

One of the transformative novelties in Life Sciences research of the last couple of decades is the onset and growth of the so-called Systems Biology, which brings about a radical change in the way we address biological problems. Although molecular biology has been traditionally considered to have been founded by physicists, this circumstance did not result in a quantitative culture and an accurate, standardised descriptive language characteristic of the hard sciences. On the contrary, with very few exceptions, the biosciences that developed since that time seldom took the opportunity to formalise the mechanisms and functions of living systems with accurate languages and codes. Systems Biology occupies this niche by analysing biological entities as comprehensible physicochemical objects with a functioning and relational logic that can be modelled, understood and reshaped.

By the same token, Synthetic Biology is not just a contemporary update of the recombinant DNA technologies of the past 30 years, along with a descriptive language imported from electrical and industrial engineering. It is also a new interpretive key for living systems as well as a declaration of intent on the use and reprogramming of biological objects for human benefit. In the same way that scientific chemistry as initiated by Lavoisier evolved into the chemical engineering that is the basis of our industrial society, biology has acquired a transforming potential that could lead to a type of industry and economy very different of the current paradigm.

The CNB SysBio Program maps in the contemporary landscape of the field by developing active research lines in environmental genomics, network biology, systemic computation and metabolic engineering. This frame (which many consider to be a veritable paradigm change) seeks to address the complexity of living systems as such, not to divide them into smaller parts—unlike the traditional reductionism of Molecular Biology. The scientific and technological potential of Systems and Synthetic Biology is immense, both in the field of Biomedicine and Industrial, Agricultural and Environmental Biotechnology.



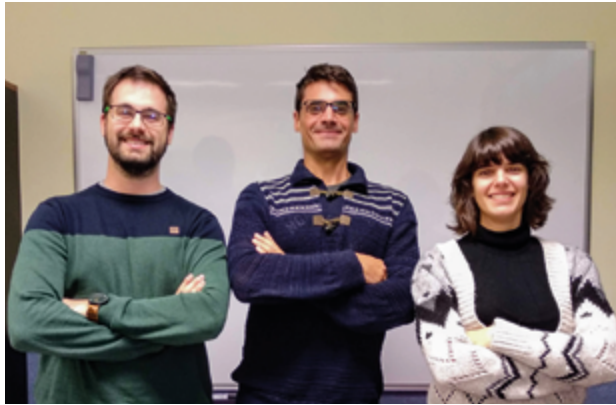
# Systems Biology

## **HEAD OF DEPARTMENT**

Víctor de Lorenzo

## **RESEARCH GROUPS**

- 1. Clocks and rulers in life**  
Saúl Ares
- 2. Molecular environmental microbiology**  
Víctor de Lorenzo
- 3. Evolutionary systems**  
Susanna Manrubia
- 4. Systems biotechnology**  
Juan Nogales
- 5. Computational systems biology**  
Florencio Pazos Cabaleiro
- 6. Logic of genomic systems**  
Juan F. Poyatos
- 7. Microbiome analysis**  
Javier Tamames & Carlos Pedrós



## Clocks and rulers in life

### GROUP LEADER

Saúl Ares

### PhD STUDENT

Pau Casanova

### MASTER'S STUDENTS

Christian Camilo Cortés  
Gabriel Rodríguez Maroto

### SELECTED PUBLICATIONS

Val-Calvo J, Luque-Ortega JR, Crespo I, Miguel-Arribas A, Abia D, Sánchez-Hevia DL, Serrano E, Gago-Córdoba C, Ares S, Alfonso C, Rojo F, Wu LJ, Boer DR and Meijer WJJ. Novel regulatory mechanism of establishment genes of conjugative plasmids, *Nucleic Acids Res* 2018; 46: 11910-11926.

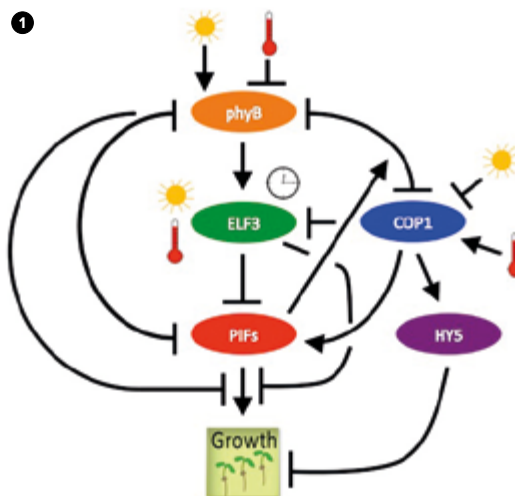
We are interested in spatiotemporal phenomena in living systems: oscillations, pattern formation and dynamics of gene expression. We work in collaboration with experimentalists to build theories of these spatiotemporal phenomena, using ideas from physics and mathematics to build models and computer simulations that help us understand the nature of the interactions underlying the dynamics of life.

We pursue this goal on a variety of research lines. Cyanobacteria are important organisms for the environment for their photosynthetic activity and their capacity to fix nitrogen into chemical forms usable for other life forms. They are also of biotechnological interest as the source of fertilisers or biofuels. We study how filamentous cyanobacteria differentiate into nitrogen-fixing cells called heterocysts, and how the patterns of heterocysts on the filament are formed.

The ability of plants to sense light and temperature allows them to tune their growth to environmental conditions. In a context of global climate change and endangered crops, it is important to understand how this occurs. In collaboration with the group of Salomé Prat in the Department of Plant Molecular Genetics, we formulate mathematical models that help to understand what are the key molecular factors to the response of plants in light and temperature.

Bacterial resistance to antibiotics is becoming a major health hazard. One of the ways in which this resistance can spread is through bacterial conjugation, a process through which bacterial cells can share pieces of DNA. We work together with the lab of Wilfried Meijer at CBMSO to understand the dynamics and regulation of conjugation in Gram-positive bacteria.

Finally, embryos are constantly growing and reshaping, differentiating new cell types and organs. Developmental biology is always an interest of the lab, and the problem of how the body of vertebrate embryos is segmented is especially close to our hearts.



1 Regulatory logic of the control of hypocotyl growth in the model plant *Arabidopsis thaliana*. Suns and thermometers represent effects of light and temperature, respectively.



# Molecular environmental microbiology

SYSTEMS BIOLOGY PROGRAMME 85

## GROUP LEADER

**Víctor de Lorenzo**

## SENIOR SCIENTISTS

Belén Calles  
Esteban Martínez

## POSTDOCTORAL SCIENTISTS

Yamal Al-Ramahi  
David Rodríguez Espeso  
Tomás Aparicio  
Pavel Dvorak

## TECHNICIANS

Sofía Fraile  
Elena Algar

## LAB EXECUTIVE ASSISTANT

Inés Merino

## PHD STUDENTS

Mª de los Ángeles Hueso Gil  
Huseyin Tas  
Elena Velázquez

## VISITING SCIENTISTS

Joseph Mougous  
(Washington University, USA)  
Hiren Joshi  
(WSCD, India)

## VISITING STUDENTS

Estela Ricaurte  
Jillian Silbert  
Ananda Sanches  
Hannes Löwe  
Coral García Gutiérrez

## SELECTED PUBLICATIONS

Dvořák P, *et al.* Bioremediation 3.0: Engineering pollutant-removing bacteria in the times of systemic biology. *Biotechnol Adv* 2017; 35: 845-866.

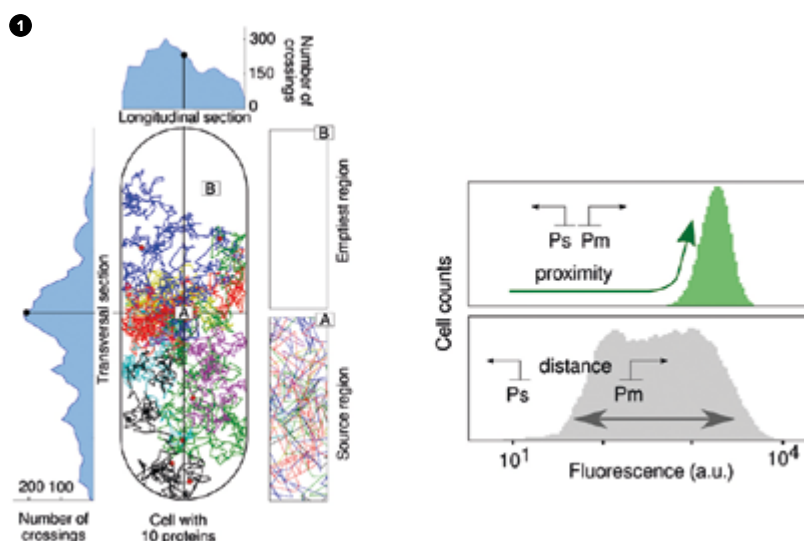
Goñi-Moreno A, *et al.* Deconvolution of gene expression noise into spatial dynamics of transcription factor-promoter interplay. *ACS Synth Biol* 2017; 6: 1359-1369.

Akkaya O, *et al.* The metabolic redox regime of *Pseudomonas putida* tunes its evolvability towards novel xenobiotic substrates. *mBio* 2018; 9: e01512-18

Dvorak P, de Lorenzo V. Refactoring the upper sugar metabolism of *Pseudomonas putida* for co-utilization of cellobiose, xylose, and glucose. *Metab Eng* 2018; 48: 94-108

de Lorenzo V. *et al.* The power of synthetic biology for bioproduction, remediation and pollution control. *EMBO Rep* 2018; 19: e45658.

The longstanding mission our team is the production of biological agents for biosensing, remediation and (wherever possible) valorisation of chemical waste that is otherwise dumped into the Environment by urban and industrial activities. The workhorse to this end is the soil bacterium *Pseudomonas putida*, which combines the ease of genetic programming that is typical of *Escherichia coli* with the safety, robustness and metabolic capabilities required in whole-cell catalysts for applications in harsh biotechnological settings. Specific activities include: [i] Development of *P. putida* as a reliable chassis for implantation of genetic and metabolic circuits. This involves a profound editing of the extant genome of this microorganism for enhancing desirable properties and eliminating drawbacks. Also, the exploitation of surface-display systems for designing complex catalytic properties altogether separated from the cell metabolism and even the design of artificial communities by means of ectopic adhesins. [ii] Genetic tools for deep refactoring of metabolic properties of *P. putida*. The list of new assets that we are developing includes a large collection of standardised plasmid and transposon vectors as well as dedicated reporter systems for parameterisation of the gene expression flow and for switching entire metabolic regimes. [iii] The TOL system borne by plasmid pWWO as a reference for metabolic circuit implantation. The two operons for toluene and m-xylene biodegradation encoded in pWWO offer a natural case of expansion of the metabolic repertoire of environmental bacteria through acquisition of new genes. [iv] Deep metabolic engineering of *P. putida*. Currents efforts attempt to develop strains that can be entirely programmed to deliver catalytic phenotypes of choice upon exposure and computation of both external and internal cues. This endeavour combines direct rational engineering with fine-tuning of gene expression by means of site-specific diversification of genomic sequences of choice through adaptation to *P. putida* of multiple automated genome engineering (MAGE) technology.



**1** Gene expression noise detected as changes in the fluorescent output of individual cells bearing transcriptional fusions to the promoters of interest reflects the distance and the intracellular microgranularity that cognate transcription factors have to go through the cytoplasm to find its target sequence (see Goñi-Moreno *et al.* 2017 for details).



## Evolutionary systems

86 SYSTEMS BIOLOGY PROGRAMME

### GROUP LEADER

**Susanna Manrubia**

### SENIOR SCIENTIST

Jacobo Aguirre

### POSTDOCTORAL SCIENTIST

Juan Antonio García-Martín

### PhD STUDENTS

Adriana Lucía-Sanz  
Pilar Somovilla

### MASTER'S STUDENTS

Oscar Gómez Balaguer  
Sergio Javier Avero Rodríguez  
Luis Marchante

### VISITING STUDENTS

Víctor Buendía  
María Caro

### SELECTED PUBLICATIONS

Lucía-Sanz A, Manrubia S. Multipartite viruses: adaptive trick or evolutionary treat? *NPJ Syst Biol Appl* 2017; 3: 34.

Yubero P, Manrubia S, Aguirre J. The space of genotypes is a network of networks: implications for evolutionary and extinction dynamics. *Sci Rep* 2017; 7: 13813.

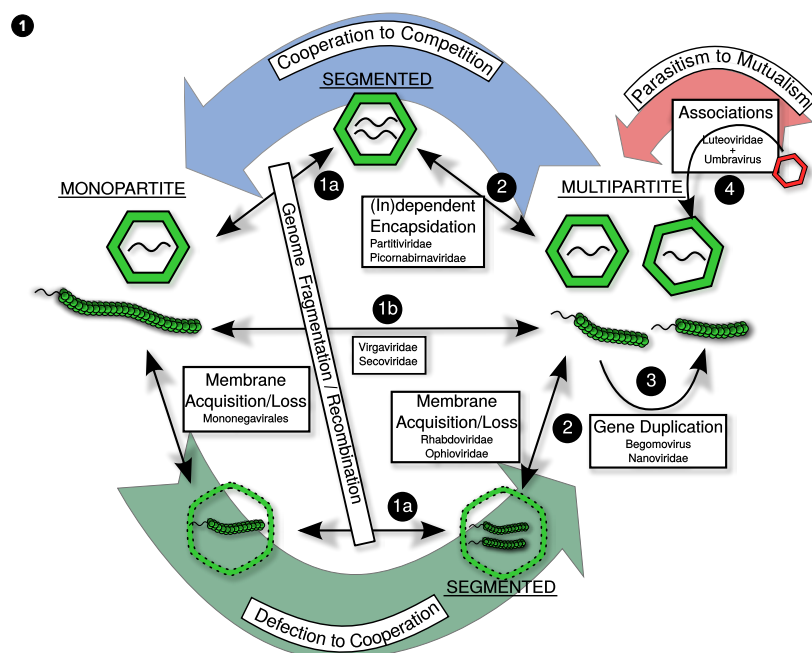
Iranzo J, Cuesta JA, Manrubia S, Katsnelson M, Koonin EV. Disentangling the effects of selection and loss bias on gene dynamics. *Proc Natl Acad Sci USA* 2017; 114: E5616-E5624.

Lucía-Sanz A, Aguirre J, Manrubia S. Theoretical approaches to disclosing the emergence and adaptive advantages of multipartite viruses. *Curr Opin Virol* 2018; 33: 89-95.

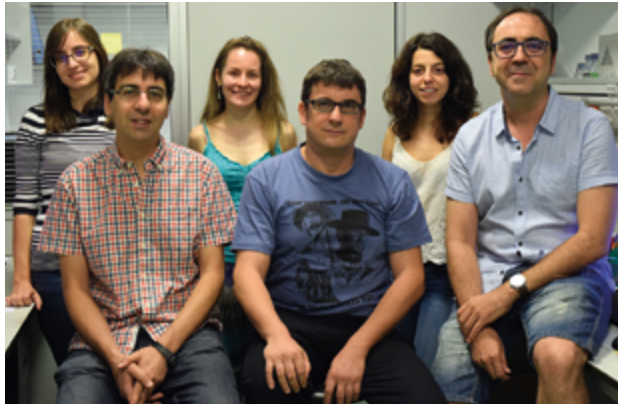
Aguirre J, Catalán P, Cuesta JA, Manrubia S. On the networked architecture of genotype spaces and its critical effects on molecular evolution. *Open Biol* 2018; 8: 180069.

The main interest of the group is the theoretical investigation of evolutionary systems of different kinds. We develop models inspired by the phenomenology observed in natural systems, chiefly molecular populations, viruses, and interacting agents from the cellular level and up. Our approach addresses either the study of fundamental properties of adapting systems—with a strong emphasis on their evolutionary origin—or, at a more specific level, tries to reproduce and eventually predict the response of such populations to endogenous and exogenous change. In this context, we investigate the properties of the genotype-phenotype map through models such as the folded state of RNA sequences, focusing on the topological structure of neutral networks of genotypes and its relevance in adaptation and molecular innovation. Another main subject is the understanding of the survival strategies of viruses, among others the relevance of multipartite genomes or the ecological effect of viral satellites.

At a higher organisational level, we are also interested in the modelisation of the interaction between agents organised in networks that vie e.g. for resources, food, or mates, as competitive interactions represent one of the driving forces behind evolution and natural selection in biological systems. Finally, we explore the application of complex systems to biotechnology through the development of analysis techniques with environmental and health purposes. We have applied graph theory to antibody microarrays in order to improve the characterisation of experimental samples, with direct application to allergy control, toxin detection in fresh water ecosystems and planetary sciences. Our studies of viral response to antiviral treatments have determined optimal modes of drug administration to minimise viral load and mutant escape



1 Multipartite viruses have genomes formed with fragments encapsidated in separated viral particles. The evolutionary origin of multipartitism is uncertain, though it could have emerged on several occasions. Current evidence suggests that *de novo* associations between independent genes, as well as fragmentation or duplication of monopartite genomes are plausible evolutionary pathways leading to multipartite genomes.



# System biotechnology

**GROUP LEADER**

**Juan Nogales Enrique**

**POSTDOCTORAL SCIENTISTS**

Beatriz García Jiménez  
Jesús Torres Bacete  
Blas Blázquez Castiñeira  
Igor Martínez Sánchez  
María Santos Merino

**PhD STUDENTS**

Lucía Agudo Algibe  
Irene Sánchez Pascual

**MASTER'S STUDENTS**

Alejandro Ronco Campaña  
Francisco J. Canalejo Molero  
Antonio Mesa Galán

**UNDERGRADUATE STUDENT**

Jorge Carrasco Muriel

**VISITING SCIENTISTS**

Cansu Uluseker  
*University of Trento, Italy*  
Silvana Díaz Herrera  
*University of Buenos Aires, Argentine*  
Fabian Moreno  
*Universidad Nacional Autónoma de Mexico, Mexico*

**SELECTED PUBLICATIONS**

Gudmundsson S, Agudo L, Nogales J. Applications of genome-scale metabolic models of microalgae and cyanobacteria in biotechnology. Chapter 4 pp.93-111 in González-Fernández C and Muñoz R (eds). *Microalgae-Based Biofuels and Bioproduct*, Woodhead Publishing Series in Energy.

Nogales J, García J, Díaz E. Degradation of Aromatic Compounds in Pseudomonas: A Systems Biology View. Book chapter, pp 1-49 In: Rojo F (ed). *Aerobic Utilization of Hydrocarbons, Oils and Lipids*. Springer International Publishing.

Armstrong RFS, ..., Nogales J, et al. Living Architecture (LIAR): Metabolically engineered building units. Book chapter, pp 170-177. In Heisel, F; Hebel, D (eds). *Cultivated Building Materials: Industrialized Natural Resources for Architecture and Construction*. Birkhauser, Berlin.

Nogales J et al. BO. Expanding the computable reactome in *Pseudomonas putida* reveals metabolic cycles providing robustness. bioRxiv 2017: 139121.

García-Jiménez B, García JL, Nogales J. FLYCOP: metabolic modeling-based analysis and engineering microbial communities. *Bioinformatics* 2018; 34: 1954-1963.

Our foundational aim is the system-level understanding of microbial metabolism as a framework for developing a broad range of novel and non-intuitive biotechnological processes. Taking advantage of metabolic modelling, systems and synthetic biology we are addressing, at different levels, the understanding and full taming of bacterial systems emergence.

**Increasing the completeness and scope of metabolic reconstructions**

We are involved in the high-quality metabolic modelling of a large set of metabolically diverse bacteria including *P. putida*, *Synechocystis*, *S. elongatus*, *A. platensis*, *Azoarcus* CIB, *S. stFA*, *P. pseudoalcaligenes* and *B. bacteriovorus*. This effort is enabling the system-level analysis of new metabolic processes while providing new computational test-beds for biotechnological applications. We are also interested in the inclusion of new metabolic modules. Current efforts are targeted on i) the modelling of endogenous reactive oxygen species (ROS), ii) the implementation of dynamic condition-specific models and iii) the inclusion of underground metabolism.

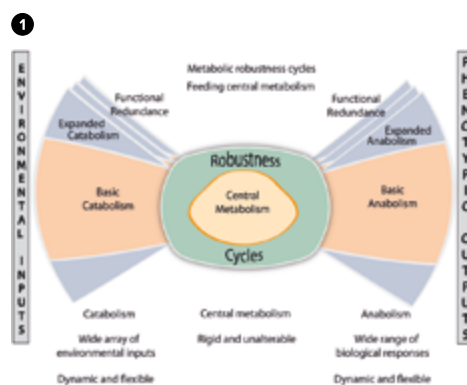
**System-level analysis of metabolic robustness in bacteria**

The robustness of a system is the property that allows it to maintain its functions despite external and internal perturbations. Through the metabolic modelling analysis of *P. putida*, we have identified metabolic cycles providing metabolic robustness. By using synthetic biology, ongoing efforts are focused on the rational engineering of such cycles under diverse biotechnological scenarios.

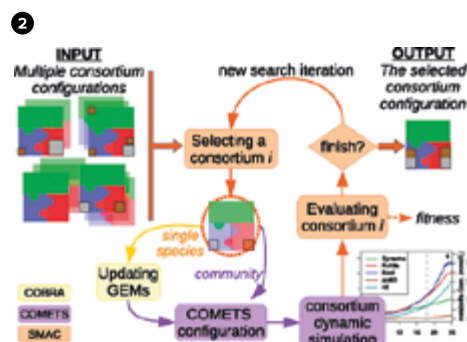
**System-level analysis and designing of microbial communities**

The division of labour in microbial consortia allows an expanded complexity and functionality in bacteria. We are interested in: i) understanding how these expanded capabilities emerge within a community and ii) how we can engineer this community-

level functionality towards biotechnological endeavours. To address these two fundamental questions, we have developed a computational platform called FlyCop for modelling and engineering synthetic microbial consortia. Further implementation of these model-based designs is allowing us to develop new synthetic biology tools for engineering microbial communities.

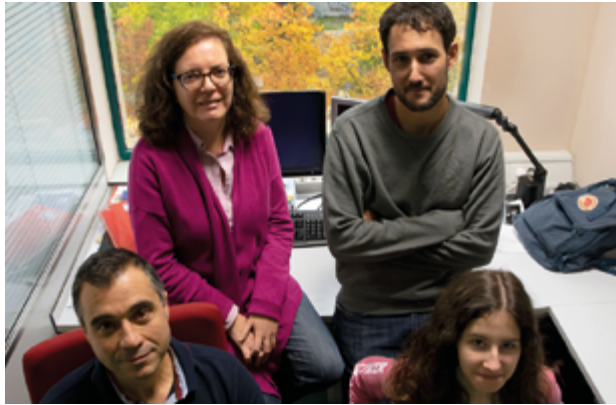


1 The bow-tie structure of the *P. putida* metabolism. *P. putida* metabolic network has increased its metabolic robustness by: i) expanding catabolism and anabolism; ii) increasing functional redundancy for many metabolic processes; and iii) incorporating buffering cycles around central metabolism (metabolic robustness cycles), acting as metabolic capacitors to promote the stable connection of catabolism and anabolism with the central metabolism under perturbations.



2 FLYCOP pipeline: Graphical representation of FLYCOP workflow. Multiple consortium configurations are systematically evaluated providing the best one maximising a given fitness.





## Computational systems biology

### GROUP LEADER

**Florencio Pazos Cabaleiro**

### SENIOR SCIENTIST

Mónica Chagoyen Quiles

### PHD STUDENT

Javier López-Ibañez Infante

### UNDERGRADUATE STUDENTS

Claudia Corona

Julia Pérez

Laura T. Martín

### SELECTED PUBLICATIONS

González-Pérez S, Pazos F, Chagoyen M. Factors affecting interactome-based prediction of human genes associated with clinical signs. *BMC Bioinformatics* 2017; 18: 340.

Alpizar A, Marino F, Ramos-Fernández A, Lombardía M, Jeko A, Pazos F, Paradelo A, Santiago C, Heck AJR, Marcilla M. A molecular basis for the presentation of phosphorylated peptides by HLA-B antigens. *Mol Cell Proteomics* 2017; 16: 181-193.

Pazos F, Garcia-Moreno A, Oliveros JC. Automatic detection of genomic regions with informative epigenetic patterns. *BMC Genomics* 2018; 19: 847.

Garrido-Martín D, Pazos F. Effect of the sequence data deluge on the performance of methods for detecting protein functional residues. *BMC Bioinformatics* 2018; 19: 67.

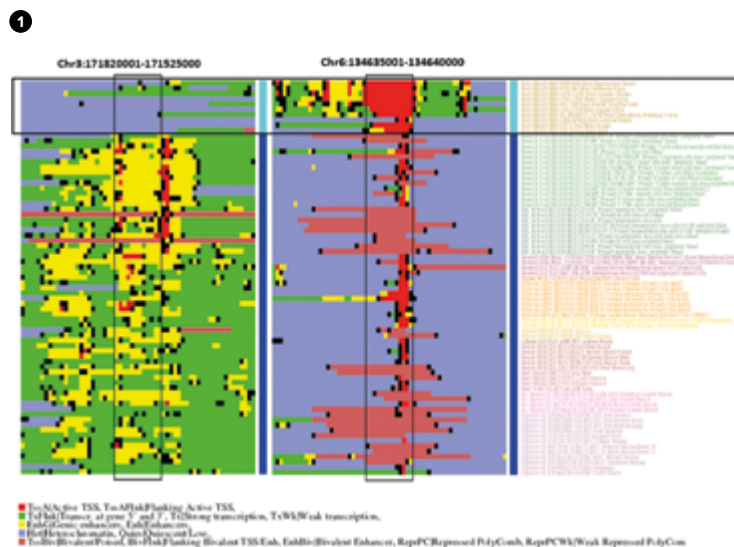
Pazos F, Chagoyen M. Characteristics and evolution of the ecosystem of software tools supporting research in molecular biology. *Brief Bioinform* 2018; doi: 10.1093/bib/bby001.

Our group is interested in different aspects of bioinformatics, computational biology and systems biology. Our goal is to obtain new biological knowledge with an *in-silico* approach which complements the *in-vivo* and *in-vitro* methodologies of biology. This mainly involves mining the massive amounts of information stored in biological databases. Besides our lines of scientific research, we also collaborate with experimental groups providing them with bioinformatics support for their specific needs and participate in different teaching projects.

We have developed evolutionary-based method for predicting sites with some functional importance in protein sequences and structures. These are based on the fact that functional sites are subject to certain evolutionary constraints whose landmarks can be detected on multiple sequence alignments.

We have also developed evolutionary-based methods for predicting interaction partners which have been accepted and followed by the community. These methods are mainly based on the hypothesis that interacting or functionally related proteins adapt to each other during the evolutionary process (co-evolution). We try to detect the landmarks that this co-evolutionary process left in the sequences and structures of the proteins.

We are studying metabolic networks (central metabolism and biodegradation) and protein interaction networks from a top-down systemic approach. Of special interest for us is the study of the complex phenomenon of protein function from a systemic perspective, trying to understand how complex functions arise by combining the molecular functions of proteins when these interact in intricate networks. We are also interested in applying this systemic approach to the study of human diseases.



**1** Example of two genomic regions with an epigenetic pattern related to brain. The sample classification is indicated with light blue (brain) and dark blue (others). The brain samples are further highlighted with a box. The sample names are on the right, coloured using the tissue-based colour schema of the Roadmap Epigenomics Consortium.



## Logic of genomics systems

SYSTEMS BIOLOGY PROGRAMME 89

### GROUP LEADER

Juan F. Poyatos

### PhD STUDENTS

Clara Moreno  
Pablo Yubero

### MASTER'S STUDENT

Alvar Alonso

### SELECTED PUBLICATIONS

Rodrigo G, Bajic D, Elola I, Poyatos JF. Deconstructing a multiple antibiotic resistance regulation through the quantification of its input function. *NPJ Syst Biol Appl* 2017; 3: 30.

Moreno-Fenoll C, Cavaliere M, Martinez-Garcia E, Poyatos JF. Eco-evolutionary feedbacks can rescue cooperation in microbial populations. *Sci Rep* 2017; 7: 42561.

Yubero P, Poyatos, JF. Large-scale analysis of the global transcriptional regulation of bacterial gene expression. *BioRxiv* 2018; 405894.

Chagoyen M, Poyatos JF. Complex genetic and epigenetic regulation deviates gene expression from a unifying global transcriptional program. *BioRxiv* 2018; 390419.

Sánchez-Gorostiaga A, Bajic D, Osborne ML, Poyatos JF, Sánchez A. High-order interactions dominate the functional landscape of microbial consortia. *BioRxiv* 2018; 333534.

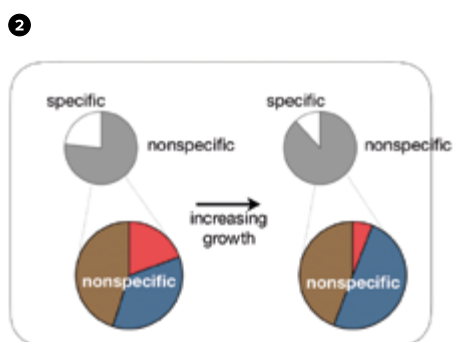
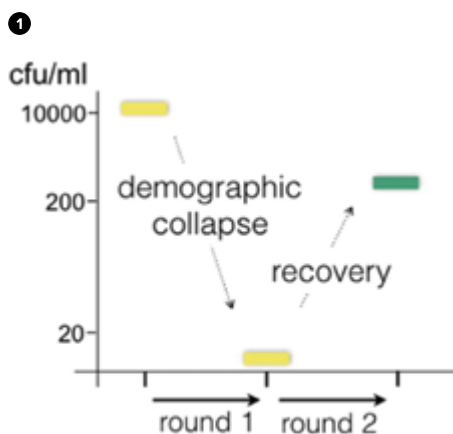
Research at the Logic of Genomic Systems Laboratory searches for design principles in biological systems. During the last years, we examined the dynamics of microbial communities, the integration of numerous regulatory signals in the triggering of an antibiotic response, and the impact of physiology on genome-wide expression.

In our study of microbial communities, we demonstrated the consequences of the coupling between ecology and evolution on community resilience (Figure 1), and the difficulty of anticipating community function. For the study of eco-evolutionary feedbacks, we used synthetic communities constituted by engineered *Escherichia coli* variants; for the study of community function, we assembled an artificial consortium constituted by natural species. Both approaches emerge as tractable experimental models to recognise ecosystem properties.

To study the intricate modulation of an *E. coli*'s response to antibiotics, we deconstructed its regulation with the use of input functions. These functions quantify the rate of transcription of the genes constituting the response with respect to the signals acting on its cognate regulators. By examining how the shape of the function changes in different situations, e.g., when a given regulator is mutated, we identified the functional implications of the associated control architecture and emphasised the role of a core dual auto-regulatory motif.

We also completed two studies in which we inspected how cellular physiology influences gene expression, what is termed the global program of regulation. We first studied the impact of the global program on gene order in bacteria. The study incorporated a large-scale characterisation of the global program, with experiments validating the analysis. In a second study, we integrated two models of resource allocation (Figure 2, cellular

“economics” is an intrinsic feature coupled to physiology) to evaluate how genetic and epigenetic regulation combine with the global regulation for the genome-wide control of gene expression. Both topics considerably advance our previous understanding of Genome Biology.



1 While the initial dynamics of a community constituted by producers (*Ps*) and non-producers of a public good (20% *Ps*, represented by a yellow rounded rectangle) leads to a demographic collapse of the full population (measured in colony forming units per ml), it also generates specific conditions, in a second round of the dynamics, to allow the recovery of *Ps* (green rectangle). This confirms the eco-evolutionary feedback in the community.

2 Partition of genome expression into five sectors that combine two previous resource allocation models. A partition based on three sectors in which the expression of their constituent genes increases (positive genes, blue), decreases (negative genes, red), or remains constant (invariant genes, brown) with increasing growth rate appears as a fine structure of a broad partition between specific and nonspecific genes.





# Microbiome analysis

**GROUP LEADERS**

**Javier Tamames de la Huerta**  
**Carlos Pedrós-Alió**

**POSTDOCTORAL SCIENTISTS**

Fernando Puente Sánchez  
Beatriz Cámara Gallego  
Arturo Marín Alguacil

**PHD STUDENTS**

Marta Cobo Simón  
Natalia García García  
Diego Jiménez Lalana

**MASTER'S STUDENTS**

Luis Alberto Macías Pérez  
Elena Montenegro de la Borbolla

**SELECTED PUBLICATIONS**

Royo-Llonch M, Ferrera I, Cornejo-Castillo FM, Sánchez P, Salazar G, Stepanauskas R, González JM, Sieracki, ME, Speich, S, Stemmann, L, Pedrós-Alió C, Acinas SG. Exploring microdiversity in novel *Kordia* spp. (Bacteroidetes) with proteorhodopsin from the tropical Indian Ocean via single amplified genomes. *Front Microbiol* 2017; 8: 1317.

Cobo M, Tamames J. Relating genomic characteristics to environmental preferences and ubiquity in different microbial taxa. *BMC Genomics* 2017; 18: 499.

Pedrós-Alió C, Acinas SG, Logares R, Massana R. The HTS contribution to marine microbial diversity. Chapter 2, pp.47-97, 2018; In JM Gasol and D Kirchman (eds.) *Microbial Ecology of the Oceans*, 3rd edition.

Alcamán-Arias ME, Pedrós-Alió C, Tamames J, Fernández C, Pérez-Pantoja D, Vázquez M, Díez B. Diurnal changes in active carbon and nitrogen pathways along the temperature gradient in Porcelana hot spring microbial mat. *Front Microbiol* 2018; 9: 2353.

Narciso-da-Rocha C, Rocha J, Vaz-Moreira I, Lira F, Tamames J, Henriques I, Martínez JL, Manaia CM. Bacterial lineages putatively associated with the dissemination of antibiotic resistance genes in a full-scale urban wastewater treatment plant. *Environmental Int* 2018; 118: 179-18.

Microbial communities (microbiomes) are key players in many scenarios, from how the biosphere works to industrial and biotechnological processes, as well as human health and wellness. We study microbiomes of diverse environments trying to learn the rules that govern the assemblage of these microbial communities. This knowledge will help to understand how they function, and to predict the effects of disturbances. Eventually, this will lead to rational design and manipulation of microbiomes.

We focus mostly on marine microbial communities, but we are actively working in many other microbiomes from different environments. We study extreme environments because their microbiotas show fascinating adaptations to the harsh conditions. We work with human-associated microbiomes, such as the gut and the vagina, because of their potential to improve our health. We are also interested in other habitats, such as wastewaters and soils.

We use mostly bioinformatics tools to study the composition and functionality of microbiomes. Metagenomics is the basis of our work, since it provides the basic material: DNA sequences from environmental samples. The analysis of these sequences informs about the presence of diverse organisms and the content of their genomes, and the latter

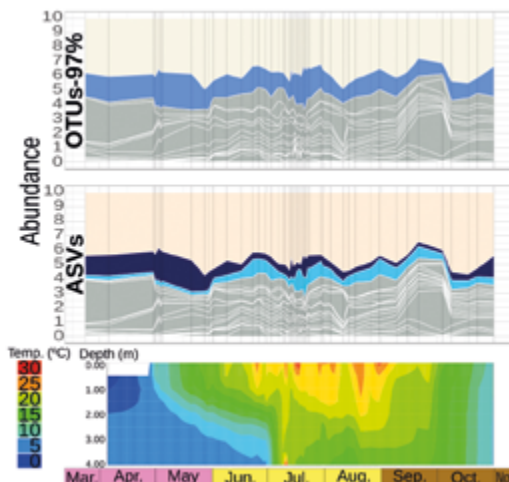
can be linked to functionality. We also carry out experimental work addressing interactions between members of microbiomes.

1



1 Microbial mats in Porcelana Geyser (Southern Chile), where we are studying metagenomics and metatranscriptomics of the thermophilic bacteria.

2



2 Bacterial community composition in a Wisconsin Lake. Blue colours show the presence of *Polynucleobacter* OTU (97%, top panel) or as its component strains (Amplicon Sequence Variants, middle panel). While OTUs show a fairly constant presence along the year, ASVs (corresponding to different ecotypes) alternate. Lake temperature is shown in bottom panel.

