



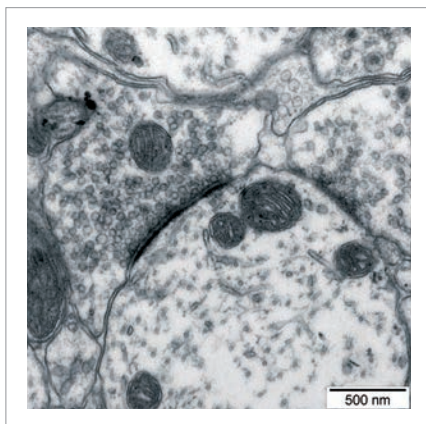
# IMAGING IBPS - ELECTRON MICROSCOPY

## OUR SERVICES

■ Four engineers provide advice on:

- methodologic choices and sample preparation;
- image acquisition in Transmission and Scanning Electron Microscopy (TEM and SEM);
- theoretical and practical training on the instruments.

Our services are fully accessible to both public and private research laboratories. Please refer to the website for pricing.



## OUR EXPERTISE

■ The facility has a long-standing and widely recognized expertise in electron microscopy, notably by introducing up-to-date technologies (cryomethods, energy-filtered imaging). We offer highly-skilled sample preparation and expert viewing in TEM and SEM for ultrastructural and immuno-localization analysis, correlative light and electron microscopy.

## OUR TECHNOLOGY

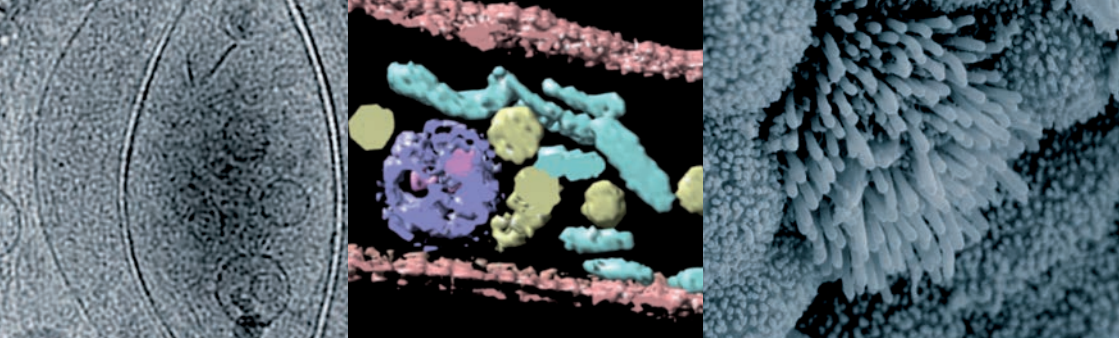
■ We have access to a wide range of equipment for the preparation and viewing of a large variety of biologic models, from bulk specimens or cell cultures to thin films or nanoparticles. Samples can be prepared using conventional chemical approaches or cryomethods associating rapid sample immobilization with an optimal preservation of their integrity (high-pressure or plunge freezing, freeze substitution, freeze-fracturing and freeze-etching).

## CONTACT

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## IMAGING IBPS - ELECTRON MICROSCOPY



### DEVELOPMENTS

■ We pioneered the introduction of cryo-methods in France to provide optimal preservation of biological samples by minimizing artefacts.

■ Our facility has introduced energy-filtered imaging in TEM, which allows chemical microanalysis on biological samples (e.g. sulfur localization in marine organisms) and three-dimensional reconstruction of thick sections by tomography and cryo-tomography.

■ As of January 2016, our platform will house a high-resolution SEM coupled to cryopreparation and automatic imaging of serial sections. This will permit high-resolution viewing of cells and tissues maintained in their native state, at the subcellular and molecular levels, and high contrast TEM-like imaging, with a very wide field of view and 3D visualization of large volumes.

#### Key publications

- Marie H. et al. (2015). Superparamagnetic Liposomes for MRI Monitoring and External Magnetic Field-Induced Selective Targeting of Malignant Brain Tumors. *Adv. Funct. Mater.* 25, 1258-69.
- Baudoin J. P. et al. (2012). Tangentially Migrating Neurons Assemble a Primary Cilium that Promotes Their Reorientation to the Cortical Plate. *Neuron* 76:1108-22.
- Volland, JM. et al. (2012). Insight of EDX analysis and EFTEM: Are spherocrystals located in strombidae digestive gland implied in detoxification of trace metals? *Micros Res Tech* 75:425-32.

### EQUIPMENT

#### Sample preparation in TEM

- Vibratome (VT1000S, Leica)
- Ultramicrotomes

#### Sample preparation in cryo

- Plunge freezing in liquid ethane (CPC, Leica)
- High-pressure freezer (HPM100, Leica)
- Freeze-substitution system (AFS, Leica)
- Freeze-fracturing and freeze-drying system (BAF 400T, Balzers)

#### Sample preparation in SEM

- Automatic critical point dryer (CPD300, Leica)
- Sputtering and e-beam coater (ACE600, Leica)

#### Microscopes

- TEM 80-120kV (912 Omega Zeiss) + side-mounted digital camera (Veleta, Olympus)
- TEM 200kV (2100HC, JEOL) + post-column energy-filter (Gif-Tridien, Gatan)
- Holders for cryo-TEM, tomography and cryo-tomography (Gatan and JEOL)
- High resolution SEM (Gemini-SEM 500, Zeiss) with cryo stage and Vacuum cryo transfer system (VCT100, Leica)

#### Data Analysis Software

- Atlas 5 Array Tomography, ImageJ, TomoJ, Imod.



# IMAGING IBPS - PHOTON MICROSCOPY

## OUR SERVICES

■ Four engineers provide training, assistance and advice in photonic microscopy, cytometry and image analysis via:

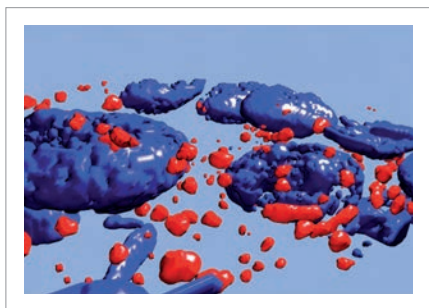
- theoretical and practical courses;
- advice on potential applications, sample preparation, technical options, and fluorochrome choice;
- individual training on the instruments and data analysis;
- assisted use of microscopes.

Our services are fully accessible via online booking to both public and private research laboratories. Please refer to the website for pricing.

## OUR EXPERTISE

■ We offer state-of-the-art imaging techniques such as F-techniques, fluorescence lifetime imaging, spectral imaging, live cell imaging, TIRF, PALM, and multicolor analysis.

We also provide expertise in sample preparation and deconvolution of confocal data as well as in data analysis.



## OUR TECHNOLOGY

■ The facility is equipped with confocal, wide-field, multiphoton and spinning disc microscopes, videomicroscopes, a macroapertome, a laser microdissection microscope, and multicolor flow cytometers. All imaging systems are configured for a wide range of applications in various biological models. Our systems are equipped with resonant scanners, hybrid detectors, motorized stages, heating and CO<sub>2</sub>-chambers, and microplate sampling devices to facilitate live cell studies.

Specific data analysis tools (ImageJ, Icy, Huygens, Metamorph, Volocity, FlowJo) are available.

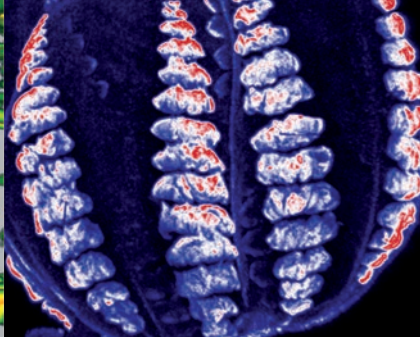
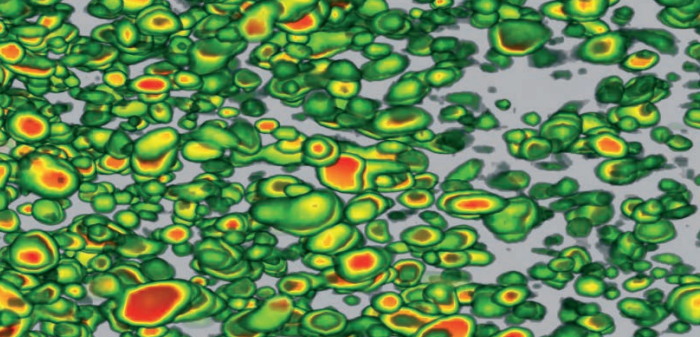
## CONTACT

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## IMAGING IBPS - PHOTON MICROSCOPY



### DEVELOPMENTS

#### ■ Development of spatial and temporal analysis tools

We have a recognized expertise in the analysis of colocalization events<sup>1, 2</sup>. In collaboration with Dr. Thomas Boudier (IPAL, Singapore), we recently developed an advanced ImageJ-implemented tool known as DiAna (Distance Analysis) based on the detection of objects and analysis of their spatial relationships.

#### ■ Optimization of sample preparation and resolution

We optimize sample preparation to improve the axial resolution of photonic devices when imaging thick biological samples such as mouse and zebrafish embryos, or mouse brain. We are developing novel high refractive index mounting media in collaboration with our industrial partner, and recently reported a marked improvement in axial resolution and imaging depth with novel mounting media. Furthermore, these media also render tissues transparent and are compatible with most common fluorochromes and fluorescent proteins<sup>3</sup>.

### EQUIPMENT

#### Confocal microscopes

- Leica TCS SP5 AOBS/upright
- Leica TCS SP5 AOBS/inverted
- Leica TCS SPE/upright

#### Multiphoton microscope

- Leica TCS SP5 MPIL/upright

#### SPINNING DISC microscopes

- Leica DMI6000/Roper/inverted
- Zeiss Axiovert/ROPER/ilas2/upright

#### Videomicroscopes

- Leica DMI6000/Metamorph/inverted
- Leica DMIRBE/Micromanager/inverted

#### FLIM-LIFA

- Leica DMIRBE/inverted

#### TIRF and SUPER-RESOLUTION

- Nikon Eclipse/inverted

#### Macro-apotome

- ZEISS AXIOZOOMER apotome

#### Laser-microdissection

- Arcturus/Nikon

#### Flow cytometer

- Miltenyi VYB and MACSQuant

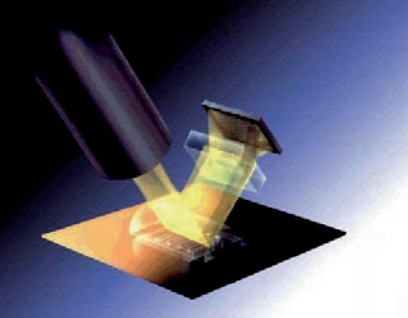
#### Data analysis software

- ImageJ, Huygens, Metamorph, Velocity, FlowJo, Venturi-One.

1. Bolte S. and Cordelières FP. (2006) A guided tour into subcellular colocalization analysis in light microscopy. *J Microsc* 224 (Pt 3): 213-32.

2. Cordelières FP. and Bolte S. (2014) Experimenters' guide to co-localization studies: finding a way through indicators and quantifiers, in practice. *Methods in Cell Biology-Quantitative Biology* 2014, 123:395-408.

3. Fouquet C., Gilles J.F., Heck N., Dos Santos M., Schwartzmann R., Cannaya V., Morel M.P., Davidson R.S., Trembleau A., Bolte S. (2015) Improving axial resolution in confocal microscopy with new high refractive index mounting media. *PLoS One*. 10(3):e0121096.



## PROTEOMICS IBPS - MOLECULAR INTERACTIONS

### OUR SERVICES

■ The engineer in charge of the facility provides user support for sample preparation and data analysis and contributes to methodologic and technologic developments:

- quality control: estimation of sample purity before immobilization by capillary electrophoresis (Experion) and equipment maintenance;
- choice of coupling chemistry, control of surface specificity and ligand stability;
- tracking of stability of interactions and regeneration efficiency, automated sample processing;
- kinetic study ( $k_{\text{off}}$ ,  $k_{\text{on}}$ ,  $K_d$ ,  $K_a$ );
- analysis of results and preparation of data for publication.

Our services are fully accessible to both public and private research laboratories. Please refer to the website for pricing.

### OUR EXPERTISE

■ The facility has strong expertise in the analysis of protein/protein interactions and of more complex interactions between biomolecules of different biochemical natures (nucleic acids, lipids, sugars, ions, etc.).

### OUR TECHNOLOGY

■ The BIACORE® device is a biosensor that uses Surface Plasmon Resonance (SPR). It enables us to study, without a specific sensor, real-time interaction characteristics between two molecules on a bio-specific surface, the ligand being immobilized on the sensor surface and the analyte being injected. The SPR quantifies refraction index changes on the surface, which are due to the formation and dissociation of molecular complexes and are linked to mass variations at the biosensor surface.

### EQUIPMENT

**Biacore 3000** (GE Healthcare)

- SPR analysis system

**Experion** (Bio-rad)

- Capillary electrophoresis system

### CONTACT

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# PROTEOMICS IBPS - PEPTIDE SYNTHESIS

## OUR SERVICES

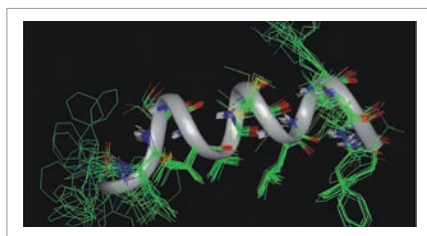
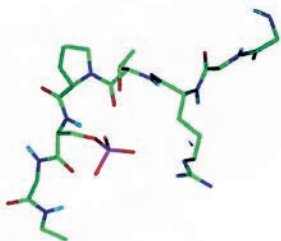
■ The facility provides peptide synthesis with or without modifications under the following conditions:

- typical turnaround time of 2-4 weeks per peptide;
- peptide quantity: from 1 to 100 mg;
- large number of possible modifications;
- peptide purity guaranteed  $\geq 95\%$ ;
- quality control.

Our services are accessible to both public and private research laboratories. Please refer to the website for pricing.

## OUR EXPERTISE

■ The engineer in charge of the facility provides peptides, with or without post-translational modifications, along with peptide purification. We can also advise users on project specifics.



## OUR TECHNOLOGY

■ Peptide synthesis is carried out via chemical approaches on a solid support, with automated peptide synthesizers using microwaves for each step of the synthesis. These synthesizers enable shorter reaction times and lower reagent consumption. Peptides are released then purified by reversed-phase HPLC. They are provided as powder with a  $\geq 95\%$  purity degree.

## EQUIPMENT

**Liberty Blue** (CEM corporation)

- microwave

**HPLC** (Goebel)

- Semi-préparative & analytic

## CONTACT

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# PROTEOMICS IBPS - MASS SPECTROMETRY

## OUR SERVICES

■ We will help you choose the best strategy for your projects. We perform:

- routine analyses;
- assistance in sample preparation;
- tailored analysis for purified molecules or shotgun proteomics;
- assistance in data processing (database search, statistical analyses, etc.);
- long-term research projects;
- training and access to a MALDI-TOF instrument.

Our services are fully accessible to both public and private structures. Please refer to the website for pricing.

## OUR EXPERTISE

■ We have strong expertise in the analysis of small molecules, polymers, peptides, proteins and oligonucleotides, in simple or complex mixes. We can perform specific sample preparation including desalting and concentration, protein extraction and digestion, proteome frac-

tionation (1D gels, liquid chromatography), phosphopeptide enrichment, and choice of the ionization mode. We also perform data processing, such as protein identification and quantification.

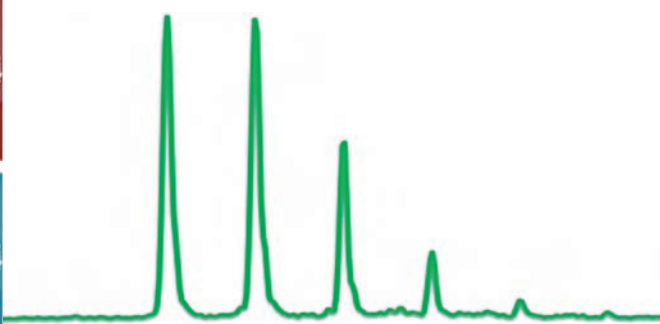
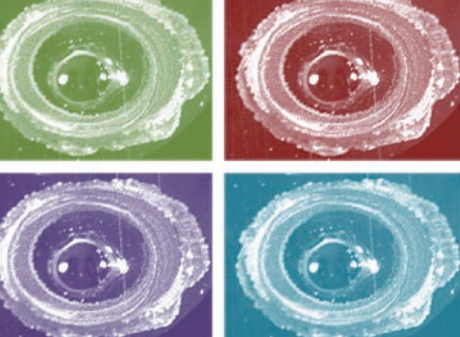
## OUR TECHNOLOGIES

■ The facility is equipped with state-of-the-art technologies in mass spectrometry, HPLC separation and data processing for characterization of molecules and biomolecules, in particular shotgun proteomics in complex samples (whole cell lysates). We propose both electrospray (ESI) and matrix-assisted laser desorption ionization (MALDI). With four mass spectrometers, we offer a wide range of mass analyzers and detectors: time-of-flight, linear ion trap for sensitivity, Orbitrap for high precision and accuracy, and triple quadrupole for MRM. CID, HCD and ETD fragmentation modes are available. We perform analyses with microLC or nanoLC separation for complex samples.

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## PROTEOMICS IBPS - MASS SPECTROMETRY



### DEVELOPMENTS

#### ■ Isotopic labeling and label-free quantification

The quantitative comparison of proteomes under different conditions is key to understanding biologic processes. We are currently implementing the experimental and statistical tools necessary for both isotopic labeling and label-free quantification, in order to identify the best strategy for your particular needs.

#### ■ Post-translational modifications

In addition to phosphoprotein analysis, currently available at the facility<sup>1, 2</sup> we are working on other PTMs, such as lysine acetylation and methionine oxidation, through specific affinity enrichment techniques and diagonal chromatography. Other PTMs can be investigated on request.

#### ■ The mechanisms of fragmentation methods

We are interested in understanding the chemistry of the diverse fragmentation modes, and specifically electron transfer dissociation (ETD), and have evaluated the fragmentation behavior of branched or cross-linked peptides<sup>3</sup>. We will extend this study to other types of molecules.

### EQUIPMENT

#### Mass spectrometer

- ESI-LTQ Orbitrap XL ETD
- MALDI-TOF/TOF 4700 Proteomics Analyzer with optional high mass detector
- MALDI-TOF Voyager De-Pro
- ESI-QTrap

#### HPLC

- Ultimate 3000 nanoLC
- Ultimate 3000 microLC

#### Other

- Probot MALDI Spotter

#### Data analysis

- Thermo XCalibur, Proteome Discoverer, Mascot, Data Explorer, Perseus, proteome annotation.

1. L. Matheron, H. van den Toorn, A.J. Heck, S. Mohammed (2014), Characterization of biases in phosphopeptide enrichment by Ti(4+)-immobilized metal affinity chromatography and TiO<sub>2</sub> using a massive synthetic library and human cell digests, *Anal. Chem.* 86 (16), 8312-20.  
2. L. Matheron, E. Sachon, F. Burlina, S. Sagan, O. Lequin, G. Bolbach (2011), Sequence-dependent enrichment of a model phosphopeptide: a combined MALDI-TOF and NMR study, *Anal. Chem.* 83(8), 3003-10.  
3. S. Clavier, G. Bolbach, E. Sachon (2015), Photocross-linked peptide-protein complexes analysis: a comparative study of CID and ETD fragmentation modes, *J. Am. Soc. Mass Spectrom.* 26-6), 1014-26





## RODENT FACILITY



### OUR EXPERTISE

■ This facility is affiliated with the Small Animal Phenotyping network RPPA (Réseau de Phénotypage du Petit Animal) and has the quality label and support of IBISA (Infrastructure en biologie, santé et agronomie). An animal welfare committee ensures new European standards on animal experimentation are implemented, and the facility is affiliated with the Ethics Committee in Animal Experimentation Charles Darwin (C2EA No. 05).

### OUR SERVICES

■ The Rodent Facility provides:

- breeding and housing of mouse and rat lines;
- surgery;
- a broad battery of behavioral tests to thoroughly phenotype rats and mice;
- functional exploration using bioluminescence and fluorescence microscopy on the whole animal;
- gene transfer by stereotaxic injection using viral vectors.

■ The service comprises two zones of conventional statute a breeding area and an experimental area. In both areas, a technical team of ten provides health monitoring, animal care and welfare, and implements the procedures governing animal experimentation.

### CONTACT

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## RODENT FACILITY



### DEVELOPMENTS

■ A behavioral core-facility developed by the Neuroscience Paris-Seine unit offers various tools for the functional analysis of mouse models. It is equipped to perform a broad variety of behavioral tests related to:

- learning and memory: watermaze, Barnes maze, conditioned fear, object recognition, Y-maze, conditioned place preference;
- motor function: actimetry, rotarod;
- anxiety: plus maze test, open field;
- depression: social defeat, suspension test by the tail, forced swimming test.

■ A PhotonIMAGER OPTIMA allows functional exploration of the whole animal by bioluminescence and fluorescence. The facility has access to a containment room level 2 (A2L2). We are also equipped for the injection of viral vectors (typical lentivirus, AAV, Sindbis) containing «repair», «reporter» or optogenetic probes (for modulating neuronal activity) in mouse or rat brain regions. This area is equipped with stereotaxic injection posts in a sterile environment.

### EQUIPMENT

#### Surgical Block

- Binocular microscope KAPS MA T005
- Binocular microscope KAPS MA T007
- Compact anesthetic unit with 4 anesthesia masks
- Oxygen concentrator
- Induction systems

#### Behavior Core Facility

- *In vivo* bioluminescence and fluorescence imager
- Watermaze
- Barnes maze
- Rotarod
- Actimetry

#### Gene transfer platform

- 2 stereotaxic instruments
- 2 microscopes
- 2 biosafety cabinets (PSM)



# BIOINFORMATICS IBPS - ARTbio

ARTbio works with the Galaxy system, a collaborative open source platform dedicated to scientific and biomedical research. The Galaxy servers enable computational data analyses with a user-friendly interface. They provide both traceability and reproducibility of the analyses which can be shared for collaboration and publication.

## OUR SERVICES

- We assist you in the experimental and computational design of high-throughput sequencing analyses using Galaxy servers.
- We help you choose the tools and workflow best adapted to your analyses.
- We provide advanced training in Galaxy usage.

Our services are fully accessible to both public and private structures. Please contact us for pricing.

## OUR EXPERTISE

- We have an extensive knowledge of the Galaxy software and its use, from raw data acquisition to publication.
- We constantly integrate newly launched software and methods into the Galaxy toolpack.
- We ensure project quality and optimal interaction with users by using continuous integration technologies

and the AGILE guidelines.

- We continuously improve our Galaxy expertise through our own research in RNA biology, epigenetics, metagenomics and bioinformatics, which we publish in peer reviewed scientific journals.

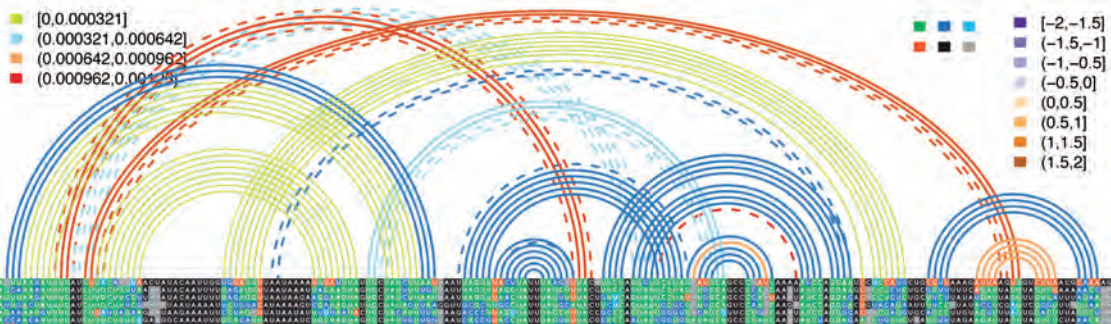
## OUR TECHNOLOGY

- We use the R, Python, Perl and Bash programming languages, the Git and Mercurial revision control software, and continuous integration tools such as Planemo and Jenkins.
- We implement virtualization and container technologies (e.g. Docker) in order to make analyses reproducible in any hardware infrastructure.
- We can increase our computing resources on demand thanks to cloud infrastructures such as that provided by the *Institut Français de Bioinformatique*.

## CONTACT

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## BIOINFORMATICS IBPS - ARTbio



### DEVELOPMENTS

#### ■ Project support

We have recently provided advanced support to many Next Generation Sequencing (NGS) projects, including studies of epigenetic functions of piRNAs<sup>1</sup>, antiviral RNA interference<sup>2</sup> or roles of miRNAs in stem cell differentiation<sup>3</sup>.

#### ■ Tools

We developed and made publicly available the « mississippi » suite of tools (for mi, si and pi RNA) for mining small RNA sequencing datasets<sup>4</sup>. We are currently releasing a set of Galaxy workflows aimed at detecting viruses or identifying new viral species from small RNA sequencing datasets<sup>5</sup>. We are also developing the DockerToolFactory, which allows execution of customized R, python, perl or bash scripts without leaving the Galaxy environment<sup>6</sup>.

#### ■ Methodology developments

We are working to improve continuous integration (based on virtualization methods (e.g. Planemo, Jenkins CI, Virtual machines, Docker and Deployment in Cloud).

### EQUIPMENT

#### Servers

- Server Dell 24 core, 128 GB RAM, 12 TB RAID storage.
- Server Dell 16 core, 96 GB RAM, 25 TB RAID storage.
- Access to IFB cloud infrastructure ([www.france-bioinformatique.fr](http://www.france-bioinformatique.fr))

#### Galaxy servers online

- <http://mississippi.fr> (public)
- <http://lbcd41.snv.jussieu.fr> (restricted access)

1. A. de Vanssay et al., Paramutation in *Drosophila* linked to emergence of a piRNA-producing locus. *Nature*. 490, 112-15 (2012).

2. P. Miesen et al., Distinct sets of PIWI proteins produce arbovirus and transposon-derived piRNAs in *Aedes aegypti* mosquito cells. *Nucleic Acids Res.* (2015), doi:10.1093/nar/gkv590.

3. A. Jouneau et al., Naive and primed murine pluripotent stem cells have distinct miRNA expression profiles. *RNA*. 18, 253-64 (2012).

4. [https://testtoolshed.g2.bx.psu.edu/view/mvdbeek/mississippi\\_toolsuite/](https://testtoolshed.g2.bx.psu.edu/view/mvdbeek/mississippi_toolsuite/)

5. [https://toolshed.g2.bx.psu.edu/view/drosoff/suite\\_visitor2/](https://toolshed.g2.bx.psu.edu/view/drosoff/suite_visitor2/)

6. <https://bitbucket.org/mvdbeek/dockertoolfactory>





## AQUATIC ANIMAL FACILITY



The aquatic animal facility is dedicated to research on several aquatic models. We provide housing and breeding of the following species: *Danio rerio* (zebrafish), *Xenopus laevis* (amphibian), cichlids, polypters and *Ciona intestinalis* (ascidian). Additional animal models will be housed in the near future, such as *Xenopus tropicalis* (amphibian) and *Clytia hemisphaerica* (cnidaria).

The facility is affiliated with the UPMC Small Animal Phenotyping network (RPPA) and has the quality label and support of IBISA.

### OUR SERVICES

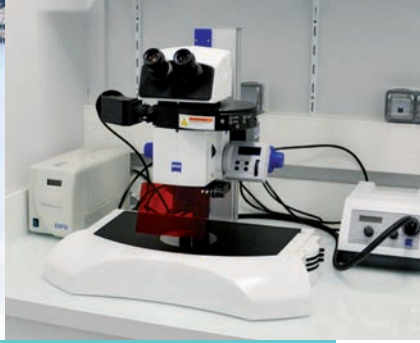
■ An engineer and 4 zootechnicians manage the animal husbandry, cleaning and maintenance of the tanks and installations. They carry out mating and embryo collection according to user request including embryo bleaching before shipping zebrafish lines to external laboratories. In addition, the following manipulations can be carried out for zebrafish:

- maintenance of lines and genotyping of adult fish via PCR;
- animal crossing, identification of mutant/transgenic animals by phenotypic or fluorescence analyses;
- cryopreservation of lines by sperm freezing and in vitro fertilization;
- preparation of zebrafish embryo media and injection dishes;
- regular update of the database containing all zebrafish lines and batches present in the facility.

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## AQUATIC ANIMAL FACILITY



### OUR TECHNOLOGY

■ The facility houses an integrated system for 15,000 adult zebrafish (1700 tanks) and a quarantine zone (60 tanks). In addition to wild type lines, it maintains more than 50 transgenic and mutant zebrafish lines.

The facility provides:

- 3 injection setups for zebrafish embryos (stereomicroscopes equipped with a micromanipulator and an injector), available as self-service for users ;
- 1 stereomicroscope equipped with fluorescence to observe and identify transgenic animals ;
- 1 injection setup under fluorescence for *Xenopus* embryos ;
- 1 water purification and treatment system.

### DEVELOPMENTS

■ Transgenic techniques for *Xenopus*, and genomic engineering with CRISPR/Cas9 technology in zebrafish are being developed and will be available soon.

## EQUIPMENT

### BREEDING

#### **Zebrafish room**

1700 tanks of different capacities : 1L, 3L, 8L of which 60 tanks have a reversed circadian rhythm.

#### ***Xenopus laevis* room**

72 tanks of 27L with quarantine possibility

#### ***Xenopus tropicalis* room**

48 tanks of 3L and 9L

#### **Ascidacea room**

8 tanks of 38L

### EXPERIMENTATION

#### **3 zebrafish injection setups**

- Stereomicroscope with transmitted light
- Micromanipulator
- Microinjector

#### **1 injection setup for *Xenopus***

- Stereomicroscope with light fiber
- Micromanipulator
- Microinjector

#### **2 setups for screening transgenic lines**

- Fluorescence Stereomicroscope (Royal Blue, Cyan, Green, UV, White)
- Fluorescence Stereomicroscope (GFP, RFP, DAPI)

#### **1 horizontal pipette puller**

#### **4 temperature-controlled cabinets**

(14°C, 23°C, 28°C, 33°C)

**Liquid nitrogen container** for fish sperm cryopreservation