RESEARCH CENTRE

Inria Paris Centre

IN PARTNERSHIP WITH:

Institut Pasteur

2024

ACTIVITY REPORT

Project-Team

INBIO

Experimental and Computational Methods for Modeling Cellular Processes

IN COLLABORATION WITH: Centre de Bioinformatique, Biostatistique et Biologie Intégrative

DOMAIN

Digital Health, Biology and Earth

THEME

Modeling and Control for Life Sciences

Inria

Contents

Project-Team INBIO

Creation of the Project-Team: 2019 November 01

Keywords

Computer sciences and digital sciences

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A6.1.4. – Multiscale modeling

A6.3.1. – Inverse problems

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Other research topics and application domains

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B1.1.10. – Systems and synthetic biology

B2.4.2. – Drug resistance

B5.10. – Biotechnology

B9.8. – Reproducibility

1 Team members, visitors, external collaborators

Research Scientist

- Gregory Batt [Team leader, INRIA, Senior Researcher, HDR]

Post-Doctoral Fellows

- Angelica Frusteri Chiacchiera [Institut Pasteur]
- Esteban Lebrun [Institut Pasteur]
- Eléonore Pourcelot [Institut Pasteur, from Oct 2024]

PhD Students

- Cecilia Capela [Institut Pasteur, from Nov 2024]
- Alicia Da Silva [Institut Pasteur]
- Henri Galez [Institut Pasteur]
- Viktoriia Gross [Institut Pasteur, until Jun 2024]

Technical Staff

- Sara Napolitano [Institut Pasteur, Engineer]

Interns and Apprentices

- Cecilia Capela [Institut Pasteur, Intern, from Mar 2024 until Sep 2024, M2 at ESPCI]
- Ines Dahlal [Institut Pasteur, Apprentice, from Aug 2024, Technician, Cergy Paris University]

Administrative Assistants

- Nelly Maloisel [INRIA]
- Mélanie Ridel [Institut Pasteur]

Visiting Scientist

- Lorenzo Pasotti [Pavia University]

2 Overall objectives

The main objective of our research is to understand, control, and optimize cellular processes in single cells and at the population level. We combine experimental and theoretical work within a single team.

Our focus is on developing methods and models that take stochasticity of intracellular processes and heterogeneity of cell populations into account. To this end, we use both mixed-effects models as well as continuous-time Markov chains and their diffusion approximations. We develop methods for efficiently calculating with such models and use them to design optimally informative experiments and to reverse engineer unknown cellular processes from experimental data. Furthermore, we deploy models in order to optimally construct and optimally control synthetic gene circuits.

We have recently started to set up our own biology laboratory at Institut Pasteur. We develop novel experimental platforms that are designed to be fully automated, controllable by our own software, and capabale of updating the experimental plan in response to incoming measurements. Optogenetic

actuation of intracellular processes, coupled to real time fluorescence measurements by microscopy or flow cytometry, then allows us to connect cellular processes with models and algorithms in real time.

The spritit of our work is that experimental platforms and circuits should be constructed with our theoretical work in mind, while our mathematical methods should be usable to adress concrete experimental questions in the lab.

3 Research program

3.1 Population dynamics emerging from randomness in single cells

Dynamics of cell populations growing in isolation or as part of some ecological system are often shaped by biochemical processes inside cells, for instance when these processes convey resistance to stressors or trigger cell fate decisions in reponse to environmental conditions. **Understanding how stochastic reaction events inside single cells affect emerging population dynamics**, and how selection effects at the population level feed back to shape single cell characteristics of cells in the population, is one of the key questions in biology. We develop **multi-scale modeling approaches** that allow us to derive emerging population dynamics from mechanistic descriptions of stochastic reaction networks inside single cells. In the past, we have used such approaches to study how stochasticity in restriction-modification systems, acting as simple bacterial innate immune systems, propagates to the ecology of bacteria and bacterial viruses and shapes the dynamics of bacterial populations. More generally, we develop and use these approaches in connection with experimental work in our lab for understanding and **controlling the dynamics of populations** in cases where **controllable system inputs inherently operate at the level of single cells** (e.g. optogenetics) but the output of interest is at the level of populations (e.g. bioproduction).

3.2 Optimal experimental design

One of the major problems in reverse engineering biochemical processes inside cells is that **cellular processes are high-dimensional and complex** with many unknown parameters while the **available data is low dimensional and corrupted by measurement errors**. Such problems can be alleviated by ensuring that the experimental plan is designed to yield data that provides as much information as possible about the unknown model parameters. We develop mathematical approaches and computational tools that can be used to calculate the expected amount of information that can be gained from a given experiment given a specification of either a stochastic model of the system (described above) or a deterministic model based on ordinary differential equations. These information calculation approaches are then coupled to optimization tools and used to plan **maximally informative experiments** in our applications.

3.3 Cybergenetics – real time control of biological processes

Cells have evolved uncountable numbers of feedback circuits to regulate their functionalities in the presence of changing environmental conditions. But can such feedback control also be externalized and placed under control of scientists? Early work on this topic suggested that **optogenetic systems, allowing for external regulation of gene expression**, have the potential to serve as an interface between cells and experimental platform that gives a computer the power to stir the functioning of cells via the application of light. We develop all the tools required to realize automated computer control of intracellular processes. On the experimental side, we develop yeast strains that are equipped with optogenetic promoters to drive various functionalities. On the mathematical side, we develop models and software to equip our experimental platforms with the appropriate programs to realize sucessful feedback control, both at the level of single cells (microscopy) and at the level of populations (bioreactors and plate reader).

3.4 Platforms for automated reactive experiments

The core scientific activity of the team is to connect mathematical methods with biological applications in our lab. The interface between the two sides, that is the experimental platforms, is therefore of crucial importance for the success of our activities. However, platforms that can be purchased by vendors are

typically delivered without the capacity to adapt the experimental plan in response to incoming measurements, a functionality that is crucially needed for deploying our computational methods (e.g. feedback control). Therefore, we develop novel experimental platforms and/or extend existing platforms with additional software and hardware that allows us to perform automated reactive experiments. Concretely, we develop a **microscopy platform and control software for yeast that uses a digital micromirror device to expose single cells to targeted light signals** that can be adjusted in real time in response to measurements taken from the cell. Furthermore, we develop a platform of 16 parallel **small scale automated bioreactors**, each equipped with controllable LEDs to allow for optogenetic gene expression and long-term reactive experiments in tightly controlled conditions. Automation of the platform is achieved via a low-cost open-source **pipetting robot that samples all reactors to a benchtop cytometer** in which single cell gene expression is measured in all sampled cells of all reactors. Finally, we develop **software to take full control of a commercial plate reader with liquid injection capabilities** (Tecan Spark). This platform allows us to use a Raspberry Pi to pilot 96 parallel reactive experiments where optical density is used as a readout of bacterial growth.

4 Application domains

4.1 Preamble

Since most of our research is at the interface of mathematics and biology, there often is no clear split between mathematical reaseach objectives and applications. For instance, feedback control of gene expression is simultaneously a mathematical and an applied problem.

4.2 Understanding resistance and tolerance to antibiotic treatments

The non-susceptibility of pathogenic bacteria to antibiotic treatments is a major health problem. Bacteria might escape treatments in two ways: being resistant or being tolerant. Whereas resistant bacteria can multiply in presence of antibiotics, tolerant bacteria can merely survive. Yet, tolerance is increasingly recognized as a major player in treatment failure. In particular, an increasing fraction of commensal and pathogenic *E coli* bacteria express extended-spectrum β-lactamases and/or carbapenemases. When individual bacteria die as a consequence of antibiotic treatments, these enzymes are released and hydrolyze the antibiotic molecules in the environment, conveying a transient protection to the remaining bacteria that lasts until the enzymes are degraded themselves. Understanding how this collective antibiotic tolerance (CAT) shapes population dynamics is difficult yet important for **optimally killing bacterial populations**: when a second antibiotic dose is applied directly after a first dose it will not be effective since the antibiotics will be degraded by the enzymes released from bacteria killed after the first dose; when the second dose is applied too late the surviving bacterial population will have regrown to a large size. Our plate reader platform allows us to apply complex temporal patterns of antibiotic treatments to bacteria over nearly two days. Parallezing such treatments in the 96 well plates allows us to generate rich data sets and to calibrate population dynamics models that can be used to optimize temporal treatment plans. One of the applied objectives of our team is to use these capacities to study a collection of fully-sequenced clinical isolates treated with a broad range of clinically important antibiotics and grown in various media. Ideally, this will lead to an approach that can be used to assay tolerance to antibiotics in hospitals instead of, or in addition to, standard antibiotic susceptibility tests, detecting resistance.

4.3 Optimization of protein production in yeast

Many proteins are of technological or therapeutical importance. The yeast *S. cerevisiae* is an interesting organism for protein bioproduction since it combines a relatively fast growth rate with good capacities to perform post-translational modifications needed for protein maturation and full functionality. However, imposing a strong demand on protein production to the cell places a significant burden on its physiology, either at the protein production level or at the maturation and secretion levels. Using systems and synthetic biology approaches, we aim at **better understanding the origins of the production bottlenecks** and then using modeling and control approaches, we aim at finding **optimal control solutions** for bioproduction. Three different strategies are envisioned. In the first approach, bioproduction stress

sensors are used to observe in real time the physiological state of the cell, and the demand is externally tuned based on the stress level of the cell population. In the second approach, the stress sensor is used to tune the response capacities of the cell to the external demand, thus creating an internal feedback loop. In the third approach, we control the fraction of the producing cells by engineering an artificial differentiation system that implements the partial differentiation of grower cells into producer cells. The optimization problem is then to find the optimum ratio based on the external environment of the cells.

5 Social and environmental responsibility

5.1 Footprint of research activities

A significant part of our daily research activities involves molecular biology work and consumes plasticware and various chemicals. We also work on lab automation and develop experimental platform to paralellize experiments. However, we work with small biorectors (15 to 50mL), so volumes of cell cultures remain very modest.

We also occasionally use a computer cluster, notably for optimization, but the jobs remain relatively modest on a yearly basis.

Henri Galez are part of a committee working on the quantification of the carbon footprint of the computational works done in the Computational Biology Department of Institut Pasteur.

5.2 Impact of research results

Regarding biological developments, we have two main research directions.

The first one deals with the optimization of bioproduction. Bioproduction is a domain of strategic importance. The field is higly technological and rapidly growing at the global scale. The market for biopharmaceuticals alone, that notably include vaccines and monoclonal antibodies, is estimated to $400B to $500B. France imports > 70% of its vaccines and > 95% of its monoclonal antibodies and lacks sovereignty. Therefore this field has a strong social, medical and economical importance.

The second research direction deals with antibiotic stewardship. The spread of antimicrobial resistance is a both a health and an ecological problem of global impact. Antibiotic stewardship aims at using these drugs in more appropriate ways. To do so, one has to better understand and quantify bacterial response to antibiotic treatments.

Therefore our two main research directions are both tightly connected with important health and social issues.

6 New results

6.1 Design and model-driven analysis of synthetic circuits with the Staphylococcus aureus dead-Cas9 (sadCas9) as a programmable transcriptional regulator in bacteria

Participants: Lorenzo Pasotti, Gregory Batt.

Synthetic circuit design is crucial for engineering microbes that process environmental cues and provide biologically relevant outputs. To reliably scale-up circuit complexity, the availability of parts toolkits is central. Streptococcus pyogenes (sp)-derived CRISPR interference/dead-Cas9 (CRISPRi/spdCas9) is widely adopted for implementing programmable regulations in synthetic circuits, and alternative CRISPRi systems will further expand our toolkits of orthogonal components. In this contribution, we showcase the potential of CRISPRi using the engineered dCas9 from Staphylococcus aureus (sadCas9), not previously used in bacterial circuits, that is attractive for its low size and high specificity. We designed a collection of around 20 increasingly complex circuits and variants in Escherichia coli, including circuits with static function like one-/two-input logic gates (NOT, NAND), circuits with dynamic behavior like

incoherent feedforward loops (iFFLs), and applied sadCas9 to fix a T7 polymerase-based cascade. Data demonstrated specific and efficient target repression (100-fold) and qualitatively successful functioning for all circuits. Other advantageous features included low sadCas9-borne cell load and orthogonality with spdCas9. However, different circuit variants showed quantitatively unexpected and previously unreported steady-state responses: the dynamic range, switch point, and slope of NOT/NAND gates changed for different output promoters, and a multiphasic behavior was observed in iFFLs, differing from the expected bell-shaped or sigmoidal curves. Model analysis explained the observed curves by complex interplays among components, due to reporter gene-borne cell load and regulator competition. Overall, CRISPRi/sadCas9 successfully expanded the available toolkit for bacterial engineering. Analysis of our circuit collection depicted the impact of generally neglected effects modulating the shape of component dose–response curves, to avoid drawing wrong conclusions on circuit functioning.

6.2 Harnessing CRISPR interference to resensitize laboratory strains and clinical isolates to last resort antibiotics

Participants: Angelica Frusteri, Lorenzo Pasotti, Gregory Batt.

The global race against antimicrobial resistance requires novel antimicrobials that are not only effective in killing specific bacteria, but also minimize the emergence of new resistances. Recently, CRISPR/Cas-based antimicrobials were proposed to address killing specificity with encouraging results. However, the emergence of target sequence mutations triggered by Cas-cleavage was identified as an escape strategy, posing the risk of generating new antibiotic-resistance gene (ARG) variants. In this contribution, we evaluated an antibiotic re-sensitization strategy based on CRISPR interference (CRISPRi), which inhibits gene expression without damaging target DNA. The resistance to four antibiotics, including last resort drugs, was significantly reduced by individual and multi-gene targeting of ARGs in low- to high-copy numbers in recombinant E. coli. Escaper analysis confirmed the absence of mutations in target sequence, corroborating the harmless role of CRISPRi in the selection of new resistances. E. coli clinical isolates carrying ARGs of severe clinical concern were then used to assess the robustness of CRISPRi under different growth conditions. Meropenem, colistin and cefotaxime susceptibility was successfully increased in terms of MIC (up to > 4-fold) and growth delay (up to 11 h) in a medium-dependent fashion. ARG repression also worked in a pathogenic strain grown in human urine, as a demonstration of CRISPRi-mediated re-sensitization in host-mimicking media. This study laid the foundations for further leveraging CRISPRi as antimicrobial agent or research tool to selectively repress ARGs and investigate resistance mechanisms.

7 Partnerships and cooperations

This year, we obtained 5 novel research grants: TrojanYeast from the ANR, the French National Research Agency, Screen2Drive from Ferments du Futur, a consortium between academic and industry partners, Screen2Learn from an Inria/IFPEN joint inititive, CyberStable from the ABIES doctoral school at Paris-Saclay, and PlatPath from the Ile-de-France region.

7.1 International research visitors

Lorenzo Pasotti, assistant professor at the Department of Electrical, Computer and Biomedical Engineering and at the Centre for Health Technologies of the University of Pavia (Italy) has been invited for three months in the InBio team.

7.2 National initiatives

- **Institut de Convergence Inception** (2016-2025) on the “Emergence of Diseases in Populations and in Individuals”, coordinated by T. Bourgeron (Institut Pasteur). Partner institutes include Institut

Pasteur, Paris Sciences et Lettres, Université de Paris, AP-HP, and research teams from CEA, CNRS, INSERM and INRA.

The Inception's goal is to develop a core structure to mobilize data resources, numerical sciences, and fundamental experimental biology in a range of health issues. It uses integrative biology, social science and data science to understand the emergence of diseases in populations and in individuals. Inception provides funding for the PhD work of Viktoriia Gross.

- **PPR Antibiorésistance Anoruti** (2021-2025) on the "Analysis of non-response to antibiotics in vivo: application to Escherichia coli urinary tract infections", coordinated by I. El Meouche (Inserm).

  The objective of Anoruti is to identify the different factors involved in the fact that some bacteria sensitive to an antibiotic in vitro do not respond to treatment in vivo.

- **PPR Antibiorésistance Seq2Diag** (2021-2026) on "Whole genome sequencing and artificial intelligence to characterize and diagnose antibiotic resistance and capacity to escape treatment", coordinated by P. Glaser (Institut Pasteur).

  Genomic sequencing has revolutionized microbiological surveillance and molecular epidemiology. The objective of the Seq2Diag project is to provide a proof of concept for its use in hospital and veterinary laboratories as a diagnostic tool for in silico antibiotic sensitivity testing.

- **ANR JCJC SmartSec** (2022-2024) on "Matching maximal host capacities: stress-informed, self-tuning bioproduction circuits", coordinated by Francois Bertaux (Lesaffre) with Gregory Batt (Inria and Institut Pasteur).

  Bioproduction requires diverting resources normally used by host cells for growth and self-replication towards the production of desired molecules. Achieving maximal resource diversion without compromising the essential functions of the host is of critical importance, but is particularly challenging. To tackle this challenge, SmartSec aims at designing host-aware circuits, with application to the production of secreted proteins.

- **Inria/IFPEN PhD fellowship Screen2learn** (2023-2026) on "A screening and learning approach for protein secretion in yeast", obtained by Alicia da Silva, supervised by Gregory Batt (Inria/Institut Pasteur) and Senta Blanquet (IFPEN).

  This project aims to generate data and train a prediction tool for optimizing the production of secreted proteins in yeast. We will quantify secretion levels in different genetic contexts and for libraries of enzyme variants. We will screen for libraries of novel enzymes involved in vegetable biomass degradation, with application to second generation biofuel production.

- **Ferments du Futur Precompetitive projects Screen2Drive** (2024-2026) on "CRISPR-based screens to identify key factors to drive yeast consortia dynamics in fermented food ", cooddinated by Gregory Batt (Inria and Institut Pasteur) and Thibault Nidelet (INRAE).

  The optimization of fermentation processes is hindered by a too superficial understanding of interactions between yeast species. The Screen2Drive project uses CRISPR-based functional screens and deep-sequencing to identify key genes altering yeast interactions. Our expected goals are to improve fermentation results and develop genetic tools to engineer non-model yeasts.

- **ANR Générique TrojanYeast** (2024-2028) on "Engineering probiotic yeasts to prevent and treat Clostridia-induced intestinal infections", cooddinated by Gregory Batt (Inria and Institut Pasteur), with Bruno Dupuy (Institut Pasteur) and Pierre Lafaye (Institut Pasteur).

  This project aims to engineer a probiotic yeast to fight Clostridioides difficile and Clostridium perfringens gut infections. This yeast will produce endolysins to kill the bacteria and nanobodies to neutralize their toxins. We will utilize modular cloning, lab automation, and anaerobic culture platforms to screen and optimize these constructs. If successful, this approach could offer a novel and effective alternative to antibiotics.

- **ABIES doctoral school PhD fellowship CyberStable** (2024-2028) on “ Cybergenetic solutions to enforce genetic stability in synthetic biology applications ", obtained by Cecilia Capela, supervised by Gregory Batt (Inria and Institut Pasteur) and Sara Napolitano (Institut Pasteur and Inria).

  In CyberStable, we investigate the effects of a bioproduction burden on genetic stability in yeast. We will quantify the impact of induction demands on cell physiology, stress, and genetic stability for various hard-to-secrete proteins. We will also use an artificial differentiation system to engineer more stable production systems. By understanding these complex processes, our research aims to improve the efficiency and reliability of synthetic biology applications.

7.3 Regional initiatives

- **Equipment grant BioConvS Region Ile-de-France PlatPath** (2024-2025) on “Automated platform to engineer pathogenic strain libraries via optimized conjugation", coordinated by Sara Napolitano (Institut Pasteur and Inria) and Angelica Frusteri (Institut Pasteur and Inria).

  This project aims to develop an automated platform for constructing collections of engineered pathogenic bacteria through optimized bacterial conjugation. The platform will include a liquid handler robot, a plate reader, a biosafety cabinet, and control software. It will enable the high-throughput and robust engineering of bacterial collections, particularly for studying antimicrobial resistance in clinical isolates.

8 Dissemination

8.1 Promoting scientific activities

8.1.1 Scientific events: organisation

Gregory Batt is a member of the programme committee of the 10th International Conference on the Foundations of Engineering in Biology (FOSBE 2024) and a member of the scientific committee of the 32nd International Conference on Yeast Genetics and Molecular Biology (Yeast 2025).

Henri Galez has been a member of the organization committee for the Computational Biology Department retreat that gathered around 100 people in Annecy over 4 days.

8.1.2 Journal

Gregory Batt has been a reviewer for Nature Communications and Cell Reports.

Lorenzo Pasotti has been a reviewer for Nature Communications, BMC Bioinformatics, and PLoS One. He is a topic editor for Frontiers in Microbiology.

8.1.3 Invited talks

Gregory Batt gave invited presentations at the Annual Symposium of the Belgian Society for Microbiology (BSM 2024, Brussels, Belgium), at the Pasteur/EMBL workshop "Building bridges in infection biology" (Paris), at the "Physics meets biology" meeting of the Center of Theoretical Biological Physics of Rice University (Paris) and a Bio-processing workshop at Tours University (Tours).

He also gave an invited seminar at the Pasteur Qbio seminar series.

Lorenzo Pasotti gave an invited talk at the Engineered Living Materials 2024 conference (Saarbrucken, Germany) and an invited seminar at the Department of Bioengineering of University of Maryland (College Park, USA).

8.1.4 Scientific leadership and expertise

Gregory Batt has been a core member of the working group on AI and technologies, in the context of the establishment of the strategic plan of Institut Pasteur. This has lead to the production of a sort document on a proposed strategy for Pasteur.

Gregory Batt has been a member of the thesis advisory committees of Manon Perrot (Institut Pasteur) and Felix Knote (University of Würzburg).

Esteban Lebrun has been a jury member at the 2024 International Genetically Engineered Machine (iGEM) competition in Paris, a global synthetic biology event, gathering more than 4000 people.

Henri Galez and Alicia da Silva independently recieved a best poster prize at the poster session of the Computational Biology Department Retreat of Institut Pasteur (Annecy).

Cecilia Capela recieved a Best Industry Internship Award (3rd prize) from ESPCI Paris for her internship on the "Development, automation and optimization of a DNA printer for enzymatic DNA synthesis" at DNA Script.

Henri Galez recieved a Best Job Interview prize in a challenge organized by the ABIES doctoral school of Paris Saclay University (Saclay).

8.1.5 Research administration

Gregory Batt is the director of the Computational Biology department at Institut Pasteur. Department heads are responsible for research animation (organization of department seminars and of department retreats), are involved in group leader recruitments (regular G5 calls), are involved in the mentoring of recently hired group leaders, have a campus-wide coordination role as representatives of the group leaders and of all department members, and have an advisory role to the direction on scientific and administrative topics (department head meetings).

Moreover, since October 2024, he is a representative of the department directors (DDrep) to discuss with the direction, and participates to the comité de direction (CoDir) of Institut Pasteur.

He is also a member of the freeze clean initiative, aiming at rationalizing the park of -80°C fridges at Pasteur (the larger in Europe, costing > 3M€/year in electricity).

He is also a member of the Comité des Equipes Projets and the Bureau du Comité des Equipes Projets at Inria Paris.

Alicia da Silva and Henri Galez are PhD student representatives, Sara Napolitano is a engineer representative, and Mélanie Ridel is an administrative support representative at the Computational Biology Department Council at Institut Pasteur.

8.2 Teaching - Supervision

8.2.1 Teaching

Lorenzo Pasotti gave courses on "Bioinformatics and Synthetic Biology" at the Bioengineering Master of University of Pavia, on "Bioinformatics" at the Biotechnology Master of University of Pavia, and on "Bioengineering and Instrumentation in Sport" at the Sport Science Bachelor of University of Pavia (Italy).

8.2.2 Supervision

Gregory Batt is of has been (co-)supervising two PhD students:

- Viktoriia Gross, “An integrative approach to characterize and predict cell death and escape to beta-lactam antibiotic treatments". Started in Oct. 2020 and defended in Oct. 2024. Supervision by Imane El Meouche, Erick Denamur and Gregory Batt.

- Alicia da Silva, “A screening and learning approach for protein secretion in yeast". Started in Oct. 2023. Supervision by Senta Blanquet, Etienne Jourdier and Gregory Batt.

Sara Napolitano and Gregory Batt are co-supervising two PhD students:

- Henri Galez, “Engineering an autocrine-like system for screening libraries of protein secreting strains in yeast". Started in Sept. 2022. Supervision by Sara Napolitano and Gregory Batt.

- Cecilia Capela, “Cybergenetic solutions to enforce genetic stability in bioproduction applications". Started in Nov. 2024. Supervision by Sara Napolitano and Gregory Batt.

Henri Galez, Sara Napolitano, and Gregory Batt supervised the internship of Cecilia Capela (M2 student, ESPCI).

Sara Napolitano is supervising Ines Dahlal, a dual-education student in "bachelor universitaire de technologie" with specialization in Medical Technology and Biotechnology at Cergy Paris University.

8.3 Popularization

Gregory Batt has presented InBio's work in a talk entitled "Automated experimental platforms for functional characterization of genetically engineered microbial systems" at the "Bits in Biology Paris" venue. Bits in Bio aims at gathering academics and industry innovators on topics related to biology and AI.

Henri Galez participated to the Journées du Patrimoine at Institut Pasteur to show the campus and to popularize science.

He also organized interventions in high-school classes as a satellite event of the computational biology departement retreat in Annecy.

9 Scientific production

9.1 Publications of the year

International journals

[1] A. Frusteri Chiacchiera, M. Casanova, M. Bellato, A. Piazza, R. Migliavacca, G. Batt, P. Magni and L. Pasotti. 'Harnessing CRISPR interference to resensitize laboratory strains and clinical isolates to last resort antibiotics'. In: *Scientific Reports* 15.1 (2nd Jan. 2025), p. 261. DOI: 10.1038/s41598-024-81989-5. URL: https://inria.hal.science/hal-04930229.

[2] D. de Marchi, R. Shaposhnikov, S. Gobaa, D. Pastorelli, G. Batt, P. Magni and L. Pasotti. 'Design and Model-Driven Analysis of Synthetic Circuits with the Staphylococcus aureus Dead-Cas9 (sadCas9) as a Programmable Transcriptional Regulator in Bacteria'. In: *ACS Synthetic Biology* 13.3 (15th Mar. 2024), pp. 763–780. DOI: 10.1021/acssynbio.3c00541. URL: https://inria.hal.science/hal-04928755.

Doctoral dissertations and habilitation theses

[3] V. Gross. 'Une approche intégrative pour caractériser et prédire la mort cellulaire et l'échappement aux traitements antibiotiques par beta-lactamine'. Université Paris-Saclay, 3rd Oct. 2024. URL: https://theses.hal.science/tel-04778378.