Biosystems & Integrative Sciences Institute

Report 2015

BioISI
Biosystems and Integrative Sciences Institute

Ciências ULisboa

Contents

BioISI Identification

Name of the Research Unit: Biosystems & Integrative Sciences Institute

Unit Acronym: BioISI

Scientific Director: Margarida D. Amaral

Scientific Areas:

Multidisciplinary/Interdisciplinary Research

Life and Health Sciences	Biomedicine
Exact Sciences & Engineering	Physics
Natural Science & Environment	Bio-based Product Technology or Food Sciences

Profile of the Research Unit

- Basic Research: 75%
- Applied research: 25%

Keywords

Molecular Systems Biology	Integrative Sciences
Agent and Systems Modelling	Biological Physics

Total Funding: 3 499 766 € (583 294 €/yr)

FCT Evaluation (2014): 24/25 - Excellent

Emails: Director: BioISIdirector@fc.ul.pt / Secretariat: BioISInfo@fc.ul.pt | Webpage: https://www.fc.ul.pt/pt/unidade/bioisi

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Introduction

BioISI is a new institute, merging 3 research centres (BioFIG, CFMC, LabMAg) officially created in January 2015 to understand and address biological questions using integrative -Systems- approaches at the forefront of life sciences research at both national and international scales: https://www.fc.ul.pt/pt/unidade/bioisi

By gathering scientists from bio-, physics and computational sciences, **BioISI** benefits from a unique multidisciplinary environment which (together with its core-facilities) is offered to its researchers and advanced students. This fosters creative thinking to solve problems through integrative approaches.

Vision. **BioISI**'s vision is to develop research of excellence on biosystems and integrative sciences so as to become the leading centre at the forefront of research in this area Portugal with a very significant international position, given its key international links.

Mission. To achieve its goal **BioISI** pursues 5 major missions: **1) Research in BioSystems & Integrative Sciences** – **BioISI** aims to solve emergent complex problems in biology and medicine, from molecules to cells, organisms to populations using Systems approaches. Outcomes contribute to improve human health and well-being as well as better foods. **2) Technology & Instrumentation** – gathering physicists and computational scientists together with biologists in one institute, puts **BioISI** in a privileged, unique multidisciplinary position in Portugal to develop new instruments (e.g., new development of novel atomic force microscopy for bio-applications, innovative biodevices or generation of software and databases for the life sciences). **3) Facilities and Services** – at **BioISI** facilities researchers can both learn about and use the most appropriate current technique to approach a specific scientific problem. They include facilities for bioimaging, physics, computing, mammalian cell culture, plant house, etc. **4) Teaching and Training** – **BioISI** hosts the multidisciplinary BioSys PhD Programme on Biological Systems, Functional & Integrative Genomics (www.fc.ul.pt/en/pagina/7688/phd-programme-biosys) already with 33 enrolled PhD students and which was evaluated as an "*Exceptionally strong PhD program with essentially no weaknesses*" and also participates in two more PhD programmes DAEPHYS – Applied & Engineering Physics and EnviHealth&Co – Environmental Health. Other training includes a Post-doctoral programme, mentoring young PIs to establish independently, and training of external visitors in collaborations, use of facilities, and practical workshops. **5) Knowledge/ Technology Transfer (KTT)** – as 25% of **BioISI** activities are on applied research, interacting with the socio-economic environment is thus an important **BioISI** activity. **BioISI** uses UL-INOVAR, the KTT office of ULisboa to protect the intellectual property developed by its members.

Institutions. **BioISI** coordinating institution is FCUL – Faculty of Sciences of the University of Lisboa (www.fc.ul.pt) and the managing institution is the FCUL Foundation (FFCUL). FCUL supplies space and general infrastructures to its ~30 research centres. **BioISI** members are associated to 4 FCUL departments: Chemistry & Biochemistry, Plant Biology, Physics and Informatics.
FFCUL acts as the legal front institution of FCUL's research centres (including **BioISI**) by supporting R&D activities with financial and administrative management of projects.

Other **BioISI** affiliated institutions include: **INSA** (Portuguese National Institute of Health, a State Laboratory of the Ministry of Health) having biomedical and public health research as its main activities; as well as **FCUP** (the Faculty of Sciences, a major school within University of Porto) and **UMinho** (University of Minho, a research university), each with one plant team in **BioISI** and being geographically well placed for Biotech key goals concerning plant research. In 2015 members from **UTAD** (University of Trás-os Montes) also joined **BioISI**.

Strategy. The rapid technological progresses and the country economic constraints leave Portuguese research centres in a disadvantageous position to achieve ambitious cutting-edge goals. Thus, bringing **BioISI** into its vision will only be enabled through key collaborations (networking and partnerships) with top international institutions, namely through: promoting collaborative projects; co-supervision PhD students and post-docs; updating in technology advances; and accessing their cutting-edge facilities. This is an excellent way of internationalizing Portuguese science and setting very high standards for national research institutions.

Proposed research. Biological systems display complex properties that cannot be predicted from studying isolated parts. **BioISI** aims to solve emergent complex problems in biology and medicine, from molecules to cells, organisms to populations using a Systems approach. Addressing such complexity calls for integrative analyses combining high-throughput Omics techniques with quantitative science and computational tools to describe and predict dynamical behaviour. The joining of researchers from Biology, Physics and Informatics will enable the **BioISI** to address these biological questions with a perspective from exact sciences which is unprecedented to each of the three previous centres. **BioISI** research focuses on 4 main Thematic Lines (TLs) comprising: Biomedicine (BioMed); Biotechnology & Bioresources (Biotech); Condensed Matter & Biological Physics (CM&BioPhys); Bioinformatics & Modelling (B&Mod). Outcomes will contribute to improve human health, well-being, foods, as well as to innovate instrumentation and create novel biodevices, keeping the country at the forefront of innovation and generating economic opportunities.

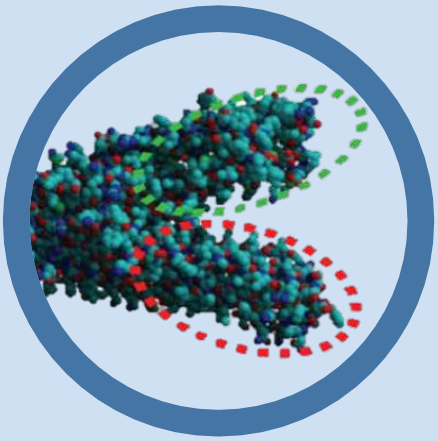
Communication & Outreach activities. These activities are carried out by the **BioISI** Communication & Outreach Working Group (C&O-WG) which organizes BioISI seminars and other events, working jointly with FCUL press office to disseminate activities, major achievements, prizes, etc.

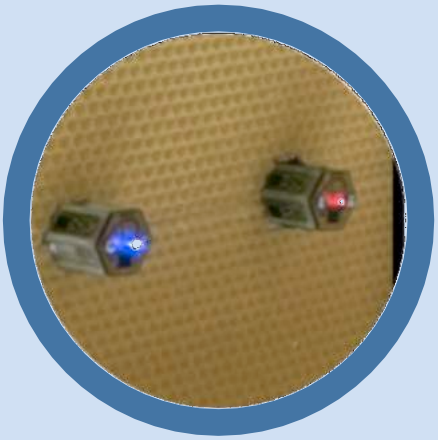
A **Company Liaison Working Group** (CL-WG) fosters **BioISI** Industrial Relations in collaboration with Tech-Labs (www.teclabs.pt) FCUL's organization for the creation and economic valorising of scientific knowledge.

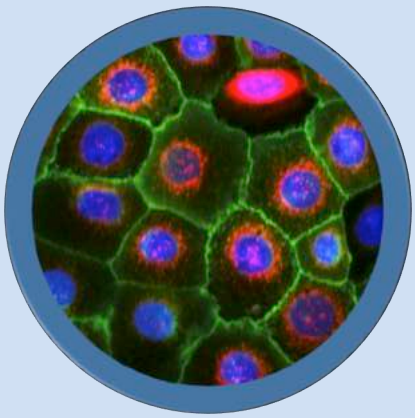
In this somewhat difficult first year of activity, **BioISI** had to face many challenges, among which a drastic reduction in its proposed budget (of 57%). This has inevitably led to a significant readjustment of its goals, downgrading some of its proposed activities and expected indicators. Nevertheless, we are confident that we have a good plan to move forward but we need expert advice to help us.

We thus with to address a big 'Thank You' to our Scientific Advisory Board (SAB) members for taking some of their time to critically evaluating our research, and for guiding our progress and so help us route our science into the next level.

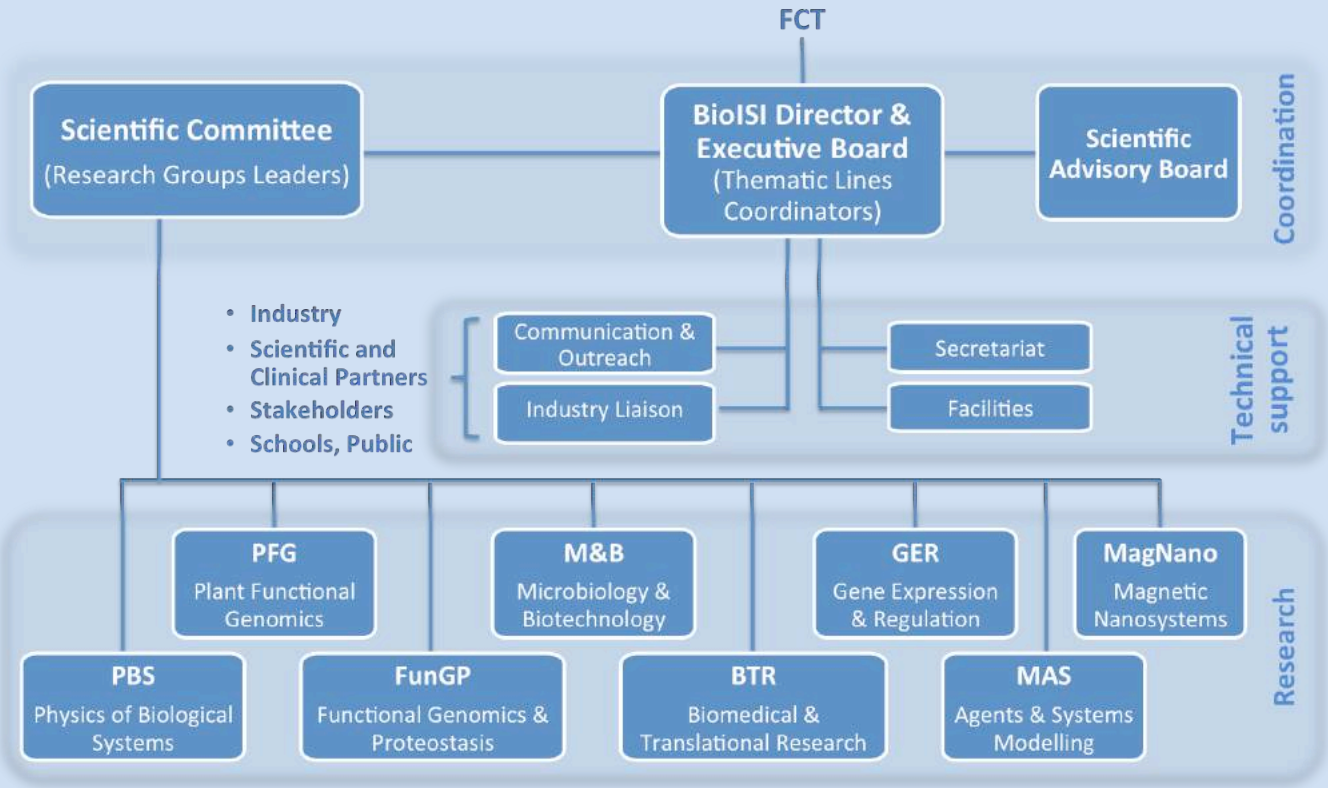
Margarida Amaral







BioISI Organization



Scientific Advisory Board:

Rainer Pepperkok (Molecular & Cell Biology). EMBL- European Molecular Biology Laboratory, Heidelberg (Germany)

Lothar Willmitzer (Plant Molecular and Cell Biology). Max-Planck Institute for Molecular Plant Physiology, Potsdam (Germany)

Juan Valcarcel Juarez (Genomics and Systems). CRG-Centre de Regulacio Genomica & ICREA, Barcelona (Spain)

Michael Gill (Systems Medicine). Institute of Molecular Medicine, Trinity College Health Sciences Centre,Dublin (Ireland)

Eugene Shakhnovich (Physics). Biophysics Laboratory, Harvard University, Cambridge (MA, USA)

Dario Floreano (Informatics). EPFL- Laboratory of Intelligent Systems, Lausanne (Switzerland)

Institutions:

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

Ciências ULisboa Faculdade de Ciências da Universidade de Lisboa

Instituto Nacional de Saúde Doutor Ricardo Jorge

FC Faculdade de Ciências Universidade do Porto

Universidade do Minho Escola de Ciências

Universidade de Trás-os-Montes e Alto Douro utad

BioISI Thematic Lines

Biomedicine

The main focus of BioISI research in the Biomedicine thematic line (BioMed-TL) is to gain a better mechanistic understanding of diseases, with an emphasis on those with a genetic basis. To this end BioISI researchers will use the advances resulting from the knowledge of the human genome by analysing how each individual gene contributes to processes associated with diseased states.

BioMed-TL research will thus range from basic biomedical research in genetics and genomics, molecular & cell biology and Omics to more translational areas such as addressing fundamental challenges in personalized medicine for better diagnosis, prognosis and therapies. The latter coincides with the health streamline priority of H2020 of personalising health and care.

Key Actions

1) Translating genes and genomics into personalized and systems medicine
2) Elucidating mechanisms of disease
3) Development of innovative therapeutic strategies and drug discovery
4) Pharmaco-genetics and pharmaco-resistance tests

Research Groups Involved in the BioMed – TL:

PBS | FunGP | M&B | GER | BTR | PBS | MagNano | MAS

Biotechnology & Bioresources

The research to be performed in the Biotechnology & Bioresources thematic line (Biotech-TL) is framed by the H2020 societal challenges: Health and Wellbeing [Functional foods for disease prevention, environmental rehabilitation, new drugs from marine organisms], food security and sustainable agriculture; and by the H2020 key enabling technologies: Advanced materials [nutraceuticals], Biotechnology.

Research will be conducted to acquire knowledge and develop modular tool kits that will enable rapid responses to unforeseen challenges, such as the emergence of new plant or diet-related diseases, changes in the distributions of plant pathogens and vectors, the emergence of new environmental conditions or the impact assessment of new bio-based products.

Key Actions

1) Plant health and crop improvement
2) Plants as Biofactories
3) Phytoremediation
4) Microbial pharmacogenomics
5) Marine microbial biotechnology
6) Wine microbial biotechnology

Research Groups Involved in the Biotech – TL:

PBS | FunGP | M&B | BTR | PBS | MagNano | MAS

Condensed Matter & Biological Physics

The thematic line Condensed Matter & Biological Physics (CM&BioPhys-TL) merges together the expertise of experimental condensed matter physicists (MagNano group) and theoretical biological physicists (PBS group) and takes advantage of the unique research opportunities offered by the multidisciplinary environment of BioISI to foster interdisciplinary work through tailored interactions among members of these two Physics groups and members of all Biology groups (FunGP, GER, PFG, BTR, B&M). The research program of CM&BioPhys-TL develops around three Key Actions (KA) as flagship projects as described below.

Key Actions

1) Development and/or refinement of Atomic Force Microscopy (AFM)/Force Feedback Microscopy (FFM)
2) Development of novel simulation approaches to study protein (mis)folding
3) Optimization of nanostructured magnetic systems for application to biosensors/biodevices

Research Groups Involved in the CM&BioPhys – TL:
PBS | FunGP | M&B | GER | BTR | PBS | MagNano

Bioinformatics & Modelling

The main scientific goal of Bioinformatics & Modelling thematic line (B&Mod-TL) is twofold: to research fundamental properties of bio inspired models and to gather BioISI research around the common goal of cell system modelling.
B&Mod-TL aggregates research of BioISI concerning computational models and tools for molecular, biological, biomedical and social systems. The scope of modelling in BioISI is vertical in terms of systems, from physical basis of biological systems to social organisation of such systems. Agent based modelling and simulation are basic techniques widely used in the B&Mod-TL.
Seven research groups of BioISI (indicated in each key action) have activities that converge into B&Mod-TL. In common all work with numerical and algorithmic models of living systems for which computational implementations are fundamental. In particular, we can identify computer processing activities typical of B&Mod-TL.

Key Actions

1) Pre-processing pipelines for data analysis
2) Data mining tools and data analysers
3) Development of new computational tools to manage, integrate and interpret the data

Research Groups Involved in the B&Mod – TL:
PBS | FunGP | M&B |GER | BTR | PBS | MAS

PFG Group

Plant Functional Genomics

www.fc.ul.pt/en/pagina/7678/pfg

Study of multiple aspects of plant growth and development with emphasis on functional aspects aiming biotechnological applications:

- Characterization of signalling and secretory pathways regulating growth and morphogenesis
- -omics analysis of plant (and fruit) development and responses to biotic interaction (parasitic and symbiotic) and abiotic stresses
- Plant responses to pollutants and their use as remediation tools

Major Achievements:

- Functional characterization of a 4KO of Physcomitrella patens PTEN (Phosphatase and tensin homolog) shows the protein is a growth repressor of both rhizoid and gametophore development.
- Transcriptome and metabolome analysis in Vitis vinifera cv. Trincadeira berries upon infection with Botrytis cinerea revealed changes in jasmonic acid, ethylene, polyamines, and auxins and up-regulation of WRKY transcription factors, pathogenesis-related proteins, glutathione S-transferase, stilbene synthase, and phenylalanine ammonia-lyase.
- RNA-Seq and gene network analysis revealed activation of an ABA-dependent signalosome during the cork oak root response to drought.
- 2 research projects initiated with members of MagNano, MAS and GER groups

Selected Publications:

L. Saavedra, R. Catarino, T. Heinz, I. Heilmann, M. Bezanilla, R. Malhó (2015) Phosphatase and tensin homolog (PTEN) is a growth repressor of both rhizoid and gametophore development in the moss Physcomitrella patens. Plant Physiology 13: pp 1197. doi.org/10.1104/pp.15.01197

Patricia Agudelo-Romero, Alexander Erban, Cecília Rego, Pablo Carbonell-Bejerano, Teresa Nascimento, Lisete Sousa, José M. Martínez-Zapater, Joachim Kopka, Ana Margarida Fortes. (2015) Transcriptome and metabolome reprogramming in *Vitis vinifera* cv. Trincadeira berries upon infection with *Botrytis cinerea*. Journal of Experimental Botany 66 (7), 1769-1785.

Costa ML, Sobral R, Costa MMR, Amorim MI, and Coimbra S. (2015). Evaluation of the presence of arabinogalactan proteins and pectins during *Quercus suber* male gametogenesis. Annals of Botany 115: 81–92.

Pereira AM, Nobre MS, Pinto SC, Lopes AL, Costa ML, Masiero S and Coimbra S. (2015). "Love is strong, and you're so sweet": JAGGER is essential for persistent synergid degeneration and polytubey block in Arabidopsis thaliana. Molecular Plant (accepted).

Magalhães A, Verde N, Martins I, Costa D, Lino-Neto T, Castro H, Tavares RM, Azevedo (2015) RNA-Seq and gene network analysis uncover activation of an ABA-dependent signalosome during the cork oak root response to drought. Frontiers in Plant Science (accepted)

Figure 1

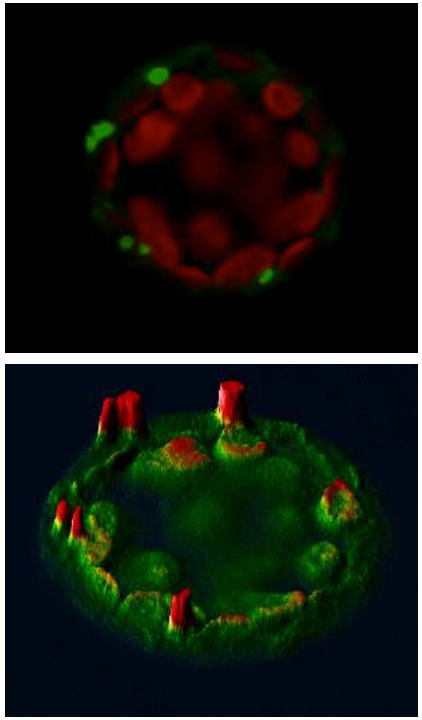
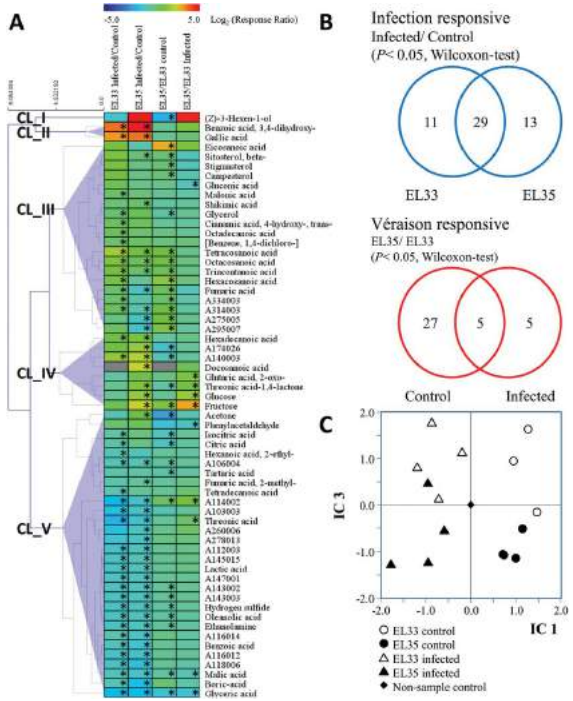


Figure 2



Group Leader
Rui Malhó

Integrated PhDs from:

Ciências ULisboa

U.PORTO

Universidade do Minho
Escola de Ciências

UNIVERSIDADE DE TRÁS-OS-MONTES E ALTO DOURO
utad

PFG Group Members: 45

Post Docs: 8

PhD Students: 11

Academic staff: 17

Key Funded Projects:

Sexual Plant Reproduction – Seed formation. Project 690946 – SexSeed. H2020 MSCA-RISE-2015. 01 March 2016, ends 28 February 2020. Total amount 720000.00€, BioISI 193500.00€. Coordination

EvoMod- Origem e estabelecimento evolutivo de um módulo transcricional que controla a assimetria floral, PTDC/BIA-PLA/1402/2014- FCT, 1 January 2016- 31 December 2018 160.416,00 €, BioISI Coordination

PTDC/AGR-FOR/3356/2014- FCT - Characterisation of cork formation and reproductive biology in a cork hybrid population, 1 January 2016- 31 December 2018, 57.115,00 €, Partners.

PTDC/BIA-BIC/4113/2012-FCT - Conservation of plant biodiversity in the Macaronesian Hotspot: Integrating phylogenetic, taxonomic, and ecological approaches to study the Cape Verde endemic flora; Starting date 01-07-2013 – End date 30-06-2016; 56.327,00€. Partners

Figure 1: Distribution of GFP-PTEN fusion protein in moss protoplasts
Figure 2: Transcriptomic and metabolic analysis of grape berries

FunGP Group

Functional Genomics & Proteostasis

www.fc.ul.pt/en/pagina/7681/fungp

Biomedicine: translating genes and genomics into personalized & systems medicine; elucidating mechanisms of disease; developing innovative therapeutic strategies & drug discovery; performing pharmaco-genetics & pharmaco-resistance tests.

1. Novel cellular epithelial models for Cystic Fibrosis studies
2. Molecular and cellular mechanisms of quality control of the endoplasmic reticulum (ER) and secretory traffic of CFTR protein
3. Translational studies for better biomarkers for CF disease diagnosis and prognosis
4. Systems approaches to tackle mechanisms of CF, neurodegeneration, metabolic disorders and cancer
5. Studies of membrane proteins associated with human diseases, e.g. CF-related ion channels anoctamins
6. Signalling/ signal transduction pathways in CF and cancer
7. Drug development for CF, cancer, neurodegeneration, metabolic disorders and malaria

Major Achievements:

- **Personalized medicine in CF:** Validation of old drugs for rare mutations using patient-derived materials [Awatade et al, EBiomedicine 2014]
- **Mechanisms of neurodegeneration and cancer:**
  - Aggregation mechanisms of Superoxide dismutase 1 [Estacio et al, BBA 2015; Leal et al, Metallomics 2015] and Aβ Peptide [Reybier et al, Angewandte Chemie 2015];
  - Calcium dysregulation in ALS [Leal & Gomes, Front Cell Neurosci 2015]
  - Rac1b signaling in colorectal cancer [Henriques et al, Cancer Lett 2015]
- **Therapeutic strategies for Cystic Fibrosis:**
  - Elucidation of the mechanism of membrane stabilization of rescued F508del-CFTR [Loureiro et al, Sci Signal 2015];
  - Description of the mechanism of action of the most promising pro-drug in clinical trial for CF (VX-809) to correct F508del-CFTR - the most frequent CF-causing mutation [Farinha et al, Pharm Res Perspect 2015]
  - Evaluation of triazines in CF [Srivastava, RSC Adv 2015]
- **Functional consequences of CFTR mutations:** Assessment of splicing variants in CF [Sharma et al, Hum Mut 2014; Ramalho et al, J Cyst Fibr 2015; Igreja et al, Hum Mut 2015]
- **Integrated view of cellular processes in health and disease using post-genomic approaches:**
  - Development of high-throughput methods and tools to study CFTR traffic [Botelho et al, Sci Rep 2015]
  - Analysis of global gene expression in cystic fibrosis and other respiratory disorders [Clarke et al, Genomics 2015]

Figure 1

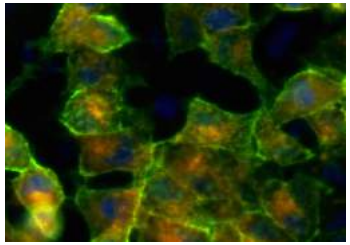


Figure 2

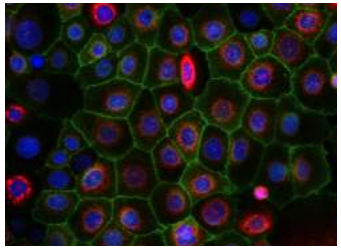


Figure 3

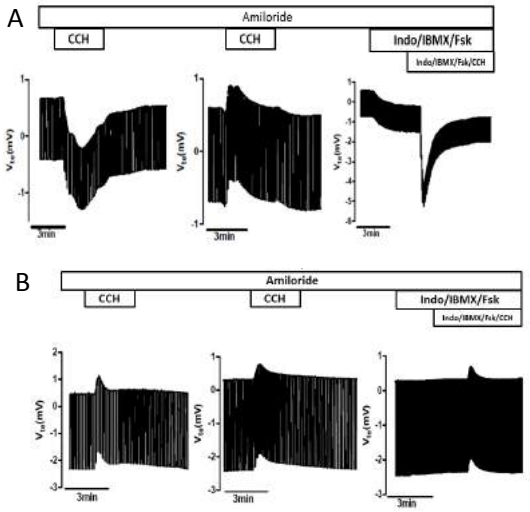
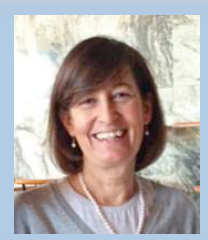


Figure 1: Fluorescent labeling of the CFTR protein in bronchial epithelial cells

Figure 2: Respiratory epithelial cells expressing a secretory membrane protein in the endoplasmic reticulum (red) or the plasma membrane (green)

Figure 3: Transepithelial voltage measurements in rectal tissues. Original recordings of the effects of cholinergic (CCH, 100 µM) and cAMP-dependent (IBMX, 100 µM and Fsk 2 µM) basal activation on healthy control (A) and Cystic Fibrosis tissue (B)



Group Leader

Margarida Amaral

PI's


Luka Clarke


Carlos Farinha


José Pedro Gil


Cláudio Gomes


Paulo Matos

Post Docs: Hugo Botelho| Ines Pankonien | Susana Igreja | Patrícia Barros | Sónia Leal | Bárbara Henriques

PhD Students: Joana Lérias (BioSys)| Sara Canato (BioSys)| Nikhil Awatade (BioSys)| Luís Sousa (BioSys)| João Santos (BioSys)| Madalena Pinto (BioSys)| Daniel Cruz (BioSys)| Margarida Quaresma (BioSys)| Ana Matos (BioSys)| Joana Cristovão | Tânia Lucas | Verónica Felício

Technicians: José Múrias

Selected Publications:

Amaral MD (2015) Novel Personalized Therapies for Cystic Fibrosis: Treating the Basic Defect in All CF Patients. J Intern Med 277: 155-66.

Botelho HM, Uliyakina I, Awatade NT, Proença MC, Tischer C, Sirianant L, Kunzelmann K, Pepperkok P, Amaral MD (2015) Protein Traffic Disorders: an Effective High-Throughput Fluorescence Microscopy Pipeline for Drug Discovery. Sci Rep 5: 9038.

Farinha CM, Sousa M, Canato S, Schmidt A, Uliyakina I, Amaral MD (2015) Increased efficacy of VX-809 in different cellular systems results from an early stabilization effect of F508del-CFTR. Pharmacol Res Perspect 3: e00152

Leal, S.S. and C.M. Gomes, Calcium dysregulation links ALS defective proteins and motor neuron selective vulnerability. Front Cell Neurosci, 2015. 9: p. 225.

Loureiro CA, Matos AM, Dias-Alves A, Pereira JF, Uliyakina I, Barros P, Amaral MD, Matos P (2015) A NHERF1 PDZ domain switch retains rescued F508del-CFTR at the cell surface by preventing CHIP recruitment. Sci Signal. 8(377), ra48. Doi: 10.1126/scisignal.aaa1580.

Key Funded Projects:

2015 Proteotoxic insults and synaptic dysfunction in the aging brain. Bial Foundation Research Grant (Portugal). 2015-2018. Project coordinator: Cláudio Gomes.

2015 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL15XX0) "*CFTR mRNA Stability Studies for PTC Mutations*". Budget: 222K$; 2 yrs. PI: MD Amaral.

2015 "Pesquisa de novos alvos moleculares para adjuvar a correção farmacológica da F508del-CFTR", funded by Programa Gilead GÉNESE (PGG/055/2014). 20K €. PI: Paulo Matos.

2016 FCT/POCTI (PTDC/BIM-MEC/2131/2014) "*DIFFTARGET-Novel Factors of CFTR Traffic Related to Epithelial Cell Differentiation: Potential Therapeutic Targets for Cystic Fibrosis*". Budget: 200K€; 3 yrs. PI: MD Amaral.

2016 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL15XX1) "*RNA LIFE – Novel RNA Regulators as Potential Drug Targets for Cystic Fibrosis*". Budget: 324K$; 2 yrs. PI: MD Amaral.

M&B Group

Microbiology & Biotechnology

www.fc.ul.pt/en/pagina/7680/mb

M&B-BioISI focused on innovative integrated approaches in several areas of M&B and linking group know-how and expertise with SMEs and industry.

R&D translation to society was further achieved through promotion of new start-ups and participation of PhD members in networks of key value chains (Bluebio Alliance, Rede Agro).

Major Achievements:

Yellow and White M&B

- Selection and integrative analysis of saccharomyces and non-saccharomyces yeasts as novel starters for wine industry
- Unveiling yeast genomic expression programs in mixed-culture wine fermentations, adaptive yeast response to stress and links of yeast nitrogen metabolism with wine aroma and quality
- Selection and characterization of an inhibitor of fungal chlorophenol methyltransferase to prevent cork taint in wines
- Development and validation of molecular methods for detection of bacterial and fungal pathogens in food and water and evaluation of their pathogenic potential

Blue M&B

- Characterization of marine microbes for bioactivity profiles and evaluation of sea host-associated microbiomes
- Positioning of a group member as a national and EU Comission reference for marine biotech and as a driver for Bluebio Alliance
- R&D translation through creation of biotech start-up BioMimetx and help to co-found new start-ups in life sciences

Black M&B

- Determination of mechanism of action of a new family of glycoside antimicrobial agents with activity against B. anthracis

Grey and Green M&B

- 1st identifications of R. solanaceraum biovar 1 and fireblight disease (E. amylovora) in Portugal
- Novel microbial strains for biodegradation of FOG and hydrocarbon contaminated wastewaters
- Identification of turf-grass diseases through Green Project phytopathology service

Gold and Red M&B

- New approaches for mining genomic data
- Production of NCBI reference genomic sequences for B. suis biovar 2 and pan-genome analysis in Brucella
- Report of 1st human case of WNV Neuroinvasive Disease in Portugal
- Role of discrete Gim proteins in STN apart of prefoldin and cytoskeleton
- Development of yeast-based genetic tools to screen oxidative drugs

Figure 1

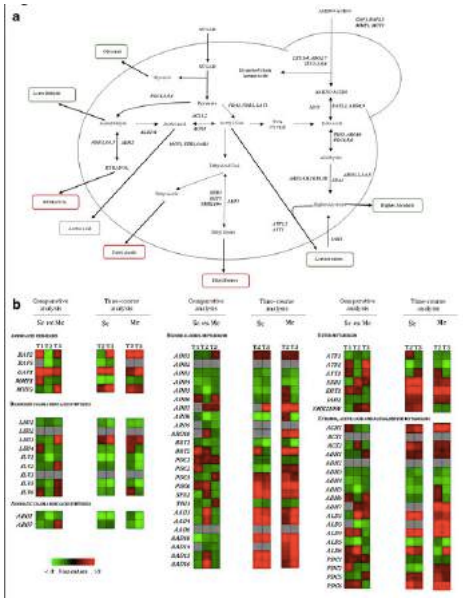


Figure 2

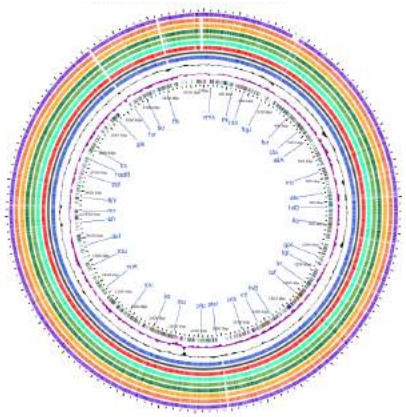
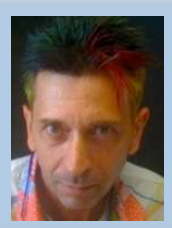


Figure 1: Biochemical pathways involved in flavor-active compounds formation in single and mixed cultures of wine yeasts

Figure 2: 22q11.2 Copy Number Variants in CHD



Group Leader

Rogério Tenreiro

Integrated PhDs

Key Funded Projects:

BlueGenics - From Gene to Bioactive Product: Exploiting Marine Genomics for an innovative and Sustainable European Blue Biotechnology Industry. EU. FP7- KBBE-2012-6- 311848, Large Scale Cooperation FP7 consortium. 2012-2016. Total funding: 6 M€. No BioISI amount. BioISI Partner: H. Vieira as Expert/Consultant (previous participant as BIOALVO). [Blue M&B]

FACIB - New drugs from sugars against infections by Bacillus species. COMPETE, QREN and FEDER. AdI 21547. Proponent Company: CIPAN. Partners: FCUL. 2011-2015. Total funding: 525 k€. FCUL PI: A. Rauter (CQB). M&B-BioISI funding: 178 k€. M&B-BioISI PI: R. Dias. [Black/Gold M&B]

LEVEalliance - a portfolium of natural and adaptively evolved non-saccharomyces yeasts for the production of lower ethanol content wines. COMPETE, QREN and FEDER. AdI 38918. Proponent Company: Proenol Lda. Partners: FCUL. 2013-2015. Total funding: 534 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 211 k€. [Yellow/White M&B]

PATHOALERT - New diagnostic methods of pathogenic and emergent microbes in food and water: a molecular and cytological approach for detection and evaluation of pathogenic potential. POR Lisboa, QREN and FEDER. AdI 30211. Proponent Company: Biopremier SA. Partners: FCUL. 2013-2015. Total funding: 576 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 304 k€. [Red/Yellow M&B]

SMARTWINE - Smarter wine fermentations: integrating Omics-tools for development of novel mixed-starter cultures for tailor-made wine production. FCT, COMPETE, FEEI. PTDC/AGR-TEC/3315/2014, 2015-2019. Total funding: 196 k€. No BioISI amount. PI: A. Mendes-Faia (UTAD/BioISI). [Yellow/White M&B]

Selected Publications:

Barbosa C, Mendes-Faia A, Lage P, Mira NP, Mendes-Ferreira A (2015). Genomic expression program of Saccharomyces cerevisiae along a mixed-culture wine fermentation with Hanseniaspora guilliermondii. Microb Cell Fact. 28;14:124.

Bernardini A, Corona F, Dias R, Sánchez MB, Martínez JL. (2015). The inactivation of RNase G reduces the Stenotrophomonas maltophilia susceptibility to quinolones by triggering the heat shock response. Front Microbiol. 19;6:1068

Cruz J, Cruz L, Tenreiro R. (2015). First Report of Xanthomonas campestris pv. raphani Causing Leaf Spot Disease of Brassica oleracea in Portugal. Plant Disease 99(2):282.

Rogers, AD, Brierley A, Croot P, Cunha M, Danovaro R, Devey C, Hoel A-F, Ruhl HA , Sarradin PM, Trevisanut S, van den Hove S, Vieira H, Visbeck M. (2015). Delving Deeper: Critical Challenges for 21st century deep-sea research. Larkin, K.E., Donaldson, K and McDonough, N. (Eds). European Marine Board Position Paper 22, Ostend, Belgium. 224pp.

Zé-Zé L, Proença P, Osório HC, Gomes S, Luz T, Parreira P, Fevereiro M, Alves MJ. (2015). Human case of West Nile neuroinvasive disease in Portugal, summer 2015. EuroSurveill. 20(38):

BTR Group

Biomedical & Translational Research

www.fc.ul.pt/en/pagina/7679/btr

Understanding how genetic, epigenetic, clinical, lifestyle and environmental determinants and modulators interact to influence health, disease and treatment efficacy; integrating large human datasets and translating findings into personalized medicine tools for improved diagnosis and intervention using Systems Medicine frameworks.

Major Achievements:

- The comprehensive collection of health and disease determinants in a representative population sample from Portugal (e_COR project) revealed a high prevalence of cardiovascular risk factors, contributed to a broader understanding of CVD physiopathology with biomarker identification, and provided evidence for improved prevention approaches.
- The first homozygous patient with two novel PCSK9 functional GOF mutations leading to hypercholesterolemia was characterized; Novel CNVS in the 22q11.2 region were identified in CHD patients from the Azores, where extensive consanguinity and familial aggregation of CHD is documented.
- A study linking iron metabolism, immune cells and atherogenesis showed that an inflammatory microenvironment promotes macrophage iron retention and lipid accumulation, eventually contributing to plaque destabilization and atherosclerosis progression.
- A clinical, social and genetic study of age-related hearing loss showed gender differences in hearing threshold, age and genetics variants, and more depression symptoms in elderly individuals with lowest hearing levels.
- The population structure of pharmacogene variation in Portugal was defined, paving the way to pharmacogenetic analysis of neuropsychiatric disease and CVD drug response.
- A systems framework applied to a large dataset of autism patients and parents showed an increased correlation of measured autistic traits between unaffected mothers transmitting genetic variants and their affected sons, reinforcing the hypothesis of female protective factors in ASD.
- Extensive genetic variant overlap between patients with ASD and other neurodevelopmental disorders was documented, indicating that specific diagnosis of ASD is unlikely through genetic analysis, and reinforcing GWAS conclusions of genetic overlap among mental disorders.

Figure 1

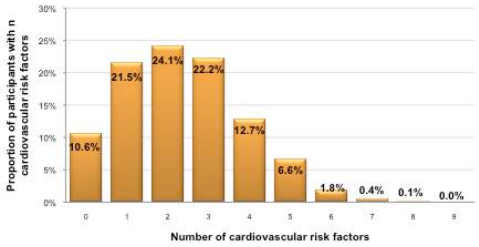


Figure 2

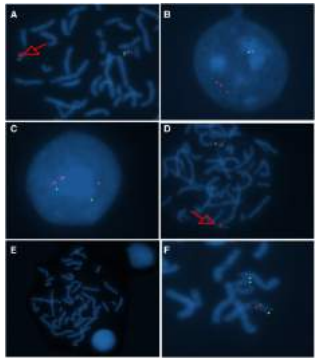


Figure 3

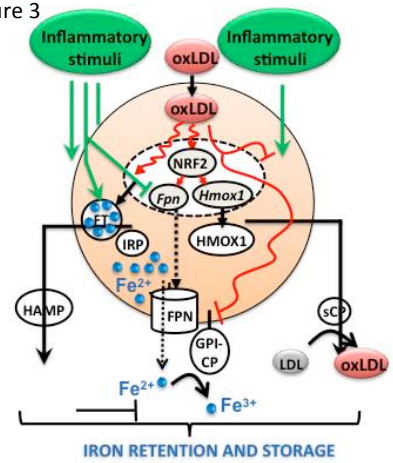


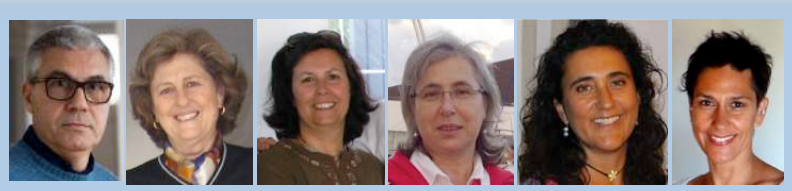
Figure 1: e_COR project results – close to 25% of the Portuguese population has 3 CVD risk factors, including hipertension, obesity and diabetes

Figure 2: 22q11.2 Copy Number Variants in CHD patients

Figure 3: Iron metabolism, inflammation and atherogenesis - molecular mechanism.

Group Leader
Astrid Vicente

PI's



João Lavinha | Graça Fialho | Helena Caria | Luísa Mota-Vieira | Mafalda Bourbon | Luciana Costa

Post Docs: Ana Catarina Alves | Célia Rasga | Claudia Branco | Inês Conceição | Tiago Matos

PhD Students: Ana Margarida Medeiros | Ana Rita Marques (BioSys) | Cibelle Mariano (BioSys) | Cristina Caroça | Haúla Haider | Joana Chora | Muhammad Asif (BioSys) | Niccolo Rosi (BioSys)

Technicians: Joana Canilho | Joana Duarte

Selected Publications:

Alves AC, Etxebarria A, Medeiros AM, Benito-Vicente A, Thedrez A, Passard M, Croyal M, Martin C, Lambert G, Bourbon M. (2015) Characterization of the First PCSK9 Gain of Function Homozygote. J Am Coll Cardiol. 10;66(19):2152-4.

Melo MS, Balanco L, Branco CC, Mota-Vieira L. (2015). Genetic variation in key genes associated with statin therapy in the Azores isalnds (Portugal) healthy population. Ann Hum Biol. 42(3):283-9.

Branco CC, Gomes CT, de Fez L, Bulhões S, Brilhante MJ, Pereirinha T, Cabral R, Rego AC, Fraga C, Miguel AG, Brasil G, Macedo P, Mota-Vieira L. (2015) Carriers of the complex allele HFE c.[187C>G;340+4T>C] have increased risk of iron overload in São Miguel Island population (Azores, Portugal). PLoS One. 9:e108534.

Network and Pathway Analysis Subgroup of Psychiatric Genomics Consortium. (2015) Psychiatric genome-wide association study analyses implicate neuronal, immune and histone pathways. Nat Neurosci. 18(2):199-209.

Guerreiro C, Silva B, Crespo ÂC, Marques L, Costa S, Timóteo Â, Marcelino E, Maruta C, Vilares A, Matos M, Couto FS, Faustino P, Verdelho A, Guerreiro M, Herrero A, Costa C, de Mendonça A, Martins M, Costa L. (2015) Decrease in APP and CP mRNA expression supports impairment of iron export in Alzheimer's disease patients. Biochim Biophys Acta. 1852(10 Pt A):2116-22.

Key Funded Projects:

Autism Spectrum Disorders in Europe **(ASDEU).** 2015-2018. Funded by the Health Programme of the European Union DG-SANCO, 144 000€. Partner Astrid Vicente

Joint Action on Chronic Diseases CHRODIS-JA, 2014 – 2016, Funded by the Health Programme of the European Union DG SANCO, 66 000€, Partners – Luciana Costa, Astrid Moura Vicente

Assessment of the reduction of low-density lipoprotein cholesterol (LDL-C) by REGN1500, 2014-2015. Funded by Regeneron Pharmaceuticals Inc., 121 900€. Principal Investigator- M Bourbon.

Identifying the earliest signs of autism - integration of behavioral, clinical and genetic information for early autism diagnosis in a at-risk population 2012 – 2015, Fundação para a Ciência e a Tecnologia (FCT/MCTES), 120 000€; Principal Investigator - Astrid Moura Vicente

Prevalence of cardiovascular risk factors in the Portuguese population (e_COR), 2009-2015. Funded by Science and Technology Foundation (FCT) and INSA,177 000€, Principal Investigator- M Bourbon.

GER Group

Gene Expression and Regulation

www.fc.ul.pt/en/pagina/7682/ger

Our research focuses on the characterization of eukaryotic genomes and gene expression programs at the transcriptional and post-transcriptional levels and their connection to signalling pathways, ranging from the underlying molecular mechanisms, to their impact on systems regulation and disease.

Major Achievements:

Nonsense-mediated mRNA decay (NMD) is a surveillance pathway that detects and degrades mRNAs carrying premature termination codons (PTCs), preventing the accumulation of deleterious truncated proteins. Our research uncovered the complex determinants of the 'AUG-proximity effect', whereby some mRNAs harboring PTCs are resistant to decay, establishing a new model for the regulation of this process with potential therapeutic impact for the targeting of truncated proteins in hereditary diseases and cancer. Continuing our studies on the impact of misregulated gene expression in cancer, namely splicing, we have shown that the escape of colorectal tumor cells from B-Raf-induced senescence is linked to the increased expression of the Rac1b splice variant. Cancer cells also display aberrant expression of multiple non-coding RNAs. In particular, our research highlights the potential contribution of satellite-derived ncRNAs to this process. We further report a new miRNA regulator of the TCR signaling response in naive CD4 T cells, connecting T cell activation to HIV infection

Key Publications:

Henriques A, Barros P, Moyer MP, Matos P, Jordan P (2015). Expression of tumour-related Rac1b antagonizes B-Raf-induced senescence in colorectal cells. **Cancer Lett**. 369(2):368-75.

Pereira FJC, Kong J, Silva AL, Liebhaber SA, Romão L (2015). The extension of the AUG-proximity effect for nonsense-mediated decay inhibition is determined by the mRNA secondary structure. Nucleic Acids Research, 43: 6528-6544.

Ferreira DP, Meles S, Escudeiro A, Mendes-da-Silva A, Adega F, Chaves R (2015) Satellite Non-Coding RNAs: the emerging players in Cells, Cellular Pathways and Cancer. Chromosome Research 23(3):479-493.

Amaral AJ, Andrade A, Foxall RB, Matoso P, Matos AM, Soares RS, Tendeiro R, Serra-Caetano A, Guerra-Assunção JA, Gonçalves G, Gama-Carvalho M, Sousa AE (2015). Deep sequencing of human naive CD4 T cells identifies miR-34c-5p as a novel regulator of T cell activation and HIV replication. Submitted to Cell Host and Microbe

Figure 1

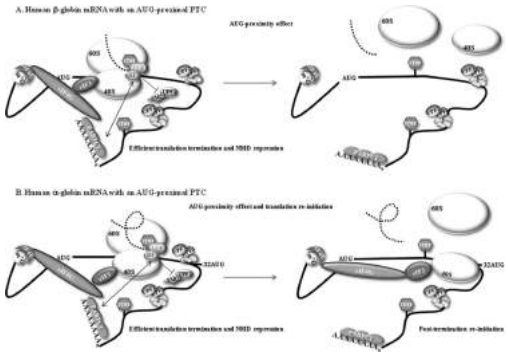


Figure 2

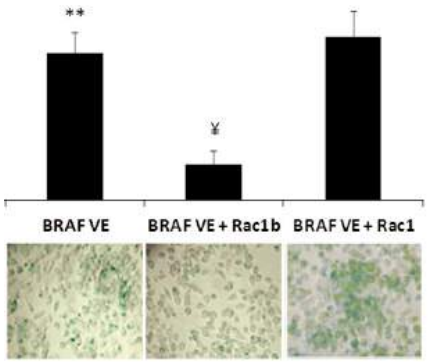


Figure 3

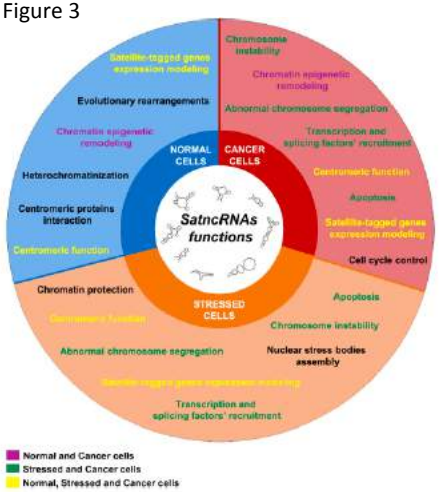


Figure 4

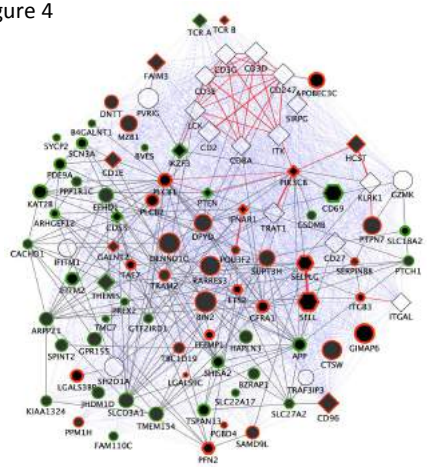


Figure 1: A model for the effect of an AUG-proximal premature termination codon (PTC or stop codon).

Figure 2: Expression of tumor-related Rac1b antagonizes B-Raf-induced senescence in colorectal cells

Figure 3: Satellite non-coding RNAs: the emerging players in cells, cellular pathways and cancer.

Figure 4: Protein interaction network between genes regulated by miR-34c-5p in Jurkat T cells and HIV-1 proteins.

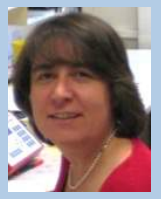
Group Leader
Margarida Gama-Carvalho

PI's


Raquel Chaves


Francisco Pinto


Peter Jordan


Luísa Romão

Post Docs: Andreia Amaral | Christian Ramos | Juliane Menezes | Maria Filomena Adega | Vânia Gonçalves

PhD Students: Andreia Henriques (BioSys)| Hugo Santos (BioSys)| Paulo Costa (BioSys)| Daniel Olivença (BioSys)| Cláudia Loureiro (BioSys)| Nuno Domingues (BioSys)| Joana Silva (BioSys)| Daniela Ferreira | Ana Cristina Mendes da Silva | Ana Cláudia Escudeiro | Joana Pereira | Rafaela Santos

Other researchers: Gerson Amaral | João Paulo Silva | Marina Garcia-Vaquero | Nuno Costa | Cláudia Estima | André Gabriel | Cláudia Onofre | Susana Meles | Ana Luísa Borges |Ana Maria Vieira da Silva

Key Funded Projects:

Perturbation of the intestinal barrier function in Inflammatory Bowel Diseases: role of the Rac1b /cytokine axis; Portuguese Society of Inflammatory Bowel Disease (GEDII), 01/2016-12/2017, 15.000 €

Tumor cell plasticity through alternative splicing in response to a 3D pro-inflammatory microenvironment; Maratona da Saúde- Cancro 2014, 07/2015 – 06/2017, 25 000 €

Translational regulation of human erythropoietin (EPO) by an upstream open reading frame (uORF) and its impact on myocardial ischemia, FCT/PTDC/BIM-MED/0352/2012, 07/2013 -12/2015, 110 k€

Common RNA-dependent pathways for motor-neuron degeneration in spinocerebellar muscular atrophy and amyotrophic lateral sclerosis, JPND-CD/0002/2013, May 2015 - April 2018, 138 847€

Nonsense-mediated mRNA decay in genetic diseases and cancer: key players, mechanisms, and a novel approach for suppression therapy, PTDC/BIM-MEC/3749/2014, 03/2016 - 02/2019 199 662€

PBS Group

Physics of Biological Systems

www.fc.ul.pt/en/pagina/7736/pbs

The PBS group develops its activity on the two extreme scales of biology: the microscopic scale of biomolecules and the macroscopic scale of populations. Its major topical themes are protein physics (focusing on folding and aggregation) and population dynamics (focusing on epidemic spread). From a methodological standpoint the PBS research activities rely heavily on the development and use of analytic and computer simulation methods rooted on statistical physics.

Major Achievements:

The group's major research achievements were obtained in the context of the following research topics:

Complex Adaptive Networks (CAN) – Following previous work on the topic we provide an improved mean field approximation yielding stationary degree distributions of two-state adaptive networks. Until now this degree distributions could only be obtained through statistics on simulations (1).

Disease Spread (DS) – We showed that the periodicities observed for measles time series crucially depend on the interplay between human mobility and local population size: this interplay is responsible for selecting specific mechanisms for the dynamics of the disease and influences in turn the time series observed globally on larger geographical regions (2). (Figure 1 and video)

Physics of Protein Folding (PPF) – We provided first evidence that native interactions between the terminal regions of the polypeptide chain (*i.e.* termini coupling) is a major determinant of the height of the free energy barrier that separates the folded from the denatured state in a two-state folding transition, therefore being a critical modulator of protein folding rates and thermodynamic cooperativity (3). (Figure 2)

Selected Publications:

1. Stefan Wieland and Ana Nunes (2015) Analytic description of adaptive network topologies in a steady state, Phys. Rev. E, 91, 060801(R) (Rapid Communication)

2. Ramona Marguta and Andrea Parisi (2015) Impact of human mobility on the periodicities and mechanisms underlying measles dynamics, J. R. Soc. Interface, 12, 20141317

3. Heinrich Krobath, Antonio Rey, Patrícia F.N. Faísca (2015) How determinant is N-terminal to C-terminal coupling for protein folding? Phys. Chem. Chem. Phys. 17, 3512-3524

Figure 1

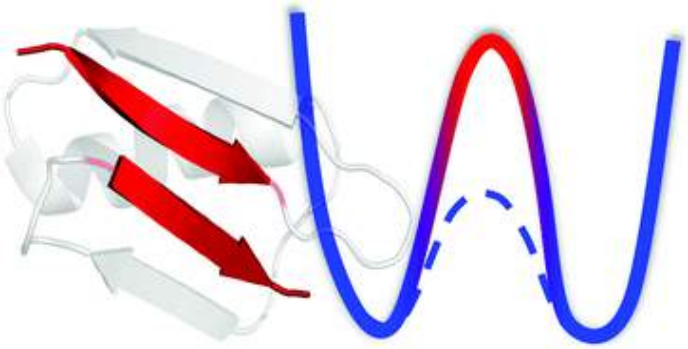
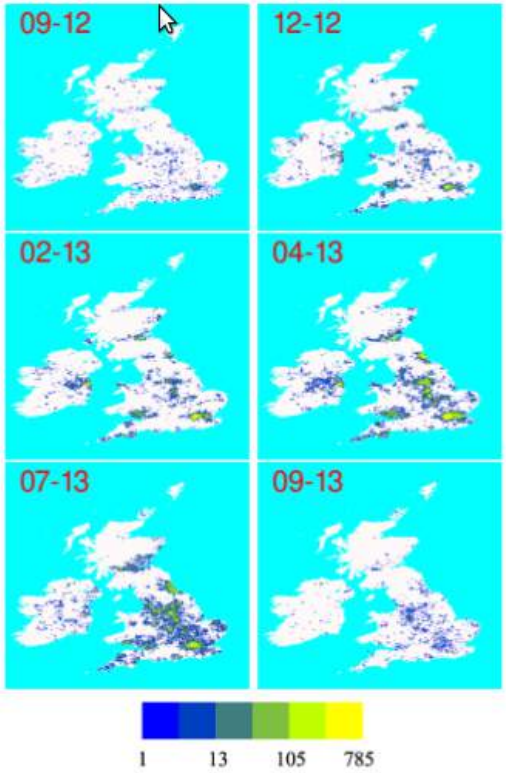


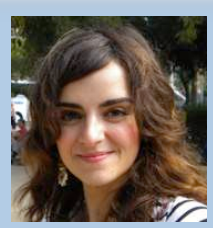
Figure 2



Group Leader
Patrícia Faísca

PI's


Ana Nunes


Sílvia Estácio


Andrea Parisi

Post Doc: Sílvia Estácio (left June 2015)

PhD Students: Rui J Loureiro (BioSYS)

Figure 1: Effect of termini interactions on the thermodynamics of the two-state folding transition. When the termini interactions are 'switched-off' the activation energy of folding decreases (dotted line of the free energy profile).

Figure 2: Snapshot of a simulation of spread of measles on the British isles for a specific value of human mobility parameter during One simulation year. Video: https://www.youtube.com/watch?v=JF0EdSjEx_E#action=share

MagNano Group

Magnetic Nanosystems

www.fc.ul.pt/en/pagina/7737/magnano

MagNano is a group of physicists with a strong expertise on magnetic and atomic systems, nanophysics and nanotechnology methods, housing several high-resolution experimental techniques and a strong competence in their use and development. Within BioISI the group will use the accumulated know-how to tackle relevant issues and innovative applications in biology and life sciences, taking advantage of the unique research multidisciplinary environment offered by this institute.

Major Achievements:

- Force Feedback Microscopy (FFM) development: Rodrigues et al; Patent WO/2013/057426. Atomic force microscopy specific technique allowing measurement of the interaction curve between two systems at all distances.
- Development and consolidation of FFM technique for: measurement of water meniscus; tuning of micro and nanomechanical oscillators; investigation of local mechanical impedance of living cells; development of biological physics studies (FCT project: EXPL/FIS-NAN/1395/2013)
- Investigation of magnetic nanoparticles for magnetic hyperthermia cancer therapy applications (FCT project:PTDC/CTM-Bio/2102/2012)
- Analysis of complex spectra from excited ions (FCT project: PTDC/FIS/117606/2010)

Selected Publications:

Luca Costa and Mario S. Rodrigues (2015) "Influence of spurious resonances on the interaction force in dynamic AFM", *Beilstein J. Nanotechnol. 6* (2015) 420;

Miguel V Vitorino, Simon Carpentier, Alain Panzarela, Mário S Rodrigues, Luca Costa (2015) "Giant resonance tuning of micro and nanomechanical oscillators" *Scientific Reports* 5 (2015) 7818;

Mendo SG, Alves AF, Ferreira LP, Cruz MM, Mendonça MH, Godinho M, Carvalho MD. (2015) Hyperthermia studies of ferrite nanoparticles synthesized in the presence of cotton. New J. Chem. 39:7182 (2015) 93.

Holzhacker C, Stöger B, Carvalho MD, Ferreira LP, Pittenauer E, Allmaier G, Veiros LF, Realista S, Gil A, Calhorda MJ, Müller D, Kirchner K. "Synthesis and reactivity of TADDOL-based chiral Fe(II) PNP pincer complexes-solution equilibria between κ2P,N- and κ3P,N,P-bound PNP pincer ligands", Dalton Trans. 44:13071 (2015) 86.

J. M. Sampaio, T. I. Madeira, M. Guerra, F. Parente, P. Indelicato, J. P. Santos and J. P. Marques. "Relativistic calculations of K, L and M-shell fluorescence, Coster-Kronig, and Auger yields for Ne, Ar, Kr, Xe and Uuo". Phys. Rev. A 91 (2015) 052507.

J. M. Sampaio, T. I. Madeira, M. Guerra, F. Parente, P. Indelicato, J. P. Santos and J. P. Marques. "Relativistic calculations of K, L and M-shell fluorescence, Coster-Kronig, and Auger yields for Ne, Ar, Kr, Xe and Uuo". Phys. Rev. A 91 (2015) 052507.

Figure 1

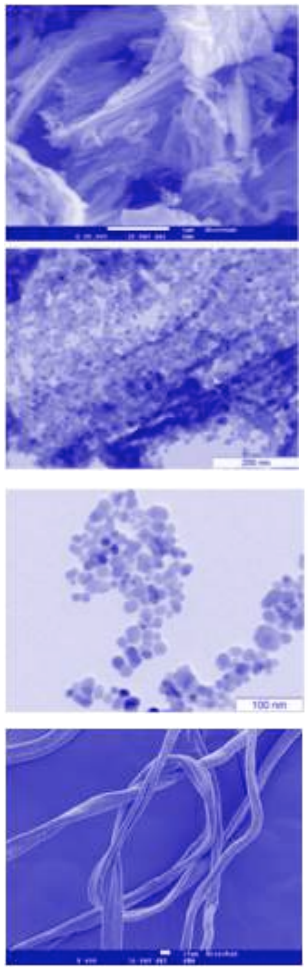


Figure 2

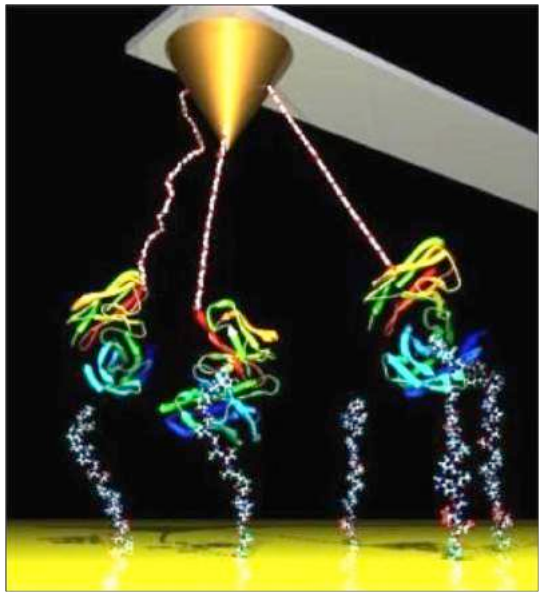


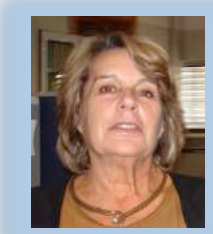
Figure 1: A: SEM (top) and TEM (bottom) images of magnetic nanoparticles prepared using cotton threads. B: TEM images of magnetic nanoparticles C: SEM image of cotton threads

Figure 2: Atomic force microscopy is an astonishing technique that can take images with molecular resolution. AFM tips can be functionalized with target proteins to map specific molecules and/or to force probe interactions between specific molecules.

Key Funded Projects:

Molecular and Mechanical Forces in Biology measured with Force Feedback Microscopy, FCT project, Start date - 01/01/2016 – 3 years, BioISI total Amount – 145.500,0 €, Total Amount of the project - 199.979,00€, Coord Mário Silveira Rodrigues

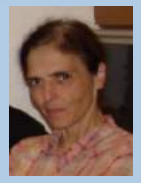
Multifunctional Luminescent Spin Labile Hybrid Materials, FCT project, Start date - 01/01/2016 – 3 year, BioISI total Amount – 27.500,00 €, Total Amount of the project - 191.879,00€, BioISI Partner – Liliana Ferreira



Group Leader

Maria Margarida Godinho

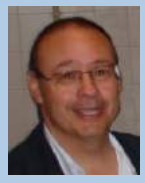
PI's



Margarida Cruz

Liliana Ferreira

Mário Rodrigues



José Pires Marques

Post Docs: Mário S. Rodrigues | Andrii Vovk

Other Integrated members: Guiomar Evans | Thomas Peter Gasche | António Casaca | Teresa Madeira Amorim | Jorge M. Sampaio | Pedro Amorim

PhD Students: Miguel Vargas Vitorino | Cátia Silva | Bruno Ribeiro

MAS Group

Agent and Systems Modelling

www.fc.ul.pt/en/pagina/7738/mas

MAS research focuses three main themes:

- Artificial intelligence approaches of agent and multi-agents systems, mobile robotics, artificial life, and natural language
- Complex multi-agent systems, including agent visualisation and animation, and social simulation
- Data mining and knowledge discovery

Major Achievements:

- National and EU-funded projects – FCT (Novelty guided evolution through grammars; Virtual tutors; MAS negotiation and risk management in electric energy markets), EU (ASSISIbf)
- H. Coelho keynote speeches at Artificial Economics 2015, Porto; EPIA 2015, Coimbra; IEEE Engineering Day, Aveiro; 3rd WCCS 2015, Marrakech, Morocco
- Chairs of key major international artificial intelligence events – S. Silva Editor-in-chief of GECCO 2015 and L. Correia co-chair with T. Soule of "Artificial Life / Robotics / Evolvable Hardware (ALife)" track
- Three PhD supervisions completed
- Collaboration with a variety of research groups: Inst. Tecnol. Tijuana, Mexico; Univ. Southampton, UK; ISCTE-IUL; ISEGI; Univ. Coimbra; Fac. Farmácia; Fac. Arquitectura, IBEB (besides the ones involved in projects)
- R. Antunes post-doc Marie Soklodowska Curie grant shared with Univ. Genève, Switzerland
- Best paper award: Lemos C, Lopes RJ, Coelho H. (2015) Quantitative Measures of Crowd Patterns in Agent-Based Models of Street Protests, IEEE 3rd World Conference on Complex Systems (WCCS15), Marrakech (Morocco)

Figure 1

Figure 2

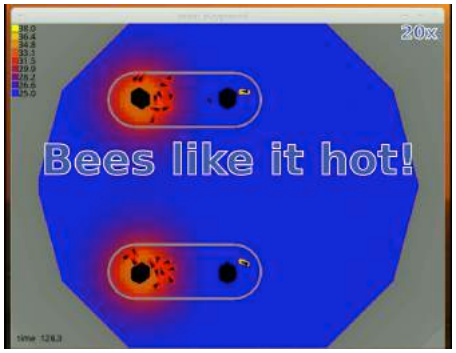
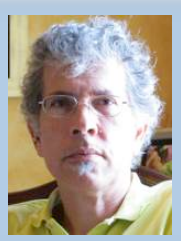


Figure 1: Mobile augmented reality – model of the brain
Figure 2: ASSISIbf bee/robot joint decision making



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Key Funded Projects:

EU-FP7 Animal and robot Societies Self-organise and Integrate by Social Interaction (ASSISIbf)", 1/Feb/13 - 31/Jan/18 (BioISI funding 515.776 EUR). Main contractor Univ. Graz (Austria) / local coordinator L. Correia

FCT VIRTUAL TUTORING. Funding FFCUL / BioISI: 60.967€, of total 199.706€. Main contractor Univ. Aberta / Local coordinator AP Cláudio.

FCT EXPL/EEI-SII/1861/2013 - "A Novidade guia a Evolução através de Gramáticas", PI P Urbano. April 2014 to March 2015, BioISI fund. 22,594 €

FCT PTDC/EEL/122988/2010 MAN-REM – Negociação Multi-Agente e Gestão de Risco em Mercados de Energia Elétrica. Local coord. H. Coelho, BioISI fund. 6 k€

Selected Publications:

Castelli M, Trujillo L, Vanneschi L, Silva S. (2015) Geometric Semantic Genetic Programming with Local Search. Proc. GECCO '15, pp. 999–1006

Gomes J, Mariano P, Christensen AL. (2015) Cooperative Coevolution of Partially Heterogeneous Multiagent Systems. Proc. AAMAS 2015. pp. 297–305

Nunes D, Antunes L. (2015) Modelling structured societies: A multi-relational approach to context permeability. Artificial Intelligence vol. 229: 175-199

Soeiro J, Cláudio AP, Carmo MB, Ferreira HA. (2015) Visualizing the Brain on a Mixed Reality Smartphone Application. Proc. EMBC'15, pp 5090-5093

Silva F, Urbano P, Correia L, Christensen AL. (2015) odNEAT: An algorithm for decentralised online evolution of robotic controllers. Evol. Comp., 23(3):421–449

BioISI Facilities

BioISI equipment that is used by several groups (internal, external, industry) is organised into shared facilities, run by service staff in a cost effective way. Up-to-date facilities constitute an important instrument to recruit the most talented young scientists and significantly contribute to advanced training: PhD, MSc students, workshops.
In 2015-2020, resources will be applied to maintain, update, and support BioISI facilities with expert staff, so that their usage can be applied to maximize expertise and technologies to solve specific biological problems.

The goals of BioISI facilities are:

1) Providing excellent services with state-of-the-art equipment, user support and appropriate computational infrastructure;
2) Turning BioISI into a key player in the creation and operation of the next generation of biological research infrastructures within ULisboa;
3) Making lab available to society initiative goals (FabLabs as proposed by the PRP-National Reform Plan for Portugal) by which citizens, companies, researchers and public institutions work together (in co-creation) to innovate faster and more effectively.

Current BioISI facilities cover the following areas:

- **BioImaging**: hosting fluorescence wide-field and confocal, electron microscopy and automated microscopy
- **Physics**: hosting several high-resolution techniques (SQUID magnetometry, Mössbauer spectroscopy, magneto-optic Kerr effect, atomic force microscopy, etc.)
- **Computing** (data management system): organized and run by BioISI jointly with other FCUL centres
- **Other smaller facilities include:** mammalian cell culture, plant house; NGS (at INSA)

BioISI Facilities Coordinator: Rui Malhó

BioISI Imaging Facilities: Telmo Nunes | Luís Marques

BioISI Facilities website: www.fc.ul.pt/en/pagina/7673/facilities

BioISI Outreach Activities

School visits to labs

E.S. António Damásio – April 30th

Colégio S. João de Brito – June 8th

University open-door days – April 29th

Visits to the microscopy facilities and Fun-GP labs

European Researcher's Night – September 25th

Citizen Science: 'The patient in the Lab – personalized solutions for Cystic Fibrosis' – an interactive demo

Technology: 'The invisible world of flowers' – SEM observations; 'Robots that communicate with beeas and fish' – multimedia presentation

Spot-light presentation: A toast to the 10º aniversary of the European Researchers Night in Portugal with biotech sparkling wine from the Bugworkers lab

Noites de Ciências – October 29th

Regular conference series for the public organized by the Astronomic Laboratory – BioISI invited topic "The Nobel Prize in Chemistry 2015"

Science and technology week - November 23rd to 29th

Workshops for the general public: 'The genome just one click away' **and** 'From a magnifying glass to atomic force microscopy – searching for the minions'

Hangout session: 'Wine with science"

Contacts: BioISIcom@fc.ul.pt

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BioISI Publications

International Journals

PFG Group

L. Saavedra, R. Catarino, T. Heinz, I. Heilmann, M. Bezanilla, R. Malhó (2015) Phosphatase and tensin homolog (PTEN) is a growth repressor of both rhizoid and gametophore development in the moss Physcomitrella patens. Plant Physiology 13: pp 1197.

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Nunes D, Antunes L. (2015) Modelling structured societies: A multi-relational approach to context permeability, Artificial Intelligence vol. 229, pp 175-199

Pombinho P, Carmo MB, Afonso AP. (2015) Adaptive Mobile Visualization – The Chameleon Framework, Computer Science and Information Systems, ComSys, 12(2): 445-464

Power D, Watson RA, Szathmáry E, Mills R, Powers S, Doncaster CP, Czapp B. (to appear) What Can Ecosystems Learn? Expanding Evolutionary Ecology with Learning Theory, Biology Direct (accepted in 2015)

Silva F, Duarte M, Correia L, Moura Oliveira S, Christensen AL. (to appear) Open Issues in Evolutionary Robotics, Evolutionary Computation (Posted Online November 18, 2015)

Trujillo L, Naredo E, Urbano P. (to appear) The Training Set and Generalization in Grammatical Evolution for Autonomous Agent Navigation, Soft Computing journal (accepted in 2015)

Trujillo L, Muñoz L, Galván-López E, Silva S, (to appear) neat Genetic Programming: Controlling bloat naturally, Information Sciences, Volume 333, 10 March 2016, Pages 21-43

Watson RA, Mills R, Buckley CL, Kouvaris K, Jackson A, Powers ST, Cox C, Tudge S, Davies A, Kounois L, Power D. (to appear) Evolutionary Connectionism: Algorithmic principles underlying the evolution of biological organisation in evo-devo, evo-eco and evolutionary transitions, Evolutionary Biology (accepted in 2015)

Books

PFG Group

Fortes A.M., Pais M.S. (2015) Grape (Vitis species). In: Simmonds, M.S.J., Preedy, V.R. (Eds.), Nutritional Composition of Fruit Cultivars. Academic Press, 257–286.

Casetta E, Marques da Silva J (2015) Facing the big sixth - from prioritizing species to conserving biodiversity. In; E. Serrelli, N. Gontier, eds, Macroevolution - Explanation, Interpretation, Evidence, (pp 377 – 403), Interdisciplinary Evolution Research, Volume 2, Springer International Publishing.

Garcia-Oliveira A.L., Poschenrieder C., Barceló J., Martins-Lopes P. (2015). Breeding for Al tolerance by unravelling genetic diversity in bread wheat. In: Aluminum Stress Adaptation in Plants. (Eds) Panda SK, Baluska F, Springer, pp. 125-153, DOI: 10.1007/978-3-319-19968-9.

M&B Group

Santos-Sanches I, Chambel L, Tenreiro R. (2015). Pulsed-Field Gel Electrophoresis (PFGE): application in population structure studies of bovine mastitis-causing streptococci. In: Methods in Molecular Biology. Molecular Diagnosis in Veterinary Laboratory Practice - Reviews and Protocols. Part III – Molecular Profiling of Veterinary Relevant Microbial Pathogens. Chapter 23: 323-334. Springer. Eds. Mónica V. Cunha & João Inácio. doi: 10.1007/978-1-4939-2004-4_23.

Pereira AP, Oliveira JM, Mendes-Ferreira A, Estevinho L. M., Mendes-Faia A. (2015). Mead and other fermented beverages. In: Current Developments in Biotechnology & Bioengineering (A comprehensive series of seven volumes) Series Editor-in-chief: Ashok Pandey (India) Volume III: Food and Beverages Industry Volume Editors-Ashok Pandey (India), Guocheng Du (China), Maria Angeles Sanroman (Spain), Carlos Ricardo Soccol (Brazil), Claude-Gilles Dussap (France). (In press)

BTR Group

Chora, J, Matos,TD, Arguello,P, Fialho,G, Caria,H. (2015) Surdez associada à idade: resultados preliminares. Coleção: E-book Seminários de Investigação - Entre a Teoria, os Dados e o Conhecimento (III). ISBN: 978-989-99447-0-1

GER Group

Mendes-da-Silva A, Adega F, Chaves R (2015) Importance of Fluorescent In Situ Hybridization in Rodent Tumors. In: Syed A. Aziz and Rekha Mehta (Eds) Technical Aspects of Toxicological Immunohistochemistry. System Specific Biomarkers. Springer Publishers (in press).

MAS Group

Antunes L, Louçã J, Almeida P, Guéniot A. (2015) Complexity At the Limit of the (Im)possible, Ghost Editions. pp 130, ISBN 978-989-98298-7-9.

Caraça, J. M. and Coelho, H. (Eds.) Power, Leadership and Complexity, in honor of professor António Gouveia Portela, Proceedings of the 12th Arrábida Workshop on Complexity 2012, IST Press, 2015.

Coelho, H. Idealização de Mentes, FL-DF Compêndio em Linha de Problemas de Filosofia Analítica, Centro de Filosofia da Universidade de Lisboa, http://hdl.handle.net/10451/18108, Maio de 2015.

Kołodziej J, Correia L, Molina JM (Eds). (2015) Intelligent Agents in Data-intensive Computing, Vol 14 of Studies in Big Data. Springer, 2015.

Book Chapters:

Castelli M, Vanneschi L, Silva S, Ruberto S. (2015) How to Exploit Alignment in the Error Space: Two Different GP Models, in Genetic Programming Theory and Practice XII, Riolo R, Worzel WP, Kotanchek M (Eds), pp. 133-148, Springer.

Coelho, H. On Power and Leadership in Artificial Communities, in Caraça, J. M. e Coelho, H. (Eds.) Power, Chapter Leadership and Complexity, in honor of professor António Gouveia Portela, Proceedings of the 12th Arrábida Workshop on Complexity 2012, IST Press, 2015.

Correia L, Manso A. (2015) Amultiset model of multi-species evolution to solve big deceptive problems, In Nathalie Gontier (Ed) Reticulate Evolution, pp 297–337. Springer, 2015.

Flores, C., Respício, A., Coelho, H., Bez, M., Fonseca, J. M. and Barros, P. (2015) Method for Building a Medical Training Simulator with Probabilistics Networks: Intelligent Simulator for Decision Making in Health Care (SimDeCSSimulation for Medical Training), in Cruz-Cunha, M. M. (Ed.) Encyclopedia of E-Health and Telemedicine, IGI Global (to appear).

Mariano P, Correia L. (2015) Partner Selection Delays Extinction in Cooperative and Coordination Dilemmas. Multi-Agent-Based Simulation XV, Ed. Francisco Grimaldo, Emma Norling. Lecture Notes in Computer Science. Springer International Publishing, pp. 88–103.

Mariano M, Correia L. (2015) Partner selection delays extinction in cooperative and coordination dilemmas, in F Grimaldo, E Norling (Eds), Multi-Agent-Based Simulation XV, vol 9002, LNCS, pp 88–103. Springer International Publishing, 2015.

Silva F, Correia L, Christensen AL. (2015) Modelling synchronisation in multirobot systems with cellular automata: Analysis of update methods and topology perturbations, in GCh Sirakoulis, A Adamatzky (Eds), Robots and Lattice Automata, volume 13 of Emergence, Complexity and Computation, pp 267–293. Springer.

Trigo, P. and Coelho, H. (2015) Multi-Agent Simulation of Electricity Markets Power and Influence in a Game Experience, in Caraça, J. M. e Coelho, H. (Eds.) Chapter Power, Leadership and Complexity, in honor of professor António Gouveia Portela, Proceedings of the 12th Arrábida Workshop on Complexity 2012, IST Press.

Computational Applications:

MAS Group

StopBully- serious game for mobile devices and PC. The target audience are children 10-12 years old and the main purpose is to prevent bullying and promote empathy.

Brain AR/VR- application for smartphone to visualize 3D models of the brain in AR and VR

Virtual Pharmacy- interactive application (for PC) conceived to improve non-prescription medicines consultation skills in undergraduate Pharmacy students

SolAR- mobile application to visualize solar radiation data in AR

BeeFish mobile game (soon in App Store) – dissemination product of ASSISIbf project

BioISI Theses

MSc theses:

PFG Group

Ana Catarina Guerreiro Marques (2015) "A sinalização por Ácido Jasmónico e a resistência a fungos biotróficos em videira"- MESTRADO EM BIOLOGIA MOLECULAR E GENÉTICA, FCUL

João Ilídio Lopes, 2015. A Olivicultura na Região de Trás-os-Montes Percurso Profissional 1989-2013. Master in Agronomic Engineering, University of Trás-os-Montes and Alto Douro, Vila Real. (Supervisor: Paula Martins-Lopes)

FunGP Group

Adriana Falcão (2015) Agregação e formação de amilóides por proteínas neuroinflamatórias S100A8 e S100A9 e implicações em processos neurodegenerativos. MSc in Biochemistry química. Faculdade Ciências e Tecnologia, Universidade Nova de Lisboa (Supervisor: Cláudio M. Gomes)

Ângela Alves (2015) "Desenvolvimento de um biossensor celular para o estudo translacional da Fibrose Quística e outras doenças respiratórias crónicas". MSc in Biochemistry, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal (Supervisor: Paulo Matos; Co-Supervisor: Carlos M Farinha).

João Coelho (2015) " Signalling pathways in Cystic Fibrosis: a cross-talk between CFTR trafficking and inflammation mechanisms" MSc in Biochemistry, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal (Supervisor: Carlos M Farinha).

Madalena Pinto – MSc student in Biochemistry. Thesis: "ANO6 - A novel ion channel regulator with extended functions and significance in disease". Supervisor: Margarida Amaral

Andreia Duarte (Nov 2015) "Avaliação das propriedades regenerativas vs. oncogénicas do tratamento com rhHGF em culturas de células epiteliais brônquicas derivadas de doentes com fibrose quística. MSc in Biochemistry, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal (Supervisor: Paulo Matos).

GER Group

Nuno Costa (2015). The mechanism of nonsense-mediated mRNA decay. MSc in Biochemistry (FCUL). Supervisor: Luisa Romão

Ana Catarina Maia Rocha (2015). Development of New Cellular Models for Step-by-Step Analysis of Astrogliogenic Pathways . MSc in Molecular Biology and Genetics. Supervisors: Federico Herrera and Margarida Gama-Carvalho

MAS Group

Bruno Penha, "Aging effects in speech statistical learning - a behavioral and computational study". Mestrado em Ciência Cognitiva, da ULisboa. Supervisor: Tânia Fernandes, co-supervisor: Luís Correia

Cátia Sofia Campos Raminhos, "StopBully- Jogo sério para prevenir o bullying e promover a empatia", Mestrado em Engenharia Informática, supervisors: Ana Paula Cláudio and Maria Beatriz Carmo

José Tiago Quenino Soeiro, "Visualização de dados médicos em Realidade Aumentada", Mestrado em Informática, supervisors: Ana Paula Cláudio and Maria Beatriz Carmo

Vítor Manuel Gonçalves Pinto, "Humanos virtuais em ambientes de treino de competências sociais na área da saúde", Mestrado em Engenharia Informática, supervisors: Ana Paula Cláudio and Maria Beatriz Carmo

Silvana Isabel Candeias da Silva, " Visualização de dados sobre radiação solar em Realidade Aumentada", Mestrado em Engenharia Informática, supervisors: Maria Beatriz Carmo and Ana Paula Cláudio

PhD theses:

PFG Group

Maria Leonor Gonçalves, 2015. Wine Authenticity – a Genomic Approach. PhD in Comparative Molecular Genetics and Technology, University of Trás-os-Montes and Alto Douro, Vila Real. Public defence on the 15th of December. (Supervisors: Henrique Guedes-Pinto and Paula Martins-Lopes)

João Paulo de Sousa Coutinho, 2015. Genetic characterization of Fagaceae by molecular and cytogenetic approaches. PhD in Comparative Molecular Genetics and Technology, University of Trás-os-Montes and Alto Douro, Vila Real. Public defence on the 16th of December. (Supervisors: Henrique Guedes-Pinto and Paula Martins-Lopes)

FunGP Group

Inna Uliyakina – PhD thesis in Biochemistry (FCT fellowship SFRH/BD/69180/2010) Thesis: "Analysis of CFTR Mutants in Epithelial Cells/Tissues and Testing of CFTR-Repairing Therapies". Supervisor: Margarida Amaral: Classification: Summa cum Laude.

M&B Group

Ana Paula Rodrigues Pereira. 2015. Optimization of mead production: design of different strategies for improvement of alcoholic fermentation. PhD thesis UTAD. Supervisor: A. Faia (UTAD/BioISI).

Marta Isabel Cerejo. 2015. TAU interactors: new drug tagets. PhD thesis MIT-Portugal | UNL. Co-supervisor: H. Vieira (FCUL/BioISI).

BTR Group

Liliana Alves da Silva Marques “Iron homeostasis in immune mononuclear cells: a potential role in atherogenesis”, Faculdade de Ciências da Universidade de Lisboa

GER Group

Susana Manuela Alves Meles (2015) The Rattus norvegicus cell model: an integrated analysis of chromosome architecture, genes and satellite non-coding sequences. PhD thesis in “Genética Molecular Comparativa e Tecnológica”, UTAD, Vila Real, Portugal. Supervisor: Raquel Chaves and Co-supervisor: Filomena Adega.

Ana Maria Correia Vieira da Silva (2015) The patchwork pattern of rodent genomes: species-specific organization of orthologous DNA sequences. PhD thesis in “Genética Molecular Comparativa e Tecnológica”, UTAD, Vila Real, Portugal. Supervisor: Raquel Chaves and Co-supervisor: Henrique Guedes-Pinto.

MAS Group

Francisco Mateus Marnoto de Oliveira Campos, “Embodied Cognition approaches to mobile robot navigation”. Doutoramento em Informática. Supervisor: Luís Correia, co-supervisor: João Calado. ULisboa, March 2015

Mateus Padoca Calado, Serviço de Emergência Médica Angolano: Optimização Utilizando Sistemas Multi-Agente, Doutoramento em Informática, Faculdade de Ciências da Universidade de Lisboa, 25 September 2015, supervisor: Luis Antunes.

Nuno Montenegro, CITYPLAN - contributo para o desenvolvimento de uma metodologia e ferramenta computacional para apoio ao desenho urbano, July 2015, co-supervisor: Paulo Urbano.

BioISI Funded Projects

PFG Group

2013 Conservation of plant biodiversity in the Macaronesian Hotspot: Integrating phylogenetic, taxonomic, and ecological approaches to study the Cape Verde endemic flora (PTDC/BIA-BIC/4113/2012); Fundação para a Ciência e a Tecnologia (FCT); 7/2013 - 6/2016; BioISI (Partner) Amount - 56.327,00 Total Amount of the project 110.202,00, Maria Romeiras

2013 Aqua+(PRO): Desenvolvimento de um novo processo de gestão de rega inteligente para produção de pera Rocha em pomares de alta densidade na região do Oeste, Programa de Desenvolvimento Rural do Continente (PRODER), 2013 – 2015, BioISI (partner) 180 000€, Anabela Bernardes da Silva

2014 PRODER Nº 57059; Titulo: Desenvolvimento de processos de produção e extracão de resina de pinheiro para a melhoria da eficiência, racionalização e expansão da atividade. (2014-2017) Parceiros: UTAD e GIFF (Montante 108550.67 €)

2015 Sexual Plant Reproduction – Seed formation. Project 690946 – SexSeed. H2020 MSCA-RISE-2015. Starts 01 March 2016, ends 28 February 2020. Total amount 720000.00€, BioISI 193500.00€. Sílvia Coimbra – Coordinator

2016 EvoMod- Origem e estabelecimento evolutivo de um módulo transcricional que controla a assimetria floral, PTDC/BIA-PLA/1402/2014- FCT, 1 January 2016- 31 December 2018 160.416,00 €/196.716,00 €, BioISI Coordinator- Manuela Costa

2016 Characterisation of cork formation and reproductive biology in a cork hybrid population, PTDC/AGR-FOR/3356/2014- FCT, 1 January 2016-31 December 2018, 57.115,00 €/199.987,00 €, Partner- Manuela Costa

FunGP Group

2014 CF Trust Strategic Research Centre Award (Ref. SRC 003) "*INOVCF- Innovative non-CFTR Approaches for Cystic Fibrosis Therapies*". Total budget: 750K£. FCUL Budget: 178.4K€; 4 yrs. PI: M Gray, Newcastle (UK). PI for the FCUL group: MD Amaral.

2015 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL15XX0) "*CFTR mRNA Stability Studies for PTC Mutations*". Budget: 222K$; 2 yrs. PI: MD Amaral.

2015 ERARE15-pp-010/JTC 2015 "*INSTINCT - Induced Pluripotent Stem Cells for Identification of Novel Drug Combinations Targeting Cystic Fibrosis Lung and Liver Disease*". Budget (FFCUL): 124K; 3 yrs. Principal Investigator (U Martin, Univ. Hannover, Germany). FCUL PI: MD Amaral.

2015 "Pesquisa de novos alvos moleculares para adjuvar a correção farmacológica da F508del-CFTR", funded by Programa Gilead GÉNESE (PGG/055/2014). 20K €. PI: Paulo Matos.

2015 "A sinalização pró-inflamatória como novo alvo terapêutico na fibrose quística", funded by Programa Gilead GÉNESE (PGG/039/2014). 15K €. PI: Carlos M Farinha.

2015 Proteotoxic insults and synaptic dysfunction in the aging brain. Bial Foundation Research Grant (Portugal). 2015-2018. Project coordinator: Cláudio Gomes.

2016 CFF Cystic Fibrosis Foundation, USA (Ref. AMARAL15XX1) "*RNA LIFE – Novel RNA Regulators as Potential Drug Targets for Cystic Fibrosis*". Budget: 324K$; 2 yrs. PI: MD Amaral.

2016 FCT/POCTI (PTDC/BIM-MEC/2131/2014) "*DIFFTARGET-Novel Factors of CFTR Traffic Related to Epithelial Cell Differentiation: Potential Therapeutic Targets for Cystic Fibrosis*". Budget: 200K€; 3 yrs. PI: MD Amaral.

2016 FCT/POCTI (PTDC/EEI-ESS/4923/2014) "*MIMED - Mining the Molecular Metric Space for Drug Design*". Budget: 127K€; 3 yrs. PI: A Falcão

2016 FCT/POCTI (PTDC/QEQ-SUP/4283/2014) "*FARMTRANSANION-Anion transmembrane transport promoted by drug-like molecules: building a library of anion carriers inspired in Ataluren (PTC124)*". Budget: 200K€; 3 yrs. PI: V Félix.

2016 Gilead GÉNESE Programme (Ref PGG/008/2015) "*Predicting Clinical Drug Efficacy of CFTR Protein Modulators Using Intestinal Organoids and Nasal Cells from Patients with Cystic Fibrosis*". 30K€, 1 yr. Principal Investigator: MD Amaral.

M&B Group

EU projects

BlueGenics - From Gene to Bioactive Product: Exploiting Marine Genomics for an innovative and Sustainable European Blue Biotechnology Industry. EU. FP7- KBBE-2012-6- 311848, Large Scale Cooperation FP7 consortium. 2012-2016. Total funding: 6 M€. No BioISI amount. BioISI Partner: H. Vieira as Expert/Consultant (previous participant as BIOALVO). [Blue M&B]

EUPHRESCO II PSADID – Bacterial canker of kiwifruit: Development and harmonisation of methods for diagnosis, detection and identification of *Pseudomonas syringae* pv. *actinidiae*. 2013-2015. EU project (IT, PT, FR, SP, CH, NZ). Non-competitive funding. Total funding: 90 k€. INIAV funding: 15 k€. No BioISI amount. PI: L. Cruz (INIAV/BioISI). [Green M&B]

MaCuMBA - Marine Microorganisms: Cultivation methods to improving their biotechnological Application. EU. FP7- KBBE-2012-6- 311975. Large Scale Cooperation FP7 consortium. 2012-2016. Total funding: 9 M€. No BioISI amount. BioISI Partner: H. Vieira as Expert/Consultant (previous participant as BIOALVO). [Blue M&B]

National basic research projects

Molecular and Mechanical Forces in Biology measured with Force Feedback Microscopy. FCT . PTDC/FIS-NAN/6101/2014. 2015-2018. Proponent: FFCUL (BioISI). Total funding: 197 k€.

PI: M Rodrigues (BioISI-MagNano). M&B Partner: L. Fernandes (IPL/BioISI). [White M&B]

New arboviruses isolated in Portugal. Risk assessment and Public Health application. FCT. PTDC/SAU-SAP/119199/2010. 2011-2015. Proponent: INSARJ. Total funding: 125 k€. No BioISI amount. BioISI Partner: L. Zé-Zé (INSARJ/BioISI). [Red M&B]

Q Fever- from diagnosis to eco-epidemiological investigation of *Coxiella burnetii* in the context of human infection. FCT. PTDC/SAU-SAP/115266/2009. 2011-2015. Proponent: INSARJ. Total funding: 178 k€. No BioISI amount. BioISI Partner: L. Zé-Zé (INSARJ/BioISI). [Red M&B]

Study of ulcerogenic *Helicobacter pylori* strains isolated from children: a contribution to get insight the pathogenesis of the peptic ulcer in pediatrics. FCT. PTDC/BIM-MEC/1051/2012. 2013-2015. Proponent: INSARJ. Total funding: 74 k€. M&B-BioISI funding: 23 k€. BioISI Partner: A. Tenreiro (FCUL/BioISI). [Red M&B

BIOCLUB - Designing biofertilizers by mimicking plants' recruitment of rhizospheric partners. FCT. PTDC/AGR-PRO/1852/2014. 2015-2018. Proponent: FFCUL (CE3C). Total funding: 199 k€. No BioISI amount. BioISI partner: R. Tenreiro (FCUL/BioISI). [Grey/Green M&B

HOSTSTREP II - Specific evaluation of the host and pathogen-host interactions agent in *Streptococcus* PTDC/CVT-EPI/6685/2014. 2015-2018. Total funding: 199 k€. No BioISI amount. BioISI partner: L. Chambel (FCUL/BioISI). [Red M&B]

National SME-associated projects

FACIB - New drugs from sugars against infections by *Bacillus* species. COMPETE, QREN and FEDER. AdI 21547. Proponent Company: CIPAN. Partners: FCUL. 2011-2015. Total funding: 525 k€. FCUL PI: A. Rauter (CQB). M&B-BioISI funding: 178 k€. M&B-BioISI PI: R. Dias. [Black/Gold M&B]

InovPomo - Improvement of the production process of pears and apples through the conservation and characterization of plant material. PRODER PA 49448. INIAV and SOATI. 2014-2016. Total funding: 160 k€. No BioISI amount. PI: L. Cruz (INIAV/BioISI). [Green M&B]

LEVEalliance - a portfolium of natural and adaptively evolved non-saccharomyces yeasts for the production of lower ethanol content wines. COMPETE, QREN and FEDER. AdI 38918. Proponent Company: Proenol Lda. Partners: FCUL. 2013-2015. Total funding: 534 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 211 k€. [Yellow/White M&B]

PATHOALERT - New diagnostic methods of pathogenic and emergent microbes in food and water: a molecular and cytological approach for detection and evaluation of pathogenic potential. POR Lisboa, QREN and FEDER. AdI 30211. Proponent Company: Biopremier SA. Partners: FCUL. 2013-2015. Total funding: 576 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 304 k€. [Red/Yellow M&B]

SMARTWINE - Smarter wine fermentations: integrating Omics-tools for development of novel mixed-starter cultures for tailor-made wine production. FCT, COMPETE, FEEI. PTDC/AGR-TEC/3315/2014, 2015-2019. Total funding: 196 k€. No BioISI amount. PI: A. Mendes-Faia (UTAD/BioISI). [Yellow/White M&B]

TAINTLESS - Preventing wine cork flavour by using selective inhibitors of enzymes involved in biosynthesis of organic halogenated compounds. COMPETE, QREN and FEDER. AdI 23045. Proponent Company: Cork Supply Portugal SA. Partners: IST, FCUL. 2012-2015. Total funding: 867 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 151 k€. [Yellow/White M&B]

BIOPEPPERtec - Production of fermented peppers paste and pepper serum vinegar: integrated approach in the implementation of biotechnological processes. POCI and POR Lisboa. P2020 project nº 3321. Proponent Company: Mendes Gonçalves SA. Partner: FCUL. 2016-2018. Total funding: 599 k€. FCUL PI: R. Tenreiro (FCUL/BioISI). M&B-BioISI funding: 351 k€. [Yellow/White M&B]

RESISTIR - Intelligent information system to control infection and personalized antibiotherapy. POCI and POR Lisboa. P2020 project nº 3379. Proponent Company: MAXDATA Software SA. Partner: FCUL. 2016-2018. Total funding: 1.02 M€. FCUL PI: R. Dias (FCUL/BioISI). M&B-BioISI funding: 531 k€. [Red/Gold M&B]

BTR Group

2015 -2018 Autism Spectrum Disorders in Europe **(ASDEU)** Funded by the Health Programme of the European Union DG-SANCO, 144 000€. Partner Astrid Vicente

2015-2018 ALHTOUR – Assisted Living Technologies for the health tourism sector (CSA action of H2020-TWINN-2015), European Commission, 2015-2018; to be defined (total FCUL= 322 752,50); Partner - Helena Caria

2015-2016 FH Genetic diagnosis - Development and validation of support documentation for the molecular diagnosis of Familial Hypercholesterolaemia, 2015-2016. Funded by Genediag.exe, 20 000€. Principal Investigator - M Bourbon.

2014-2016 Joint Action on Chronic Diseases CHRODIS-JA, 2014 – 2016, Funded by the Health Programme of the European Union DG SANCO, 66 000€, Partners – Luciana Costa, Astrid Moura Vicente

2014-2016 LAL _D.pt - Molecular study of LIPA gene in patients with unexplained severe dyslipidaemia, 2014-2016. Funded by Synageva BioPharma Corp. 56 124€ Principal Investigator.- M Bourbon

2014-2017 COST Action TINNET (Action number BM1306); Funding by European Commission; 2014-2017; Partner - Helena Caria

2014-2015 Assessment of the reduction of low-density lipoprotein cholesterol (LDL-C) by REGN1500. Funded by Regeneron Pharmaceuticals Inc., 121 900 €. Principal Investigator- M Bourbon.

2014-2015 Bem Entender a Saúde - projeto BENS, 2014 – 2015 Funded by Fundação Calouste Gulbenkian (FCG), 30 000€; Principal Investigator - Astrid Moura Vicente

2013-2015 Economics of Chronic Diseases (EConDA), Funded by the Health Programme of the European Union DG Sanco, 80000€; BioISIPartner - Mafalda Bourbon

2012-2015 Identifying the earliest signs of autism - integration of behavioral, clinical and genetic information for early autism diagnosis in a at-risk population 2012 – 2015, Funded by Fundação para a Ciência e a Tecnologia (FCT/MCTES), 120 000€; Principal Investigator - Astrid Moura Vicente

2009-2015 Prevalence of cardiovascular risk factors in the Portuguese population (e_COR), 2009-2015. Funded by Science and Technology Foundation (FCT) and INSA, 177 000 Euros, Principal Investigator- M Bourbon .

2012-2015 Prevalence of hepatic steatosis in Portugal, 2012-2015. Funded by Gilead Pharmaceutical, 50 000 Euros, Team member-M Bourbon

2010-2015 Novel genes causing Familial Hypercholesterolaemia, 2010-2015. Funded by Science and Technology Foundation (FCT), 199.727,00 Euros, Principal Investigator.

2012 Age-related hearing loss: Genetic risk factors and social impact, Funded by Fundação para a Ciência e a Tecnologia (PTDC/NEU-BEN/1192/2012) 146 616€; Principal Investigator Helena Caria

GER Group

2015 New insights into the regulation of insulin-sensitive glucose transporters by WNK protein kinases, FCT PTDC/SAU-MET/117236/2010, Jan 2012-Jun 2015, 120 000€

2015 Tumor cell plasticity through alternative splicing in response to a 3D pro-inflammatory microenvironment; Maratona da Saúde- Cancro 2014, July 2015-Jun 2017, 25 000 €

2015 Translational regulation of human erythropoietin (EPO) by an upstream open reading frame (uORF) and its impact on myocardial ischemia, FCT/PTDC/BIM-MED/0352/2012, July 2013-Dez 2015, 110 000€

2015 Common RNA-dependent pathways for motor-neuron degeneration in spinocerebellar muscular atrophy and amyotrophic lateral sclerosis, JPND-CD/0002/2013, May 2015-April 2018, 138 847€

2016 Perturbation of the intestinal barrier function in Inflammatory Bowel Diseases: role of the Rac1b /cytokine axis; Portuguese Society of Inflammatory Bowel Disease (GEDII), Jan 2016-Dez 2017, 15 000 €

2016 Nonsense-mediated mRNA decay in genetic diseases and cancer: key players, mechanisms, and a novel approach for suppression therapy, PTDC/BIM-MEC/3749/2014, March 2016-Feb 2019 199 662€

MagNano Group

2015 Colaboração na Experiência ATLAS do LHC (CERN/FIS-NUC/0005/2015), funded by FCT. Budget: 16.800,00 € (total amount of the project: 400.000€); 2 years; BioISI PI: Guiomar Evans

2016 "Multifunctional Luminescent Spin Labile Hybrid Materials", funded by FCT. Budget: 27.500,00€ (total amount of the project: 191.879,00€); 3 years, BioISI PI: Liliana Ferreira

MAS Group

2013-2018 Animal and robot Societies Self-organise and Integrate by Social Interaction (ASSISIbf)", No 601074, FP7-ICT-2011-9 of EU (BioISI funding 515.776 EUR). Main contractor Univ. Graz (Austria) / local coordinator

FFCUL TUTORIA VIRTUAL - o tutor virtual artefacto mediador da aprendizagem no ensino superior online (VIRTUAL TUTORING – the virtual tutor as learning mediating artifact in online university education). Funding FFCUL / BioISI: 60.967€, of total de 199.706€. Main contractor Univ. Aberta / Local coordinator Ana Paula Cláudio.

2013 FCT one year exploratory research project EXPL/EEI-SII/1861/2013 - "A Novidade guia a Evolução através de Gramáticas", coordinated by Paulo Urbano. Ended in March 2015

2010 PROJETO FCT PTDC/EEL/122988/2010 MAN-REM – Negociação Multi-Agente e Gestão de Risco em Mercados de Energia Elétrica.