, J. and Casals, A. (2014). A recurrent neural network approach for 3D vision-based force estimation. *4th International Conference on Image Processing Theory, Tools and Applications (IPTA),* Paris, France, 1-6. Published by IEEE

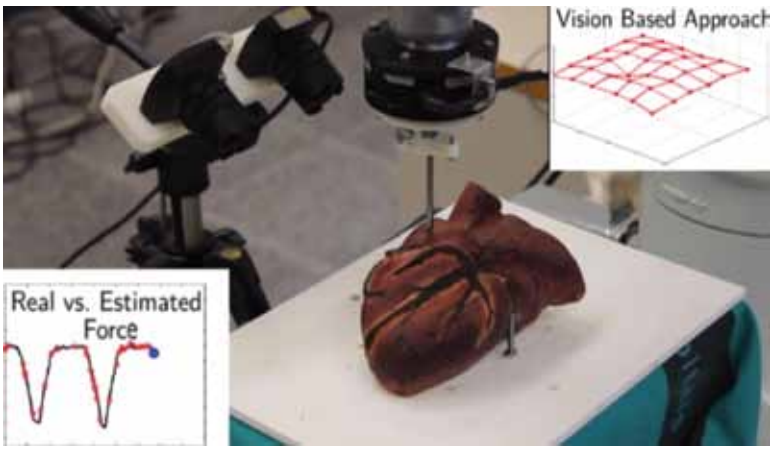
Research Prof. José L. Pons Bioengineering group, CSIC, Madrid, Spain

Prof. Joerg Raczkowsky Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

Scientific equipment and techniques

- Basic electronics laboratory equipment
- A 50' 3D monitor
- 6D magnetic positioning sensors (Polhemus)
- Ultrasound probe: B-Ultrasonic Diagnostic Equipment Model WED-2000
- 2 PC with multiprocessor architecture (Tesla C2050)
- A BCI working platform based on an Emotiv Epoc headset (EEG acquisition system)
- KUKA lightweight robot specially designed for mobility and interaction with humans and a priori unknown environments. It is equipped with a control environment developed by the team to program anatomic constraints to operate in virtual environments
- Computer controlled LED-based lighting system for the operating room
- Experimental robotized kitchen composed of a robot, several adapted cupboards, a kitchen counter and a PC for robot and environment control
- 2 robot operated 3 degrees of freedom surgical instruments
- Baxter: Robot Baxter research edition, with two sensorized arms and with integrated vision The robot operates under OROCOS and is provided with an anticollision application for a safe operation of its two arms.
- A Robotic arm with a two fingers gripper, Mico research edition, from Kinova.
- A 3-finger adaptive robot gripper, from Robotiq

Figure 2: Sequence of a sit-to-stand experiment with the assistance of the HYPER neuroprosthesis and reurorobot.



Biomaterials for regenerative therapies

Junior group leader: Elisabeth Engel

Senior researchers: Oscar Castaño, Miguel Angel Mateos, Soledad Pérez

Postdoctoral researcher: Soledad Pérez

PhD students: Claudia Navarro, Xavier Puñet, Aitor Sánchez, Riccardo Levato, Joan Martí, Irene Cano

Masters students: Cristina Rodríguez, Fabien Gaihier, Benjamin Gauvin, Antoine Micallef

Undergraduate student: Marc Batista

Technician: Belén González

Research in the Biomaterials for Regenerative Therapies group is devoted to the development and knowledge transfer to industry of innovative biomaterials and scaffolds for tissue regeneration.

We design, fabricate and characterise bioactive and biodegradable materials and investigate their interactions with biological entities, both in terms of their fundamental aspects and with specific applications for tissue engineering purposes in mind. The aim is the repair and functional restoration of tissues or organs by means of 3D scaffolds, cells and signals.

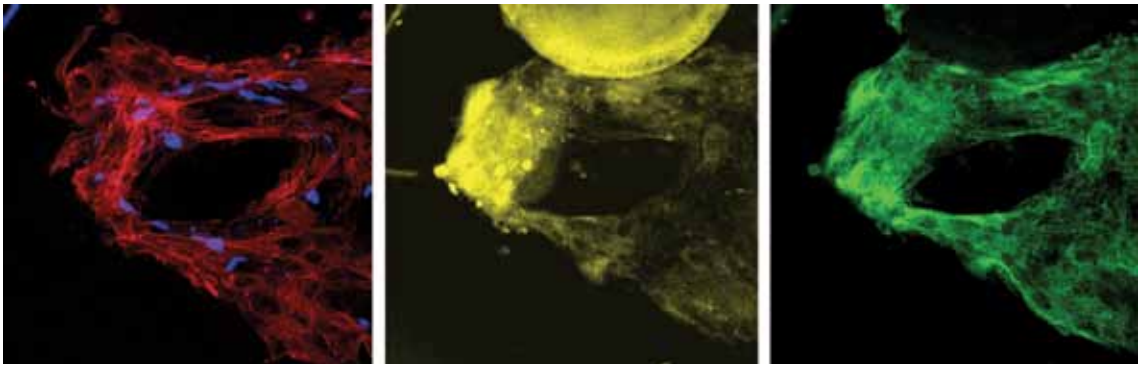
Two main research areas are being developed in the group. 1) The production of polymeric biomaterials using different fabrication techniques. The use of a jet break-up polymer precipitation technique to produce microparticles for cell delivery has allowed the use of them as a part of a bioink for rapid manufacturing processes (Levato R, *et al. Bioprocessing,* 2014), enhancing cell viability and proliferation for bone engineering applications. For central nervous tissue regeneration, the application of electrospun nanofibers in aligned distribution has been demonstrated to promote revascularization of the scaffold implanted in the mice cortex and proliferation of neuroprecursor cells (Álvarez A, *et al. Biomaterials,* 2014).

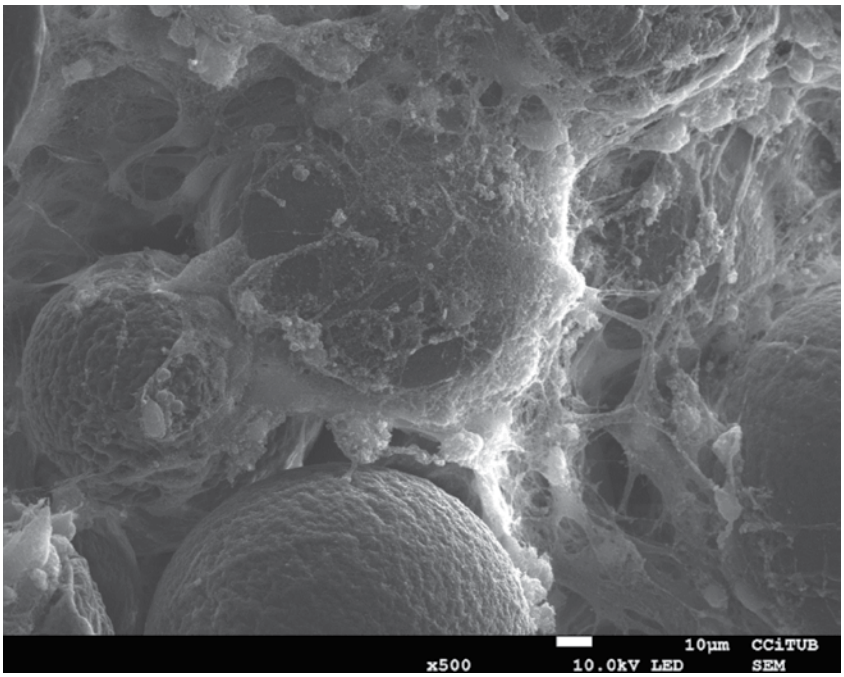
2) The other strategic area is the production of structured bioactive nanocomposites that can enhance vascularization and bone regeneration, either by electrospinning, rapid prototyping or microparticles production. Recent advances have shown the capability of electrospun nanocomposites to induce angiogenesis in bone regeneration *in vivo* (Castaño O, *ACS Appl Mater Interfaces*, 2014). Thus, rapid prototyping composite scaffolds for bone regeneration have been functionalized with fibronectin. The presence of the nanoparticles of glass enhanced the immobilization of the protein (Won JE, *et al. Biotechnol Lett.*, 2014).

In 2014, the group was granted RecerCaixa funding for a project related to tendon regeneration that has allowed us to develop a prototype for tendon regeneration that will be validated *in vivo* in 2015.

We also succeeded in raising funds via crowdfunding (on the Goteo platform) in order to validate a new dressing for treating vascular ulcers, Dermoglass. We are now working on developing a prototype to validate it in a preclinical study to demonstrate the efficacy of the dressing.

Immunofluorescence of 21-day scaffolds revealed the presence of representative ECM proteins such collagen and laminin. *L-r:* Actin DAPI, collagen I, laminin





Cells clearly forming ECM bridges, establishing interparticular connections.

Filed patents

- **Glass nanoparticles** (Filing date 9th April 2014)
Inventors: Engel, E., Planell, J. A., Castaño, O. and Navarro, M. (Universitat Politècnica de Catalunya, Fundació Institut de Bioenginyeria de Catalunya)
Ref. number: PCT/IB2014/000522

Research projects

- **THE GRAIL** Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer.
PI: **Elisabeth Engel, Soledad Pérez** (scientific coordinator)
EU - Cooperation - HEALTH

- **nAngioFrac** Angiogenic nanostructured materials for non-consolidating bone fractures.
PI: **Elisabeth Engel, Oscar Castaño** (scientific coordinator)
EU - EURONANOMED - PI11/03030

- Grup de recerca consolidat (2009-2014).
PI: **Josep A. Planell**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (2009 SGR 474)

- Andamios diseñados para promover una vascularización eficiente para fracturas óseas no consolidadas.
PI: **Oscar Castaño** (scientific coordinator)
MINECO MAT2011-29778-C02-01

Publications

- Salvagni, E., Berguig, G., Engel, E., Rodriguez-Cabello, J. C., Coullerez, G., Textor, M., Planell, J. A., Gil, F. J. and Aparicio, C. (2014). A bioactive elastin-like recombinamer reduces unspecific protein adsorption and enhances cell response on titanium surfaces. *Colloids and Surfaces B: Biointerfaces*, 114: 225-233

- Tejeda-Montes, E., Smith, K. H., Rebollo, E., Gómez, R., Alonso, M., Rodriguez-Cabello, J. C., Engel, E. and Mata, A. (2014). Bioactive membranes for bone regeneration applications: Effect of physical and biomolecular signals on mesenchymal stem cell behavior. *Acta Biomaterialia*, 10 (1): 134-141

- González-Vázquez, A., Planell, J. A. and Engel, E. (2014). Extracellular calcium and CaSR drive osteoinduction in mesenchymal stromal cells. *Acta Biomaterialia*, 10 (6): 2824–2833 (2014).

- Álvarez, Z., Castaño, O., Castells, A. A., Mateos-Timoneda, M. A., Planell, J. A., Engel, E. and Alcántara, S. (2014). Neurogenesis and vascularization of the damaged brain using a lactate-releasing biomimetic scaffold. *Biomaterials*, 35 (17): 4769-4781

- Serra, T., Ortiz-Hernandez, M., Engel, E., Planell, J. A. and Navarro, M. (2014). Relevance of PEG in PLA-based blends for tissue engineering 3D-printed scaffolds. *Materials Science and Engineering C*, 38 (1): 55-62

- Castaño, O., Sachot, N., Xuriguera, E., Engel, E., Planell, J. A., Park, J. H., Jin, G. Z., Kim, T. H., Kim, J. H. and Kim, H. W. (2014). Angiogenesis in bone regeneration: Tailored calcium release in hybrid fibrous scaffolds. *ACS Applied Materials and Interfaces*, 6 (10): 7512-7522

- Almeida, C. R., Serra, T., Oliveira, M. I., Planell, J. A., Barbosa, M. A. and Navarro, M. Impact of 3-D printed PLA- and chitosan-based scaffolds on human monocyte/macrophage responses: Unraveling the effect of 3-D structures on inflammation. *Acta Biomaterialia*, 10 (2): 613-622

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- Mateos-Timoneda, M. A., Castano, O., Planell, J. A. and Engel, E. (2014). Effect of structure, topography and chemistry on fibroblast adhesion and morphology. *Journal of Materials Science: Materials in Medicine*, 25 (7): 1781-1787
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- Bioactive biomaterials design and development for skin regeneration based on controlled ion release signaling.
PI: **Elisabeth Engel**
MINECO MAT2012-38793

- Tendon Tissue Engineering: A Helping Hand for Rotator Cuff Tears (BIOTENDON)
PI: **Elisabeth Engel, Miguel A. Mateos-Timoneda** (scientific coordinator)
RecerCaixa

- Desarrollo de un nuevo producto de terapia avanzada para la regeneración y reconstrucción de la superficie ocular.
PI: **Elisabeth Engel, Miguel A. Mateos-Timoneda** (scientific coordinator)
Technology transfer project with Ferrer

Collaborations with other research centres

Dr. Ernest Mendoza Applied Nanomaterials Laboratory, Research Centre in Nanoengineering, Technical University of Catalonia (UPC, BarcelonaTech), Spain

Dr. Izabella Rajzer Institute of Textile Engineering and Polymer Materials, University of Bielsko-Biala, Poland

Dr. José María Mora Servei de cirurgia ortopédica i traumatológica, Consorci Hospital de Terrassa, Spain

Dr. Matilde Alonso Dept. de Física de la Materia Condensada, Universidad de Valladolid, Spain

Dr. Mercè Alsina Servicio de Dermatología, Hospital Clínic de Barcelona, Spain

Dr. Soledad Alcántara Grup de Desenvolupament Neural, IDIBELL, University of Barcelona, Spain

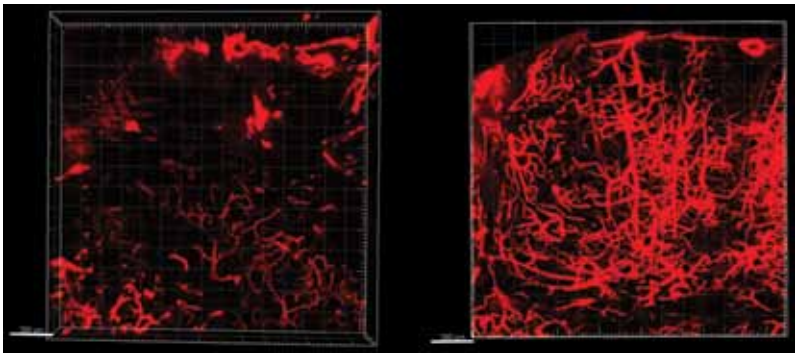
Prof. Aldrik Velders Microwave and Sustainable Organic Chemistry Department, University of Twente and Wageningen Nuclear Magnetic Resonance Centre (WNMRC), The Netherlands

Prof. Didier Letourneur Laboratoire de Bioingénierie Cardiovasculaire, INSERM, University Denis Diderot-Paris 7, Paris, France

Prof. Dirk Grijpma, Department of Biomaterials Science and Technology, University of Twente, Twente, the Netherlands

Prof. Francesco Serino Department of Vascular Surgery, Istituto Dermatologico dell'Immacolata (IDI), Rome, Italy

Nanofiber scaffolds implanted in mice cortex for 12 months. Random fibers (*left*) do not allow the entrance of the vessels inside the scaffold, while aligned fibers (*right*) show a complete re-vascularization of the scaffold.



Dr. Jerónimo Blanco Institut de Ciències Cardiovasculars de Catalunya and CSIC, Barcelona, Spain

Dr. Joelle Amedee INSERM, University of Bordeaux Segolen, Bordeaux, France

Dr. José Becerra Ratia Dept. Biología Celular, Genética y Fisiología, Universidad de Málaga, Spain

Dr. José Carlos Rodríguez-Cabello Dept. de Física de la Materia Condensada, Universidad de Valladolid, Spain

Dr. Julia Buján Dept. de Ciencias Morfológicas y Cirugía, Facultad de Medicina, Universidad de Alcalá de Henares, Spain

Dr. Małgorzata Lewandowska Faculty of Materials Science & Engineering, WUT Warsaw University of Technology, Poland

Dr. Manuel Doblaré Group of Structural Mechanics and Materials Modelling, Institute of Engineering Research, (I3A), Universidad de Zaragoza, Spain

Dr. Margarita Calonge Institute of Ophthalmobiology (IOBA), Universidad de Valladolid, Spain

Dr. María Vallet Regí Facultad de Farmacia, Universidad Complutense de Madrid, Spain

Dr. Mário Barbosa New Therapies group, Institute for Biomedical Engineering (INEB), University of Porto, Portugal

Prof. Mateo Santin Brighton Studies in Tissue Mimicry and Aided Regeneration (BrightSTAR) Research Group, University of Brighton, UK

Prof. Wouter J.A. Dhert & Dr. Jos Malda Department of Orthopaedics, University Medical Center Utrecht, The Netherlands

Scientific equipment and techniques

- Surface characterization equipment (contact angle, Z potential, nanoindenter)
- Cell culture facilities
- Molecular Biology equipment: protein and DNA electrophoresis
- Thermocycler (PCR)
- Rapid prototyping tool
- Peptide synthetiser
- Combustion furnace
- Electrospinning device
- Spin-coater
- Vibrational viscosimeter
- ElectroForce® BioDynamic® test instrument

- Levato, R., Visser, J., Planell, J.A., Engel, E., Malda, J, Mateos-Timoneda, M.A. (2014). Biofabrication of tissue constructs by 3D bioprinting of cell-laden microcarriers. *Biofabrication*, 6, 3
- Sachot, N., Engel, E. and Castaño, O. (2014). Hybrid organic-inorganic scaffolding biomaterials for regenerative therapies. Current Organic Chemistry, 18 (18): 2299-2314

Book chapters:

- Castaño, O. and Planell, J. A. (2014). *Cements*. In: *Bioceramics with clinical applications* (ed., John Wiley & Sons, Ltd: 193-247 (2014).
- Pérez-Amodio, S. and Engel, E. (2014). *Bone Biology and Regeneration*. In: *Bio-Ceramics with Clinical Applications* (ed. Vallet-Regí, M.), John Wiley & Sons, Ltd: 315-342 (2014).

Nanomalaria

(joint unit IBEC/CRESIB)

Head of Joint Unit: Xavier Fernàndez-Busquets

PhD students: Joana Azevedo, Ernest Moles, Elisabet Martí

Undergraduate student: Aida Montserrat

Established in 2010, the Nanomalaria Group is a Joint Unit affiliated with IBEC and the Barcelona Centre for International Health Research (CRESIB, Hospital Clínic-Universitat de Barcelona), receiving support from both, and located in the Esther Koplowitz Centre near the Hospital Clínic.

The current activity of the Nanomalaria group is focused on the development of nanomedicine-based systems to be applied to malaria prophylaxis, diagnosis and therapy.

Malaria is arguably one of the main medical concerns worldwide because of the number of people affected, the severity of the disease and the complexity of the life cycle of its causative agent, the protist *Plasmodium spp*. The clinical, social and economic burden of malaria has led, in the last 100 years, to several waves of serious efforts to control and eventually eradicate it, but without success. With the advent of nanoscience, renewed hopes have appeared of finally obtaining the long sought-after 'magic bullet' against malaria in the form of a nanovector for the targeted delivery of antimalarial drugs exclusively to *Plasmodium*-infected cells. Nanotechnology can also be applied to the discovery of new antimalarials through single-molecule manipulation approaches for the identification of novel drugs targeting essential molecular components of the parasite. Finally, methods for the diagnosis of malaria can benefit from nanotools applied to the design of microfluidic-based devices for the accurate identification of the parasite's strain, its precise infective load, and the relative content of the different stages of its life cycle, whose knowledge is essential for the administration of adequate therapies. The benefits and drawbacks of these nanosystems have to be considered in different possible scenarios, including economy-related issues that are hampering the development of nanotechnology-based medicines against malaria with the dubious argument that they are too expensive to be used in developing areas. Unfortunately, it is true that the application of nanoscience to infectious disease has been traditionally neglected, with most research resources overwhelmingly biased towards other pathologies that are more prominent in the developed world. Thus, extra ingenuity is demanded from us: malaria-oriented nanomedicines not only need to work spotlessly, they have to do so in a cost-efficient way because they will be deployed in low-income regions.

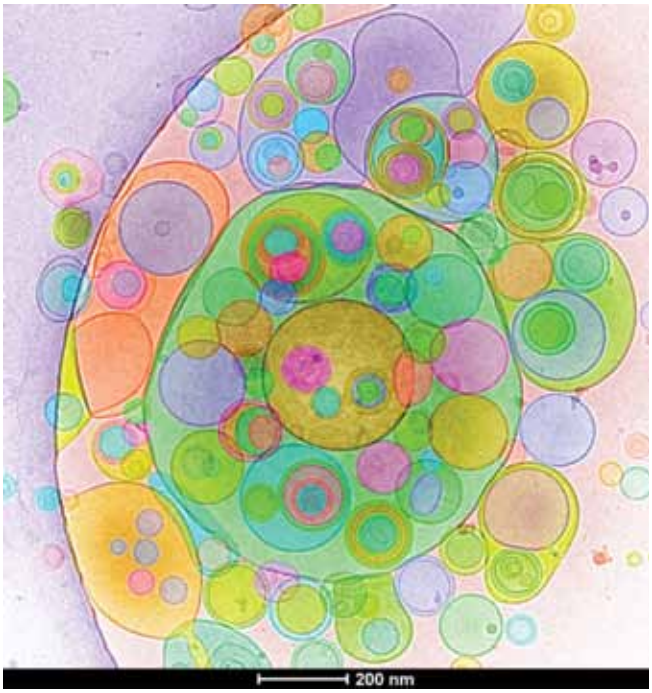


Figure 1. Cryo-transmission electron microscope image of liposomes being assayed for the encapsulation of drugs specifically targeted to red blood cells infected by the malaria parasite *Plasmodium falciparum*. CryoTEM image artistic editing by Marc Cirera, www.marccirera.com.

The driving force of the Nanomalaria group is our personal commitment to applying nanomedicine to infectious diseases of poverty though our current research lines: (i) Exploration of different types of encapsulating structure (liposomes, synthetic and natural polymers), targeting molecule (protein, polysaccharide, nucleic acid), and antimalarial compound (e.g. new structures derived from marine organisms and antimicrobial peptides) for the assembly of nanovectors capable of delivering their drug cargo with complete specificity to diseased cells. (ii) Study of metabolic pathways present in *Plasmodium* but absent in humans, with the aim of identifying specific enzymes as therapeutic targets. (iii) Use of single-molecule force spectroscopy strategies for the biodiscovery of new antimalarial and antibiotic agents. (iv) Design of new methods for the targeted drug delivery to *Plasmodium* stages in the mosquito vector. (v) Investigation of novel drugs against insect-borne diseases working through radically new mechanisms. (vi) Extension of our activities to new pathologies including leishmanisasis, Chagas' disease, and tuberculosis. Our current efforts are centered on the engineering of innovative therapeutic strategies requiring minimal clinical assays and therefore amenable to being applied in the field in years instead of decades.

Figure 2. Artistic rendering of the specific targeting of liposomes (small structures surrounded by a white envelope representing a polyethylene glycol layer designed to confer increased blood residence time) to red blood cells infected by the malaria parasite *Plasmodium falciparum*. The parasitized cell in the center is represented open to show intracellular pathogen-derived organelles and liposomes delivering their cargo. Drawing by Elisabet Baró.

Publications

- Caddeo, C. *et al* (2014). Topical anti-inflammatory potential of quercetin in lipid-based nanosystems: *In vivo* and *in vitro* evaluation. *Pharmaceutical Research*, 31 (4): 959-968
- Manca, M. L. *et al* (2014). Molecular arrangements and interconnected bilayer formation induced by alcohol or polyalcohol in phospholipid vesicles. *Colloids and Surfaces B: Biointerfaces*, 117: 360-367 (2014).
- Le Roux, D. *et al* (2014). Novel S-adenosyl-L-methionine decarboxylase inhibitors as potent antiproliferative agents against intraerythrocytic Plasmodium falciparum parasites. *International Journal for Parasitology: Drugs and*

Research projects

- **NANOMALNET** Exploration of new efficient targeting molecules for nanovector-mediated antimalarial drug delivery (2012-2015).
PI: **Xavier Fernàndez-Busquets**
MICINN (BIO2011-25039)

- Amphoteric polyamidoamines as innovative tools to selectively direct antimalarial drugs towards Plasmodium-infected red blood cells (2014-2016).
PI: **Xavier Fernàndez-Busquets**
Fondazione CARIPLO (2013-0584)

- Group for the study of self-aggregating proteins (2014-2016).
PI: **Salvador Ventura Zamora**
Consolidated Research Group certified by the Generalitat de Catalunya (2014-SGR-938)

Collaborations with other research centres

Prof. Dario Anselmetti Universität Bielefeld, Germany

Prof. Maria Antònia Busquets University of Barcelona, Spain

Prof. Elisabetta Ranucci Università degli Studi di Milano, Italy

Prof. José Manuel Bautista Universidad Complutense de Madrid, Spain

Dr. Matthias Rottmann Swiss Tropical and Public Health Institute, Basel, Switzerland

Dr. José Antonio García Salcedo Instituto de Parasitología y Biomedicina "López-Neyra", Consejo Superior de Investigaciones Científicas (CSIC), Granada, Spain

Prof. Robert Sinden Imperial College London, UK

Dr. Israel Molina Hospital Universitari Vall d'Hebron, Barcelona

Prof. José Luis Serrano Instituto de Nanociencia de Aragón, Zaragoza

Prof. Manuel Llinas Pennsylvania State University, USA

Dr. Santiago Imperial University of Barcelona, Spain

Dr. Eduardo Prata Vilanova Universidade Federal do Rio de Janeiro, Brazil

Dr. Maria Manconi Università de Cagliari, Sardinia, Italy

Dr. Krijn Paaijmans CRESIB, Barcelona, Spain

Dr. José Luis de Paz Instituto de Investigaciones Químicas CSIC-University of Seville, Spain

Dr. Ellen Faszewski Wheelock College, Boston, USA

Prof. Lyn-Marie Birkholtz University of Pretoria, South Africa

Prof. Bernard Degnan University of Brisbane, Australia

Dr. Francisco J. Muñoz Parc de Recerca Biomèdica de Barcelona, Spain

Prof. Salvador Ventura Universitat Autònoma de Barcelona, Bellaterra, Spain

Dr. Iñigo Angulo-Barturen GlaxoSmithKline, Tres Cantos, Madrid, Spain

Prof. Max Burger NOVARTIS AG, Basel, Switzerland

Dr. Juan José Valle-Delgado Aalto University, Helsinki, Finland

Scientific equipment and techniques

- Zeiss Primostar microscope
- Shake 'N' Stack (Thermo Hybaid) hybridization oven
- Rotatory evaporator RS 3000-V (Selecta)
- *Plasmodium falciparum* cell cultures

Drug Resistance, 4 (1): 28-36 (2014).

- Urbán, P. *et al* (2014). Use of poly(amidoamine) drug conjugates for the delivery of antimalarials to Plasmodium. *Journal of Controlled Release*, 177 (1): 84-95
- Ramos-Fernández, E., Tajes, M., Palomer, E., Ill-Raga, G., Bosch-Morató, M., Guivernau, B. *et al* (2014). Posttranslational nitro-glycative modifications of albumin in Alzheimer's disease: Implications in cytotoxicity and amyloid-β peptide aggregation. *Journal of Alzheimer's Disease*, 40 (3): 643-657
- Movellan, J., Urbán, P., Moles, E., de la Fuente, J. M., Sierra, T., Serrano, J. L. and Fernàndez-Busquets, X. (2014). Amphiphilic dendritic derivatives as nanocarriers for the targeted delivery of antimalarial drugs. *Biomaterials*, 35 (27): 7940-7950
- Paaijmans, K. and Fernàndez-Busquets, X. (2014). Antimalarial drug delivery to the mosquito: An option worth exploring? *Future Microbiology*, 9 (5): 579-582
- Pujol, A. *et al.* (2014). Application of quantum dots to the study of liposome targeting in leishmaniasis and malaria. *International Journal of Theoretical and Applied Nanotechnology*, 2 (1): 1-8
- Urbán, P. and Fernàndez-Busquets, X. (2014). Nanomedicine against malaria. *Current Medicinal Chemistry*, 21 (5): 605-629
- Fernàndez-Busquets, X. (2014). Toy kit against malaria: Magic bullets, LEGO, Trojan horses and Russian dolls. *Therapeutic Delivery*, 5 (10): 1049-1052
- Marques, J. *et al* (2014). Application of heparin as a dual agent with antimalarial and liposome targeting activities toward *Plasmodium*-infected red blood cells. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 10 (8): 1719-1728
- Tajes, M. *et al* (2014). The blood-brain barrier: Structure, function and therapeutic approaches to cross it. *Molecular Membrane Biology*, 31 (5): 152-167

Nanoscale bioelectrical characterization

Group leader: Gabriel Gomila

Senior researcher: Laura Fumagalli

Postdoctoral researcher: Lázaro René Izquierdo

PhD students: Maria Chiara Biagi, Marc Van der Hofstadt

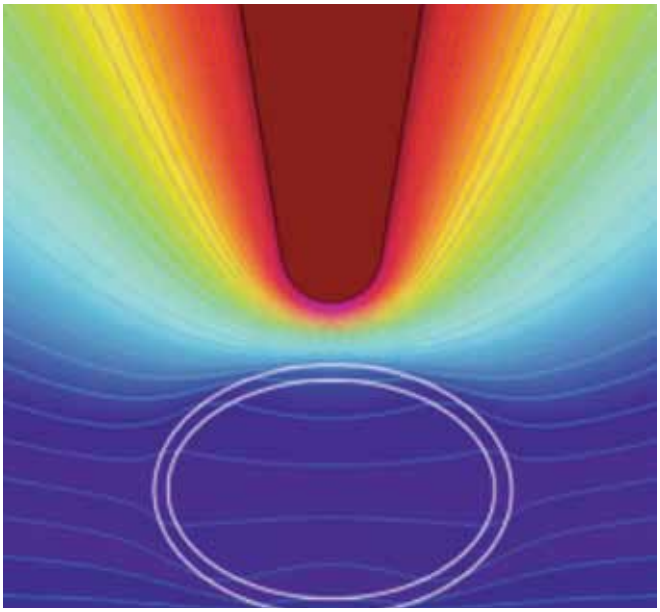
The main goal of our research group is to develop new experimental setups based on atomic force microscopy and theoretical frameworks enabling the measurement of the electrical properties of biological samples at the nanoscale (for example, biomembranes, single viruses or single bacteria).

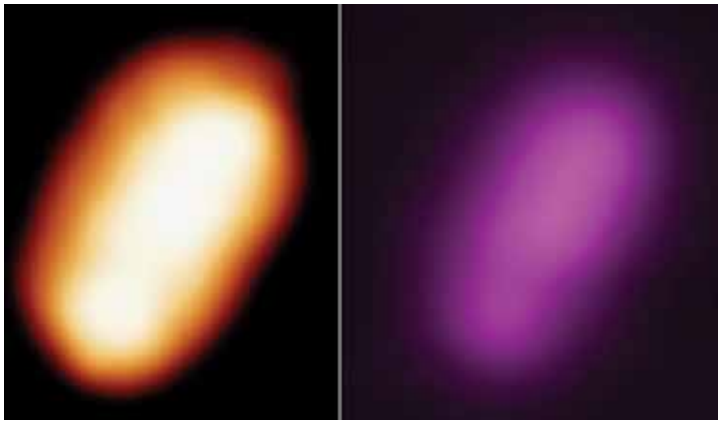
Our main objective is to contribute to develop new label-free biological characterization methods and new electronic biosensors.

During 2014 we have quantified for the first time the dielectric properties of the most important biomolecule of life, DNA. The value obtained is four times larger than previously assumed values. This result will have important implications in the evaluation of DNA electrostatic interactions with proteins and drugs. We have also been able to determine the electric polarization response of single bacteria cells for the first time. Important differences between gram types have been found, which we could associate to the different structure and hydrophilic character of the cell wall.

Finally, we have expanded our electrical measuring capabilities to the high frequency range (> GHz) with the use of the Scanning Microwave Microscope. We contributed to the development of a novel calibration method not requiring a calibration sample and, hence, of simple implementation. Application to test systems and bacteria samples have been undertaken.

Electrical potential distribution corresponding to the electric interaction between a voltage biased nanometric sharp conducting tip of radius 5 nm and a single virus particle. The virus is represented as core-shell structure with a protein shell 2.5 nm thick and a DNA core 32 nm high and 55 nm wide. From the calculated electric potential distribution the polarization force acting on the sharp tip can be calculated and compared to experimental measurements. With this procedure we determined the dielectric polarization response of DNA giving a relative dielectric constant of $\varepsilon_r \sim 8$, four times higher than conventionally assumed.





Topographic (left) and dielectric (right) images of a *Salmonella Thymuirium* bacterium measured with an electrostatic force microscope. Quantification of the dielectric image gives a bacterium relative dielectric constant of ε_r= 7 when measured in ambient conditions. This value is higher than the one obtained in dry air conditions (ε_r= 5) and reveals information on the hydration properties of the cell wall and of its hydrophilic or hydrophobic character.

Publications

- Dols-Perez, A., Fumagalli, L. and Gomila, G. (2014). Structural and nanomechanical effects of cholesterol in binary and ternary spin-coated single lipid bilayers in dry conditions. *Colloids and Surfaces B: Biointerfaces*, 116: 295-302
- Castillo-Fernandez, O., Rodriguez-Trujillo, R., Gomila, G. and Samitier, J. (2014). High-speed counting and sizing of cells in an impedance flow microcytometer with compact electronic instrumentation. *Microfluidics and Nanofluidics*, 16 (1-2): 91-99
- Caló, A., Reguera, D., Oncins, G., Persuy, M. A., Sanz, G., Lobasso, S., Corcelli, A., Pajot-Augy, E. and Gomila, G. (2014). Force measurements on natural membrane nanovesicles reveal a composition-independent, high Young's modulus. *Nanoscale*, 6 (4): 2275-2285

Research projects

- **NANOELECTOMOGRAPHY** Electrical nanotomography based on scanning probe microscopy for nanomaterials and biological samples (2014-2016).
  PI: **Gabriel Gomila**
  MINECO (TEC2013-48344-C2-1-P)
- **AFM4NanoMed&Bio** European network on applications of Atomic Force Microscopy to NanoMedicine and Life Sciences (2010-2015).
  PI: **Gabriel Gomila** (Management Committee Substitute Member)
  EU COST Action TD1002
- **V-SMMART Nano** Volumetric Scanning Microwave Microscopy Analytical and Research Tool for Nanotechnology (2012-2015)
  PI: **Gabriel Gomila**
  European FP7-NMP-SME project
- **NANOMICROWAVE** Microwave Nanotechnologies for Semiconductor and Life Sciences. (2013-2016).
  PI: **Gabriel Gomila**
  European FP7-PEOPLE-ITN project

Collaborations with other research centres

Prof. Jose L. Carrascosa Department of Structure of Macromolecules, Centro Nacional de Biotecnología, Spain

Dr. Manel Puig Departament d'Electrònica, University of Barcelona, Spain

Dr. Ferry Kienberger Agilent Technologies Austria, Linz, Austria

Dr. Adriana Gil Nanotec Electronica S.L., Madrid, Spain

Prof. Modesto Orozco Institut de Recerca Biomèdica, Barcelona, Spain

Prof. Marco Sampietro Laboratorio di Strumentazione Analogica e Materiali Polimerici, Politecnico di Milano, Italy

Prof. Joan Bausells Centro Nacional de Microelectrónica de Barcelona-CSIC, Spain

Scientific equipment and techniques

- Cypher Atomic Force Microscope (Asylum Research)
- 2 Cervantes Atomic Force Microscopes (Nanotec Electronica)
- Easy Scan 2 Atomic Force Microscope (Nanosurf)
- AxioImager A1m Reflection Optical Microscope (Zeiss) equipped with a AxioCam ERc5s (Zeiss)
- HF2LI digital lock-in amplifier (Zurich Instruments)
- CompactStat portable electrochemical interface and impedance analyzer (Ivium Technologies)
- 2 eLockIn204 4-phase Lock-In amplifiers (Anfatec)
- Keithley 6430 sub-femtoAmp remote sourcemeter (Keithley)

- Gramse, G., Kasper, M., Fumagalli, L., Gomila, G., Hinterdorfer, P. and Kienberger, F. (2014). Calibrated complex impedance and permittivity measurements with scanning microwave microscopy. *Nanotechnology*, 25 (14): 145703 (8)
- Gomila, G., Gramse, G. and Fumagalli, L. (2014). Finite-size effects and analytical modeling of electrostatic force microscopy applied to dielectric films. *Nanotechnology*, 25 (25): 255702 (11)
- Birhane, Y., Otero, J., Pérez-Murano, F., Fumagalli, L., Gomila, G. and Bausells, J. (2014). Batch fabrication of insulated conductive scanning probe microscopy probes with reduced capacitive coupling. *Microelectronic Engineering*, 119: 44-47
- Esteban-Ferrer, D., Edwards, M. A., Fumagalli, L., Juarez, A. and Gomila, G. (2014). Electric polarization properties of single bacteria measured with electrostatic force microscopy. *ACS Nano*, 8 (10): 9843–9849
- Cuervo, A., Dans, P. D., Carrascosa, J. L., Orozco, M., Gomila, G. and Fumagalli, L. (2014). Direct measurement of the dielectric polarization properties of DNA. *Proceedings of the National Academy of Sciences of the United States of America*, 111 (35): E3624-E3630
- Fumagalli, L., Edwards, M. A. and Gomila, G. (2014). Quantitative electrostatic force microscopy with sharp silicon tips. *Nanotechnology*, 25 (49): 495701 (9)

Nanoprobes and nanoswitches

Group leaders: Pau Gorostiza (ICREA research professor) and Fausto Sanz

Senior researchers: Ismael Díez, Marina Inés Giannotti, Mireia Oliva

Postdoctoral researcher: Nadim Darwish

PhD students: Albert Cortijos, Aida Garrido, Berta Gumí, Montserrat López, Helena Masanas, Silvia Pittolo, Marta Pozuelo

Masters students: Pepita Pla, Iro Tsintzou

Undergraduate student: Federica Botta

Senior technician: Núria Camarero

Publications

- Bautista-Barrufet, A., López-Gallego, F., Rojas-Cervellera, V., Rovira, C., Pericàs, M. A., Guisán, J. M. and Gorostiza, P. (2014). Optical control of enzyme enantioselectivity in solid phase. *ACS Catalysis*, 4 (3): 1004-1009
- Izquierdo-Serra, M.*et al.* (2014). Two-photon neuronal and astrocytic stimulation of azobenzene-based photoswitches. *Journal of the American Chemical Society*, 136 (24): 8693-8701
- Palacios-Padrós, A. *et al* (2014). Growth of ordered anodic SnO2 nanochannel layers and their use for H2 gas sensing. *Journal of Materials Chemistry A*, 2 (4): 915-920
- Pérez-Madrigal, M.M. *et al.* (2014). Electronic, electric and electrochemical properties of bioactive nanomembranes made of polythiophene:thermoplastic polyurethane. *Polymer Chemistry*, 5 (4): 1248-1257
- Pérez-Madrigal, M.M. *et al.* (2014). Thermoplastic polyurethane:polythiophene nanomembranes for biomedical and biotechnological applications. *ACS Applied Materials and Interfaces*, 6 (12): 9719-9732
- Redondo-Morata, L., Giannotti, M. I. and Sanz, F. (2014). Structural impact of cations on lipid bilayer models: Nanomechanical properties by AFM-force spectroscopy. *Molecular Membrane Biology*, 31 (1): 17-28
- Lagunas, A. *et al* (2014). Large-scale dendrimer-based uneven nanopatterns for the study of local arginine-glycine-aspartic acid (RGD) density effects on cell adhesion. *Nano Research*, 7 (3): 399-409
- Artés, J. M., López-Martínez, M., Díez-Pérez, I., Sanz, F. and Gorostiza, P. (2014). Conductance switching in single wired redox proteins. *Small*, 10 (13): 2537-2541
- Artés, J. M., López-Martínez, M., Díez-Pérez, I., Sanz, F. and Gorostiza, P. (2014). Nanoscale charge transfer in redox proteins and DNA: Towards biomolecular electronics. *Electrochimica Acta*, 140: 83-95

The group's research focuses on developing nanoscale tools to study biological systems. These tools include instrumentation based on proximity probes, such as electrochemical tunnelling microscopy and spectroscopy, that we apply to investigate electron transfer in metal oxides and individual redox proteins.

These studies are relevant to the development of biosensors and molecular electronics devices. In particular, based on our development of nanoscale field-effect transistors using individual redox protein, we have recently published a method to measure conductance switching in single redox proteins "wired" between two electrodes.

Another set of nanotools that we are developing is based on molecular actuators that can be switched with light, such as azobenzene, which can be chemically attached to biomolecules in order to optically control their activity. We have demonstrated for the first time two-photon stimulation of neurons and astrocytes with azobenzene-based photoswitches. We have also developed several bioactive compounds that have been engineered to be regulated by light. These "optopharmacological" compounds include peptide inhibitors of protein-protein interactions involved in clathrin-mediated endocytosis, and two ligands of G protein-coupled receptors (adenosine and metabotropic glutamate receptors), which are important therapeutic targets.

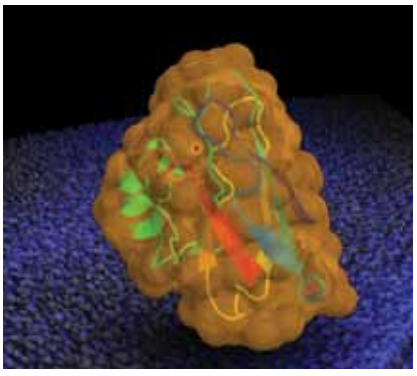
Research projects

- **THERALIGHT** Therapeutic Applications of Light-Regulated Drugs (2013-2014).
PI: **Pau Gorostiza** (coordinator)
ERC Proof of Concept Grant (ERC-PoC)

- **FOCUS** Single Molecule Activation and Computing (2011-2014).
PI: **Pau Gorostiza** (Coordinator: Vincent Torre)
European Commission Future and Emerging Technologies proactive 7: Molecular Scale Devices and Systems FP7-ICT-2009 8.7 (270483)

- **Single-BioET** Single-molecule junction capabilities to map the electron pathways in redox bio-molecular architectures (2012-2015).
PIs: **Ismael Díez** and **Pau Gorostiza**
Marie Curie FP7-PEOPLE-IRG (International Re-integration Grants)

- **OPTOPHARMACOLOGY** Therapeutic applications of optopharmacology (2014-2016).
PI: **Pau Gorostiza**
MINECO (CTQ2013-43892-R)



Crystal structure of redox protein azurin (Protein Data Bank entry: 1AZU) displaying its solvent accessible surface (gold) superimposed on the tertiary structure (rainbow) and a red sphere indicating the copper ion. When an atomically flat gold electrode is coated with azurin, the protein can be imaged under potentiostatic control by electrochemical tunneling microscopy (3D rendering of a 100x100nm^2 area shown in blue), and its electron transfer properties can be investigated by current-distance spectroscopy (Juan Manuel Artés *et al.*, 2011, *ACS Nano*).

- Optogenetic pacemaking to rewire neural circuits (2012-2014).
PI: **Pau Gorostiza** (Coordinator: Artur Llobet)
Fundació Marató de TV3, Grants for Research in Neurodegenerative Diseases

- Bioelectrochemistry and nanotechnology (2014-SGR-1251).
PI: **Fausto Sanz**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca (SGR 2014-2016)

Collaborations with other research centres

Prof. Amadeu Llebaria Institut de Química Avançada de Catalunya (IQAC-CSIC), Barcelona

Prof. Ernest Giralt Dept. de Química Orgànica, Universitat de Barcelona

Prof. Miquel Àngel Pericàs Institut Català d'Investigació Química (ICIQ), Tarragona

Dr. Piotr Bregestovski Institut de Neurobiologie de la Mediterraneé (INMED), Marseille

Dr. Mireia Oliva Dept. de Farmàcia i Tecnologia Farmacèutica, Universitat de Barcelona

Dr. Artur Llobet Dept. Patología y Terapéutica Experimental, Universitat de Barcelona

Dr. Joan Torrent Escola Universitària d'Òptica i Optometria de Terrassa, Spain

Prof. Dirk Trauner Chemistry Dept., UC Berkeley, USA

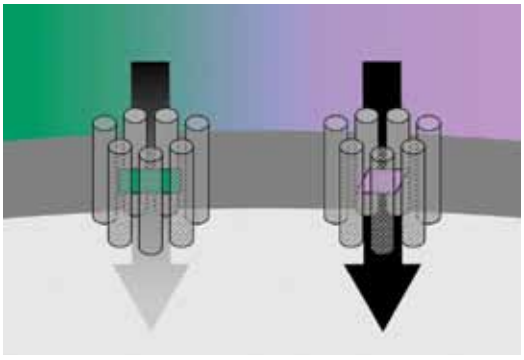
Prof. Carles Solsona Pathology and Experimental Therapeutics Dept, UB

Prof. Francisco Ciruela ICREA / Universitat de Barcelona, Spain

Prof. Jesús Giraldo & **Dr. Jordi Hernando** Universitat Autònoma de Barcelona, Spain

Scientific equipment and techniques

- iMic molecular imaging system
- Electrochemical scanning tunnelling microscope (STM) for molecular imaging
- Asylum Research Molecular Force Probe
- Multimode SPM Nanoscope III (SCT-UB)
- Autolab potentiostat
- Patch clamp setup with Heka EPC10 amplifier
- Molecular Imaging Electrochemical STM

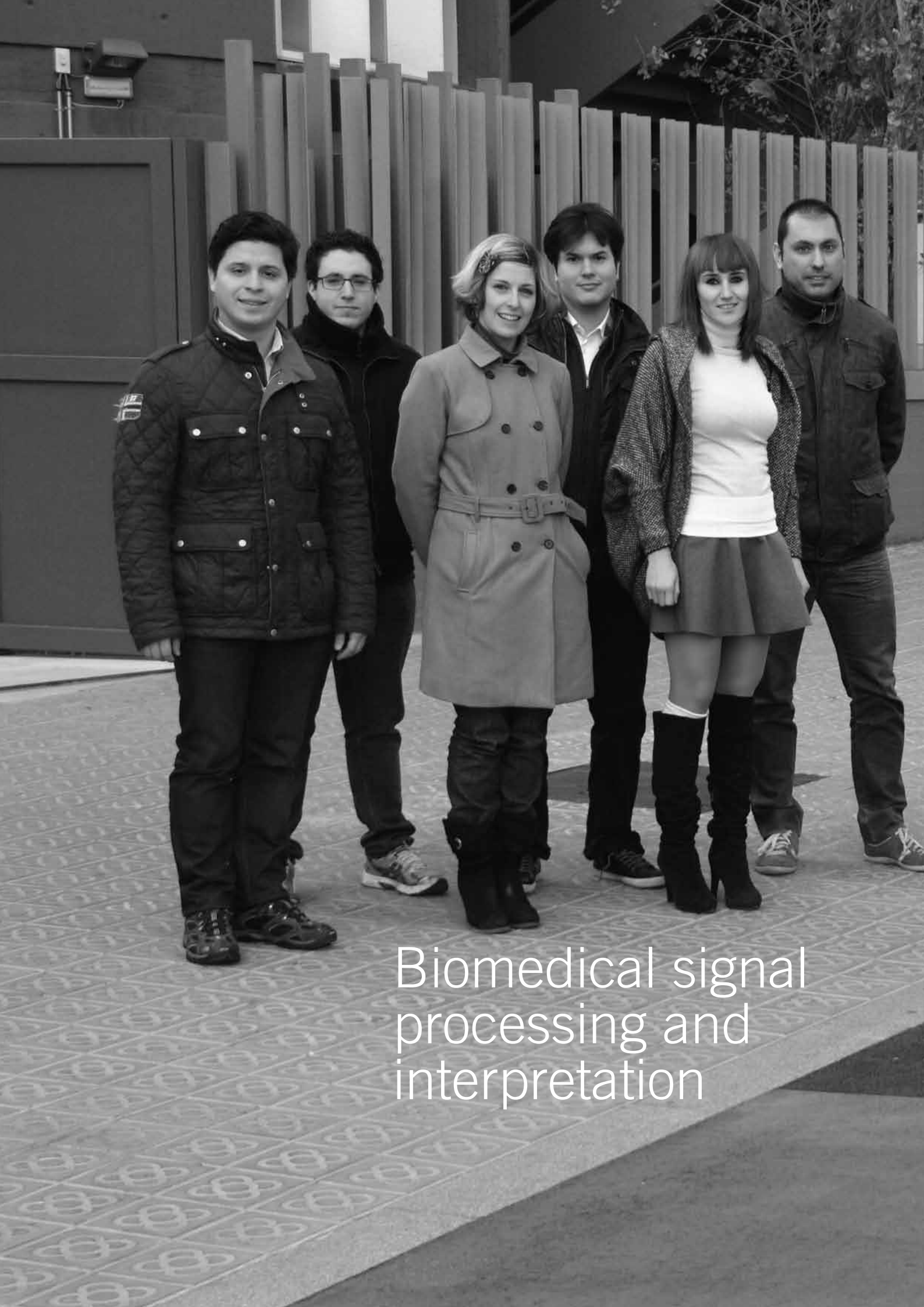


Schematic representation of a light-regulated drug bound to a 7-transmembrane receptor. Under violet illumination, the drug is inactivated and the receptor produces normal intracellular signaling. In the dark or under green light, the drug inhibits the receptor and interferes with signaling in a reversible way. (Pittolo, S. *et al*, 2014).

- Bahamonde, M. I. *et al* (2014). Photomodulation of G protein-coupled adenosine receptors by a novel light-switchable ligand. *Bioconjugate Chemistry*, 25 (10): 1847-1854
- Darwish, N., Aragonès, A. C., Darwish, T., Ciampi, S. and Díez-Pérez, I. (2014). Multi-responsive photo- and chemo-electrical single-molecule switches. *Nano Letters*, 14 (12): 7064-7070
- Eckelt, K., Masanas, H., Llobet, A. and Gorostiza, P. (2014). Automated high-throughput measurement of body movements and cardiac activity of Xenopus tropicalis tadpoles. *Journal of Biological Methods*, 1 (2): e9
- Gomez-Santacana, X., Rovira, X., Dalton, J. A., Goudet, C., Pin, J. P., Gorostiza, P., Giraldo, J. and Llebaria, A. (2014). A double effect molecular switch leads to a novel potent negative allosteric modulator of metabotropic glutamate receptor 5. *MedChemComm*, 5 (10): 1548-1554
- Pittolo, S. *et al* (2014). An allosteric modulator to control endogenous G protein-coupled receptors with light. *Nature Chemical Biology*, 10 (10): 813-815
- Torrent-Burgués, J., Cea, P., Giner, I. and Guaus, E. (2014). Characterization of Langmuir and Langmuir-Blodgett films of an octasubstituted zinc phthalocyanine. *Thin Solid Films*, 556: 485-494
- Aragonès, A. C., Darwish, N., Saletra, W. J., Pérez-García, L., Sanz, F., Puigmartí-Luis, J., Amabilino, D. B. and Díez-Pérez, I. (2014). Highly conductive single-molecule wires with controlled orientation by coordination of metalloporphyrins. *Nano Letters*, 14 (8): 4751-4756

Book chapters:

- Bautista-Barrufet, A., Izquierdo-Serra, M. and Gorostiza, P. (2014). *Photoswitchable Ion Channels and Receptors*. In: *Novel Approaches for Single Molecule Activation and Detection* (ed. Benfenati, F., Di Fabrizio, E. and Torre, V.), Springer Berlin Heidelberg: 169-188



Biomedical signal processing and interpretation

Group leader: Raimon Jané

Senior researchers: José Antonio Fiz, Beatriz Giraldo, Abel Torres

Senior postdoctoral researcher: Jordi Solà-Soler

Postdoctoral researcher: Leonardo Sarlabous

PhD students: Oiane Urra, Manuel Lozano, Luis Estrada, Andrés Arcentales

Masters students: Sara Argerich, Sergio De la Iglesia, Roger Gallart, Javier Rodríguez, Juan Pablo Téllez

Undergraduate student: Jorge Armando Pinto

Technicians: Maria Puy Ruiz de Alda, Mirella López

Publications

- Sarlabous, L., Torres, A., Fiz, J. A. and Jané, R. (2014). Evidence towards improved estimation of respiratory muscle effort from diaphragm mechanomyographic signals with cardiac vibration interference using sample entropy with fixed tolerance values. *PLoS ONE*, 9(2): e88902
- Fiz, J. A., Jané, R., Lozano, M., Gómez, R. and Ruiz, J. (2014). Detecting unilateral phrenic paralysis by acoustic respiratory analysis. *PLoS ONE*, 9(4): e93595
- Jané R. (2014). Engineering sleep disorders: from classical CPAP devices toward new intelligent adaptive ventilatory therapy. *IEEE Pulse*, 5(5):29-32

Conference proceedings:

- Correa, L. S., Giraldo, B., Correa, R., Arini, P. D. and Laciar, E. (2014). Estudio de la Pausa Espiratoria en Pacientes con Enfermedades Obstructivas en proceso de desconexión de la Ventilación Mecánica. VI Latin American Congress on Biomedical Engineering (CLAIB 2014). Paraná, Argentina Published by Springer
- Chaparro, J. A. and Giraldo, B. F. (2014). Power index of the inspiratory flow signal as a predictor of weaning in intensive care units. *36th Annual International Conference of the IEEE (2014)*, Chicago, USA. Published by IEEE
- Estrada, L., Torres, A., Sarlabous, L., Fiz, J. A., Gea, J., Martinez-Llorens, J. and Jané, R. (2014). Estimation of bilateral asynchrony between diaphragm mechanomyographic signals in patients with Chronic Obstructive Pulmonary Disease. *ibid*
- Sola-Soler, J., Fiz, J. A., Torres, A. and Jané, R. (2014). Identification of Obstructive Sleep Apnea patients from tracheal breath sound analysis during wakefulness in polysomnographic studies. *ibid*
- Tellez, J. P., Herrera, S., Benito, S. and Giraldo, B. F. (2014). Analysis of the breathing pattern in elderly patients using the hurst exponent applied to the respiratory flow signal. *ibid*

The group's research addresses the design and development of advanced signal processing techniques and the interpretation of biomedical signals to improve non-invasive monitoring, diagnosis, disease prevention and pathology treatment.

Our main objective is to improve diagnosis capability through the characterization of physiological phenomena and to enhance early detection of major cardiac and respiratory diseases and sleep disorders.

We propose and design new signal processing algorithms and develop new biosignal databases, with the collaboration of our hospital partners. To validate the clinical information of new surface signals, we have developed specific invasive/non-invasive protocols and animal models. The group focuses its research in a translational way to promote the transfer of our scientific and technological contributions. Currently, our prototypes are used in hospitals for research purposes and for future industrial developments.

Highlights in 2014

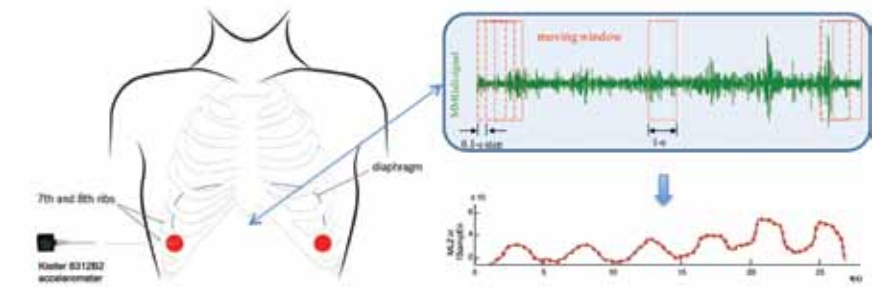
Obstructive Sleep Apnea and Sleep Disorders

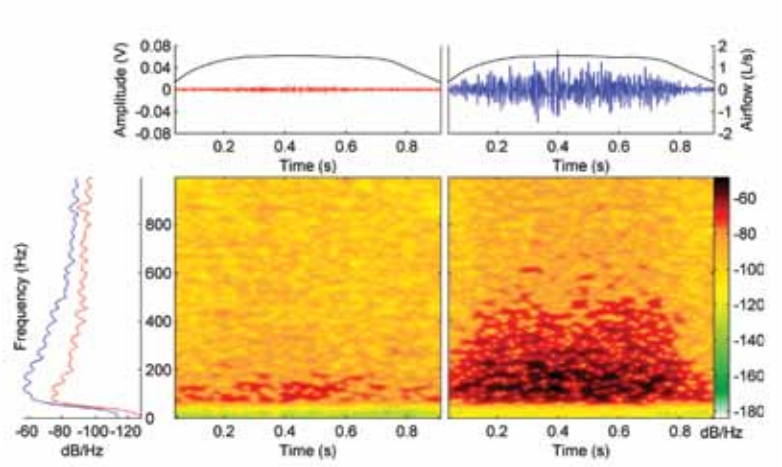
- Assesssment of classical CPAP devices and new intelligent adaptive ventilatory therapy in Sleep Disorders (*IEEE Pulse*, 5(5): 29-32).
- A new method for identification of Obstructive Sleep Apnea patients from tracheal breath sound analysis during wakefulness in polysomnographic studies (*IEEE-EMBC 2014*, 4232-4235, *SLEEP* 2014, v37: A359), with the Hospital Germans Trias i Pujol, Badalona.
- Proposal of new sleep transition indexes for describing altered sleep in patients with Sleep Apnea Hypopnea Syndrome (SAHS) (*IFMBE Proceedings 2014*, 41: 1017-1020), with the Hospital Germans Trias i Pujol, Badalona.

Chronic Obstructive Pulmonary Disease and Asthma

- Improved estimation of respiratory muscle effort from diaphragm mechanomyographic signals using sample entropy with fixed tolerance values (*PLOS ONE*, 9 (2): e88902).
- Detecting unilateral phrenic paralysis by non-invasive acoustic respiratory analysis (*PLOS ONE*, 9 (4): e93595), with the Joint Research Unit between IBEC and the research Institute of the Hospital Germans Trias i Pujol, Badalona (IGTP).

Novel ICT method to non-invasive evaluate the mechanical activation of inspiratory muscles in Chronic Obstructive Pulmonary Disease patients.





New acoustic method for better diagnosis in patients with diaphragmatic paralysis

- Estimation of bilateral asynchrony between diaphragm mechanomyographic signals in patients with Chronic Obstructive Pulmonary Disease (*IEEE-EMBC 2014*, 3813-6), with the Hospital Germans Trias i Pujol, Badalona, and the Hospital del Mar, Barcelona.
- Respiratory rate detection by empirical mode decomposition method applied to diaphragm mechanomyographic signals (*IEEE-EMBC 2014*, 3204-7), with the Hospital Germans Trias i Pujol, Badalona.
- Evaluation of Laplacian diaphragm electromyographic signals in a dynamic inspiratory maneuver (*IEEE-EMBC 2014*, 2201-2204 and *IFMBE Proceedings 2014*, 41: 977-980), with the Universidad Politécnica de Valencia.
- Analysis of normal and adventitious respiratory sounds for assessment of asthma (*IFMBE Proceedings 2014*, 41: 981-984) with the Joint Research Unit between IBEC and the research Institute of the Hospital Germans Trias i Pujol, Badalona (IGTP).

Cardiac and cardiorespiratory diseases and ageing

- Analysis of blood pressure variability in healthy subjects (*IFMBE Proceedings 2014*, 41: 1021-1024), with the Hospital de Sant Pau, Barcelona.
- Analysis of the breathing pattern in elderly patients using the hurst exponent applied to the respiratory flow signal (*IEEE-EMBC 2014*, 3422-3425), with the Hospital de Sant Pau, Barcelona
- Power index of the inspiratory flow signal as a predictor of weaning in intensive care units (*IEEE-EMBC 2014*, 78-81), with Escuela Colombiana de Ingeniería, Bogotá.

Neurorehabilitation and Biofeedback

- Evaluation of spatial characteristics of upper-limb movements from EMG signals for neurorehabilitation assessment (*IFMBE Proceedings 2014*, 41: 1795-1798) with the Robotics group at IBEC.
- Synergy analysis as a tool to design and assess an effective stroke rehabilitation (*IEEE-EMBC 2014*, 3550-3553)
- Proposal of emerging rehabilitation techniques in cerebral palsy (*Emerging Therapies in Neurorehabilitation* 2014, 4:23-49)

- Estrada, L., Torres, A., Garcia-Casado, J., Prats-Boluda, G., Yiyao, Y.-L. and Jané, R. (2014). Evaluation of Laplacian diaphragm electromyographic recording in a dynamic inspiratory maneuver. *ibid*
- Estrada, L., Torres, A., Sarlabous, L., Fiz, J. A. and Jané, R. (2014). Respiratory rate detection by empirical mode decomposition method applied to diaphragm mechanomyographic signals. *ibid*
- Urra, O., Casals, A. and Jané, R. Synergy analysis as a tool to design and assess an effective stroke rehabilitation. *ibid*
- Estrada, L., Torres, A. and Jané, R. (2014). Evaluación de la asincronía bilateral y toracoabdominal mediante señales mecanomiográficas. *XXXII Congreso Anual de la Sociedad Española de Ingeniería Biomédica (CASEIB 2014)*, Barcelona, Spain. Published by Sociedad Española de Ingeniería Biomédica
- López Picazo, M., Solà-Soler, J., Fiz, J. A. and Jané, R. (2014). Sincronización de sistemas de monitorización para el estudio de ronquidos en las distintas fases del sueño en pacientes con SAHS. *ibid*
- Lozano, M., Fiz, J. and Jané, R. (2014). Análisis de la intensidad de los sonidos respiratorios para el diagnóstico de la parálisis frénica unilateral. *ibid*
- Sarlabous, L., Torres, A., Fiz, J. A., Gea, J., Martínez-Llorens, J. M. and Jané, R. (2014). Relación entre la presión inspiratoria pico y la activación mecánica de los músculos inspiratorios durante respiración tranquila en pacientes con EPOC. *ibid*
- Urra, O., Casals, A. and Jané, R. (2014). Study of synergy patterns during the execution of stroke rehabilitation exercises. *ibid*
- Solà-Soler, J., Fiz, J. A., Torres, A. and Jané, R. (2014). Evaluación de la vía aérea superior en sujetos con SAHS mediante análisis del sonido respiratorio durante vigilia. *ibid*

- Téllez, J., Herrera, S., Benito, S. and Giraldo, B. (2014). Estudio del patrón respiratorio en pacientes ancianos. *ibid*

Books:

- Jané, R., Caminal, P., Giraldo, B., Solà-Soler, J. and Torres, A. (2014). *Libro de Actas del CASEIB 2014.* (ed. Barcelona, Spain. CASEIB-IBEC (2014).

Book chapters:

- Estrada, L., Torres, A., Garcia-Casado, J., Ye-Lin, Y. and Jané, R. (2014). Evaluation of Laplacian diaphragm electromyographic recordings in a static inspiratory maneuver. In: *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013* (ed. Roa Romero, L. M.). London, Springer International Publishing. 41: 977-980
- Giraldo, B. F., Calvo, A., Martínez, B., Arcentales, A., Jané, R. and Benito, S. (2014). Blood pressure variability analysis in supine and sitting position of healthy subjects. *ibid*, 1021-1024
- Urra, O. and Jané, R. (2014). New sleep transition indexes for describing altered sleep in SAHS. *ibid*, 1017-1020
- Urra, O., Casals, A. and Jané, R. (2014). Evaluating spatial characteristics of upper-limb movements from EMG signals. *ibid*, 1795-1798
- Lozano, M., Fiz, J. A. and Jané, R. (2014). Analysis of normal and continuous adventitious sounds for the assessment of asthma. ibid, 981-984
- Torres, A., Fiz, J. A. and Jané, R. (2014). Cancellation of cardiac interference in diaphragm EMG signals using an estimate of ECG reference signal. *ibid*, 1000-1004 (2014).
- Lambrecht, S., Urra, O., Grosu, S. and Pérez, S. (2014). Emerging rehabilitation in cerebral palsy. In: *Emerging Therapies in Neurorehabilitation* (ed. Pons, J. L. and Torricelli, D.). London, Springer Berlin Heidelberg. 4: 23-49

Research projects

- **MIMCRID** Multimodal invasive and non-invasive biomedical signal interpretation and modelling in cardiac, respiratory and neurological disorders (2011-2013).
PI: **Raimon Jané** (Coordinator)
MINECO

- Respiratory sounds analysis.
PI: **Raimon Jané**
Health Sciences Research Institute, Germans Trias I Pujol Foundation

Collaborations with other research centres

Dr. J. Mark Ansermino Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, Canada

Prof. Antonio Bayes Genis Grup ICREC, Servei Cardiología Hospital Universitari Germans Trias i Pujol, Barcelona

Dr. Salvador Benito Hospital de la Santa Creu i Sant Pau, Barcelona

Prof. Dr. Konrad Bloch Pulmonary Division, University of Zurich, Switzerland

Prof. Armin Bolz Institute of Biomedical Engineering, University of Karlsruhe, Germany

Prof. Manuel Doblaré Grupo de Mecánica Estructural y Modelado de Materiales, Universidad de Zaragoza, Spain

Prof. Guy Dumont Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, Canada

Prof. Ramon Farré Unitat de Biofísica i Bioenginyeria, Facultat de Medicina, Barcelona

Dr. Javier García-Casado Instituto Interuniversitario de Investigación en Bioingeniería y Tecnología Orientada al Ser Humano, Universidad Politécnica de Valencia

Dr. Joaquim Gea Servei Pneumologia, Hospital del Mar-IMIM, Barcelona

Dr. Alfredo Hernández Laboratoire Trataiment du Signal et de l'Image, Université de Rennes 1, Instituto Francés de Salud (INSERM), France

Dr. Eric Laciar Departamento de Electrónica y Automática, Universidad Nacional de San Juan, Argentina

Prof. Pablo Laguna Instituto de Investigación de Aragón (I3A), Universidad de Zaragoza, Spain

Dr. Barry Mersky Audiodontics, LLC, Bethesda, Maryland, USA

Prof. Dr. Thomas Penzel Interdisciplinary Sleep Center, Charité University Hospital, Berlin, Germany

Dr. Josep Morera Prat Servicio de Neumología. Hospital Germans Trias i Pujol, Badalona, Spain

Prof. Winfried J. Randerath Institut für Pneumologie, Klinik Bethanien, Solingen, Germany

Dr. Juan Ruiz Servei de Pneumología de l'Hospital Germans Trias i Pujol de Badalona

Dr. Matthias Schwaibold MCC-Med GmbH & Co. KG, Karlsruhe, Germany

Prof. Dr. Lotfi Senhadji Laboratoire Traitement du Signal et de l'Image (LTSI), Université de Rennes 1, Institut National de la Santé et de la Recherche Médicale (INSERM), France

Prof. Leif Sörnmo Signal processing group, Lund University, Sweden

Prof. Dr. Jaume Veciana Grupo de Nanociencia Molecular y Materiales Orgánicos del Instituto de Ciencia de Materiales de Barcelona (NANOMOL-CSIC), Barcelona

Prof. Andreas Voss University of Applied Sciences, Jena, Germany

Scientific equipment and techniques

- Research laboratory with full equipment for acquisition and processing of biomedical signal to test new sensors and to define clinical protocols (preliminary tests and control subjects)
- Non-invasive Vital Signs Monitor for small lab animals (mice and rats) (Mouse-Ox Plus)
- BIOPAC system for multichannel cardiac and respiratory biomedical signal acquisition
- Databases of biomedical signals from hospitals and animal laboratories
- Snoring analyzer equipment (SNORYZER)
- Sensors, electrodes and microphones to obtain cardiac, respiratory, neural, muscular and sleep biomedical signals
- Polisomnographic equipment available in the Sleep Laboratory of collaborator hospital
- Beat to beat arterial blood pressure and haemodynamic monitor equipment
- Computing server for high performance biomedical signals

- Arizmendi, C., Viviescas, J., González, H. and Giraldo, B. (2014). Patients classification on weaning trials using neural networks and wavelet transform. In: *Studies in Health Technology and Informatics* (ed. Mantas, J., Househ, M. S. and Hasman, A.), IOS Press. Volume 202, *Integrating Information Technology and Management for Quality of Care*: 107-110

Microbial biotechnology and host-pathogen interaction

Group leader: Antonio Juárez

Postdoctoral researchers: Mário Hüttener, Manuela Dietrich

PhD student: Francesca Staffieri

Masters students: Alejandro Prieto, Eleonora Tassinari, Óscar Zhu

Technicians: Mª Carmen Jaramillo, Sònia Aznar

Structure and function of bacterial proteins that modulate virulence expression; bacterial plasmids and their role in transmission of multidrug resistance markers; application of nanotools of bacterial biotechnology

1. Structure and function of bacterial proteins that modulate virulence expression

Protein–protein and protein–DNA interactions play key roles in the ability of virulent bacteria to adapt to the host environment and cause disease. A group of proteins is currently the focus of our research: nucleoid-associated proteins (NAPs) that contribute to DNA architecture and modulate gene expression. We are interested in unravelling the role played by two of these proteins – Hha and H-NS – in the regulation of virulence and of plasmid transfer. *Escherichia coli* pathotypes such as enteroaggregative *E. coli* are the subject of our research. Owing to their key modulatory functions, these proteins are interesting targets to combat bacterial infections.

2. Bacterial plasmids and their role in transmission of multidrug resistance markers

A main concern with bacterial infections is the selection of isolates that are resistant to several antimicrobial drugs. The transmission of the ability of bacterial cells of simultaneously resist several antimicrobial drugs is accomplished, in many instances, by plasmids. These genetic elements can be transmitted from one cell to another, and modify the phenotype of the recipient cell. We have recently shown that multidrug resistance plasmids in Salmonella require specific plasmid proteins to be stably maintained in this microorganism. These proteins could be considered as targets to combat multidrug resistance.

3. Application of nanotools of bacterial biotechnology

3.1. Dielectrophoresis (DEP). We have previously shown that dielectrophoresis can be a valuable tool for bacterial cell sorting and characterization. We are currently using different chip designs (2D and 3D carbon electrodes) to: a) study the effect of electric fields on bacterial cell physiology; b) combine DEP with other molecular protocols for detection and identification of different types of cells. Recent results have shown that DEP chips can be used to increase PCR detection of yeast cells.

3.2. Atomic force microscopy (AFM). Conventional AFM approaches have been shown to be powerful techniques for characterizing both biomaterials and biomolecules. In a joint project with the Nanoscale Bioelectrical Characterization group (page 56), we intend to use electrical-AFM to characterize the bacterial cell envelope. We also plan to use this approach to analyze the structural and physiological properties of bacterial living cells.

Publications

- Paytubi, S., Aznar, S., Madrid, C., Balsalobre, C., Dillon, S. C., Dorman, C. J. and Juárez, A. (2014). A novel role for antibiotic resistance plasmids in facilitating Salmonella adaptation to non-host environments. *Environmental Microbiology*, 16 (4): 950-962 (2014).
- Dietrich, M., Pedró, L., García, J., Pons, M., Hüttener, M., Paytubi, S., Madrid, C. and Juárez, A. (2014). Evidence for moonlighting functions of the θ subunit of Escherichia coli DNA polymerase III. *Journal of Bacteriology*, 196 (5): 1102-1112 (2014).
- Gibert, M., Juárez, A., Zechner, E. L., Madrid, C. and Balsalobre, C. (2014). TrhR, TrhY and HtdA, a novel regulatory circuit that modulates conjugation of the IncHI plasmids. *Molecular Microbiology*, 94 (5): 1146-1161 (2014).
- Esteban-Ferrer, D., Edwards, M. A., Fumagalli, L., Juarez, A. and Gomila, G. (2014). Electric polarization properties of single bacteria measured with electrostatic force microscopy. *ACS Nano*, 8 (10): 9843–9849 (2014).
- Oliva, A. M., Homs-Corbera, A., Torrents, E., Juarez, A. and Samitier, J. (2014). Synergystic effect of temperature and electric field intensity in *Escherichia coli* inactivation. *Micro and Nanosystems*, 6 (2): 79-86
- del Moral Zamora, B., Azpeitia, J. M. Á., Farrarons, J. C., Català, P. L. M., Corbera, A. H., Juárez, A. and Samitier, J. (2014). Towards point-of-use dielectrophoretic methods: A new portable multiphase generator for bacteria concentration. *Micro and Nanosystems,* 6 (2): 71-78
- Hüttener, M., Dietrich, M., Paytubi, S. and Juárez, A. (2014). HilA-like regulators in *Escherichia coli* pathotypes: the YgeH protein from the enteroaggregative strain 042. *BMC Microbiology*, 14 (268): 1-10

Research projects

- **REGVIRBAC** Regulación de la virulencia bacteriana por proteinas que reconocen conformaciones locales del ADN (2014-2016)
PI: **Antonio Juárez**
MINECO (BIO2013-49148-C2-1-R)

- **REGENTERO** Proteínas restringidas a la familia *Enterobacteriaceae*: implicación en la transferencia génica horizontal y virulencia (2011-2014).
PI: **Antonio Juárez**
MICINN (BFU2010-21836-C02-01)

- **INTERMODS** Interconexiones de módulos plasmídicos y los genomas de bacterias patógenas (2008-2015).
PI: **Antonio Juárez** (managed by UB)
MINECO, Consejo Superior de Investigaciones Científicas (CSIC)

- **MEJORAVE2** Mejora sanitaria y de productos cármicos de ave.
PI: **Antonio Juárez**
Industrial project with Mevet, S.A / CZ Veterinaria, S.A.

- RMN de biomolècules i biología molecular bacteriana (2014-SGR-1260)
PI: **Antonio Juárez**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca (SGR 2014-2016)

Collaborations with other research centres

Prof. Josep Casadesús Universidad de Sevilla, Spain

Prof. Charles Dorman Trinity College, Dublin

Prof. F. García del Portillo Centro Nacional de Biotecnología, Madrid, Spain

Dr. Gabriel Gomila IBEC (page 56)

Prof. Mike Hughes University of Surrey, UK

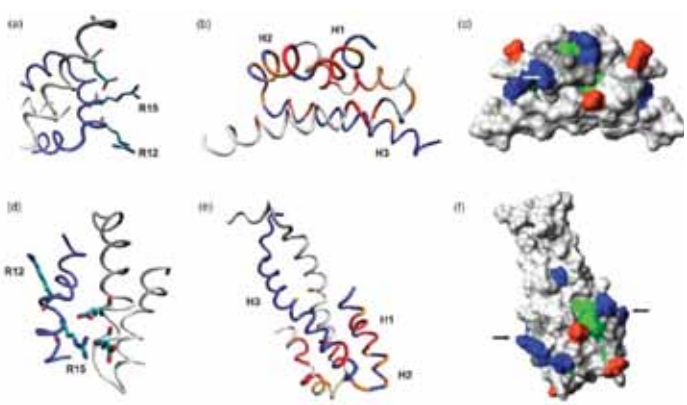
Dr. Rodrigo Martínez-Duarte École Polytechnique Fédérale de Lausanne, Switzerland

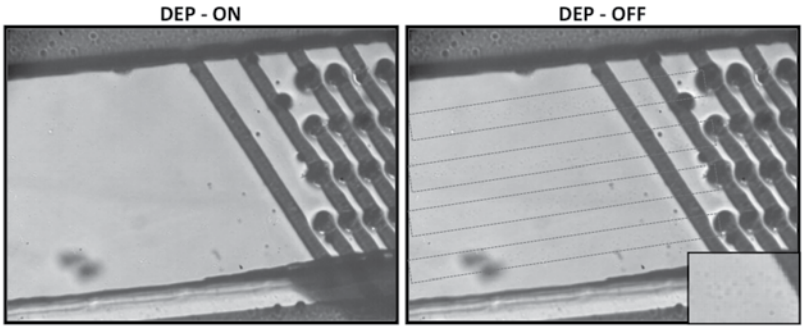
Prof. Miquel Pons Organic Chemistry Dept., University of Barcelona, Spain

Prof. Josep Samitier IBEC (page 103)

Dr. Eduard Torrents IBEC (page 108)

Hha perturbing H-NS structure

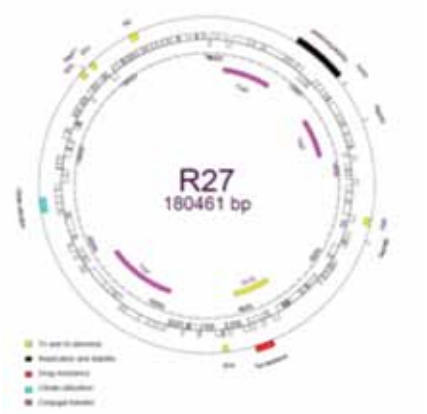




Trapping of *Escherichia coli* cells in a dielectrophoresis chip.

Scientific equipment and techniques

- Thermocycler (PCR)
- Protein and DNA electrophoresis
- Process of biomolecule production
- Protein expression and purification systems
- Technology of microbial culture facilities
- Dielectrophoresis equipment



Salmonella R27 plasmid

Book chapters:

- del Moral Zamora, B., Azpeitia, J. M. Á., Farrarons, J. C., Català , P. L. M., Corbera, A. H., Juárez, A. and Samitier, J. (2014). Towards point-of-use dielectrophoretic methods: A new portable multiphase generator for bacteria concentration. *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013*. Seville (Spain)
- Oliva, A. M., Homs, A., Torrents, E., Juarez, A. and Samitier, J. (2014). Effect of electric field and temperature in E.Coli viability. *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013*. Seville (Spain)

Signal and information processing for sensing systems

Group leader: Santiago Marco

Senior researcher: Agustín Gutiérrez

Postdoctoral researchers: Jordi Fonollosa, Raquel Obregón, Juan Manuel Jiménez

PhD students: Ariadna Bartra, Lluís Fernández, Ana Maria Solórzano

Undergraduate students: Laia Garrit, Laura Mateu, Ana Rodríguez, Raquel Rodríguez

Technicians: Rudys Magrans, Núria Cañaveras, Javier Burgués, Sara Rica

Current smart instrumentation using multi-sensors and/or spectrometers provides a wealth of data that requires sophisticated signal and data processing approaches in order to extract the hidden information.

In this context, we are interested in intelligent chemical instruments for the detection of volatile compounds and smells.

These systems can be based on an array of nonspecific chemical sensors with a pattern recognition system , taking inspiration from the olfactory system. Some spectrometries, e.g. Ion Mobility Spectrometry, are capable of very fast analysis with good detection limits but poor selectivity. These technologies have been proposed for the fast determination of the volatolome (volatile fraction of the metabolome), instead of the reference technique of gas chromatography – mass spectrometry.

Our group develops algorithmic solutions for the automatic processing of Gas Sensor Array, Ion Mobility Spectrometry (IMS) and Gas Chromatography – Mass Spectrometry (GC-MS) data for metabolomics and food samples. In a parallel activity, our group is working on the detection of drowsiness in drivers using vehicle dynamic measures.

Our research in 2014 included the following:

Computational Olfaction:

- We have developped a computational model of the peripheral olfactory system in vertebrates. The model provides insight on the different computational role of mitral cells and tufted cells.

Signal and Data Processing for smart chemical Instrumentation:

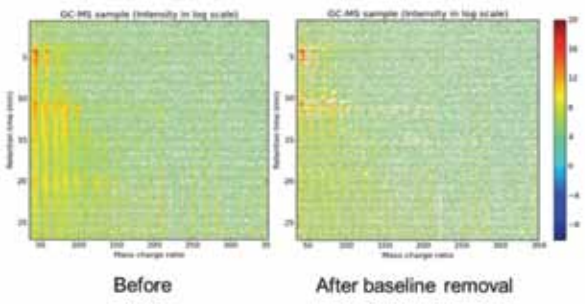
- We have proposed a new method to determine the limit of detection based on information theory. The method models the analytical instrument as a Binary Source Information Channel. The method is able to cope with non-gaussian noise and prior information.
- We have identified weak model validation practices as a major shortcoming of current research in volatolome analysis. We have proposed more strict validation practices.

Artificial Olfaction:

- We have tested Bayesian chemical source localization algorithms in real environments using autonomous robots. The localization capability of the proposed algorithm improves previous proposals in the literature.
- We have built a biomimetic olfactory system implementing controlled sniffing to show that gas flow modulation improves early odorant detection.
- In collaboration with Universitat de Lleida (Dr. J. Palacin) and University of Örebro (Prof. A. Lilienthal) we are testing chemical source localization algorithms with autonomous robots.

Automotive Sensor Systems:

- In cooperation with automotive company FICOSA, we have developed algorithmic solutions to estimate the driver drowsiness using vehicle sensor data available from the bus CAN. During this year we have developed a highly optimized embedded version for a FICOSA client.



Development of a baseline correction for GC-MS data.

Autonomous Robot fitted with a Field Asymmetric Ion Mobility Spectrometer for Chemical Source localization experiments.

Research projects

- **SMART-IMS** Procesado de Señal para Espectroscopia de Movilidad de Iones: Análisis de Fluidos Biomédicos y Detección de Sustancias Tóxicas.
PI: **Santiago Marco**
MINECO

- **BIOENCODE** Estudio comparativo de la capacidad de codificación de información química de sistemas biológicos y artificiales.
PI: **Agustín Gutiérrez**
MINECO

- Intelligent signal processing for sensor systems in bioengineering (2009-2013).
PI: **Santiago Marco**
AGAUR, Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (2009-SGR-753)

- **SOMNO-ALERT® P-10** Drowsiness Detection in drivers (2010-2014).
PI: **Santiago Marco**
Industrial project with FICOSA

- Transduccion biomimetica para olfaccion artificial (2013-2014).
PI: **Agustín Gutiérrez**
MINECO, Europa Excelencia

- **SAFESENS** Sensor Technologies for Enhanced Safety and Security of Buildings and its Occupants
PI: **Santiago Marco**
ENIAC project (European project with a mix of public-private funding)

Publications

- Fonollosa, J., Vergara, A., Huerta, R. and Marco, S. (2014). Estimation of the limit of detection using information theory measures. *Analytica Chimica Acta*, 810: 1-9
- Martinez, D., Teixidó, M., Font, D., Moreno, J., Tresanchez, M., Marco, S. and Palacín, J. (2014). Ambient intelligence application based on environmental measurements performed with an assistant mobile robot. *Sensors*, 14 (4): 6045-6055
- Marco, S., Gutiérrez-Gálvez, A., Lansner, A., Martinez, D., Rospars, J. P., Beccherelli, R., Perera, A., Pearce, T. C., Verschure, P. F. M. J. and Persaud, K. (2014). A biomimetic approach to machine olfaction, featuring a very large-scale chemical sensor array and embedded neuro-bio-inspired computation. *Microsystem Technologies*, 20 (4-5): 729-742
- Marco, S. (2014). The need for external validation in machine olfaction: emphasis on health-related applications. *Analytical and Bioanalytical Chemistry*, 406 (16): 3941-3956
- Bennetts, V., Schaffernicht, E., Pomareda, V., Lilienthal, A., Marco, S. and Trincavelli, M. (2014). Combining non selective gas sensors on a mobile robot for identification and mapping of multiple chemical compounds. *Sensors*, 14 (9): 17331-17352
- Fresco-Cala, B., Jimenez-Soto, J. M., Cardenas, S. and Valcarcel, M. (2014). Single-walled carbon nanohorns immobilized on a microporous hollow polypropylene fiber as a sorbent for the extraction of volatile organic compounds from water samples. *Microchimica Acta*, 181 (9-10): 1117-1124
- Polese, D., Martinelli, E., Marco, S., Di Natale, C. and Gutierrez-Galvez, A. (2014). Understanding odor information segregation in the olfactory bulb by means of mitral and tufted cells. *PLoS ONE*, 9 (10): e109716

- Palleja, T., Balsa, R., Tresanchez, M., Moreno, J., Teixido, M., Font, D., Marco, S., Pomareda, V. and Palacin, J. (2014). Corridor gas-leak localization using a mobile Robot with a photo ionization detector sensor. *Sensor Letters*, 12 (6-7): 974-977

Book section:

- Martínez, D., Pallejà, T., Moreno, J., Tresanchez, M., Teixidó, M., Font, D., Pardo, A., Marco, S. and Palacín, J. (2014). A mobile robot agent for gas leak source detection. In: *Trends in Practical Applications of Heterogeneous Multi-Agent Systems*. The PAAMS Collection (ed. Bajo Perez, J. *et al*), Springer International Publishing. 293: 19-25

Conference proceedings:

- Oller-Moreno, S., Pardo, A., Jimenez-Soto, J. M., Samitier, J. and Marco, S. (2014). Adaptive Asymmetric Least Squares baseline estimation for analytical instruments. *11th International Multi-Conference on Systems, Signals & Devices (SSD)*, Castelldefels, Spain. Published by IEEE
- Martínez, D., Moreno, J., Tresanchez, M., Teixidó, M., Font, D., Pardo, A., Marco, S. and Palacín, J. (2014). Experimental application of an autonomous mobile robot for gas leak detection in indoor environments. *17th International Conference on Information Fusion*. Published by IEEE.
- Sheik, S., Marco, S., Huerta, R. and Fonollosa, J. (2014). Continuous prediction in chemoresisitive gas sensors using reservoir computing. *Procedia Engineering*, 87, 843-846.
- Fernandez, L., Gutierrez-Galvez, A., & Marco, S. (2014). Robustness to Sensor Damage of a Highly Redundant Gas Sensor Array. *Procedia Engineering*, 87, 851-854
- Güney, S, Fernandez, L. and Marco, S. (2014). Calibration transfer between e-noses. *22nd Signal Processing and Communications Applications Conference (SIU)*, Trabzon, Turkey. Published by IEEE.

Collaborations with other research centres

Dr. Lourdes Arce
Dept. Química Analítica, Universidad de Córdoba, Spain

Dr. Alexandre Perera and Prof. Pere Caminal
Centre de Recerca en Enginyeria Biomèdica, Universitat Politècnica de Catalunya, Barcelona, Spain

Prof. Krishna Persaud
Chemoreception Group, University of Manchester, UK

Dr. J. Fonollosa and Prof. Ramon Huerta
Biocircuits Lab, University of California in San Diego, USA

Prof. J. W. Gardner
Microsensors and Bioelectronics Lab, Dept. of Electric and Electronic Engineering, University of Warwick, UK

Prof. Achim Lilienthal and Dr. Marco Trincavelli
Mobile Robotics and Olfaction Lab, University of Örebro, Sweden

Dr. Ivan Montoliu
Nestlé Institute of Health Sciences, Laussane, Switzerland

Dr. Jordi Palacín
Robotics Lab, Universitat de Lleida, Spain

Scientific equipment and techniques

- Gas chromatograph/mass spectrometer (Thermoscientific) with robotic head-space sampler
- 2 Infusion pumps K-systems
- 6 channel vapor generator plus humidity control (Owlstone, UK)
- Ion Mobility Spectrometer: Gas Detector Array (Airsense Analytics GmbH)
- Computing and General Purpose Electronic Instrumentation
- Field Asymmetric Ion Mobility Spectrometer (Owlstone, UK)
- Corona Discharge Ion Mobility Spectrometer (3QBD, Israel)
- Ultraviolet Ion Mobility Spectrometer (Gas Dortmund, Germany)

Experiments using a mechanical ventilator to investigate on the influence of breathing dynamics on the response of artificial olfaction systems.

Biomimetic systems for cell engineering

Junior group leader: Elena Martínez

PhD students: Gizem Altay, Albert Garcia, Verónica Hortigüela, Maria Valls

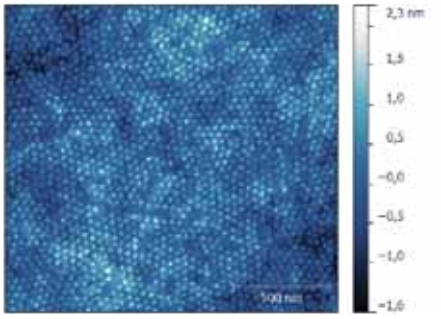
Master student: Jari Iannucci

Undergraduate students: Claudia Insa, Gabriela Korbelová, Ariadna Nistal

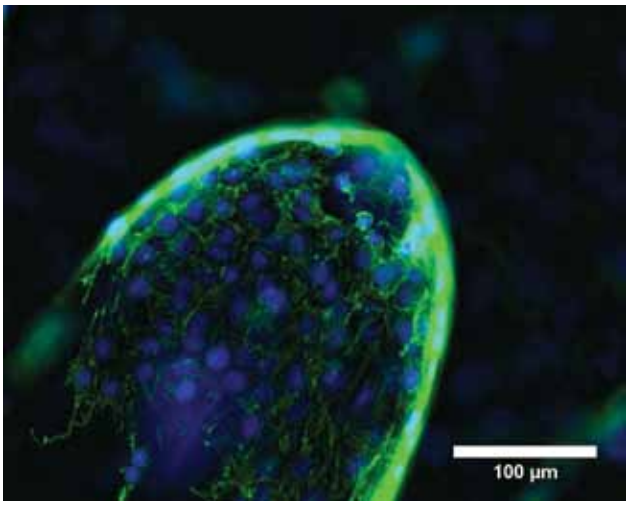
In vitro assay platforms involving human cells are increasingly important to study tissue development, tissue regeneration, construct models of disease or develop systems for therapeutic screening that predict the human *in vivo* context.

The main conceptual problem of the standard *in vitro* cell-based assays is that they rely on two dimensional monolayer cellular cultures, which fail to replicate the complexity of living systems. There is an urgent need to create technological platforms with complex cell culture systems that mimic better the tissue-like cellular microenvironment.

Our lab is interested in the development of new biomimetic systems for cell-based assays that account for the structural, physiological and biochemical features of the *in vivo* cellular microenvironment. Specifically, we develop systems that mimic the heterogeneity of the tissue extracellular matrix for cell engineering. Advanced designs include the structural anisotropy intrinsic to tissues such as heart muscle or bone, the binding of specific ligands and the capability of generating gradients of regulatory signals. These biomimetic systems will provide the interface between biological questions and engineering tools to (i) develop new insights into environmental regulation of cells, (ii) investigate diseases, and (iii) develop new therapies for regenerative medicine.



Atomic force microscopy picture of a thin layer of PS-b-PMMA copolymer. The two phases of the block copolymer self-assembled into an ordered nanostructure.



Mouse fibroblasts seeded on a PEG-AA micropillar functionalized with fibronectin.

Research projects

- Diagnóstico y pronóstico de cáncer de próstata mediante nanobiosensores híbridos multianalito (2011-2013).
PI: **Josep Samitier, Elena Martinez** (coordinator)
MINECO, Instituto de Salud Carlos III. Subprograma de Proyectos de investigación en salud (FIS)

- **CARDIO-STEM** Terapias regenerativas con células madre para el fallo cardíaco (2009-2014).
PI: **Josep Samitier**
MINECO, ACI-E Medicina Regenerativa

Collaborations with other research centres

Prof. Josep Samitier IBEC (page 103)

Prof. Ángel Raya IBEC (page 92)

Dr. Núria Montserrat Center of Regenerative Medicine in Barcelona (CMRB), Barcelona (Spain)

Dr. Daniel Riveline ISIS/IGBMC, Strasbourg (France)

Dr. Matthew Dalby University of Glasgow, Glasgow (UK)

Prof. Ramón Eritja Institut de Recerca Biomédica (IRB), Barcelona (Spain)

Prof. Fernando Albericio Institut de Recerca Biomédica (IRB), Barcelona (Spain)

Prof. Vasco Teixeira Universidade do Minho, Braga (Portugal)

Scientific equipment and techniques

- Micro and nanofabrication techniques:
  - Biomolecule gradients produced by microfluidics
  - Large-area nanostructured polymer surfaces produced by diblock copolymers
  - 3D microstructures on hydrogel materials
  - Mini-bioreactor for 3D cell culture
- Characterization techniques:
  - Surface Plasmon Resonance (SPR) measurements on polymer materials
  - Atomic Force Microscope (AFM) expertise
  - Optical Microscopes (white light/epifluorescence)
  - Focused Ion Beam (FIB) / Scanning Electron Microscopy (SEM) of biological specimens
- Equipment:
  - Biological safety cabinet (class II)
  - High precision syringe pumps
  - Peristaltic pumps
  - Access to the Nanotechnology Platform (IBEC Core Facilities): equipment for hot embossing lithography, polymer processing and photolithography, chemical wet etching, e-beam evaporation and surface characterization (TOF-SIMS)
  - Access to the Scientific and Technological Centers (University of Barcelona): equipment for surface analysis (XPS, AFM, XRD) and microscopy techniques (SEM, TEM, confocal)

Publications

- Castaño, A. G., Hortiguela, V., Lagunas, A., Cortina, C., Montserrat, N., Samitier, J. and Martinez, E. (2014). Protein patterning on hydrogels by direct microcontact printing: application to cardiac differentiation. *RSC Advances*, 4 (55): 29120-29123
- Comelles, J., Caballero, D., Voituriez, Hortigüelaa, V., Wollrab, V., Godeau, A. L., Samitier, J., Martínez, E. and Riveline, D. (2014). Cells as active particles in asymmetric potentials: Motility under external gradients. *Biophysical Journal*, 107 (7): 1513-1522
- Oberhansl, S., Castaño, A. G., Lagunas, A., Prats-Alfonso, E., Hirtz, M., Albericio, F., Fuchs, H., Samitier, J. and Martinez, E. (2014). Mesopattern of immobilised bone morphogenetic protein-2 created by microcontact printing and dip-pen nanolithography influence C2C12 cell fate. *RSC Advances*, 4 (100): 56809-56815

Cellular and Respiratory Biomechanics

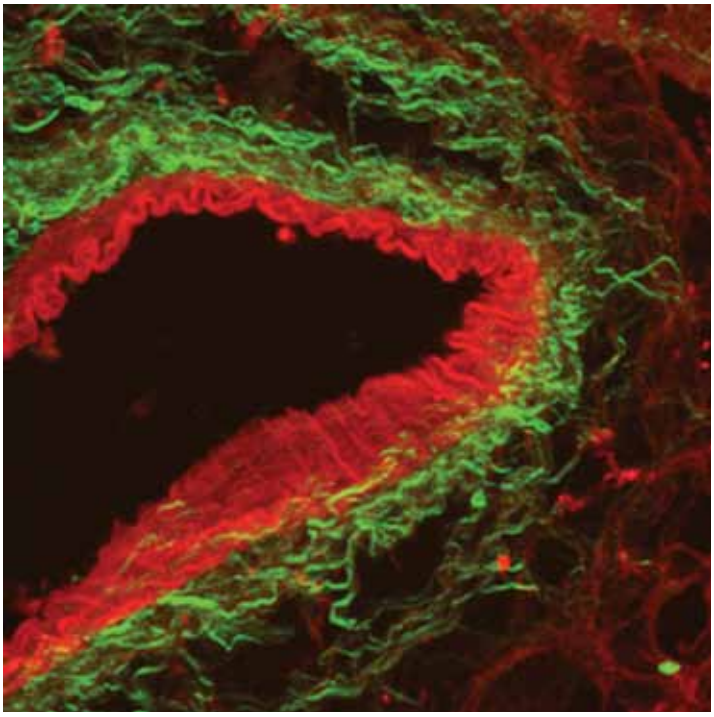
Group leader: Daniel Navajas
Junior group leader: Pere Roca-Cusachs
Postdoctoral researchers: Jordi Alcaraz, Alberto Elosegui
PhD students: Noelia Campillo, Anita Kosmalska, Roger Oria
Masters students: Víctor González, Manuel Jiménez, Ignasi Jorba

The research of our groups is focused on biomechanics; that is, the study of the mechanisms and physiological implications underlying mechanical force in biology. This research is organized into two different research lines.

The respiratory biomechanics line, led by Prof. Daniel Navajas, studies the mechanical behavior of the respiratory system, and how it is altered in respiratory diseases. The biophysical mechanobiology line, led by Prof. Pere Roca-Cusachs, studies the basic physical and molecular mechanisms by which cells detect and respond to forces.

Respiratory biomechanics (Daniel Navajas)

Our goal is to gain a deeper understanding of cellular and respiratory biomechanics in order to improve the diagnosis and treatment of respiratory diseases. The work is organized into two interrelated areas, focused on respiratory mechanics at both the systemic and the cellular level. We use basic and translational approaches in a multidisciplinary framework involving close cooperation with clinical groups. At the systemic level, we study the mechanical properties of airways and lung tissues and the mechanical dysfunctions associated with respiratory diseases. In the last period, our research has been mainly addressed to the study of sleep apnea syndrome (SAOS). We have improved continuous positive airway pressure devices for SAOS treatment. By using a novel murine model of SAOS we have shown that SAOS induces early release of mesenchymal stem cells (MSCs). We have also shown that injection of MSCs reduces SAOS-induced inflammation. We have revealed that cancer progression is associated with intermittent hypoxia. At the cellular level, we have developed an AFM technique to probe micro/nano-mechanical properties of the extracellular matrix (ECM) of decellularized tissue scaffolds. This innovative approach allowed us to reveal for the first time the local mechanical properties of the lung and heart cell niche. We have implemented several protocols for lung and heart decellularization and assessed the effect in mechanical and histological properties of the scaffold. By using induced pluripotent stem cells (iPSCs) we have shown that low O2 tension enhances the generation of lung progenitor cells.



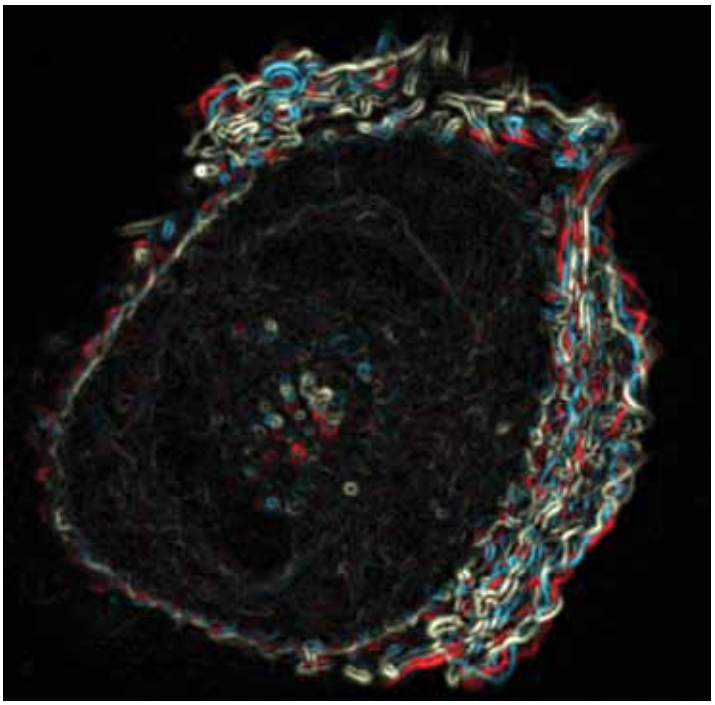
Vessel section from a decellularized lung showing the tunica intima, rich in elastin (red), and the tunica adventitia, with high concentration of collagen fibers (green). The image was obtained by two-photon and second harmonic generation microscopy. Melo *et al.* Tissue Eng Part C, 2014)

Biophysical mechanobiology (Pere Roca-Cusachs, Junior Group Leader)

Every time we blink, move a hand, draw a breath, or walk, cells in our body exert, transmit, withstand, and detect forces. This mechanical interaction with the environment determines how cells proliferate, differentiate, and move, and regulates development, tumorigenesis or wound healing. Just like biochemical stimuli initiate signaling cascades, mechanical forces affect the links and conformation of a network of molecules connecting cells to the extracellular matrix.

Our research aims precisely at unraveling the mechanisms that these molecules use to detect and respond to mechanical stimuli like forces or tissue rigidity, triggering downstream cell responses. To this end, we combine biophysical techniques like magnetic tweezers, Atomic Force Microscopy, traction microscopy, and microfabricated force sensors with molecular biology and advanced optical microscopy. Using this approach, we have recently unveiled a molecular mechanism that cells employ to detect and respond to the rigidity of their environment, which could be crucial in breast tissue and breast cancer (Elosegui-Artola *et al.*, 2014, *Nature Materials*). We have also revealed the different mechanical roles of several adhesion molecules: whereas some are responsible for withstanding forces, others detect and transmit those forces (Roca-Cusachs *et al.*, 2013, *PNAS*, and Roca-Cusachs *et al.*, 2009, *PNAS*). Ultimately, when we determine the molecular mechanisms that communicate cells with their environment, we will understand how forces determine development when things go right, and tumor formation when they go wrong.

Movement of the actin cytoskeleton of a breast myoepithelial cell, shown by superimposing images of the actin cytoskeleton in different timeframes.



Publications

- Nonaka, P. N., Campillo, N., Uriarte, J. J., Garreta, E., Melo, E., de Oliveira, L. V. F., Navajas, D. and Farré, R. (2014). Effects of freezing/thawing on the mechanical properties of decellularized lungs. *Journal of Biomedical Materials Research Part A*, 102 (2): 413-419
- Melo, E., Garreta, E., Luque, T., Cortiella, J., Nichols, J., Navajas, D. and Farré, R. (2014). Effects of the decellularization method on the local stiffness of acellular lungs. *Tissue Engineering - Part C: Methods*, 20 (5): 412-422
- Isetta, V., León, C., Torres, M., Embid, C., Roca, J., Navajas, D., Farré, R. and Montserrat, J. M. (2014). Telemedicine-based approach for obstructive sleep apnea management: Building evidence. *Interactive Journal of Medical Research*, 3 (1): e6
- Elosegui-Artola, A., Bazellières, E., Allen, M. D., Andreu, I., Oria, R., Sunyer, R., Gomm, J. J., Marshall, J. F., Jones, J. L., Trepat, X. and Roca-Cusachs, P. (2014). Rigidity sensing and adaptation through regulation of integrin types. *Nature Materials*, 13 (6): 631-637
- Andreu, I., Luque, T., Sancho, A., Pelacho, B., Iglesias-García, O., Melo, E., Farré, R., Prósper, F., Elizalde, M. R. and Navajas, D. (2014). Heterogeneous micromechanical properties of the extracellular matrix in healthy and infarcted hearts. *Acta Biomaterialia*, 10 (7): 3235-3242
- Dalmases, M., Torres, M., Márquez-Kisinousky, L., Almendros, I., Planas, A. M., Embid, C., Martínez-Garcia, M. A., Navajas, D., Farré, R. and Montserrat, J. M. (2014). Brain tissue hypoxia and oxidative stress induced by obstructive apneas is different in young and aged rats. *Sleep*, 37 (7): 1249-1256
- Melo, E., Cárdenes, N., Garreta, E., Luque, T., Rojas, M., Navajas, D. and Farré, R. (2014). Inhomogeneity of local stiffness in the extracellular matrix scaffold of fibrotic mouse lungs. *Journal of the Mechanical Behavior of Biomedical Materials*, 37: 186-195

- Nonaka, P. N., Uriarte, J. J., Campillo, N., Melo, E., Navajas, D., Farré, R. and Oliveira, L. V. F. (2014). Mechanical properties of mouse lungs along organ decellularization by sodium dodecyl sulfate. *Respiratory Physiology and Neurobiology*, 200: 1-5
- Uriarte, J. J., Nonaka, P. N., Campillo, N., Palma, R. K., Melo, E., de Oliveira, L. V. F., Navajas, D. and Farré, R. (2014). Mechanical properties of acellular mouse lungs after sterilization by gamma irradiation. *Journal of the Mechanical Behavior of Biomedical Materials*, 40: 168-177

Research projects

- Precondicionamento biofísico de células madre mesenquimales para el tratamiento de la lesión pulmonar aguda provocada por sobreventilación en modelo animal.
PI: **Daniel Navajas**
Fondo de Investigación Sanitaria, Ministerio de Economía y Competitividad (PI14/00280)

- Biomecànica cel·lular i integrativa.
PI: **Xavier Trepat**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (2014-SGR-927).

- Mechanical signaling driving stem cell differentiation in the lung. Lung-on-a-chip model.
PI: **Daniel Navajas**
Fondo de Investigación Sanitaria, Ministerio de Ciencia e Innovación (PI11/00089)

- **NANONET** Nanomechanics of intermediate filament networks.
Chair: E. Hol
Management Committee Member: **Daniel Navajas**
European Commission COST Action (BMBS-BM1002)

- **CHROMED** Clinical tRials fOr elderly patients with MultiplE Disease.
PI: Ramon Farré (UB/IDIBAPS)
European Commission, FP7-HEALTH-2012-INNOVATION-1 Project 306093-2

- **AFM4NanoMed&Bio** European network on applications of Atomic Force Microscopy to NanoMedicine and Life Sciences.
Management Committee Member: **Daniel Navajas**
European Commission COST Action (BMBS-TD1002)

- Identifying molecular mechanical pathways in cells (2012-2015).
PI: **Pere Roca-Cusachs**
Proyectos de investigación fundamental no orientada, Ministerio de economía y competitividad (BFU2011-23111)

- Mechanical pathways in cells: from molecular mechanisms to cell function (2012-2015).
PI: **Pere Roca-Cusachs** Coordinator: **Daniel Navajas**
Career Integration Grants (CIG) Marie Curie Action within the framework of EU-FP7 (MecPath 303848)

- Stromal stiffness in tumor progression (2013-2016).
PI: **Pere Roca-Cusachs**
Fundació la Marató de TV3

- Red de Excelencia en Mecanobiología.
PI: **Pere Roca-Cusachs**
Ministerio de Economía y Competitividad (MINECO)

Collaborations with other research centres

Prof. Ramon Farré Unit of Biophysics and Bioengineering, Dept. Physiological Sciences, School of Medicine, University of Barcelona/IDIBAPS, Barcelona, Spain

Prof. J. M. Montserrat Service of Pneumology, Hospital Clinic/IDIBAPS, Barcelona, Spain

Prof. M. Sheetz Biological Sciences, Columbia University New York, USA

Prof. A. Artigas Intensive Care Service, Hospital Sabadell, Spain

Prof. A. Pedotti Bioengineering Dept., Politecnico di Milano, Italy

Prof. J. Cortiella Laboratory of Tissue Engineering and Regenerative Medicine, University of Texas Medical Branch, Galveston, USA

Prof. James Hone Mechanical Engineering, Columbia University, USA

Prof. Miguel Ángel del Pozo Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

Dr. Nils Gauthier Mechanobiology Institute, Singapore

Scientific equipment and techniques

- Fluorescence resonance energy transfer (FRET) microscopy
- Confocal Microcopy
- Traction Microscopy
- Live cell fluorescence microscopy
- Cell stretching
- Cell culture
- Magnetic Tweezers
- Atomic Force Microscopy
- Surface Micro/Nano-patterning

Senior researcher: Jérôme Noailly
Postdoctoral researchers: Andy Olivares, Simone Tassani
PhD students: Carlos Ruiz, Themis Toumanidou
Masters student: Justin Jay Reagh
Undergraduate students: Alexandre Bonet, Sarah Lydia Vizel

Biomechanics and mechanobiology

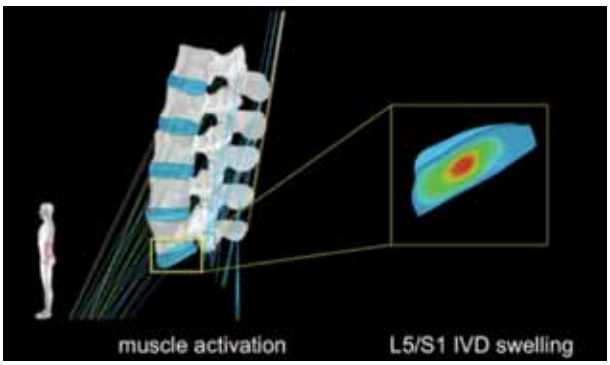
Research in the group of Biomechanics and Mechanobiology focuses on the musculoskeletal system, mainly on (i) the interactions between tissue multiphysics and biological processes, and (ii) how these interactions can affect the functional biomechanics of organs.

Numerical methods that combine different modelling and simulation techniques are used to describe both the tissues at the organ level, and the tissue-cell interactions at the tissue and cellular levels. The numerical concepts developed are tested against in vivo and in vitro data, which allows model validations, as well as educated interpretations of reported evidences.

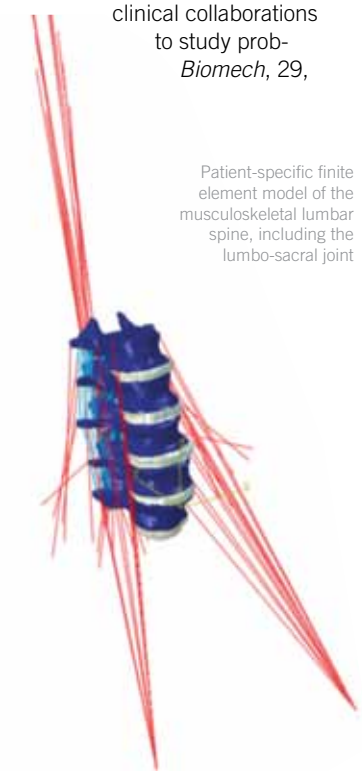
On one hand, emphasis is given in the study of the multiscale transfer of mechanical load effects from the system level to the cell level in different cases of simulated treatments or organ/tissue condition. On the other hands, advanced tissue models are used to link observable phenotypes to possible mechanisms of spatiotemporal tissue regulation. Calculations are based on both multiphysics and biophysical concepts to predict different cell environments over time.

Most tissue and biophysical models developed so far aimed to study one of the most complex organs of the musculoskeletal system, namely the spine. Thorough knowledge about the functional biomechanics of the lumbar spine has been acquired along the time in relation to computational simulations (*J Biomech*, 40, 2414-25; *Biomech Model Mechanobiol*, 10, 203-19). In order to capture as best as possible the communications between organ and tissue biomechanics, studies of advanced tissue models have been performed, in relation to the vertebrae (*Mater Lett*, 78, 154-58), to the intervertebral discs (*J Mech Behav Biomed Mater*, 4, 1224-41; *Comput Meth Biomech Biomed Engin*, 16, 923-8) and to the muscles (*J Biomech*, 45, S484). In particular, these models allowed thorough identification of the tissue parameters expected to alter cell nutrition in a deforming intervertebral disc (*PLoS Comput Biol*, 7, e1002112), leading to further relations between tissue condition and cell viability (*J Biomech*, 47, 1520-25; *Osteoarthritis Cartilage*, 22, 1053-60). Care is also taken to assess the physical meaning of the tissue model parameters (*Front Bioeng Biotechnol*, 3, Article 5), and the organ/tissue-scale simulations are confronted to bioreactor experiments (*Poromechanics V*, 2193-2201) and enhanced by both stochastic modelling.

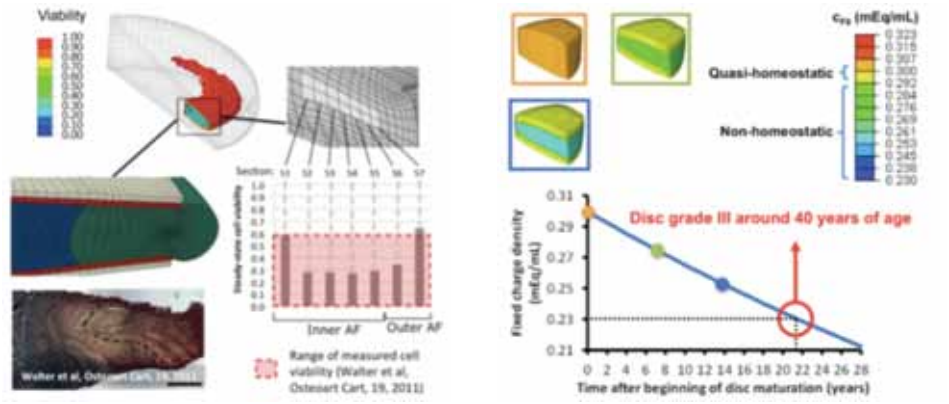
The numerical stability of these models is also one target of the explorations performed within the group (*J Mech Behav Biomed Mater*, 26, 1-10), in order to ensure the coupling to lower scale biophysical models. Also, models have been used to for implant simulations focussed either on clinical (*J Appl Biomat Biomech*, 4, 135-42), or on design questions (*Eur Spine J*, 21, S675-87). Beyond the spine domain, both knowledge and know-how acquired are being transferred to the exploration of the cardiovascular system. Also, on-going clinical collaborations are contributing to the adaptation of the numerical methods to study problems and treatment solutions related to the lower limbs (*Clin Biomech*, 29, 444-50).



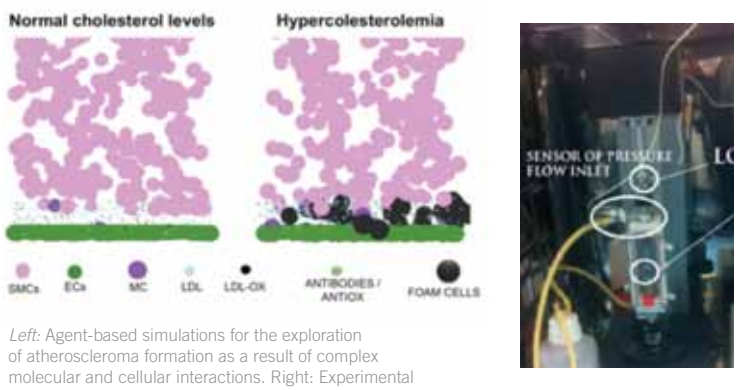
Prediction of mutual interactions between strain-induced muscle activation (left) and intervertebral disc (IVD) pressurization (right) during night rest simulations in a finite element model of the lumbar spine (L1 to L5/S1 IVD)



Patient-specific finite element model of the musculoskeletal lumbar spine, including the lumbo-sacral joint



Left: Cell viability predictions given by different mechanotransduction assumptions within a bovine intervertebral model subject to steady-state overloads. Right: Prediction of proteoglycan turnover as a result of the nutrition-dependent cell anabolic activity



Left: Agent-based simulations for the exploration of atherosclerema formation as a result of complex molecular and cellular interactions. Right: Experimental simulation of blood flow in artery samples under bioreactor conditions.

Publications

- Sánchez Egea, A. J., Valera, M., Parraga Quiroga, J. M., Proubasta, I., Noailly, J. and Lacroix, D. (2014). Impact of hip anatomical variations on the cartilage stress: A finite element analysis towards the biomechanical exploration of the factors that may explain primary hip arthritis in morphologically normal subjects. *Clinical Biomechanics*, 29 (4): 444-450

Research projects

- **MySpine** Functional prognosis simulation of patient-specfic spinal treatment for clinical use (2011-2014)
PI: **Jérôme Noailly**
EU – Cooperation – FP7-ICT-2009.5.3

- **THE GRAIL** Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer
PI: **Elisabeth Engel** (partner)
EEU - Cooperation – FP7- HEALTH.2011.1.4-2

- Investigación de la biomecánica y mecanobiología de las fracturas de la meseta tibial mediante un modelo de elementos finitos
PI: **Jérôme Noailly**
Clinical contract

Collaborations with other research centres

Dr. Josep Maria Font Universitat Politècnica de Catalunya BarcelonaTech, Barcelona

Prof. Antoni Susín Universitat Politècnica de Catalunya BarcelonaTech, Barcelona

Dr Ludovic Humbert Universitat Pompeu Fabra, Galgo Medical SL, Barcelona

Dr. Joan Carles Monllau, Dr Ion Carrera Hospital de la Santa Creu i Sant Pau, Barcelona

Dr. Màrius Valera Hospital de la Santa Creu i Sant Pau, Barcelona

Dr Gianluca Vadalà Campus Bio-Medico University of Rome, Italy

Prof. Mauro Alini AO Research Institute – AO Fundation, Davos, Switzerland

Dr Benjamin Gantenbein, Dr Samantha Chan University of Bern, Switzerland

Prof. Stephen Fergusson ETH Zurich, Switzerland

Dr. Aron Lazary, Dr Péter Pál Varga National Center for Spinal Disorders, Budapest

Prof. Christian Hellmich Vienna University of Technology - Institute for Mechanics of Materials and Structures, Vienna

Prof. Marie-Christine Ho Ba Tho Compiègne University of Technology, Compiègne, France

Prof. Hans-Joachim Wilke Institute of Orthopaedic Research and Biomechanics, University of Ulm, Germany

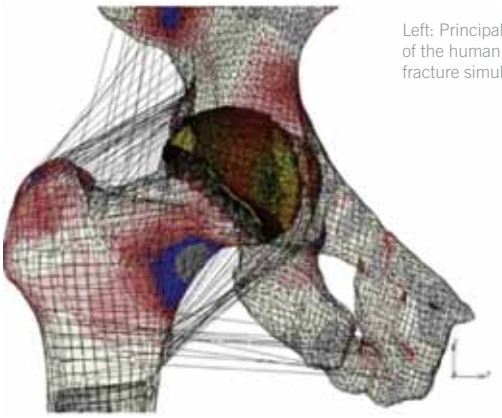
Prof. Keita Ito Eindhoven University of Technology, Eindhoven, The Netherlands

Prof. Damien Lacroix, Dr José Pozo, Prof. Alejandro Frangi University of Sheffield, UK

Dr Juan Fernando Ramírez Patiño Universidad Nacional de Colombia, Medellín, Colombia

Scientific equipment and techniques

- High performance computing infrastructure (48 cores, 256 GB RAM and over 11TB disc space, machine virtualization)
- Image reconstruction, Agent-based modelling, and Finite Element software technologies
- Bose ElectroForce BioDynamic bioreactor system (orthopaedic, cardiovascular, and customized configurations)
- Microfluidic chamber



Left: Principal stress predictions in a model of the human hip joint. Right: Tibial plateau fracture simulation.

- Malandrino, A., Noailly, J. and Lacroix, D. (2014). Numerical exploration of the combined effect of nutrient supply, tissue condition and deformation in the intervertebral disc. *Journal of Biomechanics*, 47 (6): 1520-1525 (2014).
- Malandrino, A., Lacroix, D., Hellmich, C., Ito, K., Ferguson, S. J. and Noailly, J. (2014). The role of endplate poromechanical properties on the nutrient availability in the intervertebral disc. *Osteoarthritis and Cartilage*, 22 (7): 1053-1060

Conference proceedings:

- Malandrino, A., Lacroix, D. and Noailly, J. (2014). Exploring the link between mechanical load and cell death in the invertebral disc: A theoretical study of mechno-regulated hypermetabolism and metabolic transport. *8th Combined Meeting Of Orthopaedic Research Societies (CORS)*, Venice, Italy. Published by The British Editorial Society of Bone & Joint Surgery

Book chapters:

- Noailly, J., Malandrino, A., Galbusera, F. and Jin, Z. (2014). Computational modelling of spinal implants. In: *Computational Modelling of Biomechanics and Biotribology in the Musculoskeletal System* (ed. Jin, Z.). Cambridge, UK, Woodhead Publishing. Biomaterials and Tissues: 447-484

Control of stem cell potency

Group leader/ICREA research professor: Ángel Raya

Postdoctoral researchers: Raquel Ferrer, América Martínez, Adriana Rodríguez

PhD students: Carlos Félix Calatayud, Juan Crespo, Claudia Di Guglielmo, Anna Garcia, Isil Tekeli, Juan Luís Vázquez

Masters student: Jonathan De Smedt

Senior technicians: Senda Jiménez, Yvonne Richaud

Technician: Cristina García

During embryo development, the potency of the zygote is deployed through coordinated and stereotypical changes in cell behaviors and processes of tissue patterning, ultimately resulting in the formation of an entire, highly complex organism in a relatively short period of time.

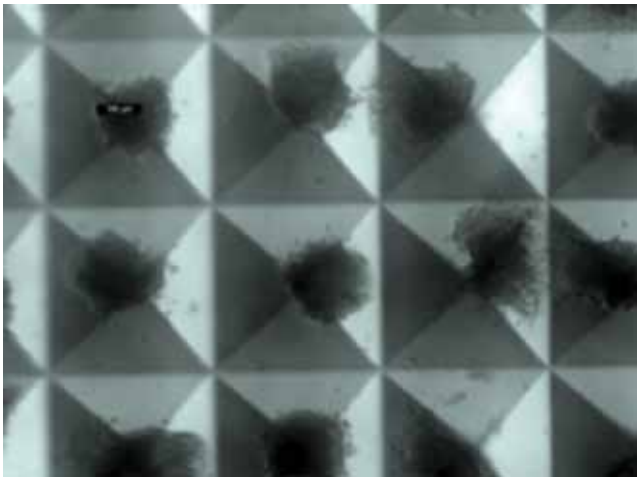
Throughout this process, the developmental potency of individual cells, i.e. their ability to give rise to cells of a different type than their own, is progressively lost, so that somatic cells in adult individuals retain very limited potency (such as in rare adult stem cells) or show no potency at all.

Our laboratory is interested in understanding the mechanisms that govern the degree of potency of human somatic cells, and how it can be experimentally increased for conditions where doing so may be of biomedical relevance. Specifically, the context in which we investigate these issues is mainly centred on the paradigm of cardiac regeneration/repair.

Heart-related diseases are the main cause of mortality in the world, with ischemic heart disease being the single most frequent condition accounting for the death toll. This results from the very limited ability of the mammalian heart to regenerate on its own, and underscores the pressing biomedical need to finding ways for potentiating this ability (heart regeneration) and/or providing new cardiac cells to replace the lost or damaged ones (heart repair). We pursue the first approach by studying the process of heart regeneration in the zebrafish, an organism with a remarkable capacity for regeneration. Natural regeneration is a biologically fascinating phenomenon in which somatic cells may regain developmental potency, and we hope that understanding the molecular and cellular mechanisms that control this process will help devising strategies to potentiate the regeneration of adult mammalian hearts.

For achieving heart repair, in turn, our research is aimed at generating functional human heart muscle cells that could be used for transplantation. For this purpose, we investigate ways to manipulate the developmental potency of human somatic cells so they become pluripotent (i.e. regain the potency of cells in the early embryo), and then study how these so-called induced pluripotent stem cells (iPSC) can be instructed to differentiate into functional cardiomyocytes. In addition, since iPSC can be generated from disease-carrying cells, many laboratories including ours are exploring the possibility of using patient-specific iPSC to generate disease-relevant cell types in which to investigate the pathogenic mechanisms of disease initiation and/or progression.

Overall, our research takes advantage of a variety of experimental paradigms (zebrafish heart regeneration, human iPSC generation and differentiation), approached from a multi-disciplinary perspective, ranging from bioengineering approaches to 3D stem cell differentiation to single-cell genetic lineage tracing analyses and genetic manipulation of human cells, aimed at tackling important current issues in biology and biomedicine, such as the mechanisms that control the establishment and maintenance of developmental potency, the initiation and progression of the regenerative process, and the differentiation and functional maturation of human cardiomyocytes, and the development of genuinely human models of human disease.



Human iPS cells aggregated to form embryoid bodies

Research projects

- Aproximación de bioingeniería a la regeneración/reparación cardiaca.
PI: **Ángel Raya**
MINECO, Investigación fundamental no orientada.

- Human pluripotent stem cells and zebrafish heart regeneration as experimental tools to understand cardiac muscle cell differentiation (2009-2012)
PI: **Ángel Raya**
MINECO, Investigación fundamental no orientada.

- **HEMO-iPS** Use of patient-specific induced pluripotent stem cells to improve diagnosis and treatment of Hemophilia A
PI: **Ángel Raya**
ISCIII; E-Rare JTC 2011

- **CELLSCAFF-CART** Reparación de Cartílago Articular mediante Ingenieria de Tejidos *in situ*: modelo *in vivo* (iPSC) (2010-2013).
PI: **Ángel Raya**
MINECO; Fomento de la cooperación científica internacional (FCCI) ACI-Promociona

- Zebrafish heart regeneration and human pluripotent stem cells as models to understand human cardiac muscle cell differentiation
PI: **Ángel Raya**
EMBO

- Estudios de funcionalidad de suplementos adicionales de cultivo para mantener el estado indiferenciado de células madre humanas con pluripotencia inducida
PI: **Ángel Raya**
Industrial contract with GRIFOLS S.A.

Publications

- Navarro, S., Moleiro, V., Molina-Estevez, F. J., Lozano, M. L., Chinchon, R., Almarza, E., Quintana-Bustamante, O., Mostoslavsky, G., Maetzig, T., Galla, M., Heinz, N., Schiedlmeier, B., Torres, Y., Modlich, U., Samper, E., Río, P., Segovia, J. C., Raya, A., Güenechea, G., Izpisua-Belmonte, J. C. and Bueren, J. A. (2014). Generation of iPSCs from genetically corrected Brca2 hypomorphic cells: Implications in cell reprogramming and stem cell therapy. *Stem Cells*, 32 (2): 436-446

Collaborations with other research centres

Anne Weber/Anne Dubart Inserm, Le Kremlin-Bicêtre Cedex, France

Manuel Galiñanes Hospital Universitari Vall d'Hebron, Barcelona, Spain

Patrizia Dell'Era Università degli Studi di Brescia, Italy

Miquel Vila Institut de Recerca, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Eduard Tolosa Hospital Clínic, Barcelona, Spain

Pedro Muniesa Facultad de Veterinaria, Zaragoza, Spain

José López Barneo Instituto de Biomedicina (IBiS), Sevilla, Spain

Daniel Grinberg/Lluïsa Vilageliu University of Barcelona, Spain

Rafael Garesse Instituto de Investigaciones Biomédicas "Alberto Sols"/UAM, Spain

Antonia Follenzi Universita' del Piemonte Orientale, Novara, Italy

Sheng Ding Scripps Research Institute, La Jolla, USA

Jordi Barquinero Institut de Recerca, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Jordi Alberch/Josep M. Canals Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Spain

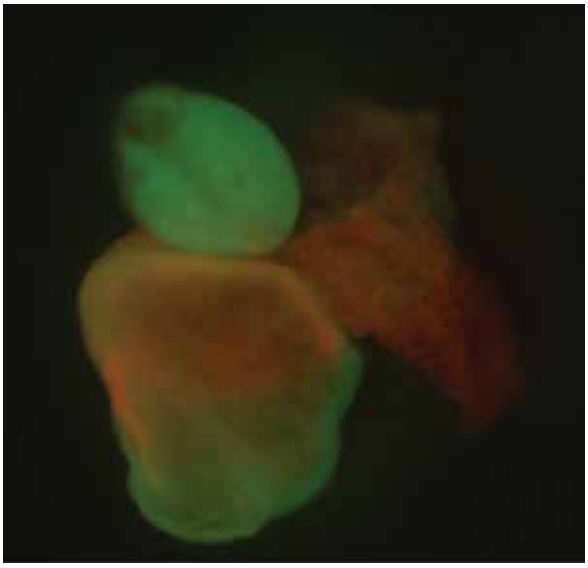
Jerónimo Blanco/Núria Rubio Centro de Investigación Cardiovascular CSIC-ICCC, Barcelona, Spain

Francisco J. Blanco Complejo Hospitalario Universitario A Coruña, Spain

Antonella Consiglio Institute of Biomedicine of the University of Barcelona (IBUB), Spain

Ludovic Jullien Ecole Normale Supérieure, Paris, France

Heart of a transgenic zebrafish showing mosaic recombination

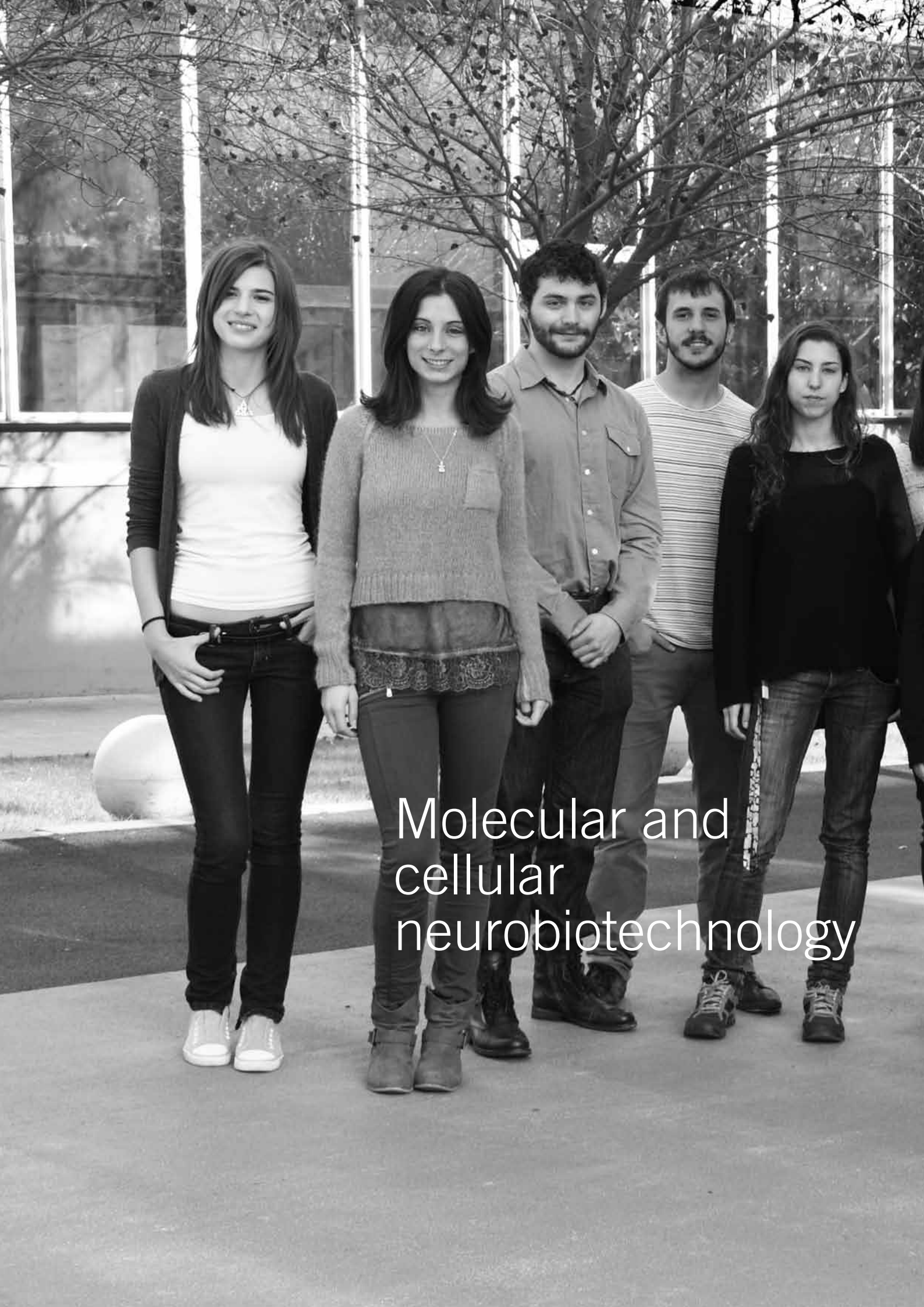


Ana Maria Cuervo Albert Einstein College of Medicine, Bronx, USA

Lorenzo Monserrat Complejo Hospitalario Universitario A Coruña, Spain

Scientific equipment and techniques

- hES/iPS cell culture station
- Zebrafish transgenesis
- Molecular biology facilities
- Stereomicroscope for picking hES colonies
- Cell culture facilities



Molecular and cellular neurobiotechnology

Group leader: José Antonio Del Río
Postdoctoral researchers: Rosalina Gavín, Ariadna Pérez, Vanessa Gil
PhD students: Agata Mata, Andreu Matamoros, Cristina Vergara
Undergraduate students: Anna Prieto, Lorena Sueiro
Technician: Miriam Segura

Our research interests are focused on four main aspects of developmental neurobiology and regeneration:

1) Analysis of cell migration and functions of Cajal-Retzius cells during cortical development.

Cajal-Retzius cells are transient pioneer neurons that migrate from specific regions of the developing brain (e.g. the cortical hem) to cover the complete neocortex. Functions of these cells are associated to the migration of the cerebral cortex, with altered migrations of Cajal-Retzius cells further impairing the development of the neocortex. In recent years we determined that an extracellular protein produced by radial glia, Sema3E, modulates the migration of these cells in mouse embryo (published in *Nature Communications*).

Current experiments are directed:

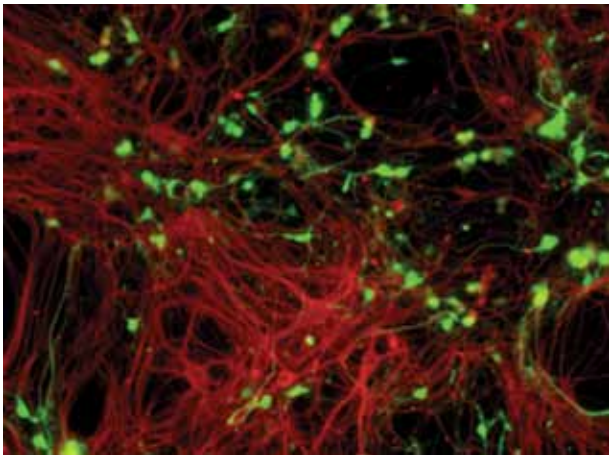
- to modulate their migration and function by using optogenic tools;
- to determine their cell lineage in the developing brain;
- to analyse their migratory behaviour in microfluidic devices;
- to determine new factors modulating their migration;
- to characterize the interplay between angiogenic factors and neural migration.

2) Cell therapy and pharmacological treatment to potentiate axon regeneration in lesioned central nervous system.

In the last few years we have focused on genetically modifying olfactory ensheathing cells (OECs) to be able to increase their survival and migration in the lesioned spinal cord. Results were recently published in *Cellular and Molecular Life Science*. In our experiments, OECs were genetically modified to overexpress the ectodomain of Nogo Receptor to increase their migration in inhibitory substrates. Current experiments by our group in collaboration with Profs J. Rogers and J. Fawcett (UK) aim to modify these cells to be able to degrade the second inhibitory molecules present in lesioned spinal cord: the chondroitin sulphate proteoglycans. From the pharmacological point of view we are developing singular peptides to enhance axon regeneration.

3) Neurodegenerative diseases.

We recently determined the role of a natural neural protein PrP^c in the evolution of Alzheimer's disease (published in *Molecular Neurobiology*). Results point to PrP^c as neuroprotective factor in Alzheimer's. Further experiments will continue in this direction, and also will be expanded to Parkinson's disease. Our hypothesis is that PrP^c is a cross-link protein between different neurodegenerative diseases presenting taupathy.

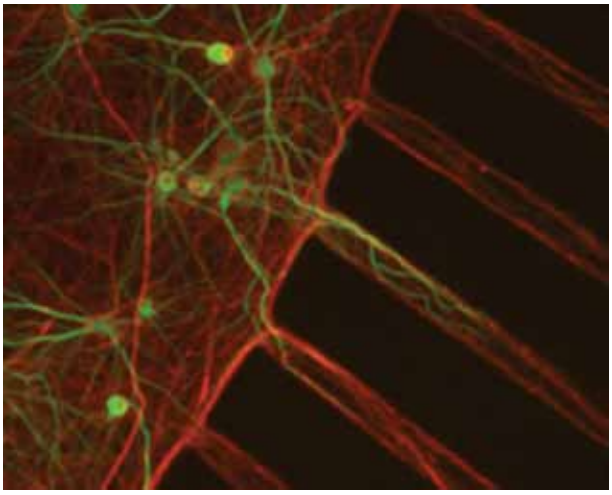


Example of fluorescence microscopy picture showing one example of cultured motorneurons (red) and glial cells (green) in microfluidic lab on a chip devices after 15 days in culture.

4) Development of new lab on a chip devices for neurobiological research.

We recently developed a new device able to reproduce the neuromuscular junction in a single chip (published in *RSC Advances*). Thus current experiments of our group in collaboration with groups of IBEC and CIBER-BBN aimed at developing new lab on chip devices to mimics and modulate particular neurobiological processes. For example: axonal lesions that mimic Wallerian-like degeneration, molecular gradient generation for migrating neurons and *in silico* 3D modeling for neurodegenerative diseases.

Fluorescence microscopy picture showing one example of cultured hippocampal neurons extending their neuritis inside a microchannel in a microfluidic lab on a chip device after 15 days in culture. The axon of the neurons is labeled in green and the dendrites in red.



Research projects

- **PRIORITY** Protecting the Food Chain from Prions: Shaping European Priorities through Basic and Applied Research (2009-2014).
PI: **José Antonio del Río**
European FP7-KBBE project (222887)

- **NEURODEV** Nuevas funciones de PlexinD1/Sema3E, PrP^C y las proteínas asociadas a la mielina durante el desarrollo de la corteza cerebral de roedores y en neurodegeneración. (2013-2015).
PI: **José Antonio del Río**
MINECO, BFU2012-32617

- **DEMTEST** Biomarker based diagnosis of rapid progressive dementias – optimization of diagnostic protocols (2012-2015).
PI: **José Antonio del Río**
Instituto de Salud Carlos III

- Bases cel·lulars i moleculars en neurodegeneració i neuroregeneració (2014-SGR-1218).
PI: **José Antonio del Río**
Consolidated Research Group certified by the Generalitat de Catalunya (SGR 2014-2016).

Publications

- Seira, O. and del Río, J. A. (2014). Glycogen synthase kinase 3 beta (GSK3β) at the tip of neuronal development and regeneration. *Molecular Neurobiology*, 49 (2): 931-944
- Bribián, A., Nocentini, S., Llorens, F., Gil, V., Mire, E., Reginensi, D., Yoshida, Y., Mann, F. and Del Río, J. A. (2014). Sema3E/PlexinD1 regulates the migration of hem-derived Cajal-Retzius cells in developing cerebral cortex. *Nature Communications*, 5: 4265
- Llorens, F., Ferrer, I. and del Río, J. A. (2014). Gene expression resulting from PrP^C ablation and PrP^C overexpression in murine and cellular models. *Molecular Neurobiology*, 49 (1): 413-423
- Gil, V., Nocentini, S. and del Río, J. A. (2014). Historical first descriptions of Cajal-Retzius cells: From pioneer studies to current knowledge. *Frontiers in Neuroanatomy*, 8 (2014/05/26): Article 32 (9)
- Tong, Z., Seira, O., Casas, C., Reginensi, D., Homs-Corbera, A., Samitier, J. and Del Río, J. A. (2014). Engineering a functional neuro-muscular junction model in a chip. *RSC Advances*, 4 (97): 54788-54797

- **NEUROPRION** Análisis del papel de PrP^C como mediador de la hiperfosforilación de tau en enfermedades neurodegenerativas (2012-2015).
PI: **Rosalina Gavín Marín**
Fondo de investigaciones Sanitarias de la Seguridad Social

- **IPS-PrP** Fundación Vasca de Investigación e Innovación BIOEF (2013-2015)
Scientists in Charge, IBEC subproject: **José A. del Río** and **Ángel Raya** (page 92)
BIO12/AL/004

Collaborations with other research centres

Prof. Javier de Felipe Instituto Cajal, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

Dr. Fernando de Castro Hospital Nacional de Parapléjicos, Toledo, Spain

Dr. Adolfo Lopéz de Munain Hospital de Donostia, San Sebastian, Spain

Dr. Jokin Castilla CiC Biogune, Bilbao, Spain

Prof. Jose Manuel García Verdugo Facultad de Ciencias, Universidad de Valencia, Spain

Prof. Jose Manuel García Aznar Nanotechnology Institute, Zaragoza, Spain

Prof. Fernando Albericio Institute for Research in Biomedicine (IRB), Barcelona

Dra. Miriam Royo Institute for Research in Biomedicine (IRB), Barcelona

Dr. Elisabeth Engel (page 47), **Prof. Josep Samitier** (page 103), **Prof. Xavier Trepat** (page 112), **Prof. Ángel Raya** (page 92), IBEC

Prof. Jesús Ávila and **Prof. Francisco Wandosell** Consejo Superior de Investigaciones Científicas (CSIC), Universidad Autónoma de Madrid, Spain

Prof. Isidro Ferrer Institut d'Investigació Biomèdica de Bellvitge, University of Barcelona, Spain

Prof. Marc Tessier-Lavigne Genentech, Inc., South San Francisco, USA

Prof. Fanny Mann Developmental Institute of Marseille Luminy, Université de la Méditerranée, Marseille, France

Prof. Yutaka Yoshida Division of Developmental Biology, Cincinnati Children's Research Foundation, Cincinnati, Ohio, USA

Scientific equipment and techniques

- Neural stem cell culture
- Microscopy facility (Olympus BX61 and Olympus IX71 with LCi culture system)
- Electroporation system (BTX 600)
- Pressure microinjection system
- Protein expression and purification systems
- Technology of neuronal culture facilities (2D and 3D)
- Lentiviral production and characterization
- Gradient thermocycler (PCR)
- Protein and DNA electrophoresis
- *In situ* hybridization oven

Nanobioengineering

Group leader: Josep Samitier

Senior researchers: David Caballero, Antoni Homs, Anna Lagunas, Mònica Mir

Postdoctoral researchers: Margarita Alvira, ZiQiu (Tommy) Tong, Samuel Dulay

PhD students: Luís Botaya, Marta Sanmartí, Bogachan Tahirbegi, Luís Rigat, Roberto Paoli, Wilmer Pardo, Rosella Zaffino

Masters student: Judit Perez

Technicians: Xavier Coromina, Miriam Funes, David Izquierdo

The Nanobioengineering group is a truly multidisciplinary team composed by researchers coming from very diverse backgrounds (chemistry, physics, material science, electronic engineering, pharmacy and molecular biology) and working together in applying nanotechnology to the development of new biomedical systems and devices, mainly for diagnostic purposes, and integrated microfluidic devices for organ-on-chip.

The main activities of the group involve the surface functionalization of materials integrated with microfluidics systems for the study of biomolecule and cell interactions to develop organ-on-chip or for the development of new biosensors that will be integrated in lab-on-a-chip devices.

The goal is to fabricate microsystems containing living cells that recapitulate tissue and organ level functions *in vitro* and new portable diagnosis devices that can be used as Point-of-Care systems. The projects carried out by the group are focused on clinical and industrial problems and are related to four convergent research lines:

1. Biosensors and Lab-on-a-chip for clinical diagnosis and food safety applications

- DNA sensors and platform arrays for cancer biomarker detection
- Antibody-based sensors for detection of pathogenic microorganisms
- Sensor array for *in vivo* ischemia Monitoring
- Sensors to mimic the chemical detection of plant roots for robotic applications
- Microfluidic chip for reagent handling in POC diagnosis devices
- Microfluidic chip using hydrodynamic focusing for bacteria counting and sorting

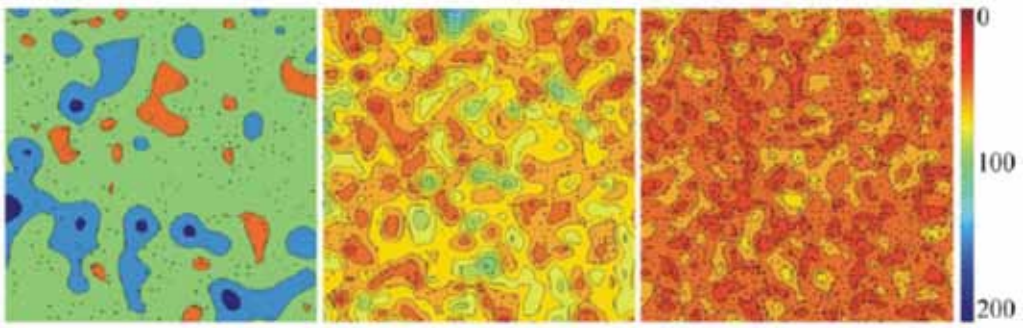
2. Nanotechnology applied to biomolecule interaction studies and micro/nano-environments for regenerative medicine applications

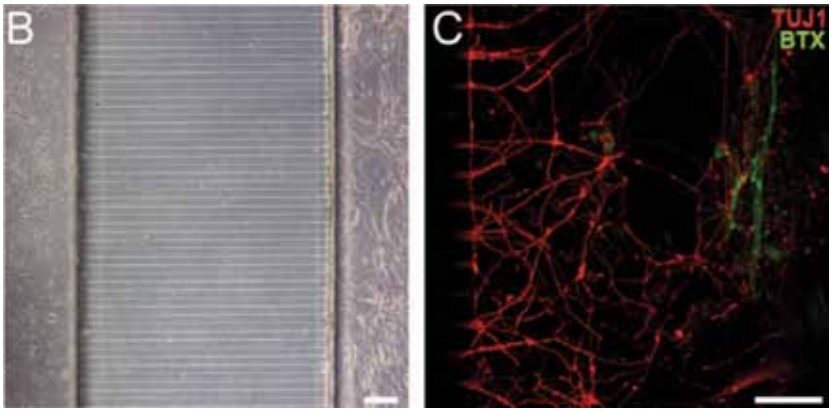
- Design, production and characterization of micro/nanoenviroments with different biocompatible materials for cell behavior studies (adhesion, proliferation, differentiation)
- Design, production and characterization of scaffolds with a topography and chemical composition controlled at the nanoscale for regenerative therapies based on stem cells
- Biophysical description of cellular phenomena (cell migration, differentiation) using micro/nanotechnologies, cell biology tools and soft matter physics.
- Magnetic nanoparticles-biomolecules interactions and their applications

3. Microfluidic systems for biological studies and Organ-on-Chip devices

- Microfluidic chip for blood/plasma filtering
- Spleen on a Chip development
- Nanoporous based systems for kidney on chip developments

Nanopatterning of RGD-Cys-D1 on Au(111) surfaces.





Neuro muscular junction formation in compartmentalized microfluidic devices.

Research projects

- **PLANTOID** Innovative Robotic Artefacts Inspired by Plant Roots for Soil Monitoring
PI: **Josep Samitier**
EU- FP7-ICT-FET-Open

- **OligoCODEs** Universal Diagnostic Platforms Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices
PI: **Josep Samitier**
MINECO

- **CARDIO-STEM** Terapias regenerativas con células madre para el fallo cardíaco (2009-2014).
PI: **Josep Samitier**
MINECO, ACI-E Medicina Regenerativa

- Desarrollo de una nueva tecnología lab-on-a-chip para la detección y cuantificación de secuencias de ADN/ARN (biomarcadores).
PI: **Josep Samitier**
Industrial project with GENOMICA S.A.U.

- Suport al desenvolupament i integració de sistemes de "point-of-care" pel diagnòstic mèdic de malalties respiratòries (dins del projecte TheraEDGE).
PI: **Josep Samitier**
Industrial project with BIOKIT, S.A.

- Grup de recerca consolidat (2009-2014).
PI: **Josep Samitier**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2009)

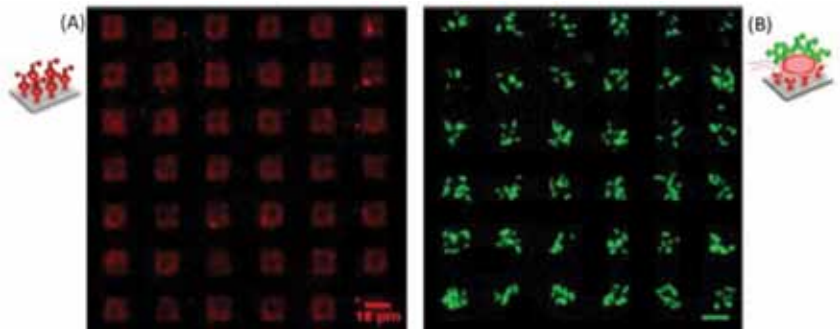
- **LABINACHIP** Nuevos métodos para la fabricación de dispositivos microfluídicos
PI: **Josep Samitier**
Convenio con Tallers Fiestas

- Joint Unit Genomica S.A.U-IBEC
PI: **Josep Samitier**
Joint Research Unit for close interaction on various R&D activities related to health-care

Publications

- Tong, Z., Seira, O., Casas, C., Reginensi, D., Homs-Corbera, A., Samitier, J. and Del Río, J. A. (2014). Engineering a functional neuro-muscular junction model in a chip. *RSC Advances*, 4 (97): 54788-54797
- Castaño, A. G., Hortiguela, V., Lagunas, A., Cortina, C., Montserrat, N., Samitier, J. and Martinez, E. (2014). Protein patterning on hydrogels by direct microcontact printing: application to cardiac differentiation. *RSC Advances*, 4 (55): 29120-29123
- Oberhansl, S., *et al* (2014). Mesopattern of immobilised bone morphogenetic protein-2 created by microcontact printing and dip-pen nanolithography influence C2C12 cell fate. *RSC Advances*, 4 (100): 56809-56815
- Comelles, J. *et al* (2014). Cells as active particles in asymmetric potentials: Motility under external gradients. *Biophysical Journal* 1077, 1513-1522
- Juanola-Feliu, E. *et al* (2014). Design of a customized multipurpose nano-enabled implantable system for in-vivo theranostics. *Sensors* 1410, 19275-19306
- Caballero, D., Samitier, J., (2014). Different strategies for the fabrication of cell culture chambers for live-cell imaging studies. *Chips and Tips* 1412, 1-5
- Rigat-Brugarolas, L. G. *et al* (2014). A functional microengineered model of the human splenon-on-a-chip. *Lab on a Chip* 1410, 1715-1724
- Castillo-Fernandez, O. *et al* (2014). High-speed counting and sizing of cells in an impedance flow microcytometer with compact electronic instrumentation. *Microfluidics and Nanofluidics* 161-2, 91-99
- Tahirbegi, I. B. *et al* (2014). *In vivo* ischemia monitoring array for endoscopic surgery. *Biosensors and Bioelectronics* 61, 124-130
- Van Heirstraeten, L. *et al* (2014). Integrated DNA and RNA extraction and purification on an automated microfluidic cassette from bacterial and viral pathogens causing community-acquired lower respiratory tract infections. *Lab on a Chip* 149, 1519-1526

- Zaffino, R. L., Mir, M., Samitier, J., (2014). Label-free detection of DNA hybridization and single point mutations in a nano-gap biosensor. *Nanotechnology* 2510, 105501 (8)
- Lagunas, A. *et al* (2014). Large-scale dendrimer-based uneven nanopatterns for the study of local arginine-glycine-aspartic acid (RGD) density effects on cell adhesion. *Nano Research* 73, 399-409
- González, L., Otero, J., Agusil, J. P., Samitier, J., Adan, J., Mitjans, F., Puig-Vidal, M., (2014). Micropattern of antibodies imaged by shear force microscopy: Comparison between classical and jumping modes. *Ultramicroscopy* 136, 176-184
- Mir, M., Lugo, R., Tahirbegi, I. B., Samitier, J., (2014). Miniaturizable ion-selective arrays based on highly stable polymer membranes for biomedical applications. *Sensors* 147, 11844-11854
- Rigat-Brugarolas, L.G., Homs, A., Samitier, J., (2014). Reservoir poly(dimethylsiloxane) cap fabrication. *Chips and Tips* 1410, 1-4
- Prieto-Simón, B., Samitier, J., (2014). "signal off" aptasensor based on enzyme inhibition induced by conformational switch. *Analytical Chemistry* 863, 1437-1444
- Rigat-Brugarolas, L.G., Homs, A., Samitier, J., (2014). Simple alignment marks patterning for multilayered master fabrication. *Chips and Tips* 143, 1-7
- Tahirbegi, I. B., Alvira, M., Mir, M., Samitier, J., (2014). Simple and fast method for fabrication of endoscopic implantable sensor arrays. *Sensors* 147, 11416-11426
- Rigat-Brugarolas, L.G., Homs, A., Samitier, J., (2014). Simple fabrication of three-dimensional ramped microstructures using SU-8 negative photoresist. *Chips and Tips* 143, 1-5
- Oliva, A. M., Homs-Corbera, A., Torrents, E., Juarez, A., Samitier, J., (2014). Synergystic effect of temperature and electric field intensity in Escherichia coli inactivation. *Micro and Nanosystems* 62, 79-86



Fluorescence images of anti-*E.coli* O157 antibody pattern before and after bacteria detection.

Collaborations with other research centres

Prof. Fernando Albericio Institut de Recerca Biomédica (IRB), Barcelona, Spain

Dr. José Antonio Andrades, Universidad de Málaga, Spain

Prof. Joan Bausells Centro Nacional de Microelectrónica (CNM-CSIC), Barcelona

Prof. Albert van den Berg University of Twente, The Netherlands

Prof. Andre Bernard Institut für Mikro- und Nanotechnologie (MNT-NTB), Buchs, Switzerland

Prof. H. Börner Max Planck Institute of Colloids and Interfaces, Golm, Germany

Prof. Josep Maria Canals University of Barcelona, Spain

Dr. Matthew Dalby University of Glasgow, Glasgow, UK

Prof. Paolo Dario Scuola Superiore Sant'Anna (SSSA), Pontedera, Italy

Prof. Ramón Eritja Institut de Recerca Biomédica (IRB), Barcelona, Spain

Prof. E. Faszewski Wheelock College, Boston, USA

Prof. G. Fuhr FhG Biomedicine, St. Ingbert, Germany

Dr. Juan C. Izpisúa Centro de Medicina Regenerativa (CMRB), Barcelona, Spain

Dr. Nicole Jaffrezic Université Claude Bernard Lyon 1, France

Dr. Graham Johnson Uniscan Instruments Ltd, Buxton, UK

Dr. Mª Pilar Marco Institute of Chemical and Environmental Research, Barcelona

Prof. Jean-Louis Marty Université de Perpignan Via Domitia, France

Prof. Barbara Mazzolai IIT Center for Micro-BioRobotics (CMBR), Pontedera, Italy

Dr. Edith Pajot Biology of Olfaction and Biosensors group (BOB) at INRA, Jouy-en-Josas, France

Dr. M. Lluïssa Pérez Dept. Farmacología, University of Barcelona, Spain

Dr. Hernando del Portillo Centro de Investigación en Salud Internacional de Barcelona (CRESIB), Barcelona, Spain

Dr. Jaume Reventós Hospital Vall d'Hebrón, Barcelona, Spain

Prof. L. Reggiani Nanotechnology Laboratory, INFM, Lecce, Italy

Prof. Daniel Riveline Laboratory of Cell Physics ISIS/IGBMC, Strasbourg

Prof. M. Sampietro Politecnico di Milano, Italy

Prof. Molly M. Stevens Imperial College, London, UK

Dr. Christophe Vieu Laboratoire d'analyse et d'architectures des systèmes (LAAS-CNRS), Toulouse, France

Industry partners:

Biokit S.A. (Werfen group); Genomica S.A.U. (Zeltia group); Tallers Fiestas S.L.; Enantia S.L.; Microfluidic ChipShop GmbH

Scientific equipment and techniques

- Nanofabrication and nanomanipulation
  - Automatized microcontact printing system (custom-made)
- Characterization
  - Surface Plasmon Resonance (SPR)
  - Potentiostates
  - Optical Waveguide Lightmode Spectroscope (OWLS)
  - Atomic Force Microscope (AFM)
  - Optical Microscopes (white light/epifluorescence)
  - Impedance spectroscopes
  - Precision Impedance Analyzer
  - Sub-femtoamp Remote SourceMeter Instrument
- Molecular/cell biology
  - Biological safety cabinet (class II)
  - Microwell plate readers
  - Protein and DNA electrophoresis systems
  - Nanodrop spectrophotometer
  - CO^2 incubator for cells: Galaxy® 48 S, 48 L, 230 V/50/60 Hz, Estándar
  - Cell culture cabin: Cabina De Seguridad Biológica, Modelo Bioii-Advance 3
- Microfluidics
  - High precision syringe pumps
  - Peristaltic pumps

Sensor array for *in vivo* ischemia detection.

- del Moral Zamora, B., Azpeitia, J. M. Á, Farrarons, J. C., Català, P. L. M., Corbera, A. H., Juárez, A., Samitier, J., (2014). Towards point-of-use dielectrophoretic methods: A new portable multiphase generator for bacteria concentration. *Micro and Nanosystems* 62, 71-78

Conference proceedings:

- Oller-Moreno, S., Pardo, A., Jimenez-Soto, J. M., Samitier, J. and Marco, S. (2014). Adaptive Asymmetric Least Squares baseline estimation for analytical instruments. *11th International Multi-Conference on Systems, Signals & Devices (SSD)*. Castelldefels-Barcelona, Spain. SSD 2014 Proceedings, 1569846703. IEEE

Book chapters:

- del Moral Zamora, B., Azpeitia, J. M. Á, Farrarons, J. C., Català, P. L. M., Corbera, A. H., Juárez, A., Samitier, J., (2014). Towards point-of-use dielectrophoretic methods: A new portable multiphase generator for bacteria concentration. In: *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013* (ed. Roa Romero, L. M.). London, Springer International Publishing. 41: 856-859
- Oliva, A. M., Homs, A., Torrents, E., Juarez, A., Samitier, J., (2014). Effect of electric field and temperature in E.Coli viability. *ibid,* 1833-1836
- Rigat-Brugarolas, L. G., Bernabeu, M., Elizalde, A., de Niz, M., Martin-Jaular, L., Fernandez-Becerra, C., Homs-Corbera, A., del Portillo, H. A., Samitier, J., (2014). Human splenon-on-a-chip: Design and validation of a microfluidic model resembling the interstitial slits and the close/fast and open/slow microcirculations. *ibid,* 884-887
- Juanola-Feliu, E., Colomer-Farrarons, J., Miribel-Català, P., González-Piñero, M. and Samitier, J. (2014). Nano-enabled implantable device for glucose monitoring. In: *Implantable Bioelectronics* (ed. Katz, E.). Weinheim, Germany, Wiley-VCH Verlag GmbH & Co. KGaA: 247-263

Bacterial infections: antimicrobial therapies

Junior group leader: Eduard Torrents

PhD students: Anna Crespo, Lucas Pedraz, Aida Baelo

Masters student: Ana Jareño Martínez

Technician: Pep Astola

Infectious diseases constitute a tenacious and major public health problem all over the world. The emergence and increasing prevalence of bacterial strains that are resistant to available antibiotics demand the discovery of new therapeutic approaches.

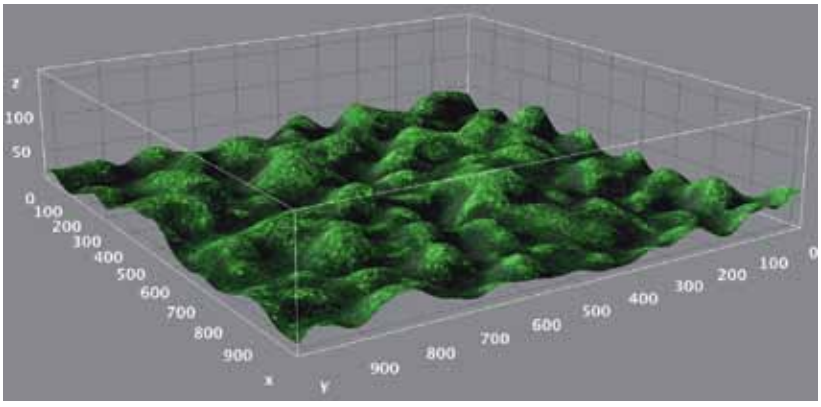
In addition, there is an urgent need for reliable and rapid detection of infecting bacteria and its pattern of resistance to antibiotics.

Bacterial DNA synthesis open new horizons in the discovery of new antibacterial targets due to remarkably differences to the eukaryotic system. The enzyme ribonucleotide reductase (RNR) catalyzes the reduction of ribonucleotides to the corresponding deoxyribonucleotides (dNTP) and thereby provides the building blocks for DNA synthesis and repair. Three different classes will limited sequence similarities have been described for this essential enzyme: class I (nrdAB/nrdEF) is oxygen dependent; class II (nrdJ) is indifferent to oxygen; and class III (nrdDG) is oxygen sensitive. The balance of the different dNTPs has to be carefully regulated and the RNR enzymes as well as its expression play important roles. In the bacterial world it is not known which transcriptional regulators are required to control the expression of the different RNR genes and their role in pathogenesis.

Our lab aims to investigate new antimicrobial therapies to combat bacterial infections with different objectives:

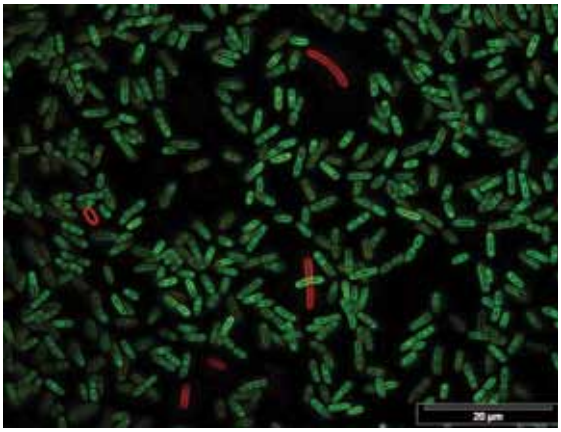
- First, to establish the molecular basis for the regulation RNR genes, their importance in virulence and biofilm formation;
- Second, the identification and screening of new molecules for the highly selective inhibition of bacterial RNR;
- Third, by using nanomedicine techniques the development of novel and specific nanoparticles to deliver existing antibiotics or new identify antimicrobial drugs, especially when the bacteria are growing in biofilm, close to the physiological conditions of the disease and where the current chemotherapy fails;
- Finally, we will use lab-on-a-chip technology, and in particular dielectrophoresis, to study the electrical fields in bacterial cell physiology and also to concentrate bacterial pathogens and facilitate their detection, especially for the identification of bacteria which are multi-resistant to different antibiotics.

We believe these projects will be beneficial to society since we explore the use of different bioengineering approaches to elucidate ways to diagnose and eradicate multi-drug resistant bacteria.



Surface plot analysis of *Pseudomonas aeruginosa* wild type PAO1 four-day old biofilm. Biofilm was form in a continuous flow cell system and visualized under the confocal scanning laser microscopy.

Structural superposition of NrdA (class I) and NrdD (class III) subunits of ribonucleotide reductase.



Pseudomonas aeruginosa treated with novobiocin.

Publications

- Torrents, E. (2014). Ribonucleotide reductases: Essential Enzymes for bacterial life. *Frontiers in Cellular and Infection Microbiology*, 4: 1-9
- Oliva, A. M., Homs-Corbera, A., Torrents, E., Juarez, A. and Samitier, J. (2014). Synergystic effect of temperature and electric field intensity in Escherichia coli inactivation. *Micro and Nanosystems*, 6 (2): 79-86
- Cendra, M. M. and Torrents, E. (2014). Enzims essencials per a la vida. *Treballs de la Societat Catalana de Biologia*, 65: 64-67

Book chapters:

- Oliva, A. M., Homs, A., Torrents, E., Juarez, A. and Samitier, J. (2014). Effect of electric field and temperature in E.Coli viability. *XIII Mediterranean Conference on Medical and Biological Engineering and Computing 2013*, Seville (Spain)

Filed patents

- **Primary hydroxylamines and uses thereof** (Filing date 2nd April 2014)
Inventors: Torrents, E., Albericio, F. and Miret, L. (Fundació Institut de Bioenginyeria de Catalunya, Fundació Institut de Recerca Biomédica)
Ref. number: EP14382032.2

Research projects

- Ribonucleotide reductasas: una nueva diana terapéutica contra organismos patógenos en enfermos de fibrosis quística.
PI: **Eduard Torrents**
Federacion Española de Fibrosis Quística "PABLO MOTOS" 2012-2014

- Inhibición de la síntesis del ADN bacteriano como diana contra organismos patogenos en enfermos de fibrosis quistica.
PI: **Eduard Torrents**
Federacion Española de Fibrosis Quística "PABLO MOTOS" 2013-2015

- **RNRpathotarget** Redes reguladoras de la expresión génica de las distintas ribonucleotidil reductasas en bacterias
PI: **Eduard Torrents**
MINECO

Collaborations with other research centres

Prof. Fernando Albericio Institut de Recerca Biomèdica (IRB), Barcelona, Spain

Dr. Elisabeth Engel IBEC (page 47)

Dr. Esther Julián Dept. de Genètica i de Microbiologia, Universitat Autònoma de Barcelona, Spain

Prof. Britt-Marie Sjöberg Dept. Molecular Biology and Functional Genomics, Stockholm University, Sweden

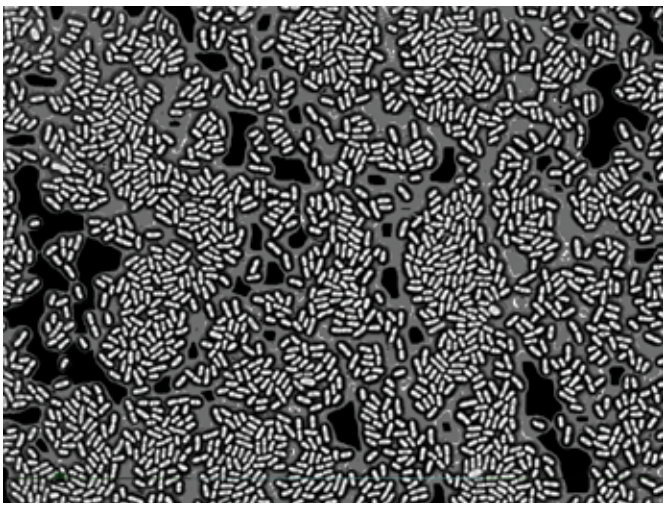
Dr. Nicolas Barnich Pathogénie Bactérienne Intestinale, Université Clermont 1, Clermont-Ferrand, France

Dr. Joan Gavaldà Infectious diseases, Vall d'Hebrón Hospital and Research Institute, Barcelona, Spain

Scientific equipment and techniques

- Gradient thermocycler (PCR)
- Molecular biology facilities
- Protein and DNA electrophoresis
- Bacterial expression systems for heterologous protein production
- Protein purification systems (FPLC; Biologic DuoFlow System From Bio-Rad)
- Technology of microbial culture facilities.
- Pressure microinjection system
- Drosophila melanogaster as a model host for bacterial infections
- Continuous flow system model for bacterial biofilm development
- Single Channel Fiber-Optic Oxygen Meter with microsensor

Free living *Pseudomonas aeruginosa.*



Integrative cell and tissue dynamics

Group leader/ICREA research professor: Xavier Trepat

Postdoctoral researchers: Vito Conte, Anna Labernadie, Andrea Malandrino, Raimon Sunyer, Romaric Vincent, Dobryna Zalvidea

PhD students: Agustí Brugués, Laura Casares, Simón García, Carlos Pérez, Pilar Rodríguez, Marina Uroz

Masters student: Carlos Ureña

Technician: Natalia Castro

The ability of eukaryotic cells to migrate within living organisms underlies a wide range of phenomena in health and disease.

When properly regulated, cell migration enables morphogenesis, host defense and tissue healing. When regulation fails, however, cell migration mediates devastating pathologies such as cancer, vascular disease and chronic inflammation.

Our research focuses on understanding the fundamental biophysical mechanisms underlying migration both at the single cell level and at the tissue level.

Making cellular forces visible

To study cell and tissue dynamics we develop new technologies to measure physical forces at the cell-cell and cell-matrix interface. By combining these technologies with computational analysis of cell shape and velocity we obtain a full experimental characterization of epithelial dynamics during tissue growth, wound healing and cancer cell invasion.

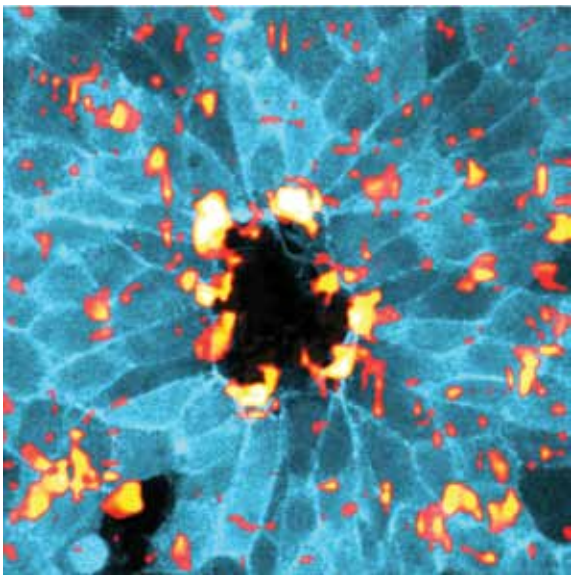
Mechanical waves and collective cell guidance

Our new tools led to the discovery of a mechanical wave – which we called "X-wave" – that propagates through expanding cell sheets. This mechanical wave is a natural candidate to trigger mechanotransduction pathways during wound healing, morphogenesis, and collective cell invasion in cancer. We also discovered a new mechanism, plithotaxis, by which cells align their shape and migration velocity to minimize intercellular shear stresses.

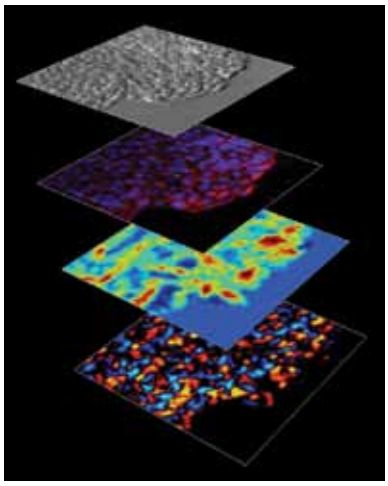
Microfabrication and wound healing

Using microfabrication technologies, we designed new ways to decipher the mechanisms of wound healing. By doing so we uncovered a new understanding of how cells move and work together to close a gap in a tissue. We showed that a new mechanism applies in which cells assemble supracellular contractile arcs that compress the tissue under the wound. By combining experiments and computational modeling, we showed that contractions arising from these arcs make the wound heal in a quicker and more robust way. In addition we developed new assays to show that epithelial skin cells can build 'suspended bridges' to seal gaps in the absence of extracellular matrix.

Map of the physical forces exerted by cells during wound healing. Cells are labelled in blue, forces are shown in red and yellow, and the wound is the central black region.



Our lab has developed techniques to simultaneously map cell velocities, cytoskeletal structure, intercellular stresses, and cell-substrate tractions (from top to bottom).



Research projects

- **GENESFORCEMOTION** Physical Forces Driving Collective Cell Migration: From Genes to Mechanism (2009-2014).
PI: **Xavier Trepat**
European Research Council IDEAS Starting Grants

- The mechanome of epithelial adhesion: unveiling the mechanisms of intercellular force detection, resistance, and transmission (2013-2015).
PI: **Xavier Trepat**
MINECO

- Physical forces driving fibroblast-led cancer cell migration (2014-2015).
PI: **Xavier Trepat** (fellow: **Anna Labernadie**)
Marie Curie Intra-European Fellowships

- Mechanics of Monolayer Migration (2011-2016).
Co-Investigator: **Xavier Trepat** (PI: Jeffrey Fredberg)
National Institutes of Health, USA

Collaborations with other research centres

Julien Colombelli Institute for Research in Biomedicine (IRB), Barcelona, Spain

Eduard Batlle IRB, Barcelona, Spain

Roger Guimerà Univeristat Rovira i Virgili, Tarragona, Spain

Roberto Mayor University College London, UK

Erik Sahai Cancer Research, UK

Benoit Ladoux Université Paris 7, France

Jim Butler & Jeff Fredberg Harvard University, Boston

Scientific equipment and techniques

- Soft Lithography
- Micro/Nano fabrication
- Cell stretching
- Live Confocal Microcopy
- Magnetic Tweezers
- Magnetic Twisting Cytometry
- Monolayer stress microscopy
- Traction microscopy

Publications

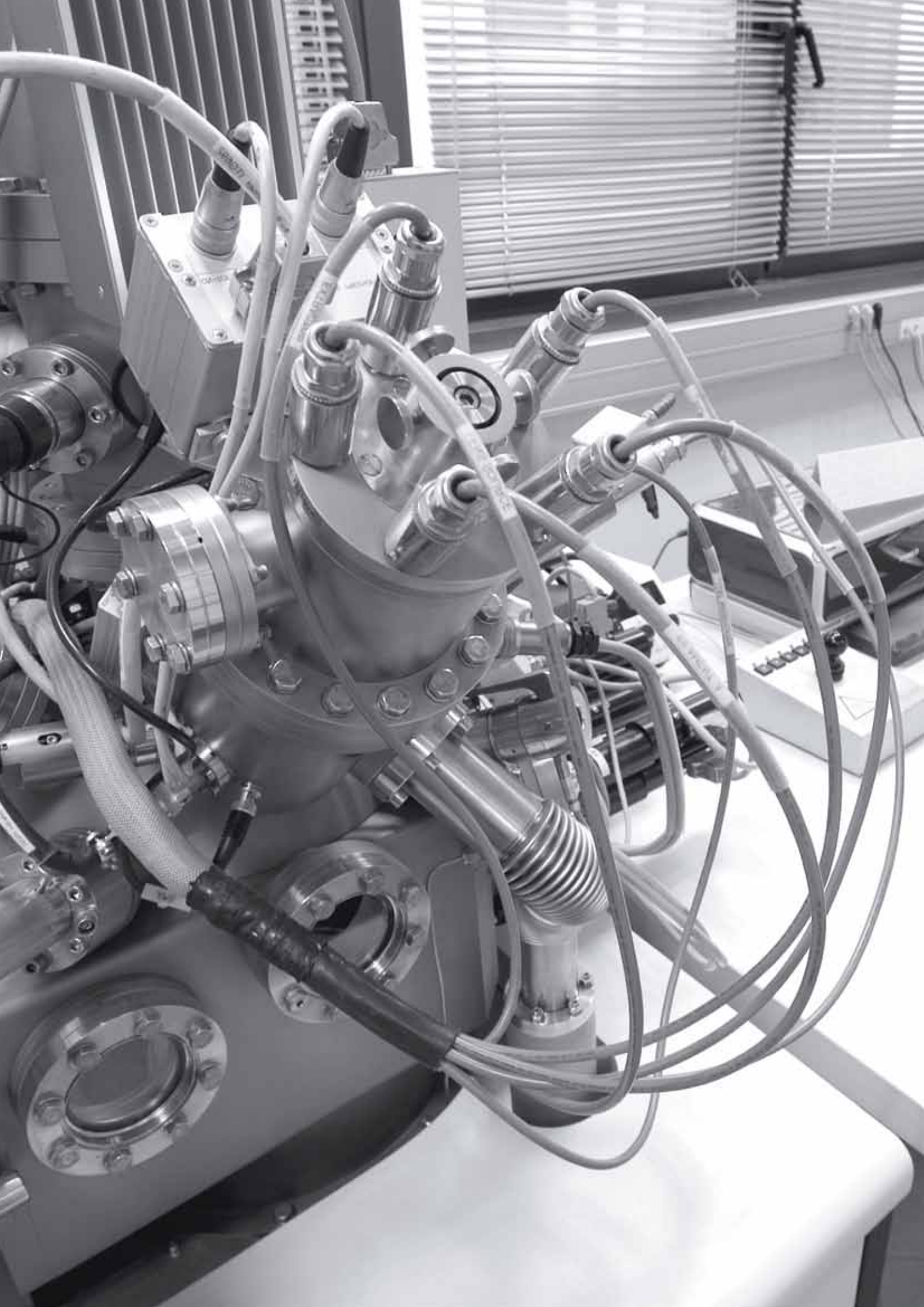
- Elosegui-Artola, A., Bazellières, E., Allen, M. D., Andreu, I., Oria, R., Sunyer, R., Gomm, J. J., Marshall, J. F., Jones, J. L., Trepat, X. and Roca-Cusachs, P. (2014). Rigidity sensing and adaptation through regulation of integrin types. *Nature Materials*, 13 (6): 631-637

- Vedula, S. R. K., Hirata, H., Nai, M. H., Brugués, A., Toyama, Y., Trepat, X., Lim, C. T. and Ladoux, B. (2014). Epithelial bridges maintain tissue integrity during collective cell migration. *Nature Materials*, 13 (1): 87-96

- Brugués, A., Anon, E., Conte, V., Veldhuis, J. H., Gupta, M., Colombelli, J., Muñoz, J. J., Brodland, G. W., Ladoux, B. and Trepat, X. (2014). Forces driving epithelial wound healing. *Nature Physics*, 10 (9): 683–690

Book chapter:

- Vedula, S. R. K., Ravasio, A., Anon, E., Chen, T., Peyret, G., Ashraf, M. and Ladoux, B. (2014). Microfabricated environments to study collective cell behaviors. In: *Methods in Cell Biology* (ed. Piel, M. and Théry, M.), Academic Press. 120: 235-252



Core Facilities

Core Facilities

IBEC provides its researchers with extensive research facilities and a scientific–technical infrastructure distributed over interdisciplinary open lab spaces. It is designed and managed to facilitate research and promote the cooperation and exchange of knowledge between IBEC scientists.

In this way, researchers share not only the space itself but also the equipment, bench space, and qualified technical staff, thereby helping to reduce research costs.

Apart from routine laboratory equipment, the Core Facilities provide additional sophisticated, stae-of-the-art equipment to support the groups' research. They are organized into two different categories: in-house equipment (only for internal users) and the Nanotechnology Platform (open to external users).

In-house equipment

- Chromatography System Biologic LP – Bio-Rad
- Spectrophotometer – Nanodrop
- Multimode microplate reader Infinite M200 Pro – Tecan
- Spectrophotometer UV-Visible – Shimadzu
- Microplate Reader Benchmark Plus – Bio-Rad
- StepOnePlus Real Time PCR System – Applied Biosystems
- DNA Engine Thermal Cycler – Bio-Rad
- T100 Thermal Cycler – Bio-Rad
- ImageQuant LAS 4000 mini – GE Healthcare
- GelDoc XR+ System – Bio-Rad
- Liquid handling robot Freedom Evo – Tecan

Head of Core Facilities
Isabel Oliveira

Nanotechnology Platform Coordinator
Mateu Pla-Roca

Laboratory Technicians
Laura Gómez, Cristina Rivero, Jenifer González

Nanotechnology Platform Technicians
Judit Linacero, Marina Cazorla

Undergraduate student
Tania Bordoy

Vocational student Lenin Lescano

Nanotechnology Platform

The Nanotechnology Platform is part of the institute's long-term strategic plan to create new Core Facilities in nanofabrication and bionanocharacterization.

Currently, the platform is an accessible and versatile research facility featuring 150m^2 of class 10,000 cleanroom space and laboratories offering state-of-the-art equipment for the fabrication and characterization of micro- and nanodevices and structures.

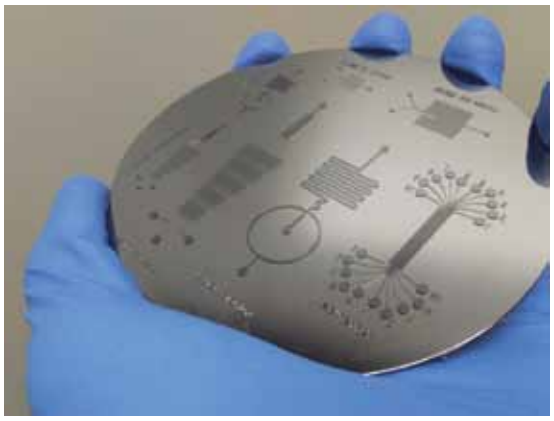
Our aim is to facilitate advanced research by providing services in the fields of nanoscience and nanotechnology for all academic and industrial researchers. Some of the many areas of application include nanobioengineering, BioMEMS, materials science, tissue engineering, optic and biomaterials.

IBEC's Nanotechnology Platform offers scientific and technological support that includes the design, development and analysis of devices, materials, and processes, so that academic researchers and companies alike may use the platform to develop their innovative ideas.

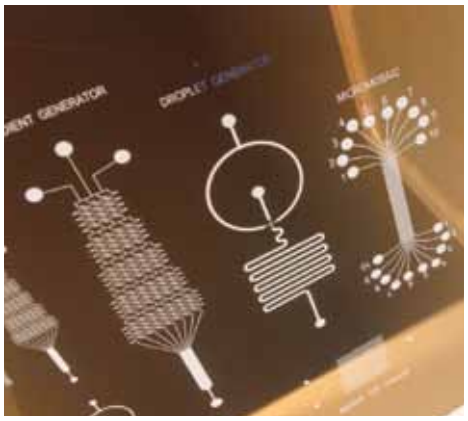
Services

- Access to 10,000 class cleanroom.
- Training on and self-use of the following equipment: interferometer, profilometer, optical microscope, spin-coater, plasma cleaner and Mask Aligner.
- Training on microfluidic chips design, fabrication and interfacing with pumping systems
- Fabrication:
  - Design and fabrication of customized microfluidic chips using photolithography and replica molding (rapid prototyping in PDMS silicone)
  - E-beam lithography technique for the manufacture of micro- and nano-structures.
  - Replication of micro nanostructures in thermoplastic polymers by hot embossing and nano-imprint lithography
  - Fabrication of Transparency and Cr photomasks for photolithographic process
  - RIE and wet-etching for silicon and glass micro and nanostrcuturation
  - Thin layer deposition of materilas (Au, Al, Ti, Cr, SiO2, etc.)
  - Microelectrode fabrication
  - Fabrication of molds for microcontact printing and micromolding in capillaries

Mold on a silicon wafer fabricated using photolithography containing seven microfluidic systems



Photomask with distinct microfluidic designs such a gradient generator, a droplet generator or a fluidic system for immunoassays



Users' publications

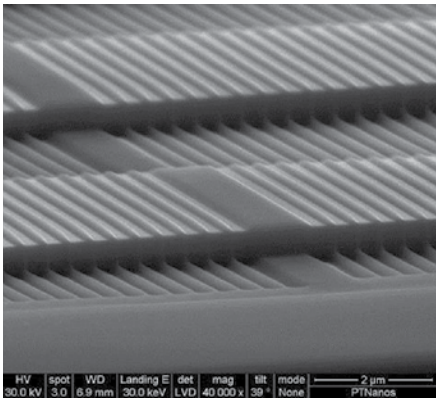
- Rigat Brugarolas, L. G., Elizalde Torrent, A., Bernabeu, M., de Niz, M., Martin Jaular, L., Fernandez Becerra, C., Homs Corbera, A., Samitier, J. & del Portillo, H. A. (2014). Functional microengineered liolmodel of the human splenon-on-a-chip. *Lab Chip*, 14(10):1715-24
- H A Moreno, S Hussain, R Amade & E Bertran (2014). Growth and functionalization of CNTs on stainless steel electrodes for supercapacitor applications. *Materials Research Express 1*, 035050
- Ziqiu Tong, Oscar Seira, Cristina Casas, Diego Reginensi, Antoni Homs-Corbera, Josep Samitier and J. Antonio Del Rio (2014). Engineering a functional neuro-muscular junction model in a chip. *RSC Adv.*

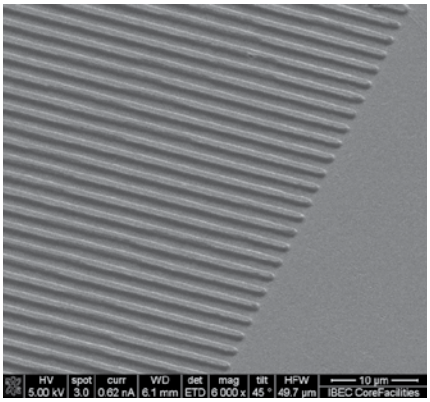
- Characterization:
  - Sample characterization using ToF-SIMS:
    - Surface microanalysis of organic and inorganic materials
    - Complete mass spectra of surfaces
    - Chemical mapping of elements and molecular distribution
    - Sample depth profile, implantation profiles and interface analysis.
  - SEM morphological and topographical characterization of a diverse range of samples.
  - Surface topographic analysis by using optical interferometry and mechanical profilometry.

Equipment

- Time-of-Flight Ion Mass Spectroscopy (ToF-SIMS)
- Ultra-High Resolution Field Emission Scanning Electron Microscopy (SEM)
- E-beam Lithography (EBL)
- Nanoimprint Lithography (NIL)
- Hot-Embossing Lithography (HEL)
- UV-Photolithography Mask-aligner
- Direct Write Laser Lithography
- Thermal and E-beam metal evaporator
- Reactive Ion Etching (RIE)
- Inteferometer
- Profilometer
- Chemical Bath
- Spinner
- Plasma Cleaner
- Optical microscope
- UV lamp for curing processes

Left: SEM image of PMMA Surface micro-nanostructured with using e-beam lithography; *right:* polylactic acid (PLA) with 1 micrometer wide and 500 nm tall microstructures fabricated using hot-embossing





Activities in 2014

During our two years of operation, 59 researchers from eleven IBEC groups, 82 researchers from 19 other public institutions, and 16 from ten private companies have become users of the Nanotechnology Platform. In 2014 the average of users and services performed by the platform was 28 and 187 per month, respectively.

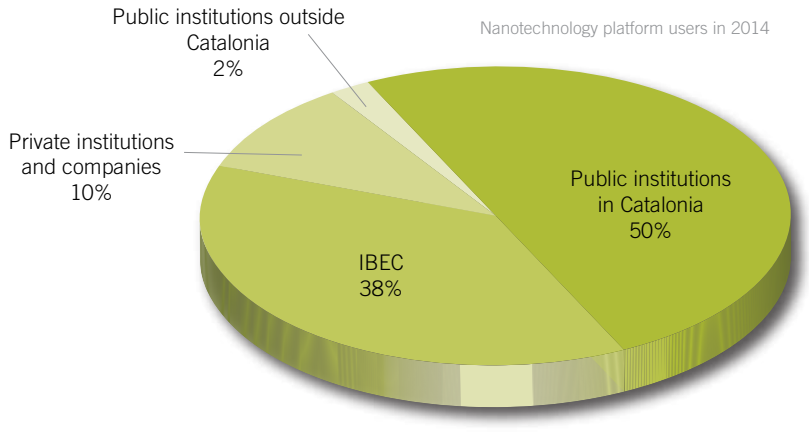
In addition, the Nanotechnology Platform facilitated introductions on micro- and nanofabrication techniques to students on the following courses: Master in Biomedical Engineering (University of Barcelona (UB)/Technical University of Catalonia (UPC)), Master in Nanoscience and Nanotechnology (UB); Bachelor in Biomedical Engineering (UB). We organized a seminar in vacuum pumping systems (performed by Iberia Vaccum S.A) and participated in several dissemination and networking activities, such as:

- "Presentació del Programa de Competències Cientifiques" event, organized by the Generalitat's Department of Education.
- Expoquimia 2014, "Jornada Nanoseguridad: Presente y futuro de los nanomaterials". Oral presentation: "Nanomedicina: nuevas aplicaciones de los nanomateriales".
- Nanobiomed 2014, Industrial Forum. Oral presentation: "Nanotechnology Platform: Opportunities for your research".
- Networking and Innovation Day 2014.
- Lessons Learned 2014: "Compartint experiències per a impulsar la competitivitat".

During 2014 the Nanotechnology Platform was listed on BioCores@BCN, an online tool launched by the CRG which is part of the pan-European initiative Core for Life. It aims to help scientists and other customers find the local scientific service, technique or equipment they need for their biomedical or life sciences research.

The Nanotechnology platform was also included in MINECO's updated ICTS (Infraestructuras Científicas y Técnicas Singulares) map as part of NANOBIOSIS (Infraestructuras Integradas de Producción y Caracterización de Nanomateriales, Biomateriales y Sistemas en Biomedicina) an integrated platform for research-oriented medical applications.

For more information about the Nanotechnology Platform, or to register as a user, please visit www.ibecbarcelona.eu/IBEC/core-facilities.html or follow us on LinkedIn.

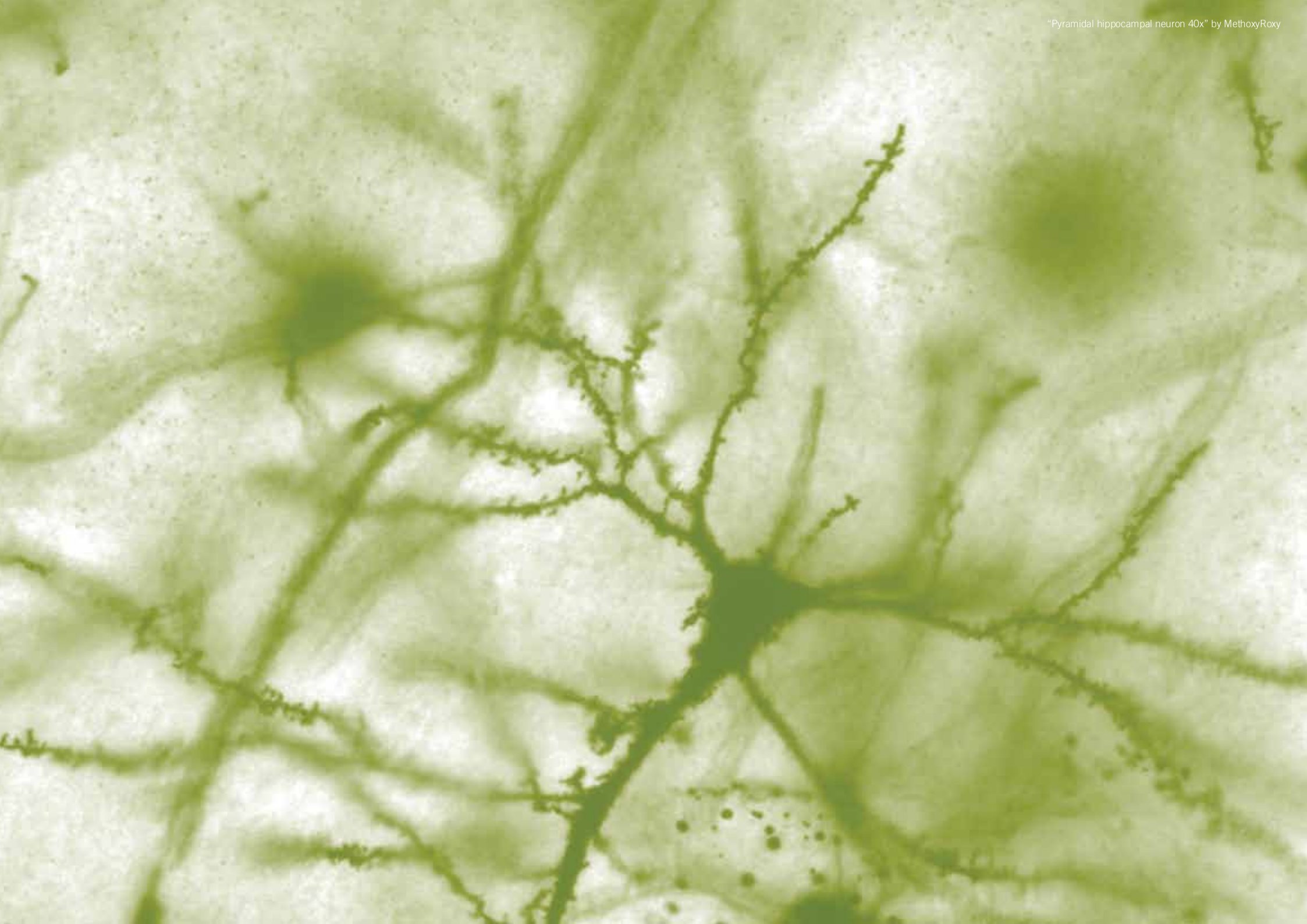


Users

- University of Barcelona
- Technical University of Catalonia (UPC)
- Centre de Recerca en Enginyeria Biomèdica (CREB)
- Fundació Institut de Recerca en Energia de Catalunya (IREC)
- Instituto de Investigación Sanitaria - Fundación Jimenez Diaz
- Institut de Recerca Biomedica (IRB)
- Institut de Microelectronica de Barcelona (CNM)
- Centre de investigación en nanociencia i nanotecnologia (CIN-2)
- Institut Català de Nanociència i Nanotecnologia (ICN2)
- Institut de Ciència de Materials de Barcelona (ICMAB)
- Universidad Politécnica de Madrid
- Universidad de Zaragoza
- Universidad de Valladolid
- Institut Químic de Sarrià
- Infinitec Activos S.L.
- Universidad Miguel Hernandez
- Institut de Biologia Molecular de Barcelona (IBMB-CSIC)
- Fundació CTM Centre Tecnològic

New users (2014):

- Universitat Autónoma de Barcelona (UAB)
- Institute of Environmental Assessment and Water Research (IDAEA-CSIC)
- Institut de Quimica Avançada de Catalunya (IQAC-CSIC)
- Fundació IGTP - Ciencies de la Salut Germans Trias i Pujol
- ViaFactor BV
- Advanced Nanotechnologies, S.L.
- BSH Electrodomésticos España, S.A.
- Cosingo - Image Optic Spain, S.L.
- Technoform Bautec Iberica, S.L.
- BCN Peptides, S.A.



"Pyramidal hippocampal neuron 40x" by MethoxyRoxy

Networking

Partnerships

While most of IBEC's funds come from the Generalitat de Catalunya, the University of Barcelona and the Technical University of Catalonia, an increasing proportion comes from national and international competitive research funding, ranging from large instruments such as the EU's Framework Programmes to independent or national foundations. Both projects and people are funded, with IBEC proud to be able to claim four group leaders with their own support from one of the most prestigious sources, ICREA, in 2014.

The Catalan Institution for Research and Advanced Studies (ICREA) is supported by the Catalan Government to recruit top scientists for the Catalan R&D system to lead new research groups, strengthen existing ones and set up new lines of research. The foundation works closely with Catalan universities and research centres through long-term agreements that allow ICREA researchers to participate in research groups in these centres.

In 2014, four of IBEC's group leaders were ICREA research professors: Ángel Raya (Control of Stem Cell Potency group, page 92), George Altankov (Molecular Dynamics at Cell-Biomaterial Interface, page 38), Xavier Trepat (integrative Cell and Tissue Dynamics, page 112) and Pau Gorostiza (Nanoprobes and Nanoswitches, page 60).

IBEC and the Centre de Recerca en Salut International de Barcelona (CRESIB), part of the Barcelona Global Health Institute (ISGLOBAL), signed an official agreement in 2010 to facilitate collaboration in certain areas of common interest. This led to the establishment of a mixed unit of personnel from both institutes to develop diagnostic and therapeutic nanomedicine-based systems to be applied to malaria (Nanomalaria group, page 52).

The agreement, which will continue as is until 2015, is focused on knowledge transfer to the clinic.

Spain's Centro de Investigación Biomédica en Red (CIBER), a legal entity financed by the Instituto de Salud Carlos III, creates large multidisciplinary and multi-institutional networks of research centres that will integrate basic and clinical research.

Several IBEC groups work in programmes within CIBER, such as **CIBERBBN**, which covers bioengineering, biomaterials and nanomedicine. Research is focused on disease prevention, diagnostics systems and technologies for specific therapies, such as regenerative medicine and nanotherapies.

Another programme within CIBER, **CIBERES** – Centro de investigación en red de enfermedades respiratorias – involves Cellular and Respiratory Biomechanics group leader **Daniel Navajas** (page 82) and addresses respiratory illnesses.

CIBERNED, which covers neurodegenerative diseases, maintains its own legal personality as it is managed by Fundación CIEN. It is composed of 63 research groups working on basic and clinical research.

Ongoing CIBERBBN projects during 2014

- **CHONDRONANONET** Nanopatterned Cell Carriers for Improved Architectural Communication Networks in Chondrogenesis towards Osteoarthritic Joint Repair
  PI: **Josep Samitier** (coordinator); **Pau Gorostiza**; **Anna Lagunas**

- **E-LEUKEMIA** The nanoconductance of redox proteins of the respiratory chain and its physiopathological implication in leukemia
  PI: **Pau Gorostiza** (coordinator); **Josep Samitier**; **Anna Lagunas**

- **TO-GLIOTHER** Towards Clinical Stem Cell Glioblastoma Therapy
PI: **Elisabeth Engel**

- **NANO3B** Novel nanocarriers as delivery systems across the Blood-Brain barrier
PI: **Fausto Sanz**

- **NANOXEN++** *Xenopus tropicalis* as an optogenetic and optopharmacological platform
PI: **Pau Gorostiza** (coordinator)

- **BIOSURFACES** Biofunctionalization of titanium implant surfaces
PI: **George Altankov**

- **BIOWOUND** Bioactive materials for wound healing based on controlled ion release
PI: **Soledad Pérez** (scientific coordinator)

- **BIOROTATOR** Tendon Tissue Engineering for Rotator Cuff Tear**s**
PI: **Miguel Angel Mateos** (scientific coordinator)

- **INTER-CARDIO** Computer-assisted interpretation of electrical signals: a step forward in understanding and treating cardiac diseases
PI: **Raimon Jané**

- **OLIGOCODES** Universal Diagnostic Platforms Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices.
PI: **Josep Samitier**

- **MUDIRES-2PSD** Multimodal Diagnosis by Signal Interpretation of the Respiratory System oriented to Pulmonary Diseases and Sleep Disorders
PI: **Raimon Jané** (coordinator); **Daniel Navajas**

- **ULTRASEN-4BIO-2MD** Characterization and evaluation of novel ultrasensitive piezoresistive all-organic sensors for biomedical signals applied to multimodal diagnosis
PI: **Raimon Jané** (coordinator)

- **NANOLYSO** Nanomedicine-based enzyme replacement therapy for the treatment of lysosomal storage disorders
PI: **Fausto Sanz**

- **BIOGELANGIO** Biomimetic extracellular matrices for angiogenic activation and anti-inflammatory activity in regenerative medicine.
PI: **Miguel Angel Mateos** (scientific coordinator)

- **Bioproterial** Biological activity of matrix proteins at the cell-material interface.
PI: **George Altankov**

- **ES-CELLTHERAPY** Use of human pluripotent stem cells as vehicles for localized delivery of therapy to brain tumors.
PI: **Ángel Raya**; **Elisabeth Engel**

- **NACRE** New Approaches for Cartilage Regeneration.
PI: **Ángel Raya**; **Miguel Angel Mateos**

- **NANOMEDIAG** Nanobioanalytical platforms for improved medical diagnosis of infections caused by pathogen microorganisms.
PI: **Josep Samitier**

- **SCAFFTIDE 3D** 3D scaffolds and implants functionalized and reinforced with recombinant protein polymers for regenerative medicine.
PI: **Miguel Angel Mateos**

Ongoing CIBERNED projects during 2014

- Generación de un modelo neuronal dopaminérgico a partir de células madre pluripotentes inducidas de pacientes con enfermedad de Parkinson asociada a mutaciones en el gen LRRK2.
PI: **Ángel Raya**

- Red española de investigación en enfermedades neurológicas PRY-114
PI: **Jose Antonio del Río**

Research Agreements and MoUs

IBEC pursues opportunities to collaborate on a long-term basis with other world-class national or international research institutes with an agreement or Memorandum of Understanding (MoU), with particular emphasis on clinical translation.

Affiliated groups and associated groups

IBEC's relationship with the University of Barcelona (UB) and the Polytechnic University of Catalonia (UPC) is described on page 24. As a result of this connection and because of the history of IBEC's foundation, the following IBEC groups are also affiliated to one of the two universities.

University of Barcelona

- Nanoscale Bioelectrical Characterization (page 56)
- Nanoprobes and Nanoswitches (page 60)
- Microbial Biotechnology and Host-Pathogen Interaction (page 70)
- Signal and Information Processing for Sensing Systems (page 74)
- Cellular and Respiratory Biomechanics (page 92)
- Molecular and Cellular Neurobiotechnology (page 98)
- Nanobioengineering (page 103)

Polytechnic University of Catalonia

- Robotics (page 42)
- Biomaterials for Regenerative Therapies (page 47)
- Biomedical Signal Processing and Interpretation (page 64)

In addition, IBEC has some associated groups, also at the UPC and UB, whose members may use our laboratories and facilities.

Memoranda of Understanding

Memoranda of Understanding formalise the participation of IBEC and the partner institute in cooperative scientific projects, promote the exchange of researchers, aid dissemination of information, the sharing of resources and the organization of joint events and activities.

By 2014, IBEC had MoUs in place with the following organisations:

- The **council of Sant Feliu de Guíxols**, to work together on a museum exhibit on the history of health and medicine in Catalunya, "Curar-se en salut". Sant Feliu de Guíxols' Museu d'Història hosts the exhibition, which opened in November 2014 and includes audiovisual displays, visual metaphors, historical material and other artefacts to show the long fight that medicine has taken to reach present-day standards. IBEC's part of the exhibition focuses on the present day situation of medicine as well as reflecting on the future. The institute developed the exhibition's content with its scientific expertise, and both sides will work together to conduct educational workshops related to research in bioengineering and nanomedicine.
- The Centre de Recerca en Salut International de Barcelona (**CRESIB**), the Center for Research in Environmental Epidemiology (**CREAL**) and the Instituto de Diagnóstico Ambiental y Estudios del Agua (**IDAEA-CSIC**) to carry out a project

Sant Feliu de Guíxols' Museu d'Història

to study DDT concentration detection in treated surfaces to tackle malaria.

- Institut De Recerca I Tecnologia Agroalimentaries (**IRTA**), Barcelona.
- **Fundació Clínic/Hospital Clínic**, Barcelona.
- Bellvitge Institute for Biomedical Research (**IDIBELL**), Barcelona.
- National Institute for Materials Science (**NIMS**), Tsukuba, Japan.
- Institute of Tissue Regeneration Engineering (**ITREN**), Dankook University, Korea.
- University of Warwick's **Centre for Cognitive and Neural Systems**, UK.
- Vall d'Hebron Research Institute (**VHIR**), Barcelona.
- Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (**IGTP**), Badalona.
- Interstaatliche Hochschule für Technick Buchs (**NTB**), Switzerland.
- **Barcelona Macula Foundation**.
- Fundació Joan Costa Roma (**JCRF**), Terrassa.
- The Open University of Catalonia (**UOC**).
- **CIBER** (page 124); under a special agreement, IBEC's Nanotechnology Platform (see page 116) is considered an integrated service platform within the CIBERBBN programme, thus facilitating access to all researchers within the network.
- **Università degli Studi di Brescia**

Institutional Initiatives

In its role as the country's leading research institute in bioengineering and nanomedicine, IBEC manages or is a partner of national and international initiatives with a range of goals including bringing together entities to network and share resources, providing advice and support, organising events, or acting as a representative, collective voice or expert consultant for stakeholders or funders.

NANOMED SPAIN

The Spanish Nanomedicine Platform (NanoMed Spain) is a forum managed by IBEC that brings together public research centres, hospitals, companies and government representatives to unite public and private interests in the development of common strategies. NanoMed Spain represents the interests of its stakeholders in the burgeoning and multidisciplinary area of nanomedicine, and is supported by the Spanish Ministry of Economy and Competitiveness (MINECO), through the Spanish Programme for R+D+I oriented to Societal Challenges.

The activity of NanoMed Spain in 2014 was focused on:

- The continued co-organization of the Annual Conference of the Biomedical Research Technology Platforms (Barcelona, 4th-5th March 2014), together with the Spanish platforms for Innovative Medicines, Biotechnology, and Health Technology and aiming to facilitate public-private collaboration, with a main focus on nanomedicine for healthy aging as well as international cooperation initiatives and spin-off creation experiences. In parallel, a programme of express bilateral contacts between NanoMed Spain members and National Contact Points was also held. A proposal for Public Innovative Procurement promoted by MINECO was introduced at Foro Transfiere (Málaga, 12-13th February 2014).
- Commitment with innovation and knowledge transfer is supported by strong alliances with the Patents and Trademarks Spanish Office (OEPM), as shown by the OEPM-crossplatform day

The Annual Conference of the Biomedical Research Technology Platforms, held in March

(Madrid, 11th March) that crystallized in a new technological alert which informs on the last published patents related to nanopharmacology, available on our web page, www.nanomedspain.net.

- Ongoing activities of the cross-platform Nanosafety group, along with the Plataforma de Seguridad Industrial (PESI), Plataforma de Materiales (MATERPLAT) and the Plataforma de Química Sostenible (SusChem). The Group organized an outreach workshop for the chemical sector taking advantage of the forum provided by the international fair EXPOQUIMIA (29th Sept-2nd Oct 2014), attended yearly by thousands of professionals at international level. The Nanomedicine-Nanosafety Group Section is now represented at the AENOR Experts Group by Dr Judith Sendra (Endor Nanotechnologies).
- Involvement in the new Working Party on Biotechnology, Nanotechnology and Converging Technologies (BNCT) of the OECD, which will start work in January 2015. The Working Party for BNCT will provide expert input on nanoengineering and issues related to the convergence of technologies. They will guide the development and implementation of global BNCT-related projects, identify funding sources, and provide a voice for BNCT matters to the different national systems. Josep Samitier is one of the four delegates nominated for Spain.
- Coordinating and fostering the Spanish participation in the first calls of HORIZON 2020 (2014-2020), in all nanomedicine topics. As well as contributing to the definition of topics and coordinating stakeholders' opinions, training activities have been in the agenda to update companies and organizations on aspects regarding the managing of projects (23rd April 2014, regarding finance managing in H2020). Out of the proposals submitted to 2014 H2020 calls, the success of the Spanish community the area of establishing pilot lines to scale-up the production of novel nanopharmaceuticals from the lab-scale to the quantities needed for clinical testing has been particularly remarkable: two funded consortia, NANOPILOT and NanoFacturing, are led by two Spanish organizations (CIDETEC and MIDATECH) and have several more Spanish partners.
- Participation in a bilateral high-level meeting Spain–Japan, to strengthen collaborations in science and innovation (12th-19th October 2014). The Platform's activities resulted in nanomedicine being one of the focus topics on the agenda of the meeting, led by the Spanish Secretary of State for Research, Development and Innovation, and with Josep Samitier as one of the experts on the Committee.

The European Commission's Ro-cKETs project

Integration between Key Enabling Technologies will be essential for economic growth, competitiveness and innovation in Europe in the coming years. In order to tap into the high cross-fertilization potential of these technologies, in 2013 the European Commission launched a study "Methodology, work plan and roadmap for cross-cutting KETs activities in Horizon 2020" (RO-cKETs). The project (2013-2014) was commissioned by Directorate General (DG) for Internal Market, Industry, Entrepreneurship and SMEs and was coordinated by D'Appolonia. IBEC's Knowledge Exchange Unit provided its expertise to identify innovative products in the pharmaceutical and medical technology sectors, as well as livestock and agriculture, which are to be enabled by the integration of nano/advanced materials/biotechnology and/or electronic and photonic techniques.

The study outlines how the combination of different Key Enabling Technologies can contribute to addressing the challenges facing European industry, economy and society. The main scope of the study has been to produce a shared methodology and a proposal for a cross-cutting KETs roadmap and workplan for the European Commission, which will provide input to the preparation

of the cross-cutting KETs part of future Horizon 2020 work programmes. Taking the demand side as a starting point, the study is helping the Commission to identify the most promising areas of innovation for cross-cutting KETs that address clear industrial and market needs in a broad range of industrial sectors.

The final report and roadmap are available at http://ec.europa.eu/growth/industry/key-enabling-technologies/eu-actions/ro-ckets/index_en.htm.

A voting member of the European Technological Platform on Nanomedicine (ETPN) since 2008, IBEC has contributed as an invited expert body, through its director and the Institutional Projects Unit, to 'Roadmaps for Nanomedicine Towards 2020'. This key document in the area of nanomedicine was drawn up to advise the European Commission on future R&D investment needed to ensure successful translation of the results of research into the related sectors of medical and pharmaceutical technologies.

The European Technology Platform on Nanomedicine organised its 2014 Annual Event & General Assembly in San Sebastian, Spain. The event took place on 15th and 16th October 2014, with the local organization being carried out by the Nanobasque Agency, supported by NanoMed Spain.

This year's annual event aimed at providing in-depth details on the practical implementation of the ETPN recommendations for a strong translational nanomedicine sector in Europe as well as unveiling future priorities for nanomedical research and innovation until 2020. Josep Samitier was invited to present the current scenario of nanomedicine in Spain, as well as to participate in a new section of national and regional organizations to promote translational activities in nanomedicine across Europe.

As nanomedicine is indeed entering a concrete implementation phase for the Translation Hub concept developed by the ETP Nanomedicine, notably through the latest calls in Horizon 2020, and is experiencing an increased interest from the research and industrial communities, from national authorities in Europe but also outside Europe, this event has been the opportunity to consolidate the ETPN efforts to shaping a functioning nanomedical sector in Europe for the benefit of patients.

Josep Samitier in a video made for the ETPN Annual Event 2014

Strategic Alliances

Several organisations exist at a local or national level to consolidate research efforts in particular fields, coordinate and encourage greater visibility for the activities of research centres, or bring together similar entities with a common goal from different regions.

EIT selects IBEC consortium for new KIC on health

A consortium of 144 European companies, research institutes and universities – including IBEC – was selected at the end of 2014 by the European Institute of Innovation and Technology (EIT) as the Knowledge and Innovation Community (KIC) on healthy living and active ageing, EIT Health.

With a total of €2.1 billion it is one of the largest public funded initiatives for health worldwide. For the next seven years, the partners – which also include INSERM (France), Imperial College (UK), Roche, Siemens and Philips – will develop innovative products, education and services addressing the challenge of demographic change in Europe. By 2018, EIT Health is aiming to create 70 start-ups per year and have a million students participating in educational online programmes per year.

IBEC will play a key role in the project, as Barcelona has been selected as one of Innolife's six co-location centres, serving as a regional cluster to bring together the partners of the KIC and ensure that its innovation potential is fully realised. At the time of writing, IBEC Director Josep Samitier is interim director of this Spanish node.

The EIT is an independent EU body set up in 2008 to spur innovation and entrepreneurship across Europe. The EIT's first three KICs on climate change, ICT and sustainable energy – Climate-KIC, EIT ICT Labs and KIC InnoEnergy – were selected in 2009. As well as EIT Health, EIT Raw Materials was also launched in 2014. The EIT will launch the next call for KIC Proposals in 2016 focusing on Food4Future and Added-value Manufacturing, with a further call tentatively planned for 2018, addressing Urban Mobility.

Clúster de Tecnologies de la Salut

In June 2014, IBEC became a member of a new alliance aimed at promoting and contributing to the competitiveness of the health technology sector in Catalonia.

Following in the footsteps of other such initiatives as Biopol'H and Bionanomed Catalunya, the Clúster de Tecnologies de la Salut brings together research organisations, companies, hospitals and other bodies to compete globally by promoting innovation and internationalization of partners and improving conditions within the sector.

The Clúster is an initiative of ACCIÓ, the Generalitat's Agency of Competitiveness for Companies in Catalonia. This network will focus particularly on partners that are work-

ing on developing technologies for healthcare, rather than basic research. The other members include the Universitat Politècnica de Catalunya (UPC) on the research side, Barcelona's Hospital Clínic among the healthcare bodies, and companies Telstar and the Sibel Group.

There are around 15,000 people currently employed in the health technologies sector in Catalonia.

IBEC is a member of the Health UB Campus (HUBc) project, led by the University of Barcelona, is a recognised Campus of International Excellence that brings together about 30 training institutions, research and knowledge transfer in health sciences, mainly around the campus of the Medical and Hospital San Juan de Dios, the campus Health Sciences with the University Hospital of Bellvitge, ICO, IDIBELL, and Barcelona Innovation Zone.

IBEC Director Josep Samitier held the position of director of HUBc until 2013.

EIP on AHA

In 2013, under the umbrella of the HUBc, several research activities at IBEC were accepted as 'commitments' by the European Commission's European Innovation Partnership on Active and Healthy Ageing (EIP on AHA). This policy-influencing initiative alongside H2020 brings together public and private stakeholders to develop new innovations which can improve the quality of life of older people while creating market opportunities for business.

In 2014, a "scaling up" strategy for the good practises developed throughout the EU constituted the next step in the development of the EIP on AHA. Partners are working within 32 Reference Sites, which are regions, cities, or integrated hospitals/care organisations that implement a comprehensive, innovation-based approach to active and healthy ageing and can give concrete evidence and illustrations of their impact on the ground. IBEC is a member of the Catalonia Reference Site.

BIOCAT coordinates, develops and promotes the biotechnology, biomedicine and medical technology sectors in Catalonia, to make the region an international reference in terms of high quality research, competitive networks and an increasingly dynamic knowledge transfer system. IBEC has worked closely with BIOCAT on such projects as BioNanoMed Catalunya, an alliance of research centres, hospitals and companies launched in 2011 to share know-how and resources and facilitate new developments in nanomedicine.

In 2013-14, along with BIOCAT and the UB, IBEC was a leading member of the consortium which prepared the winning proposal for the Knowledge and Innovation Communities (KIC) on 'Healthy living and active ageing' of the European Institute of Innovation and Technology (EIT) (see EIT-Health, previous page).

The Virtual Physiological Human (VPH) Institute is an international not-for-profit organisation whose mission is to ensure that emergent techniques based on theoretical modelling for patient virtualization are fully realised, universally adopted and effectively used both in research and the clinic.

As a regular member of the VPH Institute, IBEC actively supports the promotion of VPH technologies towards the improvement of current healthcare through the use of personalized and integrated *in silico* medicine. Jérôme Noailly, senior research associate in the Biomechanics and Mechanobiology group, and principal investigator of the VPH European project MySpine at IBEC, is IBEC delegate and member of the Policy Affair Working Group.

Other strategic alliances

During 2014 IBEC continued to be a member or partner of the following organisations or initiatives:

- Associació Catalana d'Entitats de Recerca (ACER)
- CERCA Institute (the Government of Catalonia's means of supervising, supporting and facilitating the activities of Catalan research centres).

Technology Transfer

Breakthrough innovation can only happen if research discoveries leave the lab and reach the market and users. Translating discoveries into market-ready products requires effective liaison with industry, as well as knowledge of intellectual property protection and exploitation.

The technologies that meet our criteria for commercialization are developed into products and therapies through collaborations and alliances with other research organizations, companies and clinicians, and by the creation of new start-ups. IBEC researchers are supported by the Knowledge Exchange Unit along the tech transfer and translation processes.

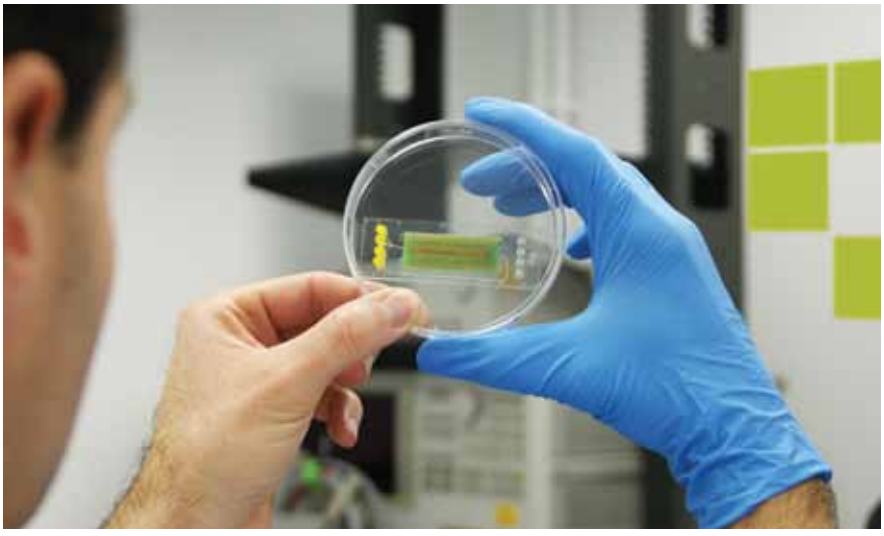
IBEC/Genomica joint unit

In July 2014 IBEC and Genomica S.A.U. (Grupo Zeltia), the leading Spanish company in molecular diagnostics, signed a collaboration agreement for the creation of a Joint Research Unit that will provide an operational framework for close interaction on various R&D activities related to healthcare.

The unit, which will be located at IBEC's headquarters in Barcelona, will see researchers and industry technicians sharing a host of know-how and in-house capabilities to develop and bring to market point-of-care diagnostic products and other medical devices and technologies.

IBEC's researchers in the unit will supply the scientific knowledge with their expertise in biosensors, micro- and nanofabrication, signal processing and bioengineering, while the members from Genomica's side will offer market intelligence, clinical evaluation and regulations, and diagnostics know-how.

It's the first time that IBEC's researchers will physically work together alongside industry personnel, though the institute already has several existing collaborations and research agreements – with companies such as Ferrer International and Ficosa, as well as Genomica itself – related to the development of specific projects and the transfer of technologies.



Adding value to Dermoglass

A promising, clinically-oriented material born at IBEC's benches is Dermoglass, a dressing that stimulates wound healing and revascularization for the treatment of skin ulcers. Led by Elisabeth Engel (Biomaterials for Regenerative Therapies group, page 47), Dermoglass is now protected under a PCT patent application submitted on April 2014. Preclinical assays, which were made possible by a round of crowdfunding in 2013, took place during 2014.

To attract possible investors, Dermoglass was presented to the 1500 professionals at the MIHEALTH international Forum in Barcelona on 21-22 May 2014 as one of the "Innovation Capsules". In addition, it was chosen as one of the top ten ideas submitted to the 4th edition of Valortec, a contest run by ACC1Ó to support the commercialization process of technology-based innovations. As a result, the team was coached by a group of experts at the end of 2014 to prepare their business case with the help of the Knowledge Exchange Unit.

Bringing a new antimicrobial agent to the fore

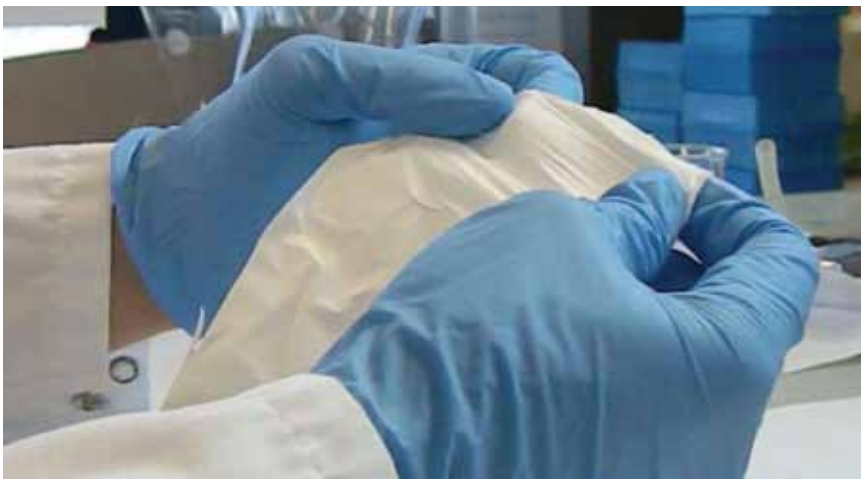
A fruitful collaboration between the Institute for Research in Biomedicine (IRB Barcelona) and IBEC has resulted in a potential new antimicrobial agent. Using a chemical library Fernando Albericio's lab at the IRB and the Bacterial Infections: Antimicrobial Therapies group (page 108) synthesized and tested their molecules on a variety of microorganisms, finding potent activity against key microorganisms and complex microbial structures as biofilms, with low toxicity profiles. These findings may open the way for new antibacterial therapies against chronic bacterial infections, which Eduard has studied for more than ten years.

The invention was analysed by the Knowledge Exchange Unit, and protection was filed on 30th January 2014 (EP14382032.2). A joint ownership agreement between IRB and IBEC has been signed, and now both institutes are working to establish contacts with industry, as a private-public partnership has been deemed the most convenient way to develop the promising candidates further.

A step closer to market for MicroGradientPage

August 2014 saw the kick-off of Xavier Trepat's (page 112) project, "MicroGradient-Page: Micro Gradient polyacrylamide Gels for High Throughput Electrophoresis Analysis", which is funded by an ERC Proof of Concept grant. With Raimon Sunyer as executive leader, this improved method for the preparation of miniaturized polyacrylamide gels goes a step further by taking pre-existing standard

Dermoglass, developed in the Biomaterials for Regenerative Therapies group (page 47)



methods and adding several improvements including high throughput, low cost and efficacy. MicroGradientPage will soon proceed to a prototype stage for more testing.

Industrial property related to MicroGradientPage is being evaluated for protection in order to ensure freedom to operate. The exploitation plan to be elaborated – a collaboration of the researchers, the Knowledge Exchange Unit and external consultants – is a key deliverable from the project. Analysis of the global scenario, including competitors and market opportunities, plus recruiting feedback from the final users will define the possible products.

THERALIGHT: From frontier science to drug development

ERC Proof of Concept funding in 2013-2014 has allowed Pau Gorostiza's group (page 60) to demonstrate that drugs can display enhanced therapeutic effects and reduced side effects by means of remote regulation of their activity with light. Light-regulated bioactive ligands of G protein-coupled receptors (GPCRs) identified through the OpticalBullet project, funded by his ERC Starting Grant, were candidates for animal tests and for the identification of biomedical applications where light regulation can provide a competitive advantage. The compound Alloswitch-1 (S. Pittolo *et al.*, 2014, *Nature Chemical Biology*), a negative allosteric modulator (NAM) of mGluR5 with indications in Parkinson's disease, displayed outstanding advantages *in vitro*.

The project has been centred on a complete characterization of Alloswitch-1, with results including satisfactory pharmacological profiles *in vitro* and *in vivo* (oral bioavailability). *In vivo* assays using an established rat model proved that Alloswitch-1 produced effects comparable to mild mGlu5 NAMs, but it has not been possible to achieve a robust opto-regulation. However, Alloswitch-1 has been established as a compound with interesting commercial properties, a large medicinal chemistry space for lead optimization, and sufficient protection for exploitation purposes (PCT filed on 27th September 2013).

Obra Social "la Caixa": Finalising the SRIs

2014 was the final year of the Strategic Research Initiatives (SRIs) programme, funded by Obra Social "La Caixa". The SRIs boosted multidisciplinary collaborations across the institute with the aim of yielding new tools for biomedical research and clinical practice. The programme included four SRIs, whose most significant outputs include:

- **CellNanoMech Cell mechanobiology: from nanoscale mechanisms to early diagnostic strategies**
  The translation of mechanobiology approaches to improve clinical research in cancer, particularly breast cancer (Elosegui-Artola *et al.*, 2014, *Nature Materials*), as well as to respiratory diseases. MicroGradientPage (see left) is a by-product of the developed techniques.

- **MyoPatch Bioengineering functional human myocardial tissue**
  In the framework of the quest for a biomimetic experimental model of physiologically-competent, mature myocardium, a new electromechanical platform to mature cells has been developed.

- **NanoLabPath Nano-bio-info platform for pathogen detection and diagnosis**
  Set up of the joint unit with Genomica (page 132), as well as promising results:

  Van Heirstraeten, L. *et al* (2014). Integrated DNA and RNA extraction and purification on an automated microfluidic cassette from bacterial and viral pathogens causing community-acquired lower respiratory tract infections. *Lab on a Chip* 149, 1519-1526

  Rigat-Brugarolas, L. G. *et al* (2014). A functional microengineered model of the human splenon-on-a-chip. *Lab on a Chip* 1410, 1715-1724

  Mir, M., Lugo, R., Tahirbegi, I. B., Samitier, J., (2014). Miniaturizable ion-selective arrays based on highly stable polymer membranes for biomedical applications. *Sensors* 147, 11844-11854

- **NeuroMEMs NeuroBiotechnology for Regenerative Neuroscience**
  Development of novel devices to enable neurobiology research such as a 3D biomimetic model for nerve cells (Tong, Z. *et al*, 2014, *RSC Advances*, 4 (97): 54788-54797). The platform has been used to study the mechanisms of action and potential improvement of olfactory ensheathing cells based therapy for spinal cord lesion. (Reginensi, D. *et al.*, 2015, *Cell Mol Life Sci.*)

Clinical Translation

IBEC counts on the collaboration of medical doctors to provide input on the clinical aspects of its research, so that results are easily extended to clinical practice. In this way, IBEC benefits from its privileged position as technological counterpart of the major hospitals in the Barcelona area, four of which (Hospital Clínic, Sant Pau, HSCSP and Bellvitge) are recognized as Biomedical Research Institutes of Excellence by the Spanish government. IBEC's framework agreements and collaborations with these nearby hospitals allow easy access to clinical samples and patients.

BIOTENDON's road to preclinical assays

A research project which was awarded funding under the RecerCaixa programme in 2013, BIOTENDON, is a collaboration between IBEC's Biomaterials for Regenerative Therapies group and clinicians from the Hospital Terrassa. The project aims to create a new nanofibrous polymeric scaffold with the appropriate biological signals and committed tendon cells to help surgeons repair rotator cuff tears in the tendons or muscles of the shoulder.

This joint research is framed under a collaborative project agreement signed in January 2014, with the objective of performing *in vitro* tests including characterization, optimization and functionalization of the device, as well as validation assays to assess the efficacy of the medical device in *in vivo* tendon models. The close collaboration between researchers and clinicians will ensure that the product developed by BIOTENDON meets clinical needs and represents a substantial benefit for the huge amount of elderly patients suffering from rotator cuff tears. If successful, the project will create a marketable medical device that can improve the healing process and avoid the usual problem of re-ruptures, a typical problem when a tear is bigger than 2.5cm in length. In addition, the device will be able to be used in other tears on the body, such as the Achilles tendon.

Robotics rehabilitation for children

Existing devices used in physiotherapy and rehabilitation which reproduce walking patterns in patients using robotic systems are currently limited to rehabilitation centres, since they are extremely expensive, are impractical for personal use at home; they also tend to be addressed specifically to adults. A project involving IBEC's Robotics group (page 42) and Hospital Sant Joan de Déu in Barcelona and funded by the RecerCaixa Programme started in 2014 focused on the development and evaluation of a robotic system based on a standard treadmill that works in a similar way to the current complex robotic systems found in rehabilitation centres, but which can be adapted to patients of any size and needs, and used in the home. The treadmill will have a motorized handle that lets the patient control the degree of support on the belt, and two retractable arms that help make controlled walking movements just by holding the patient's feet.

The platform will also be useful for research into the effects of rehabilitation robotics on patients' progress, with physiological sensors that estimate the degree of fatigue and the need to adapt the therapy at any time. The system will also be equipped with visual feedback to motivate and stimulate the patient, and the design of the equipment would not only be adaptable to children but also to the elderly.

IBEC-TCUB: Synergies in regenerative medicine

IBEC and the University of Barcelona, through its Cell Therapy programme (TCUB), signed an agreement in 2014 to join forces regarding research in bioengineering and regenerative medicine in order to develop advanced therapies, including tissue engineering and stem cell-based therapeutic products. IBEC's capabilities in translational research will be enhanced with the creation of "mixed" research teams in the areas of reference. TCUB is the first "pilot plant" for Advanced Therapies (cell, gene) in Catalonia.

The first consequence of the agreement is the preferential access that IBEC research groups will gain to the TCUB's equipment and expertise. This scientific facility is located at the central building of the UB's Faculty of Medicine at Hospital Clínic. TCUB boasts an area of 300m^2, with two rooms with cell cultures for preclinical research on human stem cells, including pluripotent stem cells.

TCUP is completed by a Good Manufacturing Practice (GMP) unit, comprising three equipped clean rooms, providing the right conditions for the standardization of protocols and procedures. The Unit's services are perfect for early-phase clinical trials.

VHIR-IBEC alliance in Infectious Diseases

Eduard Torrents' Bacterial Infections: Antimicrobial Therapy group (page 108) has signed a close collaboration agreement with Vall d'Hebron Institut de Recerca (VHIR)'s Infectious Diseases group, as a result of synergies being identified since the institutional Memorandum of Understanding between the two centres started in May 2012.

The group's research has proved to complement that of the lab led by Drs Albert Pahissa and Joan Gavaldà at VHIR, offering much potential for collaboration. While the IBEC group is interested in different bioengineering approaches to elucidate ways to diagnose and eradicate multi-drug resistant bacteria, the VHIR group focuses on community-acquired and nosohusial infections, HIV, and tropical or traveller diseases, driven by daily clinical practice. This combination is expected to bridge the gap between fundamental microbiological knowledge and making new therapies available to patients.

The agreement between the two groups is a forward step for IBEC in fulfilling its mission to forge links with clinicians and bring its health-related research results closer to patients. For both sides, the close collaboration will accelerate the development of activities and maximise the use of resources – such as scientific equipment at IBEC being made available to the clinicians – and knowledge-sharing.

Working together against respiratory diseases

A joint research Unit between IBEC and Hospital Universitari Germans Trias i Pujol (IGTP) is coordinated by Raimon Jané, head of IBEC's Biomedical Signal Processing and Interpretation group (page 64), and the hospital's Miquel Àngel Gasull.

In 2013, the Joint Research Unit developed a collaborative project in respiratory sound analysis. The clinicians performed experiments with patients with asthma and other respiratory diseases, while advanced signal interpretation techniques developed by IBEC's group improved the capability of early diagnosis in these kinds of diseases. This study crystallized in the *PLOS One* paper "Detecting Unilateral Phrenic Paralysis by Acoustic Respiratory Analysis" published in April 2014, where their non-invasive methodology to assess respiratory function is shown to be able to reinforce the reliability of the diagnosis and monitoring of these patients.

They also developed a new method to evaluate the signals produced by the respiratory muscles to detect and quantify the level of muscular weakness caused by pathologies such as COPD. The study was conducted in the hospital's Respiratory Function Laboratory.

Eduard Torrents (centre) and Joan Gavaldà at VHIR

Events and Communications

140 Events and meetings in 2014

144 IBEC Seminars and PhD Discussions

146 Outreach activities in 2014

150 Media coverage in 2014

Events and meetings in 2014

Throughout the year

Institutional and scientific projects

Throughout the year, IBEC hosts meetings for the consortia of its ongoing institutional and scientific projects.

February

■ 7 February

Reunió de l'Assemblea General Ordinària ACER

The Associació Catalana d'Entitats de Recerca (ACER) held its General Assembly at IBEC in February. Forty representatives of the ACER partners were in attendance. The assembly comprised a comprehensive review of ACER's activities in recent months.

■ 18-19 February

Training sessions in Leadership and Management Skills

Nine group leaders and heads of unit took part in a training course organised by the Human Resources Unit to help fulfil their leadership roles.

■ 19 February

Innolife Executive Committee meeting

The Executive Committee of InnoLife, a consortium of 144 European companies, research institutes and universities, met in the run-up to sending their proposal for the EIT's Knowledge and Innovation Community (KIC) on healthy living and active ageing. In May there were meetings of the constitution and the communication working group, also held at IBEC.

Below: 'Café amb la Recerca' in May

At the end of 2014, the partners – which as well as IBEC include INSERM (France), Imperial College (UK), Roche, Siemens and Philips – were to discover that their proposal had been successful, and that Innolife (now known as EIT Health) had been selected as the new KIC.

March

■ 11-13 March

Oral Presentation Skills in English course

Eleven first- and second-year PhD students took part in an intermediate course – "Say it so it stays" – to improve their competence and confidence in presenting in English at scientific conferences. In April and May, there were similar courses given at a more advanced level for older students and first- and second -year postdocs ("Progressing towards proficiency").

■ 13 March

Fira d'Empreses

This careers fair, organized by the University of Barcelona's physics and chemistry faculties, helps undergraduate students of these subjects to find out more about potential employers or furthering their studies, as well as improving the university's relations with the business sector. IBEC attended the fair to offer university leavers advice and information about continuing their career at the institute as masters or PhD students.

April

■ 23 April

La justificació financera en els projectes d'Horitzó 2020

Fifty participants attended an informative session organised by AGAUR that gave a practical overview of the financial aspects governing Horizon 2020. Aimed at researchers, managers and companies interested in participating in projects funded by the programme, the session was given by CET Auditores S.L., who have issued more than 2,400 financial certificates for projects under the EC's 6th and 7th Framework Programmes.

May

■ 15 May

Cafè amb la Recerca

Together with the Institute for Research in Biomedicine (IRB), IBEC took part in the inaugural event of the Catalan Foundation for Research and Innovation (FCRI)'s 'Café amb la Recerca' initiative, which was held at IBEC. Josep Samitier, director of IBEC, and Joan Guinovart, director of IRB, presented their research at the pilot episode of the scheme, which aims to provide a friendly meeting point for research organizations, businesses and investors to get together and identify ways to collaborate. The business people in attendance came from companies such as AXA, Reig-Jofre, Nature Bisse, Semillas Fitó, Damm, Lipotec, Lucta and AB Médica Grup, among others.

June

■ 5 June

International Course on Tissue Banking and Advanced Therapies

Organised by the TPM-DTI Foundation, this course covered tissue banking and cell donation in compliance with the agreed professional requirements, a tour of IBEC's facilities, and talks by IBEC researchers Josep Samitier, Daniel Navajas, Elisabeth Engel and Elena Martínez. 37 international participants benefitted from the day.

■ 30 June

'Interrogations at the Biointerface' Advanced Summer School

24 young researchers from Spain, Italy, Portugal and even further afield were at IBEC to learn about the state-of-the-art of stem cell research and regenerative medicine, as well as learning some essential lab techniques, in the fourth "Interrogations at the Biointerface" Advanced Summer School. The Summer

School, which is co-organised annually by IBEC, the Instituto de Engenharia Biomédica (INEB) and the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUB), both in Portugal, features a stellar line-up of speakers for three days and then introduces PhD students and early post-docs to advanced experimental techniques for a day. Speakers at the lectures preceding the lab sessions – which were also open to general attendees – included Kevin Healy (University of California at Berkeley), Matthias Lütolf (EPFL), Michel Puceat (INSERM), and Wolfram-Hubertus Zimmermann (Institute of Pharmacology in Goettingen, Germany), as well as IBEC's own Pere Roca-Cusachs.

July

■ 9 July

Basic Concepts in Image J for Image Analysis and Quantification

24 PhD students, masters students and postdocs enjoyed a course on ImageJ, the scientific image processing software, given by junior group leader Pere Roca-Cusachs. The course was jointly organised by IBEC's PhD Committee and aimed to help participants achieve basic skills in the analysis and quantification of microscopy images using the program.

September

■ 10 September

Emotional Management on Stage

Twelve participants explored how to manage their physical, emotional and personal skills during public presentations, getting tools and tips to boost self-confidence and improve body language and self-expression.

■ 29 September

7th IBEC Symposium

IBEC's 7th Symposium welcomed most of the institute's staff and scientists, its ISC members, and many visitors for the day-long event on 'Bioengineering for Future Medicine'. It was the first time that the annual symposium has had one of the institute's three main areas of application as its theme. The speakers and flash presentations reflected the fact that IBEC's many diverse areas of research are united in their quest to help make personalised medicine, hand-held diagnostic platforms, wearable monitoring devices and other technological advances a reality.

This year, a new addition to the programme was the Innovation and Clinical Translation session, in which Santiago Marco presented the latest news on his group's project to develop a driver drowsiness detector with FICOSA, including some useful tips about working with industry. Luís Rigat (Nanobioengineering) and Anita Kosmalska (Cellular and respiratory biomechanics) were the winners of the best flash presentation and poster awards.

Poster session at the 7th IBEC Symposium

CASEIB 2014

October

■ 15 October/20-23-27 and 29 October

Scientific Writing courses

"An introductory course in scientific writing" for 15 first- and second-year PhD students and masters students took place in mid October. Later in the month, eleven third and fourth-years students took the intermediate level entitled "How to write clearly and efficiently", which covered the goals of research publishing, psychological barriers to effective communication, and the purpose and motivation behind each part of a manuscript.

November

■ 13 November

ACER 'Escola de Tardor'

ACER's 4th autumn school dealt with open access in scientific research. Lluís Anglada, director of Libraries, Information and Documentation at the Consorci Serveis Universitaris de Catalunya gave a talk entitled "Open Access: The new paradigm of publishing".

■ 18 November

NanoBioMed2014

The NanoBio&Med 2014 international conference, co-organised and sponsored by IBEC, took place at the UB's Faculty of Medicine. The four-day event aimed to cover current research and recent developments in the fields of nanobiotechnology and nanomedicine. IBEC director Josep Samitier and researchers Anna Lagunas, Pau Gorostiza, Mateu Pla, Luis Rigat, Roberto Paoli and Daniel Navajas were among the contributors, and the institute was present with an information stand.

■ 26-27-28 November

CASEIB 2014

The annual congress of the Sociedad Española de Ingeniería Biomédica (CASEIB 2014) was organized by IBEC at Barcelona's CosmoCaixa museum, as Biomedical Signal Processing and Interpretation group leader Raimon Jané (page 64) is SEIB's president. CASEIB 2014 is a forum for scientists, industry professionals and biomedical and clinical engineers interested in learning about and discussing the research, education, and clinical and industrial applications in the field of biomedical engineering. 130 people attended this year's meeting.

December

■ 18 December

Christmas celebration

A salsa lesson was on the agenda at the 2014 IBEC Christmas celebration, which was attended by most of IBEC's staff and researchers.

IBEC Seminars and PhD Discussions Sessions

Throughout the year, international experts, scientists who work with our research teams on certain projects, and some of the IBEC group leaders are invited to give lectures as part of the IBEC Seminars programme. The aim of these events is to provide an overview of the state-of-the-art research in various fields and to give the audience the opportunity to discuss recent developments with the guest speakers.

In addition, the PhD Discussions Sessions are intended to encourage the participation of PhD students, providing a forum where they can present the results of their research and discuss it with fellow students and researchers. Throughout 2014, four PhD students presented their work in these sessions. Additionally, in order to help IBEC students in their career development and provide them with additional skills, an invited speaker gave a lectures on Reference Management Software.

■ 17 January

Carlos Torrens
Head of Shoulder Surgery Unit, Department of Orthopedics, Hospital del Mar, Barcelona / Associate Professor, Faculty of Medicine
Shoulder joint. Common pathologies and their biomechanical implications

■ 7 February

Jérôme Noailly
IBEC, Biomechanics and mechanobiology (page 88)
Numerical explorations of cause-and-effect relationships in the functional regulation and diseases of the musculoskeletal system: a focus on the spine

■ 7 March

Raúl Pérez-Jiménez
Nanobiomechanics Group, CIC nanoGUNE/ Ikerbasque Foundation for Science
Molecular nanomechanics in human health

■ 14 March

Samuel Sánchez
Max Planck for Intelligent Systems, Stuttgart, Germany
Smart nano-bio-devices in nanorobotics and nano-bio-engineering

■ 18 March

Mustafa Suphi Erden
Learning Algorithms and Systems Laboratory, Ecole Polytechnique Fédérale de Lausanne, Switzerland
Skill identification and closed-loop robotic assistance for fine manipulation tasks

■ 4 April

Elisabeth Engel
IBEC, Biomaterials for regenerative therapies (page 47)
Instructive biomaterials for regenerative medicine

■ 11 April

Fàtima Bosch
Center of Animal Biotechnology and Gene Therapy and Department of Biochemistry and Molecular Biology, School of Veterinary Medicine, Universitat Autònoma de Barcelona
Towards a Gene Therapy for Neurological and Somatic MPSIIIA

■ 14 May

Matt Cooper
Institute for Molecular Bioscience · The University of Queensland
The biophysics of drug action and biosensor design

■ 22 May

Marco Arrigoni
Director of Marketing - Coherent
From in-vivo imaging to all-optical physiology: new ultrafast lasers allow to image deeper and excite more fluorescent probes with finer control.

■ 23 May

Jordi Alcaraz
Faculty of Medicina, UB
Translational biomechanics in lung fibrosis and cancer

■ 29 May

Mª Arrate Muñoz Barrutia
Staff Scientist, Center for Applied Medical Research of the University of Navarra, Pamplona, Spain
Associate Professor, Engineering School, University of Navarra (TECNUN), San Sebastián, Spain
About lung cancer: A multi-level image-based perspective

■ 6 June

José Manuel García-Aznar
University of Zaragoza, Aragón Institute of Engineering Research, Dept. of Mechanical Engineering, Zaragoza (Spain)
Exploring some mechanical mechanisms underlying cell migration: a numerical approach

■ 13 June

Conxita Solans
Institut de Química Avançada de Catalunya (IQAC) del Consell Superior d'investigacions Científiques (CSIC)
The key role of surfactant self-assemblies in the development of advanced drug delivery systems

■ 13 June

Ignacio Casuso
INSERM, Lab for biological AFM, Marseille
Protein interactions by High Speed Atomic Force Microscope

■ 20 June

Ismael Díez Pérez
Physical Chemistry Department, University of Barcelona/Nanoprobes and Nanoswitches group, IBEC (page 60)
Charge Transport in Single-Molecule Wires: from synthetic to biological backbones

■ 11 July

Esther Vázquez
Institut de Biotecnologia i de Biomedicina, Universitat Autònoma de Barcelona/ CIBER-BBN/Department de Genètica i de Microbiologia, UAB
Building versatile therapeutic vehicles by self-assembled recombinant proteins in a fully de novo design strategy

■ 22 July

Dimitrije Stamenovic
Boston University
Biomechanical imaging: mapping cell stiffness and prestress with subcellular resolution

■ 19 September

Tatiana Coelho-Sampaio
IBEC/Institute of Biomedical Sciences, Federal University of Rio de Janeiro
Ordinary laminin or polymerized laminin? Why does it matter for nervous system regeneration and bioengineering.

■ 10 October

Josep Maria Canals
Facultat de Medicina, Universitat de Barcelona
Advanced therapies to solve unmet medical needs, Cell therapy program at the University of Barcelona

■ 16 October

Vladimir Baulin
Universitat Rovira i Virgili (URV), Tarragona, Spain
Membrane activity of biomolecules due to shape and size variation

■ 24 October

Guillaume Charras
London Centre for Nanotechnology and Department of Cell and Developmental Biology, University College London, UK
Short and long time-scale rheology in suspended monolayers

■ 5 December

Filip Meysman
Royal Netherlands Institute of Sea Research/ Department of Analytical, Environmental and Geo-Chemistry, Vrije Universiteit Brussel
A new record in biological electricity: filamentous bacteria transport electrons over centimeter-scale distances

■ 11 December

Malgorzata Lewandowska
Warsaw University of Technology, Poland
Physicochemical characterization and in vitro degradation of hybrid PLA nanofibres/ bioactive glass nanoparticles scaffolds for bone tissue engineering applications

■ 12 December

Salvador Aznar Benitah
ICREA Researcher, Head of stem cells and cancer laboratory, IRB Barcelona
Spatiotemporal regulation of adult stem cells *in homeostasis, ageing, and cancer*

Outreach activities in 2014

Throughout the year

Group visits

Throughout the year, several groups of students from high schools in Barcelona and Catalonia visited IBEC: Escola Natzaret on 20th February (32 participants), Escola Suissa de Barcelona on 18th March (17 participants), Escola Roig Tessàlia on 10th April (23 participants), and Escola Miquel Martí i Pol on 24th April (20 participants).

Three organizations from outside the area also visited IBEC during 2014: Cambridge University and Ikast-Brande Gymnasium, Denmark, on 20th March (12 + 50 participants) and the University College for Bachelors in Biotechnology, Belgium, on 11th June (23 participants).

ESCOLAB

Every year, IBEC takes part in the ESCOLAB initiative of the City Council of Barcelona, which introduces groups high school students into the city's research laboratories to encourage scientific vocation.

In 2014 IBEC welcomed three groups of students to the institute as part of ESCOLAB: a group of 17 from Escola Sant Josep Teresianes on 5th March; 20 from Escola Monlau on 2nd April; and 24 more from the same school on 10th December.

IBEC Researchers from the Nanobioengineering, Bacterial Infections: Antimicrobial Therapies (page 108), Cellular and Respiratory Biomechanics (page 82), Signal and Information Processing for Sensing Systems (page 74), Robotics (page 42), Nanobioengineering (page 103), and Biomaterials for Regenerative Therapies (page 47) groups contributed to the group or ESCOLAB visits with talks or activities.

Entrevistas de Bachillerato

An initiative at IBEC to help nurture the scientific minds of the future, the Entrevistas de Bachillerato, pairs high school students with IBEC PhD students to talk about subjects such as nanotechnology for the

Students from Barcelona's Escuela Suiza during their visit to IBEC

Generalitat representatives and teachers visiting IBEC at the 'Presentació del Programa de Competències Científiques' in April

pupils' final baccalaureate work. Five such one-to-one encounters took place throughout 2014, with IBEC's young researchers from the Nanobioengineering (page 103), Robotics (page 42), Biomaterials for Regenerative Therapies (page 47) and Molecular and Cellular Neurobiotechnology (page 98) groups resolving questions and doubts and sharing new ideas to help with the school projects.

Recerca a Secundària

The initiative Recerca a Secundària is addressed to 16-year-olds who are about to begin their research projects at school. This scheme offers these students the opportunity to be assessed by a tutor from the Parc Científic de Barcelona (PCB). During the year, the tutor gives advice on recommended reading, and students are also offered the chance to gain hands-on experience in their laboratory. In 2014 IBEC researchers Alexandre Casadevall, Andy Olivares, Irene Cano, Juan Pablo Téllez and Mirella Picazo took part, tutoring a total of 14 students.

February

■ 5 February

Course for STEM teachers

Fourteen university teachers from the fields of science, technology, engineering, and mathematics (STEM) took part in a course held at IBEC on "Biomaterials: new materials fro regenerative therapies" in an initiative organised alongside the Generalitat's Education Department.

April

■ 7 April

Generalitat's education event held at IBEC

IBEC welcomed members of the Generalitat's Department of Education and about 150 teachers through its doors in April, when the Department held its event 'Presentació del Programa de Competències Científiques' in a research institute for the first time.

The visitors, who included the Consellera d'Ensenyament Irene Rigau, enjoyed demonstrations and explanations about IBEC's research in biomaterials and robotics and the Nanotechnology Platform at a 'mini-fair' of stands manned by IBEC researchers, as well as visits to the labs in the Helix.

Afterwards they headed into the PCB's Auditori Antoni Caparrós for the conference, during which representatives from the government's Ordenació Curricular (Curriculum Planning) department presented support tools that help students to solve problems using scientific and technical knowledge, as well as mastering the processes of scientific and technological activity, to teachers. It included a talk by IBEC Director Josep Samitier entitled 'La nanotecnologia aplicada a la medicina'.

■ 8 April

Fira Recerca en Directe

The 'Live Research' fair at Barcelona's La Pedrera is organized by the Parc Científic de Barcelona (PCB) with the support of the Obra Social CatalunyaCaixa. It aims to present research to the general public, with researchers demonstrating and explaining their methods and goals in an accessible way. This year the Integrative Cell and Tissue Dynamics group (page 112) gave their time and expertise at the fair.

May

■ 7 and 9 May

Professors i Ciència course

IBEC was one of the 13 research centres to be chosen to take part in Fundació Catalunya–La Pedrera's 2014 edition of Professors i Ciència, an excellence programme for the specialized training for secondary school science teachers.

The foundation elected some of Catalonia's leading research centres and institutes to take part in the programme, which will provide an opportunity for about 230 teachers to receive specific training on various subjects to take back to the classroom within the research centres. IBEC's six-hour course, "Una finestra al desenvolupament embrionari del sistema nerviós", was held in May, and was run by Vanessa Gil and Ariadna Pérez, researchers from José Antonio del Río's Molecular and Cellular Neurobiotechnology group (page 98).

June

■ 14-15 June

Festa de la Ciència 2014

IBEC took part for the third time in the council-organised Festival Ciència, Tecnologia i Innovació – formerly known as the Festa de la Ciència – in Barcelona's Parc de la Ciutadella. The event was founded in 2007 to showcase the science being done in the city's universities, research centres and technology companies via exhibitions, talks and demonstrations. Since then it has grown into an extensive program of activities for all ages, transforming Barcelona into a 'giant laboratory' for the general public to do experiments.

Elisabet Martí from the Nanomalaria group (page 52) and Rosa Letizia Zaffino from Nanobioengineering (page 103) teamed up with IrsiCaixa, coordinators of the EU project NanOpinion, to man the Mobile Station in the Espai Glorieta. This eye-catching installation featured examples of products that use nanotechnologies – such as a hydrophobic shirt, a water bottle to purify water, and waterproofing sprays – as well as questionnaires to fill in about public opinions about nanotechnology, and multimedia information materials.

Laura Casares (pictured left) and Pilar Rodríguez of the Integrative Cell and Tissue Dynamics group (page 112) conducted interactive experiments that demonstrate the transmission of forces between cells during migration, and how to measure them. This event, "Les cèl·lules fan força!", was organized by the Parc Cientific de Barcelona and took place in the Darwin tent.

■ 17 June

Nanopinion workshop

In a collaboration with IrsiCaixa's Unit of Public Engagement on Health Research, IBEC gave a workshop as part of the European project "NanOpinion", which aims to monitor public opinion on nanotechnology, paying special attention to public education.

November

■ 22 November

Launch of exhibition at Sant Feliu de Guíxols

Saturday saw the inauguration of the exhibition "Curar-se en salut" at the Museu d'Història de Sant Feliu de Guíxols, an initiative of the town's council with the involvement of two CERCA centres, IBEC and Girona's Institut d'Investigació Biomèdica (IDIBGi), among other bodies. The vice-president of the Government of Catalonia, Joana Ortega i Alemany, and Minister of Health Boi Ruiz i Garcia were in attendance at the unveiling. The exhibition travels through the past, present and future of health and medicine via several thematic areas. It presents heath as something to be treasured, pays tribute to the work of health professionals and scientific advances, and explores the ways in which citizens can have a level of responsibility for their own health.

As well as looking back at eras when healthcare was not so accessible as now, the exhibition also looks forward to the future of medicine, which is the part in which IBEC has contributed. The 'Medicine of the Future' section presents some of the various small-scale diagnostic devices developed at IBEC, as well as its research into areas such as nanocapsules for drug delivery, and the concept of personalised medicine.

■ 26 November

Nit de la recerca

A first for outreach in 2014 was IBEC's participation in La Nit de la Recerca on 26th September. The 'night of research' is organized by the European Commission in collaboration with a range of public and private institutions, and offers a programme of science-related activities. The IBEC contributors were Luís Rigat and Roberto Paoli from the Nanobioengineering group (page 103), who contributed with face-to-face interview sessions to explain what being a scientist is really like, and a poster about organs on a chip.

Launch of the exhibition "Curar-se en salut" at the Museu d'Història de Sant Feliu de Guíxols

Selected media coverage in 2014

■ 16 January

La Vanguardia

"Ángel Raya, nou director del centre"

La Vanguardia published a special report about IBEC group leader Ángel Raya (page 92) taking over as director at Barcelona's Centro de Medicina Regenerativa (CMRB).

■ 6 February

La Vanguardia

"El consejo europeo de investigación otorga dos nuevas distinciones a Cataluña"

The news about Xavier Trepat's (page 112) Proof of Concept grant from the ERC appeared in *La Vanguardia*.

■ 24 February

ABC

"Un nuevo método facilitará el manejo de la EPOC"

The press release about the Biomedical Signal Processing and Interpretation group's new non-invasive method to monitor patients with respiratory diseases was covered in the health section of Spanish national daily newspaper *ABC*.

La Vanguardia supplement, March 2014

■ 18 March

RTVE and others

"Crean en España el primer bazo dentro de un chip capaz de actuar como este órgano humano"

The press release about the design of the first-ever functional 3D splenon capable of reproducing the function of the spleen, which is to filter red blood cells (page 15), by researchers from IBEC and CRESIB received lots of media coverage.

■ 23 March

La Vanguardia

"Buenos días, robot"

IBEC group leaders Alícia Casals (page 42) and Santiago Marco (page 74) featured in a Sunday supplement about robots in *La Vanguardia*.

The article discussed how living with robots is no longer science fiction, and how increasing interaction with robots in public and private could impact our working and personal relationships. The journalist mentioned the work done by Santiago on olfactory robots, and quoted Alícia on her work and on the subject of robotics advances in general.

■ 23 March

La Vanguardia (Diners)

"Catalunya i els ajuts Proof of Concept"

A *La Vanguardia* article about the ERC Proof of Concept grants awarded in Catalonia featured that of IBEC group leader Xavier Trepat (page 112).

■ 7 April

El Periódico de Catalunya

“La ciencia avanza hacia fármacos que se activan cuando les da la luz”

An *El Periódico* article about and interview with Pau Gorostiza (page 60) on his work on light-activated drugs.

■ 8 April

Diari de Girona

“Ensenyament introdueix noves competències en ciència i tecnologia”

Diari de Girona coverage of the visit of the Generalitat’s Department of Education, including Consellera d’Ensenyament Irene Rigau, and about 150 teachers to the PCB for their event ‘Presentació del Programa de Competències Científiques’ (see page 9).

■ 15 April

El Mundo (Innovadores)

“Laboratorio en un chip”

An article in *El Mundo* presented the development at IBEC, the UB and Biokit S.A. of a miniature diagnostic platform for respiratory infections such as pneumonia and infectious bronchitis.

■ 5 May

ABC and others

“Descubren cómo se endurece el tejido en el cáncer de mama”

Alberto Elosegui and Pere Roca-Cusachs’ *Nature Materials* paper (page 17) got lots of press coverage in newspapers, TV and radio (*ARA, El Periódico, El Punt Avui, La Razón, La Vanguardia, Diario Médico, El País,* etc). In the study, they describe for the first time how mammary cells detect tissue stiffening, which is key to the development of breast cancer. The publication’s visibility was boosted by a well-attended press conference at Barcelona’s Palau Macaya, which was organized jointly with the Obra Social “la Caixa”, which supported the work in part.


Sociedad

La ciencia avanza hacia fármacos que se activan cuando les da la luz

Cromosoma

Pau Gorostiza in *El Periódico*

■ 3 June

El Mundo (Innovadores)

“El físico que innova en biología”

Integrative cell and tissue dynamics group leader Xavier Trepat (page 112) was profiled in *El Mundo*’s ‘Innovadores’ supplement. In the interview, which introduced him as a scientist “off the charts”, he talked about his move from a physics background to looking at biological questions, and how his three ERC grants helped him to compete in difficult times and attract the best talent.

■ 11 June

El Mundo (Innovadores)

“Ingenieros en ciencias de la vida”

In an *El Mundo* article dedicated to IBEC, the newspaper discusses the lines of investigation at the institute that lead to the realisation of the three areas of application of bioengineering: future medicine, regenerative therapies and active ageing.


INNOVADORES

Qué gusto de premiado

El físico que innova en biología

Xavier Trepat in *El Mundo*

■ 16 June

El Mundo

"Democratizar la ciencia, acercar la nanotecnología"

On 16 June *El Mundo* published an article about Barcelona's Festa al Parc de la Ciutadella, specifically about the NanOpinion Mobile Station which was co-organised by IBEC and IrsiCaixa, as well as the nanotechnology workshop held at IBEC the following day.

■ 20 June

El Punt Avui

"Enginyeria biomèdica al museu guixolenc"

An article in *El Punt Avui* about the new museum exhibition on the history of health and medicine in Catalunya, "Curar-se en salut", at Sant Feliu de Guíxols' Museu d'Història, a joint initiative with IBEC.

■ 30 June

La Xarxa

"Implants per autoregenerar el cervell"

The Biomaterials for Regenerative Therapies group (page 47) appeared on science programme 'El problema de Gettier'. Junior group leader Elisabeth Engel talks about the group's development of a tuned implant that could aid the regeneration of brain tissue, particularly in cases of pre- and postnatal injury. Made by La Xarxa, the programme is broadcast on various regional TV channels at different times.

■ 7 July

Gaceta Médica

"PrP^{c}, sobreexpresada en las fases asintomáticas de EA"

A *Gaceta Médica* article about a study published in Molecular Neurobiology, in which Molecular and Cellular Neurobiotechnology group (page 98) researchers reveal that our nervous system's naturally protective response to the onset of Alzheimer's may contribute to the fact that patients do not suffer memory loss until the disease has progressed further.

■ 8 July

Diario Medico

"Hallada la vía que regula la migración de células de la capa I en el córtex"

A *Diario Médico* article about the study published in *Nature Communications* by the Molecular and Cellular Neurobiotechnology group (page 98) on the existence of a signaling molecule, Semaphorin 3E (Sema3E), which, by joining PlexinD1 (its specific receptor present in Cajal-Retzius cells) is able to modulate the action of the CXCL12 / CXCR4 system.

■ 4 August

La Vanguardia

"Los científicos descubren cómo las células del cuerpo humano curan las heridas"

The news about the Integrative Cell and Tissue Dynamics group's (page 112) paper in *Nature Physics* was covered in *La Vanguardia*.

■ 13 November

Televisió L'H

"Pessics de ciència"

Miguel Angel Mateos from the Biomaterials for Regenerative Therapies group (page 47) was interviewed for Televisió L'Hospitalet after his participation in this year's Setmana de la Ciència, for which he gave a talk entitled "Regeneració de teixits : com nou" at the Centre Cultural Sant Josep on Wednesday.

■ 14 November

El Mundo (Innovadores) and others

"Un robot capaz de transportar fármacos a una célula cancerígena, mejor innovación del año"

Samuel Sánchez, who will join IBEC as a new group leader in January 2015, has been awarded the title 'Innovador del año' by *MIT Technology Review*, the best of their 10 selected "Innovadores menores de 35 España 2014", for his pioneering contributions in the field of micro- and nanomotors, such as self-propelled nanorobots for biosensing applications. He featured in articles and interviews in *La Vanguardia, El Confidencial, El Mundo,* Antena3, RAC1 and more.

■ 7 December

La Vanguardia (Dinero)

"Quirófanos asistidos por un robot"

La Vanguardia reported that Rob Surgical Systems, the IBEC/UPC spin-off company, started validating its Bitrack Surgical Robot System for minimally invasive laparoscopic surgery.Aiming to address the current shortcomings of laparoscopic surgery, the robot has been designed under the technical direction of Dr. Josep Amat (UPC) and Alicia Casals' Robotics group (page 42), with medical direction from Dr. Javier Magriña from Arizona's Mayo Clinic, an expert in Da Vinci surgical robots.

■ 9 December

El Periódico

"Los ojos y la voz de la ciencia mejoran la vida"

El Periódico revisited IBEC's series of scientific talks on nanobiotechnology, robotics and tissue engineering which were held at libraries and civic centres in Barcelona at the end of 2013.

■ 11 December

La Vanguardia

"Barcelona será sede de una red europea de I+D+i en salud"

Coverage of IBEC's consortium's winning proposal for the EIT's Knowledge and Innovation Community (KIC) on healthy living and active ageing, EIT-Health. For the next seven years, the 144 partners will develop innovative products, education and services addressing the challenge of demographic change in Europe (see page 131).

IBEC in *El Mundo*

>INSTITUTO DE BIOINGENIERÍA DE CATALUÑA

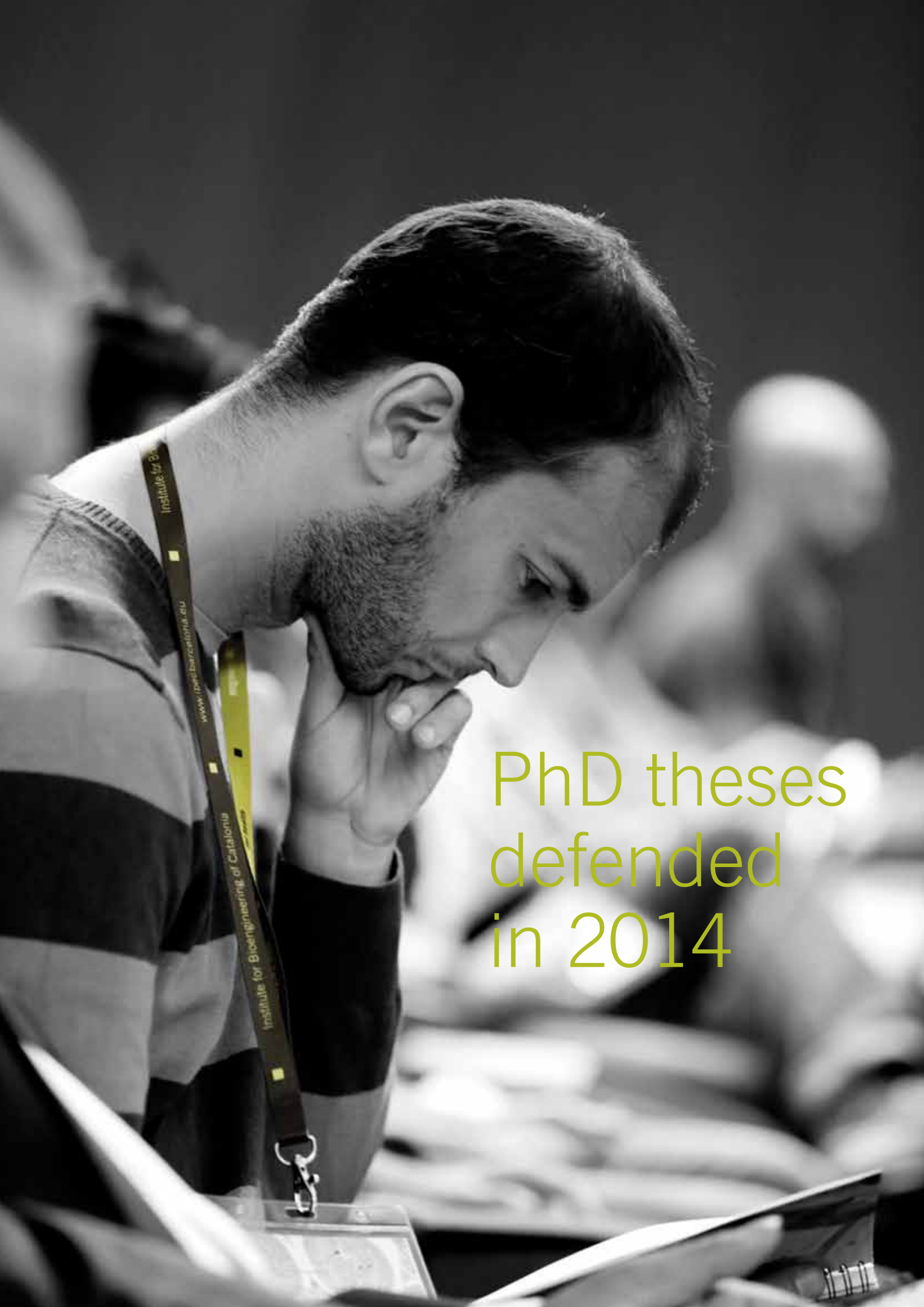
- El centro se está posicionando fuertemente en crear avances en un chip
- La ciencia básica es el 'core' pero transfieren a empresas y crean 'spin off'
- Uno de sus investigadores ha recibido ya tres premios ERC

> INVESTIGACIÓN

Ingenieros en ciencias de la vida

En el IBEC se investigan tres grandes aplicaciones de la bioingeniería: la medicina del futuro, las terapias regenerativas y el envejecimiento activo. Por **Andrea Pelayo**

+INFO
EXPERTO "BIO"



PhD theses defended in 2014

PhD theses in 2014

The data shows the date of the defence, the name of the student, his or her group at IBEC, the title of the PhD thesis and the awarding body.

■ 6 March

Sara Nocentini
Molecular and cellular neurobiotechnology (page 98)
Potential of genetically modified ensheathing cells for regeneration after spinal cord injury (UB)

■ 29 April

Tiziano Serra
Biomaterials for regenerative therapies (page 47)
Development of 3D-printed biodegradable composite scaffolds for tissue engineering applications (UPC)

■ 6 May

Mercè Izquierdo
Nanoprobes and Nanoswitches (page 60)
Photoswitchable glutamate receptors to control neurotransmission with light (UB)

■ 16 June

Ana Mª Oliva
Nanobioengineering (page 103)
Estudio de los procesos celulares inducidos por campos eléctricos en sistemas de Lab-on-a-chip (UB)

■ 3 July

Nadège Sachot
Biomaterials for regenerative therapies (page 47)
Design of Hybrid Fibers for Bone Tissue Engineering (UPC)

■ 25 July

Zaida Álvarez
Biomaterials for regenerative therapies (page 47)
Lactate-Releasing PLA scaffolds for brain regneration (UPC)

■ 23 September

Marilia Barreiros Dos Santos
Nanobioengineering (page 103)
Development of a multi-electrode impedimetric biosensor: detection of pathogenic bacteria and mycotoxins (UB)

■ 14 October

Andrés Martín
Nanoprobes and Nanoswitches (page 60)
Desarrollo de péptidos fotoconmutables para el control de la actividad celular (UB)

■ 24 October

Laura Casares
Integrative cell and tissue dynamics (page 112)
Epithelial dynamics on soft hydrogels in response to stretch (UB)

■ 20 November

Antonio Bautista
Nanoprobes and Nanoswitches (page 60)
Design and Synthesis of Photoswitchable Molecules for Biological Applications (URV)

■ 25 November

Daniel Esteban
Nanoscale bioelectrical characterization (page 56)/Microbial biotechnology and host-pathogen interaction (page 70)
Electric polarization properties of single bacteria measured with electrostatic force microscopy. Theoretical and practical studies of Dielectric constant of single bacteria and smaller elements (UB)

■ 4 December

César Parra
Nanobioengineering (page 103)
Microfluidic devices with integrated biosensors for biomedical applications (UB)

Cover image: Autofluorescence confocal microscopy image of plastids in the parenchyma cells of Arabidopsis thaliana *seedling cotyledons. Nanomalaria group (page 52)*

Compiled and produced by the Communications and Outreach Department, IBEC.
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