CENBG-Université de Bordeaux – CNRS/IN2P3

AIFIRA : Applications Interdisciplinaires des Faisceaux d'Ions en Région Aquitaine

Scientific committee IN2P3 - 25/02/2020

Abstract

AIFIRA is a small scale ion beam facility equipped with a single stage electrostatic accelerator delivering beams of light ions (H+, D+, He+) in the MeV energy range. The accelerator (Singletron™, HVEE, The Netherlands) has been commissioned in 2006 and is particularly suitable for producing focused microbeams as well as secondary fields of mono-energetic neutrons or γ. AIFIRA delivers beams presenting a high brightness (74 A m^{-2} rad^{-2} eV^{-1}) and a high energy stability ($\frac{\Delta E}{E} = 10^{-5}$) in 5 beamlines dedicated to specific applications. Since 2007 the accelerator is opened about 200 days per year to academic research groups and companies. Experiment proposals are discussed twice a year (June and December) by a local committee and beamtimes are allocated on a semester basis.

AIFIRA is used for fundamental and applied research. Most of the research conducted on the facility covers three main areas:

- **Ion beam analysis (IBA) at various scales (from µm to mm)**. IBA techniques provide quantitative information on sample composition and especially trace elements (down to ppm). They are used in various research areas: Characterization of materials and thin layers, archaeometry and expertise on art items, life science and studies of the impact of exogenous compounds on living cells, geology and geochemistry of terrestrial and extraterrestrial samples.

- **Targeted micro-irradiation with charged-particles at the cellular scale**. This technique is used to elucidate the fundamental mechanisms of the radiation-induced cellular response. The charged-particles available at AIFIRA are similar to the ones involved in natural radioactivity (α-particles) and radiotherapy (protons).

- **The production of well characterized mono-energetic neutron and γ fields** suitable to calibrate radiation protection detectors and dosimeters and to conduct fundamental research on nuclear data relevant for new generation of power plants.

Measurements for industries and private companies are conducted partly in the frame of collaborations with the academic users and mostly through the activity of the technology transfer unit ARCANE which handles ion beam analysis measurements for SMEs or bigger companies at the regional and national levels.

AIFIRA is also a technical support for teaching and professional training. The ion beam techniques and instrumentation are used to address fundamental and practical aspects of radiation matter interactions, nuclear instrumentation, radiation metrology and radiation protection.

1. Description of the facility

a. Instruments

AIFIRA is based on a single stage electrostatic accelerator delivering beams of light ions (H+, D+, He+) in the MeV energy range. The accelerator (Singletron™, HVEE, The Netherlands) is particularly suitable for producing focused microbeams as well as secondary fields of mono-energetic neutrons or γ. It delivers ion beam with a high brightness (74 A m^{-2} rad^{-2} eV^{-1}) and a high energy stability ($\frac{\Delta E}{E} = 10^{-5}$) in 5 beamlines dedicated to specific applications.

The five beamlines available at AIFIRA are:

- A « macro-beam » used for sample analysis at the mm scale.

- A « external beamline » dedicated to ion beam analysis of big and/or fragile samples that cannot be inserted in vacuum chambers. The beam is extracted in air through a thin kapton or silicon nitride window.

- A nuclear microprobe used for quantitative imaging at the micrometer scale (so-called microbeam line).

- A microbeam dedicated to targeted irradiation of living cells with a counted number of particles and the micrometer accuracy (so-called micro-irradiation beamline). The particles are extracted in air through a silicon nitride window or a thin diamond detector.

- A beamline designed for the production of neutron and gamma fields (so-called “Physics beamline”).

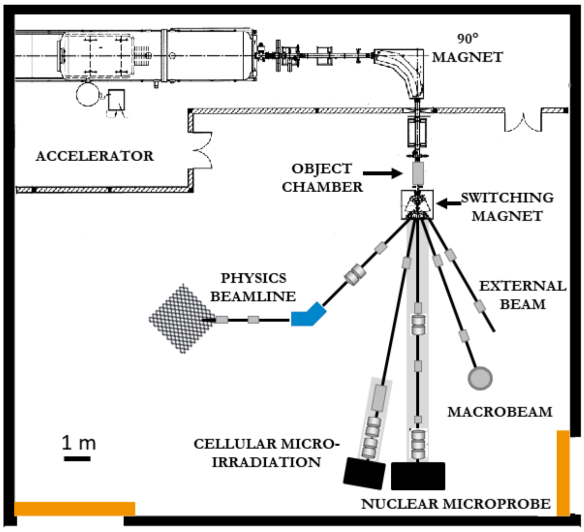

Figure 1: Schematic view of the AIFIRA facility

Figure 2: Panoramic view of the AIFIRA experimental hall

b. Organization and staff

AIFIRA is operated by a team of 3 people: one associate professor and two engineers. This team is organized as follows:

- A scientific coordinator (Philippe Barberet, associate professor univ. Bordeaux, 20 % FTE): head of the platform and in charge of the scientific and funding aspects.
- A operation manager (Stéphanie Sorieul, engineer CNRS/IN2P3, 80% FTE): In charge of the user support, beamtimes operation and communication.
- A technical coordinator (Philippe Alfaurt, engineer CNRS/IN2P3, 50 % FTE) : In charge of the maintenance of the accelerator and beamlines

The activity and developments on the platform are also supported by the CENBG technical groups (instrumentation, mechanics and computing) and rely widely on the scientific expertise of the CENBG research groups.

Besides the support to research projects by the CENBG staff, the services for private structures are performed by the CENBG technology transfer unit ARCANE (http://www.adera.fr/cellules/arcane-caracterisation-analyse-nucleaire-aquitaine). ARCANE is administrated by the ADERA association ("Association pour le Développement de l'Enseignement et des Recherches auprès des universités, des centres de recherches et des entreprises d'Aquitaine"). ARCANE uses 20 % of the AIFIRA beamtime and performs about 80 services per year for a total amount of about 200 k€.

The scientific and technical topics are discussed in the frame of a local committee gathering engineers and researchers from CENBG and having a specific expertise in the various analysis and irradiation techniques available at AIFIRA. This committee appraises the experiment proposals twice a year and advises the AIFIRA staff regarding the scientific and technical needs. Monthly meetings are organized to follow the beamtimes allocated to external or CENBG users, to discuss the technical problems and to propose solutions. The technological survey and the state of the art of the instrumentation and techniques are also discussed regularly by the experts of the committee. The composition of the experts committee is provided in table 1.

Name	Affiliation @ CENBG	Expertise
Philippe Barberet	iRiBio / AIFIRA	Scientific coordinator of AIFIRA. Microanalysis and micro-irradiation. Beam handling.
Stéphanie Sorieul	Instrumentation / AIFIRA	Operating manager. Ion beam analysis and irradiation of materials. Scientific support. Beam handling. Radiation protection.
Philippe Alfaurt	Instrumentation / AIFIRA	Technical coordinator of AIFIRA. Maintenance, vacuum and automatism. Beam handling
Laurent Daudin	Instrumentation	Detectors, electronics and data acquisition.
Ludovic Mathieu	ACEN	Nuclear physics and neutron production. Radiation protection
Stéphane Roudeau	ICS	Radiation protection and microanalysis
Guillaume Devès	iRiBio	Microanalysis of biological samples
Hervé Guégan	ARCANE	Ion beam analysis and services to labs and companies. Ion beam irradiation and production of 6 MeV γ fields.

Table 1: Composition of the AIFIRA local committee.

In addition to the local committee, a user's meeting is organized once a year to discuss the feedback from users originating from the different communities represented at AIFIRA.

c. Funding

The AIFIRA running costs are covered by three types of funding:

- Regular support from the two parent institutions: IN2P3 and the university of Bordeaux. The contribution of IN2P3 is of 15 k€ per year and the university of Bordeaux covers the cost of fluids and building maintenance for a total amount of about 20 k€ per year.
- Contribution of the ARCANE technology transfer unit. In counterpart of accessing 20 % of the AIFIRA beamtime, the ARCANE unit pays 15 k€ per year to cover the corresponding running costs.
- AIFIRA own funds coming from external users fees. Presently the contribution is of 500 € / day for users from CNRS and/or university of Bordeaux and 1000 € / day for others. These amounts are being re-evaluated by CNRS and will probably change in the near future.

Besides the regular running costs, bigger equipment and investments are covered by specific proposals submitted to funding institutions either by the AIFIRA team or CENBG research groups. In the last years, the main funding institutions were the Région Nouvelle Aquitaine (via a specific call "plateforme mutualisée"), Europe (AIFIRA was associated to Marie-Curie RTN and I3 consortia), INSERM (via the physicancer call) and the CNano cluster. Projects dedicated to the development of new activities or instruments are also funded by the CNRS MITI mainly on the frame of the iRiBio group scientific activity (see section 5).

d. Users

A list of the laboratories that used the AIFIRA facility in the last years is given in table 2.

CNRS - IN2P3	CNRS - hors IN2P3	Autres
CENBG (UMR5797)	ICMCB (UPR9048/INC)	IRSN (LMDN)
LPC (UMR6533)	CRP2A (UMR5060/INSHS)	CEA (LIST/DSL)
IPHC (UMR7178)	CBM (UPR4301/INC)	IRSN (LE2M)
IPNL (UMR5822)	CELIA (UMR5106/INP)	
	PLACAMAT (UMS 3626/INC)	
	LCP (UMR8000/INC)	
	ECOLAB (UMR5245/INEE)	
	MFP (UMR5234/INSB)	
	INCIA (UMR5287/INSB)	
	CIRIMAT (UMR5085/INC)	
	PACEA (UMR5199/INEE)	
	Institut Fresnel (UMR7249/INSIS)	
	LAB (UMR5804/INSU)	

Table 2: list of the AIFIRA users

2. Scientific activity

The activity of the platform mainly covers three areas: (i) elemental analysis, (ii) detector characterization and (iii) radiation biology. This document summarizes most of the research projects in these three areas conducted in the last five years. Smaller scale projects or punctual experiments were also performed in the same period, they will not be described in the following but the corresponding papers are given at the end of the bibliography list.

a. Elemental analysis using ion beams

Ion beams in the MeV energy range offer relevant techniques to quantify trace or major elements in materials with the ppm (part per million) sensitivity. Combined together, these techniques give access to most of the elements of the periodic table. The ion beam analysis (IBA) techniques used in routine at AIFIRA are summarized in table 3.

Analysis technique	Acronym	Information provided
Particle-Induced X-ray Emission	PIXE	Concentration of all elements with Z>11 with a sensitivity of a few tens of ppm. Based on the detection of X-Rays from atomic deexcitation.
Rutherford Backscattering Spectrometry	RBS	Quantitative analysis of surfaces and interfaces. Good resolution in depth. Based on the detection of backscattered ions.
Elastic Recoil Detection Analysis	ERDA	Quantification of hydrogen. Based on the hydrogen elastic recoil under light ion irradiation.
Nuclear Reaction Analysis	NRA	Quantification of light elements by nuclear reactions (He, Li, Be, B, C, N, O, F). Based on the detection of charged-particles produced by the nuclear reaction. Isotopic analysis.
Particle-Induced Gamma-Ray Emission	PIGE	Quantification of light elements by nuclear reactions leading to the emission of specific γ rays.
Scanning Transmission Ion Microscopy	STIM	Mapping of thin samples areal mass by measuring the ions transmitted energy through the sample.
Ion Beam Induced Charge	IBIC	Mapping of the charge collection in electronic devices under ion irradiation.

Table 3 : IBA techniques used routinely at AIFIRA and the corresponding acronyms. The acronyms are preceded by µ (e.g. µPIXE) when the technique is conducted with a microbeam.

✓ Analysis at the millimeter scale

AIFIRA is equipped with two beamlines dedicated to ion beam analysis at the millimeter scale: the so-called “macro beamline” and “external beamline”.

The macro beam line is used routinely to conduct PIXE, RBS, NRA and PIGE measurements on thin layers either in the frame of the ARCANE activity or for collaborators from academic laboratories. This beamline is used extensively used by the ARCANE technology transfer unit in the frame of contracts with companies and laboratories. From the academic side the "macro beamline" was mainly used for RBS and NRA characterization of materials by collaborators from ICMCB (INC / university of Bordeaux) in the frame of the development of Lithium-ion microbatteries [1–4].

AIFIRA is one the few facilities equipped with an external beamline designed for ion beam analysis of cultural heritage samples. A regular activity is conducted in collaboration with the IRAMAT-CRP2A laboratory (Institut de recherche sur les Archéomatériaux – Centre de recherche en physique appliquée à l'archéologie). PIXE analysis is used to assess the trace elements contents in obsidian samples collected in the mediterranean basin. These trace elements concentrations provide information on the origin of the samples and thus on exchanges between populations of the neotlithic period. Several articles on this topic have been published in the last years, including methodological papers promoting the ion beam techniques for archaeometry [5,6].

✓ Micro-analysis and imaging

The ion beam analysis techniques mentioned previously (table 3) can be implemented on the microbeam line. The beam spot is focused down to a size ranging from 300 nm to a few micrometers and is raster scanned on the sample. The composition is measured locally and maps showing the localization of the chemical elements are produced. Thus, microanalysis provides quantitative measurements of the sample composition at the ppm level and at the micrometer scale. This approach is particularly relevant for mapping and quantifying chemical elements in living cells, small organisms or tissue sections. In the last years, µPIXE analysis has been extensively used in the frame of several projects to quantify inorganic elements. The methodological approach can be divided in two types of studies:

- Single cell analysis aiming at characterizing the internalization of exogenous elements (metals, nanoparticles) at the single cell scale as well as its impact on endogenous elements (e.g. P, S, K, Ca). This approach has been implemented either to better understand the role of metals or their toxicity in neurobiology[7–9] or to study the internalization and the toxicity of metal or metal oxide nanoparticles[10]. The strength of the AIFIRA facility in that field is that µPIXE is one of the only analytical technique combining quantitative information (elemental concentrations at the ppm level) and mapping capabilities. Thus, it allows to measure precisely the quantity of internalized compounds in a significant number of single cells in a population. This is of particular importance for studying the biological response following the exposure to exogenous compounds that are not internalized equally from one cell to the other. Such studies have required instrumentation developments handled by the technical groups at CENBG. For example, we installed multiple Si(Li) detectors to increase the detection efficiency and thus decrease the acquisition time and we developed the possibility to perform batch acquisition to allow full time measurements (24h a day) and thus increase the number of samples analyzed per day of beamtime. Besides these technical developments, the iRiBio group (Ionizing radiation and biology) performed several methodological developments regarding the sample preparation, correlative imaging and data processing. These developments have been published and opened to the community[11–13].

  These research projects conducted by local teams have led to an interest of the community for the capabilities of µPIXE analysis. Several external groups have used the AIFIRA facility in the frame of their research on nanotoxicology[14–17]. More recently the extension of the capabilities of µPIXE for the quantification of metals, rare earth or nanoparticles at the single cell level for other reseach fields has been investigated. This concerns:

- The exposure of cells to metallic nanoparticles as radio-enhancer in radiation therapy. One of the fundamental question in that field is how these nanoparticles are internalized, where and in which amount. This project is coordinated by a team from LPC (UMR 6533).

- The exposure to new radioactive isotopes for vectorized radiotherapy. In such studies, cells are exposed to molecules containing radioactive isotopes and the internalization of this molecule leads to a dose deposition inside the biological cell. µPIXE performed on cell exposed to molecules marked with non radioactive isotopes of the same elements can provide relevant information on the quantity of internalized atoms and their localization (nucleus vs. cytoplasm). This project is coordinated by a team from INCIA (UMR 5287).

Two feasibility studies have been performed in 2018-2019 and will probably lead to extensive studies in the coming years (see perspectives).

- Analysis of tissues or sections to quantify inorganic elements. Microanalysis is also performed by external groups for various applications. In the last years these techniques have been routinely used to:
  - Characterize and optimize the interaction of biomaterials with biological tissues [18–20]. This project is driven by the “Chemical physics of biomaterials and nanostructures” group at LPC, Clermont-Ferrand. In this frame, µPIXE is used to (i) study the bioactivity process at bioactive glasses / living tissues interface, (ii) evaluate the capacities of the doped materials to release relevant quantities of trace elements in tissues.
  - Characterize sedimentary samples to study the conditions of primitive life on earth (project run by the CBM, Orléans) [21–23]. Here µPIXE experiments are conducted to quantify the presence of hydrothermally transported inorganic elements in analogous sediments. This allowed to identify the physical and chemical conditions in which prebiotic chemical reactions can take place. In the frame of this project, new methodological approaches are also developed. The development of correlative imaging involving raman spectroscopy and ERDA measurements performed at AIFIRA providing the hydrogen content of well defined area of the sample was presented at the last Ion Beam Analysis international conference (IBA 2019, Antibes, France).

b. Detector characterization

In the last five years, a significant amount of beamtime has been dedicated to the characterization and calibration of ionizing radiation detectors and dosimeters.

First, two projects aiming at a precise characterization of the charge collection in dosimeters based on semi-conductors were conducted at AIFIRA. The micrometer size of sensitive volumes require the use of a charged-particle microbeam to probe locally this ion beam induced charge. The first project is conducted by the DeSIs group at IPHC Strasbourg. It aims at characterizing two type of neutron dosimeters based on CMOS chips and neutron-proton or neutron-alpha conversion. In this project the AIFIRA microbeam was used to probe the charge induction and collection following alpha-particle or proton irradiation at the micrometer scale in the CMOS pixelated sensor [24–26]. The second project is driven by collaborators from the “laboratoire capteurs diamants” (LCD, CEA-LIST Saclay). This project aims at designing and optimizing microdosimeters based on single crystals CVD diamonds[27]. In that frame the microbeam is regularly used to characterize prototypes designed at LCD. This project is running until the end of 2020 and is funded by CEA and INSERM.

The AIFIRA primary beams (protons or helium) and the secondary neutron or γ fields are also used as references to calibrate detectors used in nuclear physics experiments. In the last years, The ACEN group at CENBG has developed a research program to answer the need of a significant reduction of the uncertainties on nuclear data for many actinides. In particular, a good knowledge of fission cross sections in the MeV neutron energy range is a key point for accurate simulations of reactors for which the maximum of the neutron spectrum is around 1-2 MeV (Fast Neutron Reactors). For this purpose, the group developed a gaseous proton-recoil detector for neutron flux measurements. Protons beam of well-known energy are used to calibrate this proton recoil detector at AIFIRA [28,29].

Besides gaseous detectors, the proton beam was also used recently to calibrate Thomson parabola developed for characterizing proton and helium beams produced and accelerated in the MeV energy range by high power lasers. The ENL group at CENBG used AIFIRA proton beams of increasing energies (0.7 to 2.5 MeV) to calibrate the response of the detectors. The use of AIFIRA beams as references allowed to measure precisely the characteristics of light ion beams produced at the PICO2000 laser (LULI, Palaiseau)[30].

3. Cellular micro-irradiation

The cellular targeted micro-irradiation activity significantly increased in the last five years. A dedicated beamline, developed by the iRiBio group and the technical groups of CENBG was commissioned in 2012/2013. This beamline is designed to target cellular compartments (nucleus / cytoplasm) with a counted number of charged-particles. The end-station is equipped with a time-lapse fluorescence microscope used to record the cell early response in the first seconds to minutes after irradiation. This original equipment triggered new research projects and collaborations. First, in the frame of a Marie Curie research initial training network (“Supporting Postgraduate Research with Internships in industry and Training Excellence" (SPRITE)), the iRiBio group developed the methodology to record and analyze the recruitment of proteins at DNA sites damaged by single or multiple ions [31]. Systematic measurements at various LETs and doses have been performed and are being coupled to track structure simulations. This approach should allow a better understanding of the relation between the amount and the complexity of the radiation-induced DNA lesions and the cell early response. Specific developments of thin diamond detectors (below 2 µm in thickness) were also performed to offer the opportunity to irradiate precisely with single ions[32]

Besides DNA targeted effects, the micro-irradiation beamline was also used in the frame of a collaboration with the SNAKE facility (Universität der Bundeswehr, Munich) to address the specific radiation-induced response of mitochondria. Joint experiments conducted with carbon beams (SNAKE) and proton beams (AIFIRA) allowed to target specifically the mitochondrial network and measure the behavior of fluorescent probes related to the mitochondrial membrane polarization. These experiments showed a partial or complete membrane depolarization related to the dose[33].

In the last years, the micro-irradiation technique was also extended to multi-cellular organisms. Preliminary experiments were performed to precisely irradiate a single cell in C. elegans embryo with a controlled number of protons[34]. This approach opens new perspectives for the investigation of low-dose and non-targeted effects. This topic will be investigated in the frame of the RADIANCe project (supported by CNRS PRIME80) that started in 2019 and is aiming at characterizing the radiation-induced effects on the RNA metabolism of C. elegans.

Finally, biophysics experiments have also begun recently on the micro-irradiation beamline. The so-called INSIDE project ("IN SItu DEtection of DNA fragmentation induced by proton collision") was initiated in 2019 and is aiming at measuring the probabilities of single or double strand fragmentation of DNA in liquid water when irradiated by a proton beam controlled in dose, time and impact parameter. The DNA fragmentation will be investigated through the measurement of diffusion constants and radius of gyration using fast fluorescence time-lapse imaging online. These parameters were chosen as they can be heavily modified by the fragmentation of the DNA molecule. The first experiments using the AIFIRA beams have been conducted in 2019 and demonstrated the capability of the set-up to record fast Brownian motion online and to control the irradiation time with the ms precision.

3. Position of the AIFIRA facility

The AIFIRA facility was commissioned in 2006 to:

- Sustain the specific skills developed at CENBG on the Van de Graaff accelerator: ion beam analysis, nuclear microprobes and nuclear physics experiments based on neutron fields produced using light ion beams.
- Open the analysis and irradiation techniques to the scientific community

The main features of AIFIRA are the possibility to perform imaging or targeted irradiation at the micrometer scale and the use of an external beamline that opens analytical techniques to archaeometry.

✓ Microbeams

AIFIRA is the leading facility at the national scale concerning microbeam technologies and applications. The nuclear microprobe is the one presenting the smallest beam size and the only one suitable to perform ion beam analysis at the single cell scale. The only other similar analytical tool in France is the one installed at CEA-IRAMIS which is mainly dedicated to light element analysis by nuclear reaction. To date, AIFIRA is also the only French facility with a running activity on cell targeted micro-irradiation. The AMANDE-MIRCOM facility (IRSN Cadarache) has recently been equipped with a micro-irradiation beamline (developed and commissioned by the CENBG technical groups) but, up to date, no radiation biology studies have been published.

At the international level, AIFIRA is involved in the "Ion Beam Analysis" (IBA) and "Nuclear Microprobe Technologies and Applications" networks. The scientific coordinator of AIFIRA is a member of the scientific boards of the related international conferences. The facility and the iRiBio group are also regularly involved in European networks (Marie Curie ITN or Integrated Infrastructure Initiatives). AIFIRA is recognized as a leading facility for the applications of ion microbeams to life sciences and is well recognized in the field of targeted cellular irradiation.

✓ External beamline

AIFIRA is one of the two french facilities, with the AGLAE facility at Louvre, presenting a regular activity applied to cultural heritage. The external beamline allows to perform PIXE and PIGE experiments in air on fragile artefacts. Even if the number of proposals received in that field remains low, ion beam analysis techniques are competitive in specific applications requiring multi-elemental measurements and good sensitivity (ppm).

4. Evolution of the facility

The evolution of the AIFIRA facility and the related scientific activities is oriented towards three main aspects:

✓ Improvement of the ion beam analysis capabilities

The three next years will be devoted to the evolution of the external beamline in the frame of a program funded by the Région Aquitaine. This project aims at installing state of the art silicon drift detectors (SDD) for X-Ray spectrometry. This evolution should allow to acquire at higher count rates and thus to increase the number of sample analyzed per unit beam time. This technical evolution is also mandatory since the Si(Li) detectors used on the platform are not supported anymore by the manufacturers. The update of the detection system will be completed by a renewing of the beamline components (vacuum pumps, motors and pipes) and an update of the motorized stage used to position the sample. This update should allow to perform automatic acquisitions overnight and imaging via multi-spot analysis.

Besides this complete evolution of one of the beamlines, analysis and quantification of light elements should also be developed. Currently, this concerns mainly:

- Hydrogen analysis using elastic recoils detection for which we have a connection with the PLACAMAT platform (UMS3626) to inter-calibrate complementary analysis techniques. A first stone of this intercalibration project was set recently by providing hydrogen quantification for Ti-alloy samples. The results will be correlated with Glow-Discharge spectrometer measurements in order to elucidate the diffusion mechanism involved in the hydrogenation of Ti-alloys (Collaboration with LCTS, Bordeaux (UMR5801)).
- Fluorine quantification on the external beamline for archaeometry applications. Feasibility experiments have been conducted in collaboration with IRAMAT-CRP2A to quantify F in bones. This first try was very promising but underlined the need for further work on data normalization. This work will be continued in the future since PIGE is one of the only quantitative technique to quantify Fluorine with a few ppm sensitivity without destroying the sample.

✓ Micro-analysis of biological samples

As mentioned previously, the µPIXE technique is relevant for quantifying the internalization of exogenous elements in living cells. Several projects are planned for the near future:

The first one concerns the quantification of internalized gold nanoparticles in cancer cells. µPIXE is one of the only technique allowing the measurement of the amount of gold at the single cell level. This is particularly relevant in the frame of the exposure of cells to metallic nanoparticles as radio-enhancer in radiation therapy. The project will most probably start in 2020 and is coordinated by a team from LPC (UMR 6533).

The second project aims at characterizing the exposure to new radioactive isotopes for vectorized radiotherapy. In this study, cells will be exposed to molecules containing radioactive isotopes with the aim of the internalization of this molecule and a radioactive dose deposition inside the cell volume. µPIXE is planned to be performed on cell exposed to molecules marked with non radioactive isotopes of the same elements in order to provide relevant information on the quantity of internalized atoms and their localization (nucleus vs. cytoplasm). This project will be submitted at the European FET (Future and Emerging Technologies) call and is coordinated by a team from INCIA (UMR 5287).

✓ Micro-irradiation of multicellular models

The cellular micro-irradiation is also developing towards the selective irradiation of multicellular models. The technique has been adapted to target selectively cells or organs in the C. elegans nematode at various development stages. New developments to couple irradiation at controlled doses with RNA sequencing are in progress in the frame of the RADIANCe PRIME80 project.

At longer term, we plan to collaborate with the "Bioimaging & OptoFluidics laboratory" group at LP2N (UMR5298) to develop the possibility to irradiate encapsulated cellular aggregates of a few tens of µm in size. This approach allows the investigation of the radiation-induced response in cells while taking into account the 3D characteristics of the tissues in a very reproducible way.

✓ Detector characterization

There is a growing need for characterizing precisely small size or pixelated ionizing radiation detectors. The µIBIC technique available at AIFIRA is particularly relevant for that and microbeam are very competitive for such measurements. We are working at advertising the capabilities of the AIFIRA facility in that field based on the publish results we obtained in the last years and we are aiming at increasing the beamtime devoted to this activity.

5. Resources

a. Funding and spending

The global running cost of the platform, without taking into account the staff expenses is of 90 k€ per year:

- 60 k€ for running costs and maintenance of the accelerator and the 5 beamlines
- 20 k€ for electricity and fluids
- 10 k€ to cover accidental breakdown of big equipment

The platform regular incomes are of 50 k€ / year:

- 15 k€ from IN2P3
- 15 k€ from the ARCANE technology transfer unit
- 20 k€ from the university of Bordeaux

These incomes are completed by the user fees that represent an average of 10 k€ / year.

Altogether, the incomes cover the regular expenses but provisioning to anticipate important breakdowns cannot be done at present. These expenses have up to now been covered by own funds obtained through European projects overheads or the contract for developing a microbeam line for IRSN. These funds are now almost exhausted and a new strategy have to be defined to face such problems.

The investment on beamlines are covered by funding from specific projects:

- Appels à projets "Plateforme mutualisée" from Région Nouvelle Aquitaine. Since 2015, three projects were funded to (i) install a fluoresence recovery after photobleaching (FRAP) set-up on the micro-irradiation beamline (2014-2017, 80 k€), (ii) upgrade the physics beamline (2016-2019, 80 k€) and (iii) upgrade the external beamline (2019-2022, 66 k€)
- Projects from the iRiBio team at CENBG. Since 2015, projects in the following calls allowed to buy equipment for the AIFIRA platform:
    - MITI CNRS Défi « Instrumentation aux limites » - DIRAC project)
    - MITI CNRS Défi « Nano » - PROTONS project
    - MITI CNRS Défi « Modélisation du vivant » - INSIDE Project
    - NEEDS - projects ECHOS and DOSE-ECHOS

- AAP INSERM « physique, mathématiques, sciences de l'ingénieur appliqués au cancer » - DIADEM project

Altogether these projects allowed to invest 60 k€ for AIFIRA equipment in the last five years (detectors, electronics, ion sources, sample holders …).

b. Staff

As mentioned in section 1.b, the platform is operated by three persons (representing 1.5 FTE). Even if the human resources devoted to the platform allows to provide about 200 days of beamtime per year, they remain rather low to operate one accelerator and five beamlines. We would like to highlight the fact that these resources have decreased recently (2019) since the engineer in charge of the operation is now in charge of a the radiation protection at CENBG (decrease from 100 % FTE devoted to AIFIRA to 80%).

At present, the main thread for the AIFIRA facility is related to the knowledge in maintenance, vacuum systems and automation. These technical know-how are relying on only one person (Philippe Alfaurt, technical coordinator of the platform, 50% FTE). This particular aspects is extremely important to maintain a regular activity on the platform and it should be consolidated with a second person with suitable technical skills. Unfortunately, despite several demands in that sense, no support could be obtained in the last years from the parent institutions. A short term contract (1 year engineer) will be funded in 2020 by the university of Bordeaux to temporarily support the AIFIRA activity. At the time of writing this document we have no certainty about the sustainability of this support.

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