Highlighting **the challenges of the 21st century**

Reflection on results obtained on the SMIS beamline.

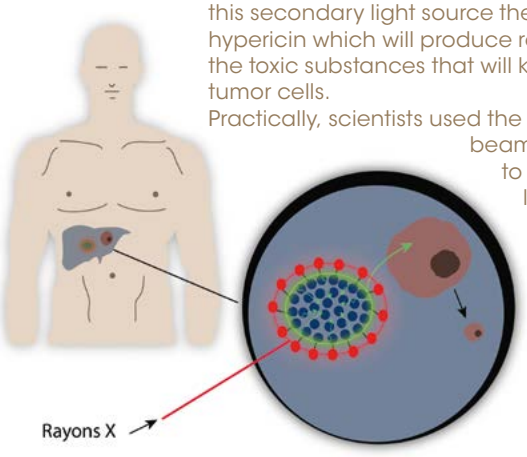
An essential purpose of research is to assist society in identifying the challenges of tomorrow and implementing the necessary solutions. To address the problems we face, it is essential to establish links between the different scientific disciplines and create greater international cooperation. Research at synchrotron SOLEIL also reflects societal concerns.

DISCO-METROLOGY

Medecine - a nanoflash-light to activate drugs in solid tumors

Light has been used in medicine for decades, until now. Photodynamic therapy (PDT) relies on the use of substances which become toxic for their immediate environment when subjected to visible light. The major limitation of the technique: only the reachable zones can be treated (skin, esophagus, lungs…). The whole issue is about vectorising these substances in the tumor before illuminating them to trigger the reaction. Scientists from SOLEIL Synchrotron and the Center of Molecular Biophysics of Orléans had the idea to trigger a chain reaction allowing them to access deeper tumors.

First step, a liponanoparticle micellar structure, with peripheral lanthanides, comes flanking a photosensitizer, the hypericin, which allows vectorising this highly hydrophobic substance until it reaches the zone to be treated. Step 2, the whole area is irradiated by X-rays that initiate the chain reaction. Actually, lanthanides (ex: Gadolinium or Europium) present a long-known luminescence property: when submitted to X-rays, they reemit ultraviolet or visible light. Step 3, this secondary light source then irradiates the central hypericin which will produce reactive oxygen species, the toxic substances that will kill the surrounding tumor cells.
Practically, scientists used the METROLOGY and DISCO beamlines of SOLEIL in order to irradiate liponanoparticles and collect the associated luminescence spectra. They thus showed that the presence of lanthanides did indeed allow emitting a UV-visible radiation which matches the absorption spectrum of hypericin. They then characterized the light energy transfer between those two molecules. They later measured with mass spectrometry the increasing of production of reactive oxygen species, consequence of the light absorption of hypericin. Furthermore, the UV-luminescence properties of the micellar structure allowed the scientists to monitor them inside the cells, and even inside the nuclei.
This system benefits from being extremely versatile: it is indeed possible to enlarge this method to other photosensitizers, or other liponanoparticles already tailored for specific targets. When current photodynamic treatments amount to no more than superficial therapies, the use of the penetrating capacity of X-rays promises to bring new perspectives in the issue of treating deep tumors and also offers perspectives in magnetic resonance imaging.



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Our synchrotron radiation facility is a large-scale research infrastructure (LSRI), which, thanks to its multidisciplinary nature, can address many challenges facing our society, including health, biology, energy, pollution, food production, etc. By programming more than 4,000 research visits each year, SOLEIL is increasingly at the heart of international scientific cooperation, essential to the implementation of global solutions to the problems facing us today. With its 27 beamlines (soon increasing to 29) using different techniques and energy fields, SOLEIL is providing effective tools to meet current research needs and offers a unique platform for study.

As well as the examples presented in this issue of Rayon de SOLEIL, the involvement of our synchrotron in social issues is varied and transversal: all our beamlines are active on these issues, either by their in-house research, or from visiting users. Without being exhaustive, let us scan over some of the research at SOLEIL that covers social issues.

In 2015, with the organization of COP21 (2015 UN Climate Change Conference), France is a central player in the global coordination of measures to control the climate and the environment. SOLEIL has been contributing to this effort for several years. Examples include the study of proxy data, providing natural archives of former or current environmental changes. These climate indicators may

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ROCK - SAMBA

ENERGY - A SOCIETY TURNING TO HYDROGEN

One of the great issues facing our society is to find alternatives to fossil fuels, the reserves of which are dwindling day by day. Clean energy production based on renewable resources is becoming more widespread but this is creating new challenges because of its intermittent nature and its distribution over the country. The use of hydrogen as a clean energy reserve is now being considered for many applications in everyday life, especially to power our cars or our homes. It can be produced from a natural energy source (wind, biomass, solar panels, etc.) but is unfortunately available today only in an intermittent and localized manner. We will be able to talk of the hydrogen age only when we are able to use it without geographical or supply restraints for the conversion of electrical energy into chemical energy and vice versa. We must have enough efficient ways to produce hydrogen cleanly for use in devices such as fuel cells, and the conversion of energy in these batteries must be sufficiently effective to compete with fossil fuels. To solve these two problems, the search is on for low-cost effective catalysts over the long term.

Hydrogen (H_2) of purity compatible with the fuel cell can be produced by converting ethanol from biomass in the presence of alumina-supported cobalt-based catalysts. In collaboration with the Institute of Chemistry of Araraquara (Brazil), researchers on the ROCK beamline undertook to follow on the scale of a few seconds, using time-resolved X-ray absorption measurements, the speciation of cobalt phases when the catalyst is working and losing efficiency. It was shown that the activity of such a catalyst vis-a-vis H_2 production was stable over a long period when metallic cobalt, active in the conversion of ethanol into H_2, coexisted on the alumina surface with a divalent species of cobalt, CoO, used for reoxidizing the coke formed on the catalyst surface. The proportion of the two species must be close to CoO/Co(0) = 1/3. This result was confirmed by studying the regeneration of the activity of the catalyst poisoned by coke formation. If pulses of oxygen are introduced in the medium, the production of H_2 picks up significantly after the coke has been re-oxidized to CO_2 and the CoO/Co(0) ratio is close to 1/3, despite the re-oxidation of the metallic cobalt, inherent with the introduction of oxygen.

In a fuel cell, hydrogen is oxidized to produce electricity directly. These hydrogen oxidation and oxygen reduction reactions are mediated through a proton permeable membrane and an electrical conductor; these reactions are not, therefore, explosive, but controlled. The price to pay is that among the catalysts required for these reactions, the most effective is platinum, which is both very expensive and rare. Fortunately, new low-cost catalysts are emerging. Among these, those based on non-noble metals such as iron, cobalt or molybdenum, or noble but more abundant such as gold, are beginning to compete with platinum on performance. In close collaboration with a research group of the Charles Gerhardt Institute, UMR 5253, CNRS, University of Montpellier, the SAMBA research group were able to clarify one of the most obscure and controversial issues in the study of iron based catalysts in the reduction of oxygen: determining the structure of the active site. Simulating the XANES spectra of Fe obtained on very effective catalysts but with low iron content, they found that the active site consisted of an iron atom linked to four nitrogen atoms, in a structure similar to porphyrin (close to that which coordinates to iron in our blood) and can be located at the edges of a graphene sheet.
This new revelation opens the way for a more rational approach to the study of these systems: one step closer to the hydrogen age.

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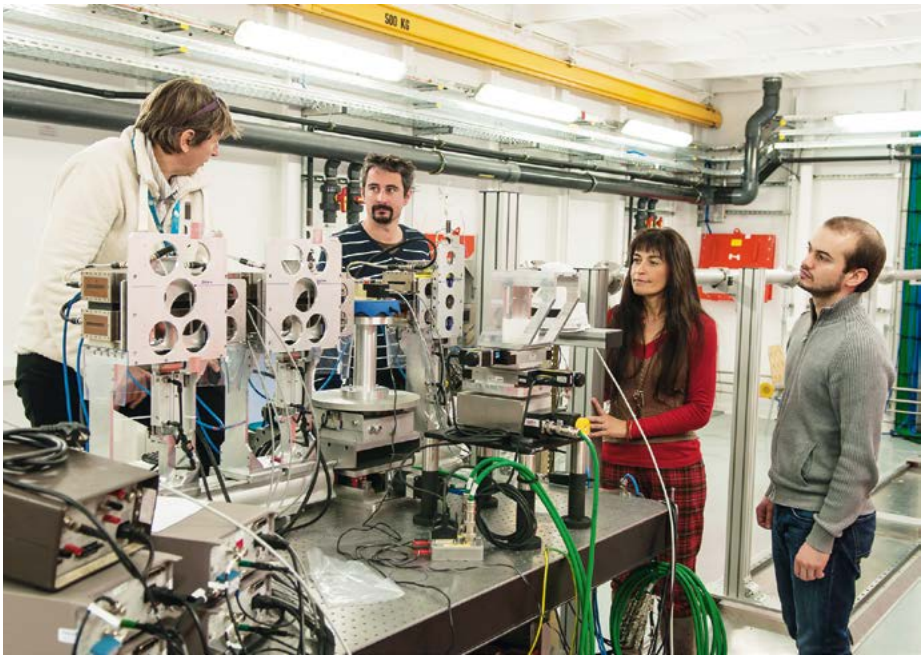

The beamline team working in the ROCK experimental hutch

MARS

Environment – Radionuclides and sea water

From left to right: Christophe Den Auwer, Mélody Maloubier and Maria Rosa Beccia (Nice Sophia Antipolis University) and Pier Lorenzo Solari (MARS beamline).

What happens to natural radionuclides or those resulting from nuclear activity in the environment, particularly in sea water? Take, for example, the Fukushima nuclear accident in 2011, with its nuclear reactor on the coast. Land contamination should also be considered because radionuclides can be transported via waterways to the sea, which appears as the ultimate receptacle. This question is even more crucial given that very few studies have been carried out on this subject.
Establishing a model for understanding how radionuclides are dispersed in seawater and evaluating their impact on man needs to take into account multiple parameters such as current fields, advection and diffusion, exchanges between water and suspended matters, wind and chemical speciation, i.e. the chemical form in which radionuclides exist in the environment. Speciation is often difficult to establish because radionuclide concentrations are extremely low (e.g. 10^{-17} M in the Mediterranean for 239,240-plutonium, thus well below ppb), but it is an essential factor if one wants to properly understand the dispersion of radionuclides after an accident. Moreover, the toxicity and bioavailability of those elements often depends on their speciation, hence this factor is important for its toxicological impact.
A research group from the Nice Chemistry Institute (Nice Sophia Antipolis University/ CNRS), with the CEA-DAM-DIF, have been trying to establish a link (in cooperation with the environment laboratory of the International Agency of Atomic Energy (IAEA), Monaco) between the speciation of actinide radionuclides, more specifically in sea water, and their assimilation by marine organisms, to better understand the biochemical transfer mechanisms involved.
Initially, the researchers studied the speciation of uranium (VI) and neptunium (V) in seawater. Uranium is a specific case because it occurs naturally in the earth's crust but can be locally concentrated by human activity (e.g. mining). Its natural concentration in seawater is extremely low (around 10^{-8}M in the Mediterranean). These are quantities below the detection threshold for many spectroscopic

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be in the form of shells and skeletons of marine organisms, biominerals studied by combined X-ray microscopy and spectroscopy on the LUCIA beamline, or by photoemission spectroscopy (XPS) on TEMPO. Fish otoliths are also sensitive witnesses to environmental variations, as shown by X-ray diffraction, absorption and fluorescence on the DIFFABS beamline.

In the context of energy transition, developing the energy of tomorrow is also important. The SAMBA and ROCK beamlines are particularly active and specialized in this field with their research on catalysis and batteries (see p.17). Furthermore, on CRISTAL, our researchers are studying the structure of abundant and low-emission materials (Cu_2ZnSnS_4) that can be used as absorbers in solar cells, with the aim of improving their energy conversion efficiency. The DESIRS beamline, for its part, has already welcomed several researchers whose combustion studies could help improve engine efficiency and thus reduce pollution.

Food production is also a recurrent research theme at SOLEIL, which has a particularly strong partnership with the National Institute for Agricultural Research (INRA), with three of its research engineers working full time on our premises. After a first edition in 2012, we are currently preparing a new book to celebrate 10 years of this fruitful collaboration, which will show all the richness and

techniques used to determine chemical speciation.
To work around this problem while remaining as representative as possible of the natural environment, the group studied natural seawater solutions doped with actinide at 5.10^{-5} M, a concentration above X-ray spectroscopy detection limits, but still lower than that of major ions in seawater.
EXAFS (Extended X-ray Absorption Fine Structure) measurements were made on MARS, the SOLEIL beamline dedicated to the study of radioactive samples. Coupled with time-resolved laser spectroscopy (TRLS), the EXAFS results showed that uranium was linked to three carbonate groups, with the $Ca_2UO_2(CO_3)_3$ complex found not to be bioavailable. By comparing the spectra obtained on MARS beamline with theoretical data from thermodynamic models, the researchers suggested that neptunium (V) was, meanwhile, present in two forms in seawater: NpO_2^+ and $NpO_2CO_3^-$.
These first results validate the interest and relevance of this approach, a compromise between the use of model systems and direct environmental measurements, often inaccessible to spectroscopy.

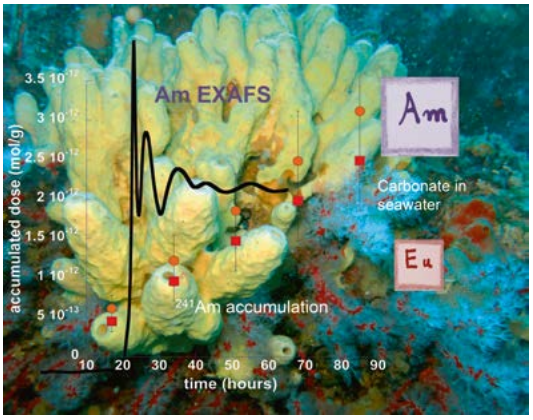

Figure 1: In the background of the photograph of *Aplysina cavernicola*, the accumulation curves of Am-241 over time (two specimens). In black, an example of an Am L_3-edge EXAFS spectrum.

The group then turned to the speciation of 241-americium, a heavy trivalent actinide, and its accumulation in a Mediterranean sponge, *Aplysina cavernicola*. Among living marine organisms, sponges are known for their ability to bind heavy metals, which makes them good sentinel biomonitors candidates.
The methodology used consisted in doping seawater with americium to 5.10^{-5} M and comparing with europium, an element in the lanthanide family, which has stable chemical properties close to those of americium.
The use of TRLS (mentioned above), attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) (which allows the study of ion coordination methods) and finally scanning electron microscopy (giving morphological information about the complexes formed) complemented the EXAFS data for the seawater set-up, but also for the contaminated sponge *Aplysina cavernicola*.
It appeared that the marine sponge specimens tested accumulated 241-americium linearly over time (Figure 1). *A. cavernicola* thus fixes it under the chemical form it adopts in seawater. But what is that form? The combined results of the 4 techniques cited suggest the form $NaAm(CO_3)_2.nH_2O$ and the equivalent $NaEu(CO_3)_2.nH_2O$.
The next steps in this research will be to determine the biological and chemical transformations of these carbonate complexes after uptake by the marine organisms under consideration.

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diversity of the research. From yeast cell metabolism for applications in green chemistry, as revealed by infrared on SMIS, to the tomography of plants under drought conditions on the PSICHE beamline, via the secrets of gum arabic on SWING and DISCO, many and varied are the topics of interest in nutrition and biotechnology at SOLEIL.

SOLEIL is also deeply involved in solving biological and health problems, with two beamlines, PROXIMA 1 and PROXIMA 2, specialized in the crystallography of macromolecules (see p.20 article on dengue and legionella), as working out their 3D structure is often an essential step in the design of new drugs. Beside structural biology, SOLEIL is also involved in early diagnosis (e.g. of liver or kidney disease) and is focusing on disease development, with the aim of developing more suitable treatments (e.g. graft quality analysis before liver transplant - a protocol developed on SMIS, then exported directly to the hospital). The DISCO beamline is also a major contributor in these issues, in cell biology, for example, where individual cells can now be isolated and studied: the improved localization of glioblastoma tumor cells before radiation therapy, the study of antibiotic-resistant bacteria and the better targeting of antitumor treatment, etc. (see p.16, collaboration with the METROLOGY beamline). SOLEIL is also working with the pharmaceutical industry by hosting a structural biology research lab, built and

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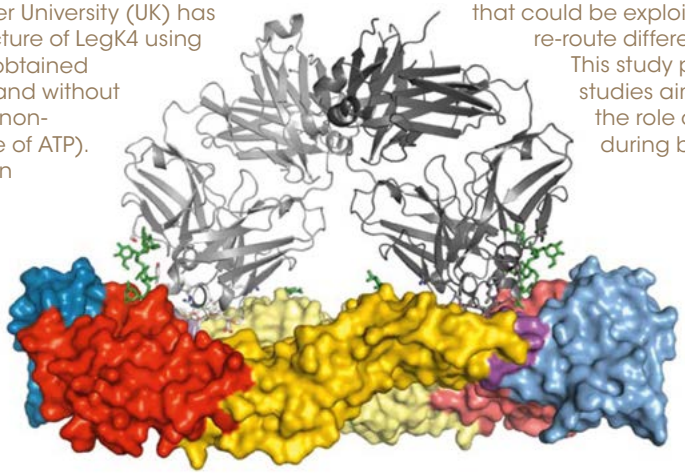
PROXIMA2

Legion fever and dengue: X rays against bacteria and virus

This year, beamline PROXIMA2 has contributed to major findings concerning two pathogens: the bacteria called Legionella pneumophila and virus DENV, respectively responsible for the Legion fever, an aggressive form of pneumonia, and the dengue virus, which can develop into a hemorrhagic, and therefore mortal, fever.

In the case of the study of Legionella, researchers combined biocristallography with the SAXS technique on beamline SWING. The study focuses on LegK4, one of the proteins used by the bacterium to hijack the cellular machinery of the host cell (i.e. an epithelial cell in the lung, or a macrophage) to reproduce rapidly within it. To do so the bacteria targets phosphorylation cascades which often act as switches to control cellular processes. The intervention of LegK4 consists in phosphorylating host cell proteins in the manner of parasites to impact their activity. A group of researchers from IBCP and CIRI in Lyon as well as Leicester University (UK) has solved the crystal structure of LegK4 using X-ray diffraction data obtained from the enzyme with and without substrate (AMP-PNP, a non-hydrolyzable analogue of ATP). The structure reveals an atypical eukaryotic-like kinase domain, which is responsible for phosphorylation, along with several unique features—nucleotide binding does not involve the canonical glycine-rich activation loop, but is instead mediated by unusual amino acids in nearby structural elements. Another remarkable specificity of LegK4 lies in its ability to self-assemble to generate a dimeric interface never observed up to that point in the protein kinase super-family, as confirmed by SAXS. Complementary enzymatic studies demonstrate that LegK4 is a constitutively active enzyme (even without being activated by phosporylation) and the structural data suggests that the dimer assembly stabilizes the active conformation in the absence of phosphorylation.

Sequence comparisons indicate that some of these elements may be found in other members of this protein family. This new structure also points toward specific mechanisms of kinase regulation that could be exploited by the bacteria to re-route different host pathways. This study paves the way for further studies aiming at understanding the role of eukaryotic-like kinases during bacterial infection.



3D structure of the antibody complexes for all four serotypes bound to the dengue virus envelope protein. ©Institut Pasteur.

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operated by an industrial partner, giving it easy access to synchrotron tools.

Finally, technological issues raised by data inundation, or Big Data, that will make profound changes in such areas as health, transport, energy, and electronic component miniaturization, are also the subject of SOLEIL experiments: the study and optimization of materials (graphene or organometallic compounds, for example) for use in spintronics or nanoelectronics on the DEIMOS, HERMES or CASSIOPEE beamlines and ferroelectric thin films on ANTARES are all cutting-edge topics

Another sizeable challenge to society is human evolution, discovering our history, understanding and preserving our heritage, to which some of our researchers devote their studies. Many in-house and visitor research experiments on «ancient materials» are conducted at SOLEIL. One example is the recent results obtained on ANTARES, showing the degradation of the gilded bronze on the «Gates of Paradise», a Ghiberti masterpiece in the Baptistery of Saint John in Florence, thanks to a high resolution photoemission study of artificially corroded gilded bronze replicas. Note that the PUMA beamline, optimized for the study of ancient materials, is under construction

Dengue is the most widespread viral disease in our planet's tropical regions. There are four strains of dengue virus. While a patient produces antibodies specific to one serotype during an initial infection, these do not confer effective protection against subsequent infection by the other serotypes. These specific antibodies may even constitute a risk factor for developing a dengue hemorrhagic fever in the case of a subsequent infection by any of the 3 other forms. This explains the need for a vaccine providing simultaneous and efficient protection against all four virus serotypes.

Although a team from Imperial College London had already identified and isolated antibodies that simultaneously neutralize all four virus serotypes in a cohort of infected patients, the mode of action of these antibodies remained unknown. Researchers from Institut Pasteur and CNRS then carried out a crystallographic analysis to study the antibodies in complex with protein E, which constitutes the virus envelope and on which antibodies are known to bind as part of the immune response. Through X-ray diffraction analyzes performed on beamline PROXIMA2 and at ESRF, the researchers were able to solve the structure of these complexes and to identify the binding site on protein E. The latter is similar for all four virus serotypes, and therefore gives it obvious potential as a vaccine target.

Based on this structure, the researchers also discovered why this antibody binding site is found in all serotypes despite the viral flow that it represents: although a mutation on this site would enable the virus to evade the immune system, it would however highly limit its diffusion, since a protein which is essential to viral replication also binds to this site. The researchers have thus highlighted a true double Achilles' heel for the virus. Introduced in a patient, antigens mimicking this site would potentially be able to trigger an immune response targeting all four dengue serotypes simultaneously, thus constituting a prime vaccine candidate against dengue.

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Discussions on the PROXIMA2 beamline.

and will open to users in 2017. SOLEIL also hosts the IPANEMA platform, a mixed CNRS and Ministry of Culture and Communications Unit, aimed at making it easier for the Ancient Materials community to have access to synchrotron techniques.

In addition to its research, SOLEIL is also introducing various measures, such as the Smart Building project, alongside the Chamber of Commerce and Industry (CCI) of Essonne and the Advancity Sustainable Cities Cluster, in which some of our energy data are recorded and analyzed by SMEs to suggest possible areas for improvement.

Finally, we are continuing our science awareness program for the general public, schools and universities, in order to build lasting relationships between science and society (see e.g. p.24 and back cover).

These are just a few examples of research at SOLEIL dealing with societal challenges. New scientific perspectives are opening up all the time, for example with the NANOSCOPIUM and ANATOMIX beamlines. You will find all this information and much more, on our website.