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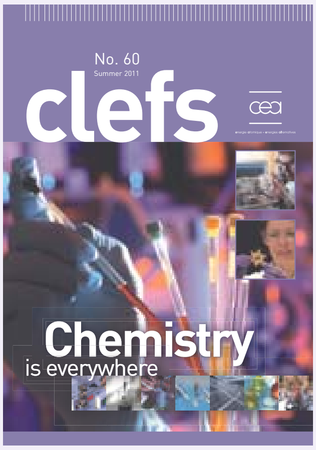
Chemistry is everywhere



Clefs CEA No. 60 – SUMMER 2011

Main cover picture
Dyed polymers for photovoltaic cells. For many years, CEA has been applying all aspects of chemistry, in all its forms. Chemistry is at the very heart of all its major programs, whether low-carbon energies (nuclear energy and new energy technologies), biomedical and environmental technologies or the information technologies.
P. Avavian/CEA – C. Dupont/CEA

Inset
top: Placing corrosion samples in a high-temperature furnace.
P. Stroppa/CEA

bottom: Gas sensors incorporating "packaged" NEMS.
P. Avavian/CEA

Pictogram on inside pages
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Chemistry is everywhere

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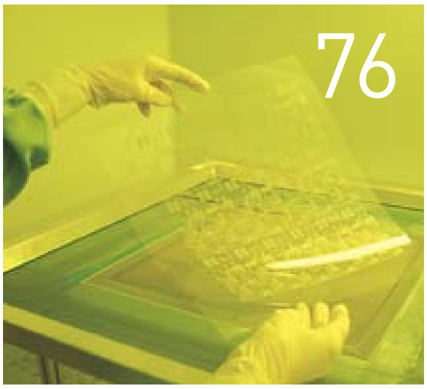
III. CHEMISTRY FOR HEALTH AND ENVIRONMENT

IV. CHEMISTRY FOR THE INFORMATION TECHNOLOGIES



CEA, a major player in the field of research, development and innovation

French Alternative Energies and Atomic Energy Commission (CEA) is active in four main fields: energy, defense and global security, information technologies and biomedical technologies, associated with first-rate fundamental research and the design and operation of very large research infrastructures.

CEA is a unique public organization and occupies pride of place in the French research landscape, where it is now the major operator in scientific and technological research in low-carbon energies, in addition to its existing, traditional roles.

CEA operates 10 centers around France and thanks to its internationally recognized expertise it is consulted by the public authorities for its opinions and its ideas on a variety of topics. It stands at the crossroads between the industrial, scientific and academic worlds and has forged strong ties with industry, while developing close collaboration with universities. In this respect, CEA is a stakeholder in national alliances coordinating French research in the fields of energy (ANCRE), life sciences and health (AVIESAN), numerical sciences and technologies (ALLISTENE) and the environmental sciences (AllEnvi). Particular emphasis is also placed on education and public information, in order to promote the transfer of knowledge and foster the science-society debate.

Foreword

2011 celebrates the International Year of Chemistry,

a distinction awarded by the 63rd General Assembly of the United Nations. For this scientific discipline that is omnipresent, be it in domestic or industrial applications, this distinction is a well-earned one, because chemistry is the key to the development of most of the technological solutions of tomorrow, in particular in the field of energy: energy storage, exploitation of new energy sources, materials strength, and so on.

CEA recognized this very early on and for many years has been applying chemistry in all its forms (from fundamental research to process engineering) and in all its aspects (modeling, physico-chemistry of solutions and interfaces, soft matter, analytical chemistry, chemistry of materials and nanomaterials, corrosion, electrochemistry, organic synthesis, life sciences chemistry, chemistry under ionizing radiation, radiochemistry, etc.). In the nuclear field, chemistry is involved at all steps in the cycle, from the mine to the fabrication of fuel and the containment of waste. Nonetheless, even if current processes can boast remarkable performance, the scientific bases which underpin them are still raising many fundamental questions.

The separation sciences are thus a major issue in the design of the nuclear systems of the future, in particular with regard to the search for new extractants, capable of offering the necessary selectivity while remaining stable under irradiation, but also in understanding the transfer mechanisms at the interfaces. CEA is also developing a huge knowledge database around actinides chemistry and chemistry under irradiation – topics that are studied very little by the academic world because they are highly specific to the nuclear field, but which have given the scientific community experimental techniques and models that are advanced and creative. Actinides chemistry remains a complex field owing to the scarcity of experimental data, the acquisition of which demands large facilities, but also to the fact that it is hard to describe these elements with the usual modeling techniques. Yet the commitment to a sustainable and safe nuclear industry makes it essential to acquire and master these data. Hence the development of modeling techniques covering all scales: from modeling by quantum chemistry of actinide ions in solid state or in solution, to the simulation of industrial liquid/liquid extraction operations used in the facilities at the La Hague plants.

Similarly, chemistry under ionizing radiation, which is highly specific to CEA activities, created a network for coordinating the experimental and theoretical work on this subject. The challenge is not so much to study the phenomenon of the creation of radicals as to understand the chemistry arising from this creation. This is an extremely complex road, in particular when the media considered are close to actual media: mixtures in solution, alloys, polymer coverings, etc.

In the same way as the space and transport industries, the nuclear industry, both civil and defense, is

L. Godart/CEA

the source of many major technological and scientific advances in the field of materials. For example, the construction of the Megajoule Laser triggered new research into the chemistry of innovative materials. CEA is thus a benchmark in all areas of the field of metallurgy, a science at the crossroads between physics and chemistry: structural metallurgy, mechanics, corrosion, etc. With regard to corrosion, the stakes involved go far beyond the boundaries of the nuclear industry, despite specific aspects linked to coupling with irradiation: corrosion in the strict sense of the term for the alteration of metals and alloys, corrosion in a broader sense concerning the alteration of glasses. In any case, the understanding of the phenomena involves a multidisciplinary approach combining ageing experiments and modeling.

Another strong sign is that since 2010, CEA has been known as the Alternative Energies and Atomic Energy Commission – a name change that clearly reflects its commitment to the new energies. Here again, chemistry is omnipresent: electrochemistry, catalysis, materials and nanomaterials, modeling and soft matter. CEA is heavily involved in the field of electrical transport and is working to achieve a significant increase in on-board energy, bringing down costs and proposing recyclable materials to make savings in the resource and reduce the environmental impact, without forgetting studies into biomass, a large "consumer" of chemistry and process engineering. To design new sources of energy, another approach is to draw inspiration from mechanisms at work in living organisms, which encouraged CEA to explore new avenues: the capacity of micro-organisms to produce substrates with a high energy value and the development, through a biomimetic approach, of processes for obtaining hydrogen from solar energy.

The interface between chemistry and the life sciences is particularly well-developed at CEA, especially with regard to new biomedical technologies. Chemistry can then be seen as a means of understanding how living organisms work (new probes for imaging, enzyme inhibitors, etc.) through the use of rationalized molecular chemistry, but also screening, in particular for toxicology research. The development of chemical methods for isotopic marking, used for studying the structure, the dynamics and the engineering of biomolecules, was a major source of innovation for health, medical diagnosis and biotechnologies and has recently contributed to the study of the toxicology of nanoparticles, an extremely delicate subject, in which all the components of CEA are involved, through a cross-disciplinary program.

Finally, the chemists at CEA have a crucial role to play in the development of the new information and communication technologies: chemistry of polymers, surface modification, the physico-chemistry of self-assemblies are decisive for one major aspect of nanoelectronics – the integration of nano-objects (nanowires, nanotubes, graphene) and for 3D electronics. In the near future, the development of micro and nanotechnologies promises a number of major breakthroughs involving sensors and signal processing and analysis, for diagnosis, environmental monitoring and civil security (chemical and biological terrorism threat, pandemics).

"Chemistry is the key to the development of most of the technological solutions of tomorrow."

The analytical sciences are an everyday feature of work at CEA, involving highly creative chemistry that is constantly pushing back the boundaries: detection of traces in complex matrices or on surfaces, development of portable miniaturized systems, selective sensors, etc. The challenges are numerous and meeting them implies calling on the multidisciplinary expertise present at CEA which for many years has been engaged in environmental toxicology, developing studies in speciation, in diffusion of contaminants of all types, and contributing to establishing structure/properties relationships for molecular, supramolecular and, now, nanometric species.

2011, *the International Year of Chemistry*, ushers in a highly stimulating period for all chemists. The next few years promise to be rich in challenges in health, food, energy, security and domestic comfort. The chemists at CEA, with their wide range of expertise, have everything needed to play a major role in all these fields. They also have one major advantage: a remarkable multidisciplinary environment offering them access to large facilities and innovative concepts and objects. Meeting these challenges is thus within their grasp. The articles in this issue of *Clefs CEA* aim to prove it.

> **Valérie Cabuil**
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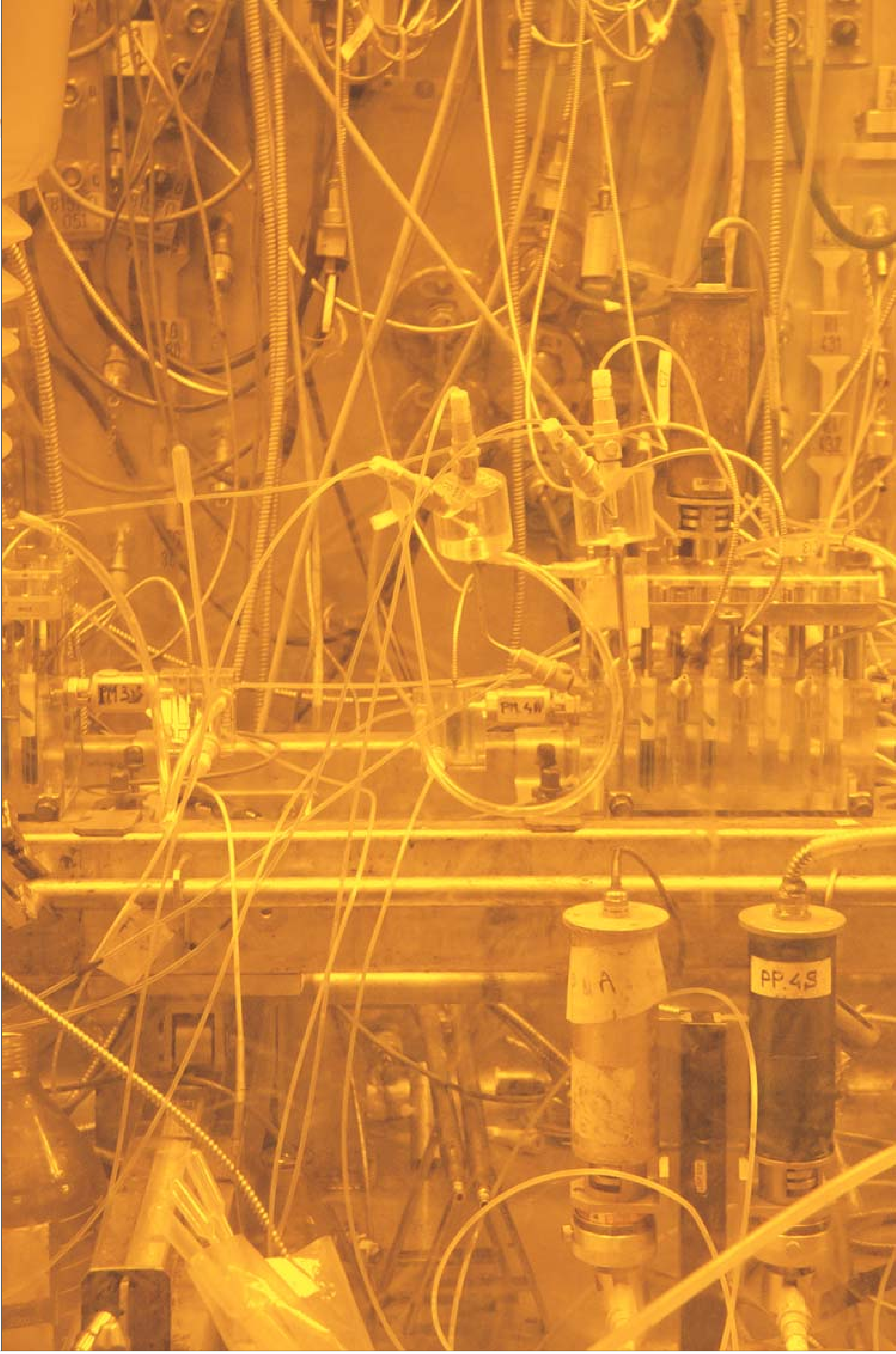
Adviser to the High Commissioner for Atomic Energy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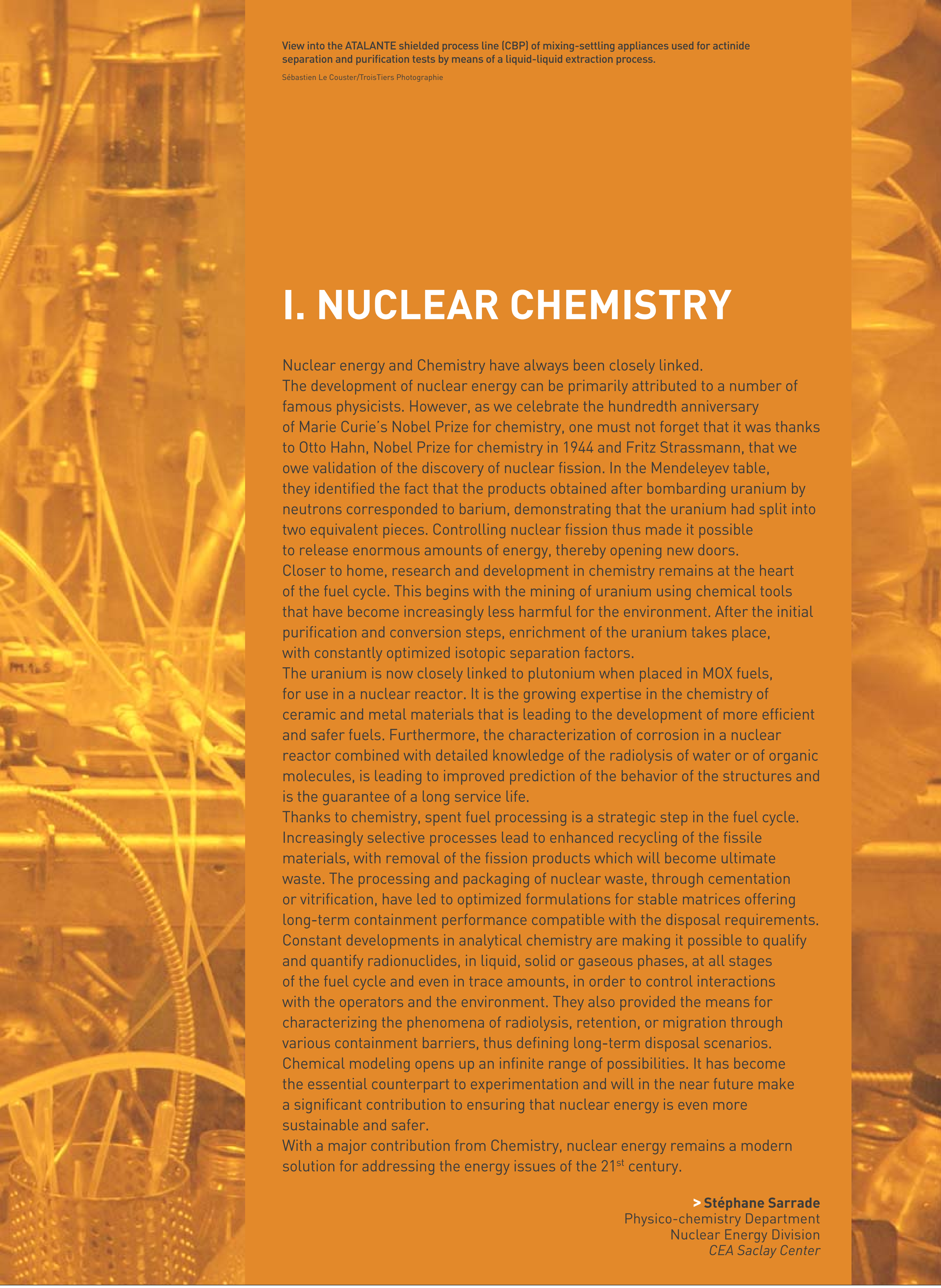

View into the ATALANTE shielded process line (CBP) of mixing-settling appliances used for actinide separation and purification tests by means of a liquid-liquid extraction process.

Sébastien Le Couster/TroisTiers Photographie

I. NUCLEAR CHEMISTRY

Nuclear energy and Chemistry have always been closely linked.
The development of nuclear energy can be primarily attributed to a number of famous physicists. However, as we celebrate the hundredth anniversary of Marie Curie's Nobel Prize for chemistry, one must not forget that it was thanks to Otto Hahn, Nobel Prize for chemistry in 1944 and Fritz Strassmann, that we owe validation of the discovery of nuclear fission. In the Mendeleyev table, they identified the fact that the products obtained after bombarding uranium by neutrons corresponded to barium, demonstrating that the uranium had split into two equivalent pieces. Controlling nuclear fission thus made it possible to release enormous amounts of energy, thereby opening new doors.
Closer to home, research and development in chemistry remains at the heart of the fuel cycle. This begins with the mining of uranium using chemical tools that have become increasingly less harmful for the environment. After the initial purification and conversion steps, enrichment of the uranium takes place, with constantly optimized isotopic separation factors.
The uranium is now closely linked to plutonium when placed in MOX fuels, for use in a nuclear reactor. It is the growing expertise in the chemistry of ceramic and metal materials that is leading to the development of more efficient and safer fuels. Furthermore, the characterization of corrosion in a nuclear reactor combined with detailed knowledge of the radiolysis of water or of organic molecules, is leading to improved prediction of the behavior of the structures and is the guarantee of a long service life.
Thanks to chemistry, spent fuel processing is a strategic step in the fuel cycle. Increasingly selective processes lead to enhanced recycling of the fissile materials, with removal of the fission products which will become ultimate waste. The processing and packaging of nuclear waste, through cementation or vitrification, have led to optimized formulations for stable matrices offering long-term containment performance compatible with the disposal requirements.
Constant developments in analytical chemistry are making it possible to qualify and quantify radionuclides, in liquid, solid or gaseous phases, at all stages of the fuel cycle and even in trace amounts, in order to control interactions with the operators and the environment. They also provided the means for characterizing the phenomena of radiolysis, retention, or migration through various containment barriers, thus defining long-term disposal scenarios.
Chemical modeling opens up an infinite range of possibilities. It has become the essential counterpart to experimentation and will in the near future make a significant contribution to ensuring that nuclear energy is even more sustainable and safer.
With a major contribution from Chemistry, nuclear energy remains a modern solution for addressing the energy issues of the 21st century.

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Advances in the **separation chemistry** of actinides

The development of sustainable nuclear energy demands rigorous management of the materials it uses, both to preserve natural resources and to minimize the environmental impact of the waste produced. The separation chemistry of actinides lies at the heart of the processes used to recover recyclable materials from the spent fuel and to package ultimate waste.


CEA

View of the CBP (shielded process chain) in the ATALANTE facility at CEA/Marcoule, where experiments and technical feasibility demonstrations are carried out on the various actinide separation concepts developed.

With the Acts of 30th December 1991 and 28th June 2006, the French legislator threw down a number of major challenges to the chemists concerning the separation chemistry of actinides (An). Chief among them is the development of "industrial-scale" processes able to reduce the quantity and harmfulness of high level, long-lived radioactive waste, regardless of the various recycling scenarios envisaged. Strand 1 of the 1991 Act, concerning the management of this waste, asked the researchers to study: "*[…] the separation, for subsequent transmutation, of the long-lived radioactive elements contained in the radioactive waste*". The Radiochemistry and Processes Department (Département radiochimie et procédés/DRCP) at CEA played a major role in these studies, which are the keys to the development of the nuclear energy of tomorrow.

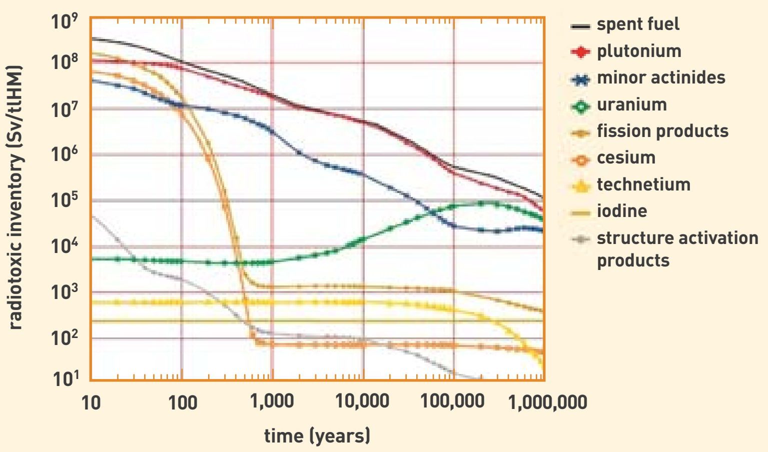

Figure 1.
Evolution of the radiotoxic inventory, expressed in sieverts per ton of initial heavy metal (uranium) (Sv/tIHM), of spent UOX fuel (based on Uranium OXide) unloaded after burnup of 60 GW·d/t.

What elements to separate and with what type of process?

This task required an evaluation of the feasibility and the potential benefits of individual, differentiated management of certain long-lived radionuclides present in the spent fuel, currently left in the vitrified waste. Once the plutonium (Pu) has been separated, the minor actinides (MA), americium (Am) firstly and then curium (Cm) and neptunium (Np), make the most significant contribution to the radiotoxic inventory of the spent fuel (Figure 1). They would thus seem to be the radioelements that require priority management by separation-transmutation in order to effectively reduce the long-term radiotoxic inventory of the waste. Their particular situation also places them at the heart of the research being carried out into separation-transmutation.

To summarize, the stakes of these studies are to produce data allowing an evaluation of the prospects for industrial implementation of An separation processes, for both of the transmutation modes envisaged in a fast neutron reactor (FNR), that is:

- *heterogeneous mode* transmutation based on differentiated management of uranium (U) and Pu with regard to the MA (Am, Cm and Np), these latter being recycled in the form of U-based targets or blankets. The issue here is the concept known as "advanced separation" which aims to produce "cleaner" waste;
- *homogeneous mode* transmutation, during which the MA are recycled by dilution in the entire fuel with U and Pu. In the case of the FNR, core management in particular implies different U/An enrichment depending on the position of the fuel in the core, hence the integration into the grouped separation concept, known as GANEX (Global ActiNides EXtraction), of an upstream U separation step. GANEX has the two-fold advantage of reducing the proliferating

character of the process and the end-products while still pursuing the goal of "cleaner" waste. Consistently with these two transmutation modes, different scenarios are being studied (Figure 2).

The researchers were very rapidly to opt for separation processes using a solvent, on the basis of the positive experience feedback from the PUREX process employed in the La Hague (Manche) plants to recover U and Pu. Only this type of process is capable of ramping up to an industrial scale by offering very high separation performance, both in terms of recovery rates but also purification of U and Pu, while producing extremely limited quantities of technological waste.

A scientific approach firmly based on modeling

With regard to the choice of molecules and the development of processes, the researchers adopted the following scientific approach:

- design of new molecules based on bibliographical studies, supplemented by molecular scale modeling tools;
- detailed understanding of the An(III) complexation and extraction mechanisms through thermodynamic and kinetic studies at the molecular and/or supramolecular level. At this stage, the use of molecular scale modeling tools proved to be invaluable in interpreting the observed phenomena (Focus A, *Advances in modeling in chemistry*, p. 17);
- study of the degradation of the extractant molecules under the effect of acid hydrolysis and radiolysis, associated with the development of treatments for regenerating the degraded solvents (see *Understanding the chemical mechanisms of radiolysis*, p. 21);
- the acquisition of shared data essential for establishing models capable, by means of the PAREX (PARtitioning by EXtraction) simulation code, of calculating the schemes to be implemented to test An(III)/lanthanides Ln(III) separation;

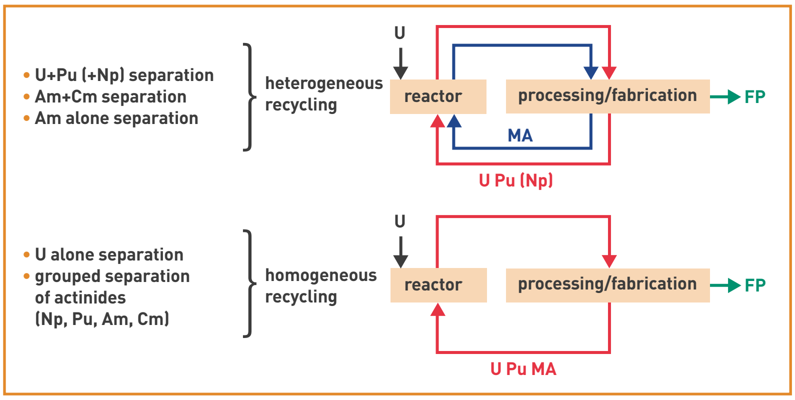

Figure 2.
The scenarios studied according to the envisaged transmutation modes (heterogeneous and homogeneous). MA and FP stand for minor actinides and fission products respectively.

- the performance of tests to integrate the calculated schemes, using laboratory contactors on inactive solutions, then on simulated intermediate-level solutions (with MA) and finally on high-level solutions (produced by spent fuel processing). The results of the PAREX code simulation are then compared with the results of each test in order to check the pertinence of the model and target any additional tests necessary (iterations with the previous steps); Figure 3.

Separation strategies

The steps in the three An separation strategies are presented: Am+Cm separation then separation of the Am "alone", as part of a heterogeneous mode transmutation, and grouped separation of the An, as part of a homogeneous mode transmutation.

Separation of americium and curium

Am and Cm are the main contributors to the radiotoxic inventory of the effluents produced by the PUREX/COEX^{TM} process (after Pu separation);

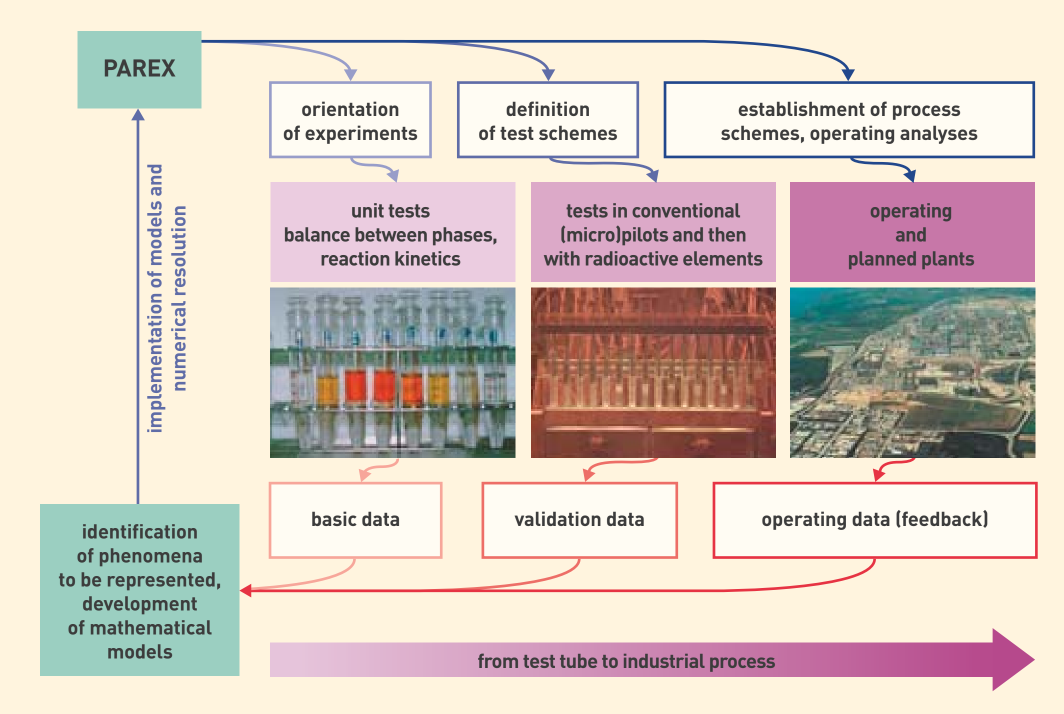

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Figure 3.
Modeling/simulation approach designed to support the development studies for actinide separation concepts. This iterative approach between modeling and experimentation is a means of rationalizing the acquisition of basic data and limiting the number of integration tests. It also has the advantage of building on the knowledge obtained within the simulation code, which could be put to good use for continued development of the process and/or transposition to an industrial application.


CEA

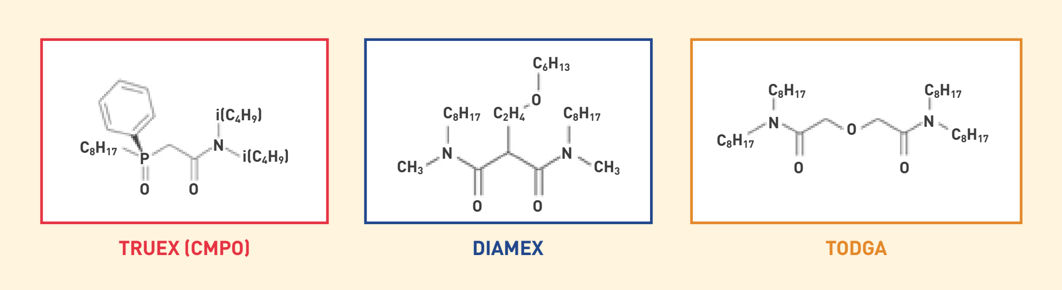
View of the CBP pulsed columns in the ATALANTE facility. Their operating principle is to circulate the solvent (light phase) from bottom to top in a vertical cylinder against the flow of the immiscible aqueous phase (heavy). They are 4 meters high and thus representative of the equipment used on an industrial scale.

see *Chemistry and chemical engineering, the COEX process*, p. 12. These two elements are therefore the ideal target for separation-transmutation studies. The difficulty to be overcome when defining molecules capable of separating Am and Cm from a PUREX/COEX$^{\text{TM}}$ raffinate is linked above all to the considerable similarity in the chemical behavior of the two families of An(III) and Ln(III) elements (5f and 4f elements respectively, see *The chemical specificities of actinides*, p. 10). The An(III) are "hard" cations, in other words they form purely ionic type bonds. It is therefore necessary to use "hard donor" based ligands, in other words oxygenated ligands, to extract them (*Pearson HSAB theory*). In order to reinforce the extractant power of these ligands while ensuring good selectivity with regard to the nitric acid proton, the researchers resort to a multidendate extractant with a chelate effect. However, these families of extractants only offer low selectivity with respect to Ln, which are also "hard" cations. The solution was found in the fact that the spatial expansion of the 5f orbitals is slightly greater than that of the 4f orbitals, as the An(III) are "slightly softer" cations than the Ln(III), in other words, more able to form partially covalent bonds. For An(III)/Ln(III) separation, "soft donor" nitrogen ligands must be used. Unfortunately, these ligands offer low selectivity in relation to the other FP fission products (transition metals d) and to the proton.

The researchers will produce a two-stage strategy to achieve separation of the An(III). A first step involving co-extraction of the An(III) and Ln(III) is used on a PUREX raffinate, by means of a multidentate oxygenated "hard donor" extractant. A second An(III)/Ln(III) separation step, starting from the solution produced in the previous step (An(III)+Ln(III) mixture), that is less acid than the PUREX raffinate, is performed using nitrogen "soft donor" ligands.

For the first step, the Separation Process Chemistry department (Service de chimie des procédés de séparation/SCPS) at CEA/DRCP has developed the DIAMEX (DIAMide EXtraction) process. Comparable processes developed in the United States (TRUEX for separation of TRansUranium element by EXtraction) and Japan (TODGA for TetraOctylDiGlycolAmide) are also based on multidentate and chelating "oxygenated donor" type extractant families (Figure 4). The feasibility of using the DIAMEX process in pulsed column extractors was proven in 2005 on 15 kg of spent fuel in the shielded process chain (CBP) at ATALANTE.

For the second step, the SANEX process, the researchers developed various multidentate nitrogen extractants. Their studies were part of European collaborative programs and demonstrated that two families were particularly effective: bis-triazinyl-pyridines or bis-triazinyl-bis-pyridines. Unfortunately, these molecules offer either insufficient resistance to radiolysis, or inadequate extraction kinetics. Hence the search for a new concept. This will consist in co-extracting An(III) and Ln(III), and then separating them by selective stripping of the An(III) using a hydro-soluble complexing agent. For example, the American TALSPEAK process (Trivalent Actinide-Lanthanide Separation by Phosphorous reagent Extraction from Aqueous Complexes) utilizes polyaminocarboxylic acids.



TRUEX (CMPO)

DIAMEX

TODGA

Figure 4.
Bidendate (CMPO and diamide of the DIAMEX process) or tridendate (TODGA) extractants necessary for co-extraction of An(III)/Ln(III) with chelating effect. CMPO: octyl[phenyl]-N, N-diisobutylCarbamoylMethyl Phosphine Oxide; TODGA: TetraOctylDiGlycolAmide.

Today, by combining the advantages of the DIAMEX and TALSPEAK processes, the chemists can carry out this separation directly, in a single step, starting from the PUREX raffinate: this is the DIAMEX-SANEX process. Its principle is based on selective extraction of Am, Cm and Ln by means of a diamide, DiMethylDiOctylHexylEthoxyMAlonamide (DMDOHEMA) of high-acidity. An(III)/Ln(III) separation is then carried out at a pH close to 3 by selective stripping using a polyaminocarboxylic acid, Hydroxy-Ethylene-Diamine-TriAcetic acid (HEDTA). However, in the medium where the complexing agent proved to be effective, the DMDOHEMA no longer extracts the cations. Hence the need to use another extractant: bis(2-EthylHexyl)Phosphoric acid (HDEHP), which is effective in this acidity region and which will therefore be added to the diamide.

Separation of americium "alone"

The production of a pure Am flow requires not only An(III)/Ln(III) and An(III)/other FP separation, but also separation of Am and Cm, two elements characterized by a very similar chemical behavior. Based on the DIAMEX-SANEX process, this separation is built around a two-fold observation: DMDOHEMA extracts Am slightly better than Cm, while the diglycolamides family, in particular TetraEthylDiGlycolAmide (TEDGA), complexes Cm better than Am.

Understanding this system required numerous inactive and glove-box studies, as well as major analytical developments, in particular to comprehend the fate of the TEDGA in the system. As an aqueous complexing agent, the TEDGA can complex the Ln(III) and the An(III) in various forms, or can be protonated by nitric acid (Figure 5). Development of the final system, proven during a series of tests in ATALANTE, would imply a detailed understanding of all these phenomena.

A high-level validation test for the entire process, called EXAm (EXtraction of Americium), was carried out in March 2010 in the ATALANTE CBP. This test was a world first. It demonstrated the feasibility of the single-cycle Am recovery concept on a real, high-level solution. Excellent performance was obtained, including 99.2% recovery of the Am during extraction-scrubbing (98.5% over the entire process), along with a Cm decontamination factor of better than 500.

Grouped actinide separation

This operation takes place in two stages. First of all *selective extraction of U* (see *Uranium chemistry: significant advances*, p. 11), a step based on the use of molecules from the $RC(O)NR'_2$ monoamide family. By modifying their structure, it becomes possible to optimize their extractant properties. To achieve this, ramification of the alkyl substituent R ($—C_nH_{2n+1}$) on the carbon atom adjacent to the carbonyl function (C=O) boosts U(VI)/Pu(IV) selectivity, even at high nitric acidity, and thus allows selective extraction of U without the addition of another reagent. Among the various monoamides available, the DEHiBA (N,N-Di-(Ethyl-2-Hexyl)-isoButyrAmide) molecule was selected for its ability to achieve the desired selectivity .

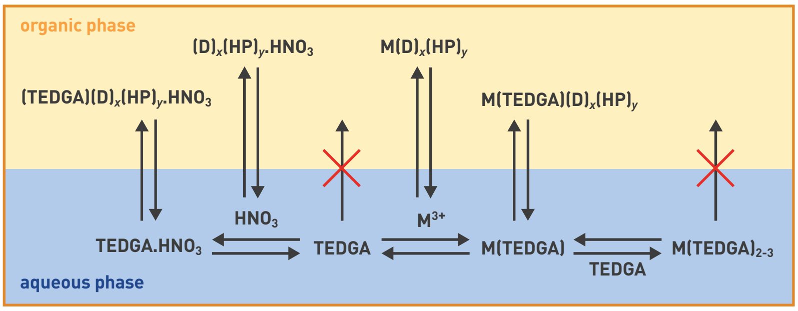


Figure 5.
Summary of the phenomena occurring in the presence of TEDGA, showing the complexity of the various balances involved (M: An(III) or Ln(III), D: diamide, HP: HDEHP). Even though found preferentially in aqueous phase, the TEDGA co-extracts partially in organic phase with nitric acid (HNO_3) or the cations (M^{3+}). TEDGA alone and $M(TEDGA)_{2-3}$ are not extractable.

Then comes the actual GANEX cycle, that is *grouped separation of An (Np, Pu, Am, Cm)*. The particularity and importance of this step are linked to the ability of the process to manage the An in the various oxidation states in a nitric solution: +III (Am, Cm), +IV (Np, Pu), +V (Np), +VI (U, Np). The studies conducted by the SCPS indicate that the extractant system in the DIAMEX-SANEX process, unlike conventional extractants, leads to the quantitative extraction of the An, regardless of their degree of oxidation in solution, provided that the nitric acid in the medium be higher than 3 mol/L. Hence the choice of this process, preferred for its robustness, as the starting point for this grouped separation of the An. With regard to An recovery in aqueous phase, the studies show that joint stripping of all the An (Np, Pu, Am, Cm) proves to be quantitative and selective with respect to the extractable FP (Ln, Y, Zr, Fe). There are however two preconditions for this operation: the presence of a reducing agent to strip the Np in the form of Np(IV) and Np(V) in aqueous phase, but also a temperature rise from 23 to 45°C in order to accelerate the kinetics of Pu and Np stripping.

In 2008, the success of the validation tests for these two steps in the ATALANTE CBP clearly demonstrated the feasibility of the GANEX concept on a real, high-level solution.

The performance of the processes demonstrated on actual solutions means that it is today possible to meet the needs of the various separation-transmutation scenarios. This is a major step forwards. Even if many points still need to be optimized, the studies inevitably required will be able to draw on the progress already made in modeling/simulation and multi-scale approaches, in collaboration especially with the ICSM (Marcoule Institute for Separative Chemistry).

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The chemical specificities of actinides

The chemistry of actinides (An) is a young science(1) resulting from the work on radioactivity (1896) and quantum theory (1900). This enabled the discoverer of plutonium – Glenn T. Seaborg – to deploy a periodic classification in 1944 incorporating the 4f and 5f subshell (Figure). In addition to these concepts, the development of An chemistry has been guided by a multidisciplinary approach (analytical chemistry, spectroscopy, microchemistry, etc.)(2).

With atomic numbers (Z) between 90 and 103, the An have very heavy nuclei and a large number of electrons. To compare their behavior to that of the lanthanides (Ln) would be an over-simplification, even if sometimes useful. The rise in Coulomb attraction with Z stabilizes the f orbitals, leading to a regular reduction in the size of the +III and +IV ions (actinide and lanthanide contraction). Moreover, the f orbitals manifest a restricted radial extension in relation to the s and p sublayers, which limits their reactivity. For the Ln, the greater localization of the 4f electrons (*versus* 5f) explains the dominance of the +III oxidation state (o.s.). On the other hand, for the "light" An (from Pa to Am), the lesser localization of 5f electrons increases their participation in the chemical bonds and leads to different o.s.: from +III to +VII, which makes them similar to transition metals. For the "heavy" An, the greater localization of 5f electrons makes them comparable to Ln(III).

Extremely varied chemical properties

It is hard to summarize the chemical properties of the An, given the large number of o.s. The An(III) and An(IV) ions are hydrated with a first, well-structured layer of water molecules (8 to 10), while the An(V) and An(VI) take the form of actinyl ions (AnO_2^{n+} with n = 1 or 2)(3) – except Pa – with 5 water molecules in the equatorial plane. The An(VII) are oxocations (AnO_3^+) in an acid environment and oxoanions ($AnO_4(OH)_2^{3-}$) in a basic environment. This multitude of o.s. is made even more complex by disproportionation reactions and the kinetic charge transfer constraints.

For the aquo ions (hydrated), the higher charge of the An(IV) and their size makes these cations a very hard *Pearson* acid and thus highly reactive. For example, hydrolysis of the An(IV) is no longer negligible for acidities of less than 1 mol/L. For plutonium, it should be noted that polycondensation of the hydrolyzed forms leads to the appearance of colloidal phases in which the reactivity is poorly understood. As most of the bonds with the An(IV) are ionic, an increase in the reactivity with Z is generally observed. The reactivity of the An(III) is far less and, for example, their hydrolysis is low. For the actinyls, the charge localized on the metal cation is far higher than that of the ion – about 3 for the An(VI) – and that localized on the oxygen atoms is correspondingly lower. This property gives the An(VI) a reactivity that is higher than that of the An(III) (in the case of low steric hindrance) and the An(V) comprise cation-cation interactions, characteristic of an exacerbation of the reactivity of the oxygen atoms. To date, the An(VII) have been little studied and only fragmentary data is available.

There are multiple coordination numbers: they range from 8 to 12 for aquo ions and from 4(+2) to 6(+2) for actinyls, with extremely varied coordination polyhedrons for the two families. Finally, it must be pointed out that An reactivity decreases with the softness of the donor atoms – as defined by Pearson(4) – leading to bonds in which the covalency increases.

This base of knowledge, although already robust, still needs to be further supplemented in order to achieve the goal of obtaining a clearer understanding of An chemistry. Subjects as important as controlling and predicting their behavior in the fuel cycle (modeling of the behavior in a solution, optimization of separation, understanding the effects induced by ionizing radiation, development of new fuels, etc.) and in the environment (behavior in the geo- and biosphere, monitoring of non-proliferation through measurement of ultra-traces of nano-samples) or the acquisition of fundamental data, can only be addressed by the scientists through enhanced understanding of these elements.

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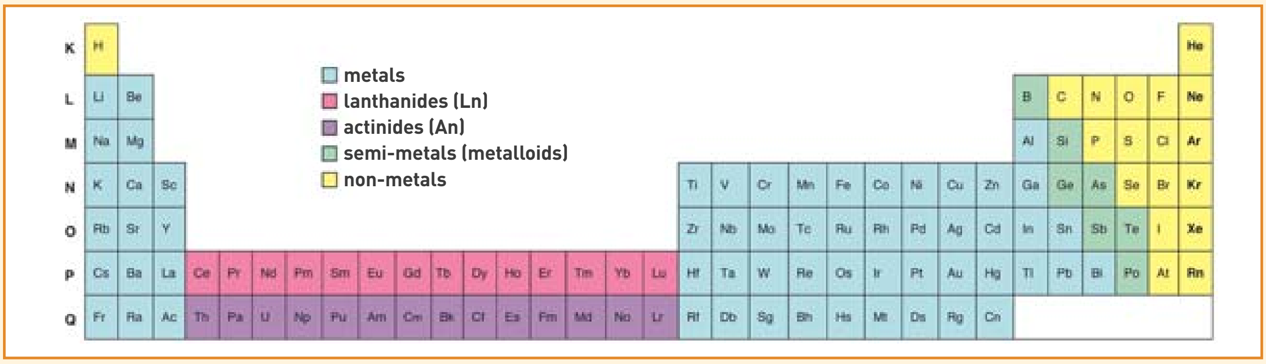

Figure.
The An family (electronic configuration $[Rn]5f^n6d^m7s^2$) consists of 14 radionuclides (15 with actinium): from thorium to uranium for the natural elements and from neptunium to lawrencium for the artificial ones. However, 3 isotopes of plutonium are not of anthropogenic origin: ^{244}Pu (primordial), ^{239}Pu (neutron capture by spontaneous fission of ^{238}U and double β^- decay), ^{238}Pu (double β^- decay of ^{238}U).
The electronic configuration of Ln is $[Xe]4f^n5d^m6s^2$.

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(1) Uranium, thorium and protactinium were discovered in 1789, 1829 and 1917 respectively; actinium was discovered in 1899.

(2) See «Le traitement-recyclage du combustible nucléaire usé», Monograph by the CEA Nuclear Energy Division, Éditions du Moniteur (2008).

(3) These ions consist of a central metal cation linked to two oxygen atoms in a linear molecular assembly ($An(V)O_2^+$ and $An(VI)O_2^{2+}$).

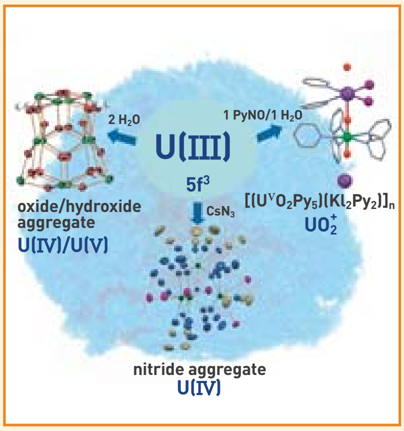
(4) The notion of hardness (and softness) proposed by R. Pearson corresponds to a classification according to the ionic (hard) or covalent (soft) nature of a bond. The most conventional donor atoms are halide ions (in particular fluoride ions which form very stable and volatile compounds), oxygen, nitrogen and sulfur atoms (the last 3 being increasingly soft).

Uranium chemistry: significant advances

The decision to opt for nuclear power for energy production in France and around the world requires a clearer understanding of the molecular chemistry of the actinides, in particular the redox processes involved in the processing of spent fuel, in the migration of actinides into the environment and in the development of more efficient fuels. This requirement triggered an upsurge in interest for the chemistry of uranium among the global scientific community. The study of uranium chemistry does not entail as restrictive conditions as those of its neighbors: neptunium and plutonium, which are highly radioactive. It does however have numerous similarities and can therefore provide fundamental structural information on actinides in general. Like its neighbors, uranium undergoes hydrolysis, oxidation and disproportionation reactions which make the chemistry of these species in water highly complex.

The many states of uranium

The researchers at the Ionic Recognition and Coordination Chemistry Laboratory of the CEA Institute for Nanosciences and Cryogenics (Inac/RICC) are exploring the chemistry of uranium in non-aqueous media to gain a clearer understanding of the molecular mechanisms involved in the selective extraction, hydrolysis and aggregate formation reactions. In an anhydrous medium, fleeting or unusual species can be prepared and their reactivity studied without being burdened by thecomplexity of the aqueous medium.

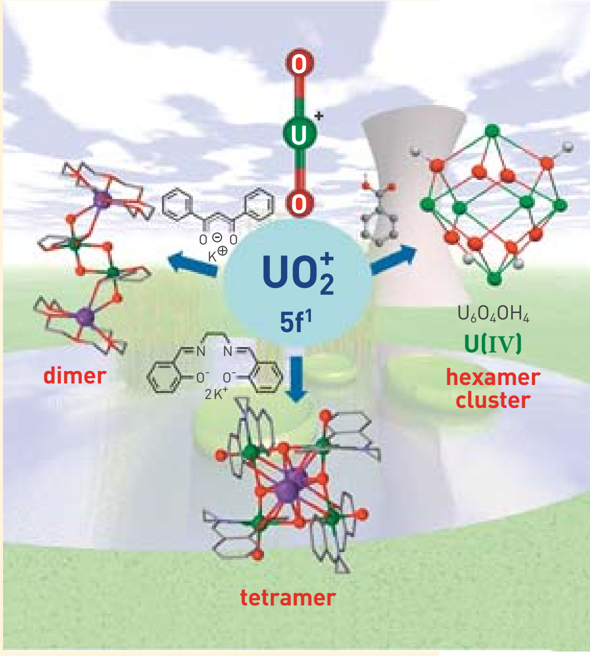


CEA/DSM

Figure 1.
The reaction of U(III) with water (H_2O) led to the isolation of several aggregates in which uranium atoms with a degree of oxidation V or IV are kept together by groups of O^{2-} (oxide ions) and OH^- (hydroxide ions) [G. Nocton *et al*, *Angew. Chem., Intl. Ed. Engl.*, 46, 2007, p. 7574], while the reaction with a mixture of water and pyridine oxide (PyNO) made it possible to isolate the first stable complex of uranyl with a degree of oxidation V [L. Natrajan *et al.*, *J. Am. Chem. Soc.*, 128, 2006, p. 7152]. The reaction with azide ions produces a rare example of an aggregate of uranium(IV) ions bound by nitride (N^{3-}) and azide (N_3^-) groups, and thus extremely rich in nitrogen [G. Nocton *et al.*, *Angew. Chem., Intl. Ed. Engl.*, 47, 2008, p. 3040].

Initial research conducted in an anhydrous medium at the RICC, correlated the structural and electronic differences observed in the interaction of uranium(III) and the lanthanides(III) with nitrogen or sulfur molecules and the effectiveness of these molecules in An(III)/Ln(III) separation *via* liquid-liquid extraction. The results obtained revealed key information for the development of more efficient extractants.

Recent work at the RICC on the redox reactivity of trivalent uranium U(III) in an organic medium with molecules such as water or an azide ion (N_3^-) in stoichiometric quantities, led to extremely interesting uranium aggregates (Figure 1). Those produced in the reaction with water accurately model the soluble nanoparticles of the actinide oxides involved in the migration of actinides in the environment or responsible for aggregation problems in the fuel processing cycle. The aggregates formed in the reaction with CsN_3 are potential molecular precursors for the development of new and more efficient fuels.



CEA/DSM

Figure 2.
The first stable polynuclear complexes (dimer and tetramer) of uranium(V) were isolated in an anhydrous medium [G. Nocton *et al.*, *J. Am. Chem. Soc.*, 130, 2008, p. 16633 ; V. Mougel *et al.*, *Angew. Chem.*, 2009, p. 1843]. These species shed light on the disproportionation mechanism. The reaction with organic acids leads to soluble compounds of uranium(IV) which accurately model the species responsible for the migration of actinides [V. Mougel *et al.*, *Chem. Commun.*, 46, 2010, p. 8648 ; B. Biswas *et al.*, *Angew. Chem.*, *Intl. Ed.*, 50, 2011, p. 5745].

Another significant advance was the discovery at the RICC of a compound containing the uranyl ion with a degree of oxidation (V) UO_2^+, obtained by oxidation of uranium(III). The chemistry of the actinides with high degrees of oxidation (V, VI) plays a crucial role in the development of new spent fuel separation strategies and in the development of pollution clean-up strategies. In the natural environment, uranium exists in two major forms: soluble uranyl(VI) UO_2^{2+} and insoluble uranium(IV) (therefore not mobile), but fleeting species of uranyl(V) can also be involved in the processes of biological or mineral reduction of uranyl(VI) which generate soluble polymetallic species. The chemistry of uranyl(V) is also essential as a model for the chemistry of neptunyl(V) NpO_2^+. The chemistry of uranyl(V), a species hitherto considered to be too unstable to be isolated – owing to its tendency to disproportionate, was totally unexplored. During the disproportionation reaction, two uranyls(V) react with each other to form a uranyl(VI) and a uranium(IV). Recently, chemists in Grenoble succeeded in blocking this reaction and stabilizing polymetallic complexes of uranyl(V), opening the door to a systematic study of the reactivity and the electronic and magnetic properties of these compounds (Figure 2). This work provides important information for the understanding of the reaction pathways leading to insoluble compounds of uranium.

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Chemistry and chemical engineering, the COEX process

The COEX™ process, which is the fruit of the R&D conducted at CEA in partnership with Areva NC, is a significant innovation in the processing and recycling of fuel. COEX™ is an adaptation of the PUREX process utilized at La Hague (Manche), and is helping to optimize management of plutonium and uranium, paving the way for changes to the cycle for future nuclear systems.

During the *processing* of spent fuel, beginning with its dissolution, the recyclable materials – mainly uranium and plutonium – are separated out by liquid-liquid extraction from the non-reusable elements such as fission products. From PUREX to COEX™, the main difference is that the plutonium is no longer purified alone, in separation cycles devoted solely to this actinide, but always in the presence of uranium, thus offering an additional barrier against proliferation.

This result stems in particular from COEXtraction processes, producing a purified aqueous solution of plutonium and uranium. These mixed elements are then coprecipitated in solution through the controlled addition of oxalic acid (Figure 1): this operation allows quantitative recovery of the plutonium with the uranium in the same solid phase. This mixed oxalate is then heat-treated to produce the COEX™ end-product, a mixed oxide of plutonium and uranium (Figure 2).

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Figure 1.
Close-up of the oxalic coprecipitation of the purified solution of plutonium and uranium resulting from the coextraction cycles. The mixture of the uranium and plutonium solution on the one hand and of the oxalic acid on the other, to produce the mixed oxalate coprecipitate, takes place in a vortex effect reactor, in other words a reactor magnetically agitated by a magnetized bar.

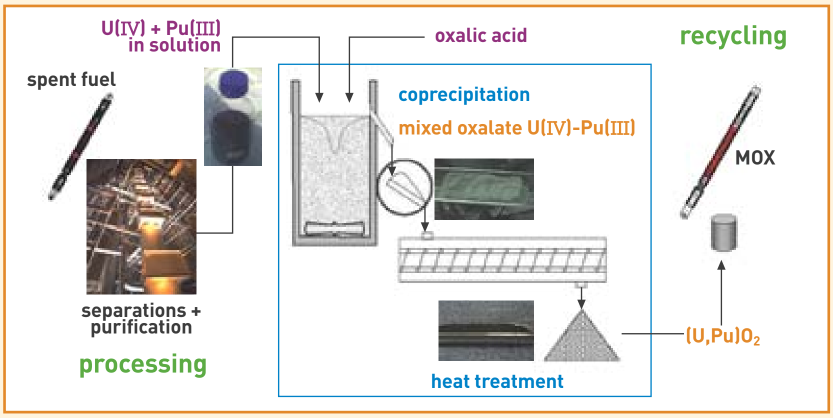

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Figure 2.
Coprecipitation of plutonium and uranium and then calcination into a mixed oxide, at the end of the COEX™ process and upstream of recycling into a MOX type fuel.

Sébastien Le Couster/TroisTiers Photographie

Preparation of an oxalic coprecipitation test in laboratory L15 at ATALANTE for modeling of the process.

This return to a solid state paves the way for the next step in the cycle: *recycling* of this plutonium with the uranium in a new MOX (*Mixed OXide*) type fuel, a close mixture of plutonium and uranium oxide. This fuel is intended both for light water reactors (LWR) and for the future fourth generation fast neutron reactors (FNR) for which it will be the reference fuel.

As for the chemistry of actinides, it lies at the heart of this process, in particular through the adjustment of the liquid-liquid extraction conditions (an aqueous phase and a non-miscible solvent containing the tri-*n*-butyl phosphate extractant), with a view to separating and purifying the plutonium while keeping it associated with the uranium. The specificity of plutonium and that of uranium, at their various degrees of oxidation, contribute to controlling this selectivity. Through the use of pulsed columns or centrifugal extractors, chemical engineering can cascade the contact between and then separation of the non-miscible phases, in other words the required number of separation/purification stages (stipulated by the process modeling), and achieve very high decontamination factors.

With regard to the return to the solid state, a key step in recycling, the oxalic acid added in solution as a precipitating reagent produces a highly insoluble mixed phase, leading to single step recovery of more than 99% of the uranium+plutonium mixture, initially adjusted to U(IV)+Pu(III). This oxalic coprecipitation is today performed in a vortex effect reactor, allowing continuous operation, for which there is unique industrial operating experience feedback – this reactor is already in use at La Hague for precipitation of the plutonium at the end of PUREX – and detailed knowledge of the chemical engineering involved, in particular through modeling of how it functions. The molecular structure of the U(IV)-Pu(III) coprecipitate targeted in the process is the basis of the controlled mixture of plutonium and uranium in the solid phase. This highly homogeneous mixture is preserved at calcination into a mixed oxide $(U,Pu)O_2$, making for greater simplification in the fabrication of MOX fuels for LWR and above all for FNR.

In short, from spent fuel processing to recycling, the COEX™ process represents controlled chemistry of the plutonium+uranium mixture.

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Supercritical fluids in chemical processes

When the pressure and temperature of a fluid are simultaneously higher than their critical point values (Figure 1), the fluid is said to be supercritical. Supercritical fluids have unique physico-chemical properties, part way between those of liquids and those of gases, making them attractive for use in chemical processes. They in particular have specific gravity close to that of liquids and viscosity close to that of gases. These properties can be modulated by adjusting the pressure and temperature conditions, creating variable geometry fluids.

Supercritical CO_2: abundant chemistry for a variety of applications

Carbon dioxide CO_2 ($P_c = 73.8$ bars, $T_c = 31$ °C) is the most widely used compound in supercritical processes, owing to its moderate critical point, its abundance, its non-toxicity and its non-flammability, thus limiting its health and environmental impacts. The applications of supercritical CO_2 are extremely varied: extraction from solid substances, fractioning of liquid mixtures, synthesis of materials, and so on. An abundant chemistry has been built up around this solvent whether or not combined with low levels of additives, which can modify its properties and reinforce its solvent capacity.

In the nuclear field, chemistry inspired by liquid phase extraction has been developed for the supercritical CO_2 used as a diluent in association with extractant systems such as organophosphorus compounds or β-diketones. The Japanese Super-DIREX (Supercritical fluid DIRect EXtraction) process exploits the supercritical CO_2 - tri-*n*-butyl phosphate – nitric acid chemical system to extract actinides from spent fuel. In the United States, the same chemical system is utilized in an industrial facility to recover enriched uranium from incineration ash. The CEA Supercritical Fluids and Membranes Laboratory is studying this type of process and moving towards the design and development of additives optimized for supercritical CO_2, based on molecules containing functional groups which have a strong affinity for it, such as siloxanes.

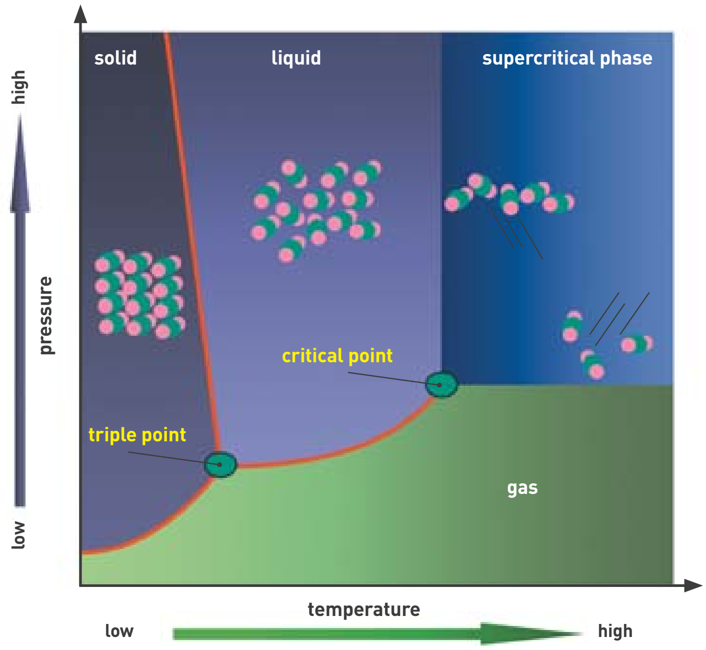

Figure 1.
Pressure-temperature phase diagram for an elementary body. Elementary bodies can be found in various well-known conventional states: solid, liquid, gas. In this diagram, the regions corresponding to these states are separated by state change curves. The vaporization curve, relative to the state change between gas and liquid, marks a break point called the critical point, corresponding to a pressure-temperature pairing specific to each elementary body and noted (P_c, T_c).
Beyond the critical point ($P > P_c$ and $T > T_c$), the notions of gas and liquid disappear: an elementary body exists in a single phase known as supercritical.

P. Dumas/CEA

Supercritical CO_2 test bench installed in the Supercritical Fluids and Membranes Laboratory at CEA/Marcoule.

Supercritical H_2O: remarkable properties for targeted applications

Owing to the temperature-related modification of the interactions between its molecules, supercritical water H_2O ($P_c = 221$ bars, $T_c = 374$ °C) exhibits solvation properties close to those of organic solvents and can solubilize organic compounds that are insoluble in liquid water. This remarkable property is exploited in chemical processes, with targeted applications in the treatment and recycling of organic waste and effluents. Supercritical water is then used as a solvent for running chemical reactions involving organic compounds, in a single-phase medium, thus allowing extremely fast reaction kinetics. The applications cover oxidation, controlled depolymerization, liquefaction and gasification.

In the nuclear field, CEA is studying oxidation in supercritical water, also called hydrothermal oxidation, for the mineralization of contaminated organic solvents. This process consists in a reaction between the organic compounds to be destroyed and an oxidant (air) in a supercritical water medium at about 300 bar and 500 °C. In these conditions, destruction rates of better than 99.9% can be achieved with residence times of a few tens of seconds. The DELOS nuclearized unit in the ATALANTE facility is designed to treat contaminated used organic solvents.

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The **chemistry** of **corrosion**

In order to maintain its economic competitiveness, while at the same time meeting ever-stricter safety requirements, the nuclear industry is working on improving and optimizing the performance and durability of its facilities. **Minimizing and controlling corrosion is a crucial issue.**


P. Stroppa/CEA

Placing stress corrosion samples in the Vénus facility in the Saclay Center.

According to the IUPAC, *corrosion is an irreversible interfacial reaction of a material with its environment, which results in consumption of the material or in dissolution into the material of a component of the environment.* The kinetics of this reaction is often the main subject of the studies performed in this field. The multiphysics, multiscale aspect is closely tied into the «science of corrosion» and involves numerous disciplines. As in other complex system sciences, the process of modeling corrosion or alteration phenomena is closely linked to experimentation and simulation.

Whether one is dealing with metal alloys, concretes, glasses, and so on, the materials used in the nuclear industry become altered at various rates in contact with the environment(s) in which they are situated, depending on the type and intensity of the loads. The physico-chemical environment determines the corrosion process modes. The associated loads can be precursors, catalysts or amplifiers of the damage to a material and lead to degraded properties, or a loss of the strength or integrity of a component, the structure or a facility. The systems studied at CEA are extremely varied and complex and can change over a period of time, given that the following have to be considered: materials that are homogeneous and heterogeneous, composite… and potentially reactive; environments and thus loads liable to lead to simultaneous, sequenced or closely coupled (multiphysics) phenomenology, that are sometimes extreme (high temperature, high pressure, irradiation, chemical concentration, mechanical stresses); a broad range of spatial scales (multiscale), from the scale of the material (nano, micro, meso) to that of the structure (macro). Furthermore, additional constraints, in particular nuclear-related, are to be taken into account, such as the notion of long-duration – for example up to several hundred thousand years in the case of geological disposal of radioactive waste – which demand approaches that are robust, reliable and predictable.

Three examples concerning different materials illustrate the problems linked to corrosion phenomena and give an idea of the developments under way in order to control them. They also illustrate the wide variety of heterogeneous chemical kinetics dealt with at CEA.

The behavior of metal materials

In an aqueous environment, such as in water reactors, the corrosion of metal materials (M) is electrochemical in nature, in other words the reaction involves a certain number x of electrons (e^-). It entails at least a metal oxidization reaction: $(M^{x+}, xe^-) \rightarrow (M^{x+}) + x(e^-)$.

This reaction is inevitably combined with at least a reduction reaction, which corresponds to the reduction of the dissolved oxygen (O_2) when present:

$$O_2 + 2\,H_2O\ \text{(water)} + 4\,e^- \rightarrow 4\,OH^-\ \text{(hydroxide ion)}$$

or, in a deoxygenated medium, the reduction of the water itself, through the following reaction:

$$H_2O + e^- \rightarrow \tfrac{1}{2}\,H_2\ \text{(hydrogen)} + OH^-.$$

Aqueous corrosion is characterized by these basic electrochemical reactions which occur either uniformly over the entire surface in question, or more unevenly. These corrosion phenomena are then conventionally separated into two groups: *generalized corrosion* and *localized corrosion*.

In pressurized water reactors (PWR), generalized corrosion is encountered on fuel element cladding. The purpose of the studies being carried out in this field is to evaluate the behavior of the zirconium alloys used in increasingly demanding operating conditions and to contribute to the development of new, stronger alloys. Another important case of generalized corrosion is that of materials such as the nickel alloys used in reactors, more particularly for the steam generator tubes. The industrial problem here is not so much material damage caused by corrosion, but more the release and transport of corrosion products, which can carry radioactive contamination.

The main localized corrosion phenomenon encountered in reactors is *stress corrosion* affecting not only the fuel element cladding, but also the nickel-based alloys and stainless steels, which can thus affect most of the nuclear island components (containment internals, vessel heads, piping, steam generator, etc.). In this field, developing models capable of predicting crack initiation and propagation is one objective, with a view to optimizing the frequency of inspections and any replacements. Numerous mechanisms are proposed in the literature to show the stress corrosion of nickel alloys (in particular Alloy 600) in the primary system environment of PWRs. In order to discriminate among these mechanisms, targeted experiments are conducted. Their aim is to acquire the missing data, in particular with regard to the role of oxygen and hydrogen, and to validate the various steps in the models. Some of the experiments were carried out on materials with a model microstructure. Finally, isotopes of oxygen and hydrogen were used to gain a clearer understanding of the role of hydrogenated and oxygenated species. Following the targeted experiments, a detailed description of the oxides present in the cracks and in the incipient cracks was proposed according to the specificities of the crack (active or not). Figure 1 gives an example of these characterizations.

Deterioration of reinforced concrete

Reinforced concrete is the material used for nuclear reactor containment buildings and for their cooling towers. It is also used for packaging of nuclear waste (containers and cemented packages) and the design of structures for the long-term management of this waste. These reinforced concrete structures not only have a role in guaranteeing mechanical strength, but must also act as a physico-chemical barrier to contain radionuclides (geological disposal). This requires concretes capable of retaining their integrity over extended periods of time, and thus requires the study of this type of material to improve the prediction and prevention of its degradation.

Concrete is characterized by an extremely alkaline pH (about 13). In atmospheric conditions, the main cause of reinforced concrete degradation is linked to the phenomenon of carbonation. The carbon dioxide (CO_2) of the air dissolves in the alkaline pore fluid of the concrete by means of the following reaction:

$$CO_2\,\text{(gas)} + H_2O\,\text{(water)} \leftrightarrow H_2CO_3\,\text{(carbonic acid)}.$$

This reaction leads to a physico-chemical change in the concrete, through the precipitation of calcium carbonates from (mainly) portlandite making up the material, *via* the following balance equation:

$$Ca(OH)_2\,\text{(portlandite)} + H_2CO_3 \leftrightarrow CaCO_3\,\text{(calcium carbonate)} + 2\,H_2O.$$

To simulate this phenomenon, the atmospheric carbonation model considers that the concrete comprises three phases – solid (cement hydrates), liquid (interstitial water), gaseous (CO_2), at the interfaces of which chemical reactions involving dissolution, precipitation, condensation and evaporation take place, in association with phenomena such as transport (water, CO_2) and microstructure evolution (pore clogging).

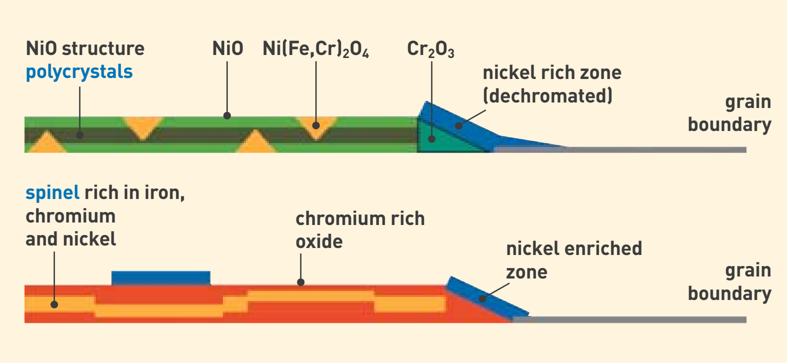

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Figure 1.
Schematic representation of the oxides contained in a stress corrosion crack formed in a nickel alloy test piece [600 alloy comprising about 14 to 17% chromium (Cr), 6 to 10% iron (Fe) and more than 72% nickel (Ni)] exposed to the primary system environment of a PWR. At the top, a grain boundary active crack; at bottom, a passive secondary crack.

Carbonation in particular leads to a drop in the pH of the concrete pore fluid to values at which the steel reinforcements are no longer passive (pH in the vicinity of 9). This reinforcement corrosion has two types of consequences for the reinforced concrete structure. On the one hand, the formation of a layer of oxides more voluminous than the initial steel which will be able to cause cracking, or even bursting of the concrete. In these conditions, the concrete's transport and containment properties are impaired. Moreover, the loss of section of the reinforcements during the corrosion process entails a loss of structural bearing strength. The life of the structure is thus shortened.

For the study and long-term modeling of interactions between cement and metal materials (CIMETAL program) in atmospheric conditions and their impact on the mechanical strength of the material, a micro-macro type approach was adopted. All of this work should in the end lead to the implementation of a coupled model taking account of the transport of aggressive agents in the cement medium, the

F. Rhodes/CEA

Study of concrete reactivity to CO_2 gas: performance of an accelerated carbonation test.

reinforcement corrosion mechanisms, damages to the concrete cover, up to and including the residual bearing capacity of the structures.

Glass alteration

For nearly twenty years, France has been treating and recycling PWR spent fuels and vitrifying the fission products and the minor actinides (mainly R7T7 glass). Glass was chosen for confining of high-level, long-lived waste, owing to its ability to withstand chemical attack, the ease with which a wide variety of chemical elements can be incorporated into its structure and the relative ease with which it can be used industrially. It is however understood that the water present in the deep geological disposal clays would be capable of altering the glass and releasing a fraction of the radionuclides it contains. The whole question is to identify the rate at which the deterioration takes place and what are the mechanisms involved.

In the presence of water, reactions take place in R7T7 type glass, as in most borosilicates, some of which can be attributed to the nature of the chemical bonds within the vitreous structure and some to the properties of the dissolved species. These reactions can be divided into four processes at work simultaneously and which can be described kinetically (Figure 2). These processes are calculated by equations in the GRAAL(1) model, which is the basis for describing the glass alteration rate in geological disposal conditions

Towards harmonization of the various approaches

The general impression is that with regard to corrosion, each case is special, with corrosion resembling a patchwork of independent phenomena. It is therefore essential for the multiphysics and multiscale aspects of the corrosion phenomena described by the physical chemists to be coupled in order to understand the overall processes and model them. Even if the space and time scales involve several orders of magnitude, the tools – whether analytical or simulation – are progressing and should in the future lead to coherent approaches for predicting the phenomena and their impact on the durability of materials.

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P.-F. Grosjean/CEA

Production by fusion of a waste containment glass for study of its long-term behavior.

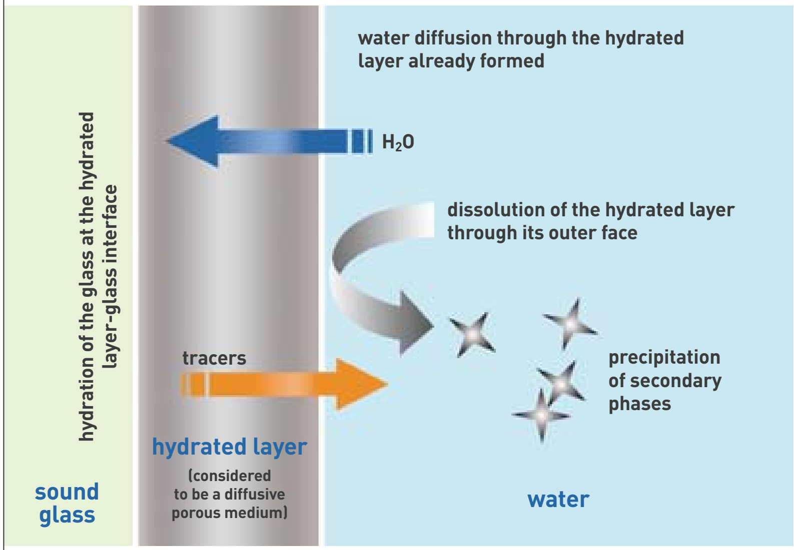

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Figure 2.
Representation of four processes simultaneously involved in glass alteration.
1. The oxide glass transforms into an amorphous, porous and hydrated oxo-hydroxide «phase». 2. The transport of water by diffusion up to the reaction interface through the hydrated layer already formed limits the hydration reaction of the glass. The hydrated layer thus plays a passivating role. 3. This layer dissolves on its outer face, with the kinetics depending on the solution renewal conditions in the vicinity of the glass. 4. Secondary phases precipitate by consuming elements forming the hydroxides layer. The glass alteration rate is measured by analyzing the evolution of the solution concentration of the marker elements (boron, sodium) released by the glass.

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(1) On this subject, see *Clefs CEA* N° 59, *The long-term behavior of glasses for waste containment purposes*, Summer 2010, p. 22-23.

FOR FURTHER INFORMATION

«La corrosion et l'altération des matériaux du nucléaire», Monograph by the CEA Nuclear Energy Division, Éditions du Moniteur (2010).

FOCUS A

Advances in modeling in chemistry

The organization of atoms at the microscopic scale is the result of attractive forces associated with their cloud of electrons. Without the latter, repulsion between the positively charged nuclei would make it impossible to form the complex edifices that constitute the subject of chemistry. Consequently, modeling of these structures in principle entails describing the electrons, a task that is made difficult owing to their number and above all to their quantum nature. The chemist is then faced with a dilemma. Either he strives to calculate the energy of an atomic configuration using the Schrödinger equation, which is only possible for a small number of atoms, or the nature of the problem requires that he take account of a large number of atoms, in which case a quantum calculation must be abandoned in favor of conventional potentials, in other words, analytical expressions which are the only way of ensuring an acceptable calculation time. A third possibility is to produce predictive models based on experimental data, without involving a detailed description of the system at the microscopic level. All areas of chemistry at CEA make extensive use of these modeling approaches, whether for nuclear applications, nanosciences, military applications, or life sciences.

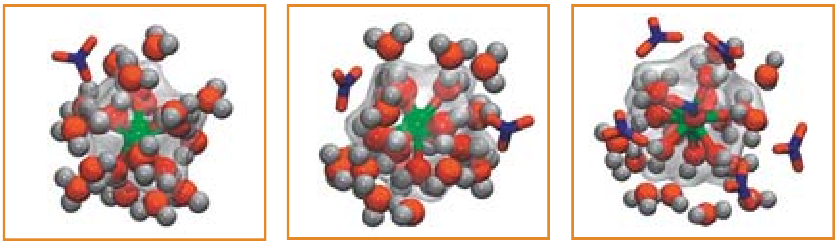
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Figure 2.
Instantaneous views of the local structure around a dysprosium(III) ion in aqueous solutions of $Dy(NO_3)_3$ at 0.5 mol/kg, 1 mol/kg and 3 mol/kg of water; atoms colors: H in white, O in red, N in blue, Dy in green.

Simulations of concentrated aqueous solutions using molecular dynamics

In the nuclear fuel cycle, the part consisting in spent fuel processing involves dissolution in nitric acid (HNO_3) and various separation stages through liquid-liquid extraction. During this process, numerous metal cations can be found in highly concentrated aqueous solutions. To understand and correctly describe the chemistry of these cations, one must be able to characterize both the structure and the thermodynamics of the species present in them.

One of the best methods for characterizing these solutions is molecular dynamics. This technique is capable of representing atoms and molecules by taking account of the thermal agitation that is essential for a pertinent representation of the solvation effects. It is possible to perform these simulations at the quantum level (Car-Parrinello simulations). If the simulation times currently accessible (a few tens of picoseconds) are able to show rapid kinetic reaction paths, they cannot however be used to obtain sufficient conformational sampling for systems exhibiting many degrees of freedom. Consequently, these methods also make it very hard to access thermodynamic data. At a less detailed level of representation of the chemical bond, the simulations based on an analytical representation of the interaction energy (resulting from conventional mechanics) make it possible to deal with a large number of atoms explicitly and thus show the molecules to be studied and the surrounding solvent with the same formalism (Figure 1). Simulations can then be performed over far longer time periods (a few tens of nanoseconds), thus making it possible to study the influence of solvation on the form and behavior of the chemical objects of interest to the chemist (Figure 2). The coupling of these methods with techniques such as those collectively referred to as "coarse-grained models" – based on interactions between pairs of ions, with an implicit solvent model – then gives access to thermodynamic data, such as the activity coefficients that are essential to describing the thermodynamics in concentrated media.

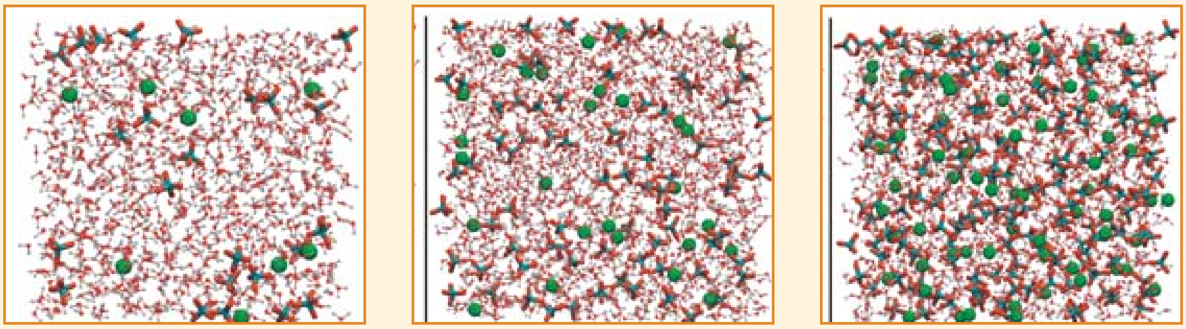
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Figure 1.
Instantaneous views of molecular dynamic simulations of dysprosium(III) perchlorate at 0.5 mol/kg, 1 mol/kg and 3 mol/kg of water; atoms colors: H in white, O in red, Cl in cyan, Dy in green.

FOCUS A

Properties of f element compounds

In recent years, the number of fields of application of the f elements (see *The chemical specificities of actinides*, p.10) has increased. This mainly concerns the lanthanide compounds with applications linked to their optical, chemical and structural or magnetic properties. For their part, actinides tend to remain associated with nuclear sciences. The experimental chemistry of f elements is today supported by numerical simulation. This is still undergoing significant expansion and remains a very real scientific challenge owing to the chemical nature of the media studied and the character of the lanthanide and actinide elements. These particular conditions mean that the "standard" theoretical simulation tools cannot always be used. Methodological developments are essential. Thanks to progress in computing and the implementation of new algorithms in the computer codes, it is only recently that it has become possible to study compounds of a realistic size.

The general objective of the work being done at CEA is primarily to model and gain a detailed understanding of the chemical behavior of radionuclides in the fields of spent nuclear fuel processing, the packaging and disposal of radioactive waste and nuclear toxicology. Secondly, the search for relationships between the orders of magnitude calculated and the properties measured should allow a qualitative orientation of the choice of one or more molecules in a family, but also, based on a new molecular pattern, an *a priori* evaluation of its properties. One of the most striking examples is the chemistry of spent nuclear fuel processing, both with regard to current processes and future prospects. The theoretical tools available are primarily quantum chemistry and classical and *ab initio* molecular dynamics. Studies are carried out at CEA using existing theoretical tools, but also by ensuring that the necessary methodological developments are made. These concern the analysis of the chemical bond, the construction of force fields including non-additive effects for conventional molecular dynamic simulations and the production of specific pseudopotentials appropriate to f elements, for *ab initio* molecular dynamics simulations. For example, the developments made with polarizable force fields, initially on lanthanides, made the first quantitative simulations possible of the dynamic properties of the hydrated Gd(III) ion complexed with a polyaminocarboxylate (applications for magnetic resonance imaging). Developments are currently being carried out with a view to simulating the dynamic and thermodynamic properties of actinide compounds that are solvated and/or complexed with organic molecules.

Another potential future use of theoretical tools is to design new f element compounds with controlled chemical, optical, magnetic or electronic properties. For example, thanks to theoretical chemistry, a new 32-electron principle based on the f elements was defined for the first time; it is comparable to the 18-electron rule for the d elements. It enables very stable actinide compounds to be designed (Figure 3), while the similar lanthanide compounds do not have properties that are as interesting. However, despite recent progress, much work is still to be done before being able to make a quantitative description of the physico-chemical properties of lanthanide or actinide compounds and producing new systems with specific properties. This research is the subject of national and international collaboration.

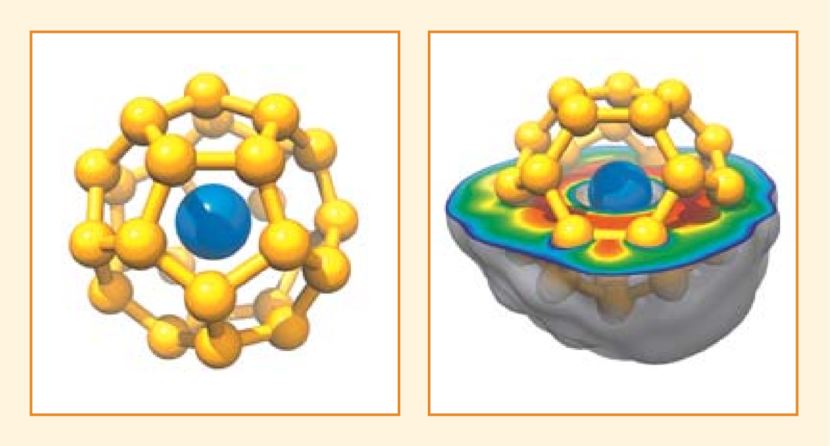
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Figure 3.
New families of extremely stable actinide-based compounds. On the left, tetrahedral symmetry complex consisting of a carbon cage encapsulating Pu^{4+} ($Pu^{4+}@C_{28}$). On the right, visualization of the electron localization function in $Pu^{4+}@C_{28}$. The color red corresponds to a maximum electron density. The calculations show that the 7s, 7p, 6d and 5f orbitals of the central f element hybridize with those of the cage to form a 32-electron system.

Explosive organic materials

Unlike the previous compounds, organic materials have simple electronic structures. However, modeling them comes up against combinatorial difficulties owing to the high number of possible configurations for the molecules. These difficulties are further aggravated when the chemist begins to look at the reactivity of these materials, because of the numerous potential mechanisms. This is in particular the case with explosives. These materials offer fertile ground for the application of new techniques reconciling the advantages of quantum chemistry with conventional molecular modeling, that is the ability to describe chemical reactions on the one hand, and the consideration of many degrees of freedom on the other. It should be remembered that an explosion is usually initiated by a shockwave. Although its initial effects on the material can be simulated by *ab initio* calculations (Figure 4), describing the subsequent steps however implies access not only to a reactive potential – in other words capable of describing the rupture and formation of chemical bonds – but also one that is effective, in other words, semi-analytical. In the same way as the conventional potentials of molecular mechanics, the reactive potentials are defined by explicit energy expressions according to geometrical variables. However, unlike non-reactive potentials, they are not able to exploit constants associated with chemical bonds, because the notion of bond is poorly defined for non-equilibrium

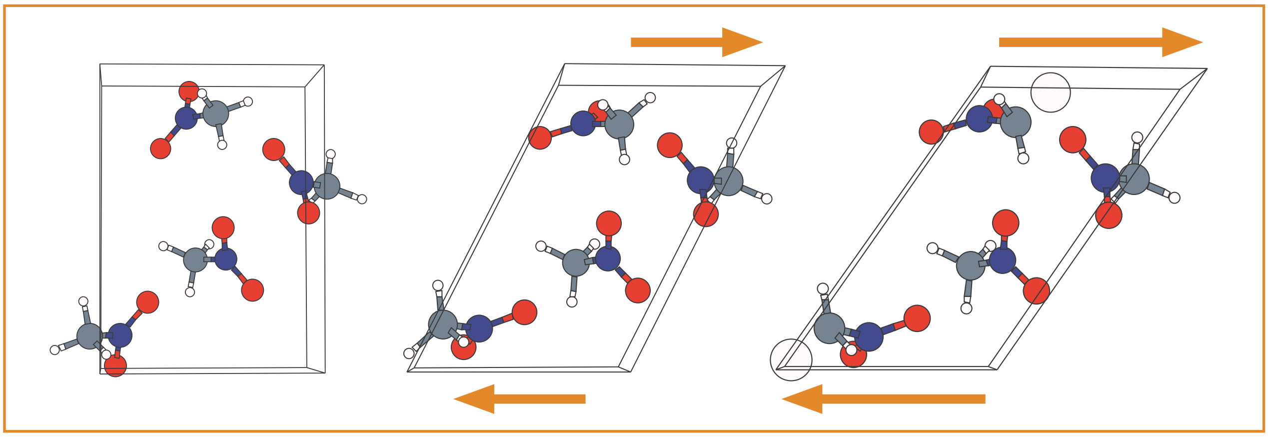
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Figure 4.
Evolution of the mesh of a nitromethane crystal (model explosive) subjected to increasing shear stress, which ends up tearing hydrogen atoms off the molecules (represented on the right by two large white spheres).

configurations. These constants are then replaced by functions which depend on a continuous bond order, calculated for each pair of atoms according to the distance separating them and according to their environment. These expressions must also be coupled with a variable electron charge model, in order to describe the changes in the electron distribution during the reactions. The search for increasingly reliable and less empirical models has been the subject of intense activity for the past decade.

Study of DNA damage

Structural DNA modifications (damage) are particularly frequent chemical processes in the cell nucleus. They are generally effectively repaired by enzymatic mechanisms. However, cellular division (mitosis) can sometimes precede damage repair. In this case, the daughter cell contains the same DNA damage as the mother cell. This is known as mutation. Mutation is the cause of cell ageing and can be the starting point for a cancerous process. It is therefore vital to understand the microscopic mechanisms.

The theoretical chemist has many different tools for modeling a chemical reaction. Of all the available methods, conceptual DFT is the paradigm of choice for comparing the reactivity and selectivity of chemically similar molecules. The essence of this method is to evaluate the energy variations and the electron density at the outset of the reaction in order to predict the most probable transition state and therefore the majority kinetic product. The variations in energy or electron density are estimated using a set of indices which numerically reflect the chemical characteristics of the studied molecule. The most frequently determined indices are the overall electrophilicity – the attraction for negatively charged species – or nucleophilicity – the attraction for positively charged species – of a molecule (reactivity) and their local distribution (selectivity).

This approach can be illustrated by considering damage known as tandem base damage, between the thymine and an adjacent purine base of a nucleotide. When this damage occurs, a covalent bond is created between the methyl group (CH_3) of the thymine and the C8 carbon of a neighboring guanine or adenine. Experimental results show that guanine is involved five times more often than adenine. The thymine radical which intervenes during the generation of this damage, is electrophilic. It will therefore be necessary to find the purine base for which the C8 carbon is the most nucleophilic. The most effective index is therefore the grand canonical dual descriptor developed at CEA in 2005-2006, which is a spatial function whose positive or negative sign respectively indicates the electrophilic or nucleophilic nature of the concerned zones. This function is represented for adenine and guanine on Figure 5. It would appear that the C8 carbon of adenine is electrophilic, while that of guanine is nucleophilic. The interaction with guanine is therefore stronger than with adenine, thus demonstrating the greater occurrence of thymine-guanine tandem base damage. This example is typical of the possible use of conceptual DFT in reactivity.

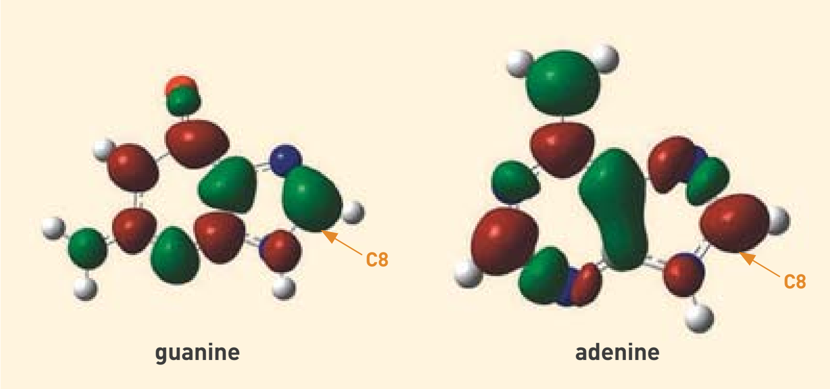

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Figure 5.
Grand canonical dual descriptors $f^{(2)}(\vec{r})$ for guanine and adenine. The positive (or electrophilic) zones are shown in red, while the negative (or nucleophilic) zones are shown in green. The C8 carbon is indicated by an arrow.

FOCUS A

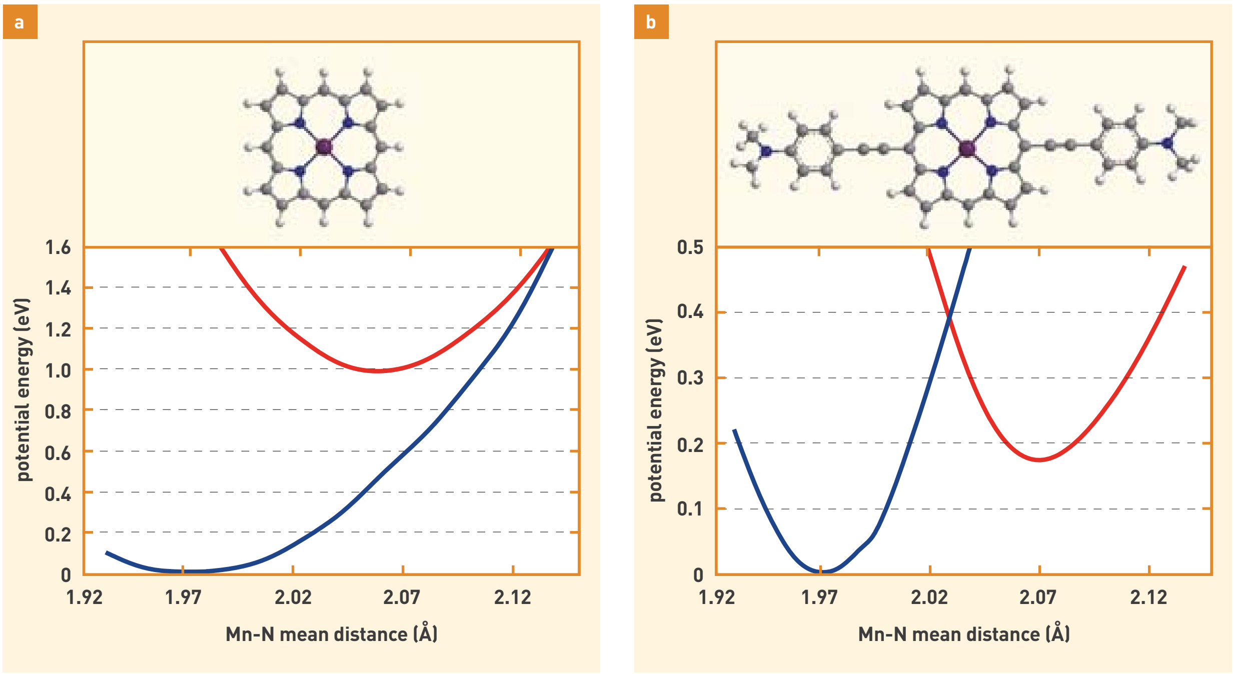

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Figure 6.
Potential energy (eV) curves for Mn porphyrins (noted P) oxidized with different charge locations, according to the mean distance between the central Mn atom and the 4 nitrogen atoms of porphyrin, Mn-N (Å). In blue: $[Mn^{III}P^{2-}]^+$ (S = 2) state; in red: $[Mn^{II}P^{\bullet-}]^+$ (S = 3) state. In figure a, porphyrin without substituent. There is a single minimum, regardless of the Mn-N distance. In figure b, porphyrin with a substituent. There are two minima, one for each state, precursors of bistability.

Theoretical chemistry and nanosciences

Molecules grafted onto nano-objects make it possible to control or enhance the properties of these nanomaterials, with significant applications in imaging, nanostructuring, sensors, or data storage. The first challenge is to calculate the key property at molecular level: light emission, magnetic transition, charge transfer, etc. The second challenge concerns the modeling of the coupling between the molecule and the nano-object. These questions are illustrated here by the modeling of "molecular memories" where molecules with a redox activity are grafted onto silicon (Si) for data storage purposes.

The molecules studied in this context are "metallated" porphyrins, comprising a redox metal (Mn, Fe, Co). Effective data storage (*via* a charge on the molecule) requires bistability, a property which entails the existence of two potential energy minima. In the case of porphyrins of Mn(III), advanced *ab initio* calculations for two different spin states S (collaboration with the Lyon ENS [École normale supérieure de Lyon]) show that a careful choice of substituents can achieve this type of bistability (Figure 6). This leads to the existence of a difference between the molecule's oxidation and reduction potentials, which is an essential precondition for "storing" a charge.

When the molecule is grafted covalently – *via* a chemical bond called a spacer – to the Si substrate, one is then faced with the question of electron transfers between the molecule and the Si, which are governed by the relative positioning of their electronic levels. The calculation of a redox molecule grafted onto a Si aggregate of a finite size, shows that there is very little hybridization between the molecule electronic levels and the Si states. More significantly, the differences between the molecular levels and those of the Si are primarily modulated by the spacer. Thus, a short spacer (vinyl function) leads to a small molecule-Si transfer energy gap, while a long spacer (≥ 6 carbon atoms) produces a larger gap. These results, which are valid for all the redox molecules used in the study, were corroborated by electrochemistry and capacitance experiments on grafted silicon substrates (collaboration with CEA's Leti Institute – Electronics and Information Technology Laboratory). The validity of the Si aggregate models was also confirmed by a periodic quantum approach, leading to the same level gaps as the molecular approach (collaboration with the Leti Institute).

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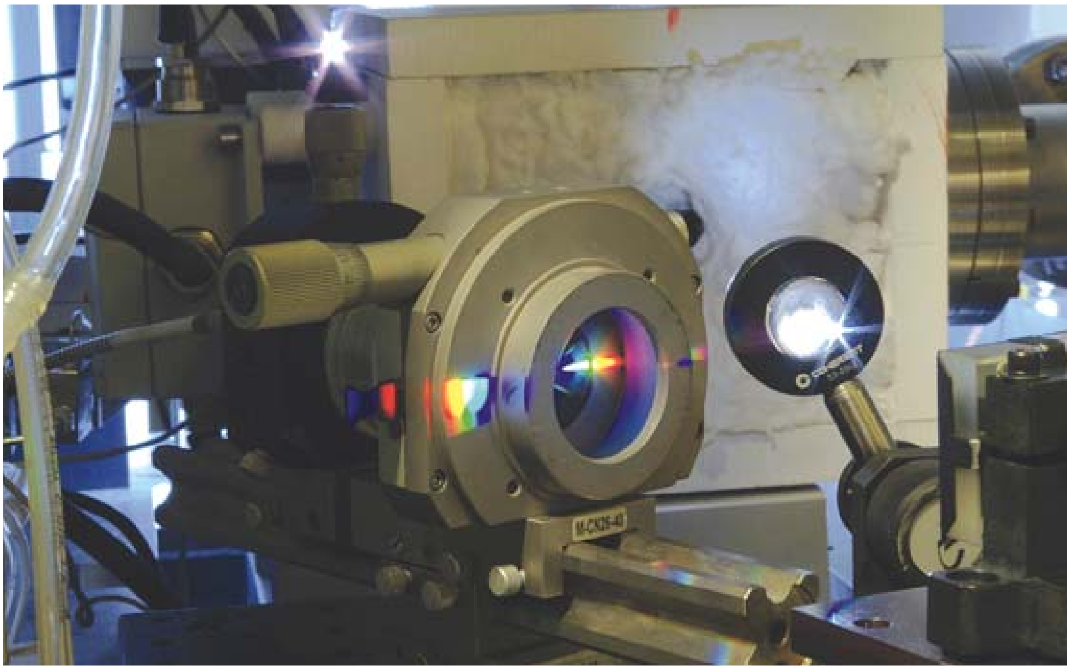
Understanding the **chemical** mechanisms of **radiolysis**

The phenomenon of radiolysis is apparent throughout the fuel cycle, resulting as it does from the interaction between nuclear radiation and matter, in particular water. It essentially causes corrosion, a loss of efficiency in the actinide extraction processes and the production of dangerous or corrosive gases. The chemistry of radiolysis, which is primarily radical, must be controlled and understood down to the smallest detail.



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Experiment conducted to determine the primary radiolytic yield of radical species. The light transmitted by an autoclave capable of containing supercritical water (374 °C, 221 bar) is scattered with a visible optical grating (from blue to red) on entering a slit which selects the wavelength sent to the detector via an optical fiber (remote detection). The time versus light intensity analysis during a brief irradiation will give the kinetics of the formation and recombination of the chemical species considered. These kinetics are closely dependent on temperature, pressure and the type of radiation used.

The phenomenon of radiolysis was observed shortly after the discovery of radium in 1898. It corresponds to the dissociation of molecules by ionizing radiation, consisting in the release of a gas – a mixture of hydrogen and oxygen – when a radium salt is dissolved in water (H_2O). It has continued to be investigated and refined and as of the early 1970s the radiolysis model comprised nearly 50 reactions for pure water. It is the most widely studied and understood chemical system in radiolysis. Up until the 1990s, databases of rate constants were produced for numerous gaseous or liquid phase solutes.

Tracking nuclear radiation

Although the first studies were carried out with the alpha radiation produced for example by radium, the chemical mechanisms were subsequently consolidated using pulsed electron beams which perfectly mimicked the effects of gamma radiation, but with a far higher radiation intensity. Observing the effect of alpha, proton, neutron or recoil nuclei radiation means that the solutions have to be polluted with radioactive salts which are then participants in the chemistry, thereby complicating the interpretation of the results. The oxidation or the reduction of these salts by the water radicals modulates the production of molecular hydrogen (H_2). This radiation exhibits high linear energy transfer (LET) and is accessible with cyclotrons, if necessary using their intrinsic time-based structure. Switching to pulsed mode makes it possible to visualize free radicals with a short life (maximum of one millisecond). Gamma and high-energy electron radiolysis is thus well understood, although this is not so much the case with higher LET radiation.

To control a radiolysis phenomenon, one must be familiar with the doses deposited in the medium and the primary radiolytic yield for the production of radical species when sufficiently diffused in the medium (Figure 1). For water at ambient temperature and pressure, between 100 ns and 1 µs after the passage of an ionizing particle, the species are uniformly distributed through the medium. Once the energy of the incoming particle is liable to cause ionization,

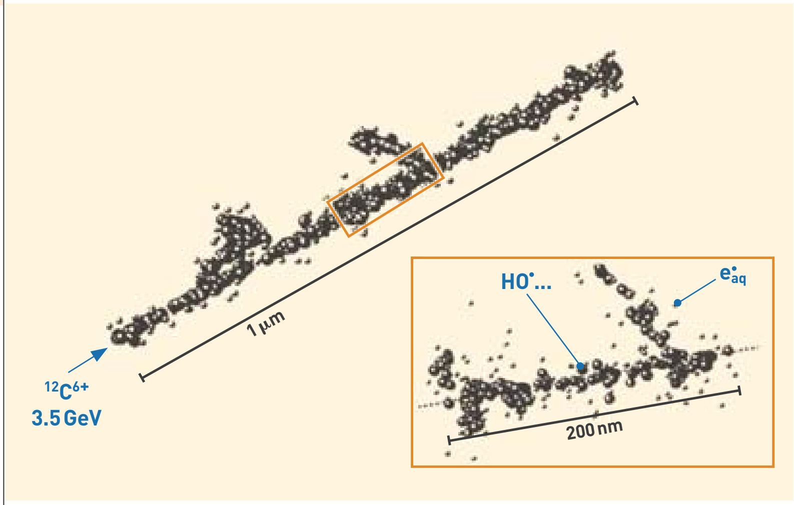

Figure 1.
Trace of ionization obtained by Monte-Carlo simulation. The resulting ionizations and radicals are symbolized by points along the ionizing particle propagation axis (here a carbon ion). Secondary axes (called delta rays) are created by energetic electrons ejected from the trace core. When the density of these delta rays becomes homogeneous, in other words when the LET increases, they form what is called the «penumbra», for which the energy deposit, in this case the value of the LET, is that of the electrons.

typically at least about ten eV, the chemistry is predictable. If the solution is well described (solutes, reactions and speed constants), it is relatively easy to predict the release of hydrogen and the production of hydrogen peroxide (H_2O_2). Things are often not so simple and far more detailed knowledge is essential. The primary yields are not known with precision for all types of radiation and there is no law that can determine them. The LET value alone cannot do this. These yields depend on the solute concentrations when higher than 0.01 mole/dm^3, because chemical capture takes place before the distribution of free radicals becomes uniform. They also depend on temperature. Furthermore, the Arrhenius law no longer applies above 250 °C when calculating the rate constants, because water also becomes a reagent rather than simply a bystander solvent. Experiments at higher temperatures are needed. In addition, the primary yields are only valid in a homogeneous medium and thus one without an interface. Recent studies have shown that the molecular hydrogen production yield is multiplied by a factor of at least 10 in nanometric and mesoscopic porosities. A thin film of water on the surface of plutonium oxide can also lead to an unusual level of radiolysis.

This data is accessible but at the expense of detailed research involving time resolutions ranging from a femtosecond to a nanosecond. Because the radiolysis model is a diffusion model, if the time scale observed is small, the spatial dimensions are also smaller. The zoom is therefore both time and space related. These studies must finally reveal the secret history of the primary yield of the species resulting from ionization, either in chemistry accelerated by temperature or by the proximity of high LET ionization, or in a chemistry that aims to be heterogeneous in the pores or at the interface between the radiolyzed molecule and the material. Moreover, these studies in extreme conditions are accompanied by modeling to bring simulation and experimentation together.

What effects on the fuel cycle?

The effects of radiolysis are omnipresent in the fuel cycle, given that they are the result of the interaction between nuclear radiation and the molecules of the water used to cool pressurized water reactors (PWR), the extractant molecules of actinides separation or the waste containment materials.

The radiolysis of PWR water

The radiolysis of water is most obvious in PWRs. Very early on, H_2 release and corrosion by H_2O_2 proved to be issues in the design of this type of reactor. The chemistry of radiolysis was controlled thanks to a clear understanding of the reaction mechanism, in particular the *chain, or Allen's reaction* between H_2 and H_2O_2:

$$H_2 + HO^{\bullet} \rightarrow H^{\bullet} + H_2O \text{ (reaction 1)}$$

$$H^{\bullet} + H_2O_2 \rightarrow HO^{\bullet} + H_2O \text{ (reaction 2).}$$

These latter occur as long as there is H_2 and H_2O_2 in solution, in other words, as long as radiolysis continues. As the primary yield of the hydroxyl radicals $HO^{\bullet}$ and of H_2 are very different, hydrogen (about 0.001 mole/dm^3) has to be injected so that the chain reaction can take place. Injecting hydrogen into the water of the PWR reactor coolant system is an integrated operation fully controlled by the licensee. In this way, it is as if there were no breakdown of the water. However, the chemistry of PWR water is complex owing to the effects of temperature, the mix of radiation in the vicinity of the fuel cladding, the additives designed to maintain the pH, and so on. The reactors of the future will not necessarily encounter the radiolysis problem, because the fourth generation fast neutron reactors, for example, will not contain any water. This is not the case of the ITER which will be water-cooled and subjected to neutron irradiation of 14 MeV.

The radiolysis of extractant molecules

The recycling of nuclear fuel, before producing ultimate waste, involves liquid-liquid extraction steps to extract and separate the minor actinides from the reusable uranium. After dissolution in concentrated nitric acid, molecules such as tri-*n*-butyl phosphate (TBP) in the PUREX process undergo radiolysis in the presence of the radiation from the dissolved fuel. Even though relatively stable, the TBP breaks down and must be recycled in order to maintain its plutonium extractant capacity. The “finer” processes (SANEX) allowing the extraction of curium and americium, utilize molecules such as the malonamides. The chemical mechanisms involved in the radiolysis of these molecules are being studied and evaluated, in terms of both the products formed under radiolysis and the transient radicals. As they have a complex architecture (sort of complexing clamp), time resolved infrared spectroscopy and mass spectrometry give access to the chemical bonds involved in radiolysis and their reaction mechanism.

The radiolysis of containment matrices

Ultimate waste is contained in several types of matrices according to its activity level. The R7T7 glasses for high-level containment would not seem to be susceptible to radiolysis. This is not the case of matrices such as concrete, which contains water with extremely alkaline pH (13-14) and undergoes considerable radiolysis leading to a release of hydrogen liable to impair the containment and escape into the facility. Studies of the radiolysis of this water subjected to mixed alpha and gamma radiation are complex and successive refinements of the models are still unsatisfactory. The high concentrations of hydroxide (HO^- ions) are disruptive, up to and including in the definition of the yields considered in the simulations. Moreover, the influence of concrete porosity considerably increases the molecular production yield known for free water, in the same way as LET would. The challenge is to establish a link between the short time scale (Monte-Carlo) and long time scale (resolution of differential equation systems) simulations.

The future challenges for chemistry under radiation

To meet the safety requirements of facilities or the performance needs of a process, but also to help understand the processes involved in radiobiology and radiotherapy, the researchers of the Radiolysis Laboratory (UMR 3299 CEA-CNRS) at the Saclay Institute of Matter and Radiation (CEA/Iramis) are faced with a number of challenges when attempting to understand the detailed mechanisms of radiolysis in extreme conditions: high LET radiation, high temperatures and pressures, interface. The goal is to produce a detailed description of an energy deposit in all types of ionization traces with Monte-Carlo simulations to back up the experiments, focusing on the initial processes in the field ranging from the picosecond to the nanosecond. This could be done by associating new ion sources, in particular those triggered by laser (Figure 2), with experiments combining microscopy and time resolution, to observe the heterogeneities in the traces and evaluate the models. The more complex molecules undergoing the effects of radiolysis will be analyzed by time-resolved spectroscopy capable of revealing the chemical bonds affected. This is also true for the new chemical systems such as ionic liquids liable to accept nuclear waste and for which numerous studies are required. Furthermore, simulations in molecular dynamics could reveal the detailed processes of certain clearly targeted reactions (Figure 3).

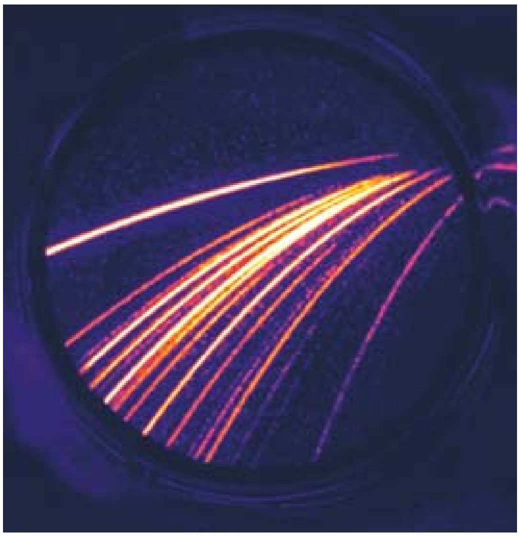
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Figure 2.
Thomson parabola: analysis of the particle beam (mainly protons and carbon ions with an energy of a few MeV) resulting from the interaction between an ultra-short laser pulse (picosecond) of very high power (terawatt) and a diamond target. Ongoing research projects are attempting to use these particles, with a high LET, to study ultra-short processes in the traces of ionization in water or polymers. The use of these particles in hadron therapy is also an objective linked to the energy deposit at the end of the trace (Bragg peak) to kill the malign tumors in certain cancers. Understanding the radiolytic mechanisms in this region is therefore crucial.

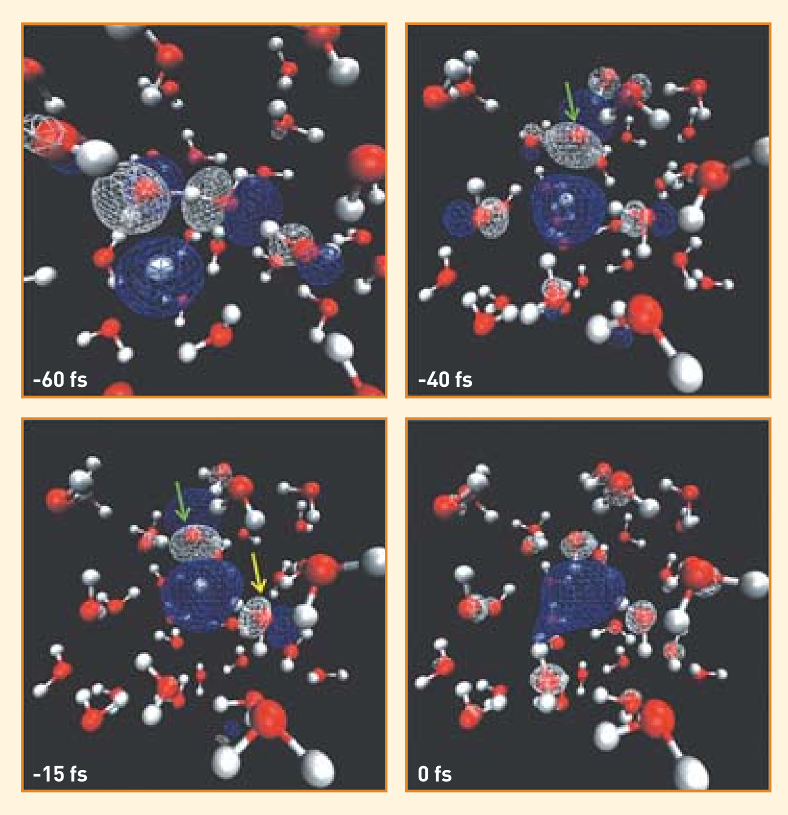

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Figure 3.
Representation of the steps in the process of the formation in water of a hydrated electron $e^{\bullet}_{aq}$ from a proton $H^{\bullet}$ and a hydroxide ion HO^-. At $t = 0$ s, it is shown in its solvation cage in blue with water molecules pointing their hydrogen atoms at it. Molecular dynamics reconstitutes the details of the interactions in an equilibrium reaction that had for a long time been nothing more than a hypothesis.

Networking

The technological and scientific hurdles involved in the radiolysis process will only be overcome by networking CEA's expertise so that radiolysis chemistry is no longer something to be endured but will be integrated into new concepts from the outset of research and the preliminary studies. This is the role of the CEA Radiolysis Network created in 2007, and in which the Radiolysis Laboratory is a coordinating member, building on the know-how accumulated and communicating with all CEA centers to facilitate exchanges of information in all the fields concerned by radiolysis.

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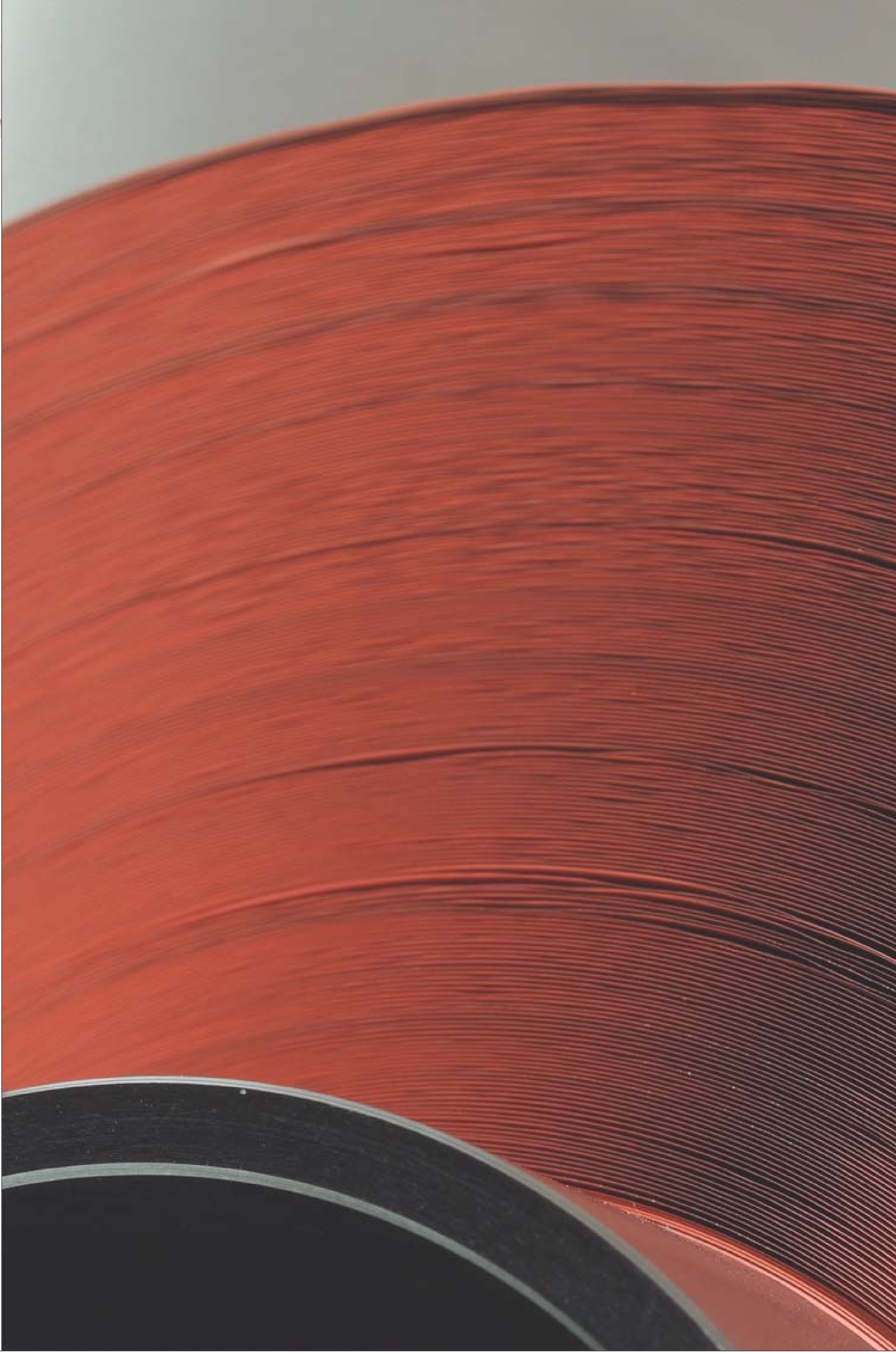

Edge of a negative electrode winding for a lithium-ion storage battery leaving the coating bench.

P. Avavian/CEA

II. CHEMISTRY AND ALTERNATIVE ENERGIES

In a national and international context which is extensively promoting low-carbon energies, CEA is involved in the new energy technologies that hold the key to a sustainable energy future. They include: the production and storage of electricity from solar energy, for both stationary and mobile applications; the production, storage and utilization of hydrogen for various applications such as electrical mobility or smoothing out the production of intermittent renewable energies; or even the use of energy from non-food biomass. This chapter illustrates the key role of chemistry, which is the cornerstone of the efficiency of energetic components. Chemistry is also the key to the development of organic photovoltaic cells, with the three-dimensional organization of matter *via* supramolecular interactions designed to encourage the dissociation of excitons into charges, or through the design of new stable conjugated molecules in which the absorption of light is tuned to match the solar spectrum. Chemistry is also a means of developing catalysts containing no noble metals, drawing inspiration from the working of metallo-enzymes, such as hydrogenases, capable of synthesizing hydrogen. This bio-inspired approach consists in creating a simple chemical environment around an abundant metal (iron, nickel, cobalt, etc.) the function of which mimics that of the living world. It was thus possible to generate current in a low-temperature fuel cell using a first bio-inspired catalyst grafted onto carbon nanotubes.

Of the storage technologies liable to meet the growing needs of stationary, nomad or mobile applications, lithium-ion storage batteries today offer the best performance in terms of energy and power density, but they can and must evolve further, for example to adapt to the particular specifications of electric transport. Chemistry is also playing an active role in developing these batteries by proposing new electrode and electrolyte materials. It is also essential to understanding and mastering all the possible reactions, whether desired or side-reactions, a vital step in the design of efficient and stable electrochemical systems capable of operating for long periods. Once again, it is the development of chemical processes that is enabling systems for recovering and recycling these storage batteries to be created as part of the sustainable development movement.

At the same time as working on vehicle electrification, CEA has for more than a decade been developing the synthesis of the second generation of biofuels from wood, forestry waste and ordinary industrial waste, or even agricultural residues. The thermochemical process adopted entails numerous fundamental studies to understand the basic physical-chemical phenomena governing the transformation of biomass materials at high temperatures. This highlights the key role of analytical chemistry (thermobalance, various spectroscopic methods and nuclear magnetic resonance (NMR) of solids) in the examination of the tars and the various gases produced in an entrained flow thermochemical gasification reactor.

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Producing **conjugated molecular architectures** for organic photovoltaics

As an inexhaustible source of power with low greenhouse gas emissions, solar energy is enjoying unprecedented growth, but if it is to truly carve out a place for itself in the energy mix, the price of photovoltaic electricity will have to come down significantly. Organic materials are easy to use and relatively inexpensive and are thus excellent candidates for the development of low-cost flexible solar cells. As an alternative to conventional silicon-based items, organic and hybrid photovoltaic cells are thus the focus of considerable research aimed at optimizing their performance.


P. Avavian/CEA

Synthesis of a photo-active copolymer intended for organic photovoltaic cell applications.

Photovoltaic technology directly converts the light energy from the Sun into electricity, *via* solar cells. The conversion of photons into electrons takes place in photo-active, semi-conductor type materials. Organic materials are cheaper to produce and purify, are lightweight, flexible, have optical and electronic properties that can be easily adjusted by chemically modifying their structures and are an ideal active material for use either alone or in combination. Organic and hybrid photovoltaic cells appeared in the 1990s and have become the product of choice in the research field, owing to their considerable energy conversion potential. One of their main advantages lies in the reduction in the cost of photovoltaic electricity. However, for the time being, these cells offer only relatively low conversion efficiency and deteriorate rapidly. In order to break into the market, they will need to offer efficiency of at least 10% and lifetimes of several years, at the same time as proposing manufacturing costs far below those of the conventional silicon-based alternative.

Promising materials for the active layer

The materials for the active layer of the new generation of photovoltaic cells are being developed *via* three approaches. The first uses evaporable molecular organic compounds, with vacuum evaporation techniques. The second uses soluble polymers or oligomers. These can be used in solution in ink form and printing technologies are sometimes employed. When these polymers are used in combination with inorganic nanoparticles, the chemists then talk of composites and hybrid cells. The last and radically different approach requires organometallic or purely organic dyes, which are grafted onto inorganic metal oxide type nanostructures. These molecules are used in combination with an electrolyte. The characteristic common to all these materials is their pi-conjugated electronic structure. A pi-conjugated molecule exhibits a primarily carbon-based chemical structure, in which the atoms are bound together in a covalent manner through an alternation of simple bonds (σ bonds created between two atoms by axial overlapping of orbitals) and double bonds (π bonds formed between two atoms by lateral overlapping of orbitals). The electrons located in the π (pi) orbitals can then delocalize over the entire architecture and thus give the material semi-conducting properties. Whichever approach is adopted, the design of new pi-conjugated materials for photovoltaic cells requires that a number of physical phenomena which contribute to generating the electric current must be taken into account, and that some of their properties directly linked to the cell operating principle be optimized.

Optimizing each operating step

The first parameter to be optimized is the absorption of light from the Sun (Figure 1). The molecules or polymers must be capable of intense absorption of the photons emitted by the Sun over a wide range of wavelengths. During this step, excitons – electron-hole pairs linked by electrostatic interaction – are generated in the material. It must then be possible to dissociate them to ensure the formation of unbound charges that will be collected on the electrodes. This phase calls on the bulk heterojunction concept, which consists in making an interface between a p type material (electron donor) and an n type material (electron acceptor). Effective dissociation of the excitons therefore requires adequate relative positioning of the energy levels of the HOMO (highest energy occupied at least by one electron) and LUMO (lowest energy, unoccupied) frontier orbitals of the two materials. Another parameter to be considered concerns the diffusion length of the excitons which, in organic materials, is no more than about ten nanometers. Consequently, for a heterojunction to be perfectly adapted, the phase segregation between the donor material and the acceptor material must lead to the formation of domains, the dimensions of which are about 10 nm. In the case of devices based on evaporable molecules, the heterojunctions are generally planar. Those based on polymers use the volume heterojunction concept (Figure 1). Once the charges are created, the molecules or polymers have to ensure that they move toward the electrodes. Hole mobility must therefore be high in the donor material and, conversely, electron mobility must be high in the acceptor material.

Based on these pre-requisites, the chemists have over the past twenty years developed semiconducting organic materials specifically for photovoltaic conversion. By combining different chemical patterns within pi-conjugated architectures, they succeeded in synthesizing materials possessing absorption ranges offset in the visible spectrum up to the near infrared and optimized charge transport properties.

Small evaporable molecules

The first organic cells using small evaporable molecules were produced in 1986. At that time, an efficiency of 1% was obtained for a planar heterojunction, utilizing a copper phthalocyanine (donor) and a derivative of perylene (acceptor); Figure 2. In recent decades, thanks to the production of new small molecules, whose molecular weight rarely exceeds 800 g/mol, the efficiency of this type of cell has been significantly improved. A major advance in this field consisted in breaking down the "work" of the cell into layers, by developing evaporable materials specifically tailored to absorb light and create charges, and others more specifically designed to transport electrons or holes. By stacking the molecules layer by layer in the appropriate way, the conversion efficiency achieved 7.7% for a size of 1 cm^2.(1) These results benefited from technological advances and the development of molecules also used in organic light-emitting diodes, a technology which already found commercial applications.

Pi-conjugated polymers

More than thirty years after the discovery of conducting polymers and eleven years after the Nobel Prize for chemistry was awarded to Hideki Shirakawa, Alan G. MacDiarmid and Alan J. Heeger for their work on this class of pi-conjugated materials, this area of research – at the boundary between chemistry and physics – is still growing rapidly.

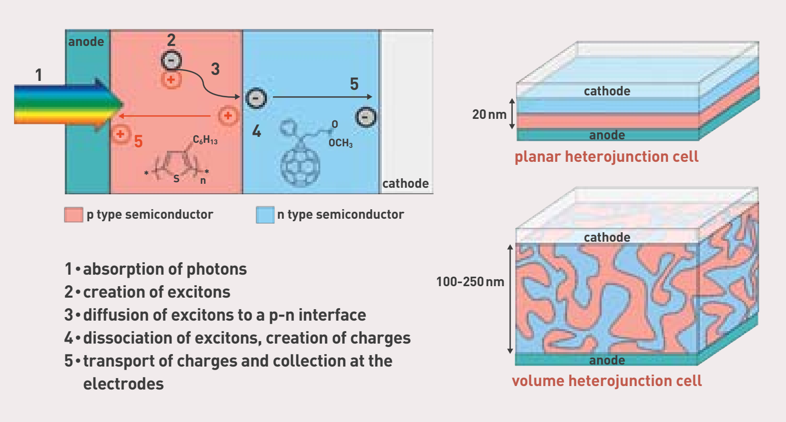

Figure 1.
Operating principle of a heterojunction cell and structure of planar and volume heterojunction structures.

Pi-conjugated polymers are extensively used in the production of volume heterojunction cells. They are used as p type semiconductors in combination with fullerene derivatives or inorganic nanocrystals (n type semiconductors). Fullerenes and nanocrystals generally exhibit a relatively limited absorption capacity. Therefore, in order to maximize photon collection, significant work has been done in recent years to develop polymers with a small gap, with large absorption ranges in the visible part of the spectrum up to the near infrared. These polymers can be homopolymers such as Poly(3-Hexyl)Thiophene, but most of the new systems are alternating copolymers, with a more complex chemical structure (Figure 2). These new materials contain electro-donor segments (rich in electrons) for example containing aromatic heterocycles such as thiophene, which will directly influence the energy position of the HOMO, and others that are electro-acceptors (less rich in electrons), which will determine the position of the polymer LUMO level. These various building blocks alternate within the chain. This strategy makes it possible to obtain materials that absorb more efficiently in the visible part of the solar spectrum and improve control of the energy position of the frontier orbitals. To be able to use these materials in liquid form, the structures are usually decorated with lateral alkyl type chains ($—C_nH_{2n+1}$). These substituents make these new systems soluble and improve control of their self-organization within the layers, helping improve their ability to transport the charges generated by the photons. By following the above-mentioned design rules, new polymers with a conversion efficiency in a solar cell of between 6 and 8.3%, have been prepared in recent years. More recently, small soluble molecules have been developed using these rules and employed successfully in this type of cell (efficiency up to 6.7%).

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(1) See the website http://www.heliatek.com.

The major part of these copolymers is produced by copolymerization of monomers correctly substituted in relation to each other, using organometallic catalysis. The coupling methods developed by John K. Stille or by Akira Suzuki, Ei-ichi Negishi and Richard F. Heck, winners of the Nobel Prize for chemistry in 2010, are extensively used in the preparation of these materials.

Organic dyes for sensitizing oxides

Organic dyes are used in hybrid cells called Dye-Sensitized Solar Cells or Grätzel(2) cells. In these photoelectrochemical cells, invented in the early 1990s, organic dyes are used to sensitize a conducting transparent oxide, usually a nanostructured titanium oxide (TiO_2). The photoactive organic dyes are grafted onto the surface of the oxide to form a monolayer. Under light irradiation, the excitons generated in this layer will be dissociated by electronic transfer in the oxide. The electrons created will thus be transferred to the cathode of the external circuit. The dyes, which are then in an oxidized state, are regenerated by a redox mediator in the electrolyte. At the present time, the most efficient dyes are organometallic complexes based on ruthenium (Ru) with record efficiency of 11%. However, these complexes are costly to produce because ruthenium is one of the rarer metals on Earth. Moreover, certain derivatives are highly toxic. This is why, in recent years, new families of purely organic dyes have been developed. The efficiency levels achieved with organic molecules are progressing rapidly and now stand at 9% (Figure 2).

Apart from the fact that these molecules are required to offer extensive and intense absorption, primarily by a pi-conjugated skeleton, they must also be designed to anchor themselves on the oxide surface in a stable fashion. To achieve this, carboxylic (—COOH) or phosphoric ($—P(O)(OH)_2$) functions are generally introduced at one end of the molecules. During operation of the cell, these molecules will undergo numerous oxidation and reduction cycles without degrading. To guarantee this integrity, groups with stable redox properties, such as derivatives of aromatic amines ($(Ar)_2N—$), are generally introduced into the purely organic compounds.


P. Avavian/CEA

Samples of pi-conjugated polymers and photovoltaic cell test prototypes manufactured from them.

This quick overview of the various approaches adopted in the organic and hybrid photovoltaic field clearly shows that chemistry is continuing to play a crucial role in the development of these new technologies, which in the coming years will doubtless constitute an additional source of renewable energy.

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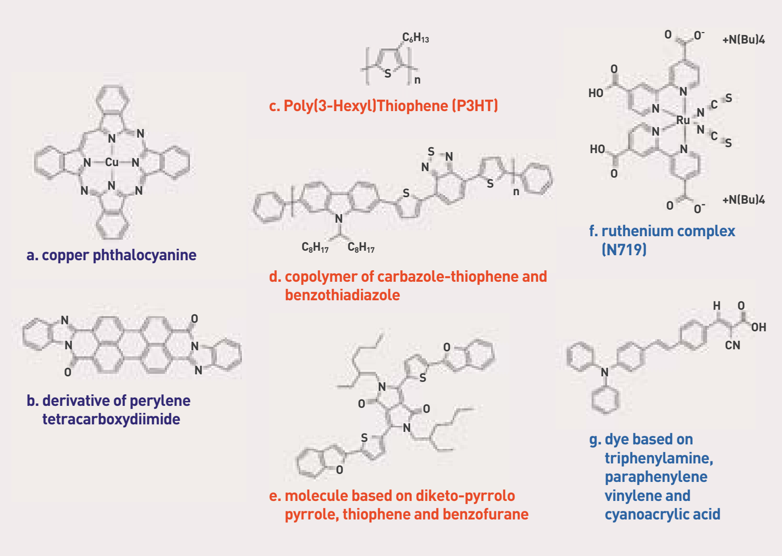

a. copper phthalocyanine

b. derivative of perylene tetracarboxydiimide

c. Poly(3-Hexyl)Thiophene (P3HT)

d. copolymer of carbazole-thiophene and benzothiadiazole

e. molecule based on diketo-pyrrolo pyrrole, thiophene and benzofurane

f. ruthenium complex (N719)

g. dye based on triphenylamine, paraphenylene vinylene and cyanoacrylic acid

Figure 2.
Examples of evaporable molecules (a, b), polymers and small soluble molecules allowing use in liquid form for volume heterojunction cells (c, d, e) and dyes for Grätzel cells (f, g).

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(2) On this subject, see *Clefs CEA* No.59, Summer 2010, p. 83.

Bio-inspired chemistry: getting rid of platinum in hydrogen applications

Enzymes are proteins expressed by living organisms to guide the thousands of reactions needed by their metabolism. They are without doubt the most effective and efficient catalysts in Life. However, their use in a technological context remains limited to fine chemistry because they remain fragile biomolecules which can only perform in a relatively limited set of conditions and usually only in water. One solution is to imitate the chemistry of their active site in order to develop "bio-inspired" catalysts. **The researchers at CEA have thus developed new highly efficient catalysts inspired by hydrogenases,** that enable platinum to be replaced in electrolyzers or hydrogen fuel cells or which can be integrated into a device producing hydrogen *via* artificial photosynthesis.

Hydrogen offers enormous potential as an energy carrier and as a means of providing long-term storage of renewable energies. Consequently, the electrolysis and photolysis of water are extremely efficient processes for producing hydrogen, a gas which can be stored and whose oxidation by the oxygen in air – ideally in a fuel cell – will enable the stored energy to be released on-demand, without generating any greenhouse gases, atmospheric pollutants or waste other than water. Unfortunately, the production of hydrogen, and its oxidation, are complex multi-electronic processes which require catalysts if they are to be usable at relatively low temperatures. Thus, reversible electrochemical devices with an H^+ proton exchange membrane (PEM) are capable of operating in fuel cell mode to produce electricity from hydrogen or, conversely, in electrolysis mode to produce hydrogen from electrical energy. Although their high efficiency opens up numerous markets for these devices, they are still far too expensive, in particular because they contain catalysts based on noble metals such as platinum (Pt) which, for a mass production run, would account for up to 20% of the price. It is therefore of the greatest interest to develop alternative catalysts using abundant and inexpensive metals of the first transition series, such as nickel (Ni), cobalt (Co) or iron (Fe). Over and above this aspect, the production of hydrogen from solar energy and water, two renewable resources, is an extremely attractive solution which would be able to provide our societies with guaranteed energy in the future. It is in the living world that the chemists may find the means of doing this.


P. Avavian/CEA

The development of bio-inspired catalysts begins with the synthesis of new ligands entailing expertise in organic chemistry. Subsequently, the coordination of these ligands with metal ions or organometallic patterns is often carried out in an argon atmosphere, through the use of special techniques.

Hydrogenases, fascinating enzyme systems

Certain organisms, bacteria or micro-algae, naturally have the ability to produce or oxidize hydrogen. For example, *Ralstonia eutropha* bacteria live thanks to a metabolism based on the reaction of hydrogen with oxygen, the same process as that at work in a fuel cell! In the same way as plants convert light energy into chemical energy (biomass) by reduction of atmospheric carbon dioxide (CO_2), the micro-algae *Chlamydomonas reinhardtii* can perform a certain form of photosynthesis, but producing hydrogen through photolysis of water. All of these activities are only possible because these organisms express fascinating metallo-enzymes called hydrogenases, which catalyze the production of hydrogen or its oxidation:

$$2\,H^+ + 2\,e^- \rightleftharpoons H_2\,.$$

Hydrogen factories

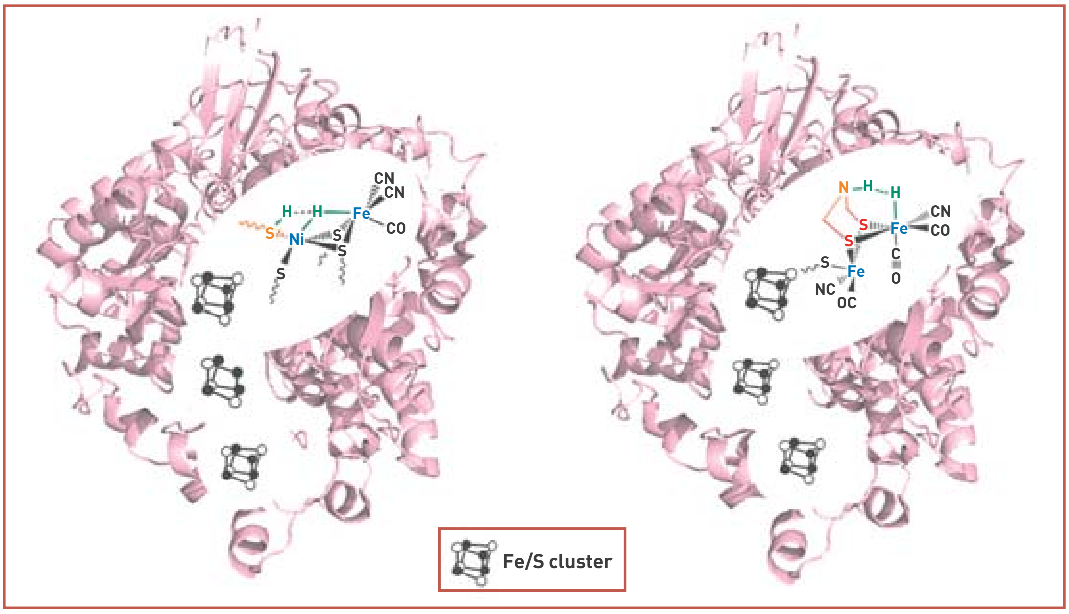
There are two families of hydrogenases (Figure 1) catalyzing the production of hydrogen or its oxidation. Their structures were determined in Grenoble in the 1990s by Juan Carlos Fontecilla-Camps' group at the Institute of Structural Biology (IBS) – a joint CEA/Life Sciences Division-CNRS-Université Joseph Fourier Grenoble 1 research unit. They differ in the metals content of their active site, comprising either nickel and iron (NiFe hydrogenases), or two iron atoms (FeFe hydrogenases). The two metal atoms are connected by sulfur (S) atoms belonging to cysteine residues of the protein chain for the NiFe hydrogenases, or constituting a dithiomethylamine ligand in the case of FeFe hydrogenases. The iron atoms are coordinated by ligands that are relatively unexpected in living organisms: carbonyl (CO) and cyanide (CN^-), which places these enzymes among the rare examples of organometallic molecules in biology. The presence of basic sites, such as the sulfur atom of a cysteine residue on the active site of NiFe hydrogenases, or the amine function of the dithiomethylamine ligand of the FeFe hydrogenases, constitutes a structural element playing a crucial role in the catalytic cycle, by facilitating the protonation or deprotonation reactions.

At the heart of the enzyme, a chain of iron-sulfur clusters (Fe/S), less than 15 Å apart, enables the electrons to circulate between the active site and the surface of the protein where the physiological partners of the hydrogenases intervene. In the same way, the IBS teams highlighted a preferential pathway within the protein for the transfer of protons and for the circulation of gases. Hydrogenases are therefore in reality small hydrogen factories with optimized electron, proton and gas transport logistics, which enables them to function at the standard potential of the H^+/H_2 pair with no electrochemical overvoltage – in other words, without requiring more energy than that strictly required by thermodynamics – and at high speed. A hydrogenase enzyme produces from 1,500 to 9,000 hydrogen molecules per second at pH 7 and 37 °C.

The bio-inspired approach

Hydrogenases are therefore a very promising potential solution for the catalysis problem mentioned earlier. As part of the *BioHydrogène* program at the CEA Life Sciences Division, the researchers at the Laboratory of Chemistry and Biology of Metals (Laboratoire de chimie et biologie des métaux/LCBM) – a joint CEA-CNRS-Université Joseph Fourier Grenoble 1 research unit – utilized this structural knowledge to develop bio-inspired catalysts. An approach such as this relies on the fact that extremely precise understanding at the molecular level of the structure of an enzyme active site can be used to make a faithful synthetic copy (*biomimetic model*) or, more broadly, to invent catalysts whose operating principles are derived from those of the active enzyme (enzymatic mechanism). This second variant in particular makes it possible to use chemical elements or combinations of atoms that Nature neither explored for reasons of bio-availability, nor selected, for example because of their toxicity during evolution. We then talk of *bio-inspired models.* Because it contains the key structural information obtained from the active site of the enzyme, where the reaction catalysis takes place, this biomimetic or bio-inspired catalyst will reproduce its activity, but while reducing both the complexity and the sensitivity to reaction conditions.

Catalysts such as this exhibit numerous advantages. They are easy to synthesize and are inexpensive to produce on a large scale, because they contain no noble or rare metals [Pt, palladium (Pd), iridium



CEA/DSV

Figure 1.
Schematic representation of the structure of NiFe hydrogenases (left) and FeFe hydrogenases (right) in the key intermediate state of their catalytic cycle. The cysteine residues (∿S), ligands of the metal centers, are symbolized by their sulfur atom. The dithiomethylamine ligand of the active site of the FeFe hydrogenases appears in red. The amine function it contains is shown in orange, as is the terminal cysteine ligand playing the same role in the active site of the NiFe hydrogenases. The interaction between a coordinated hydride ligand on the active site and a proton carried by the basic sites (orange), facilitating the reduction of protons into hydrogen or oxidation of the hydrogen, is schematically shown in green.

(Ir), rhodium (Rh) or ruthenium (Ru)]. Unlike the enzymes which inspired them, they can be used in many organic solvents, or even in water for some of them, over a wide range of temperatures and pressures. They are also less sensitive to oxidation in air. Bio-inspired catalysts do however have some drawbacks, in that they are often less active, less stable and less selective than enzymes. They are soluble and suffer from a recurring problem in homogeneous catalysis, that of their integration into a technological process. The discovery of a molecular catalyst that shows promise for an industrial application usually requires that it be grafted onto an insoluble material.

Bio-inspired hydrogenase catalysts

When the project started at the LCBM in 2002, more than 50 structural models of the active site of NiFe hydrogenases had then been described. Surprisingly, none of these complexes had been characterized as possessing a catalytic activity, whether for the production or oxidation of hydrogen.

Modeling hydrogenases

The LCBM team first of all decided to play a biomimetic and bio-inspired game, and to exploit the fascinating chemistry of ruthenium, a metal isoelectronic to iron(1), known to produce stable complexes with hydrogen or hydride ligands (H^-). A whole series of *dinuclear* Ni-Ru complexes (Figure 2) was thus developed. They proved to be capable of catalyzing the production of hydrogen in an organic solvent and in the presence of weak acids, thus becoming the first structural and functional models of NiFe hydrogenases. Thanks to a structure-function study within this series, it was possible to optimize the performance of these catalysts, step by step, both in terms of their catalysis rate and the overvoltage they need to reduce the protons to hydrogen. A detailed theoretical chemistry study using Density Functional Theory (DFT), conducted in collaboration with Martin Field of the Molecular Dynamics Laboratory (Laboratoire de dynamique moléculaire) at the IBS, demonstrated that the production of hydrogen catalyzed by the Ni-Ru complexes entails a hydride intermediate with a bridging structure (Figure 2), very similar to that determined for the catalytically active state of these enzymes. Moreover, by combining the results of this study with numerical simulations of their electrocatalytic properties, it was shown that for these catalysts and on the active site of the hydrogenases, the production of hydrogen followed a *heterolytic* mechanism involving the protonation of this intermediate hydride.

More recently, it has been possible to replace the ruthenium center by an organometallic pattern containing a metal from the first transition series. A nickel-manganese (Ni-Mn) complex and then a nickel-iron (Ni-Fe) complex were synthesized and characterized in turn (Figure 3). This latter has a composition very close to that of the active site of the NiFe hydrogenase. These complexes are active for the production of hydrogen in an organic medium, even if they require a more acid medium than their Ni-Ru analogues. They also prove to be relatively stable for the performance of several catalytic cycles and utilize the same bridging intermediate hydride.

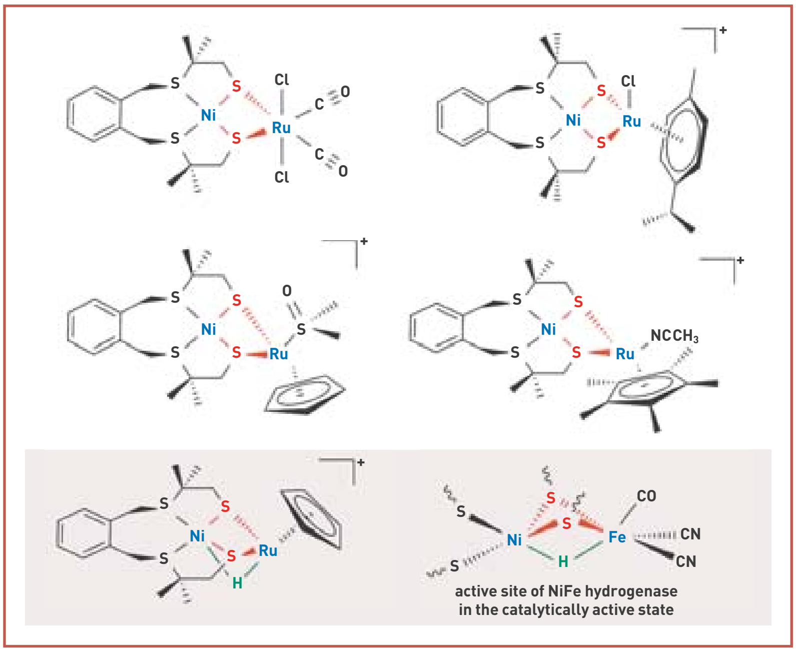


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Figure 2.
Structure of a few nickel-ruthenium compounds developed as models of the active site of NiFe hydrogenases. In the box, the structure of the intermediate hydride obtained by DFT calculation is compared with that of the catalytically active intermediate of the enzyme.

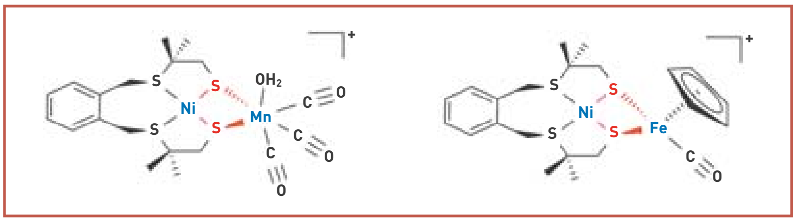

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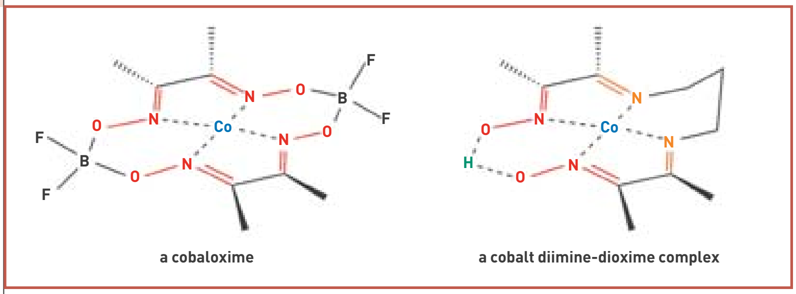
Figure 3.
Structure of nickel-manganese and nickel-iron compounds developed as structural and functional models of the active site of NiFe hydrogenases.

More efficient cobalt complexes and a photocatalytic system for producing hydrogen

Unfortunately, and the same applies for the models of the active site of the FeFe hydrogenases developed by other teams, all these dinuclear catalysts are not particularly efficient in terms of energy conversion yield. Whereas the hydrogenases function at thermodynamic equilibrium, their models all catalyze the production of hydrogen with high overvoltages, of between 500 mV and 1 V, which makes them practically unusable. This is where the second, bio-inspired variant of this approach comes into play, which requires a good understanding at a molecular level of what makes the enzymatic site so efficient. As an example, a small cobalt complex containing four oxime functions in the equatorial plane called cobaloxime (Figure 4), can be reduced at the Co(I) state at a potential very close to the physiological operating potential of hydrogenases. In the presence of protons, this compound catalyzes the production of hydrogen with limited overvoltages and high cycle frequencies.

(1) These two metals have the same number of electrons on their outer layer (valence orbital).



a cobaloxime

a cobalt diimine-dioxime complex

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Figure 4.
Structure of a cobaloxime, a first-generation cobalt-based catalyst, and a diimine-dioxime complex of cobalt developed more recently. The oxime functions are shown in red and the imine functions in orange.

P. Avavian/CEA

Experiment to photoproduce hydrogen in homogeneous phase catalyzed by the supramolecular complex described in figure 5.

In 2008, a first example of a supramolecular photocatalytic system to produce hydrogen was created at the LCBM by combining a cobaloxime with an inorganic, ruthenium based photo-sensitizer, capable of absorbing sunlight and converting it into a stream of electrons. In this way, part of the photosynthetic chain of hydrogen producing micro-algae is reproduced. Under the effect of light, the electrons supplied by triethylamine, introduced as a sacrificial element consumed during the reaction, help to transform the water into hydrogen at the cobalt centre (Figure 5), with an efficiency greater than that of the noble metal based systems (Rh, Pd, Pt) described hitherto. The quantum efficiency and the stability of these systems are today comparable with those of systems comprising the same molecular photo-sensitizers but using nanoparticles of platinum as catalytic sites. These results are a key step towards developing a water photolysis system by means of artificial photosynthesis.

More recently, a second-generation cobalt-based catalyst was developed at the LCBM. It contains a tetradentate ligand – in other words liable to engage in four bonds with a metal ion – (Figure 4) giving it exceptional hydrolysis stability, while retaining excellent catalytic performance owing to its two oxime functions, capable of fixing a proton in order to close the macrocycle. One of the key structural characteristics of the enzyme active site mentioned earlier can be found here, that is the presence of basic sites which can act as proton relays. Thanks to this function, and in a way similar to the hydrogenases, these complexes can adapt to the acid-base conditions of the medium and catalyze the production of hydrogen with low overvoltage over a wide range of pH values.

Detailed understanding of the working principles of an enzyme thus allows selection of the minimum structure necessary for the activity (here a single metal center is sufficient) followed by significant improvement of the performance of a catalyst (here by adding proton relay sites).

Characteristics such as these can be found in the catalysts developed by Daniel L. DuBois (Pacific Northwest National Laboratory, United States), which combine structural elements taken from the active sites of two types of hydrogenases. In these *mononuclear* complexes we find the nickel ion of the NiFe hydrogenases and an amine function incorporated this time into a diphosphine ligand rather than in the dithiomethylamine cofactor of the FeFe hydrogenases. With the cobaloximes and related diimine-dioxime cobalt complexes, these compounds form the second most efficient family of molecular catalysts for the production of hydrogen. It is this family of catalysts that was chosen to develop electrode materials in collaboration with the team of Serge Palacin and Bruno Jousselme at the Surface and Interface Chemistry Laboratory (Laboratoire de chimie des surfaces et interfaces) of the Saclay Institute of Matter and Radiation (CEA/Physical Sciences Division/Iramis). The ligands of a nickel bisdiphosphine complex were modified so that it could be grafted onto carbon nanotubes chosen for their high specific surface area and for their high electrical conductivity (Figure 6).

When deposited on an electrode and tested in

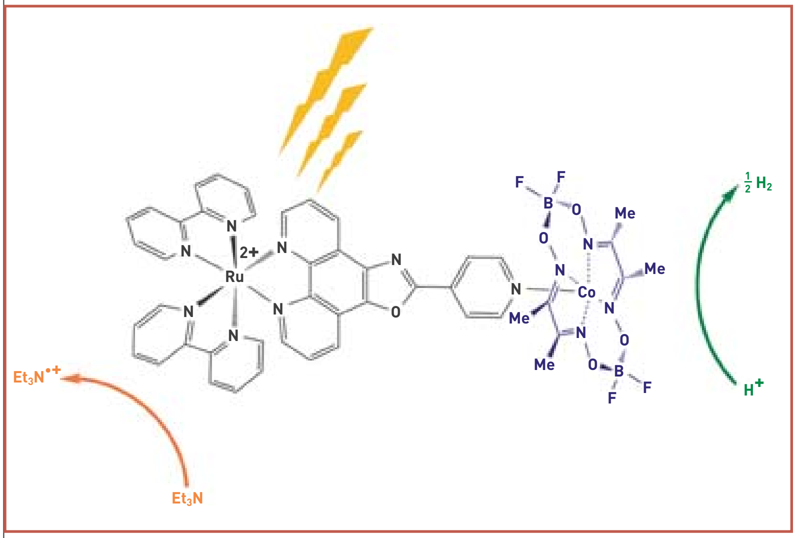

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Figure 5.
Structure and working principle of a supramolecular photocatalytic system to produce hydrogen, containing a ruthenium complex as the photo-sensitizer and a cobaloxime as hydrogen production catalyst. Triethylamine (Et_3N) provides the electrons necessary for transformation of the water into hydrogen at the cobalt.

a half-cell configuration by Nicolas Guillet at the Catalysis, Cells, Electrolysis and Modeling Laboratory (Laboratoire de catalyse, piles, électrolyse et modélisation) at the Liten Institute (Innovation Laboratory for New Energy Technologies and Nanomaterials) in Grenoble (CEA/Technological Research Division), this new material proved to be extremely stable and capable of functioning, with no overvoltage and reversibly, in a highly acid medium. These properties make it compatible with proton exchange membranes (such as Nafion®) used almost universally in electrochemical devices operating at low temperature. The use of this new material, the first with no noble metal and able to function at equilibrium, could eliminate a major scientific obstacle to the economic, large-scale development of the hydrogen sector. Full-cell tests are in fact under way at the Liten Institute. The electrical current densities obtained are still low and should continue to be improved, either by continuing to optimize the intrinsic performance of the catalyst, or by increasing the quantity immobilized on the electrode.

Promising outlook

By combining nanosciences and bio-inspired chemistry, the CEA researchers have therefore for the first time produced a material which, like platinum, is capable of catalyzing both the production of hydrogen and its oxidation. The immobilization of the bio-inspired complex on carbon nanotubes gave it both exceptional stability and new properties enabling it to work at electrochemical equilibrium. The aim now is to understand in detail the reasons for this type of activity, even if it appears clear that by connecting it to carbon nanotubes, which conduct electrons like the chain of Fe/S clusters, and by incorporating it into a Nafion® polymer, which promotes the diffusion of protons close to the catalyst, the chemist has reproduced an environment around the bio-inspired catalyst similar to that the enzyme creates for its active site! But we can go further than simply imitating an enzyme and can reproduce the activity of even more complex biological systems; artificial photosynthesis is a rapidly growing discipline which aims to draw inspiration from the working of the photosynthetic chain – a complex assembly of photo-sensitizers, proteins, enzymes and cofactors – to create a system using solar energy and water, two renewable resources, to produce hydrogen, or even liquid fuels by reduction of the carbon dioxide.

This field of research is thus opening up significant prospects for the future growth of alternative energies, by overcoming major obstacles to the development of new energy technologies.

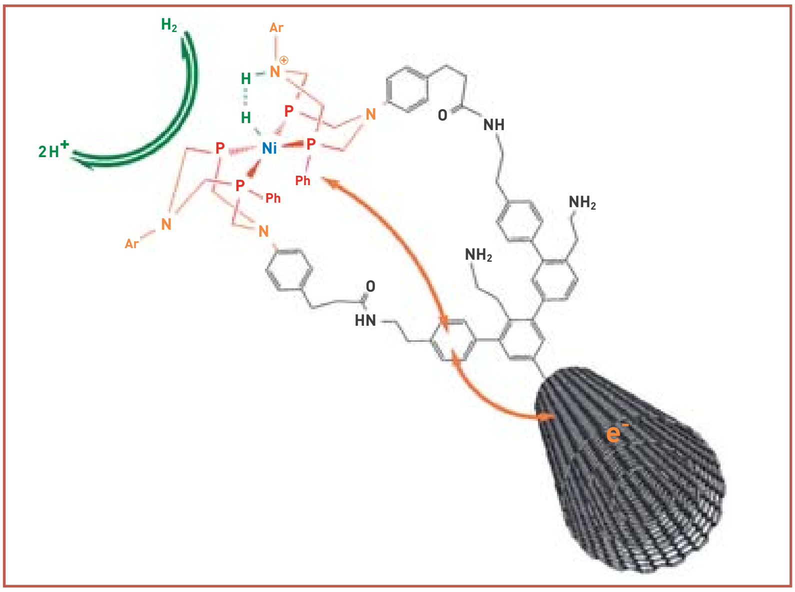

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Figure 6.
Schematic representation of the structure and reactivity of the material obtained by grafting the bio-inspired nickel-bisdiphosphine catalyst onto carbon nanotubes. The diphosphine ligand is shown in red and the amine functions it contains are shown in orange. The orange arrows show the exchange of electrons between the nanotubes and the catalyst. The interaction between a hydride ligand carried by the nickel and a proton carried by an amine function, facilitating the reduction of protons to hydrogen or the oxidation of the hydrogen, is schematically shown in green.

Fabien Collini

Electrochemical cell in half-cell configuration designed for testing the new catalysts with the technology developed at the Liten Institute.

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FOR FURTHER INFORMATION

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Chemistry in batteries

Over the past two decades, the number of products supplied by independent electrochemical storage systems (cells, storage batteries, etc.) has soared. These embedded energy sources have proven to be crucial to the development of new roaming electronic devices, hybrid and electric vehicles and biomedical instruments. The specific needs associated with each target application entail the development of appropriate storage systems. The choice of their components and how they are produced, their architectures and their assembly processes, enable the optimum solutions to be determined for each set of specifications. **CEA has for about fifteen years now been proposing innovative solutions linked primarily to lithium-ion technology, a generic solution for high-performance storage batteries, in particular through the synthesis and forming of new materials.**


P. Avavian/CEA

Left, production of positive composite electrodes using the solvent method. This process entails the production of an "ink" by dissolving an organic binder in a liquid and dispersing solid particles (active material and additives) in this mixture. This ink is then coated on the metal collector, dried and calendered to reduce its porosity.
Right, wound Li-ion storage batteries.

An electrochemical cell or storage battery is a device which is able to control an internal chemical reaction between a reducing material and an oxidizing material and to channel the electrons involved in the external circuit, thus generating an electric current. This device comprises at least two electrodes (positive and negative) and an electrolyte transporting the ions between these electrodes. These are electronic conductors, and are usually also ion conductors (mixed conductors), while the electrolyte, an ion conductor, must be an electronic insulator.

There are many types of electrochemical generators utilizing chemical compounds and various materials (Table). The main characteristic values of these systems are their rated operating voltage (V), their capacity (Ah), their specific energy and power (Wh/kg, W/kg), their energy and power densities (Wh/l, W/l), their cycleability, their calendar life and their energy efficiency. According to these criteria, it is possible to envisage them being used in a particular field of application. The technical-economic, environmental or safety aspects then have to be considered in order to evaluate the pertinence of a commercial launch. The choice of chemical compounds or materials used for the positive electrode/electrolyte/negative electrode trio, making up the active part of the device, determines the level of these characteristic values.

The materials chemistry problem for lithium storage batteries

"Standard" lithium-ion storage battery technology uses a negative electrode operating at very low potential (~ - 3 V/SHE), leading to devices which run at high voltages (3 - 4 V) and high specific energies (150 - 250 Wh/kg). This performance explains the key role played by this storage battery chemistry in the development of mobile systems and electric/hybrid vehicles. Generally speaking, Li-ion technology is based on the use of electrodes consisting of lithium insertion compounds and a compatible electrolyte conducting Li^+ ions. The insertion compounds are mixed conductors (Li^+, e^-). Their crystallographic configuration creates a host structure for the Li^+ ions, which should in principle be relatively undisturbed by Li^+ extraction/insertion during the charge-discharge cycles. The most widespread system at present uses

type	lead-acid	nickel-cadmium	nickel-metal hydride	lithium-ion	ZEBRA	redox-flow[1]
positive electrode	$Pb^{(IV)}O_2/Pb^{(II)}SO_4$	$Ni^{(III)}OOH/Ni^{(II)}(OH)_2$	$Ni^{(III)}OOH/Ni^{(II)}(OH)_2$	$Li_{1-y}MO_2$ (M = Ni, Co, Mn)		$V^{(V)}O_2^{+}/V^{(IV)}O^{2+}$
negative electrode	$Pb^{(II)}SO_4/Pb^{(0)}$	$Cd^{(II)}(OH)_2/Cd^{(0)}$	$LaNi_5/H_xLaNi_5$	Li_xC_6	molten Na^+/Na	V^{3+}/V^{2+}
electrolyte	concentrated H_2SO_4	concentrated KOH + LiOH	concentrated KOH + LiOH	aprotic[2] organic solvent + $LiPF_6$	ceramic conducting Na^+ ions (β-Al_2O_3)+ $NaAlCl_4$ (molten)	sulfonated polysulfone membrane[3] or Nafion® + concentrated H_2SO_4
rated voltage (V)	2.1	1.2	1.2	3.6 – 3.7	2.6	1.3
operating temperature (°C)	-40 – 40	-20 – 70	0 – 40	-20 – 60	250	
energy density (Wh/l)	60 – 75	50 – 150	140 – 300	250 – 600	160	not applicable
specific energy (Wh/kg)	30 – 40	40 – 60	30 – 100	150 – 250	90	not applicable

[1] May also be considered as a particular fuel cell. [2] Which lacks of acidic hydrogen. [3] Thermoplastic polymer with high chemical, thermal and mechanical stability, modified to make it proton conducting. Nafion® belongs to the family of perfluoroalkylsulfonic superacids with a formula $C_nF_{2n+1}SO_3H$. It is a copolymer of tetrafluoroethylene and perfluoro(4-methyl-3,6-dioxa-7-octene-1-sulfonic fluoride).

Table.
Characteristics of a few families representative of electrochemical storage batteries. These are generally categorized according to the nature of the electrolyte and the various pairs of electrodes used, the operating temperature and the architecture of the device considered.

$LiCoO_2$ with a lamellar structure at the positive electrode, graphite at the negative electrode, and an electrolyte consisting of a $LiPF_6$ lithium salt dissolved in a mixture of organic solvents. It operates at around 3.6 V (Figure 1).

A considerable amount of work is being done to optimize this generic system. One priority target area for progress is linked to improving the intrinsic properties of the active materials employed. This progress is made possible by changes to the chemical composition of the compounds and by the use of new material structures and morphologies. Other areas for improvement are improved control of the chemical, electrochemical and mechanical interactions between the various storage battery components.

Improving electrode active materials

The *positive electrode* active materials for Li-ion storage batteries are mainly mixed oxides of lithium and transition metals (Li-M-O: $LiCoO_2$, $LiNiO_2$, $LiNi_{1/3}Mn_{1/3}Co_{1/3}O_2$ with a lamellar structure, $LiMn_2O_4$, $LiNi_{0.5}Mn_{1.5}O_4$ with a spinel structure). They may be partly replaced by other metals (for example $LiNi_{0.8}Co_{0.15}Al_{0.05}O_2$) to improve stability. They are synthesized from metal oxides or salts in at least two steps, comprising precipitation from aqueous solutions and heat treatment (750 – 900 °C). They take the form of powders with an average granulometry of about 5 - 10 µm.

Other oxide families, said to have a *polyanionic structure*, are the subject of much work. These are compounds such as Li-M-XO_4, or even Li-M-XO_4F, (X: S, P, Si; M: V, Fe) in which the XO_4 entities provide significant structural stability and an increase in the lithium insertion potential. The most advanced compound is $LiFePO_4$ with an olivine structure. It can be synthesized in a variety of ways, including precipitation in hydro/solvothermal conditions, solid-solid reaction, production by fusion, and which must in any case lead to nanometric grains (~ 25 nm) covered with 1 - 5 nm of carbon (Figure 2). This insertion material has numerous advantages for high-capacity devices (electric vehicles, intermittent energy storage, network connection): low cost,

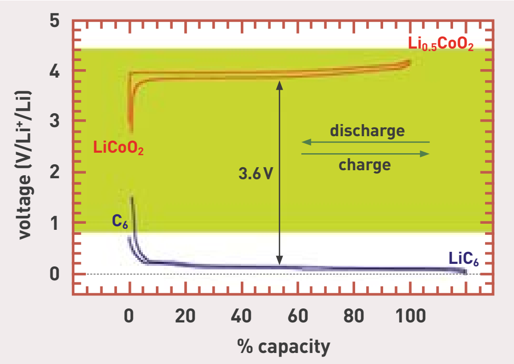
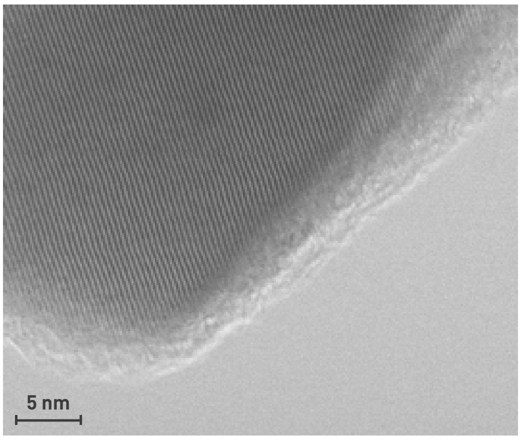


Figure 1.
Charge-discharge curves for the two electrodes making up a Li-ion storage battery. The colored zone indicates the electrochemical stability domain for the electrolyte used.



Adrien Boulineau/CEA

Figure 2.
Particle of $LiFePO_4$ coated with a nanometric carbon film. It is only in this form that the compound is able to output its full potential, as pure $LiFePO_4$ is a very poor electronic conductor.

specific capacity of 170 mAh/g, corresponding to full deinsertion of the lithium, an operating voltage of 3.45 V/Li$^+$/Li, excellent structural stability (and thus cyclability) and thermal stability (and thus safety). For all these reasons, it has been continuously developed at the CEA LITEN Institute for the past ten years.

Until very recently, graphite and other types of carbon were the only compounds used as the *negative electrodes* in Li-ion storage batteries, owing to their ability to insert/disinsert lithium at low potential (372 mAh/g, ~ 0.1 V/Li$^+$/Li) outside the electrolyte's electrochemical stability domain. The structure of the graphite is therefore not the only decisive factor in achieving the reversibility of the reaction. The second is to be able to form a compact, stable passivating layer that conducts the Li$^+$ ions, in particular by modulating the reactivity of the graphite surface and morphology and by adapting it to a given electrolyte composition.

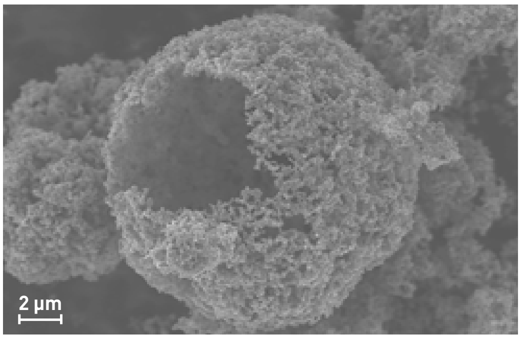
Like the other elements that can be alloyed with lithium, silicon is being examined particularly closely, given its far higher lithium insertion capacity (up to ten times that of graphite). At the same time, its volume is multiplied by four during the electrochemical formation of the alloy. It is therefore hard to maintain the integrity of the electrode and the protective function of the passivating layer during cycling and – for the time being – to achieve satisfactory stability. The goal of the research being carried out in many laboratories is to be able to solve this problem by appropriate forming of the material: incorporation of silicon into the conductive composite matrices, production of porous or (nano) structured materials, surface modifications, and so on (Figure 3).

In the case of applications such as hybrid vehicles, which can require extremely rapid charging (energy recovery at braking), a material inserting the lithium at higher potential is more suitable, in particular for safety reasons. A titanium oxide such as type $Li_4Ti_5O_{12}$ operating at 1.55 V/Li$^+$/Li is then used.

Optimizing electrolytes and composite electrodes

The *electrolytes* commonly used consist of mixtures of organic solvents, a lithium salt and small quantities of additives. For optimum operation of the storage battery, the water content must be minimal (~ 10 ppm). Combinations of solvents and salts can be adapted for different operating temperatures (from - 70 to + 85 °C) and required electrochemical stability domains. The role of the additives is to form an effective passivating layer on the negative electrode or to avoid accidental overcharging of the storage battery by creating electrochemical shuttles. It is possible to transform these liquid electrolytes into a gel by combining them with fluorinated copolymers (Lithium-ion Polymer cells).

Other types of electrolytes conducting lithium ions can be employed alone or in association with the previous ones: ceramics, vitro-ceramics or glasses, for which the ion conductivity is lower, at ambient temperature, than that of liquid electrolytes, but which make it possible to envisage operation at temperatures higher than 100 °C or to limit the diffusion of species (other than Li$^+$) from one electrode to the other; ionic liquids or molten salts at ambient temperature, for which the total ionic conductivity is very high and which, being non-flammable, would contribute to improving storage battery safety.



Cyril Paireau/CEA

Figure 3.
Hollow composite spheres consisting of nanometric silicon and carbon produced by atomization, a process which consists in transforming a solution, sprayed in the form of droplets placed in contact with a hot gas, into a powder.

The *electrodes* used are generally *composites* consisting of the active material in powder form, electronic conducting additives (carbon of various types and morphologies) and an organic binder, deposited on a metal film forming the current collector. The role of the additives is to ensure optimum electronic connection of all the particles in the active material to the current collector. These compounds can be produced and formed using two processes: a solvent method (see illustration p. 34) and a dry method based on direct mixing of the various solid components (possibly with a solid or gel polymer electrolyte) and the production of the composite film by extrusion. In any case, optimizing the performance of component electrodes demands a complete understanding of the interactions between the components, not only in their final state but also during each manufacturing step.

Electrochemical storage devices, including Li-ion storage batteries, are complex objects using an extensive range of materials, and their intrinsic properties, but also their interactions, manufacture and forming have to be understood in exhaustive detail. A wide variety of chemistry skills (solid chemistry, electrochemistry, chemistry and reactivity of interfaces, organic chemistry and polymers, catalysis, etc.) is therefore essential if one is to succeed in producing new and efficient devices. The greatest attention is currently being given to lithium-sulfur, lithium-air(oxygen), sodium-ion storage batteries and all-solid state systems.

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Battery recycling

For nearly 10 years now, CEA's Liten Institute has been conducting a program to develop high-energy Li-ion batteries, with the key aims of bringing out a new generation of active materials offering both improved performance and low production costs. These challenges are currently close to being met and materials such as boron doped $LiFePO_4$ (LFPB) and $Li_4Ti_5O_{12}$ (LTO) offer performance that is high enough to allow the technological transfer to the industrial scale, with applications in full electric ou hydrid vehicles. With a view to this transition, the recycling of used batteries and the management of production waste have to be considered.

Even if there are many industrial players in the recycling of used batteries of all types, their processes for this Li-ion technology all rely on the recovery and reuse of high valuable metals (Ni, Co, Fe, Cu) usually through pyrolysis of the full battery. For the time being, the Li-ion batteries to be processed come primarily from used portable electronic devices (computers and telephones), consisting mainly of mixed lithium and cobalt and/or nickel oxides. Lithium is not recovered. Consequently, the emergence of new active materials without cobalt and without nickel (LFPB and LTO) is seriously compromising the economic balance of current recycling processes and thus requires an extensive review of the industrial approach.

P. Avavian/CEA

Physico-chemical characterization of a leachate obtained after dissolution of Li-ion battery active materials.

P. Avavian/CEA

Leaching of Li-ion battery components.

Covering the entire manufacturing chain

Against this backdrop, the Liten has started from 2010 an R&D program covering the recycling of CEA's technology Li-ion batteries. Its aim is to develop an overall process processing not only the used batteries, but also the significant amounts of production waste generated by pre-industrial manufacturing of the batteries. This program will eventually enable Liten to cover the entire Li-ion battery manufacturing chain, from the raw materials to processing of the end-of-life product, thus confirming it as a major player in this field.

This program includes a method for making the used battery safe, as it can still retain a significant part of its electrical capacity, and actual recycling of the storage batteries. At this level, the recovery and recycling of the copper and aluminum current collectors, which on their own represent the majority of the cost of the battery, are essential. This program is also looking to recycle a large number of materials, such as the fluoride binder of the electrodes (PVDF) and the electrolyte ($LiPF_6$). With regard to the active materials (LFPB and LTO), the preferred solution, owing to the absence of high added value elements, is to return the recycled materials to the manufacturing cycle for new storage batteries. A hydrometallurgical process is therefore being developed for reuse of the lithium. Although this alkaline metal is far less costly than nickel or cobalt, its procurement is today considered to be strategic, in particular for the electric vehicle industry. The targeted technique consists in leaching the active materials in an acid solution, separating the metal elements in the solution and then synthesizing new precursors of active materials in the form of lithium carbonate (Li_2CO_3) or lithium phosphate (Li_3PO_4).

The ultimate goal of this program is to enable Liten to refine its technical-economic and environmental impact assessments for the Li-ion batteries sector and to deploy an eco-design approach in the near future. In order to meet this range of challenges, a network of partners is being set up around local academic and industrial players heavily involved in the recycling of storage batteries and chemical separation, with the aim of recovering and reusing secondary raw materials.

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Chemistry is all present in the **production of energy** from **biomass**

By 2030, transport will account for 20% of the world's primary energy consumption. Aiming to meet the commitments in terms of greenhouse gas emissions and the preservation of fossil fuel resources, **the production of second-generation biofuels from biomass, a renewable resource, is an alternative to fossil fuels**. The skills acquired at CEA in thermochemistry, as well as in running and optimizing processes, are decisive factors in the integration of the various technological steps of future industrial processes.


P. Avavian/CEA

Biomass samples. The purpose of the research carried out at CEA is to produce a high-purity synthesized gas from biomass, which can then be used to manufacture high-quality biofuels for transport.

The *first generation of biofuels*, called agro-fuels, uses the noble part of the plants (rapeseed, corn, wheat, etc.) to synthesize liquid fuels. However, CEA chose ten years ago not to propose biomass uses that compete with the food industry when working on the *second generation of biofuels*. CEA is optimizing existing and innovative technologies and processes which could supply large quantities of biofuels from wood, forestry waste, ordinary industrial waste and agricultural residues (stems, leaves, etc.). CEA is also examining the possibility of recovering energy from household waste and waste treatment sludges employing similar technologies. Technical-economic evaluations were performed based on an estimate of the available quantities of various resources, as well as on a realistic improvement in the mass and energy yield of the existing processes. This study shows that second generation biofuels should be able to meet half the current liquid fuel requirements (or about 25 Mtoe) for terrestrial transports in France.

The Biomass Technologies Laboratory (Laboratoire des technologies de la biomasse/LTB) at the Liten Institute carries out research into the various technologies of biomass conversion. Among the existing processes(1), the thermochemical route consists in heating the resource producing several chemical reactions within the mixture. Depending on the processes and the temperature levels reached, variable quantities of gases, liquids and solids (Figure 1) are produced. Gasification of the biomass is being experimentally studied at the LTB, both in process-scale facilities, as well as analytical laboratory equipment allowing the observation of the individual phenomena.

Insuring a good compatibility feedstock / process

As the potential of unexploited renewable resources is limited and extremely variable, the processes will have to be flexible enough to accept different types of biomass. Their physical and chemical properties often differ widely, and also depend on the growing and harvesting conditions of the plant – in other words, its harvesting date and growing location: this can make the process management delicate. Furthermore, even if the basic carbon, hydrogen and oxygen composition remains fairly constant whatever the biomass, the moisture content, density, calorific value, nitrogen, sulfur, chlorine, fluorine and metals contents can vary widely, as well as the ash content and composition.

In the gasification process, it is essential to characterize the inorganic elements, which are contained in far greater quantities in agricultural by-products such as straw (up to 10% of the dry matter) than in forestry biomass (1 to 3% of the dry matter). They can be found in the gas produced during gasification, and may become poisons for the catalysts used for the fuel synthesis. Inorganic compounds

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(1) On this subject, see *Clefs CEA* No. 50/51, *Fuel production by thermochemical transformation of biomass*, Winter 2004-2005, p. 42-46.

can also agglomerate in the gasification reactor, or impact the solid conversion rate. Studies being carried out with a thermobalance in the LTB showed the catalytic or inhibiting role of several inorganic species on the conversion rate, with a differential factor of more than 20 between several samples depending on their potassium and silicon contents. Such differences can impact process design. One of the solutions could be to mix different biomasses in order to obtain a solid with constant properties. Work could also be made with biomass producers to improve feedstock quality through new cultivation methods (add of fertilizer, harvesting date...) and species improvement.

Understanding the torrefaction mechanisms to optimize process performance

Entrained flow gasification is one of the technologies commonly employed for coal. Injection in such reactors requires particles with a quasi-spherical form, smaller than 500 µm. Given the fibrous nature of the biomass, it is technically very difficult to meet this specification and therefore extremely energy-consuming and expensive. Thermal pre-treatment is therefore essential in order to improve the grindability of the material, while losing as little mass as possible. For this reason CEA is working on torrefaction, which is a mild thermal reaction which conventionally takes place between 200 and 300 °C in a neutral atmosphere for several tens of minutes. The final product is hydrophobic and represents an anhydric weight loss of less than 30%. The properties of the torrefied biomass are close to those of coal: an increase in the carbon versus hydrogen and oxygen ratios, as well as in the calorific value and friability. The LTB aims to understand the mechanisms of this transformation. In particular, the use of the thermobalance tests and nuclear magnetic resonance (NMR) analysis of the solid allows identification of the chemical mechanisms involved in the degradation of the various biomass compounds, i.e.: cellulose, hemicellulose and lignin. The objective is to model the transformation and to optimize the corresponding operating conditions. Chemists are now aware of the fact that each of the constituting components exhibits its own behavior: thermally unstable hemicelluloses are very easily degraded, unlike cellulose which only breaks down significantly above 280°C and lignin which undergoes a slow degradation over a wide temperature range. Furthermore, interactions between compounds have been observed at high treatment temperatures and studies are under way to determine whether they are of purely structural or catalytic origin. During the torrefaction process, gases (CO, CO_2), water and other condensable products such as acetic acid (CH_3COOH), furfural and phenols are also emitted. It is essential to be able to predict their composition, in order to prevent corrosion of the facilities or to recover them as part of the green chemistry approach. Here again, work has been started to establish the link between the macromolecular structure of the material and the products obtained.

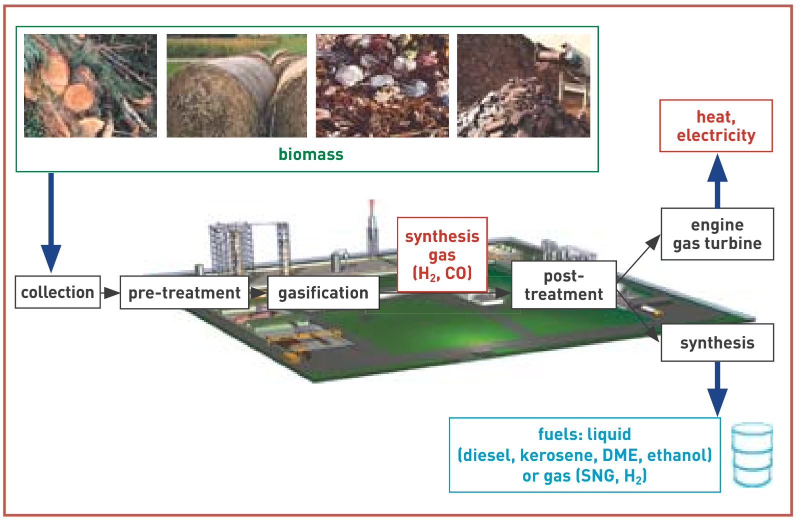

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Figure 1.
General and synthetic diagram of thermochemical transformation of biomass. Once cleaned of its undesirable compounds, the synthesis gas obtained is employed directly to produce heat and electricity or is sent to reactors for synthesis of biofuels, either liquid (diesel, kerosene, dimethyl-ether (DME), ethanol, etc.) or gas (for example methane, referred to as a Substitute Natural Gas (SNG), and molecular hydrogen H_2).

Biomass gasification: modeling complex physical and chemical phenomena

During the gasification step, the preheated biomass produces synthesis gas that will then be converted into biofuel. The LTB is mainly studying two gasification technologies: the fluidized bed reactor (temperature of 700 to 900 °C, pressure less than 5 bar) and the entrained flow reactor (temperature of 1,200 to 1,500 °C, pressure of 5 to 60 bar).
As soon as the biomass enters the reactor, it is raised to a very high temperature, leading to its pyrolysis, in other words its decomposition under the effect

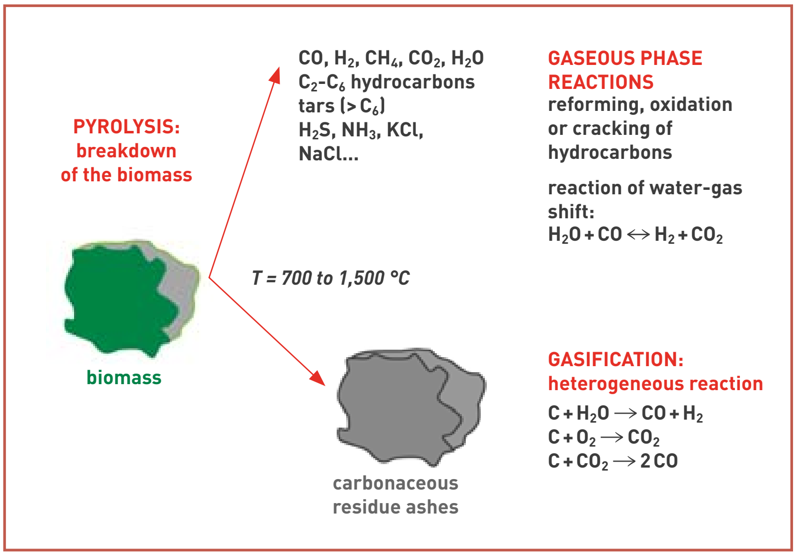

Figure 2.
Simplified diagram of the chemical reactions taking place during biomass gasification. As soon as it enters the reactor, the biomass starts to break down under the effect of the very high temperature. The pyrolysis products are incondensable gases [carbon monoxide (CO), molecular hydrogen (H_2), methane (CH_4), carbon dioxide (CO_2), ammonia (NH_3)], water (H_2O), hydrocarbons, tars, sulfides [hydrogen sulfide (H_2S)...], chlorides [potassium chloride (KCl), sodium chloride (NaCl) etc.], carbonaceous residue and ashes.

of heat (Figure 2). The products of pyrolysis are incondensable gases, hydrocarbons, water, tars, carbonaceous residue (char) and ash containing the inorganic species initially present in biomass. The first tars formed are mainly oxygenated compounds. These species rapidly evolve towards *secondary* and *tertiary* tars [alkenes, aromatic compounds and polycyclic aromatic hydrocarbons such as naphthalene ($C_{10}H_8$)] during the secondary reactions in the gas phase and under the effect of temperatures higher than 500°C. The carbonaceous residue, in contact with an oxidizing gas (oxygen, carbon dioxide or water vapor), undergoes a heterogeneous gasification reaction leading to the formation of carbon monoxide and molecular hydrogen. Reactions also take place in the gas phase, in particular the water-gas shift reaction and cracking, oxidization or reforming of hydrocarbons. Finally, the inorganic species, in particular in the form of sulphides and chlorides in gasification, are either collected in liquid phase in the process, or transported in the form of aerosols in the gas, and agglomerate in the cold areas. They can cause corrosion and exchanger clogging in industrial facilities: this is why particular attention is given to the behavior of these species.

All the chemical phenomena governing the degradation of a biomass particle are coupled with the physical phenomena involved in heat and mass transfers. Depending on the initial size of the biomass particle, some of these phenomena can appear as the limiting factor during degradation. This approach has been followed to develop a phenomenological gasification model of biomass particles at the LTB. This model includes the kinetics of each solid degradation step as well as the gaseous phase reactions, simulated with the CHEMKIN commercial software.

Better gas analysis for better gas cleaning

The composition of the gas produced is analyzed in order to quantify the efficiency of the gasification step, but also to check the concentrations of undesirable species (heavy tars, corrosive gases, inorganic "poisons"). This operation relies on a high number of complementary techniques such as catharometry, gas phase chromatography, mass spectrometry, analysis by Fourier Transform Infrared spectroscopy (FTIR) and ion chromatography. The sampling methods are specific to each type of species. Tars are either trapped in a series of impingers containing an organic solvent (isopropanol) kept at controlled temperature (between 40 and – 80 °C), or adsorbed on special fibers (Solid Phase Adsorption (SPA) technique) between 150 and 200°C. In the industrial process, before the final biofuel synthesis step, the gas is cleaned of its undesirable compounds. The particles are filtered and the gas undergoes several washing phases to remove the tars and inorganic species.

The cleaned synthesis gas can either be burnt to produce heat and electricity (cogeneration) with a higher energy yield than that of direct wood combustion, or it can be converted through catalytic reactions into liquid or gas biofuels (Figure 1).


P. Avavian/CEA

Fourier Transform Infrared spectroscopy (FTIR) analysis facility for measuring traces of inorganic compounds and tars in the synthesized gas.

The LTB team is using its chemistry skills in its studies on the biofuel process, from the feedstock characterization to the modeling of combined thermal, fluid mechanics and chemical phenomena in the gasification reactors and to the development of gas cleaning techniques. To increase the research efficiency, the LTB shares its skills with numerous French and foreign universities, research centers and industrial companies in various collaborative projects.

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Chemistry at the heart of the DSM-Low Carbon Energy program

At a time when our civilization is beginning to see the end of the fossil energy era and is witnessing the measurable and harmful effect of its practices on the biosphere, it is a matter of extreme urgency... to take the time to think carefully. Faced with this major challenge to our society, the staff at the CEA Physical Sciences Division (Direction des sciences de la matière/DSM) were asked to apply their scientific research approach to the problem: produce new ideas and concepts, evaluate and enhance them through theory, test and improve them through experimentation. The DSM-Low Carbon Energy program proposes to help these innovative concepts grow and take their first steps, by providing financing incentives. It was set up in 2010 after a rich and diverse maturing phase which saw on the one hand a multidisciplinary group of DSM researchers produce a joint strategic orientation(1) and, on the other hand, a call for ideas, issued for the entire DSM, which led to about a hundred responses.

Chemistry, the keystone of the basic science effort

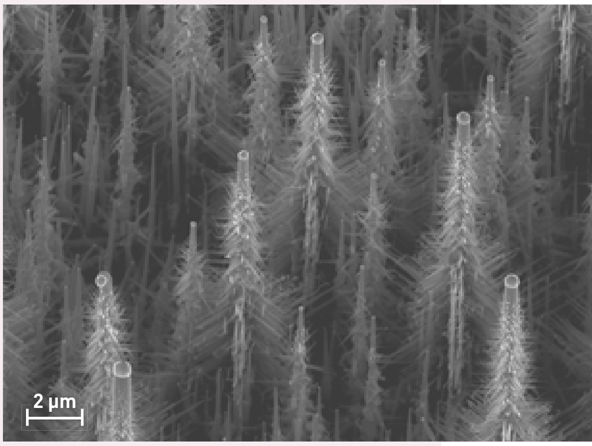
In 2010, two calls for project proposals were published. Of the thirty-four proposals received, and the 16 projects selected, nearly half directly concerned chemistry: electrochemistry or photochemistry, physical chemistry of surfaces, catalysis, structural analysis, etc. (Figure 1). This majority is hardly surprising as the main "renewed" energy resource on Earth is the stream of photons from the sun, the average energy of which is around 2 eV. Chemistry is precisely a science which has constantly juggled with energies on this scale, for the transformation and organization of molecular or solid matter.

In order to effectively and cleanly "harvest" solar energy, chemistry is very much in the front-line. For a long time, the aim for chemistry was to master molecular functions and manufacture them to order. The current energy challenge entails minimizing losses and optimizing the effectiveness of all the steps in the processes, which clearly explains the interest of the goal of "catalysis by design". It is above all in terms of the recurrent, massive reactions made possible and effective by catalysts, that energy consumption must be reduced and the barriers of potential overcome.

The 16 projects launched are exploring new membranes and new membrane-electrode assemblies for PEM (Proton Exchange Membrane) fuel cells, attempting to better understand the catalytic reactions at work in water electrolysis and in the working of the PEM, or are developing advanced measurement concepts and instruments for photovoltaic cells optimization. Two projects are also looking to open up new avenues for the reuse of CO_2, a core topic of the Energy-Climate issue.

Alongside the exploration of renewable resources, the potential for energy savings must also be addressed by long-term research. Two of the projects are looking at thermoelectricity, enabling heat losses to be converted into electrical current: this entails on the one hand working on concepts for new media in which to produce the thermoelectric effect and, on the other, to develop nanomaterials with enhanced properties.

Outside the field of chemistry and physical chemistry, significant gains in energy efficiency are also being sought through improvements to cryogenic cooling processes, through improved understanding of the losses caused by turbulence, or through a detailed understanding of the dynamics of electrical current distribution grids. "Smart" networks will become all the smarter if we can better describe and predict their interaction with the various social networks.



CEA/DSM

Silicon nano-trees are being looked at as a way of boosting the performance and efficiency of systems for the new energies: photovoltaic, superconductor, lithium batteries.

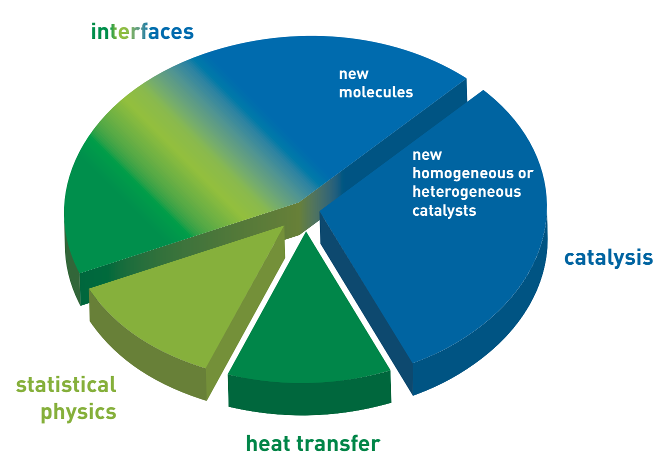


Figure 1.
Thematic breakdown of projects selected in 2010 for the DSM call for proposals: Innovative concepts for low carbon energy.

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(1) Intranet link http://www-dsmi.cea.fr/Phocea/file.php?file=Ast/19/DSM_RechercheFondamentale_Energie2010.pdf.

Detection of volatile organic compounds emitted by bacteria, through a colorimetric chemical reaction in solution and in three-dimensional materials.

P. Avavian/CEA

III. CHEMISTRY FOR HEALTH AND ENVIRONMENT

Chemistry provides us with a universal language which we can use to describe the general rules governing how living organisms work, to understand the interactions and changes involved, but also to design techniques enabling man to become an active player in his environment. Given its activities in the health-related technologies and its goal of controlling the environmental impact of its developments, nothing could be more natural than for CEA to make a strong commitment to the various aspects of this versatile science. The articles in this chapter provide concrete examples of how the chemists acquire their knowledge of the structure and the molecular reactivity of biomolecules, knowledge that they then use to produce original biosensors, new biomedical tools, or models of radionuclide migration in the environment. These numerous and seemingly independent applications nonetheless share a set of chemical methods, ranging from imaging labels to the measurement of non-covalent interactions. Following in the footsteps of Frédéric Joliot-Curie who, with his colleagues, demonstrated the benefits of radioactive labeling and tracers in physiology (e.g. synthesis of the ^{131}I-derivative of the thyroid hormone in 1944), CEA researchers pioneered labeling methods, the principle of which is now well-known: incorporating radioactive or stable isotopes, or with easily detected chemical functions, into biological or pharmacological molecules, which then become easy to monitor and map, even in infinitely small quantities in complex media. The labeled molecules can also be used to reveal the non-covalent bonds which are responsible for a large part of living organisms functioning. These reversible interactions between biological molecules or, for example, between contaminants and biochemical targets, create quantifiable balances involving the complementary approaches of solution chemistry or the chemistry of colloids and interfaces, as applicable. It thus becomes possible to make progress in defining the detailed rules controlling two remarkable properties of biological systems, high selectivity and high sensitivity, which are important in all areas of application.

The other aspect common to the articles of this chapter is the use of structural chemistry. The ability to provide a detailed description of the geometry of atoms in the molecules studied and in the reactive interfaces, provides essential data for representing the mechanisms at different levels of complexity, in particular by linking them from the atomic to the nanometric scales. This multi-scale approach is fascinating, owing both to its aesthetics (for example the magnificent form of DNA or of proteins) and to the prospects it opens up in terms of the rational engineering of new molecules for pharmaceutical or biotechnological applications.

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Chemistry of **tracers** for **medical imaging**

The use of macromolecules and nanostructures is today attracting increasing interest from the scientific community for use as imaging tracers. Their development requires the expertise of specialists in supramolecular organic and inorganic chemistry, in radiochemistry and of course of specialists in chemistry of materials, colloid and functional surface grafting. All these researchers use their know-how to build innovative molecular structures, some of which are (radio)labeled.

P-F. Grosjean/CEA

Preparation of radiopharmaceuticals: collection and weighing of a sample for synthesis (Service hospitalier Frédéric-Joliot/SHFJ).

Conventional radiography, computed tomography, echography, but also nuclear magnetic resonance imaging (MRI), optical and fluorescence imaging, positron emission tomography (PET), are all medical imaging techniques. While the first are simply able to visualize the anatomy of human organs, the latter can help understand how these organs function, without having to resort to surgery! Doctors and radiologists can today locate a damage or an unexpected growth in a tissue, with precision of about one millimeter. For patient diagnosis and therapeutic monitoring, this is a real revolution. These advances are partly due to the development in recent years of innovative molecular structures: molecules acting as probes and endowed with unprecedented pharmacological properties specific to each imaging technique.

At the CEA, the chemists are focusing their research on the three techniques previously mentioned: MRI, optical imaging and PET. These techniques all use "tracer" molecules whose chemical structures possess:

- a contrast entity, which is the origin of the image (magnetic species for MRI, radioisotopes for PET: in particular fluorine-18, and fluorophores for fluorescence imaging);
- a targeting entity, enabling the tracer injected into the patient to reach its biological target or its destination organ.

Labels for MRI and optical imaging

Unlike nuclear imaging techniques, neither uses ionizing radiation.

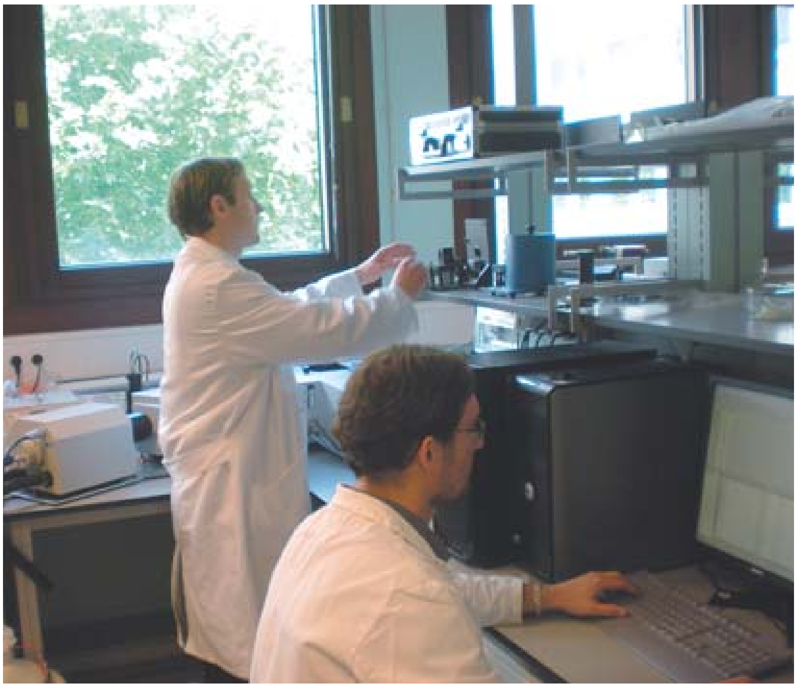
- MRI, based on the phenomenon of nuclear magnetic resonance of the hydrogen atoms nuclei, gives access to high spatial resolution with unlimited penetration through the organism. However, its low sensitivity means that the patients have to be injected with gadolinium-based contrast agents in order to improve the diagnosis, in 40% of clinical examinations. Moreover, the relaxivity of current compounds remains insufficient for molecular imaging. Remedying this presupposes obtaining more efficient contrast agents with improved relaxivity at high magnetic field. Significant advances have been made by the researchers at the Institute for Nanosciences and Cryogenics (Inac), in particular in the Inorganic and Biological Chemistry department (Service de chimie inorganique et biologique/SCIB). These advances consist in including gadolinium in macromolecular or nanometric systems and the improved design of the molecules used to complex this gadolinium. The benefit of this strategy lies in the more precise adjustment of the number of water molecules bound to the gadolinium, the exchange rate of each of these water molecules with the water in the surrounding environment, the Brownian rotation speed of the complex and the electronic relaxation – a parameter hitherto little explored. The gadolinium complexes thus obtained, based on molecules containing aromatic amines associated with carboxylate groups, show higher relaxivity than that of the contrast agents currently used for clinical examinations, while retaining good physiological stability. They also enabled the structure of the contrast agent to be correlated with its toxicity and certain molecular parameters determining the relaxivity.
- Optical imaging, a technique that complements MRI, differs in low spatial resolution but very high sensitivity. Its principle rests on the use of a camera capable of following the fate of the fluorescent labels emitting colored light (often in the visible or infrared spectrum) in the cells. The best fluorescent labels include semiconducting nanocrystals, also called quantum dots. Among these, calcium selenide-based

nanocrystals have already been used as biological labels since 1998. Thanks to quantum confinement, their emission wavelength is adjusted by their size. Depending on the material used, the emission spectrum range varies from the ultraviolet (zinc selenide/ZnSe) to the near infrared (lead sulfide/PbS, indium-arsenic/InAs alloy). These quantum dots exhibit other advantages: a broad absorption spectrum, straight emission lines, high fluorescence quantum efficiency and high photostability. The only downside is cadmium toxicity. Hence the idea from the researchers at Inac, this time from the Structures and Properties of Molecular Architectures Department (Service Structures et propriétés d'architectures moléculaires/SPrAM), to develop cadmium-free quantum dots for *in vitro* and *in vivo* biological labeling: these nanocrystals are known as "core-shell" compounds of indium phosphide (InP) for the core and zinc sulfide (ZnS) for the shell⁽¹⁾ or copper and indium sulfide ($CuInS_2$/ZnS⁽²⁾) (Figure 1 a).

A second approach, developed by the Photons, Atoms and Molecules Department (Service des photons, atomes et molécules/Spam) at the Saclay Institute of Matter and Radiation (Iramis), concerns silicon nanocrystals, which offer a number of advantages: proven absence of toxicity, luminescence in the red/infrared radiation spectrum, gaseous phase synthesis using continuous processes that can be extrapolated to a larger scale and which are therefore compatible with commercial production. After their synthesis, the technique consists in encapsulating the nanocrystals in silica particles to ensure good stability in biological media (Figure 1 b). The silica surface makes it easily available for functionalization for example by a magnetic function⁽³⁾.

The last approach is to encapsulate organic fluorophores, already approved for clinical use, in lipid nanoparticles (typical diameter of 50 nm) produced from pharmaceutical ingredients: oil, lipids and excipients⁽⁴⁾ (Figure 1 c). This technique is based on the expertise developed by the Electronics and Information Technology Laboratory (Leti/Biology and Healthcare Department).

Optical imaging and MRI complement each other and can be coupled to combine their advantages: high-resolution for MRI and high-sensitivity for optical imaging. The operation nonetheless requires the development of specific multimodal compounds. Thus, in the lanthanide family, which gadolinium (used in MRI) is a member of, other chemical elements, particularly europium and terbium, can act as optical labels using the same chelating template (containing aromatic amines associated with carboxylate groups). When compared with purely organic fluorophores, their long lives allows a better detection through time resolved experiments which suppress the fluorescence of the biological medium. They also offer strong resistance to photo-decomposition and good spectral discrimination. Lanthanide compounds, capable of efficient emission in the visible or infrared spectrum, in other words with very good quantum luminescence efficiency, have been developed⁽⁵⁾ by researchers at the LRICC of the SCIB⁽⁶⁾. The design of complexing molecules which meet the specifications of the two techniques, nonetheless remains a challenge. Molecules capable of meeting these criteria and leading to optical and magnetic probes have been produced⁽⁷⁾ and encapsulated in nanospheres of silica in order to build multimodal⁽⁸⁾ tracers. The researchers at the Inac⁽⁹⁾ are also developing bimodal probes


D. Imbert/CEA

Measurement of optical properties of terbium and europium components.

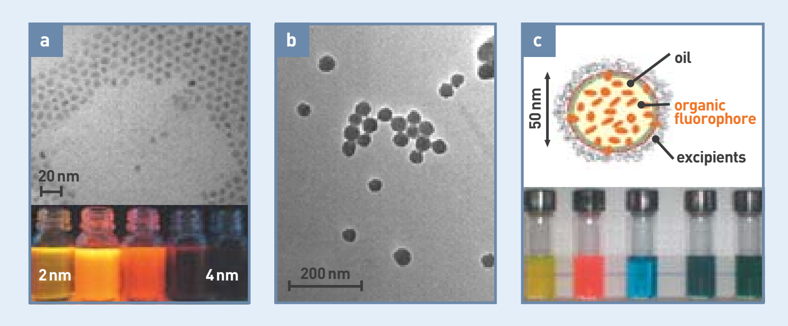


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Figure 1.
Three approaches developed for the production of fluorescent tracers.
(a) TEM transmission electron microscope image and series of nanocrystal samples: copper and indium sulfide ($CuInS_2$)/zinc sulfide (ZnS).
(b) Example of silicon nanocrystals encapsulated in a silica shell.
(c) Example of lipid nanoparticles loaded with organic fluorophores.

(1) Li L. *et al., J. Am. Chem. Soc.* 2008, *130*, 11588-11589.

(2) Li L. *et al., Chem. Mater.* 2009, *21*, 2422-2429.

(3) Doctoral thesis by V. Maurice, Université de Paris XI (5 November 2010).

(4) Texier I. *et al, J. Biomed. Opt.* 2009, *14*, 054005 ; Goutayer M. *et al., Eur. J. Pharm. Biopharm.* 2010, *75*, 137-147 ; Delmas T. *et al., Langmuir* 2011, 10.1021/la104221q.

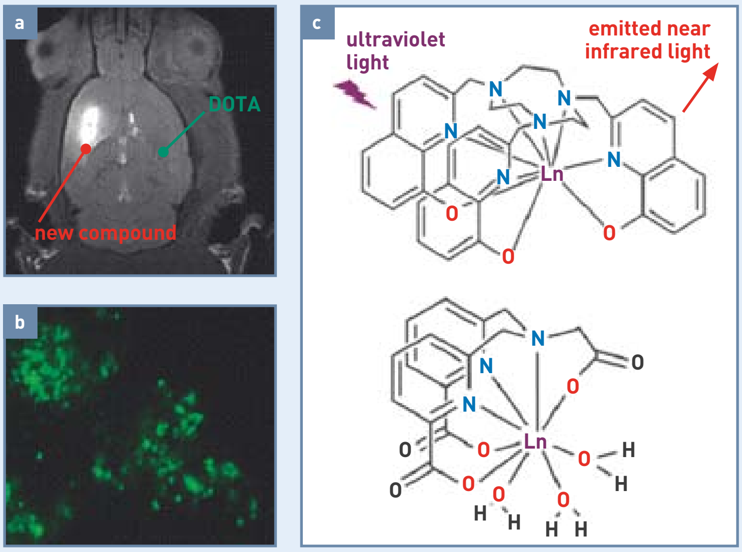
(5) Chatterton N. *et al, Angew. Chem., Intl. Ed. Engl.*, 2005, *44*, 7595-7598. Nonat A., *Inorg. Chem*, 2009, *48*, 4207-4218.

(6) Ionic Recognition and Coordination Chemistry Laboratory/Inorganic and Biological Chemistry Department (Laboratoire de reconnaissance ionique et chimie de coordination/Service de chimie inorganique et biologique).

(7) Nonat A., *Chem. Eur. J.*, 2006, *12*, 7133-7150 and 2007, *13*, 8489-8506.

(8) Samuel J., *Chem. Commun.* 2010, 2647-2649.

(9) Inorganic and Biological Chemistry Department (Service de chimie inorganique et biologique /SCIB) and Structures and Properties of Molecular Architectures Department (Service Structures et propriétés d'architectures moléculaires/SPrAM).



Left: Michel de Waard (Inserm/GIN/U836); right: CEA

Figure 2.
(a) MRI image of a rat brain 30 minutes after injection of the contrast agent; DOTA is the name of a commercial contrast agent; (b) Confocal image (optical imaging) of cells with the new labels developed (CEA, DSM, Inac-SPrAM and SCIB); (c) A few examples of new molecules leading to new magnetic (Ln = Gd) and optical (Ln = Tb, Yb) labels.

by coupling gadolinium complexes with quantum dot type fluorescent nanocrystals. Initial results are leading to nanometric contrast agents with high relaxivity, associating the magnetic and fluorescent modalities. The two images in Figure 2 were obtained with these compounds in collaboration with Michel de Waard's team at Inserm (Grenoble Institute of Neurosciences – Institut des neurosciences/GIN-U836). Moreover, in order to penetrate cells, or respond by amplification of the MRI signal during a biological process, current efforts aim to couple these compounds with molecules of biological interest (oligonucleotides, peptides, proteins, sugars, etc.).

Molecules labeled for atraumatic observation

Positron emission tomography (PET) is used in nuclear medicine departments, in particular in CEA's Service hospitalier Frédéric-Joliot (CEA/SHFJ). It is one of the high spatial resolution functional imaging techniques and stands out owing to its extreme detection sensitivity allowing *in vivo*, non-invasive and thus atraumatic detection of biological and physiological processes specific to humans. Its principle is based on the distribution (pharmacokinetics and pharmacodynamics) of a radioactive molecular structure (acting as a probe) allowing the observation of metabolic and neurochemical events and thus obtaining functional information about the target organ. A PET scan involves three phases:

- administration, generally intravenously, of a molecule labeled with a radioactive isotope (radiotracer);
- 3D visualization of the metabolic activity of an organ, by means of the emissions produced by the positrons resulting from the decay of the radioactive isotope;
- monitoring and mapping of the path of this radiotracer by means of external detection.

PET development is therefore closely linked to the availability of radiotracers specific to the pharmacological targets linked to the pathological processes to be diagnosed (neurological diseases, cancers, etc.). Of these radiotracers, fluorine-18, a short-lived positron-emitter (109.8 minutes radioactive half-life), highly efficiently manufactured by a nuclear transmutation reaction (in a cyclotron), is a radioisotope of choice for the development of innovative radiopharmaceutical products. This is illustrated in clinical oncology by the increasing use of a radiofluorinated derivative of glucose, 2-[^{18}F] fluoro-2-deoxy-D-glucose ([^{18}F]FDG). Owing to the maturity of its radiochemistry, fluorine-18 can also be used to label more complex molecular structures such as peptides, proteins and antibodies, oligonucleotides and their derivatives (Peptide Nucleic Acids/PNAs, aptamers), polysaccharides and nanoparticles or nano-objects.

Nonetheless, even if many macromolecules exhibit biological or pharmacological properties that are exceptional, or even ideal for molecular imaging, the complexity of their chemical structures and their high molecular weight require the development of special radiolabeling techniques(10), in particular when short-lived positron emitters such as fluorine-18 are used. The radiolabeling of these macromolecules, through conjugation with a prosthetic group carrying fluorine-18, is today the norm. Even if molecular fluorine was used to label peptides and despite recent developments in the chemistry of nucleophilic fluorine for single-step labeling, the prosthetic labeling of macromolecules today remains the most developed and most widely used. This strategy is comparable to a sequential process. The first phase consists in preparing a reagent with a low molecular weight carrying the fluorine-18 and the second phase in conjugating it chemoselectively and regioselectively with the target macromolecule. This approach offers the advantage of being able to dissociate the chemical preparation of the reagent labeled with fluorine-18 (multiple steps and using reagents and conditions that are rarely compatible with the chemical stability of the target macromolecules) from its covalent coupling with the macromolecule. This approach guarantees both conjugation of a single prosthetic group with the macromolecule and retention of its pharmacological and biological properties(11). Backed by highly promising methodological results in heteroaromatic radiofluorination, CEA recently focused on the preparation and use of new chemoselective reagents containing a given fluoropyridine structural pattern (Figure 3 a)(12).

A first series of compounds, chemically selective for functions containing a sulfur atom (thiols), includes

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(10) Dollé F. *et al,* Fluorine-18 chemistry for radioactive molecular imaging (radiotracer) with Positron Emission Tomography. In *Fluorine and Health: Molecular Imaging, Biomedical Materials and Pharmaceuticals*, Tressaud A. & Haufe G. (Eds), Elsevier, Amsterdam, 2008, Chap 1, 3-65.

(11) Kuhnast B. *et al, Curr. Radiopharm.* 2010, *3(3)*, 174-201.

(12) Dollé F., *Curr. Pharm. Design* 2005, *11(25)*, 3221-3235.

the molecules named [^{18}F]FPyME, a reagent with a maleimide function and [^{18}F]FPyBrA, a reagent with an alpha-bromoacetamide function. A second series of compounds, chemically selective of azide and/or alkyne functions, which can in particular be synthesized using a simplified process (single-step), opens up new prospects for labeling of macromolecules with fluorine-18, using the selective reactions of cycloadditions. This class includes the molecule named [^{18}F]FPyKYNE. The reagents [^{18}F]FPyME and [^{18}F]FPyBrA have so far been successfully used to label various macromolecules (Figure 3 b) including peptides and proteins, oligonucleotidic sequences (single strand, aptamer, SiRNA, Peptide Nucleic Acids/PNAs) and, more recently, nano-objects. Particularly noteworthy is the fluorine-18 labeling of two aptamers: D4-36, a macromolecule targeting the RET tyrosine kinase transmembrane receptor, and TTA-01, a macromolecule targeting human tenascin-C. Worth-mentioning is also the labeling of semiconductor nanocrystals (QD) encapsulated in functionalized phospholipid micelles.

Molecular imaging using MRI and PET offer wonderful prospects for fundamental research, in particular for the chemistry of tracers. It should however never be forgotten that the design of an innovative tracer, dedicated to human injection, implies precautions that are the same as those for introduction of a new drug into the pharmacopeia. The possibility of the toxicity of a product shall always be considered, even if in most cases, the patient will receive a single administration of very small quantities of the compound.

The work done by the various teams at CEA should shortly be leading to new developments in the field of patient diagnosis (non-invasive and atraumatic visualization of pathological biochemical events, at the level of the organ, the cell, or even the molecule) and treatment (validation of the therapeutic effectiveness and assistance with interventional surgery).

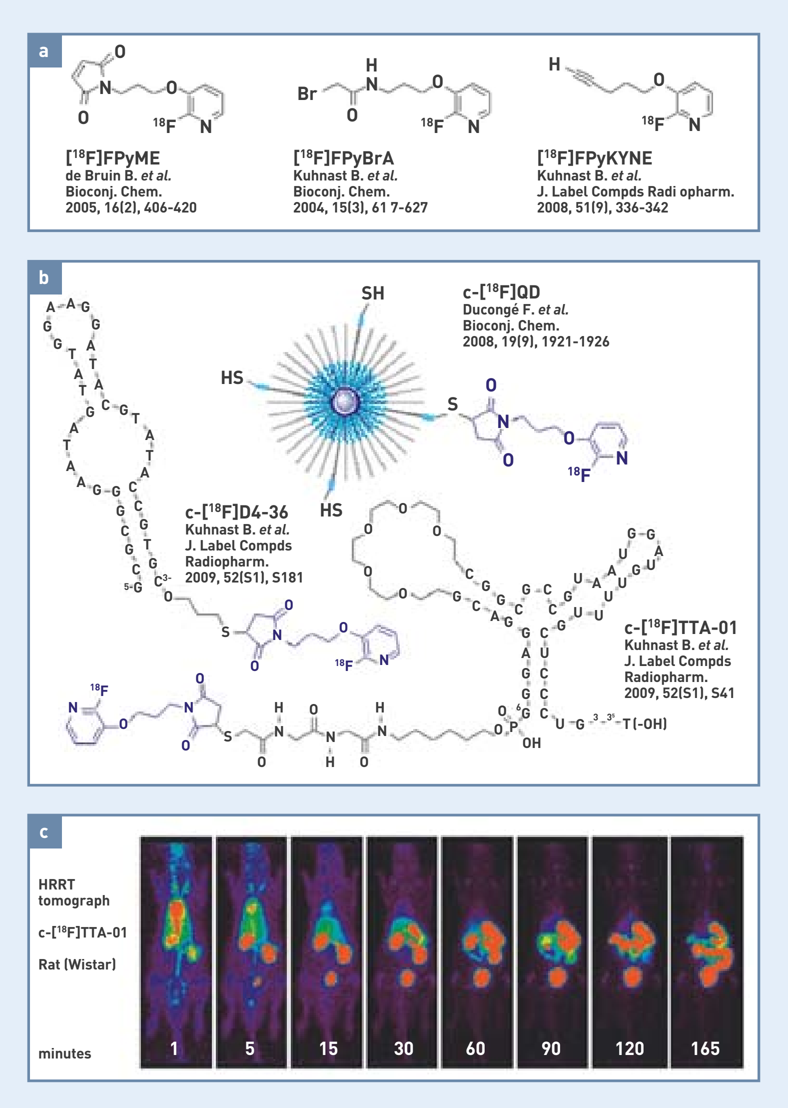

Figure 3.
(a) Reagents labeled with fluorine-18 by nucleophilic substitution in heteroaromatic series and directed chemoselectivity towards the thiol, phosphorothioate and azide functions.
(b) Application of [^{18}F]FPyME, a maleimide type radiofluorinated reagent, to the prosthetic labeling of aptamers (c-[^{18}F]D4-36 and c-[^{18}F]TTA-01) and semiconductor nanocrystals (QD) encapsulated in functionalized phospholipid micelles.
(c) Whole-body images obtained with the HRRT tomograph in rodents after *in vivo* injection of aptamer c-[^{18}F]TTA-01.

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> **Nathalie Herlin-Boime**
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> **Bertrand Kuhnast** and **Frédéric Dollé**
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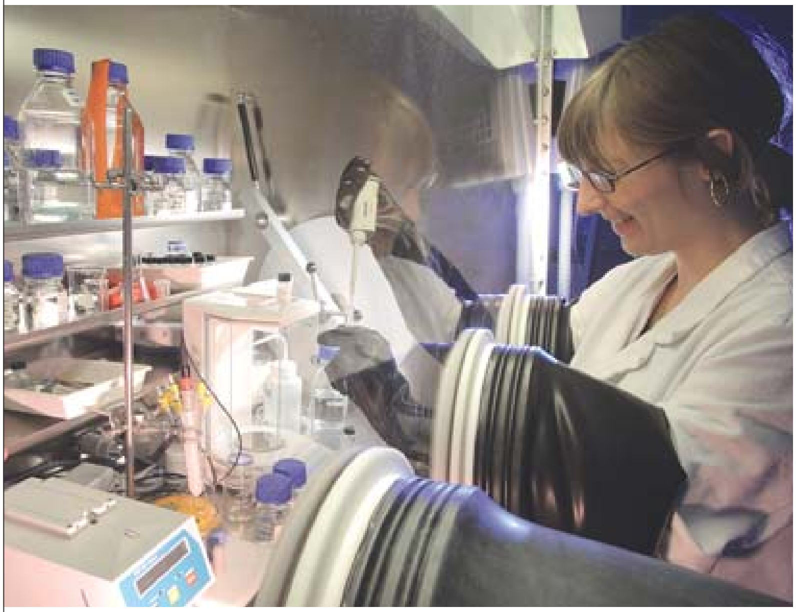
CEA/Service hospitalier Frédéric-Joliot (SHFJ)
Life Sciences Division
CEA, Orsay


C.Boulze/CEA

Positioning products in the shielded cell of the Zymate XP robot (USA) at the Service hospitalier Frédéric-Joliot (SHFJ).

Drug design for optimizing pharmacotherapeutic molecules

In order to boost the effectiveness of our drugs or to create new ones, researchers are no longer content to observe and test existing substances: they are "designing" new ones. This technique is known as Structure Based Drug Design (SBDD). It is extremely sophisticated and combines advances in chemistry, molecular and cellular biology, pharmacology, but also numerical simulation. Researchers can now predict the effects of a substance on the organism even before it is manufactured and placed on the market: this is nothing short of a revolution for the pharmacopeia.


P.Avavian/CEA

Handling chemical compounds sensitive to the oxygen in air in a glovebox containing an inert atmosphere (argon).

In ancient times, doctors would treat empirically using natural products. Centuries were to pass before science would identify the active ingredients of drugs, manufacture them by chemical synthesis, decode their action mechanisms, and so on. This continued until the 1970s, when new tools for exploration of proteins and genes would lead to an understanding of the living world at the molecular level. Hence the appearance of "pharmacophore" molecules programmed to reach their target and perform their function, leading to new drugs, a few examples of which are given here.

Wilson's disease soon vanquished?

This disease is triggered by a malfunction of the copper regulating system in the organism. It affects from 1,000 to 1,500 people in France. When it builds up in certain parts of the body, such as the eyes, the central nervous system, the liver, etc., copper can cause neurological, psychiatric or hepatic (cirrhosis) symptoms, liable to require a liver transplant.

A sickness linked to an excess of copper

Copper is a trace-element essential for growth, bone strength and the working of the red and white corpuscles. It is encountered in many types of food: crustaceans, broccoli, mushrooms or chocolate... It exists in two soluble oxidation states: the reduced state Cu (I) and the oxidized state Cu (II). When in excess in the organism, it can generate oxidizing species that are extremely harmful for the cells. Hence the need to regulate the copper concentration by a set of proteins – an operation known as homeostasis of copper.

To understand this disease, one must be aware that the deficient gene, responsible for this disease, codes for a protein transporting copper in the liver, called the Wilson disease protein(1), or ATP7B. It distributes the copper to the enzymes that need it, or excretes it to the bile duct when there is too much. When this surplus copper is no longer correctly eliminated, it builds up in the organism and the disease is triggered. There are treatments for limiting the absorption of copper through food: D-Penicillamine and trientine. This old and relatively unspecific pharmacopeia has a two-fold drawback: limited effectiveness in certain patients and significant side effects. Hence the urgent need for a new drug.

A rational approach to new and more specific treatments

For the researchers at the Institute for Nanosciences and Cryogenics (Inac), improving the Wilson's disease treatment involves the development of chelating agents capable of hunting out the surplus copper stored in the liver, without interacting with other essential metal ions. However, the molecules capable of trapping the copper in its predominant form in the cells – copper (I) – still had to be synthesized and given a system for guiding them to the liver. This molecule possesses two units: the first chelating the copper (I) and the second targeting the liver

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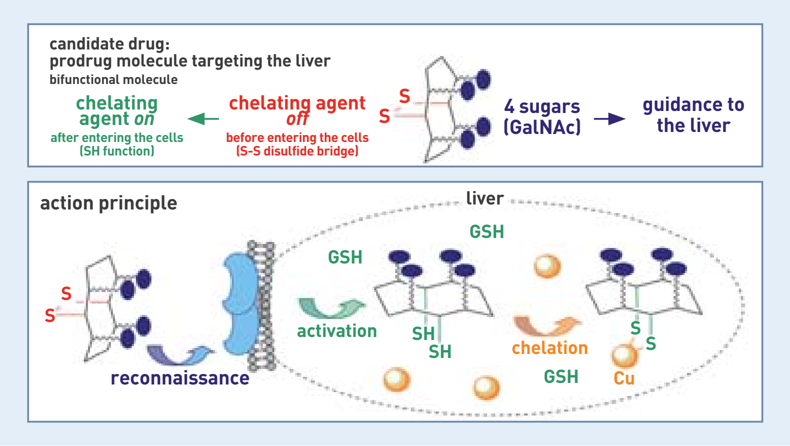
(1) WILSON (Kinnier), a British neurologist (1878-1937) who worked in particular with Pierre Curie and Joseph Babinski, holder of the Neurology Chair at King's College. He described the disease bearing his name in 1912.

cells (hepatocytes). To avoid trapping other essential metals, it generally takes a prodrug form, that is only active after it enters the target cells (Figure 1).



CEA

Figure 1.
Design and action principle of a prodrug bifunctional molecule, chelating copper(I) and guided to the liver cells. The bifunctional molecules presented comprise a system guiding them to the liver cells (sugars shown in blue). These sugars are recognized by receptors on the surface of the liver cells, enabling the chelating agent to enter these cells. The chelating agent is said to be *Off* (in red) before it enters the cells because it cannot chelate the Cu(I) ions. After it enters the cells, the chelating agent is activated by glutathion (GSH) and its state is then said to be *On*, because the thiol functions (SH in green) are released. It can then chelate the Cu(I).

- Strategy for chelating copper (I):

The proteins involved in the homeostasis of copper are those used as the models for producing copper chelating agents that are effective in the cells. Transporters, such as the copper "chaperones", or "sequestering agents" such as metallothioneins, bind the copper in the reduced state Cu(I) thanks to cysteines, in other words, natural α-amino acids with a thiol group (SH). The thiol chemical functions enable these proteins to effectively and selectively bind the copper (I). These α-amino acids act as the basic building blocks for constructing the chelating unit and obtaining molecules capable of mimicking the chelating power of living proteins. The chelating agents produced in the Inorganic and Biological Chemistry Department (Service de chimie inorganique et biologique/SCIB(2)) thus carry two or three cysteines grafted onto a chemical platform and thus offer several convergent thiol functions for trapping the copper thanks to the sulfur atoms.

- Liver cells targeting strategy:

To target the chelating agents on the liver, the SCIB exploits a property of liver cells, the surface of which exhibits numerous receptors capable of specifically recognizing sugars, such as *N*-acetylgalactosamine. One need simply insert three or four units of this type of sugar into a given molecule to encourage its interaction with these receptors and thus entry of the molecule into the liver cells. Hence the idea of "decorating" the most effective chelating agents with sugar units to guide them to the liver.

These new sulfur molecules are thus proving to be highly effective in trapping the copper, to the exclusion of the other metals in the organism (calcium, zinc, etc.). Moreover, their ability to bind the copper in liver cells was recently highlighted by the Laboratory of Chemistry and Biology of Metals (Laboratoire de chimie et biologie des métaux/LCBM)(3). These new chelating agents are thus highly promising for the fight against excess copper in the liver, which is the cause of Wilson's disease. Tests are still required to validate their use as potential drugs.

New uranium decorporating agents

Assuming an accidental release of radionuclides within a nuclear facility or into the environment, the researchers at CEA have for many years been examining the risk of acute or chronic internal contamination through inhalation, ingestion or wound, leading to chemical(4) and/or radiological(5) toxicity, depending on the causal element. Since the early 2000s, research has been intensifying in the field of nuclear toxicology, especially concerning the treatment of contamination (or decorporation). It is precisely by focusing on the chemical approach that the researchers were able to develop new decorporating agents for uranium. This approach allowed the design and synthesis of ligands capable of *in vivo* complexing of the uranyl ion (UO_2^{2+}) which is predominantly present in the biological medium, while at the same time meeting significant constraints for these ligands: strong association with metal, selectivity in relation to the biological cations (calcium, potassium, etc.), non-toxicity and good bioavailability. This result was achieved by implementing two strategies:

- a rational approach, based on physical-chemical and steric factors such as the geometrical adaptation of the ligand to the atomic dimensions of the uranyl ion by molecular modeling – an approach that was validated by the production of highly stable uranyl complexes;
- an approach based on the synthesis of banks of molecules and high-throughput screening, commonly used by the pharmaceutical industry for the design of new drugs. The researchers can now select ligands combining strong affinity and good

P.Avavian/CEA

Fluorescence microscope visualizing the Wilson protein in liver cells. The non-functionality of this protein leads to severe copper toxicosis, through build-up of copper in the tissues.

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(2) A department of the Institute for Nanosciences and Cryogenics (Inac).

(3) Laboratory of the Institute of Life Sciences Research and Technologies (iRTSV).

(4) Dose expressed in mass or moles

(5) Dose expressed in grays (Gy) or sieverts (Sv).

P.Avavian/CEA

Left: freezing a solution containing a fluorescent chelating agent.
Right: agitation of a chemical reactor during the synthesis of peptides on a solid medium.

selectivity *in vitro*. A "chemical library" comprising more than 300 ligands, has already been subjected to the screening steps. This operation, carried out at the Bio-organic Chemistry and Labeling Department (Service de chimie bio-organique et de marquage/ SCBM(6)), highlighted the remarkable properties of a family of bisphosphonate molecules (Figure 2). These compounds proved to be highly effective in complexing the uranyl ion with very high affinity constants in a physiological medium. *In vivo* tests demonstrated the decorporating effectiveness of these bisphosphonates, in terms of retention, excretion and distribution within the various organs. They also led to the selection of molecule 19E (Figure 2) capable of achieving a 10% increase in the excretion of the uranium injected and a reduction of about 50% in the uranium fixed in the kidney.

Similar important work was done on other radionuclides of interest: on the one hand for plutonium, for which there is currently a reference molecule, DTPA and a molecule currently under development, LIHOPO, as well as for cesium, for which the reference molecule is Prussian Blue. Other applications of trientine and D-penicillamine (mentioned for copper) were recently tested for treatment of contamination by cobalt (Co (II)) and polonium (Po (IV)), two cations close to soft cations like copper (Cu (I)) and which therefore have an affinity for sulfur molecules. Prospects in the field of contamination treatment on the one hand concern the vectorization of the ligands in order to improve their effectiveness and their residence time in the organism and, on the other hand, the search for formulations that can be assimilated *via* the digestive tract.

F.Rhodes/CEA

Study of the effect of uranium on wheat and rapeseed

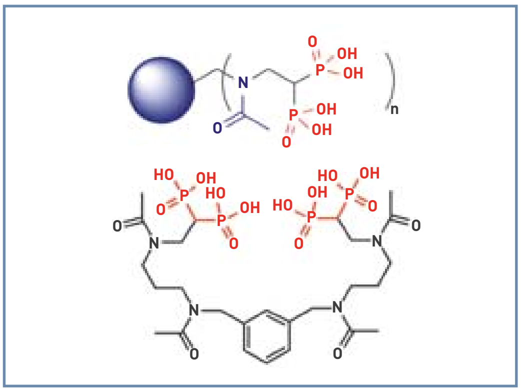

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Figure 2.
Examples of ligand structures with a uranium decorporation potential. Top: general structure of bisphosphonates; bottom: structure of the bisphosphonate 19E dipod.

Bioactive molecules for innovative drugs

Better understanding of certain biological functions for the design of new drugs presupposes prior development of biologically active molecules. Hence the studies conducted by the researchers at the SCBM, who are examining the properties of certain natural or synthetic molecules, in collaboration with teams of biologists.

Fighting cancer with glycosidase inhibitors

Glycosidases are enzymes capable of catalyzing the cleavage of sugars by hydrolysis, a process that is essential when generating molecules with a lower molecular weight (monosaccharides or disaccharides). Nonetheless, these enzymes sometimes perform aberrant glycosylation and hydrolysis that are responsible for pathologies: type II diabetes, genetic diseases (influenza, Fabry and Gaucher disease). Hence the need to develop glycosidase inhibitors, some of which are already on the market: Glucobay® (anti-diabetic), Zavesca® (treatment of Gaucher's disease), Relenza® and Tamiflu® (treatment of influenza).

Developing antiviral, but also anti-tumor agents, implied a clearer understanding of enzyme mechanisms. By studying one of them, the hydrolysis of glycosidases, the chemists at the SCBM succeeded in designing new inhibitors, analogues of the transition state of this reaction. They demonstrated how these compounds mimic the sugar structure to be hydrolyzed and present on the active site, during enzymatic catalysis. This was followed by the multi-step synthesis preparation of inhibitors derived from glucose and mannose with a diversely substituted amidine function, and then testing in the presence of glycosidases (Figure 3). One of the mannose derivates proved to be 30 times more effective than the other alpha-mannosidase(7) inhibitors, a performance making it the most powerful and most selective inhibitor as yet identified.

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(6) A department of the Institute of Biology and Technologies – Saclay (iBiTec-S).

(7) $K_i = 6$ nM (K_i = inhibition constant and nM = nanomolar).

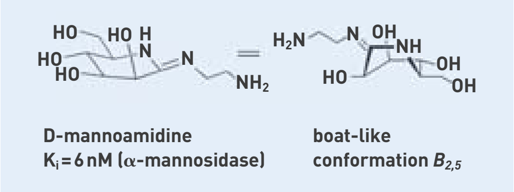

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Figure 3.
Structure of the inhibitor derived from D-mannose carrying an exocylic ethylamine function, the best synthesized mannosidase inhibitor (K_i being the inhibition constant).

At the same time, the SCBM researchers carried out studies into the kinetics of inhibition and co-crystallization with a human beta-mannosidase, taken from *Bacteroides thetaiotaomicron* bacteria. The results of RX co-crystallizations (resolution of 2.1 Å)(8) show inhibitors with an unusual "boat-like" conformation(9) with this beta-mannosidase (Figure 4). The transition state of the reaction probably adopts the same conformation, a result that no laboratory had been able to evidence hitherto. The glycoamidines synthesized in the laboratory, with a boat-like conformation(10) $B_{2,5}$, thus act as inhibitors competing with the beta-mannosidase of the *Bacteroides thetaiotaomicron* but probably also as inhibitors of the transition state. This study promises a bright future for glycosidase inhibitors as new therapeutic agents, in particular for cancer treatment.

Antioxidant molecules

Whether in the event of a radiological incident during medical treatment such as radiotherapy, a nuclear accident, an act of terrorism, etc., it is possible that ionizing radiation, high-energy radiation, can damage the tissues of living organisms(11) – DNA being one of its prime targets. Hence the development of compounds able to counter the harmful effects of this radiation on the organism – a major challenge for the CEA researchers.

It is true that a living organism has systems to protect itself against the reactive species of oxygen - antioxidant molecules (glutathione) or enzymes (*superoxide dismutase*) in particular. However, in the case of strong irradiation, they are not sufficient. Antioxidant compounds that can protect the organism and that are easily absorbable before or after the irradiation still have to be designed. A multidisciplinary team of researchers from CEA(12) brought to light an exceptionally effective antioxidant product: norbadione A (Figure 5). This compound, isolated from the *Boletus badius* mushroom and similar to pulvinic acids, acted as the starting point for the SCBM researchers in the synthesis and then evaluation of a large number of analogue molecules (Figure 6) and thus the determination of structural elements promoting antioxidant activity(13). The bioavailability of these compounds was augmented by modifying various functions and two molecules then demonstrated a significant radioprotective effect. A study project concerning the development of one of these molecules is currently under evaluation.

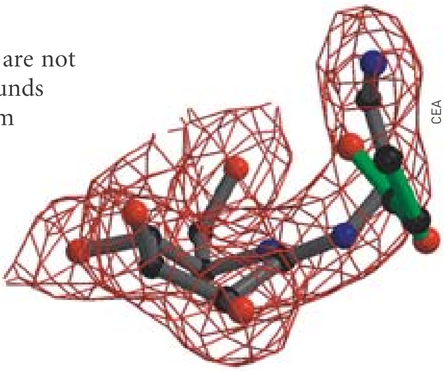

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Figure 4.
Co-crystallization of the inhibitor with BtMan2A (beta-mannosidase 2A). The bonds between the atoms are shown in grey and green, with the oxygen atoms (red), nitrogen atoms (blue) and carbon atoms (black) shown at their ends. The red envelope corresponds to the electron density map of the molecule allowing determination of the precise structure of the molecule.

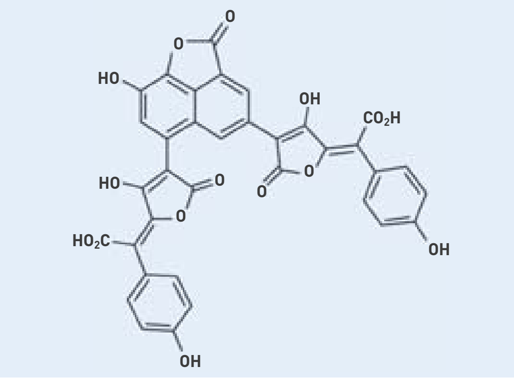

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Figure 5.
Structure of norbadione A, a pigment of *Boletus badius*.

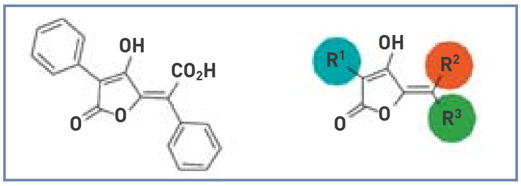

Figure 6.
Pulvinic acid, analogues with modification sites.

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Physical Sciences Division
CEA Grenoble Center

> **Éric Ansoborlo**
Radiochemistry and Processes Department
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(8) When an inhibitor shows very good affinity for an enzyme, X-ray (RX) radiocrystallography in a synchrotron can be used to obtain the electron density of the molecule, after calculation of the inverse Fourier transform; the lower the resolution value obtained, the more precise the details obtained: 2.1 Å is thus an extremely detailed result. For an atomic level resolution, 1 Å would be needed.

(9) So named because the structure of the molecule resembles an upturned boat hull.

(10) The inhibitor has the shape of a boat: the main cycle, with six atoms, can take the form of a chair or a boat and our co-crystallization study shows that on the enzymatic site, the inhibitor takes the form of a boat.

(11) It is through a reaction with the water contained in the organism, that reactive species of oxygen are produced (superoxide or hydroxyl radical ion). These species are capable of destroying biomolecules.

(12) Bio-organic Chemistry and Labeling Department (Service de chimie bio-organique et de marquage/SCBM), Pharmacology and Immunoanalysis Department (Service de pharmacologie et d'immuno-analyse/SPI), Interdisciplinary Department of Molecular Systems and Materials (Service interdisciplinaire sur les systèmes moléculaires et les matériaux/SIS2M).

(13) As part of a study financed by the Direction générale de l'armement (DGA)

New **sensitive and selective sensors**

Discriminating pathogenic bacteria for **non-invasive diagnosis of diseases, studying how to repair DNA, preventing terrorism, detecting biological toxins or evaluating the immune response of certain patients infected by the hepatitis C virus ...** No matter how seemingly different these areas of research, they all have one factor in common: the design and use of innovative sensors.

Production of chemical sensors with optical transduction, based on nanoporous materials doped with molecular probes to detect gaseous pollutants.

C. Dupont/CEA

The sensor is the basic instrument for collecting data about the environment but it must ensure that the various physical values are usable for subsequent processing. A new wave of sensors is today arriving in the laboratories, resulting from R&D in which chemistry plays a decisive role. From research to industry, the chemists are sharing common or similar investigative ground with the physicists designing innovative detection processes, the biologists who test them and the manufacturers who bring them to the market.

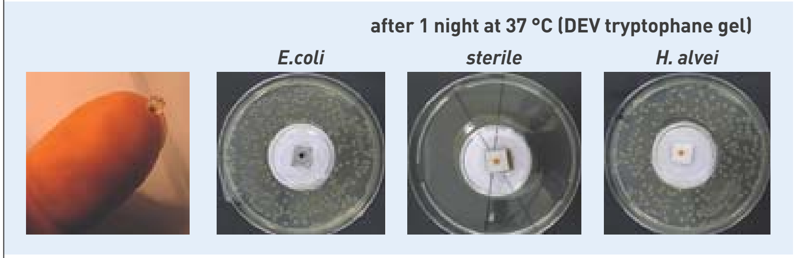

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Figure 1.
Test to detect gaseous indole generated by the bacteria. The transparent nanoporous sensor, doped with dimethyl-aminocinnamaldehyde (photo left), is placed on a glass plate containing a desiccant, positioned in the centre of the Petri dish. The desiccant is justified by the fact that the bacteria grow in a warm and wet atmosphere: the water can enter the pores and change the acidity of the nanoreactor, which then becomes less efficient.
The Petri dish contains an agar culture medium in which the bacterial colonies will grow. After 7 hours, the coloring is already visible and intensifies over time. The sensor turns green owing to the build-up of indole generated by *Escherichia coli*. The test is negative for both *Hafnia alvei*, which does not produce any, and the sterile sample. The color in this case is orange (see Figure 2).

Targeting trace levels of VOCs

Sniffing out odors to identify pathogenic bacteria and diagnose diseases non invasively: the concept is not a new one and already goes back some twenty years. Well-established labels are, for example, ammonia coupled with CO$_2$ for gastro-intestinal infections caused by the bacterium *Helicobacter pylori*. In most cases, one must be able to detect trace quantities of volatile organic compounds (VOC) emitted by these micro-organisms. Numerous laboratories around the world are active in attempting to identify these VOCs. This operation required the use of major detection resources such as gas phase chromatography (GPC), proton transfer coupled with mass spectrometry or chemical ionization, also coupled with mass spectrometry, to produce a data bank of specific markers. As numerous VOCs can be emitted at different concentrations by various bacteria, discriminating between them comes up against a two-fold obstacle: detecting certain VOCs in low quantities (ppb) and quantifying their production rate versus time. At present, however, none of the electronic or colorimetric noses available on the market or described in the literature can meet these two conditions. Hence the idea by the researchers of designing innovative sensors capable of combining high sensitivity and selectivity at the same time as being able to quantify the production rate of the metabolite. Their principle is based on nanoporous matrices of organic/inorganic hybrid polymers, produced from silicon alkoxides, using the sol-gel process, which is both simple and inexpensive. The interest of these materials, with a high specific surface area of adsorption (600 to 750 m^2·g^{-1}), lies in their multifunctionality. They act as veritable sponges, capable of accumulating VOCs, while filtering them according to the size of their pores. Moreover, once doped with molecular probes capable of reacting specifically with the target VOCs, these materials become nano-reactors enhancing the chemical reactions by offering the sensor increased selectivity.

The researchers obtained the proof of the effectiveness of this concept by attempting to discriminate between two bacteria: *Escherichia coli* and *Hafnia alvei* – the first being capable of generating indole in a culture medium containing tryptophane, while the second is not. Hence a specific sensor was produced, using a material with a sufficiently large pore size to trap indole molecules (Figure 1). This sensor was doped with a molecular probe, dimethyl-aminocinnamaldehyde (DMACA), whose reaction with indole leads to the formation of a heavily colored (blue-green) azafulvenium salt, absorbing in the visible radiation domain, with a maximum centered at 625 nm (Figures 2 and 3). The rate of formation of the azafulvenium chloride is proportional to the concentration of indole in a broad range of concentrations ($5{\cdot}10^{-7}$ to $2{\cdot}10^{-4}$ mole·L^{-1}) and the sensitivity achieved with a reagent pellet lies between 0.1 and 40 nanomoles of indole with a 20 µL sample of the solution to be analyzed. This concept could be extended to a large number of target VOCs, with numerous applications in the health and agro-industry fields. The search for markers for early diagnosis of cancers, for example, is a growth industry. Similarly, in the agro sector, monitoring the freshness of foods and early detection of food contamination by pathogenic bacteria during their transformation are of considerable importance, with major economic implications for companies.

Quantifying DNA repair with biosensors

DNA is constantly being subjected to endogenous or exogenous agents able to damage it, or responsible for mutagenesis processes or cell death. Fortunately, various enzymatic repair mechanisms can deal with this damage, eliminate it and restore the integrity of the genetic message. Deficiency in the DNA repair capability can lead to the appearance of cancers. These repair mechanisms can therefore be called "guardians of the genome". Moreover, given that the over-expression of DNA repair proteins is linked to the resistance of certain cancers to anti-tumor treatments, one of the strategies for limiting this phenomenon is to combine chemotherapy or radiotherapy with a repair inhibitor. So, given the essential role played by DNA repair systems, the aim of the researchers is to measure the enzymatic activity of these systems, as precisely as possible.

Conventionally, DNA repair by excision/resynthesis(1), is measured by means of functional tests using radioactive nucleic probes coupled with analysis by electrophoresis. The time-consuming, tiresome analytical approaches cannot be used for routine, high-throughput analysis of large numbers of biological samples. The researchers at the Nucleic Acids Lesions Laboratory(2) have developed new DNA biosensors using fluorescent detection, in solution or on a support. These new biosensors now allow quick and easy functional analysis of base excision repair (BER) enzymes or protein complexes of nucleotide excision repair (NER), two repair mechanisms based on the excision of lesions and the resynthesis of the DNA.

The goal of one of these innovative biosensors is to measure different DNA repair activities. This is a functional test, based on the use of fluorescent or profluorescent oligonucleotide probes (fluorescence initially quenched). As shown in Figure 4, the different oligonucleotides, each containing a distinct lesion, are synthesized and then used either in solution (micro-tube or micro-plate format), or fixed to a biochip type solid support. This biosensor, both miniaturized and multiplexed (simultaneous fixing of several sequences), can measure the activity of purified enzymes but also quantify activity within cell extracts (cancerous cells or skin primary cells, blood, etc.). It led to the discovery and study of repair inhibitors.

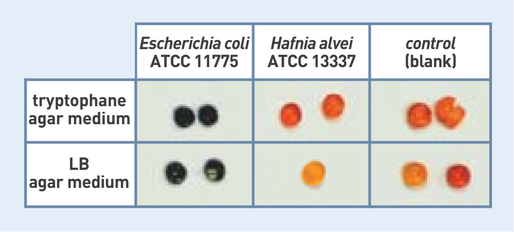

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Figure 2.
Standard strain marketed by LGC Standards, whose Research and Technology Department represents the British National Physical Laboratory for chemical and biochemical analyses: exclusive European distributor of *American Type Culture Collection* (ATCC) *biomaterial* the number of which indicates the origin of the strain.

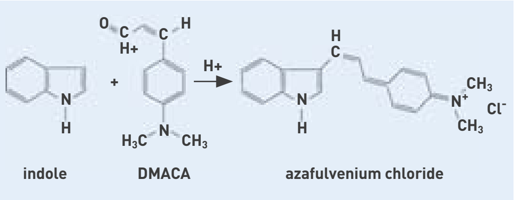

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Figure 3.
DMACA: 4-(N,N-dimethylamino)cinnamaldehyde or 4-(N,N-dimethylaminophenyl)propenal.
Azafulvenium chloride or 3-[4-(N,N-dimethylaminophenyl)-2'-propenylidene]indolinine hydrochloride.

A similar approach was developed to access DNA repair as a functional protein network. This uses the immobilization of circular plasmids carrying specific DNA lesions on biochips covered with hydrogel (Figure 5). Repair activities, belonging to different mechanisms, are quantified on it simultaneously, which makes it possible to determine specifically activated or inhibited, co-regulated or independent pathways, by means of dedicated bioinformatic tools.

Apart from the time saved and the user-friendly format, this type of approach also has the advantage of offering a new dimension and new drive to the research being carried out in DNA repair field. It will be possible, to test large populations and using high-throughput screening to identify inhibitors, to study the impact of drugs (toxic or anti-cancerous) on the repair mechanisms – the short-term objective then being to develop translational research and ensure the transition from these tests to clinical and pharmaceutical applications.

Nanotechnologies for neurotoxic gas detectors

The spread of international terrorism means that thought must be given to how to prevent potential threats, in particular from easy-to-use combat gases, which have a strong psychological effect and media impact. As shown by the sarin attack on the Tokyo metro in 1995, the use of chemical weapons by terrorists can affect large numbers of the civilian population. A rapid response to a combat gas attack requires the use of sensors performing an extremely rapid alert function, specific to the type of gas used, in order to immediately trigger protection and intervention procedures and the treatment of any injuries.

(1) This is a process involving cleavage, elimination of the lesion and then synthesis of undamaged DNA.

(2) Laboratory of the Inorganic and Biological Chemistry Department (Service de chimie inorganique et biologique/ SCIB) of the Institute for Nanosciences and Cryogenics (Inac).

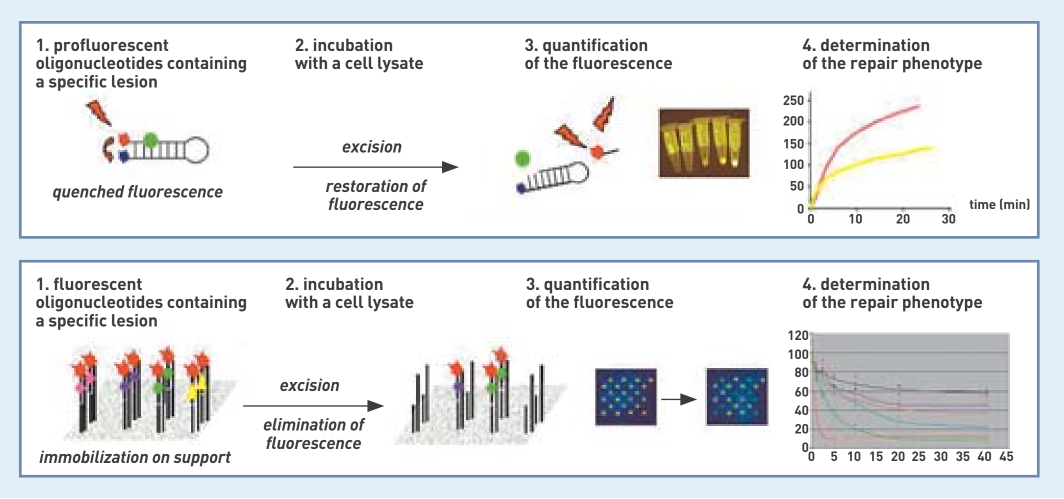

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Figure 4.
Schematic representation of the tests to detect the DNA repair activities through excision by the BER enzymes, using profluorescent oligonucleotide probes in solution (top) or fluorescent probes on support (bottom).
The top figure shows a self-complementary oligonucleotide, containing a lesion of interest, which organizes into a "hairpin" duplex in which the two chromophore molecules, situated at each end of the structure respectively, are very close. When the donor fluorochrome is excited, at a specific wavelength, the energy it emits is absorbed by the "quenching" chromophore. The fluorescence is then extinguished and no signal is measured (1). During incubation in solution with a repair enzyme recognizing the lesion, or an extract containing specific repair activities, the lesion is cleaved and the donor fluorochrome is released simultaneously in solution (2).
Its excitation at the specific wavelength leads in these conditions to the emission of fluorescence which is quantified and increases with the digestion time (3). It is thus possible in real time to monitor the kinetics of enzymatic cleavage (4); red and yellow curves: simultaneous quantification of two repair activities characteristic of a given sample.
The bottom figure shows oligonucleotides containing DNA base or sugar lesions, labeled by a fluorochrome, immobilized by hybridization on a previously functionalized glass slide, which generates fluorescent spots (diameter 250 μm). Simultaneous fixing of distinct lesions, at predetermined positions on the support, allows the test to be multiplexed and thus the performance of simultaneous quantification of several repair activities specific to each lesion (1). The biochip prepared in this way is incubated in the presence of a cell extract or of the repair enzymes to be characterized (2). Repair of the lesions fixed on the support by the enzymes contained in the biological medium is associated with the cleavage of the recognized oligonucleotides and the elimination of the fluorescence of the support. By quantification of the residual fluorescence using a scanner, the effectiveness of the cleavage of the various lesions by the enzymes contained in the medium (3) can be determined; the red spots on the biochip before the reaction turn green after cleavage. The kinetics of lesion cleavage by the enzymes in the medium are thus established and a repair phenotype is determined, characteristic of the repair capacity of the initial biological sample (percentage cleavage of each lesion). Each slide (75×25 mm) comprises 24 biochips, corresponding to 24 reactions conducted in parallel.

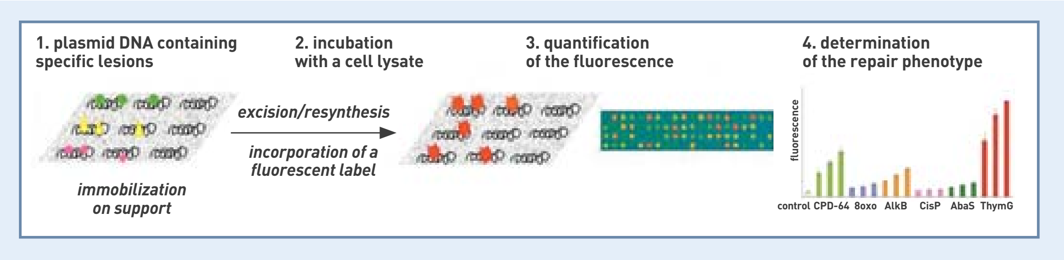

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Figure 5.
Schematic representation of the test to detect DNA repair activity by excision/resynthesis with protein complexes of BER or NER, using plasmid probes immobilized on a support.
Plasmids containing specific lesions in different quantities created by physical or chemical agents (ultraviolet radiation, oxidization, photo-sensitization, acid treatment, etc.) are immobilized at predetermined positions on a micro-support covered with a hydrogel (1). This latter allows the long-term preservation of the DNA. The biochip thus prepared is incubated in the presence of a cell extract to be characterized (2). The lesion excision and undamaged DNA resynthesis reaction by the enzymes contained in the biological extract leads to the incorporation of fluorescence (red stars), which is then measured with a scanner (3: false-color image of the biochip).
The intensity of the fluorescence measured is proportional to the quantity of lesions present on the plasmids (3 lesion/DNA ratios) and to the effectiveness of the repair enzymes present in the biological medium and specific to each type of lesion.
The histogram in (4) shows the repair phenotype of a sample, with the measurement of 6 different repair activities (one per color).

Today, there are various devices sensitive to toxic gases but which are sometimes inadequate for certain types of surveillance or intervention. In the future, the growth of nanotechnologies, in particular the coupling of chemical functionalization and nanomaterials, should open up new prospects for the production of miniature sensors that are highly sensitive and selective, for the detection of toxic compounds. Recent studies into the use of silicon nanowires functionalized by molecular chemical receptors, have highlighted an excellent capacity for immediately and extremely selectively detecting organophosphate (OP) toxic compounds – a family of neurotoxic molecules that includes sarin. The principle of these new sensors lies in the receptor molecules specific to this type of toxic compound, prepared by means of several organic synthesis steps and then grafted onto very small silicon wires about 100 nm in diameter. In the presence of the targeted toxin, the grafted molecules react with the gas and create electrical charges. In the immediate proximity of the silicon nanowire, these appreciably modify the passage of the electrical current through the silicon. Simply by measuring the electrical current in the device versus time, it is then possible to find out whether the molecules have reacted and thus whether the presence of a toxic gas has been detected (Figure 6).

Flexible, versatile chemistry for biochips

Today, thanks to miniaturized systems such as biochips, researchers can detect target molecules present in a biological sample. In this case, the molecular probes recognize the targets present in the solution to be fixed on the surface of the biochip. In the 2000s, DNA was the target of choice and the researchers optimized their chemistry so as to be able to fix this type of molecule. Since then, the spectrum of use of these objects has broadened considerably, going well beyond the DNA/DNA interaction. It is therefore now possible to detect antibody/antigen molecular assemblies (toxins, allergens, etc.), or even more complex assemblies such as antibodies with cells or bacteria. The chemistry used to fix these various molecule classes therefore has to meet a whole series of criteria:

- versatility;
- ability to adapt to the detection mode of the interaction used: fluorescence, plasmonic resonance, mechanical sensor, etc.
- ability to adapt to the micro, or even nanostructuring processes necessary for construction of the biochip.

The Chemistry for Recognition and Study of Biological Assemblies (Creab)(3) group therefore decided to work on the functionalization of thin layers of gold (a few tens of nm) owing to its particular optical properties, in particular called into play during plasmonic measurements, but also its ease of use in microelectronic processes. The group thus developed electrochemical deposition processes able to immobilize molecules on a large number of conducting surfaces, including gold. The principle is to functionalize the molecular probes by using a pyrrole and then copolymerizing them with free pyrrole on a conducting surface. As this reaction takes place in a saline aqueous medium at neutral pH, in other words in physiological conditions, it remains compatible with numerous molecules of biological interest, and the interactions measured today are proving to be many and varied. This thus opens the door to fields of application as yet very little explored. Furthermore, the deposition processes developed allow functionalization of the surfaces, not only by functionalized polymer spots a few nanometers thick and whose diameter can be adjusted over a range from a few hundred nanometers up to a millimeter, but also surfaces with micro or nanometric pores. This great flexibility allows easy adaptation to biological needs as varied as the detection of rare toxins in a sample of water, the analysis of blood cells, or even positioning of nano-objects.

There is a two-fold advantage to this great operating flexibility: that of adapting to a large number of interaction detection processes, whether optical or electrochemical, with or without tracers, and that of covering a broad range of biological applications. For example, with regard to environmental protection, the researchers now have highly sensitive systems for detecting biological agent toxins; in the medical research field, these processes can also be used to evaluate the immune response of patients infected by the hepatitis C virus, the search for biologically active oligosaccharides, the organization and characterization of human cells on microstructured surfaces, etc.

It thus remains essential for the chemistry to be developed in close collaboration with the physicists involved in the detection processes, with the biologists responsible for the applications, but also, and wherever necessary, with the relevant industries for practical implementation of the results.

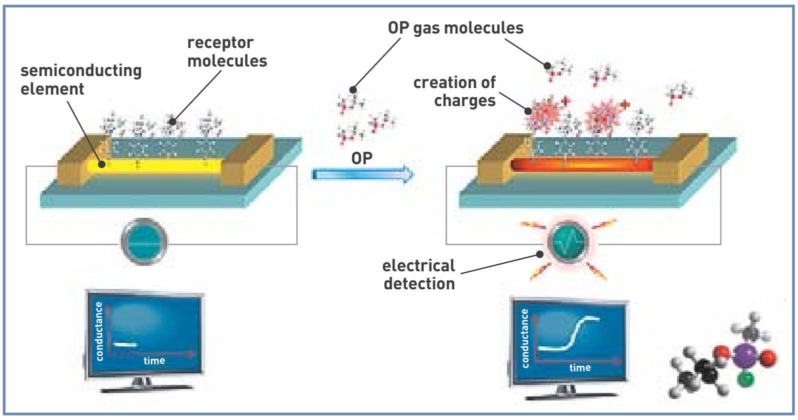

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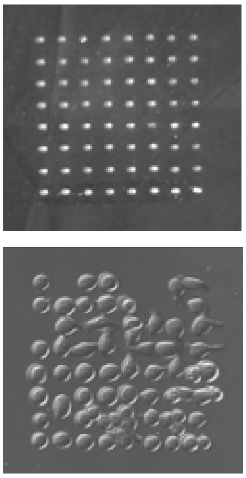
Figure 6.
Schematic representation of the silicon nanowire based detection system comprising surface-grafted sensitive molecules. The current measurement is stable before the presence of toxic compounds and an increase in the electrical conductance can be observed after the reaction by the gas molecules on the functionalized silicon nanowire. The screens show the conductance of the functionalized nanowire versus time. On the right, a representation of the sarin molecule.



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20 µm pitch matrix of micro-deposits of antibodies (top) specific to certain blood cells (T lymphocytes). Given the size of the spots (5 µm) and the size of the cells (10 µm), only one cell can fit on the spot. The antibody matrix is incubated with the biological sample and the recognized cells self-organize according to the pattern drawn. The cells can therefore be easily examined and studies can be conducted on the secretion of molecules mediating the immune activity (bottom/Roupioz et coll.).

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> **Jean-Pierre Simonato**
Liten Institute (Innovation Laboratory for New Energy Technologies and Nanomaterials)
Technological Research Division
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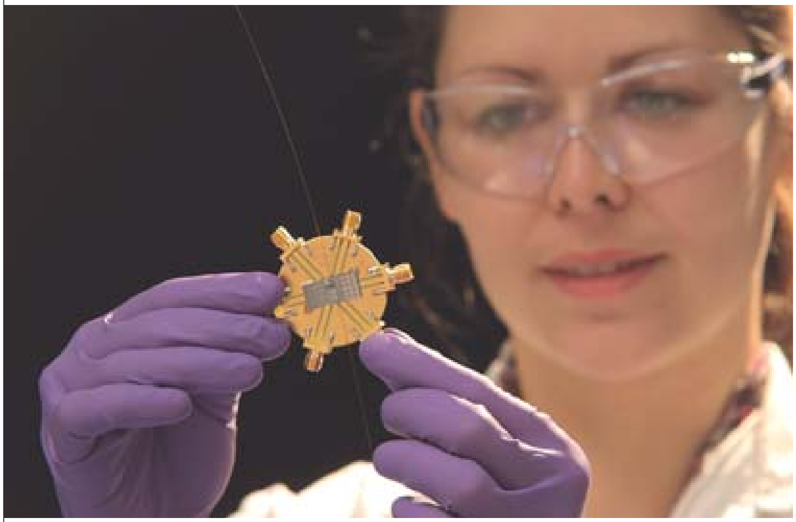
(3) This is a group belonging to the Structures and Properties of Molecular Architectures Department (Service Structures et propriétés d'architectures moléculaires / SPrAM/UMR 5819) working within the Institute for Nanosciences and Cryogenics (Inac).

Chemistry for **functional micro** and **nanosystems**

Chemistry is experiencing a radical change in both concepts and practices. **The contribution of micro and nanotechnologies is promising major breakthroughs** in the medical, environmental protection and civil security fields.



P. Avavian/CEA

Gas sensors incorporating NEMS (Nano Electro Mechanical Systems).

Since the 1970s, we have been witnessing a change in concepts and practices in chemistry, conventionally described in terms of organic and mineral chemistry, chemistry of materials and physical chemistry(1). The prospects are not so much for the discovery of a molecule leading to new applications as in the ability of chemistry to allow the construction of new, innovative, multi-functional objects. It thus stands at the crossroads between various disciplines and techniques. The processing and analysis of the signals produced by chemical and/or biological sensors incorporating micro and nanotechnologies thus throws wide the door to major breakthroughs in the fields of health (diagnosis and theranostics), environmental monitoring (quality of water and air) and civil security (chemical and biological threats, pandemics). The role of chemistry here is to provide complex multi-scale architectures in order to create chemical systems with controlled functions, compatible with manufacturing and usage constraints (in living organisms particularly). The concentration, capture, sorting, detection or delivery of chemical or biological species are among the range of these functions being produced.

Miniaturizing biological samples and shortening analysis times

Succeeding in doing this entails concentrating the metabolites from whole blood, without extracting the plasma, as is the case today. By working on the development of new drugs, the researchers have managed to change analysis techniques in two ways:

- gradual reduction in the volume of the biological samples needed for an analysis: now only 5 ml of whole blood are enough;
- the use of the same sample for simultaneously assaying the active principle, its metabolites and its associated pharmacological activity bio-markers.

This has not however solved all the problems. These assay techniques, based on liquid chromatography and mass spectrometry of plasma samples, remain complex because they require extraction of the compounds in a volume of about 100 µl of plasma. A true ethical advance for future clinical trials in patients therefore entails miniaturization of the volume of biological samples. A volume of a few microliters would avoid the highly invasive process of taking blood samples. Simply pricking the finger would be sufficient. The other advance would be the ability to work directly on the blood and thus simplify the sampling step, with the corresponding time saving and improved management of the biological samples. In this field, the researchers at the Electronics and Information Technology Laboratory (Leti) have just demonstrated the feasibility of a metabolites concentrator, using a miniaturized volume of blood of about ten microliters,

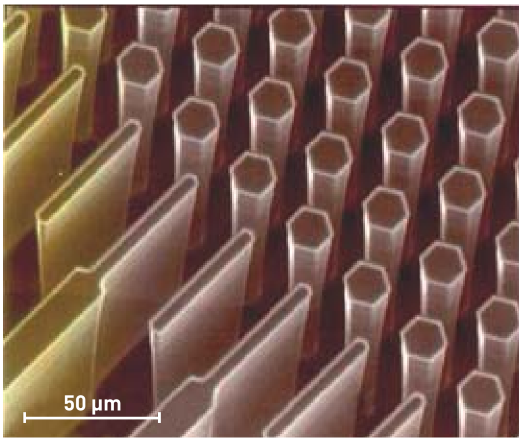


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Figure 1.
Inside a micro-reactor, structured by deep etching of silicon, observed by scan electron microscopy.

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(1) We should mention the introduction to soft chemistry concepts (J. Livage, 1997), supramolecular chemistry (J.-M. Lehn, 1987), green chemistry (P. Anastas and J. Warner, 1998), click chemistry (K.B. Sharpless, 2001) and integrative chemistry (R. Backov, 2005).

in a micro-reactor chemically structured and functionalized in gas phase after sealing (Figure 1). The results are looking promising: after elimination of the blood cells and the proteins, a drug was extracted and purified in 30 minutes, instead of the 5 hours currently needed, all from a sample of only 20 µl of whole blood.

Capturing proteins to diagnose cancers

Cancerology is today waiting for the researchers to provide it with better means of diagnosis, along with progress in therapeutic monitoring. If the available techniques are still limited, this is because they rely on assaying of the markers present in the serum of the patients, but also because they require extraction and concentration steps to be able to identify the equivalent of a grain of salt in a swimming pool! Nonetheless, a research team headed by François Berger from the Neurosciences Institute of Grenoble [Institut des neurosciences] may have made a significant breakthrough. Within this unit, researchers from the Leti made a major contribution by developing a miniaturized technique for *in situ* sampling of biomarkers in tumors. This technique consists in using a silicon substrate of 600 µmx2 cm, structured in the form of octagonal micro-columns (height: 50 µm and diameter: 80 µm) which are then chemically functionalized, for example with an anionic function, for selective capture of the proteins - by means of electrostatic interactions - after placement of this substrate using an appropriate surgical tool (Figure 2). Further sterilization of these devices in no way impairs their surface chemistry. The substrate is then directly analyzed using Seldi-TOF mass spectrometry from Ciphergen. The first tests, performed to determine the protein imprint in subcutaneous tumors induced in mice, validated this micro-biopsy principle.

Detecting ions to monitor a physiological state

As part of the European Nephron+ project, the Leti developed an Ion Selective Electrode (ISE) type sensor for continuous monitoring of the Na$^+$ and K$^+$ ions present in the plasma after a blood filtration loop through an artificial kidney fitted to a patient. To build it, the researchers included capture molecules (calixarenes, crown-ether) in a PVC membrane, an architecture that favors the measurement of the electrolyte concentration (Figure 3). This sensor is directly operational in the blood plasma and has the two-fold advantage of being biocompatible and non-toxic.

This same type of sensor was used for physiological monitoring of fire-fighters on duty, with the ion concentration in their sweat being an indicator of stress (Figure 4).

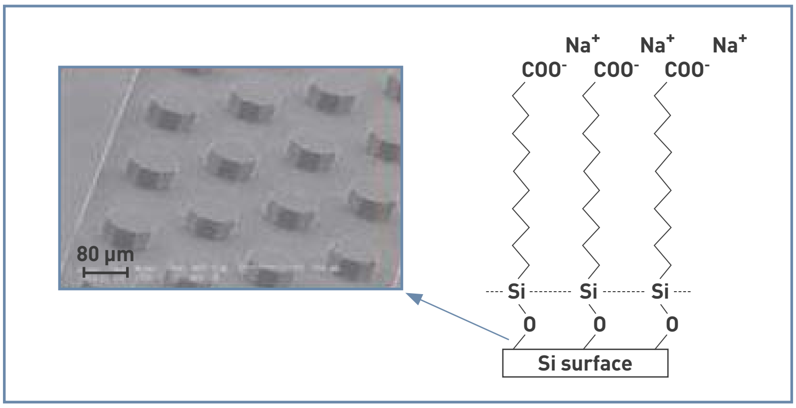

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Figure 2.
Chemistry for capture of proteins in a silicon substrate (right) and details of silicon structure observed by scan electron microscopy (left).

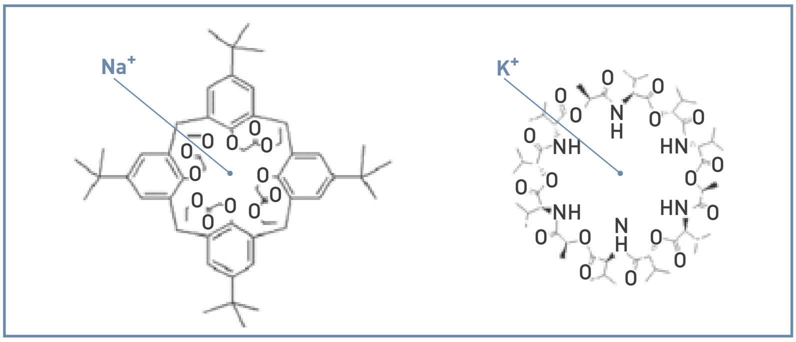

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Figure 3.
Na$^+$ and K$^+$ ion capture principle.

Preventing chemical and biological risks

Capturing, separating and detecting gases is crucial for the prevention of chemical or biological risks in the environment. The problem lies in the fact that in a complex environment (oil well, the home, river water), toxic substances are only found in trace levels, thus making their detection particularly complex. The chemists are therefore faced with a major challenge. Meeting this challenge entails the production of a compact, portable, inexpensive system offering functionalities and performance equivalent to those of gas phase chromatography coupled with mass spectrometry. The Leti researchers are working on developing such a device, capable of analyzing gas mixtures. The future device will be built around an original architecture, comprising a series of NEMS (Nano Electro Mechanical Systems) type detectors, coupled with a chromatography microcolumn.

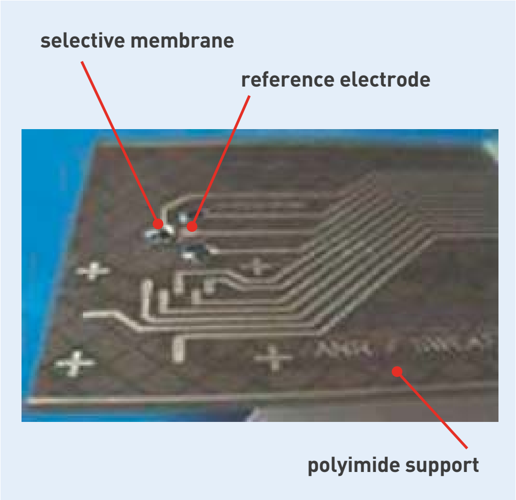

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Figure 4.
Electrochemical ion sensor on a flexible support.

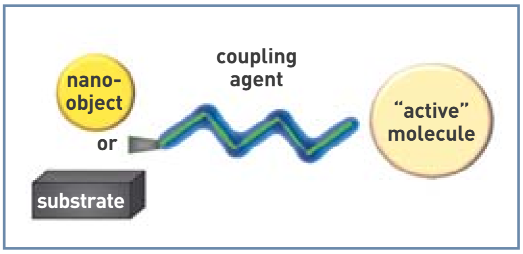

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Figure 5.
Diagram of chemical modification of a substrate or nano-object.

Integration of this type will offer both high sensitivity and rapid measurement on complex samples. This work is part of the collaboration between the Leti and Caltech, under a Nanosystem Partnership Program. The member industrial firms in this program are all involved in the detection of gas compounds in the atmosphere (acid gases for the industrial security aspects and measurement of VOCs in accordance with the REACH directive) and in developing a system for monitoring gases emitted by the chemical industry (refineries). Apart from applications in the field of chemistry, potential applications can be envisaged for health, such as the identification and monitoring of biomarkers in breath, doing away with blood samples, or detection of the respiration of bacteria!

Here, through gas-sensitive layers, chemistry can be used either for separation (in the chromatography micro-columns) or detection (on the nanometric scale structure). Reversible interactions, which are specific and selective for the gases to be detected, in the case of continuous monitoring, are obtained in this layer a few tens of a nanometer thick, localized by electrografting of diazonium salts.

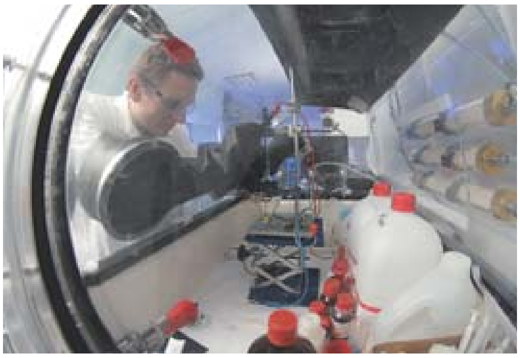
Creating a chemical interface between an object and its environment

As we could see through the previous examples, chemistry is using substrates of extremely diverse types and structures.

A coupling agent will enable a link to be established between an "inert" substrate and the function that the active molecule will be conferring on it (Figure 5).

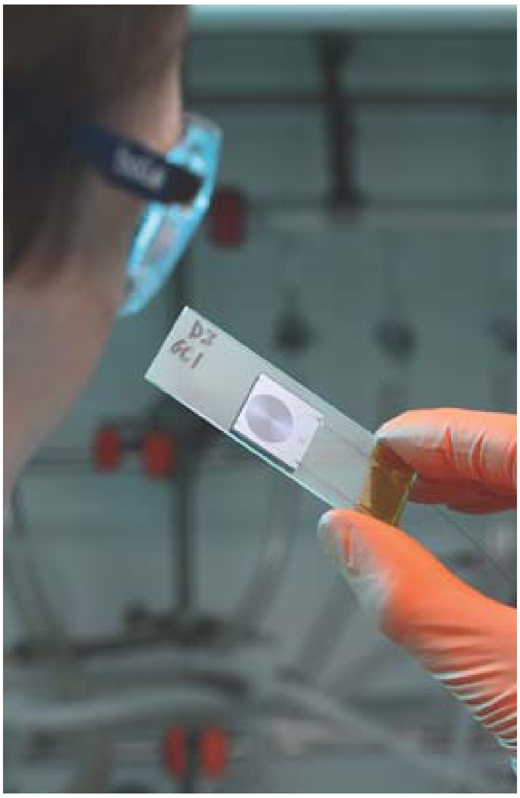
This includes bi-functional molecules, layers of functional polymers or sol-gel. Coupling of the active molecule is either *via* covalent or electrostatic bonds, or by adsorption. The nature of these molecules depends on the target application: biological molecules (DNA, proteins, enzymes, antibodies, saccharides, peptides) for applications in the field of *in vitro* diagnosis, and chemical molecules (anionic and cationic hydrophobic alkanes, polyethylene glycol, calixarenes) for applications in the field of proteomics or physiological sensors. Once these molecules and these associated processors were identified, the researchers at Leti created a sort of vast "library", in which the non-toxic chemical components and low-energy consuming reactions are the best sellers. This new interface chemistry sector only became possible thanks to the specific environment of the Leti, where knowledge of technology, micro fluids, biology and chemistry can be shared. In addition to applications in the fields mentioned earlier, the skills acquired are finding other developments in the energy sectors and new information technologies. The Leti researchers were thus able to graft the active site of a hydrogenase onto electrodes to produce a hydrogen production cell, or molecules with interesting properties for building electronic memories.

These skills, combined on the Chemistry platform of the Technological Research Division (Direction de la recherche technologique/DRT) also allowed further developments in the surface modification of soft matter, more particularly of lipid nanoparticles called Lipidots™, for applications in the field of imaging and therapy (see article p. 44).



P. Avavian/CEA

Localized electro-grafting of diazonium salts in a glove box.



P. Avavian/CEA

Silicon micro-columns for gaseous phase chromatography.

> **Françoise Vinet**
Leti Institute (Electronics and Information Technology Laboratory)
Technological Research Division
CEA Grenoble Center

Structure and activity of **proteins**

The life sciences also have their nano-machines: we call them proteins. Within or on behalf of a biological cell, each carries out one or more specific tasks, thus making possible the various processes necessary for the growth and survival of an organism. **Gaining a clearer understanding of proteins function, structure and dynamics is thus vital**, to expand the pharmacopeia if nothing else.

The function of a protein is encoded in its sequence: this determines not only its structure, but also its dynamics. The dynamics are to the structure of the proteins what the fairy's wand was to the puppet Pinocchio.

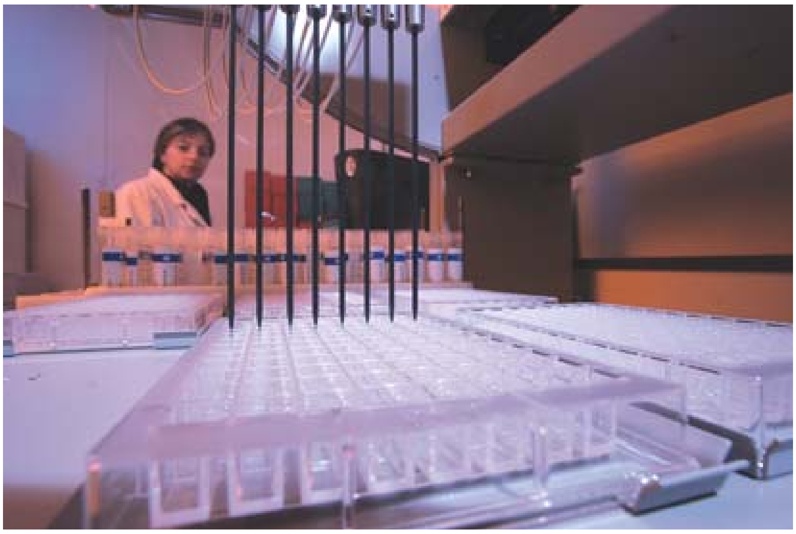
Living nanomachines

Proteins are manufactured according to the genetic instructions encrypted in the DNA, and are the "workers" of the living organism, both outside and inside the biological cells. In the complex processes at work within living organisms, each one of these proteins interprets its role or roles. In the blood, for example, hemoglobin handles the transport of oxygen, while insulin regulates the sugar levels. These highly specific roles lead to a classification of proteins according to their biological function: enzymes, hormones, receptors, antibodies, signaling, transport, storage, etc. proteins.

One of these proteins, acetylcholinesterase (AChE), is of particular interest to the researchers of the Protein Structural Dynamics team at the Institute of Structural Biology (IBS), an institute co-funded by the CEA, the CNRS and the Université Joseph Fourier. AChE is the "off switch" at cholinergic synapses, that is the synapses using acetylcholine (ACh) as a neurotransmitter. This type of synapses is encountered at neuromuscular junctions and in the areas of the brain responsible for the cognitive functions (orientation, memory, language, etc.): AChE is therefore an essential enzyme. Modulating its activity will be a factor in symptomatic treatment of glaucoma, myasthenia (*myasthena gravis*) or Alzheimer's disease. For example, for this form of dementia alone, four of the five drugs approved are reversible inhibitors of AChE. However, inhibiting it completely and irreversibly would be lethal – for example in the case of exposure to a massive dose of insecticides (methamidophos, monocrotophos, parathion, etc.) or to certain neurotoxic agents (VX, soman, sarin, and so on).

Wide diversity of three-dimensional structures

Our "genetic memory", our DNA, is written by a succession of "triplets" of a 4-letter alphabet – the bases of DNA: there are thus $4^3 = 64$ available "characters". Nonetheless, within proteins translated from DNA, one only finds 20 "natural" amino acids. The various types of amino acids are in fact coded by a variable number of DNA "characters": we then talk of degeneration of the genetic code.


P. Avavian/CEA

Protein crystallization robot.

To describe a protein in simple terms, one could imagine it as a "necklace" consisting of an alternation of twenty different "beads". The various protein "necklaces" are of varying lengths, each with a different number of types of "beads". They are primarily differentiated by their "bead" sequence: this sequence will determine the structure adopted by the protein. Thus, despite the apparent lack of diversity in the "library" of natural amino acids, proteins offer a multitude of three-dimensional structures. The sequence – or "primary structure" – of a protein also dictates its dynamics, which proves to be just as important from the biological viewpoint. It is the subtle animation of its structure, by a combination of movements of varying lengths and amplitudes, that in the end allows a protein to be biologically active. To stretch the metaphor somewhat, we could imagine a butterfly: its ability to take off depends just as much on the beating of its wings as on their shape.

Proteins can be placed in two categories: soluble proteins, bathing in an aqueous solution, and membrane proteins that are inserted into a biological membrane. In these two categories, the vast majority of proteins has a unique and specific three-dimensional structure tailored to their biological role(s). Nonetheless, proteins said to be "intrinsically unfolded" were discovered about a decade ago. They are specific in their absence of a unique three-dimensional structure and are better described by a series of conformations rapidly changing from one to another. AChE falls into the category of soluble and structured

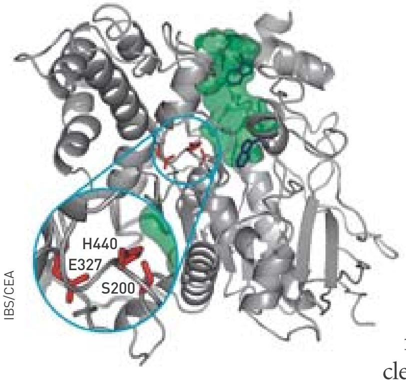


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Figure 1.
Overview of an acetylcholinesterase structure. The α-helixes and β-sheets are represented by helical ribbons and arrows respectively; these are the secondary structure elements. The green surface corresponds to the gorge leading to the enzyme's active site. The red rods show the amino acid side chains of the "*catalytic triad*", in other words a serine, a histidine and a glutamic acid in position 200 (S200), 440 (H440) and 327 (E327), respectively.

proteins. Its three-dimensional structure illustrates the two major elements of the "secondary structure" within proteins (Figure 1), that is, α-helices (represented by helical ribbons) and β-sheets (represented by arrows); these latter are connected by loops that are often little structured.

As we mentioned earlier, the main function of AChE is to "catalyze" the cleavage of the ACh neurotransmitter. AChE is thus an enzyme, in other words a protein responsible for accelerating a chemical reaction. The enzymes are invariably structured and their overall structure corresponds to the framework best suited to operation of the "active site" performing the catalysis. That of AChE only involves three protagonists from among the 600 amino acids that compose it: hence the expression "catalytic triad" (magnified and shown in red in Figure 1). This triad is to be found at the bottom of a narrow "gorge" (surface shown in green in Figure 1). Its position made it hard to understand the organization of the traffic on the substrate (ACh) and the products in the gorge. This traffic appeared all the more mysterious as AChE is among the fastest enzymes in nature (up to 20,000 ACh molecules hydrolyzed per second). This level of catalytic efficiency can only be rationalized by taking account of its dynamics. The existence of an additional exit, invisible in the structure of the enzyme when not active, was in particular postulated; its transitory opening at the base of the active site would allow rapid evacuation of the catalysis products, thus freeing up the active site for a new substrate molecule. Further on, we will see how this hypothesis was confirmed, thanks to experiments which literally "filmed" the AChE in action.

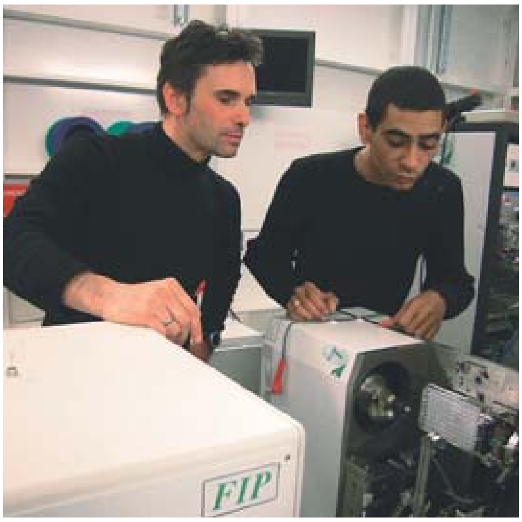
How to determine the structure of a protein?

To resolve the structure of a protein at the atomic level, the researchers now have two principal methods.

- X-ray crystallography, requiring that the protein first be crystallized. Crystallization of a protein is a lengthy process, whose outcome is always uncertain. X-ray crystallography nonetheless corresponds to a "direct measurement" enabling each of the atoms making up the protein to be localized.

High-field (800 MHz) nuclear magnetic resonance spectrometry (NMR) at the Institute of Structural Biology (IBS).

P. Avavian/CEA



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X-ray crystallography experiment at the ESRF, on the FIP (French beamline for Investigation of Proteins). This platform of the Partnership for Structural Biology, in Grenoble, is partly funded by the CEA. This beamline can in particular be used to evaluate the diffraction quality of very small protein crystals, without extracting them from their crystallization box (visible at bottom right).

- Nuclear magnetic resonance (NMR) does not require crystals but is only applicable to relatively small proteins ($\approx$ 300 amino acids). The reconstruction of a structure by NMR will always be indirect, because it is based on the measurement of the distances between atoms in the protein. The models produced are those which best meet these distance constraints. A third method, cryo-electron microscopy can, in certain favorable cases, give quasi-atomic, or even atomic level resolutions.

Consequently, 90% of the 70,000 proteins structures deposited in the Protein Data Bank (PDB) were resolved by X-ray crystallography, as against 10% by NMR. The worldwide spread of 3rd generation synchrotrons significantly contributed to this situation – for example, the European Synchrotron Radiation Facility (ESRF) in Grenoble, the SOLEIL synchrotron in Saclay or the Advanced Photon Source (APS) in Chicago. The X-ray beams output by these synchrotrons are bright and intense and in just one minute can allow performing experiments which used to take several days with a laboratory source. Synchrotron radiation has thus allowed the resolution of structures from very small crystals with very low diffracting power. This was notably the case for the structure of the ribosome, a giant macromolecular complex capable of translating genetic information into proteins, and whose crystals had the two drawbacks mentioned. Without 3rd generation synchrotrons, Venkatraman Ramakrishnan, Thomas Steitz and Ada Yonath would not have won the Nobel prize for chemistry in 2009, for their work on the structure and function of ribosomes.

Chemistry and living organisms: rational design of drugs based on protein structures

Most drugs act by targeting a specific protein, one that is involved in a particular metabolic disorder. As applicable, either activation or inhibition of this protein will be sought. With regard to AChE, the target of numerous active molecules, four of the five drugs used for symptomatic treatment of Alzheimer's disease act by altering its activity. A reduction in the level of ACh is invariably observed in the brain of victims of the disease, so reversible inhibition of the AChE will enable it to be restored and slow down the progression of the disease. The inhibiting drugs include donepezil, a molecule which binds not only to the active site base, but also to other amino acids in the gorge (Figure 2). This illustrates how understanding the three-dimensional structure of a protein can help with the rational design of a drug.

Even though chemistry remains firmly in control when it comes to synthesis, understanding the structure of a protein will greatly simplify the quest for new active molecules. The complex structures of the proteinaceous target with putative lead compounds will e.g. allow rationalizing biochemical observations and guiding the synthesis of more effective drugs. Thus a very large number of small molecules, forming a chemical library, can be screened first of all *in silico*, then *in vitro* and *in crystallo*, thus answering the following questions:

- is the molecule worth considering?
- if so, is the molecule active?
- if so, how can this activity be rationalized or even improved?

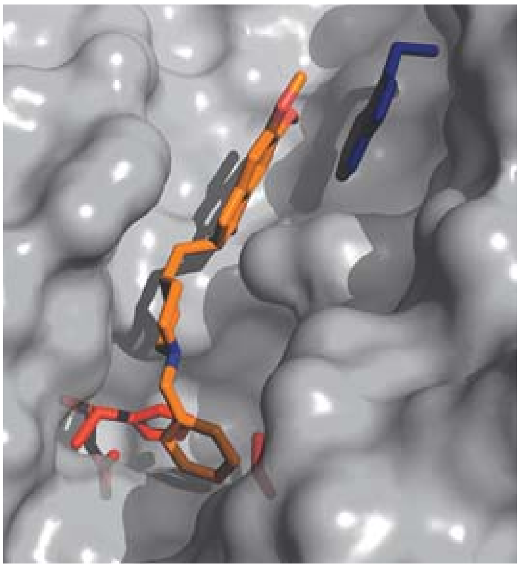
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Figure 2.
A molecule of donepezil (orange) interacts in the gorge (in green on Figure 1) with acetylcholinesterase, thus inhibiting it reversibly[(1)]. The amino acids of the catalytic triad are shown in red and a tryptophane is shown in blue at the entrance to the gorge acting as the peripheral site for substrate binding. Donepezil (commercial name Aricept^{MD}) is used for palliative treatment of Alzheimer's disease.

Until a few years ago, structure-based drug-design was limited to the "key/lock" model, whereby a drug necessarily matched the inactive structure of the active site of the target protein. Nonetheless, other active-site conformations are sometimes better for binding a potential drug. The dynamic nature of protein structures is thus taken into account with greater regularity in drug design. This necessarily increases the complexity, but better reflects the biological reality, and can sometimes make a significant difference.

Kinetic crystallography demonstrating proteins in action

We are familiar with the structure of more than 70,000 proteins but this is still nothing more than a collection of still images of dynamic objects. A clearer understanding of their working requires characterization of their structural dynamics, in other words all the conformations – similar but nonetheless different – which are accessible to them. For an enzyme, this characterization proves to be particularly important because it is these transitions between conformational sub-states that in the end provide it with its activity.

Kinetic crystallography is to conventional crystallography what cinema is to photography: its aim is to visualize the proteins "in action". In concrete terms, this entails triggering the biochemical reaction for which the protein is responsible, within the crystal, and then characterizing the various conformational sub-states between which it passes in order to perform its catalytic cycle. Here again, the use of the intense radiation from a synchrotron will be a key advantage.

In the case of AChE, it was possible to "film"(2) the traffic on the substrate and the enzymatic products from the entrance to the gorge – peripheral site – to the active site (Figure 3). Kinetic crystallography also proved the existence of backdoor exit for rapid evacuation of the products, and its synchronized opening was made possible either using a laser flash, or the synchrotron radiation itself(3).

In the near future, the 4th generation X-ray sources, capable of producing radiation one thousand billion times more intense than that of the current synchrotrons, will provide snapshots of single proteins in action (X-ray Free Electron Lasers/XFEL). The proof of concept was provided by researchers working at the XFEL of Stanford (United States)(4). Two other XFELs are already under construction: the European XFEL in Hamburg and the SPring-8 SASE Compact Source in Japan. It would admittedly be premature to state that these giant machines will become "molecular film theaters", but one thing does however appear to be certain: X-rays still have much to teach us about molecules and the living processes.

> **Martin Weik** and **Jacques-Philippe Colletier**
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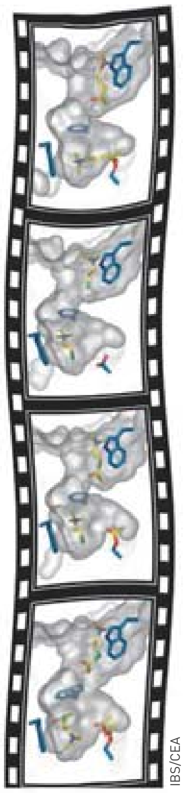
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Figure 3.
An enzyme in action. Different key steps in the traffic of the substrates and products within the acetylcholinesterase gorge (green in Figure 1), identified by means of kinetic crystallography.

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(1) Kryger (G), Silman (I), Sussman (J-L), "Structure of Acetylcholinesterase complexed with E2020 (Aricept): Implications for the Design of New Anti-Alzheimer Drugs", *Structure* 7, 297-307 (1999).

(2) Colletier (J-P), Fournier (D), Greenblatt (H-M), Stojan (J), Sussman (J-L), Zaccai (G), Silman (I) and Weik (M), "Structural insights into substrate traffic and inhibition in acetylcholinesterase", *Embo Journal.*, 25, 2746-2756 (2006).

(3) Weik (M) and Colletier (J-P), "Temperature-dependent macromolecular X-ray crystallography", *Acta Crystallographica Section D*, 66, 437-446 (2010).

(4) Chapman (H-N), Fromme (P) *et al.* "Femtosecond X-ray protein nanocrystallography", *Nature*, 470, 73-77 (2011).

From **toxicology** to **ecotoxicology**

Whether inorganic, organic or biological, **chemistry has been with us since the very beginning**. However, its major role in industry came about with the industrial revolution of the 19th century, even then raising the **question of the impact of chemical products** on the workers, the consumers and, of course, the environment.


P. Avavian/CEA

Human cell culture for toxicology studies

Progress in the protection of health and the environment has already been marked by a number of milestones: the limits placed on animal experimentation (1959)(1), the European directive classifying hazardous substances (carcinogenic, mutagenic, reprotoxic/CMR) in 1967, the creation of the American Environmental Protection Agency (EPA) dedicated to human health and the protection of nature (1970), the appearance of the concept of green chemistry in the 1990s. 2007 was marked in France by the "Grenelle" environment summit and, in the European Union, by the REACH directive (Registration, Evaluation and Authorisation of Chemicals) creating an integrated, unique system for the registration, evaluation and authorization of chemical substances. In this context, the Organization for Economic Cooperation and Development (OECD) published recommendations for chemical product testing, including details of physical-chemical properties, ecotoxicology and toxicology.

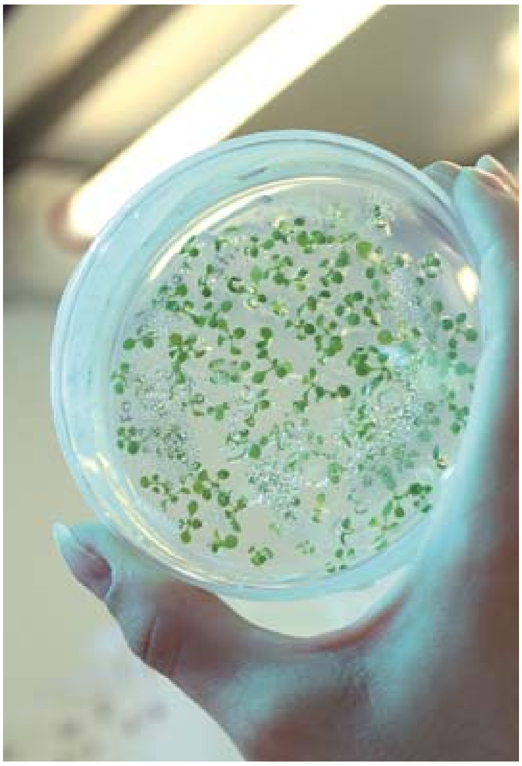
Toxicology and radiotoxicology are benefiting from the spread of scientific, technical and bioinformatic knowledge and feedback from the drugs sector. As early as 2002, CEA initiated a cross-disciplinary program dedicated to toxicology, aiming to obtain a clearer understanding of the impacts of chemical elements and/or radionuclides resulting from the use of nuclear energy (tritium, iodine, cesium, actinides) – a program which, since 2010, has included the impact of nanoparticles on ecosystems and living organisms. This multidisciplinary program is leading to CEA's chemists and biologists working closely together, as they are both keen to understand the mechanistic aspects of toxins and characterize their chemical forms.

Metals: environmental toxins

The formation of species that can be assimilated by organisms remains a key aspect of the transfer of toxic products from the environment to the living organisms. Water, which comprises complexed forms of metal with organic or inorganic ligands, is a direct mode of trophic contamination for Human. A study by the chemists and biologists

(1) "3R" principle ("replacement" by computer models, "reduction" by maximizing the information gained from each animal and "refinement" by minimizing animal suffering) developed by the British researchers William Russel and Rex Burch.

from the Laboratory of Target Protein Studies (Lepc)(2) and the Radiochemistry and Processes Department (DRCP)(3), in collaboration with Säteilyturvakeskus (STUK), showed that the association of uranium, calcium and carbonates in Finnish well water, explained the absence of any effects on the population health. At the same time, studies involving the Institute for Nanosciences and Cryogenics (Inac), the Institute of Life Sciences Research and Technologies (IRTSV)(4), in particular the Plant Cell Physiology Laboratory (PCV)(5), demonstrated that the transfer of uranium from the roots to the shoots depends heavily on the chemical form or the speciation of the uranium. However, whatever the contamination route, the metal species can pass from an entry compartment (digestive tracts, air, plant leaves or roots) to other compartments (storage organs in particular), passing through varied anatomic and cell barriers. These transfers depend on the mode of interaction between the metals and the various biological ligands capable of transforming the metal in turn from its initial form to forms that can be eliminated or stored. *In vivo* biokinetic and biodistribution studies have been able to determine the organs and compartments in living organisms in which the metal builds up and generates significant toxic effects: metabolic, endocrine, immune (for the animal world) disruptions, and impairment of growth or root development (for the plant world). The researchers at the Ibeb(6) are also working on build-up mechanisms in bacteria capable of reducing certain metal oxides (selenite, tellurite, pertechnetate, uranyl) and stocking insoluble forms in the cytoplasm or, in the form of precipitates, in their walls. For the past ten years, the consequences of chronic or acute exposure to toxic products have been studied *in vitro*, *via* the use of cell lines in culture. Although these "omics" approaches (transcriptomics, proteomics, metabolomics) cannot replace *in vivo* evaluation (animal experimentation), they can however eliminate unacceptably toxic molecules early in the process. A comparative analysis of the transcriptomes provides information about the metabolic activity of the cell through modulation of the expression of genes in toxin response situations – approaches that rely on DNA chips. A comparative analysis of cell proteomes and metabolomes, whether or not exposed to toxic products, requires the combination of separation methods, such as electrophoresis, and identification techniques using mass spectrometry of proteins. Combined approaches involving metabolomics, transcriptomics or proteomics showed that the exposure to cadmium (Cd) leads to a modulation of the sulfur metabolism in yeast *S. cerevisiae* and thus the over-production of glutathione, a molecule that is a chelating agent for cadmium. In the plant *Arabidopsis thaliana*, the exposure to cadmium resulted in the modulation of the expression of the phytochelatins involved in the sequestration of cadmium. A similar approach involving a combination of transcriptomics and proteomics highlighted significant differences in the response to uranyl exposure by human cell lines from kidney and from lung. Thus for the kidney cells, proteomics revealed modifications


P. Avavian/CEA

Germination *in vitro* of *Arabidopsis thaliana*. A nutrient agar medium underwent sterile seeding. After 48 hours at 4 °C in the dark, the boxes were placed in culture in a chamber until plantlets were obtained, able to be transferred for various operations (about a week).


P. Avavian/CEA

Synthesis of peptides. Analysis and assaying of samples containing toxic metals.

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(2) Laboratory of the Institute of Environmental Biology and Biotechnology (Ibeb/Life Sciences Division) situated in the CEA Marcoule Center.

(3) Department of the Nuclear Energy Division (DEN), situated in the CEA Marcoule Center.

(4) Institute of the Life Sciences Division.

(5) Joint research unit 5168 - CEA - CNRS - INRA - Université Joseph Fourier.

(6) Institute of Environmental Biology and Biotechnology/Life Sciences Division.

in the proteins of the cytoskeleton and transcriptomics showed finer alterations, in particular the involvement of a mineralization regulator, an approach validated by the identification of the protein involved.

The use of these overall approaches should lead to the emergence of predictive toxicology, the development of experimental models, or alternative methods such as *in silico* or QSAR methods (Quantitative Structure-Activity Relationships).

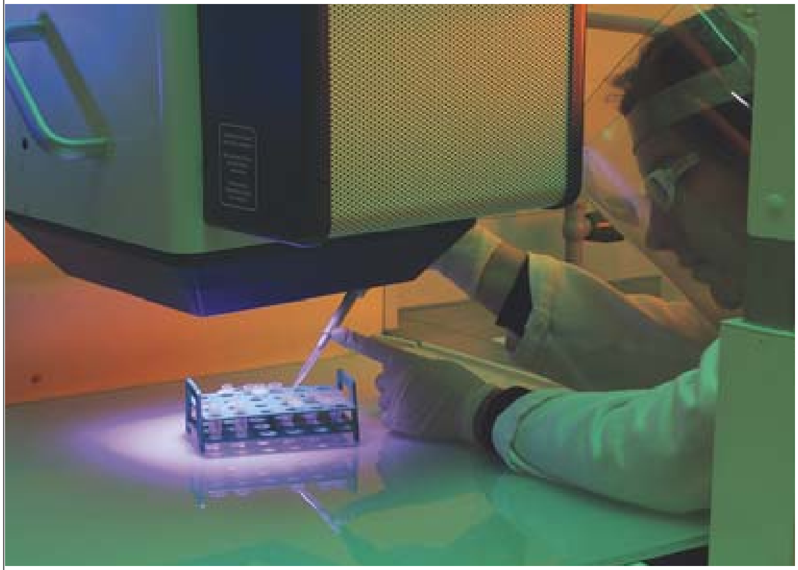
Increasingly effective analytical techniques

The development of effective analytical techniques, or an *in analytico* approach, is ideally suited to the detection of traces and leads to improved characterization of the chemical species in a given medium and access to their speciation. These techniques, used on model systems and then coupled with modeling approaches, can predict the impact of organic or mineral molecules and the pH on the bioavailability of toxins. An approach including experimentation and modeling, with the development and updating of speciation software(7) and databases(8), contributed to a better understanding of radionuclides(9). These analytical techniques will be of benefit to biology. Elementary analysis, in association with imaging techniques such as scanning electron microscopy/SEM or transmission electron microscopy/TEM, has made it possible to identify the chemical form of the metals present at cellular and sub-cellular level, in particular uranyl (in its uranium VI-phosphate form) in the lysosomes of kidney cells. The exposure of keratinocytes to cobalt leads to its preferential localization in the nucleus and the cytoplasm, along with a drop in intracellular magnesium and zinc. Mass spectrometry techniques, whether or not associated with separation methods, also offer powerful tools for characterizing the metal-ligand complexes formed. Analyses performed by Electrospray Ionization/ESI and Electrospray Mass Spectrometry/ES-MS were used to determine the various forms of the Co^{2+} in the presence of small ligands such as certain organic or amino acids and peptides present in biological media. Time-Resolved Laser Fluorescence Spectroscopy (TRLFS) can for its part be used for direct determination of the stoichiometry and complex formation constants of fluorescent elements such as uranium or rare earths: this for example led to the characterization of different uranyl/phosphate species according to the pH of the medium, to the detection of uranyl/protein complexes (transferrin) or uranyl-peptides (peptides from calmodulin).

Toxicity at the molecular level

There are several steps in understanding the molecular mechanisms involved in the toxicity of metals: firstly, identification of the target proteins transporting and/or favoring their build-up in the cells of the target organs, then determination of the physical-chemical and thermodynamic parameters characterizing and quantifying the protein/metal interactions, and finally, the resulting structural or functional consequences. The speciation of metals in complex biological media (culture media, biological fluids or cell extracts) often proves to be extremely incomplete, especially with regard to the identification of metal/protein complexes. Isolating them is an approach that renders possible identifying the potential formation of complexes. Thanks to separation chemistry techniques, the use of chromatographic methods, involving immobilization of a metal (cobalt, nickel) by a chelating agent (nitrilotriacetic acid /NTA or iminodiacetic acid/IDA) grafted onto a stationary phase, leads to isolation of the affine proteins for these metals. Teams from the Marcoule Institute for Separative Chemistry (ICSM)(10) and the Lepc achieved a breakthrough in immobilizing uranyl on a support with grafted phosphonic amines. Since then, the researchers have been using this phase, in physiological pH and ionic force conditions, to isolate and identify affine proteins for uranyl, from cell extracts. Another approach, developed at the Laboratory for Protein-Metal Interaction Studies (Lipm)(11), in collaboration with the Physico-Chemistry Department, aims to isolate the protein/metal complexes formed in the cells. This approach consists in coupling separation by electrophoresis on gel, in non-denaturing conditions, with gel mapping (by TRLFS or autoradiography) to identify the protein/metal interactions.

The speciation and identification of potential targets of the metal remain necessary but are not sufficient to describe toxicity phenomena. Thanks to the determination of physical-chemical and thermodynamic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Irradiation of human cells to study the impact of ultraviolet radiation.

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(7) Example of the CHESS (Chemical Equilibrium of Species and Surfaces) software.

(8) Example of the BASSIST database (French acronym for Base Applied to Speciation in Solution, Interfaces and SolubiliTies).

(9) This approach involves teams from CEA, the French Radioprotection and Nuclear Safety Institute (Institut de radioprotection et de sûreté nucléaire/IRSN), CNRS and several universities.

(10) Joint research unit: CEA-CNRS-UM2-ENSCM (UMR 5257).

(11) Laboratory of the Joint research unit (UMR6191): CEA/CNRS/University of Aix-Marseille.

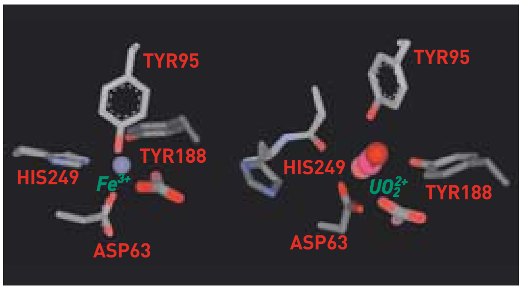

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Figure 1.
Spatial organization of ligands (histidine 249, aspartate 63, tyrosine 95, tyrosine 188 and carbonate) on the metal binding site of transferrine. Case of iron (left, shown by a blue sphere) and uranyl (right, uranium shown by a pink sphere surrounded by two red oxygen spheres). The grey segments correspond to the carbon-carbon bonds, the red segments to oxygen and the blue segments to nitrogen.

parameters, it is now possible to characterize and quantify the protein/metal interactions. Thus, using Surface Plasmon Resonance phenomena in physiological conditions and using very small quantities of proteins, the researchers at the Lepc succeeded in determining their affinity for uranyl, within a range from the nano to the micromolar and in just a few hours. This screening can cover a wide range of affinities. The main problems encountered when using conventional biophysical techniques are thus overcome, with no prior knowledge of the protein, even though it is used in very small quantities.

In the future, researchers will need to supplement these studies in order to identify the structural or functional consequences of these interactions.

Owing to their nature and their excessive concentration in the cells, some membrane proteins play a decisive role either by assimilating essential substances or by excreting toxic substances. Today, several teams from the Ibeb, the IRTSV and the IBS are working on a structural and functional study of these transporters in plants and micro-organisms. A significant result has already been obtained, with the identification of the transporters responsible for the entry or the sequestration of certain toxins in cells, or in the cellular storage compartments in the case of the vacuole of plant cells. The future will involve identifying the specific patterns dedicated to the transport of metals and their selectivity. The Membrane Exchange and Signaling Laboratory (LEMS) is already heavily involved in this field and has demonstrated that the consequence of over-expression of a type P1B-ATPase transporter, *At*HMA4 (for *Arabidopsis thaliana* Heavy Metal Associated) was an increased build-up of cadmium in the leaves. As this transporter also handles lead and cobalt, this discovery led to the filing of an international patent on the applicability of this process in the field of phytoremediation.

In humans, certain metals bind with the transferrin, a major protein of iron homeostasis. Researchers at the Ibeb have shown that the uranyl binding at the iron binding sites did not lead to the conformation change necessary for its recognition by specific cell receptors (Figure 1). A final geometry was proposed by an *in silico* approach, using an algorithm specially developed to predict the uranyl localizations within the proteins. The impossibility for the cells of internalizing the transferrine/uranyl complex was confirmed, thus validating all the *in vitro* and *in silico* results.

The data produced by this research are making a major contribution to changes in protection rules and the development of detection (biosensors), bioremediation or decorporation tools.

Chemists restoring the genome to health

DNA is a target of choice for toxins and pollutants. Any modification of its chemical structure by physical or chemical agents can lead to the appearance of mutations, a source of tumors. The impact assessment of a toxin presupposes a genotoxicology part, a discipline where chemistry plays a key role. The reactivity studies today performed on model systems have led to the characterization of the chemical nature of the DNA damage caused by genotoxic substances: breaks in chains and products modifying the chemical structure of bases (oxidation, alkylation, etc.). Analytical chemistry, organic synthesis and nuclear magnetic resonance (NMR) have contributed to identifying a new type of damage at cellular level. This lesion, generated by ionizing radiation, combines a strand break, a cross-link and a modified base (Figure 2). Other complementary studies are based on quantum chemistry approaches, in particular to shed light on the damage formation mechanisms.

The researchers are now able to identify the lesions liable to affect cells and tissues. To measure these lesions *in vivo*, analytical chemistry – by coupling mass spectrometry and liquid chromatography - enables them to precisely quantify abnormal bases

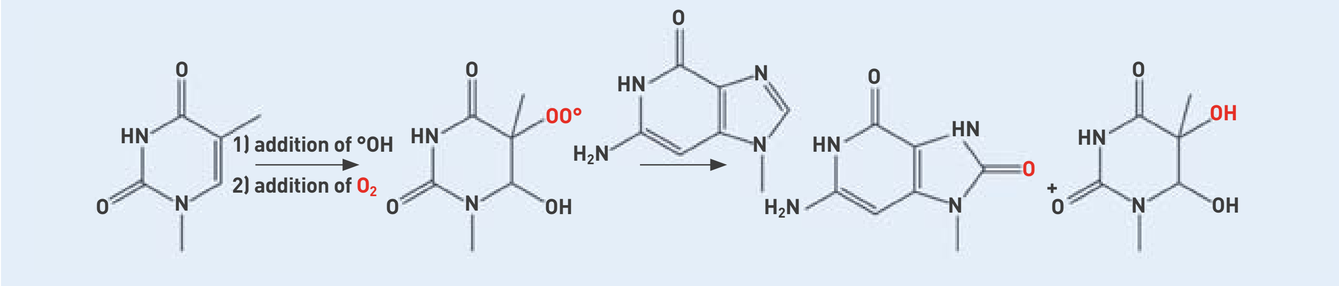

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Figure 2.
Mechanism of formation of complex oxidative lesions in DNA. The initial attack by a single radical leads to oxidation of two adjacent bases owing to the reactivity of one of the intermediate radicals. The involvement of molecular oxygen (shown in red) was brought to light by mass spectrometry.

within DNA samples that have been hydrolyzed into monomers in order to facilitate their analysis. With regard to atmospheric pollution, it is now possible to quantify the adducts to the DNA of organic molecules, in particular benzo[a]pyrene, an atmospheric carcinogenic contaminant.
The ability of cells to repair damaged DNA and eliminate the defective portions of the genome is well known. Nonetheless, this analytical approach has shown that two oxidized bases, produced in vicinal positions in the double-helix, are difficult to eliminate. Finally, unprecedented information on the repair of damage caused by exposure to solar ultraviolet radiation has been obtained on human skin.
Synthetic, characterization or analytical chemistry, remains a major field of research in genotoxicology. Collaboration between chemists and biologists within the same laboratory has enabled the CEA teams to provide the scientific community with original information.

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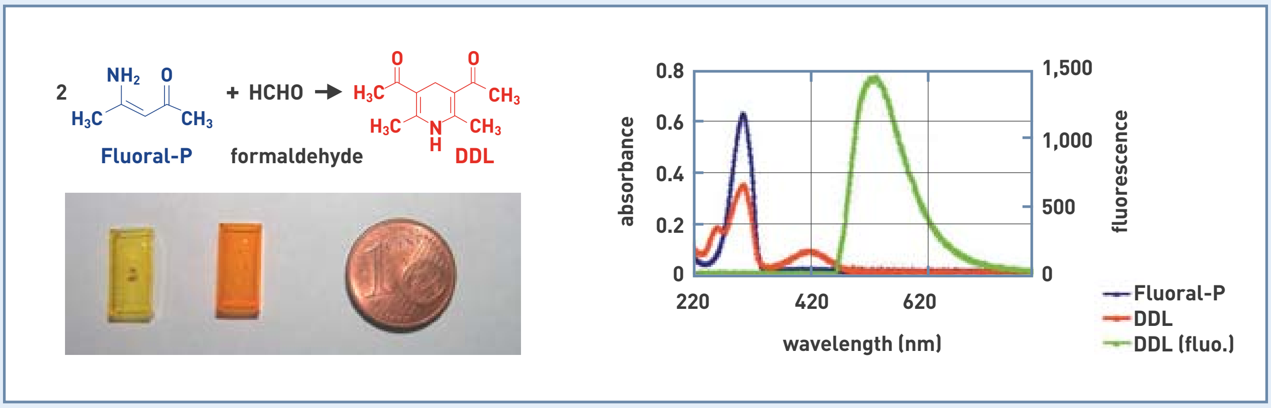
Doped sensors

Aliphatic aldehydes are major pollutants present in indoor air. The smallest of them, formaldehyde, belongs to the class of carcinogens. It can be found in products as common as plastics, resins, wood-chip panel glues, insulating foam, germicides, insecticides and fungicides, and even in antibacterial additives for food preservation. Formaldehyde is also used by the paper, leather tanning, photography, artificial silk, dyes, explosives, cosmetics, etc. industries.
In an enclosed space, the formaldehyde level varies from 1 to 100 µg·m^{-3} and up to 500 µg·m^{-3}. The French Agency for Food, Environmental and Occupational Health & Safety (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail/Anses) recommends not exceeding 10 µg·m^{-3} for chronic exposure. In order to meet this requirement, we have designed innovative sensors with strong trapping capacity, consisting of nanoporous materials, whose pore size (adaptable to the pollutant) allows initial filtering of the VOC (volatile organic compounds). A particularly selective reaction for this purpose, that of formaldehyde with Fluoral-P, produces a molecule which absorbs and "fluoresces" in visible radiation: 3,5-diacetyl-1,4-dihydrolutidine (DDL). The sensors are therefore heavily doped with Fluoral-P for a rapid reaction in the nanopores. Detection of the formaldehyde is based on measuring the absorbance or fluorescence of the DDL. The DDL formation rate is proportional to the concentration of formaldehyde, and the measurement range established to check the air quality varies from 1 to 250 ppb. Since the creation of the ETHERA start-up, inexpensive measurement devices have been created to use these sensors (see page 70). The large adsorption surface of the material, equivalent to that of activated carbon, gives the sensor a second pollution remediation function, in addition to that of detection. Other colorimetric sensors for indoor air are being studied, in particular for the volatile compounds present in the atmosphere of swimming pools, the harmfulness of which has been recently revealed.



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Left: schematic representation of the Fluoral-P reaction with formaldehyde and the optical properties of Fluoral-P and dihydrolutidine (DDL). The photo shows the sensor at two different stages of its exposure to formaldehyde: from transparent, the sensor turns yellow, orange, then dark brown when saturated. Right: absorption spectra of Fluoral-P (blue spectrum), DDL (red spectrum) and the fluorescence spectrum of DDL when illuminated at 410 nm (green spectrum).

Chemistry and **migration**

The monitoring of industrial activities and their impact on the environment, but also the acceptability of the various choices made by society with regard to industrial development and waste management, today require **increasingly detailed knowledge of the processes involved in the fate of contaminants in the environment**. The studies being conducted by the researchers at CEA are making a major contribution to the acquisition of experimental data and their integration into various migration models.

The various regulations on environmental monitoring and sustainable development now require that industrial firms implement strict monitoring of their facilities and draft clean-up plans capable of effectively dealing with any accidental contamination. Evaluating the impact of a facility in nominal and accident situations implies prior utilization of modeling tools capable of integrating data about the various processes controlling the migration of contaminants in the environment. This method also applies to the management of nuclear waste, in particular assuming the use of a solution involving disposal in a deep geological formation. Alongside the research being conducted into waste conditioning and the performance assessment of containment materials, understanding the processes controlling the fate of radionuclides is a major issue for the chemists, and rightly so, because when one considers the time-scales concerned, in other words, more than 10,000 years, these radionuclides will be released into the geosphere. It is therefore up to the researchers to build models capable of predicting the fate of these radionuclides and their impact, both on mankind and on the biosphere – over a time-frame that humans find very hard to grasp.

Against this backdrop, CEA provides Andra with scientific and technical support (definition of research programs, answers to technical questions, and so on), for assessment of the containment performance of the Callovo-Oxfordian argilite, a medium that is being recommended for siting of the future ultimate waste disposal facility.

Coupled processes

The migration of a contaminant in the environment involves numerous scientific fields, which means that the researchers have to:

- know the chemical form (soluble or particulate) in which the contaminant is released;
- understand the chemical behavior of the contaminant in solution, particularly its interaction with the other chemical species present in this solution or with solid heterogeneous phases, such as mixtures of minerals or organic substances;
- determine the transport properties of the medium itself, in which the contaminant is to be disseminated.

There is a further complication to the already complex basic processes involved in the transfer of contaminants in the medium: being able to couple these processes and thus obtain a more detailed description of the phenomena observed that is as realistic as possible. It is by integrating these processes in a model that it will then become possible to predict the migration of contaminants in the geosphere with greater confidence, but also to evaluate their impact on the environment.

P. Stroppa/CEA

For the laboratory experiments, the samples liable to be disturbed by the oxygen in air must be prepared and cut in a chamber containing a nitrogen atmosphere. The glovebox is here occupied by a wire saw for cutting compact samples.

A heterogeneous and complex natural environment

The natural environment resembles a porous medium whose complexity is based on three main factors:

- the nature and diversity of the phases (minerals, plants, micro-organisms) of which it is comprised;
- the granular heterogeneity;
- the textural organization of this medium.

This organization is made all the more complex by the fact that the researchers are working in a surface environment on soils subjected to bioturbation phenomena and to root environments or on soils marked by the imprint of human activity (urban soil, industrial wastelands, etc.). This complexity is further compounded by the natural variability of the hydric conditions of the environment, linked to its hydrogeological conditions and pluviometry.

Solution chemistry

Once released into the environment, the radionuclides and other contaminants combine with other chemical species naturally present in this environment. The mobility of radioelements in the geosphere and their interaction with mineral or organic surfaces basically depend on their chemical form in solution.

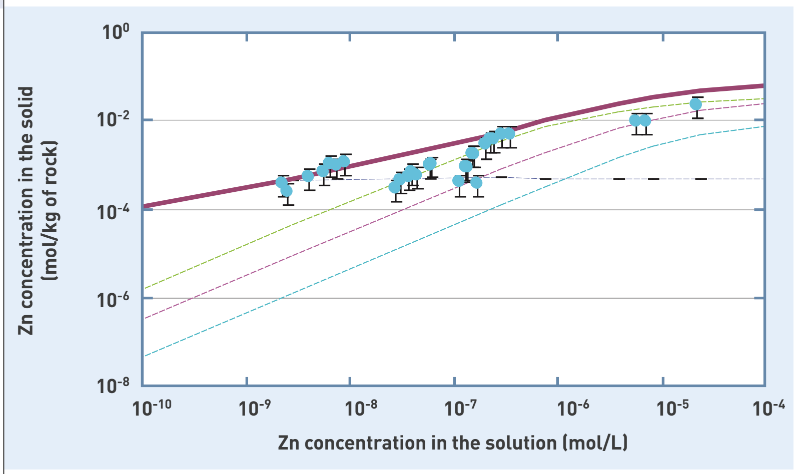

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Figure 1.
Curve for Zn^{++} retention on a natural sediment. The Zn^{++} retention on a sediment consisting of a mixture of mineral phases (calcite, quartz, clay minerals) is here represented by the contribution of the clay minerals alone. The retention properties of these phases were characterized beforehand and implemented in a model, giving a satisfactory reproduction of the retention measurements taken on the sediment. The dotted lines on the figure show the various retention sites identified on the clay minerals. The sum of these sites corresponds to the solid line.

Of the species frequently encountered in the natural environment, one finds carbonate ions, sulfates, organic acids from the degradation of organic matter, or more or less complex organic molecules secreted by plants (roots) and fungi, as well as humic substances (organic macromolecules closely linked to mineral matter). In the precise case of uranium VI(1), its complexation with the carbonate ions or organic acids increases its solubilization in the medium and thus its mobility. Other competing factors can intervene, controlled by bacterial activity. Some bacteria can therefore directly reduce the uranium or more frequently impose physicochemical conditions that are favorable to the reduction of uranium VI into IV, the effect of which is to immobilize it in place in the form of uranium oxide (UO_2) crystals. In general, the natural environment is home to a multitude of chemical reactions, all of which are in competition to varying degrees, which will determine the fate of a contaminant and its migration possibilities.

In order to understand these complex systems, the Department for the Study of the Radionuclides Behavior (Service d'étude du comportement des radionucléides/SECR) developed a number of analytical tools capable of both measuring these contaminants, even in small concentrations, and also accessing their chemical form. The results obtained in this way enable the researchers to enhance and improve a thermodynamic database, collating knowledge of actinides and fission products, necessary for modeling their behavior in the environment. This base is run under the aegis of the Nuclear Energy Agency (NEA).

Chemistry at the interfaces

These contaminants, in the form of simple or complex species, interact with the different mineral surfaces present, which can develop significant contaminant retention capacity and slow down their migration through the porous medium. In general, minerals have a surface charge (permanent charge and ionized chemical groups), where ion adsorption reactions take place. The models used by the Laboratory of Radionuclides Migration Measurements and Modeling (L3MR) to describe these adsorption reactions, are based on an exact compensation of the surface charges by counterions. The assembly formed by the mineral surface and the counterions is then considered to be electrically neutral. The L3MR has for more than a decade been contributing to identifying the retention properties of these mineral phases (carbonates, oxides, clay minerals, etc.) with respect to radionuclides (uranium, americium, curium, europium, strontium, cesium, etc.) and other common chemical species (hydrogen, sodium, potassium, calcium, magnesium, and so on). With concentrations that are generally higher than the radionuclides, these are major competitors for the adsorption of radionuclides on mineral surfaces.

Thanks to the results obtained, the researchers developed models capable of integrating all these properties for input into a thermodynamic database. The different mineral phases appear as elementary building blocks, whose properties are defined in this database. By combining these elementary blocks, it then becomes possible to describe a more complex assembly, such as a soil or sediment, and thus predict the behavior of a contaminant in this medium – which the researchers then check by means of laboratory experiments. This is a first step towards producing a model applicable to the migration of contaminants in natural environments.

These different approaches can in particular be used to identify dominant phenomena capable of regulating the migration of a contaminant. In the example of the contamination by zinc of a complex sediment in an industrial wasteland (Figure 1), the sediment retention capacity can be described satisfactorily, through the contribution of clay minerals alone.

Contaminant transport: from the laboratory to the geological site

The species which remained free in solution then migrate in the pore network of the geological medium. Their rate of displacement will primarily depend on the textural properties of the material and in particular its porosity. In low-permeability media (indurated sediments, rock, etc.) where the transport of species is dominated by the diffusion phenomenon, the rate of migration also depends on the size of these species compared with the pore diameter and their electrical charge. Negatively charged species are repelled from the pore surfaces, which are also usually negatively charged, as is the case with clay minerals. These species are thus excluded from a part of the pore space and diffuse less rapidly than the uncharged species. However, the positively charged species, which are retained on the mineral surfaces, migrate even more slowly.

In order to study the migratory behavior of chemical species in these rocks, the L3MR set up

(1) Uranium has four possible valences (III, IV, V and VI). Valences IV and VI are more common in natural environments and ores, depending on the prevailing redox conditions.

laboratory experiments (see Box). Faced with the complexity and variability of the natural medium, the researchers are continuing their investigations on different scales: from the centimeter, *via* diffusion cells, up to several decimeters in instrumented mock-ups. Column devices can be used to monitor both the migration of a contaminant (whether or not radioactive) and acquire data on the hydric and physical properties of the medium being studied (Figure 2). It then becomes possible to determine the transport properties in a variety of hydric conditions (which is normally the situation in natural systems) and then integrate them into migration models. Through its collaborative work with Andra, the L3MR contributed to setting up migration experiments directly in the geological formation within the Bure underground laboratory.

Coupling of processes or reactive transport

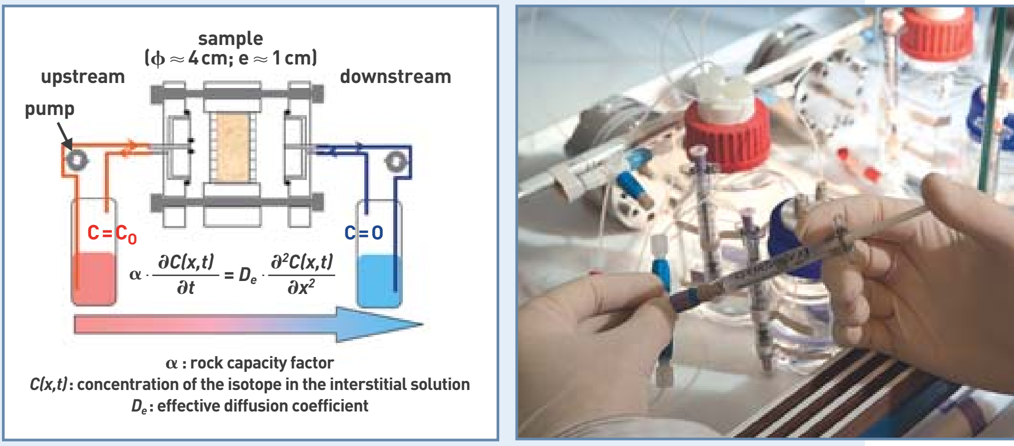
Once they have been determined, the parameters needed to describe the chemical processes, the physical properties of the porous medium (porosity) and the transport parameters (diffusion coefficient) are integrated into models coupling the various chemical processes with the transport. Using this type of model, the researchers at the L3MR are able to simulate the migration profile of a contaminant inside a porous medium, in well-controlled laboratory conditions. These results confirm the approach adopted at the L3MR, concerning both the characterization of basic processes and the choices made with respect to modeling.

Through the experiments carried out, both in the L3MR and in the underground laboratory, the researchers are able to evaluate the prediction capability of

Tracing techniques

To determine the migration properties of chemical elements, whether or not radioactive, in the environment, the researchers make extensive use of tracing techniques. These are based on the injection of a naturally rare, stable, or radioactive isotope into the medium. For studies concerning nuclear waste disposal, the researchers concentrate on radioactive isotopes that can be easily measured, even at very low concentrations. This characteristic enables the study of the migration of different species to be extended to environments that are far from the pollution source, where the concentrations are extremely low.

The diffusion cell shown on the diagram is one of the techniques used by the Laboratory of Radionuclides Migration Measurements and Modeling (L3MR) to determine the diffusion properties of a compact porous material – rock for example. Its principle is leaktight insertion of the sample inside a cylindrical body made of an inert material, holding it between two porous grids which come into contact with water from two tanks. The chemical composition of the water in these two tanks must be as close as possible to that of the water filling the pores of the medium: this is an essential precondition for maintaining the properties of the sample during an experiment which may well last from several months to more than a year. Thus, after an initial chemical balancing phase designed to prevent any evolution of the solid during the experiment, the isotope – whether or not radioactive – is injected into the “upstream” tank of the cell. In the “through” diffusion experiment the activity of the isotope is measured in the tank, over time, after leaving the sample. Adjusting the solution of Fick’s equation to the total activity and the surface diffusion flux measured enables one to obtain the diffusion properties of the tracer in the sample.



right: P. Stroppa/CEA

Schematic of a “through” diffusion cell. Left: the sample is “sandwiched” between two tanks into which the tracer is injected (upstream tank) and, in the downstream tank, the quantity of tracer which passed through the sample is measured versus time. Right: injection of the tracer solution into the diffusion cells upstream tank.

When the element diffuses too slowly, or is heavily adsorbed at the surface of the solid, the sample is then extracted from the cell, after a sufficient time, to measure the diffusion profile of the tracer in the rock. The information thus obtained in particular gives the diffusion properties. The researchers use different types of tracers. For example, tritiated water, an inert tracer, is a means of obtaining the intrinsic physical properties of the medium, in other words its porosity and effective diffusion coefficient – in this case, no chemical process is involved. Other, non-inert elements, can interact with the solid surfaces of the medium, such as certain cations which are adsorbed on the surface of clay minerals. Thus the behavior of an element is heavily dependent on its chemical nature. Tracing techniques are also used in columns, through which the passage of the tracer can be measured downstream of the column (breakthrough curve), or in the column (profiles) over time, but also during the course of *in situ* experiments.

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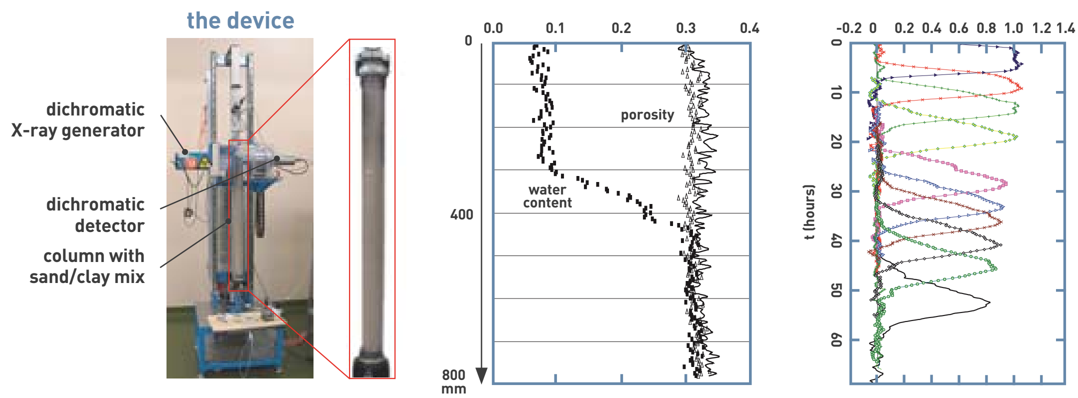

Concentration profile of a tracer versus time: each of the colors represents the concentration of the tracer at a given point of the column.

Figure 2.
BEETI (experimental bench for the study of transport in unsaturated conditions) experimental column filled with a granular material (mixture of mineral phases, sediment or soil): the migration of a contaminant and the physical properties (porosity, water content) are measured by means of X-ray absorption in the material. The X-ray generator moves along the column and gives the water content and the concentration of a tracer over its entire length, versus time.

the migration models. In configurations in which the experimental conditions are stable and well-controlled, the models can now reproduce the observations. However, applying these models to evaluating the contamination of polluted sites still poses a number of problems. In surface environments, the conditions are extremely different, often poorly defined and variable in both time and space. Validating these models requires time and space monitoring of the site's parameters (physical-chemical characteristics of the medium, pluviometry, etc.). Furthermore, to take this variability into account, the models have to incorporate the kinetics of the chemical and biological reactions liable to occur in the medium. Conducting experiments on-site, to validate the migration models or study real cases will be a means of acquiring the data necessary for studying these complex systems and improving the predictive capacity of the migration models.

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ETHERA: measuring and cleaning air with a rapid, sensitive, efficient kit

Indoor air quality has become a major issue for individuals sensitive to the air quality in their homes, allergic subjects, hospital staff, persons working in sensitive zones and so on. Faced with this growing awareness and the long-term health risks (asthma, cancer, etc.), new indoor air requirements have been mandated. These measures require innovative measurement and treatment solutions. To satisfy this need, the ETHERA company develops and markets measurement and cleaning kits capable of simplifying the diagnosis, monitoring and elimination of the chemical pollution of the air inside public and private buildings.

The interest of this quick, sensitive and highly selective technology lies in the simplicity of its direct optical measurement, which does away with the need for time-consuming and inevitably costly laboratory analyses. Its success is based on unique know-how in the engineering of nanoporous materials. These materials are synthesized using a sol-gel process, and trap and concentrate the target pollutants. Then, by integrating specific reagents, these initially transparent materials then change color according to the concentration of the pollutant. When associated with optical readers, they become colorimetric sensors. These materials offer a very high pollutant capture capacity; they can also subsequently be used to create air cleaning systems.

In the short term, ETHERA is targeting the professional measurement market for indoor air pollution in heavily regulated areas. It is already proposing individual portable dosimeters for hospital workers and diagnostic equipment for public buildings. Priority has been given to measuring formaldehyde, the most common pollutant, but new studies should soon be expanding the range to other regulated toxic gases such as benzene and trichloramine. In the medium term, ETHERA should be proposing a colorimetry kit for private individuals concerned by their indoor air pollution (carpets, paint, flooring, etc. emitting volatile organic compounds). This kit will be capable of easily detecting particularly toxic pollutants and will comprise an air cleaning system as well.

The ETHERA technology was developed in a joint CEA/CNRS laboratory: LIMPID.


ETHERA

Exposure badges comprising nanoporous materials.

> Yves Bigay
Chairman of ETHERA

FOCUS B

Analyses for health and the environment: stakes and prospects

Analytical chemistry is faced with a highly stimulating challenge, that of characterizing the species present in the environment (water, soil, air) or the biological medium liable to incorporate them. This is an ambitious goal in a number of respects: firstly because of the complex and heterogeneous nature of the environments studied, but also because the chemical elements detected (whether or not radioactive) are often to be found in ultra-trace levels (therefore hard to find) and in extremely varied physico-chemical forms. The researchers therefore have to identify and quantify the elements present, even in very small concentrations, using analysis techniques (preferably *in situ*), but also determine all the chemical forms which the element can take. The chemists use the terms "speciation" for the analyses developed to fine-tune their understanding of these forms, which determine the ability of the species to migrate in the environment, their bioavailability and consequently their toxicity. The implications of this speciation were rapidly recognized by the European Union, which decided to include this understanding of all the chemical forms in the European REACH[1] directive designed to protect the populations from industrial chemical risks.

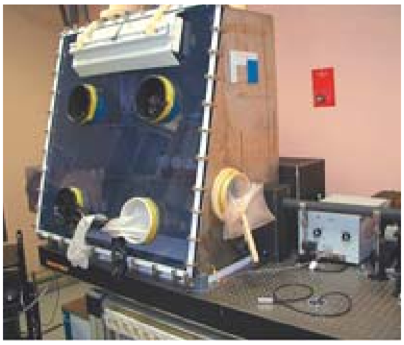
Methodology of speciation

Speciation is a combination of various analysis techniques with computer codes specially designed to determine the distribution of chemical forms from the composition of the medium and the physico-chemical balances involved. The problem lies in protecting the structural integrity of the various species so as to be able to identify them unambiguously, quantify them, or even map them. There are two complementary categories of analytical techniques.

Direct analytical techniques

These allow immediate work on a sample with no particular preparation beforehand, as with spectroscopic or mass spectrometry techniques.

- Time resolved laser spectroscopy (TRLS), also called time-resolved laser fluorescence, is a particularly appropriate technique for investigating the immediate environment of the ion. This process is non-intrusive, because it only uses photons, and exploits the fluorescence properties of certain elements, in particular the changes in this fluorescence linked to variations in the chemical environment of the element. TRLS has proven its effectiveness in characterizing species and determining complexation constants (Figure 1 and Box).
- Nuclear magnetic resonance (NMR) is more particularly used for collecting information about the structure and the stoichiometry of complexes as well as determining complexation constants; this technique does however suffer from sometimes insufficient sensitivity.
- Infrared spectrometry (IR) uses molecular absorption of IR radiation to determine the nature of the chemical bonds within a molecule and thus establish structural hypotheses. Owing to the sometimes extremely complex and specific nature of an IR spectrum, it can act as a molecular ID card.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Time-resolved laser-induced spectrofluorimetry (TRLS) device in a glovebox.

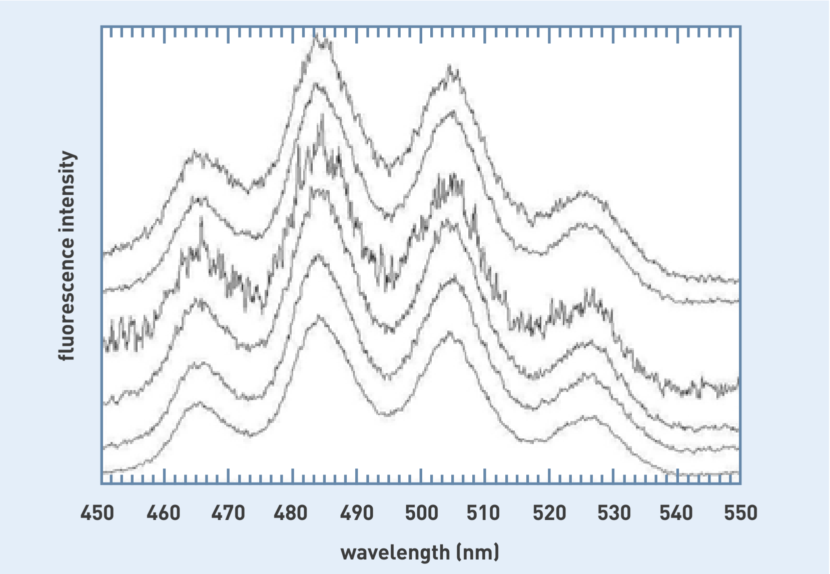

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Figure 1.
Fluorescence spectra of uranium (VI), obtained by time-resolved laser-induced spectrofluorimetry (TRLS), in 6 samples of natural well water taken in Finland, where these waters are naturally rich in uranium. Analysis of the emission bands at 465, 484, 505 and 526 nm confirms the speciation, calculated with thermodynamic data, of the U (VI), primarily in the form of ternary complexes of calcium-uranyl-carbonate.

(1) The European REACH (Registration, Evaluation and Authorization of Chemicals) directive came into force on 1st June 2007, and is an integrated system for the registration, evaluation, authorization and restriction of chemical substances. Its goal is to improve human health and environmental protection against the potential risks from chemical products, while maintaining competitiveness and reinforcing the spirit of innovation within the European chemical industry. The requirements arising from the REACH directive are managed by the European Chemical Agency.

FOCUS B

A quick description of complexation

A metal chemical element in solution in water and electrically charged becomes surrounded with molecules holding the opposite charge, called ligands, with a strength (affinity) that depends on the nature of the chemical bonds created during the interaction between the metal cation and the anion. When the affinity is not too strong, a succession of chemical balances, dependent on the concentration of ligands, tends to bind more and more ligands. For example, pentavalent plutonium (PuO_2^+), in an alkaline solution, will tend to bind with carbonaceous anions in accordance with the following balances:

$PuO_2^+ + CO_3^{2-} \rightleftharpoons PuO_2CO_3^- + CO_3^{2-} \rightleftharpoons PuO_2(CO_3)_2^{3-} + CO_3^{2-} \rightleftharpoons PuO_2(CO_3)_3^{5-}$.

For example, according to Figure 2, at pH = 7.5, the four chemical species of pentavalent plutonium will be simultaneously present in solution, at relative concentrations that are all different: 5% of PuO_2^+ and $PuO_2(CO_3)_3^{5-}$, 20% of $PuO_2(CO_3)_2^{3-}$ and 70% of $PuO_2CO_3^-$.

- Raman diffusion spectrometry will provide information on the chemical structure and composition of a sample, by subjecting it to laser radiation and then analyzing the light diffused. This is a non-destructive method complementing infrared spectroscopy.
- Spectrometry using the absorption of ultraviolet and visible radiation is based on the absorption of light radiation by matter. It is applied to measure the concentrations of chemical species in aqueous or other solutions.
- Electrochemical techniques, based on the redox phenomena occurring at the electrodes perform two roles: determining the bioavailability of the elements and then studying their complexes with organic or inorganic ligands.
- Mass spectrometry consists of a range of analysis techniques capable of detection and detailed identification either of elements (inorganic mass spectrometry), or molecules (organic or molecular mass spectrometry). In this case, the chemical structure of the molecules can be characterized in two ways: either by fragmentation, or by measuring their molecular weight with great precision. Organic mass spectrometry offers numerous combinations between the different sources of ionization and the various analyzers. With Electro Spray Ionization/ESI, that is most commonly used, the researchers can for example obtain multi-charge ions, which are of particular interest in characterizing macromolecules.


CEA

Coupling of a capillary electrophoresis (CE) device (left) with the ICPMS (Inductively Coupled Plasma Mass Spectrometry) device (right).

Indirect analytical techniques

These are based on the coupling of separation techniques (chromatographic or electrokinetic) and elemental detection techniques. This coupling makes it possible to combine the species purification/separation step with highly sensitive detection techniques.

The researchers are today also studying speciation from micro-samples, with extremely low concentration levels in complex biological or environmental media. This advance was made possible by:

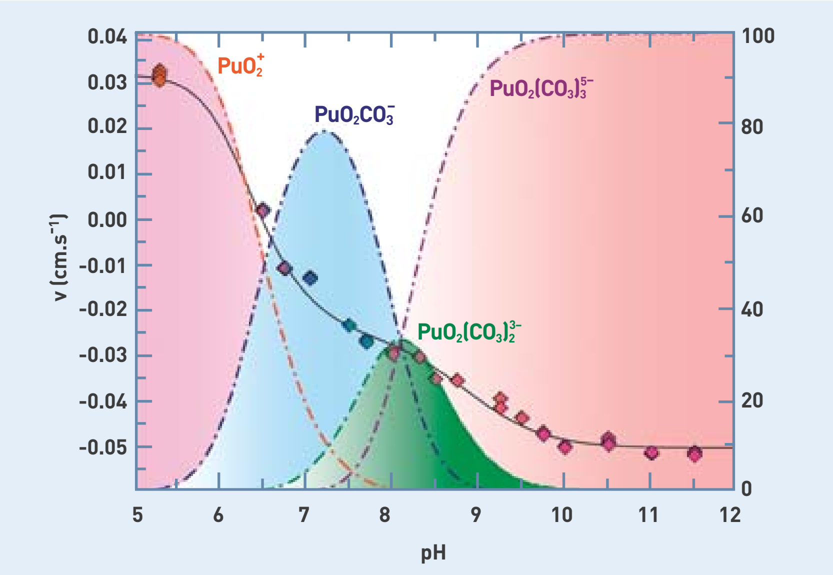
- progress in the field of nanochromatography and capillary electrophoresis; using this last technique, the researchers can separate the chemical species according to the charge/size ratio, by differential migration under the effect of an electric field; they can thus separate the species of a given element, according to their oxidation state or their chemical form, while retaining its initial chemical state;
- coupling of these analytical methods with techniques for detecting elements, such as ICPMS (Inductively Coupled Plasma Mass Spectrometry), or molecules, such as ESI-MS (Electro Spray Ionization Mass Spectrometry). With ICPMS, an extremely sensitive, elementary and isotopic analysis method, the researchers can now determine the speciation with concentrations as low as 10^{-12} mol·L^{-1} (Figure 2); current developments are therefore tending to couple the various separation techniques with organic and inorganic mass spectrometry, to provide the two types of information simultaneously. This process is a particularly interesting one, in particular for the investigation of metals (inorganic) and ligands (organic).

The interest of these different techniques lies in the complementary nature of the information obtained, but also the range of concentrations accessible. With this broad panel of analytical techniques, the researchers can therefore now accurately determine the speciation of an element in natural environmental or biological media. Finally, high-resolution imaging techniques, based on the use of ion beams or synchrotron radiation, supplement this range of physico-chemical analysis techniques, with the aim of establishing the distribution of elements in the biological compartments.

In situ analysis techniques

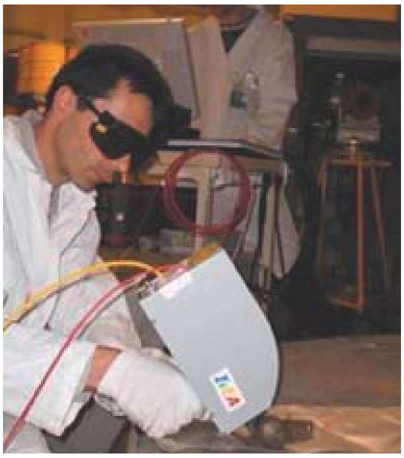
There remains the problem of the collection, conservation and processing of the samples – which are always time-consuming, complex and costly steps and liable to adversely influence the measurements. The Physico-Chemistry Department therefore developed a number of innovative systems devoted to *in situ* analyses in real-time. These systems are based on spectroscopy and the use of lasers to design and implement robust and easily transportable equipment, with performance close to that obtained in the laboratory. The most recent developments of pollutant characterization include:

- CRDS (Cavity Ring Down Spectroscopy), a technique used to detect gas traces by laser absorption spectroscopy, using laser diodes. Thanks to this compact and robust technique, illustrated below, the researchers succeeded in selectively measuring traces of small gas



CEA

Figure 2.
Relationship between the velocity v (expressed in centimeters per second) of the plutonium ion (◆) detected by EC-ICPMS (y axis, left) for a solution pH varying from 5 to 12 (x axis) and the relative proportion of the different carbonaceous species (bright pink for PuO$_2^+$, blue for PuO$_2$CO$_3^-$, green for PuO$_2$(CO$_3$)$_2^{3-}$ and salmon pink for PuO$_2$(CO$_3$)$_3^{5-}$ of the pentavalent plutonium with the same pH (y axis, right). The carbonaceous species of plutoniu PuO$_2^+$ are the most probable species in surface waters.



CEA

LIBS (Laser Induced Breakdown Spectroscopy) fiber optic device for analysis of elements, marketed by CEA's IVEA start-up.

molecules, such as carbon monoxide (CO), hydrogen sulfide (H_2S), methane (CH_4), ammonia (NH_3), nitric oxide (NO) and formaldehyde (CH_2O) in real time, using volumes of about 10 cm^3, and with detection limits of less than $5{\cdot}10^{-11}$ mol·L^{-1}. Originally intended for the nuclear and environmental protection sectors, this technique has found unprecedented applications, especially in medicine. When applied to the air expired by a patient, this type of analysis can reveal the presence of malignant cells in the human body and thus contribute to the detection of cancers.

CEA

On-board CRDS (Cavity Ring Down Spectroscopy) device for *in situ* analysis of gas pollutants. This is a system developed by the Physico-Chemistry Department (DPC) located in the CEA Saclay Center, in collaboration with the Université Joseph Fourier of Grenoble.

- Laser Induced Breakdown Spectroscopy (LIBS) is a method initially developed for analyses in a hostile environment – for example, remote-analysis of radioactive materials. It consists in focusing a laser beam on a material, to vaporize a small quantity of it (less than one µg) thus creating a microplasma. As they de-excite, the atoms and the ions thus ejected emit a spectrum of UV and visible radiation, consisting of lines of a wavelength and intensity allowing identification and quantification of the elements present in the sample. This is a particularly effective means of multi-element analysis of all types of materials, down to concentrations of one part per million (ppm or microgram per gram) for the most sensitive elements.
- Lab-on-a-chip compact analysis microsystems (only a few cm) initially designed for biology, in particular through the use of biochips for medical diagnosis, are today being used for new environmental protection developments. This advance stems from their ability to incorporate the various steps involved in the preparation (micro-extraction) and separation (electrochromatography or capillary electrophoresis) of the components in micro-channels of a few tens of micrometers – with detection based on spectrometry (fluorescence, chemiluminescence, UV and visible radiation absorption, etc.) or electrochemical techniques. These microsystems prove to be particularly effective in analyzing metal traces and organic pollutants. This can be explained by the fact that the sensors (chemical, biological, optical, etc.) can be automated to allow extremely fast analysis in the event of accidental pollution. These processes are enjoying rapid growth and the researchers are anticipating direct access to the analysis of traces in a medium as complex as that of the environment.
- Immuno-analysis methods based on the use of antibodies are in particular being used to detect and quantify biological molecules, with which they will form specific complexes. These non-exhaustive examples of the development of *in situ* analytical techniques probably represent the future for environmental monitoring and surveillance. At present, R&D efforts are being focused on autonomous, miniaturized, faster and more sensitive and selective systems, designed for absolute and relative measurements and capable of monitoring space-time variations.

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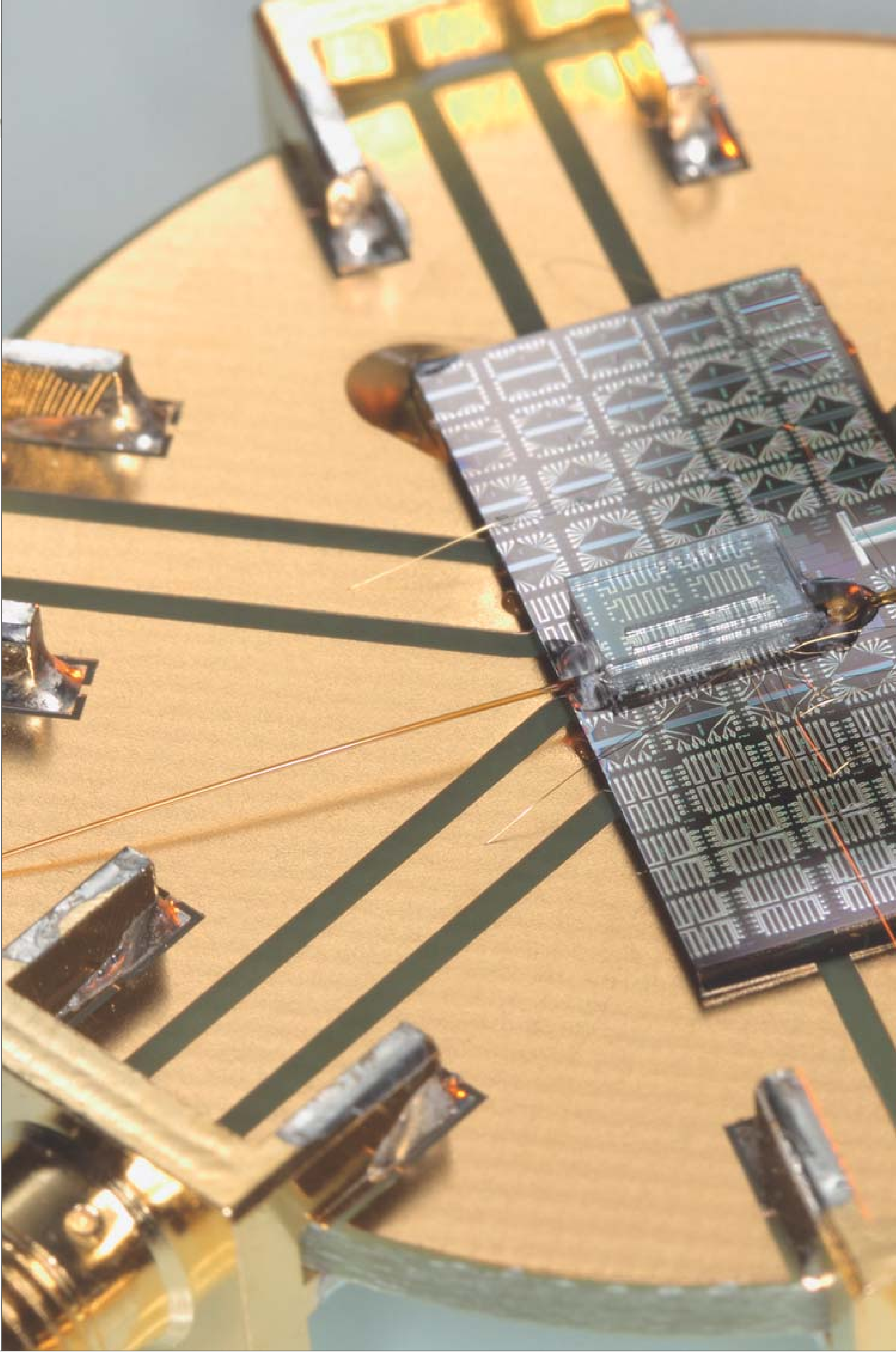

Nano Electro Mechanical System (NEMS) for gas detection.

P. Avavian/CEA

IV. CHEMISTRY FOR THE INFORMATION TECHNOLOGIES

For a number of years now, the information and communication technologies (ICT) have been accelerating so fast that they can only be described by means of roadmaps. For example, microelectronics, characterized by a two-fold evolution based on both miniaturization of components according to Moore's Law (*More Moore*) and their diversification, including the addition of sensors, communication systems or energy storage (*More than Moore*) follows the International Technology Roadmap for Semiconductors (ITRS).

This evolution in microelectronics affects all components, both logical (microprocessors, memories) and analogue (RF electronic components, systems such as MEMS and NEMS (Micro and Nano Electro Mechanical Systems), nearly all of which are silicon-based. At the same time, other sectors are developing within the ICT: flat screens, organic electronics, power electronics for energy management and electronics to support biological and medical activities. Roadmaps such as the *Roadmap for Organic and Printed Electronics*, from the Organic Electronics Association (OE-A), are covering these new sectors; the same applies to *Beyond CMOS* (Complementary Metal Oxide Semiconductor) which is going beyond the traditional limits, and which could one day replace traditional microelectronics.

Whatever the fields concerned, chemistry plays a vital role: manufacturing processes (grafting, self-assembly, electrochemistry, sol-gel processes, printing, inks, etc.), synthesis of new molecules or materials (carbon nanotubes, graphene, colloidal nanocrystals, organic components such as OLEDs (Organic Light-Emitting Diodes), functional molecules (molecules for molecular memories, photo-stimulatable molecules), applications linked to the information technologies, and so on. This overview naturally includes the relationship between chemistry and biology. Chemistry is therefore today present in most of the ICT and the *ChimTronique* cross-disciplinary program can be thanked for having spotlighted these chemistry activities similar to the bottom-up approaches commonly used in nanosciences and nanotechnologies. Of the actions covered by this program, organic, molecular and carbon electronics have recently made great leaps forward, as witnessed by the emergence of industrial transfers and the awarding of the Nobel prize for physics to André Geim and Konstantin Novoselov for their work on graphene.

Another significant aspect of this research is how it addresses complexity *via* the "system" approach, for assemblies comprising billions of electronic components of nanometric or molecular size and of variable quality. In the same way as the neurons of the human brain, these systems should be able to process all the information regardless of defective or unconnected components, or could even repair them. Chemistry, particularly its weak bonds, as well as molecular biology, should play a major role in this.

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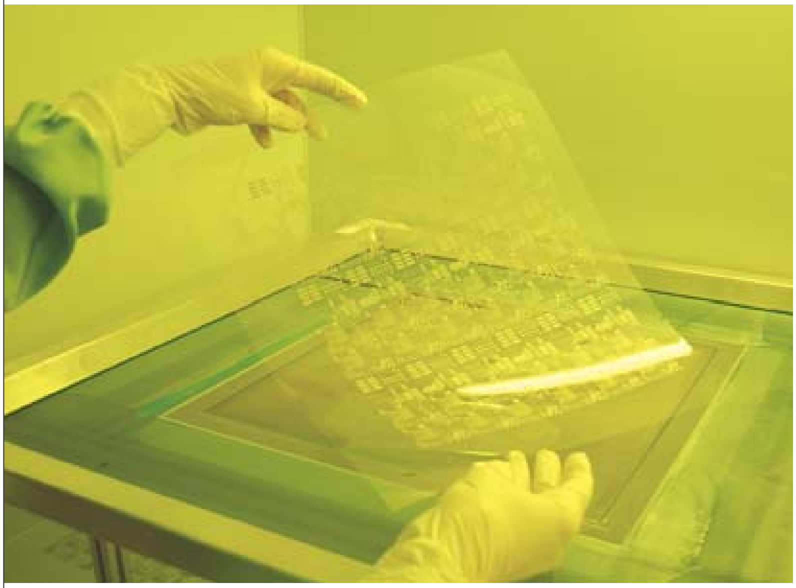
New **performance** for **organic optoelectronics**

Organic semiconductor (OSC) materials were discovered about thirty years ago and **are arousing keen interest** for potential applications in the production of integrated (opto)electronic components and devices, that can be shaped by processes with a low thermal budget and are compatible with large surface areas.



PixelVideo/CEA

Large-sized (30 x 30 cm) printed flexible plastic substrate.

Organic semiconductor (OSC) materials fall into the category of π-conjugated molecular and macromolecular (molecules and polymers) materials, with alternating saturated and unsaturated bonds. This specific arrangement of bonds between atoms (for example, carbon, hydrogen, nitrogen, sulfur and oxygen) gives rise to semiconducting behavior, which can be easily adjusted by molecular and macromolecular engineering. In order to usher in a new form of electronics based on this new generation of semiconductors, future efforts will need to focus simultaneously on improved understanding of the relationship between their structures and properties and on adapting conventional printing techniques to facilitate low-cost implementation of electronic components over large surfaces.

Structures/properties relationship

For the researchers, the challenge is to modulate the chemical structure of OSCs for two reasons:

- fine-tuning of their electronic properties by (macro) molecular engineering of their π-conjugated systems;
- obtaining the solubility needed to process them (using wet methods) by decorating their π-conjugated systems with *ad hoc* solubilizing groups.

By modulating the chemical structure of the OSC in this way, it then becomes possible to produce a formulation for organic/hydro-soluble inks or solutions that are directly usable in printing processes or spin coating, which will allow printing and/or thin film deposition of these OSCs and thus the production of the basic functions and components being sought for this field of electronics.

However, establishing a direct correlation between the composition of basic building blocks (molecules or polymer chains) and the electronic properties extracted from (sub)micron devices still remains highly problematical. The reason is the fact that various types of disorders (chemical and structural) taking place at different scales, disrupt our understanding of the electronic and energy transport processes in these OSC materials. The researchers at the Structures and Properties of Molecular Architectures Department (Service Structures et propriétés d'architectures moléculaires/SPrAM)(1) at the Institute for Nanosciences and Cryogenics (Inac), set themselves the target of overcoming these fundamental obstacles and achieving progress towards the ultimate intrinsic electronic performance (excluding the disorder effects) of these functional (macro)molecular organic materials. Increasing the current performance levels of the first generations of macromolecular and molecular OSCs(2), presupposes first of all identifying, analyzing the impact and then eradicating the various sources of disorders. This is the only possible way of obtaining organic electronic components with enhanced performance and opening the door to "all organic circuitry" of greater complexity, which will allow the development and integration of devices in the future applications from the organic electronics industry.

Molecular OSCs

With their chemical purity and their perfectly defined structural organization, single-crystals of π-conjugated materials offer ideal systems for studying the ultimate electronic transport properties of OSCs. They also allow estimation of the potential applications on organic electronic devices. The researchers at Inac thus succeeded in modifying the vapor phase growth technique for molecular OSCs and in laminating these OSCs through molecular bonding (van der Waals interactions) on a field-effect transistor with a back gate type structure comprising source and drain electrodes (gold) buried in the gate dielectric (SiO_2). Thanks to this advance, it is now possible to obtain ultra-thin single-crystals of rubrene (sub-micrometric thickness) that are conformable and capable of achieving mobility of 4.0 and

(1) Joint research unit (CEA, CNRS and université Joseph Fourier Grenoble I) 5819-SPrAM.

(2) Record mobility values for charge carriers (holes and electrons) of 0.1-1.0 $cm^2 \cdot V^{-1} \cdot s^{-1}$ in macromolecular OSCs and 5-40 $cm^2 \cdot V^{-1} \cdot s^{-1}$ in molecular OSCs.

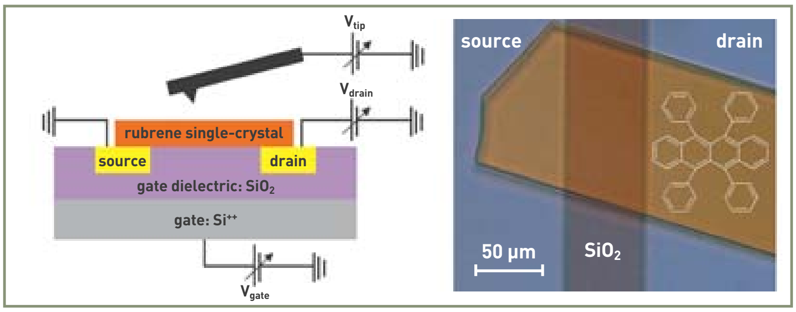


Figure 1.
Organic field-effect transistor based on a rubrene single-crystal and electrical configuration for a Kelvin probe force microscopy study on an operating device: schematic cross-section and top view with a Polarized optical microscope (insert: chemical structure of rubrene).

$6.0\ cm^2 \cdot V^{-1} \cdot s^{-1}$ in the "linear and saturation" regimes of a field-effect transistor (Figure 1). The next challenge was to exploit the dimensional characteristics of this single-crystal of rubrene and the exceptional potential for locally investigating electronic transport at the buried organic semiconductor/gate dielectric interface. By using Kelvin probe force microscopy on an operating device, the researchers succeeded in directly visualizing and identifying, analyzing and quantifying *in situ* two factors which had hitherto limited the electrical performance of OSCs:

- the existence of a potential drop at the source/rubrene contact, resulting in contact resistance, which intrinsically limits the electrical modulation capacity of the current in the transistor channel;
- the correlation between the presence or absence of electronic heterogeneities (at the OSC/gate dielectric interface in the semiconductor channel) and the trapping or non-trapping of charge carriers in the transistor channel.

Over and above the research conducted to obtain new molecular OSCs with improved purity and stability in air, these results identify the areas on which efforts need to be concentrated in order to improve the performance of electronic devices. These priorities in particular concern the effective management of the contact/OSC and gate dielectric/OSC interfaces.

Macromolecular OSCs

Thanks to macromolecular engineering of OSCs, the researchers are now able to synthesize semiconducting polymers to order. Their electronic properties can be finely modulated by adjusting the chemical composition of the π-conjugated system constituting the skeleton of the chains. At the same time, their solubility can be authorized by its functionalization by pending groups, encouraging good polymer/solvent interaction. We thus obtain a generic material platform based on materials with a semi-rigid comb-shaped architecture(3) for printing (opto)electronic components and devices.

Over the course of the last decade, the researchers have achieved remarkable results in the synthesis of new generations of semiconducting polymers with improved structure and chemical stability. However, the mobility values of the charge carriers (holes and electrons) have stagnated in the $0.1\text{-}1.0\ cm^2 \cdot V^{-1} \cdot s^{-1}$ range. The performance and complexity of the functionalities of printed organic electronic components are thus limited. Two factors can explain this:

- at the nanometric scale, certain intra-chain structural defects persist (for example, chain folding) complicating the path of the charge carriers on these chains and forcing them to make more or less efficient jumps between chains to ensure electronic percolation;
- at the mesoscopic and micronic scales, the heterogeneous nano or micro-structuring of the active layers into amorphous and crystalline zones, which are interconnected to varying degrees and hardly propitious to obtaining high performance; it is also worth noting that this deleterious effect can be aggravated by the use of macromolecular OSCs with high polymolecularity index values(4) deviating significantly from the nominal value.

By studying self-assembly on HOPG (Highly Oriented Pyrolytic Graphite) of films (sub-monolayers and multi-layers) of poly(3-dodecylthiophene-2,5-diyl), using scanning tunneling microscopy, our team recently succeeded in visualizing and identifying different types of chain folds and revealing the polycrystalline nature of the monolayers of this macromolecular OSC model system.

The researchers at the Inac recently achieved three significant breakthroughs: visualization of the repair of intra-chain defects, self-sorting of chain lengths and a significant increase in the crystalline zones triggered by thermal annealing (Figure 2). They also revealed that these fundamental processes, favorable to obtaining layers of macromolecular semiconductors with enhanced performance, can develop remarkably beyond the monolayer.

Like the results obtained on molecular OSCs, study of a model system dedicated to macromolecular OSCs highlights two avenues to be explored in order to obtain a new generation of enhanced performance semiconducting polymers:

- purification of the first generations of macromolecular OSCs into polymer materials with a calibrated molecular weight and with significantly reduced polymolecularity index values, the ultimate goal being 1.0;

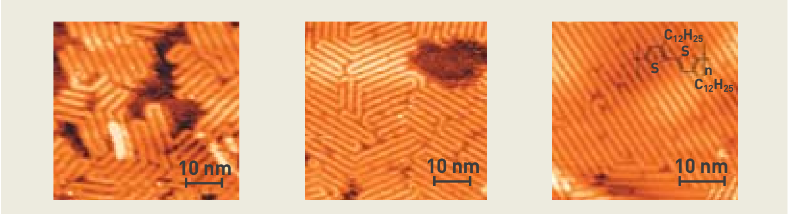


Figure 2.
Scanning tunneling microscopy images [$52 \times 52\ nm^2$] of self-assembled chains of poly (3-dodecylthiophene-2,5-diyl) on highly oriented pyrolytic graphite [sub-monolayer coverage ratio] immediately after deposition at 293 K (*left-hand panel)* from a solution with a concentration of 8 micrograms per liter in chloroform, after initial annealing at 400 K (*central panel*) and after second annealing at 467 K (*right-hand panel*). Insert in right-hand panel: repetition unit of poly(3-dodecylthiophene-2,5-diyl). $C_{12}H_{25}$: chemical composition in terms of carbon atoms (12 atoms) and hydrogen atoms (25 atoms) of the solubilizing *n*-dodecyl paraffin chains which functionalize (in position 3 of the thiophene heterocycle) the poly(thiophene) type π-conjugated macromolecular skeleton to form poly(3-dodecylthiophene).
n: this formalism allows simplification of the notation of the chemical structure of a polymer which, as its name indicates, consists of a repetition (poly) and its repetition unit (mer). n is the number of times the repetition unit is repeated (chemical structure between [ ]) of the poly(3-dodecylthiophene); for a polymer, this number is high, generally at least higher than 20.

(3) The archetype is the family of poly(3-alkylthiophene-2,5-diyl) which appeared in the early 1990s.

(4) Distribution of chain lengths of the same chemical structure deviating from a nominal value equal to one for an ideally monodisperse material.

- the design and synthesis of new macromolecular comb-shaped architectures with high molecular weights, with a low intrinsic propensity for developing chain folds and allowing real control of their structure.

Implementation and applications

The utilization of semiconducting polymer inks opens up new prospects for the development of conformable, large area, low cost organic electronic. The target applications include flexible screens based on printed OLED, RFID identification systems, or sensors. For more than five years, a multidisciplinary team of physicists, chemists and electronics specialists has been working hard on this innovative topic within the Laboratory of Printed Components (Laboratoire des composants imprimés/LCI). Their work aims to integrate low-complexity electronic functions (transistors, capacitors, induction coils, memories), made of organic materials by means of printing processes. This research is a part of various institutional projects financed by the Directorate General for competition, industry and services (DGCIS/FUI Printronics) or the 7th European framework R&D program (PROETEX(5) and COSMIC(6)).

In recent years, a large number of technical obstacles have been overcome concerning the formulation of inks, the lifetime of components, the physical modeling of devices – with this progress leading to the construction of an initial analog and digital CMOS (Complementary Metal Oxide Semiconductor) library, enabling designers to produce the first logic circuits devoted to specific applications. These circuits run at supply voltages of 5 V, compatible with portable electrical power supply sources. The CEA's excellent position on the international stage can be clearly seen through a portfolio of more than twenty patents and numerous publications.

Printing techniques

The use of printing techniques to produce devices and the formulation of active inks are the two major challenges in this field. The evolution of traditional printing tools has led to a diversification of their applications and made it possible to integrate them into industrial processes for electronics. Ink-jet printing, screen printing, gravure printing or flexography are still the most commonly used today. These wet deposition processes take place at low temperatures and allow good integration of functions (resistors, diodes, capacitors) on conformable, large-sized substrates. The attractiveness of these processes lies in their very low cost and high production rates when compared to those of the microelectronics industry.

In order to assume in full its role in this technological challenge, CEA created the Components Printing Platform for the Information and Communication and sensors Technologies (PICTIC) intended for the development of organic electronic technologies. The platform is devoted to the production of functional systems on flexible sheets and will offer industry a two-fold opportunity: pilot-scale testing of materials and printing processes, but also the manufacture of their first printed prototype circuits. This platform, which operates in "sheet to sheet" mode, produces medium-complexity circuits with pattern resolutions of about ten microns.

In order to move onto the industrialization stage, organic electronic technologies will have to provide the circuit designers with more sophisticated drawing rules, compatible with the first generations of products. They will also need to acquire appropriate modeling and simulation tools. The development of these tools is the second key area of research, after the development of the printing processes. This is being tackled by the electronics engineers, utilizing a stable and robust generation of printed components developed at the Laboratory of Printed Components.

Applications

Organic electronics aims simply to supplement and not replace inorganic silicon-based electronics, owing to its lower electrical performance. Rather than witnessing a sterile competition between the two technologies, the future will tend more to see an expansion of the existing traditional electronics market. New applications should appear, taking advantage of the low production costs and the "large conformable surface" features of organic technology. A wide variety of sectors will benefit: photovoltaics, signaling, RFID tags or chemical pressure and temperature sensors.

The Technological Research Division (DRT) of CEA spent the initial years of research on developing printing processes dedicated to individual transistors and then to CMOS functional circuits. The activity is today diversifying and new devices are being studied, such as passive RF filter type components, light-emitting diodes or organic photodetectors. Among the major spin-offs from the activities of the Innovation Laboratory for New Energy Technologies and Nanomaterials (Liten) and the know-how acquired in the field of printing, is the creation of the new Isorg company, specialized in the design and manufacture of organic photodetectors. More generally however, these technologies are targeting the Integrated Intelligent Systems (IIS) sector, primarily for mobile applications. Organic electronics is today promising to be a disruptive technology which could well lead to the emergence of a new range of technologies for information, energy, health and leisure. According to the IDTechEx consultancy firm, which specializes in the new technologies, the global market in this field should reach about 300 billion dollars by 2030. This would be equivalent to that of the traditional CMOS industry in 2009(7).

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(5) Integrated European project for the development of fiberglass based clothing textiles to improve the safety of emergency response crews, in particular the fire department, and for injured civilians, designed to optimize survival management.

(6) Complementary Organic Semiconductor and Metal Integrated Circuits.

(7) Source: *Strategic Research Agenda – by Organic Electronics Association.*

Chemistry for **molecular electronics** and **carbon electronics**

For data processing, **molecular electronics exploit the electronic transport properties of individual molecules or molecular monolayers. An extremely attractive field of research into disruptive electronics based on the synthesis of molecules with adjustable properties then emerged**. To date however, no experimental demonstration has succeeded in achieving a level of performance comparable with that of conventional electronics. Molecular electronics thus remain the preserve of fundamental research. However, the lessons learned are already trickling down to other fields such as organic electronics or photovoltaics.

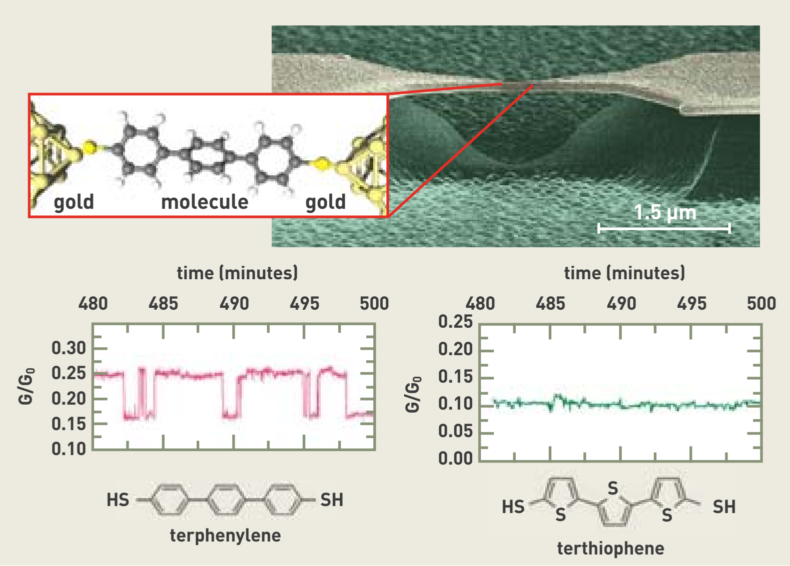
Since 1991, molecular electronics has been interested in carbon nanotubes. These objects can be manipulated in solution like molecules but are more robust and compatible with electronic manufacturing processes. Moreover, their electronic properties far exceed those of silicon. The only downside is that carbon nanotubes remain hard to synthesize, purify and position. However, since 2004, the arrival of graphene among the high-performance materials dedicated to electronics has increased electron mobility to 100,000 $cm^2 \cdot V^{-1}.s^{-1}$ as against only 1,000 $cm^2 \cdot V^{-1}.s^{-1}$ in silicon. One of the major advantages of graphene lies in its ability to synthesize over very large surfaces, which solves the problem of precise positioning of individual objects, which is so critical in the case of nanotubes. But whether molecular electronics concern small molecules, polymers, carbon nanotubes or graphene, chemistry always plays a central role.


C. Dupont/CEA

Low-temperature chemical reaction.

Synthesis and functionalization of new objects for electronics

Chemistry is involved right from the outset in the synthesis of the materials of interest. The conductivity measurements made on individual molecules, in particular those carried out at the Saclay Institute of Matter and Radiation (Iramis), show that any modification to the structure of molecules, however slight, has a significant influence on the electronic properties and stability of the metal/molecule/metal junctions (Figure 1). The ease with which a molecule carries an electric current depends on the conformation and conjugation of this molecule, but also the quality of the metal/molecule bond within the device. The organic chemist thus has highly sensitive tools for designing junctions with adjustable properties. He can design and characterize molecules meeting precise specifications. For example, derivatives of porphyrins, synthesized at the Institute for Nanosciences and Cryogenics (Inac), are specifically substituted to achieve different, electrically switchable conformations, in order to improve the stability of "molecular memory" devices.



CEA (top) and D. Dulic *et al. Angew. Chem. Int. Ed.* 2009, 48, 8273-8276 (bottom)

Figure 1.
Top, image taken with an electron microscope, showing a break-junction, on which the spacing between electrodes can be adjusted with extreme precision. Bottom, stability of conductance of such a junction for two types of molecules (20-minute sequence taken from a 24 h measurement).
In one case, the conductance fluctuates between two values, in the second, it retains the same value for several hours (G being the conductance and G_0 he conductance *quantum*).

C. Dupont/CEA

Stock of carbon nanotubes powder.

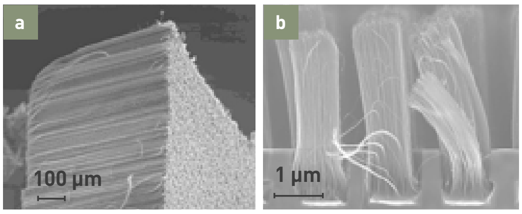
Chemistry is just as crucial for the synthesis of carbon nanotubes, particularly for the engineering of catalysts, in particular metal nanoparticles the nature and size of which to a large extent define the morphology of the synthesized nanotubes. Choosing the right combination of gases and catalysts allows precise control of the materials synthesized, in particular when using CVD (Chemical Vapor Deposition) methods, such as that using an aerosol developed at Iramis (Figure 2a) or those used by the Innovation Laboratory for New Energy Technologies and Nanomaterials (Liten) (Figure 2b).

Once the initial materials have been obtained, chemistry is once again involved, to improve their properties or their compatibility with a particular use, in particular the functionalization of surfaces. There are several processes for immobilizing molecules on a surface, according to the nature of the substrate, the quantity of molecules to be deposited (film or monolayer) or the nature of the desired bond between the surface and the molecules (covalent or non-covalent). For example, the researchers need simply modify the surface of nanoparticles by grafting organic ligands, to guarantee their stability and their solubility or to optimize their properties: particles of platinum can be used as a catalyst in fuel cells and nanocrystals in bio-imaging. With carbon nanotubes, a chemical purification step is required in order to eliminate the catalysts and the amorphous carbon. This is a key step for electronic device applications. This chemical step can also allow the separation of carbon nanotubes having metal type electronic properties from semiconductor nanotubes: this is an essential step in the production of efficient field-effect transistors. A team at Iramis recently developed and patented a very effective method for highly selective elimination of the conductivity of metallic nanotubes without affecting that of semiconducting nanotubes. This was the result of a detailed study of the reaction between diazonium salts and carbon nanotubes – a reaction that was poorly understood, even though often used for their functionalization. This study was originally part of a fundamental research program but opened the door to selectivity, leading to an efficient and useful process.

Organic and molecular nanodevices

Once synthesized, purified and, as applicable, functionalized, nano-objects can then be incorporated into nano-devices. CEA is thus producing systems such as molecular and organic memories, or devices based on carbon nanotubes and graphene.

● Molecular memories can be capacitive or resistive. In the first case, the goal is to exploit compounds with several stable charge states and to detect these states, using the channel of a transistor as a detector. In the second case, a resistive molecular memory exploits compounds with several adjustable conductivity states, such as the anchored porphyrins being studied at Inac or the metal complex based redox compounds being studied at Iramis.



CEA

Figure 2.
Images of carbon nanotubes synthesized at CEA:
(a) by aerosol CVD (Chemical Vapor Deposition) at Iramis [Photons, atoms and molecules Department (Service des photons, atomes et molécules/SPAM)];
(b) for the production of interconnections in integrated circuits at Leti and Liten.

● Carbon nanotubes are the subject of studies for use in the field of electronics. These studies show that despite electron mobility higher than that of silicon, carbon nanotubes will not allow the development of post-CMOS (Complementary Metal Oxide Semiconductor) electronics. This is due to the issue of precise placement of nano-objects within complex circuits and to the lack of homogeneity in their characteristics.

This does not prevent carbon nanotubes from playing a role in applications with different constraints. In particular, the potential of vertical bundles of nanotubes is being evaluated for the interconnection of components in integrated circuits. The conventional metal wires joining the basic transistors to their neighbors will become limited when miniaturized to the extreme. Leti and Liten are therefore developing nanotube-based interconnection technologies compatible with microelectronics (Figure 2b). One major criterion in evaluating these interconnections is the density of nanotubes obtained, and this places CEA among the best in the world. Carbon nanotubes are also looking promising for the production of rapid transistors compatible with all types of substrates. Even if they have trouble competing with silicon in conventional electronics, these transistors could well be serious rivals for uses in flexible electronics. This can be explained by their ability to combine performance superior to that of semiconducting polymers with favorable mechanical properties. A team at Iramis, in association with the Institute for electronics, microelectronics and nanotechnology (Institut d'électronique, de microélectronique et de nanotechnologie/IEMN), was thus able to carry out a first demonstration of non-optimized flexible transistors whose cut-off frequency reaches a GHz. For this type of use, the precise placement of carbon nanotubes and their heterogeneities prove to be less critical – with the nano-objects not being used individually but in large assemblies, so they can then be coupled with large-surface organic electronics deposition and structuring techniques (such as spray or inkjet deposition). An alternative to the positioning problem is to opt for graphene instead of carbon nanotubes. This is due to the capacity of graphene to grow over very large surfaces.

Leti is today actively carrying out studies to obtain the synthesis of high-quality graphene on metal or on silicon carbide. Inac and Iramis are looking to improve our understanding of the fundamental electronic properties both of graphene and of carbon nanotubes.

Finally, these two carbonaceous materials are excellent candidates for the production of transparent flexible electrodes, which are looking particularly promising for flexible screens or portable photovoltaic devices. This would imply replacing the current transparent electrodes, of the TCO (Transparent Conductive Oxide) type, which are commercially well-established and which offer a very good transparency/conductivity compromise. However, the mechanical fragility of TCOs compromises their use for applications on flexible substrates and their rising cost is an obstacle to their economic development. The production of electrodes based on carbonaceous materials offers undeniable process advantages: low temperature, compatibility with most flexible substrates, possibility of using conventional printing techniques. These devices are being studied at Liten and Iramis in particular and offer remarkable performance.

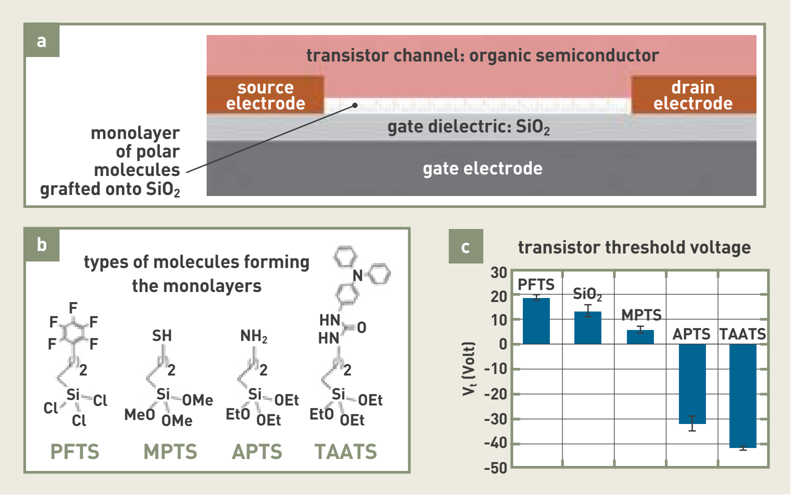
Chemistry as a means of optimizing devices and adding functionalities

For physicists, chemistry has the two-fold advantage of providing them with new objects for electronics and of improving the performance or functionalities of devices, whether or not nanometric.

In a field effect transistor type geometry (Figure 3a), chemistry can be called on as a way of modifying certain interfaces, in particular those between the electrodes and the conducting channel and that between the channel and the dielectric of the control electrode (gate). The teams at Liten and the IEMN have succeeded in demonstrating that the threshold voltage of these transistors can be accurately adjusted by grafting molecular monolayers to the gate dielectric surface of organic transistors (Figure 3). As the effect comes from the dipolar moment of the grafted molecules, it is usable for other types of channel materials, such as silicon nanowires, carbon nanotubes or graphene. The gate dielectric could also conceivably be entirely molecular. This is an advantage for flexible electronics or for use with semiconductors in which the oxide is not as efficient as silicon dioxide (SiO_2), for example germanium.

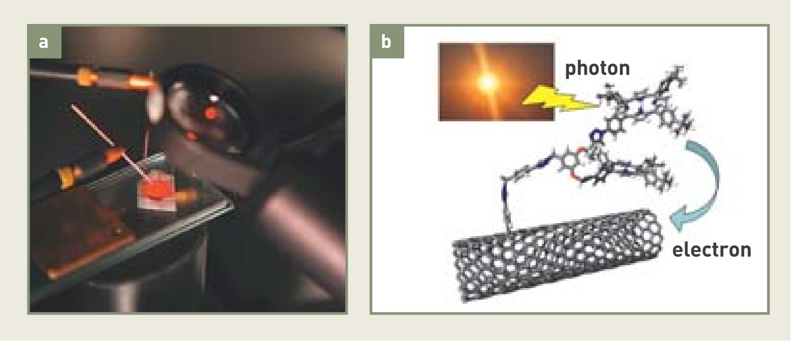
The channel of a transistor can also be chemically modified, which influences the threshold voltage, the level of doping and the conductivity of the channel. Researchers at Inac are examining the benefits of surface functionalization of silicon nanowires by organic molecules as a means of passivating these surfaces, the quality of which is essential in attaining the expected performance of the nano-object. The transport measurements and studies of the photoluminescence properties of grafted objects are techniques used to assess the impact of this functionalization.

In addition, using simulation, researchers at Inac have succeeded in determining the impact of molecular grafts on the conductivity of nanotubes and graphene. This grafting offers an additional means of improving the functionality of devices, particularly for gas sensors. Nonetheless, even if resistors and transistors based on silicon nanowires and carbon nanotubes can be used to make highly sensitive gas detectors, their selectivity is inadequate. However, by functionalizing the sensitive surface with appropriate molecules or polymers, their selectivity can be significantly improved. The researchers at Liten and Iramis have developed devices highly sensitive to different gases (ammonia, nitrogen dioxide, carbon monoxide) and even to certain types of organophosphorus neurotoxic agents. Chemistry thus offers a whole range of possibilities for functionalizing various parts of the sensor (electrodes, channel, gate dielectric) and thus boosting its sensitivity and selectivity.



C. Celle *et al.*/Organic Electronics, 10 (2009) 119-126

Figure 3.
Adjustment of the threshold voltage of an organic transistor, by chemical modification of the dielectric/channel interface. (a) Schematic diagram; (b) Type of molecules grafted; (c) Effect on the threshold voltage (V_t: voltage at which the transistor switches from insulating to conducting state) of a grafted monolayer of each type of molecule. The SiO_2 column corresponds to the non-grafted surface.



C. Dupont/CEA (left)

Figure 4.
Optoelectronic properties of functionalized nanotubes. (a) Measurement of the photoconductivity of a film of nanotubes according to the wavelength; (b) Carbon nanotube functionalized by a zinc porphyrin dendrimer.

Light-sensitivity is another functionality offered by chemistry. Figure 4 illustrates how a complex nano-object can be manufactured and utilized. The principle is to synthesize a porphyrin based dye and then graft it onto a carbon nanotube. It then becomes possible to study the photo-induced charge transfers and thus the optoelectronic properties of the new material. In this example, the dye chosen by Iramis is a first-generation dendron, comprising two chromophores, but a single anchor point on the nanotube. This configuration has the two-fold advantage of maximizing the absorption of light, while preserving the good electrical conductivity of the nanotube.

Modification of the surfaces and interfaces of nanomaterials by chemical functionalization opens the door to remarkable possibilities. This is clearly a major development area for the nanotechnologies of the future. It goes beyond the boundaries of molecular electronics and stands at the crossroads of numerous domains that will benefit from it. Complex functionalized nano-objects (such as that in Figure 4b) thus offer interesting properties in the field of organic photovoltaics. Gas detectors can also be adapted to become sensors for molecules in solution for biology, while functionalized nanoparticles are finding applications in energy and imaging.

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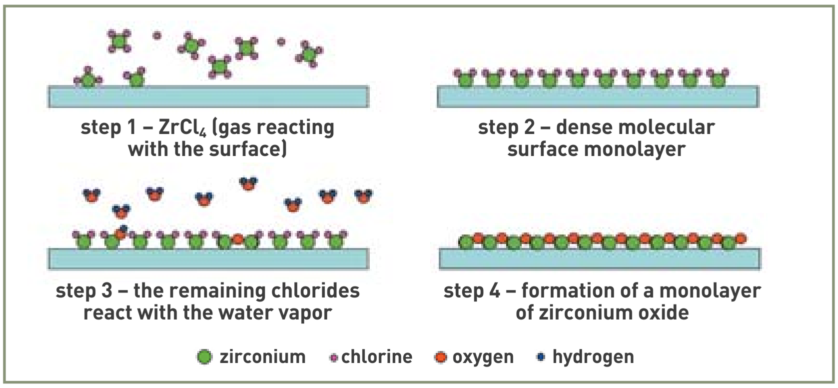
FOCUS C

The growing complexity of chemistry for the information technologies

For nearly 50 years now, the number of transistors in microprocessors has been doubling every two years. It has risen from a few units per cm^2, in 1960, to more than a billion today, with an infinitely small error rate. Late 2011, or early 2012, should see the marketing of the first "22 nm" chips, on which the half-pitch separating the identical features of the array of memory components will be about 22 nm. This size reduction is accompanied by the need for material assemblies of increasing complexity and with ultimate physical properties that are being constantly improved and better controlled. More than a hundred different materials are today integrated during the course of several hundred process steps – some not exceeding a few atomic layers in thickness.

This frenzied race requires increasingly detailed control of the chemistry of the materials used and their manufacturing processes. This control takes place in the scale of the atoms of the structure and the surface of these materials. For the chemists and researchers working in this field, the challenge is one they face on a dayly basis. Hence the development of new Atomic Layer Deposition methods. This technique (and its variants) consists in depositing an atomic layer on a material, using highly reactive organometallic precursors reacting with free chemical groups situated on the surface of the materials to be treated (Figure 1).



Jean-Christophe P. Gabriel/CEA

Figure 1.
Diagram describing the steps in a deposition cycle. ALD uses a sequence of pulsed gases. The first allows reaction with a first precursor (zirconium chloride/ZrCl$_4$) on surface groups and the formation of a first reactional monolayer. After purging, a second precursor (H_2O in the example) is then inserted into the chamber and reacts with the previous layer to form the first oxide layer. As each cycle of pulses produces exactly one monolayer of oxide, this technique allows extremely precise control (to within one atomic layer) of the final thickness of the material deposited.

P. Avavian/CEA

Surface modification in a clean room by liquid-phase silanization on a solid medium.

The chemists at the Electronics and Information Technology Laboratory (Leti) are collaborating with the suppliers and equipment manufacturers, to develop molecules that are reactive enough to adapt to these new deposition methods and determine associated process "windows". To address the rising complexity of these constructions, new precursors must be able to deposit layered materials with novel chemical compositions or more complex structures, such as innovative alloys or oxides (see article page 79). Concerning these precursors, the other essential requirement was to reduce the hazards associated with their high reactivity, prior to any risk-free commercial deployment. In short, the success of this method lies in its daily use for the production of computer processors, but also of memories (USB flash drives), light-emitting diodes, or photovoltaic cells.

Again with a view to improving control of the surface functionalization methods, the researchers at the Saclay Institute of Matter and Radiation (Iramis) have also succeeded in developing several processes giving access to new surface functionalization methodologies, that is electrografting, chemo-grafting, molecular deposition control. The specific precursors synthesized using these processes can then graft themselves onto a surface using a strong and stable chemical bond which perfectly follows the contours of the surface (Figure 2). Two

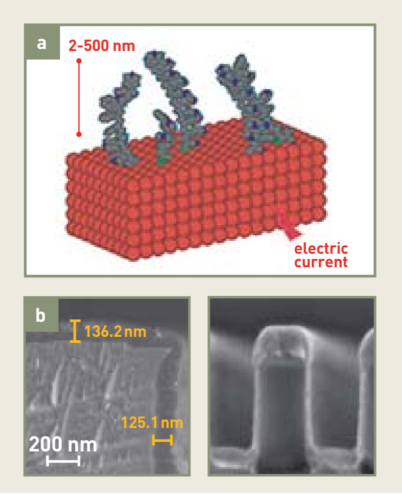


Figure 2.
(a) Electrografting can be used to produce chemical bonds leading to perfect and conforming adhesion (parallel to the surface) of a single molecular layer.
(b) The layers deposited by electrografting (left) follow the surface contours far better than when vapor phase deposition (right) is used, here observed with an scanning electron microscope.

start-ups arose from this fundamental research: the Alchimer company for marketing electrografting and PegasTech for marketing a chemo-grafting process.

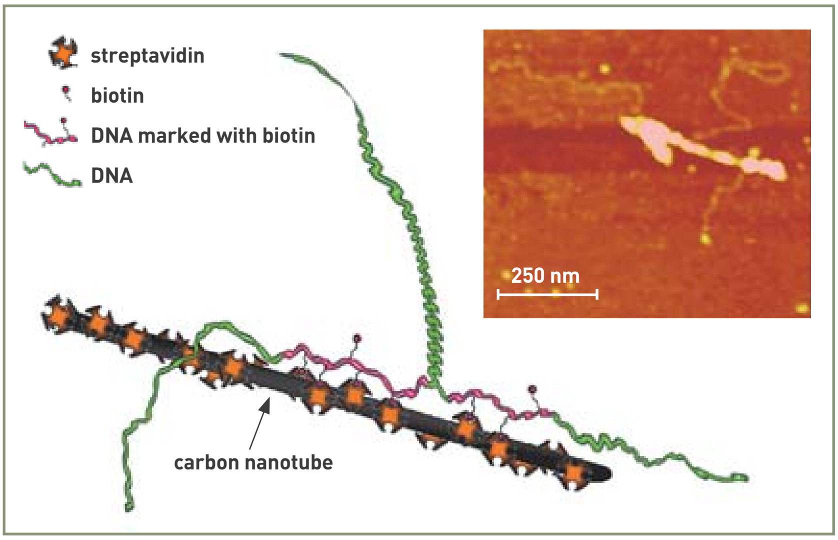
As for the molecules which the researchers are or will be using to functionalize surfaces in the future, they comply with specifications of constantly increasing complexity. These molecules are becoming true multifunction hierarchical structures in which the various molecular parts play different and complementary roles. For example, antennas for photon capture, links for the transmission of the photo-emitted electrons, controlled-size nanoparticles acting as electron reservoirs, etc. The chemists at the Institute for Nanosciences and Cryogenics (Inac) are developing this type of structure in collaboration with their colleagues at the Innovation Laboratory for New Energy Technologies and Nanomaterials (Liten) and the Leti, for the production of new-generation, high-efficiency photovoltaic or light detection components.

Nonetheless, controlling structures and materials by means of surface chemistry will not be sufficient to produce the components essential for the nanoelectronics of the future. It will be necessary to "sculpt" these layers and these materials into clearly defined structures, with nanometric precision. On this point, the industry has for the past fifty years, adopted a top-down approach, in other words, an optical process capable of replicating on a silicon plate the patterns on a reference plate called the mask (a little like producing photographs from a negative). This operation carries the name of lithography. For the illumination step, this technique uses a source of deep ultraviolet radiation, which has a wavelength far shorter than visible radiation – the shorter the wavelength, the better the resolution. Owing to the size of today's patterns, the researchers are now at the extreme limit of the potential of this technique, hence the two top-down options envisaged for the future:

- lithography using light with an even shorter wavelength (by a factor of about 10, or probably 13.5 nm);
- lithography no longer based on a beam of photons, but on a beam of electrons, which will allow nanometer-scale resolution in the laboratory.

These two options demand considerable fundamental and technological development, in terms of both the beam sources and the materials for the associated optics, the masks and their maintenance, the resins to be printed and so on. Moreover, their commercial introduction is being regularly postponed: initially scheduled for 2009 and now expected for 2015. Hence the question of whether it might be possible to replace them with a bottom-up approach using a self-assembly concept that would be simpler to implement, at least in theory. This approach would be derived from the formation of living organisms capable of constructing a complete and functional being from a single cell and some genetic code – apparently with a very low error rate (furthermore, if errors do appear, the system can deal with them). Hence the idea from the CEA chemists of adopting these bottom-up type approaches, in particular those based on the replication properties of DNA. Owing to its extraordinary capacity for molecular recognition and its sub-nanometric scale resolution, DNA is a unique tool for organizing and placing matter. The researchers at Iramis therefore use DNA as scaffolding for installing specific electronic elements/components based on carbon nanotubes (CNTs). They thus manufacture complex structures, capable of preserving the electronic properties of the CNTs. They for example obtained DNA/proteins/CNTs complexes which represent the first step towards self-assembly of CNT transistors with independent gates (Figure 3). Once the self-assembly is completed, the DNA can then be used as a metallization support, or even be transformed into a pathway interconnecting the transistors – which does not stop the List (Systems and Technology Integration Laboratory) researchers from working in parallel on error-tolerant architectures.

These few examples illustrate the pivotal role being played by chemists in the development of future electronic technologies. The researchers at CEA are spearheading these developments and are thus covering a broad spectrum of requirements in this field, ranging from the most fundamental research to technological research, in partnership and close collaboration with their academic and industrial partners.



Stéphane Campidelli and Arianna Filoramo/CEA

Figure 3.
Complex molecular associations, based on the complementarity of the biotin-streptavidin (two proteins) pairing have been synthesized. They are formed on the one hand by a double-stranded DNA molecule (dsDNA) with a T structure, to which the biotin marker is fixed (see the pink double-strand) and on the other by carbon nanotubes on which the streptavidin molecules are placed and interact weakly with the CNTs. When placed together, these molecular assemblies can form a complex by molecular recognition of the biotin-streptavidin pair. Finally, this association can be deposited on a surface to act as a semiconductor channel for an electronic transistor.

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Institutions and organizations: who does what?

Alchimer: created in 2001 as a CEA spin-off, this company specializes in the chemical functionalization of surfaces; it holds the copyright on a number of processes for the production of organic coatings of a few microns, with extremely strong adherence and adjustable functionalities; this company assesses, diagnoses, develops, designs and markets chemical formulations, with specific activities and processes for bonding these molecules to surfaces.

Andra (Agence nationale pour la gestion des déchets radioactifs): a public-sector industrial and commercial establishment (Épic) responsible for the long-term management of radioactive waste produced in France. Andra thus makes its expertise and know-how available to the French Government, in order to identify, implement and guarantee safe management solutions for all the French radioactive waste, to protect present and future generations from its inherent risks.

Anses (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail): this agency plays a role of surveillance, appraisal, research and reference over a broad field covering human health, animal health and welfare and plant health. It provides a cross-disciplinary view of health issues and is thus able to identify all the risks the humans are exposed to, depending on their various lifestyles, their consumption patterns and their environments, including professional.

Areva: a French industrial group, created in 2001 through the merger of CEA-Industrie, Cogema and Framatome. The group is responsible for managing all industrial and commercial activities, particularly in the nuclear, renewable energies and electricity transmission and distribution fields. Its subsidiaries include Areva NC (Nuclear Cycle) – formerly Cogema – covering all services linked to the fuel cycle.

British National Physical Laboratory (metrology institute): a world center of excellence in the preparation and application of the most precise measurements in standards for science and technology.

Caltech: a company which, for the past 15 years, has specialized in the manufacture of cut and machined foam packing for a wide variety of fields: electronics, technical, medical, mechanical and electrotechnical packaging, luxury packaging, IT, maintenance, industry, etc.

CNRS (Centre national de la recherche scientifique): a public-sector scientific and technological establishment carrying out its activity in all fields of research.

DGA (Direction générale de l'armement): a procurement agency for weapons programs. The DGA is responsible for the design, purchase and evaluation of systems supplied to the armed forces.

École normale supérieure (ENS) de Lyon: the Lyon ENS is a multidisciplinary higher education establishment comprising more than 2,000 students, 400 doctoral students, 350 researchers and 230 lecturer/researchers. Among its 23 laboratories, the Chemistry Laboratory (a joint CNRS-CEA-Université Lyon 1 research unit) is developing research into the fields of molecular chemistry, materials with specific properties, theoretical modeling and the structure of complex molecules.

EPA (United States Environmental Protection Agency): an independent American Government agency set up on 2nd December 1970 to study and protect nature and American citizens' health. It employs about 17,000 people.

European Union (EU): association of twenty-seven independent European States who decided to coordinate their policies, delegating certain powers to joint bodies by means of treaties. The EU is governed by two fundamental treaties: the Treaty of Rome, signed on 25th March 1957 and which came into force on 1st January 1958, and the Maastricht Treaty, signed on 7th February 1992 and which came into force on 1st November 1993. These two treaties were retained and amended by the Lisbon Treaty, signed on 13th December 2007 and which came into force on 1st December 2009.

IDTechEx: provides customized advice and consulting and research services to help its customers develop their work in the following key areas: technology and comparative market analyses, strategy definition or evaluation, competitive environment, optimum product positioning, investment security, etc.

IEMN (Institut d'électronique, de microélectronique et de nanotechnologie): a joint research unit (UMR 8520) set up in 1992 by CNRS, Lille University of Science and Technology (USTL), Valenciennes University (UVHC) and the Higher Institute for Electronics and Digital Technology (ISEN: Institut supérieur de l'électronique et du numérique); its research activity covers the fields of physics, electronics, microtechnologies and nanotechnologies. Its main laboratory is situated in Villeneuve-d'Ascq.

Institut des neurosciences: a new center of excellence aiming at a better understanding of the brain through a multidisciplinary approach, from the scale of the cell up to the whole human being, through the use of advanced technologies (Université Joseph Fourier, Grenoble University Hospital, Inserm Unit 318).

IRSN (Institut de radioprotection et de sûreté nucléaire): a public-sector industrial and commercial establishment (Épic) set up in 2001. It is the public expert on research and for the assessment of nuclear and radiological risks. Its field of expertise covers all risks linked to ionizing radiation used in industry or for medicine, as well as naturally occurring radiation (environmental radiological monitoring and intervention in a radiological emergency, human radiation protection, prevention of major accidents in nuclear facilities, reactor safety and safety in plants, laboratories, transport and waste, defense-related nuclear expertise).

Isorg (Image Sensor Organic): a pioneer in organic electronics. This company was set up as a spin-off from CEA/Liten in May 2010 and is the first in the world to produce large-surface photodetectors using printed organic electronics. It has developed an innovative technology able to transform plastic and glass surfaces into smart surfaces.

IUPAC (International Union of Pure and Applied Chemistry): a non-governmental organization, which focuses on chemistry advances and whose members are the national chemistry societies. It is the recognized authority for the development of the rules to be adopted for nomenclature, symbols and terminology of chemical elements and their derivatives.

NEA (Nuclear Energy Agency): a specialist agency of the Organization for Economic Cooperation and Development (OECD) with the role of helping its member countries to maintain and, through international cooperation, to enhance the scientific, technological and legal bases essential for a safe, environmentally friendly and economical use of nuclear energy for peaceful purposes.

OECD (Organization for Economic Cooperation and Development): an inter-governmental organization responsible for promoting policies for sustainable economic and employment growth, improved living standards and a greater freedom of trade.

PegasTech: set up in 2009 as a spin-off from CEA, this company's goal is to design, produce and market surface treatment products in various industrial sectors. Its fields of activity are environmental (water treatment, elimination of industrial pollutants) and biomedical.

Säteilyturvakeskus (STUK): Finnish nuclear safety and radiation protection regulator.

Université Joseph Fourier (UJF) Grenoble 1: situated in Grenoble, the Université Joseph Fourier is a large Comprising more than 50 laboratories, it develops first-rate research in partnership with the national research organizations, including CEA.

Glossary

A

***ab initio* (calculations):** refers to calculations based on fundamental equations of physics and which therefore require neither experimental data nor empirical parameters.

actinides (An): natural and/or artificial radioelements with an atomic number between 89 (actinium) and 103 (lawrencium). This group corresponds to the filling of the 5f and 6d electronic subshell. Actinides all exhibit very similar chemical properties; major actinides: heavy nuclei of uranium and plutonium present or formed in nuclear fuel; minor actinides: heavy nuclei formed in relatively small quantities in a reactor by successive neutron captures by fuel nuclei. These long-lived isotopes are primarily neptunium (237), americium (241, 243) and curium (243, 244, 245).

activity: the number of nucleus decays per unit of time within a radionuclide or a mixture of radionuclides. It is expressed in becquerels (Bq), with one becquerel corresponding to one decay per second and which is thus an almost infinitesimal unit. High-level activity reaches several billion becquerels per gram.

adducts: AB chemical species in which each molecular entity is formed by the direct combination of two distinct A and B molecular entities.

adsorption: a surface phenomenon in which the gas or liquid molecules bind to the solid surfaces of adsorbents through a number of processes of varying intensity; this phenomenon is extremely important in the evolution of numerous chemical reactions. Desorption is the reverse phenomenon.

aerosol: a set of solid or liquid particles of a given chemical substance in suspension in a gaseous medium.

aggregates: small grains of matter comprised of a very small number of atoms or molecules, or even cells, bound to each other by forces of varying strength, generally irreversibly.

algorithm: a theoretical method for numerical calculation on a computer by means of a programming language.

alkane: a saturated hydrocarbon of formula C_nH_{2n+2}.

alkenes: unsaturated hydrocarbons characterized by a double covalent bond between two carbon atoms. The general formula for acyclic alkenes is C_nH_{2n} where $n \geq 2$.

alkylation: a chemical reaction consisting of the transfer of an alkyl group from one organic molecule to another. It thus leads to an increase in the number of carbon atoms in an organic compound.

alloy: a metallurgical product resulting from the incorporation into a base metal of one or more metallic or other elements.

alpha radiation: a positively charged particle consisting of two neutrons and two protons.

Alzheimer's disease: a neurodegenerative disease of the cerebral tissue leading to gradual and irreversible loss of mental functions, memory in particular. It was first described by the German physician Alois Alzheimer (1864-1915).

amidine: a class of organic compounds comprising a $C(=NH)NH_2$ functional group equivalent to an amide in which the oxygen atom of the oxo is replaced by the NH group.

amino acids: a class of chemical compounds possessing two functional groups (both a $-COOH$ carboxyl group and a $-NH_2$ amine group).

α-amino-acids: chemical compounds possessing two functional groups, a carboxylic acid and an amine bound to the same carbon atom; the 20 natural amino acids are the basic components of proteins.

ammonia (NH_3): a colorless gas producing highly concentrated condensation fumes and releasing a highly unpleasant pungent odor.

amorphization: the process whereby a substance is brought to a state characterized by the absence of order in the distribution of the matter particles (amorphous state), as opposed to the crystalline state.

analogue: a substance that is similar in structure to another substance.

angström (Å): 1 Å = 10^{-10} meter.

antibody: a complex protein used by the immune system for specific detection and neutralization of antigens; secreted by cells derived from B lymphocytes: plasmocytes.

antioxidant: a molecule which neutralizes free radicals, thus preventing them from destroying biomolecules.

aptamer: a synthetic oligonucleotide, usually an RNA, capable of binding a specific ligand and sometimes of catalyzing a chemical reaction on this ligand.

***Arabidopsis thaliana*:** a small crucifer whose genome is the smallest known in the plant kingdom. Because of this characteristic, this species is used as a model for genome analysis.

aromatic (compound): a chemical compound containing a cyclic system following *Hückel's rule*. This states that a hydrocarbon is aromatic if planar and if it possesses $4n + 2$ electrons (where n is a positive integer or zero) that can be delocated into a cyclic system. Benzene C_6H_6, for example, which contains one cycle and 6 delocalized electrons, is an aromatic. This rule applies to polycyclic compounds made up of adjacent cycles, only if a carbon does not belong to more than three cycles. For example, anthracene $C_{14}H_{10}$, which is formed of three benzene nuclei, is a polycyclic aromatic hydrocarbon.

Arrhenius's law: this states that there is a linear relationship between the logarithm of a measured quantity and the inverse of the temperature, from which one can deduce an activation energy. In chemical kinetics, this law can be used to describe the variation in the rate of a chemical reaction versus temperature. The reactions with the weakest activation energies are the fastest, and vice-versa.

ATALANTE (originally standing for **ATelier Alpha et Laboratoires pour ANalyses, Transuraniens et Études de retraitement**: Alpha Workshop and Laboratories for Analyses, Transuranics and Reprocessing Investigations): a nuclear facility at CEA/Marcoule dedicated to R&D for the processing of spent fuels, from dissolution of the fuel up to vitrification of the waste, using real radioactive products and the acquisition of basic data concerning the chemistry of actinides. Sophisticated scientific analysis and processes equipments utilizing a system of confinement chambers (gloveboxes and shielded chains) allow the study of the processing processes (hydrometallurgy and pyrometallurgy) and the manufacturing of compounds for actinide recycling tests.

atomic emission spectroscopy: a physico-chemical analysis method based on the emission of photons by excited atoms returning to a lower energy level.

Atomic Force Microscopy (AFM): a method of microscopy based on measurement of the force or force gradient in the three spatial directions between a probe (the tip of which is formed of just a few atoms) and a solid surface. The pointed probe is attached to a thin blade acting as a spring, the deflection of which is measured by the deviation of a laser beam, with a computer allowing the data to be visualized.

automatic learning: a branch of artificial intelligence the aim of which is to study techniques enabling a computer to acquire behavior from knowledge. In chemistry, these techniques are in particular used to obtain procedures capable of estimating a physical value from a molecular formula.

autoradiography: an image produced directly on an emulsion or photographic film by the radiation emitted by a radioactive substance.

B

bacterium: a prokaryote (characterized by the absence of nucleus and organelles) single-cell living organism.

***Bacteroides thetaiotaomicron*:** bacteria of the mouth which are part of the normal flora of the digestive, genito-urinary and respiratory tracts.

bar: unit of pressure; 1 bar = 10^5 pascals (legal unit Pa).

Base Excision Repair (BER): a mechanism for repairing damage to an individual DNA base; such a damage is repaired by simple excision of the base, followed by cleavage of the deoxyribose and then new synthesis. This mechanism concerns relatively slight damage.

benzene (C_6H_6): a monocyclic aromatic hydrocarbon; a colorless organic compound, benzene is a carcinogenic liquid; it is a solvent widely used in the chemical industry, and an important precursor for the synthesis of drugs, plastic materials, synthetic rubber, or dyes. Benzene is a natural component of crude oil.

benzol[a]pyrene: a member of the family of polycyclic aromatic hydrocarbons (PAH).

bio-remediation: a set of processes to eliminate pollutants (organic and/or mineral) present in soils, sediments, liquid effluents by means of micro-organisms (bacteria, yeast, fungi).

bioavailability: the fraction of an element which is present in a mixture of varying complexity and capable of assimilation by an organism.

biochip: a set of DNA molecules attached to and ordered on a small surface (glass, silicon, plastic) allowing analysis of the level of expression of genes in a cell, a tissue, an organ, an organism, or a complex mixture, at a given time and in a given state, by comparison with a reference sample.

biocompatible: which is compatible with biological tissues.

biokinetics: the study of modifications and movements due to growth in a developing organism.

biomass: the mass of living matter, more than 99% vegetable, present on the surface of the Earth.

biosensors: biological devices used to capture biochemical changes within living matter and transmit them *via* a reception system to an apparatus capable of interpreting them.

biosphere: all the ecosystems on the planet, comprising all living beings and their habitat.

bioturbation: a phenomenon involving the transfer of nutrients or chemicals by living beings within an ecosystem compartment or between different compartments, but also the active mixing of soil or water layers by living species, primarily animal.

blood plasma: a liquid component of blood in which the blood cells are in suspension, constituting 55% of the total blood volume.

***Boletus badius (Xerocomus badius)*:** a basidiomycete mushroom of the Bolete family.

bottom-up: the bottom-up approach in nanotechnologies involves the controlled assembly of atoms and molecules in order to form components of a larger size. The reverse operation is said to be top-down.

Brownian motion: named after the Scottish botanist Robert Brown (1773-1858), it is the mathematical description of the random motion of a "large" particle immersed in a fluid and which is subject to no other interaction than the shocks with the "small" molecules of the surrounding fluid; this results in a highly irregular motion of the "large" particle.

C

cadmium selenide: a chemical compound of formula CdSe, semiconductor.

calixarene: a macrocycle resulting from the reaction of a phenol and an aldehyde; calixarenes exhibit hydrophobic cavities which can include small molecules or ions.

Callovo-Oxfordian argilite: a clayey rock formed 160 million years ago in a marine environment, during the Jurassic period of the secondary era. It consists of a geological layer of the Paris Basin, today situated at a depth of between 400 and 600 meters.

calmodulin: a monomer protein of 148 amino acids, capable of binding with the calcium ions present in the cell environment. This bond leads to a change in the conformation of the protein, forming a calmodulin/calcium complex.

calorific value (of a combustible material): the energy contained in materials which can be given off in the form of heat by the reaction of combustion with oxygen. Generally expressed in kJ/kg.

capacitance: measures the quantity of electrical charge stored for a given electrical potential.

capacity (of an electrochemical generator): quantity of electricity stored. Expressed in ampere-hours (Ah).

capillary electrophoresis: a method for separating components according to their rate of migration in an electrical field.

carbon monoxide (CO): one of the oxides of carbon in gaseous state in normal pressure and temperature conditions; colorless, odorless and highly toxic for mammals. It is the cause of extremely frequent and sometimes fatal domestic intoxication accidents if undetected or if appearing suddenly in the air breathed by humans.

carbon nanotube: a structure consisting of one or more rolled graphene layers, with a nanometric diameter but with a length that can reach several, or even several hundred micrometers. Depending on the type of rolling, it may be either metallic, or semiconducting.

carbonate: an ion consisting of a carbon atom and three oxygen atoms carrying a double negative electrical charge (CO_3^{2-}), or a chemical compound comprising this anion.

carcinogenic: a factor provoking, aggravating or sensitizing the appearance of a cancer (chemical product, occupational exposure, lifestyle, physical and biological agents).

catalysis: a process involving a substance (catalyst) capable of accelerating a chemical reaction, without itself undergoing any modification other than temporary.

catharometry: a gas analysis technique based on the difference in the thermal conductivity of gases. The response of the detector is proportional to the measured concentration of the substance.

cellulose: the main component of plant cell walls. It is a linear polymer consisting of glucose units. It varies relatively little with the biomass.

chelation: the establishment of several bonds by the same ligand within a complex; chelator: a ligand liable to form several coordination bonds with an ion or a molecule within a complex; chelating: qualifies a multidendate ligand liable to engage in several bonds with the same metal cation by exerting a "clamping" effect, making the assembly particularly stable (formation of a 5 to 7 link cycle with the cation).

chemiluminescence: a chemical reaction phenomenon the consequence of which is the emission of light when an excited (unstable) molecule returns to a stable state.

chemo-grafting: a self-limited functionalization method allowing controlled deposition of a molecular monolayer on a surface.

chromatography: an analysis technique in which the sample, containing one or more species, is entrained by a mobile phase current (liquid, gas or supercritical fluid) along a stationary phase (paper, gelatin, etc.). Each species moves at its own speed dependent on its characteristics and on those of the two phases; a molecule separation technique based on their different solubilities in solvents.

chromophore: a colored molecule.

cladding: a leaktight envelope around nuclear fuel, designed to confine the radioactive material, guarantee its mechanical strength inside a reactor core and transmit heat from the fuel to the coolant.

CMOS (Complementary Metal Oxide Semiconductor): a technology for manufacturing electronic components and, by extension, all the components manufactured by means of this technology.

co-crystallization: a technique which places a very good inhibitor together with its enzyme and which uses X-ray crystallography to destroy the precise conformation of the inhibitor inside the enzyme cavity.

coarse-grained model: a model used for simulation of ionic solutions without explicit representation of the solvent.

code (to): in genetics, a gene codes for a protein, in other words, induces the synthesis of a protein which possesses a clearly defined sequence of amino acids.

cognition: the range of intellectual activities and processes relating to knowledge and the function which produced it.

colloidal (phase): a mixture of ultramicroscopic particles uniformly dispersed through a substance to form a suspension or a gel.

complexation: the formation in an organic or aqueous solution of an edifice (or complex) consisting of a central metal ion to which other ions or molecules, called ligands, bind in numbers greater than the charge of the metal (for example, $LnCl_3$ is an inorganic salt, $Ln(H_2O)_9^{3+}$ is a complex). A complexing molecule (or ligand) is a chemical species capable of binding with a metal ion to form a complex.

composite: a material formed by the assembly of several other materials and exhibiting properties that each of the latter do not individually possess. It for example consists of a framework (*stiffener*) supporting the mechanical loads, and an encapsulating material (*matrix*).

computed tomography: X-ray imaging for studying anatomical structures.

computer code (or software): in a computer software, a simplified numerical representation (modeled) of a system or process, in the form of coded mathematical expressions, in order to simulate it.

conductivity: characterizes the conduction capacity (electrical, thermal) of a material.

confinement: the physical and/or chemical ability to maintain radioactive and/or toxic elements in a given place or within a given object (limiting dispersion or release).

confocal: refers to an image from an optical microscope; these are images with a very small depth of field (about 400 nm); they are obtained by positioning the focal plane of the lens at different depths in the sample; this can be used to produce a series of images from which it is possible to obtain a three-dimensional representation of the object. The object is not therefore directly observed by the user, who sees an image recreated by computer.

containment barrier: a device capable of preventing or limiting the dispersion of radioactive materials.

contrast agent: in medical imaging, a compound which artificially increases the contrast, allowing the visualization of an anatomical (for example blood vessels) or pathological (for example a tumor) structure, which would naturally offer little or no contrast and which would be hard to differentiate from the neighboring tissues.

coordination number: the number of bonds an ion is capable of establishing with electron donor atoms. For actinyl ions (AnO_2^{n+} where $n = 1$ or 2), the coordination number is split into two: that corresponding to the coordination in the equatorial belt and that of the two axial positions given between parentheses.

copper sulfide: a chemical compound of formula Cu_2S, semiconducting.

corrosion: the slow deterioration of the surface of materials by chemical agents; on metals, corrosion involves oxidation.

counterion: an ion which, in association with a surface or another ion with the opposite charge, ensures electric neutrality.

covalent bond: a bond between two atoms which saturate their last orbital by sharing one or more electron pairs.

cracking: a modification of the molecular structure of a hydrocarbon under the effect of heat, pressure and sometimes a catalyst.

CRDS (Cavity Ring Down Spectroscopy): a technique allowing the analysis of gas traces by absorption spectroscopy. The principle consists in measuring the time constant of the decay of a laser pulse injected into a resonating cavity containing the gas to be analyzed, then deducing the concentration from this measurement.

crown-ethers: heterocyclic chemical compounds which, in their simplest form, are cyclic oligomers of ethylene oxide.

CVD (Chemical Vapor Deposition): a method for preparation of layers (with a thickness that can vary from a few tens of nanometers to about a hundred micrometers) by vapor phase deposition formed by a chemical reaction from a gaseous medium of different composition.

cycleability: expressed as a number of cycles (a cycle corresponds to a charge and a discharge), it characterizes the lifetime of an electrochemical generator, in other words the number of times it can restore a capacity greater than a predetermined threshold (generally 80% of the initial capacity). It heavily depends on the type of load and the positioning of this threshold.

cycling: alternation of charging and discharging.

cyclotron: a type of circular particle accelerator in which the particles placed in a magnetic field follow a spiral path and are accelerated by an alternating electric field to energies ranging from a few MeV to about thirty MeV.

cysteine: a natural α-amino acid present in most proteins and which possesses a thiol group.

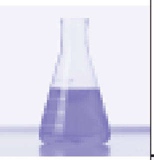
cytoplasm: comprises everything contained inside the volume bounded by the cytoplasmic membrane, except for the nucleus and certain organelles (mitochondria, lysosomes, etc.).

D

β-diketones: organic compounds possessing two ketone functions (C=O), separated by an intermediate carbon, and exhibiting chelating properties with respect to metal cations.

DDL: an abbreviation designating 3,5-diacetyl-1,4-dihydrolutidine, a cyclic compound resulting from the condensation between two molecules of Fluoral-P and formaldehyde; 2,6 lutidine, which is the dimethyl derivative of pyridine (benzene with a nitrogen atom replacing a carbon atom), exists naturally and comes from the carbonization of coal.

decorporation: a treatment using a chemical substance to eliminate radioactive or toxic elements incorporated into an organism.



degree (or number) of oxidation or oxidation state: the relative number of electrons that must be added to a metal ion in a complex to make it neutral (for example, the oxidation state (o.s.) of iron in the complex $[Fe(H_2O)_6]^{3+}$ is +III). A lower number corresponds to reduction and a higher number to oxidation.

dendron: a molecule comprising on the one hand a branch site with reactive ends and, on the other, a site able to bind with a molecular or solid support.

Density Functional Theory (DFT): a theory based on the existence of a universal functional allowing calculation of the energy of a quantum system with *n* particles on the basis of the electronic density. Conceptual DFT is a branch of this in which one seeks to extract chemical concepts and principles from DFT; other names: chemical DFT, chemical reactivity DFT.

descriptor: a numerical value that is easy to obtain from a chemical formula and which is therefore liable to constitute an input variable for automatic learning methods.

diazonium (salts): positively charged ions, consisting of an aromatic cycle carrying a "diazo" N_2 group; these compounds are used to synthesize dyes and as precursors of aryl groups for surface functionalization.

dielectric: refers to a material which contains no electrical charge liable to move and thus which cannot conduct electrical current; synonym for electrical insulator.

dimer: in chemistry, a molecule consisting of two sub-units bound together. Tetramers and hexamers comprise four and six sub-units respectively.

dimethyl-ether (DME): a chemical compound of formula $CH_3–O–CH_3$ occurring in liquid state at 20 °C under a pressure of 5.3 bar.

diode: an electronic component which lets electrical current pass in one direction only.

dipolar (moment): the origin of the existence of a dipolar moment in a molecule lies in the difference in electronegativity between the atoms.

disaccharide: a carbohydrate comprising two sugar molecules bound together.

disposal (of radioactive waste): the operation consisting in placing the radioactive waste in a special facility designed for potentially permanent disposal. This term also refers to a disposal facility designed for the conservation of the waste with no plans for subsequent recovery. Recovery would however be possible in the case of a reversible disposal facility. The deep geological disposal of radioactive waste entails placement of these substances in an underground facility specially designed for this purpose.

disproportionation: a redox reaction in which a given chemical element, present at a certain degree of oxidation in the reagents, acts as both oxidant and reductant, thus having two different degrees of oxidation in the products, one higher and the other lower than the initial degree of oxidation.

DNA (deoxyribonucleic acid): the molecule carrying hereditary genetic information; its original structure, comprising two helical wound complementary strands (double helix), enables it to duplicate into two molecules identical to each other and to the parent molecule; these are the components of chromosomes; genes are DNA segments.

DNA chip: see biochip.

donepezil: a drug with indirect parasympathomimetic action owing to its reversible inhibiting effect on acetylcholinesterase; used in light to moderately severe forms of Alzheimer's disease.

doping: the introduction of a foreign atom (doping agent) into a crystalline or amorphous array, in order to modify its properties.

dose: the quantity of energy deposited by a unit of mass in a material by means of penetrating radiation.

dosimeter: an instrument designed to measure exposure to pollutants.

double-helix: the chemical components of DNA, named A, T, C and G (for adenine, thymine, cytosine and guanine) combine to create "steps" forming the double-helix structure of DNA and always combining according to the same model: A with T and C with G.

D-penicillamine: a decay product of penicillin; a drug which has been used to treat Wilson's disease since 1956.

DTPA (Diethylene Triamine Penta Acetic acid): a member of the polyaminocarboxylates family widely used in chemistry.

E

echography: an imaging technique using ultrasounds.

ecosystem: a group of biological communities sharing a physical environment: air, water, the earth and the living organisms, including humans, interact to form an ecosystem.

eco-toxicology: a discipline at the interface between ecology and toxicology, arose from recognition of the fact that a growing number of toxins have contaminated and are continuing to contaminate all or part of the biosphere with some of them interacting with each other and with living organisms.

effluents: waste in liquid or gaseous form.

electrocatalyst: the catalyst of an electrochemical reaction, in other words involving an exchange of electrons between one or more chemical species and an electrode.

electrochemical shuttles: certain additives present in the electrolyte of a Li-ion rechargeable battery undergo oxidation reactions on the positive electrode. In their oxidized form, they then diffuse to the negative electrode, where they are regenerated by reduction. The oxidation potential of the chosen additive is a way of limiting the maximum potential to which the positive electrode will be charged. The surplus capacity injected as charge is thus consumed by the redox reactions of this electrochemical shuttle, generating the equivalent of an internal short-circuit.

electrochemistry: a scientific discipline describing chemical phenomena coupled with reciprocal exchanges of electrical energy.

electrode: a conducting element using an electric field to emit, capture or guide electrons or ions. When placed in a medium (electrolyte, etc.), electrodes can be divided into cathodes and anodes depending on whether they supply electrons to the external medium or receive them. The anode is where an electrochemical oxidation reaction occurs, while the cathode is where an electrochemical reduction reaction takes place. In a disposable or rechargeable battery, there is a positive electrode and a negative electrode.

electrografting: the "organic" equivalent of electroplating; the species generated by electrochemistry are organic reagents, precursors of an organic film covalently grafted onto the electrode.

electrokinetics: the study of electrical circuits and above all of the movement of electricity through materials, as compared with electrostatics, which studies the phenomena and laws relative to static electricity.

electroluminescence: an optical and electrical phenomenon during which a material emits light in response to an electric current passing through it, or to a strong electrical field.

electrolysis: the use of electric current passing through an electrolyte placed between two electrodes to perform a chemical reaction. In the specific case of electrolysis of water, the electric current breaks the water down into oxygen and hydrogen, given off at the two electrodes.

electrolyte: a liquid or solid medium allowing the conduction of the electric current *via* the displacement of the ions it contains.

electronic component: an element designed to be assembled with others in order to perform one or more electronic functions.

electronic or ionic conduction: the phenomenon whereby an electron or an ion moves within a material.

electronic relaxation: return to electronic spin magnetization equilibrium after disruption by a magnetic field disrupting its equilibrium (the electrons have their own kinetic moment, called spin, which gives rise to a magnetic moment); if electronic relaxation of a paramagnetic complex is too fast, this compound will not be an effective MRI contrast agent.

electronvolt (eV): unit of energy corresponding to the energy acquired by an electron accelerated by a potential of 1 volt, thus 1 eV = $1.602 \cdot 10^{-19}$ joule. Primary multiples: keV (10^3 eV), MeV (10^6 eV) and GeV (10^9 eV).

electrophoresis: a separation technique, used in chemistry and biology (with chromatography), to separate and characterize molecules; it is based on the difference in their partition coefficients between a mobile phase (buffer, solvent) and the solid phase (gel, polymer support).

Electrospray Mass Spectrometry/ES-MS: a mass spectrometry (MS) technique in which the elements to be analyzed are introduced into the apparatus in the form of a spray (Electro Spray Ionization/ESI) and then ionized, before identification of the mass of the ions thus formed.

empiricism: a method relying on experimentation alone.

energy output (of an electrochemical generator): expressed in watt-hours (Wh), it corresponds to the product of the current (in amperes A) and the voltage (in volts V) integrated over the duration of discharge (in hours h).

enrichment: the process designed to increase the content of one of the isotopes of an element.

enzyme: a molecule able to reduce the activation energy of a reaction and to accelerate by up to several million times the chemical reactions of the metabolism taking place in the cellular or extracellular environment, without modifying the equilibrium created; these proteins are the catalysts of the living world.

ESI-MS: the electro-spray source (Electro Spray Ionization/ESI) is a source of ion formation from a liquid solution, by vaporization and nebulization of this solution, in the presence of an intense electrical field. When associated with mass spectrometry (MS), it is a powerful tool for analyzing molecules.

ethanol: a colorless liquid (alcohol) with chemical formula C_2H_5OH.

extrusion: a transformation process consisting in continuously pushing a heat-softened material through a *die* which imparts its geometry to the extruded section.

F

Fabry's disease: a genetic disease, linked to the X chromosome and due to an alpha-galactosidase A enzyme deficiency. It therefore mainly attacks men. The first signs appear in childhood or adolescence with skin lesions, painful extremities, reduced sweating, anomalies of the cornea, cataracts. By adulthood, the disease can evolve to kidney failure, heart problems and strokes.

Fast Neutron Reactor (FNR): a reactor without moderator in which most of the fissions are produced by neutrons presenting energy levels of the same order of magnitude as that they had when they were produced by fission.

fast neutrons: neutrons released by fission, traveling at very high speed (20,000 km/s). Their energy is about 2 MeV.

femtosecond: 1 fs = 10^{-15} second.

Fick's equation: this is obtained by writing the conservation of matter law and considering that the diffusive flux is proportional to the concentration gradient (Fick's first law).

field-effect transistor: a semiconducting device of the transistor family, which uses an electrical field to control the shape and thus the activity of a "channel" in a semiconducting material.

fissile: refers to a nuclide whose nucleus is liable to undergo fission by absorption of neutrons. Strictly speaking, it is not the nucleus referred to as fissile which undergoes fission, but the compound nucleus formed following a neutron capture.

fission: the splitting of a heavy nucleus into two pieces, accompanied by the emission of neutrons, radiation and significant amounts of heat.

fission products: nuclides generated either directly by nuclear fission, or indirectly by the decay of fission fragments. They are gaseous (fission gases) or solid (volatile or otherwise).

flexography: a relief printing technique with flexible plastic or rubber film and a fluid ink.

fluidized bed (reactor): a reactor in which an ascending current of a fluid counteracts the apparent weight of particles of a powder product which then flows like a fluid.

Fluoral-P: the commercial name for acetylacetonamine or 4-amino-3-penten-2-one, a synthetic compound produced from acetylacetone and ammonia.

fluorescence: the emission of light triggered by the absorption of an incoming flux (of light, X-ray electromagnetic radiation or electrons) followed by rapid de-excitation of the electrons in the outer atomic layers of the luminescent body – this loss of energy leads to the emission of a new electromagnetic radiation; if its wavelength is situated in the visible part of the spectrum, there is luminescence.

fluorescent or profluorescent oligonucleotide probes: small fragments of DNA manufactured by chemical synthesis, by sequentially adding the different nucleotides carrying DNA bases in a predetermined order; the fluorescent probes are marked by a fluorescent tracer which enables their location or their transformation to be monitored, especially during the enzymatic repair process.

fluorophore: a chemical substance capable of emitting fluorescence light after excitation.

force field: a conventional model describing the potential energy of a system of particles (generally atoms). A polarizable force field implicitly includes the effect of polarization by introducing induced dipoles.

formaldehyde (H_2CO): a gas at ambient temperature better known as formol when solubilized in water. It is present in numerous products such as paints, wallpapers, detergents, glues, softeners, adhesives, forest fires, tobacco smoke. It is even produced in small quantities by the human body. It is classified as a "known carcinogen", causing nasopharyngeal cancers.

fossil energies: energies produced from geological deposits of organic fuel matter buried under the ground, such as coal, oil and natural gas.

Fourier transform: result of a complex mathematical operation which consists in "weighing" the relative weight of each frequency in a time signal in order to give a spectral representation of that signal.

Fourier Transform InfraRed spectroscopy (FTIR): an analysis technique based on the absorption of infrared radiation from the gases examined; through the detection of the vibrations characteristic of chemical bonds, it can be used to analyze the chemical functions present and thus identify the nature of the gases present. The spectra obtained are interpreted using a mathematical operation called the Fourier transform.

fourth-generation nuclear reactor: a new generation of nuclear power generating systems being studied internationally and offering improved economics and safety, less waste and a lower risk of proliferation when compared with the existing reactors or those under construction. Six reactor technologies, mostly *closed cycle* and fast neutron, were selected for the detailed design studies, using sodium, lead, supercritical water, gas (helium) or molten salt as the coolant.

free electron laser: a type of laser that functions using electrons that are not bound to an atom, hence the term "free", to create photons.

fuel (nuclear): a fissile material which, through an appropriate geometry, sustains a chain reaction within the core of a reactor; fuel element: the smallest component of a core with its own structure, containing nuclear fuel; spent fuel: fuel which can no longer sustain the nuclear reaction and is removed from the reactor.

fuel cell: a cell in which electricity is produced by the oxidation on an electrode of a reducing fuel (for example hydrogen) coupled with the reduction on the other electrode of an oxidant, such as the oxygen in air.

fuel cycle: the circuit followed by nuclear fuel. The cycle comprises mining of the ore, concentration of the fissile material, enrichment, fabrication of the fuel elements, their utilization in the reactor, their processing, the possible recycling of the heavy atoms thus recovered and the packaging and disposal of the radioactive waste.

fullerenes: carbon compounds containing at least 60 carbon atoms. The atoms are arranged in polyhedra (similar to graphite) to form spherical compounds.

functionalization: broadly speaking, the adaptation of a chemical, physical, or biological object to make it perform the desired functions. More strictly speaking, we talk of surface functionalization to bind certain chemical functional groups on a surface.

furfural: a cyclic compound with chemical formula $C_5H_4O_2$ used in particular in the chemical industry as a solvent.

fusion: an energy production process involving the fusion of light-element nuclei (hydrogen isotopes).

G

gamma radiation: a highly penetrating but only slightly ionizing electromagnetic radiation emitted in the form of photons by the decay of radioactive elements.

Gas Phase Chromatography (GPC): a technique used to separate the various molecules of a mixture. It primarily applies to gas compounds or compounds liable to be vaporized by heating, without breakdown, and is increasingly widely used in the main fields of chemistry.

Gaucher's disease: a disease due to a deficiency of an enzyme, glucocerebrosidase, essential to the breakdown of a particular lipid, glucocerebroside. When it abnormally builds up in the spleen and the liver, it leads to hypertrophy of these organs, as well as to anemia, spontaneous bruising and coagulation disorders.

gene: a sequence of deoxyribonucleic acid (DNA) which specifies the synthesis of a chain of polypeptides or a functional ribonucleic acid (RNA).

genetic code: a set of rules enabling proteins to express the information contained in the genetic material of living cells.

genome: the assembly of hereditary material comprising nucleic acids (DNA or RNA) of a cellular organelle, an organism or a species.

genotoxicology: the branch of toxicology which focuses on studying the effects of toxic substances on the genes. This discipline looks at damage to DNA, its repair and its biological consequences, especially in terms of mutations.

geosphere: all the different parts of the Earth supporting the biosphere, comprising the inner layers, the outer layer (lithosphere), the hydrosphere and the atmosphere.

glaucoma: an increase in the intraocular pressure leading to damage to the optic nerve.

glutathione: a tripeptide, formed by the condensation of glutamic acid, cysteine and glycine: γ-L-Glutamyl-L-cysteinylglycine.

glycoamidine: a molecule composed of a glucid type structure and an amine function.

glycosidase: an enzyme performing hydrolysis of sugars.

glycosylation: an enzymatic reaction consisting in creating a covalent bond between a glucid and a peptide chain or a protein.

grain boundary: the boundary between two crystallites. A crystallite is an area of matter (grain) with the same structure as a single-crystal and a size ranging from a few tens to a few hundreds of nanometers.

graphene: a two-dimensional (single-plane) crystal of carbon, which when stacked forms graphite.

graphite: one of the allotropic forms (in other words with a thermodynamically stable crystalline structure in certain temperature and pressure conditions) of carbon with a crystalline structure taking the form of graphene layers, in which each atom is bound to three of its neighbors.

gravure printing: a printing technique employed for large print runs, using etched copper cylinders or plates.

green chemistry: a concept defined in 1998 by the American chemists Paul Anastas and John Warner, which entails the application of principles to reduce and eliminate the use or generation of substances harmful to the environment, by means of new chemical processes and "clean" synthesis methods, in other words which are environmentally-friendly.

greenhouse gas: gases present in the Earth's atmosphere and contributing to global warming. The main greenhouse gases are carbon dioxide (CO_2), water vapor and methane.

H

hadrontherapy: a method for destroying cancer cells by irradiating them with a beam of accelerated particles (particularly carbon ions and protons). Its advantage over conventional radiotherapy, which mainly uses X-rays, lies in the fact that it allows precise targeting of deep tumors while causing less damage to the healthy surrounding tissues.

half-pitch: in a periodic array structure, the half-pitch represents half the distance between a node on the network and its nearest neighbor.

hemicellulose: the second component of plant cell walls. It is a ramified polymer formed of sugar units with 5 or 6 carbon atoms. Its nature significantly varies according to the biomasses.

hemodialysis: a method for blood purification by creating an extracorporeal circuit passing the blood through a dialyzer.

hemoglobin: a protein whose main function is to transport dioxygen in the human organism and other vertebrates.

hertz: a unit of frequency (Hz) of an alternating phenomenon, equal to one cycle per second; the main multiples are: the megahertz (1 MHz = 10^6 Hz) and the gigahertz (1 GHz = 10^9 Hz).

heteroaromatic radiofluorination: refers to a chemical reaction allowing the introduction of radioactive fluorine into an aromatic type chemical nucleus not exclusively consisting of carbon atoms.

heterocycles: a class of chemical compounds in which one or more atoms of a carbocycle is replaced by a heteroatom (atom other than carbon or hydrogen and non-metallic), such as oxygen, nitrogen, sulfur, etc.

hole: when an electron passes into the conduction band, a hole (vacant place) is created in the valence band; this carrier has an e^+ charge.

homeostasis: the ability of an organism to maintain its internal physiological equilibrium despite external stresses.

HOPG (Highly Oriented Pyrolitic Graphite): a substrate of graphite with oriented crystallographic axes.

hormone: a chemical messenger carried by the blood or the lymph which acts at a distance from its production site by binding with specific receptors.

humic: concerning humus, an organic soil matter formed by the decomposition of plants and plant substances.

hybrid vehicle: a vehicle which associates two energy generation modes. The currently preferred formula combines an internal combustion engine and a battery supplying an electric drive train; the first, which operates at constant speed and thus at optimum efficiency, recharges the battery which absorbs the current peaks and recovers braking energy.

hydrocarbon: a molecule comprising only carbon and hydrogen.

hydrogen sulfide (H_2S): a chemical compound of sulfur and hydrogen, responsible for the unpleasant rotten-egg smell.

hydrogenases: enzymes which reversibly catalyze the conversion of H^+ ions ("protons") into dihydrogen through the reaction: $2\,H^+ + 2\,e^- \rightleftharpoons H_2$.

hydrology: Earth science concerning the water cycle, in other words the exchanges between the atmosphere, the surface of the Earth and its subsoil.

hydrolysis: in mineral chemistry, the hydrolysis reactions of a metal cation correspond to the breakdown of a water molecule (into H^+ and OH^-), allowing the chemical reaction between this metal cation and the hydroxyl anion (OH^-).

hydrometallurgy: a process designed to extract metals from compounds, after dissolving the latter in an aqueous phase. Hydrometallurgical processes are used, for example, to extract uranium from ore and to separate the actinides from spent nuclear fuel.

hydrophobic/hydrophilic: which repels/attracts water.

I

ICPMS (Inductively Coupled Plasma Mass Spectrometry): the association of an extremely energetic atomization and ionization source, the inductive coupling plasma, with a mass spectrometer; this is one of the most sensitive element analysis techniques.

IDA: ImidoDiAcetate, a chemical molecule which complexes uranium.

immunology and immunobiology: the branch of medicine studying immunity, in other words the reactions of the organism in which an element of the antigen category appears.

incineration: a chemical treatment process involving the combustion of certain combustible radioactive wastes. This term is sometimes used with respect to nuclear transmutation, when this operation is envisaged for the management of radioactive wastes.

indium phosphide (InP): a semiconducting material used in microelectronics.

indole: an aromatic heterocyclic organic compound the name of which is derived from indigo, a blue pigment whose molecule contains two fused indole groups; it is formed of a benzene cycle and a bonded pyrrole cycle.

infrared radiation (IR): a part of the electromagnetic spectrum covering radiation with a wavelength ranging from 760-780 nm to 1 mm. Physicists subdivide the infrared spectrum into the near IR (760 nm - 4 µm), mid IR (4 µm - 14 µm), far IR (14 µm - 100 µm) and submillimetric IR (100 µm - 1 mm).

infrared spectrometry (IR): see infrared spectroscopy.

infrared spectroscopy: this technique consists in passing a beam of infrared light through a sample and analyzing the emitted light. It is based on the fact that the molecules exhibit specific frequencies at which they rotate or vibrate in correspondence with *discrete* energy levels. The frequency of the vibrations can be associated with a particular chemical bond. Infrared spectroscopy thus gives access to chemical bonds and their dynamic measurement.

insulin: an hormone secreted by the pancreas with the role of lowering the level of glucose in the blood and enabling the cells to use the glucose.

ion: an atom or molecule which has lost or gained one or more electrons and is thus electrically charged (cation: positively charged ion; anion: negatively charged ion).

ionic bond: a bond characterized by the *transfer* of electrons from one atom to another, but without *sharing* as in a covalent bond.

ionic force: one of the main factors influencing the activity of ions in an aqueous solution.

ionization: a state of matter in which the electrons are separated from the nuclei; the process in which ions are produced, by collision with atoms or electrons (*collisional ionization*) or by interaction with electromagnetic radiation (*photo-ionization*).

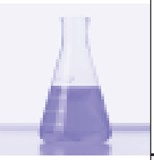
ionizing radiation: a radiation capable of directly or indirectly producing ions as it passes through matter.

ionophore: a solute which transports ions.

isopropanol: a colorless and flammable chemical compound (alcohol) of formula $CH_3CH(OH){-}CH_3$.

isotopes: forms of a given chemical element, the nuclei of which possess an identical number of protons (as well as an identical number of electrons orbiting the nucleus) but a different number of neutrons.

ITER (International Thermonuclear Experimental Reactor): a very large scale scientific experiment aiming to demonstrate the scientific and technological feasibility of fusion energy, thus paving the way for its industrial and commercial operation. ITER will be the first fusion device capable of producing 10 times more energy than it receives.



K

keratinocytes: cells accounting for 90% of the skin surface layer (epidermis) and the skin appendages (nails, hair, fur, feathers, scales).

kerosene: a mixture of hydrocarbons containing alkanes (C_nH_{2n+2}) with a chemical formula ranging from $C_{10}H_{22}$ to $C_{14}H_{30}$. It is mainly used to produce aviation fuel.

kinetic crystallography: a crystallography method aiming to determine the structure of molecules in motion.

kinetics: in chemistry, kinetics is the study of the speed of chemical reactions.

L

labeling: the introduction of radioactive or fluorescent elements (tracers or markers) into a molecule, a substance, a living organism, to enable them to be detected.

lamellar structure: constructed of a stack of successive layers. $LiCoO_2$ for example consists of layers of octahedra (CoO_6) between which the lithium is positioned and diffused.

lanthanides (Ln): the family of elements with an atomic number between 57 (lanthane) and 71 (lutecium). This group corresponds to the filling of the electron subshell 4f and 5d. The lanthanides exhibit very similar chemical properties which are also similar to those of the +III actinides of the end of the series (americium and beyond).

laser (Light Amplification by Stimulated Emission of Radiation): a light source providing monochromatic waves (of a single wavelength) that are coherent in both time and space (always in phase).

laser diode: an optoelectronic component constituting a source of coherent light, for which the beam intensity can be modified by applying a variable voltage.

leaching: placing a solid body in contact with a liquid, with the idea of extracting certain elements from it. By extension, leaching is used to describe any experiment concerning the alteration of a solid in a liquid.

lead sulfide: a chemical compound of formula PbS, semiconducting.

ligand: an organic molecule which, by means of a coordinate bond, can attach to an ion within a coordination complex.

Light Water Reactors (LWRs): a family of reactors in which ordinary water acts as both the coolant and the moderator. The LWR family includes PWR Pressurized Water Reactors and BWR Boiling Water Reactors.

light-emitting diode: an electronic component able to produce light. It consists of several superposed layers, based on inorganic or organic semiconductors, between two electrodes. By applying an appropriate electrical voltage, the electrons and the holes injected into the emission layer from the cathode and the anode recombine to form excitons (electron-hole pairs). Light is emitted (electroluminescence). The basic processes which follow one another are the opposite of the sequence employed in a photovoltaic cell.

lignin: the third main component of the plant cell walls. This is a complex three-dimensional polymer comprising phenolic units, which differ according to the biomasses.

LIHOPO: Linear Hydroxypyridinone, of the family of siderophores which are chelators of iron, synthesized and in particular secreted by micro-organisms.

Linear Energy Transfer: LET = dE/dx, where dE is a part of the energy transferred in electronic form over a track dx by the particle entering the medium. It is expressed in J/m but more commonly as eV/nm. It is possible to talk of the mean LET over the total track of the particle, or over a segment. The value of the LET for an ion increases as its energy drops, as it slows down. It is at its maximum at the end of its track, at the Bragg peak. This particularity is not one possessed by accelerated electrons, X-rays or gamma rays but it is exploited in hadrontherapy.

liquid chromatography: a quantitative, qualitative and separative analysis technique, primarily used in analytical chemistry, organic chemistry and biochemistry.

long-lived: a term applying to radionuclides with a half-life of more than 30 years.

luminescence: emission of "cold" light, as opposed to incandescence, referred to as "warm" light.

lysosome: a small-dimension cell component containing or producing various enzymes which digest or break down certain substances.

M

macro: in general, a prefix meaning large and qualifying an object with dimensions on the human scale, larger than 1 mm (for example, a macromolecule is a large molecule); however, in biology, the prefix "macro" is used to differentiate between large molecules (proteins) and their complexes of small molecules (substrates, hormones, etc.).

magnetism: a physical phenomenon which leads to the manifestation of attraction or repulsion forces between one object and another or with electrical charges in motion.

mannose: an ose (simple non-hydrolysable sugar) the basic formula of which is identical to that of glucose ($C_6H_{12}O_6$) but for which the developed formula exhibits the carbon atom (C2) of opposite configuration; mannose is thus an epimer of glucose.

mannosidase (alpha- and beta-mannosidases): an enzyme which hydrolyses a mannose function in a polysaccharide or a glycoprotein: the alpha- and beta-mannosidases are differentiated by the position of the mannose residue in the active site.

mass spectrometry: a physical analysis technique for detecting and identifying molecules of interest, by measuring their mass, and characterizing their chemical structure. Its principle lies in the gas phase separation of the charged molecules (ions) according to their mass/charge ratio.

matrix (waste): an organic or mineral matrix (glass, bitumen, hydraulic binder, ceramic) the function of which is to immobilize a waste to prevent its dispersal, and/or ensure the long-term confinement of radionuclides.

mesoscopic: situated at an intermediate scale between the nanoscopic and the microscopic scales.

metabolism: the set of molecular and energetic transformations which continuously take place in a cell or a living organism.

metabolites: organic compounds that are the intermediates or products of the metabolism.

metabolomics: the science studying all the metabolites (sugars, amino acids, fatty acids, etc.) present in a cell, an organ, an organism. It is the equivalent of genomics for DNA.

metallothionein: a protein involved in detoxification of the organism, playing a protective role for our cells against metal trace elements, previously called heavy metals (lead, mercury, cadmium, copper, zinc, etc.).

methamidophos: an organophosphorus insecticide used in many countries, especially Spain, Australia, China, Japan and the United States.

methane: as a hydrocarbon with a general formula CH_4, methane is the main component of natural gas and the biogas resulting from the fermentation of animal or vegetable organic matter. It is given off naturally in wet zones with little oxygenation such as marshes and flooded land. It also forms in the stomachs of ruminants.

micro: prefix μ for one millionth (10^{-6}). 1 micrometer (μm) or micron = 10^{-6} meter; 1 microsecond (μs) = 10^{-6} second.

microprocessor: a processor in which the components have been sufficiently miniaturized for placement on a single integrated circuit. Functionally, the processor is the part of the computer which runs the instructions and processes the program data.

microstructure: this term applies to nuclear fuel or a material and designates the shape, size and arrangement of its components (grains of a poly-crystalline material, minerals) and its voids (porosity, vacancies, etc.).

modeling: the simplified representation (model) of a system or process in order to simulate it, contained in a computer software (often called code), in the form of mathematical expressions. The mesh size, in terms of space and time, gives the resolution of the model.

mole: a unit of quantity of matter (symbol mol) in a system containing as many basic entities as there are atoms in 0.012 kg of carbon 12, or $6.03 \cdot 10^{23}$ (Avogadro's number). M = mole/liter.

molecular dynamics: a method consisting in simulating the movements of atoms within molecular systems, by applying the laws of conventional mechanics to predict the evolution of their spatial configuration over time. These movements correspond to vibrations around a minimum or to the passage from one energy minimum to another. Gives access to structural properties and to thermodynamic values.

molecule 19 E: a bisphosphonate dipod of the phosphonates family.

monocrotophos: a very highly toxic organophosphorus insecticide banned in France, the European Community and the United States (since 1991).

monosaccharides (or oses): monomers of glucides, not hydrolysable but soluble in water: glucose and mannose are two monosaccharides.

Monte-Carlo (method): a statistical method for approximating the value of an integral, using a set of points randomly distributed according to a certain probability. It consists in repeating the allocation of a numerical value depending on the running of a process involving chance and then calculating the mean of its statistical dispersion (indicating its precision) for all the values obtained.

Mtoe: millions of tonnes oil equivalent. 1 toe = 42 billion joules or 11,630 kWh.

multidendate (or polydentate): qualifies a ligand liable to engage in several bonds (a bidendate ligand is liable to engage in two bonds, a tridendate in three, and so on).

mutagenesis: a genetic approach to understanding the function of the genes, which consists in intentionally introducing mutations into a DNA sequence by means of chemical or physical agents.

mutagenic: an agent which changes the genome (DNA in general) of an organism, thereby raising the number of genetic mutations above the natural background level.

myasthenia: a neuromuscular disease of the skeletal striated muscles through impairment of neuromuscular transmission leading to fluctuating muscle weakness and excessive fatiguability; one of the most well-known auto-immune diseases.

N

***N*-acetylgalactosamine:** an ose derived from galactose.

nano: prefix n for one billionth (10^{-9}); 1 nanometer (nm) = 10^{-9} meter; 1 nanosecond (ns) = 10^{-9} second.

nanotechnologies: the range of manufacturing and manipulation processes for structures, devices and material systems, at the scale of the nanometer; as in nano-aerosols, nanomaterials, nano-objects, nanoparticles, nano-labels, nanostructures, nano-wires, biomolecules, and so on.

NEMS (Nano Electro Mechanical Systems): a device containing electrical and mechanical functionalities at the nanometric scale.

neurochemistry: a science concerned with the biochemical phenomena of the central nervous system.

neurotoxic: refers to a product that is toxic to the central nervous system.

neurotransmitter: a chemical substance which transmits signals from one neuron to another across a synapse.

nitric acid: a corrosive liquid chemical compound with formula HNO_3.

NitriloTriAcetic acid (NTA): a tricarboxylic acid ($C_6H_9NO_6$) which can bind with metal ions, by a chemical complexation reaction, and thus form hydrosoluble complexes; this is an important chelating agent with many industrial applications.

nitrogen dioxide (NO_2): a toxic gas and an atmospheric pollutant, able to absorb UV radiation, which then no longer reaches the surface of the Earth.

NMR (Nuclear Magnetic Resonance) spectroscopy: a spectroscopy technique based on the phenomenon of nuclear magnetic resonance consisting in causing a radio-frequency (RF) wave to interact with a system to be examined – the RF frequency differs according to the magnetic field and the nucleus concerned – followed by detection of the signal re-emitted by the sample (NMR signal) which provides information about the local structure around the nucleus.

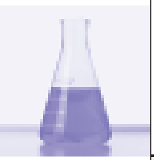
noble metals: historically, precious metals that are unaltered by air or water (silver, gold, platinum), used in jewel-making. This term now applies to other metals which are scarce in the Earth's crust and which are thus also costly (palladium, rhodium, iridium, osmium and ruthenium).

norbadione A: a pigment isolated from the *Boletus badius*; an antioxidant compound.

nuclear glass: a mineral matrix used for the confinement of high-level nuclear waste. Glass has the structure of a frozen liquid, in other words a short-range order and an absence of intermediate-range order, which enables it to accommodate most fission products and minor actinides resulting from the reprocessing of spent fuels.

Nuclear Magnetic Resonance (NMR): its principle is based on the properties of certain atomic nuclei possessing a nuclear spin, placed in a magnetic field; when subjected to electromagnetic radiation, the atomic nuclei can absorb the radiation energy and then release it; the energy involved in this resonance phenomenon corresponds to a very precise frequency that is dependent on the magnetic field and molecular factors; this phenomenon is thus capable of identifying the structure of the compounds present.

Nuclear Magnetic Resonance Imaging (MRI): this medical imaging technique can visualize the organs and soft tissues in various spatial planes, making it possible to accurately determine the position of lesions that would otherwise be invisible; this examination entails no irradiation.



nuclear medicine: the range of medical applications of radiolabels or unsealed radioactive sources.

nucleic acids: polymers consisting of a chain of nucleotides. There are two types: DNA (deoxyribonucleic acid) and RNA (ribonucleic acids).

nucleic probe: a natural or synthetic fragment of DNA or RNA (ribonucleic acid), reproducing a small part of human or another organism's DNA or RNA, used in research or in laboratory examinations (diagnostic tests).

nucleophilic: a chemical compound attracted by positively charged species, as opposed to an electrophilic compound.

nucleotide: a basic unit of nucleic acids, consisting of a purine base (adenine, guanine for example) or pyrimidine base (cytosine, thymine for example), a sugar and one or more phosphate groups.

Nucleotide Excision Repair (NER): natural systems allowing the repair of damaged DNA, in particular as a result of exposure to ultraviolet radiation or to radioactivity.

nuclide: a nuclear species characterized by its number of protons *Z* (atomic number), its number of neutrons *N* and its mass number *A*, equal to the sum of the number of protons and the number of neutrons ($A = Z + N$).

number of spin states: the number of potential spin orientations (angular momentum or momentum of intrinsic internal rotation) of an elementary or composite particle, or molecular entity, in relation to an axis of Cartesian space.

numerical simulation: the reproduction by computation of the functioning of a system, previously described by a model or a set of models.

O

OLED (Organic Light-Emitting Diode): an organic component with the property of emitting light when a voltage is applied to it.

oligomer: a polymer of small size, consisting of 4 to 20 monomers.

oligonucleotides: sequences produced artificially by synthesis.

oligosaccharides: carbohydrates formed of a small number of oses and representing a large set of molecules comprising both anti-diabetic drugs such as acarbose (designed to lower glycemia), numerous antibiotics (particularly anti-bacterial), food additives, digestion enhancers (mannane), immune defense stimulants, etc.

olivine structure (of oxides): the crystalline structure of oxides with the general formula $ABXO_4$ where X (Si for olivine) is a cation situated at the centre of a tetrahedron formed by the oxygen ions (O^{2-}), the A and B cations occupying different octahedral sites. In the case of $LiFePO_4$, the $FePO_4$ skeleton bounds the lithium diffusion channels in a single direction.

oncology: the study of cancer, its diagnosis and its treatment.

optical imaging: a medical imaging technique using the optical interference of the light emitted by an infrared source, with the tissues analyzed, to obtain an image of the tissues at different depths (virtual biopsies); at shallow depth (about one mm) it is possible to obtain high-resolution images (of about a micron); these are non-destructive and harmless techniques.

opto: a prefix indicating a relationship with what is visible or with vision.

optoelectronics: a branch of both electronics and photonics. It studies the electronic components which emit or interact with light; optoelectronic components are electronic to optical, or optical to electrical transducers, or components which use such devices to function.

organic acid: a molecule comprising a carboxyl group (–C(O)OH); these are acids and their conjugated bases are called carboxylates.

organometallic (compound): a compound associating a metal and an organic ligand containing at least one carbon-metal bond. By extension, certain complexes with a low degree of oxidation containing hydride (H^-), molecular hydrogen (H_2) or phosphine (PR_3) type ligands are often included in the family of organometallic compounds.

organometallic precursor: a molecule formed primarily of metal atoms, carbon, hydrogen and oxygen.

organophosphorus (compound): an organic compound comprising at least one phosphorus atom bound directly to one carbon.

oxidation: a reaction during which an atom or an ion loses electrons. The most common is that in which a compound combines with one or more oxygen atoms, thus forming an oxide; oxidant: which causes an atom or an ion to lose electrons.

P

package: an assembly consisting of a transportation, storage or disposal container and a clearly defined content of radioactive waste.

packaging (of radioactive waste): the series of consecutive operations to be performed to ensure that the waste is in a stable and safe form compatible with subsequent management, whether this is storage, transmutation or disposal. These operations can in particular include compacting, encapsulation, fusion, vitrification, containerization.

pandemic: an epidemic affecting an exceptionally large percentage of the population and present over a large geographical area.

parathion: a very highly toxic organophosphorus insecticide; imports are illegal in more than fifty countries, including France.

passive (or passivating) layer: a barrier capable of limiting access by corrosive species (H_2O, O_2, etc.) to a surface. It thus helps reduce the rate of corrosion of the underlying material. In a Li-ion rechargeable battery, the passivating layer (Solid Electrolyte Interphase (SEI)) formed on the negative electrode, provides protection against the electrolyte.

pentavalent plutonium: plutonium with degree of oxidation +5; in aqueous phase corresponds to molecular species PuO_2^+.

peptide: a chain comprising fewer than 50 amino acids bound by peptide links.

pertechnetate: TcO_4^- ion formed in oxidant conditions.

pH: a measurement of the concentration in hydrogen ions in a liquid. In pure water, below 7, it is acid, above which it is basic (or alkaline).

pharmacodynamics: describes the effects of an active ingredient on the organism; a detailed study of the receptor/active substance interaction. This response is a component of the desired therapeutic effect.

pharmacokinetics: the discipline studying the fate of an active ingredient contained in a drug inside the organism.

pharmacophores: active atoms consisting of a pharmacologically active part of a molecule acting as a model; used in drug design.

phenols: aromatic chemical compounds (alcohols) carrying a hydroxyl –OH function.

phosphate: in inorganic chemistry, a phosphoric acid salt resulting from the attack of a base by phosphoric acid and, in organic chemistry, an organophosphorus compound derived from phosphoric acid.

phosphonic amines: a $RCH_2NHCH_2PO_3$ type functional group, where R represents any group.

phosphopeptides: peptides containing an amino acid bound to a phosphate group.

photocatalysis: catalysis of chemical reactions under the effect of light.

photodecomposition: the destruction, under the effect of light, of the photochemical properties of an optical contrast agent.

photodetector: a photoelectric detector.

photolysis: the use of light energy to perform a chemical reaction, generally involving breaking the bond within a compound.

photosynthesis: the process whereby plants, algae and certain bacteria use solar energy to synthesize organic molecules. Plants and algae use carbon dioxide and water to do this, while giving off oxygen (O_2).

photovoltaic: the effect whereby light energy is directly transformed into electrical energy in a semiconductor.

photovoltaic cell: an electronic component which, when exposed to light (photons), generates electricity.

phytochelatins: polypeptides responsible for plant tolerance of metal ions, particularly cadmium.

π-conjugation: a chemical system is said to be conjugated when it is formed of atoms bound to each other in a covalent manner with at least one delocalized π type bond.

picosecond: 1 ps = 10^{-12} second.

plasmid: a supernumerary molecule of DNA distinct from chromosomal DNA, capable of autonomous replication and not essential to the survival of the cell.

plasmon resonance: a physical phenomenon implying an absorption of light by metal compounds (gold for example) utilized in particular for biological analysis.

pluviometry: the measurement of rainfall, generally in millimeters.

polarization: the macroscopic value corresponding to the sum, per unit volume, of microscopic dipolar moments (induced by the shift in the center of gravity of the positive charges in relation to the center of gravity of the negative charges) created at application of an external electrical field.

polarography: a particular form of voltammetry which uses a dropping mercury electrode as its working electrode; a method for analyzing oxidation and reduction in solution, it falls into the category of electrochemistry, the science which describes the chemical reactions in which electron transfers occur.

poly(3-dodecylthiophene-2,5-diyl): a macromolecular organic semiconductor (semiconducting polymer) consisting of a π-conjugated, controlled regiochemistry macromolecular skeleton (head to tail chain of 3-dodecylthiophene type monomer units) based on heterocyclic thiophene units functionalized in position 3 by solubilizing *n*-dodecyl paraffin groups ($C_{12}H_{25}$).

polyethylene glycol: a polymer of ethylene oxide with a molecular weight of less than 20,000 g/mol.

polymer: a macromolecule repeating the same structural pattern, called a monomer, in the case of a homopolymer, or at least two different monomers for a copolymer.

polymerization: the progressive addition of molecules of monomers by covalent bonds, forming a polymer (*ant.* depolymerization). Copolymerization involves at least two different monomers.

polysaccharides: polymers created by the polycondensation of a large quantity of ose molecules (starch, cellulose, etc.).

porphyrin: a molecule with a cyclic structure involved in the transport of oxygen and able to act as a bound cofactor (prosthetic group) of certain enzymes.

positron: an antiparticle associated with the electron, which possesses an electric charge of +1 elementary charge (as against -1 for the electron), the same spin and the same mass as the electron.

Positron Emission Tomography (PET): a medical imaging technique consisting in injecting a radioactive substance emitting positrons and then collecting the radiation by means of an external sensor and then finally reconstructing a cross-section image of the organ on the computer.

potential (electrochemical potential of an electrode): it is measured in relation to a standard hydrogen electrode (SHE), which acts as a reference in electrochemistry, the potential of which is set at 0 V. It is thus expressed in relation to SHE (V/SHE).

ppb: part per billion.

ppm: part per million.

precipitation: the formation in a solution of an insoluble solid substance (precipitate) by a chemical reaction between two (or more) compounds.

Pressurized Water Reactor (PWR): a reactor in which heat is transferred from the core to the heat exchanger *via* water kept at high pressure in the primary circuit, to stop it from boiling.

primary system: the closed and leaktight primary system contains the core and, by means of circulating pumps or compressors, carries the coolant which transfers its heat to a secondary system *via* a heat exchanger.

processing or reprocessing (of spent fuel): the selective sorting of the materials contained in spent fuels in order to extract those which are reusable and recyclable (uranium and plutonium) or possibly transmutable, and to package the ultimate waste.

prosthetic: a group of a heteroprotein molecule which is not an amino acid and which is bound to the protein fraction on which it confers its main properties.

protein: the main macromolecular component of cells, formed by the DNA coded chaining of amino acids.

proteomics: a science which studies proteomes, in other words all the proteins of a cell, organelle, tissue, organ or organism at a given moment and in given conditions.

protonation/deprotonation: a chemical reaction during which an H^+ proton is added to/removed from a molecule.

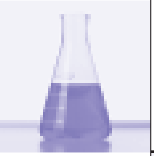
Prussian Blue: ferric ferrocyanide, chemical formula $Fe_7(CN)_{18}(H_2O)_x$, where x varies from 14 to 18.

pseudopotential: a supplementary term in Schrödinger's equation capable of simulating the effect of the electrons of the inner layers of an atom, which play no direct part in the chemical bonds. The volume of calculations required is thus significantly reduced without sacrificing too much information on the physico-chemical properties of the molecules or complexes.

pulvinic acid or **vulpinic acid** (Methyl (*2E*)-2-(5-hydroxy-3-oxo-4-phenylfuran-2-ylidene)-2-phenylacetate): an organic acid present in fungi and lichens.

PUREX (Plutonium Uranium Refining by EXtraction): a hydro-metallurgical process for reprocessing spent fuel, currently used industrially to extract from it the uranium and plutonium still of value in energy terms. The process separates these two elements from the minor actinides and fission products, considered to be waste.

PVC (polyvinyl chloride): abbreviation designating a plastic material.



pyrex: a brand of kitchenware belonging to the Arc International group, created in 1915 and traditionally best known for its thermostable glass baking dishes.

pyridinecarboxylate: an organic compound consisting of an aromatic amine (pyridine) and a carboxylate.

pyrrole (or azole): a simple and fundamental heterocyclic compound, of general formula C_4H_5N, consisting of an aromatic cycle of 5 atoms including a nitrogen atom.

Q

QSAR (Quantitative Structure-Activity Relationship): a process whereby a chemical structure is correlated with a clearly determined effect, such as biological activity or chemical reactivity.

quantum: related to the theory developed on the basis of Planck's principle of *quanta* (any manifestation of energy can only be expressed by a *discrete* value called a quantum) and on *Heisenberg's uncertainty principle* according to which it is not possible to accurately measure both the position and speed of a particle at the same time.

quantum chemistry: a branch of theoretical chemistry which applies quantum mechanics to molecular systems, to study the chemical processes and properties.

quantum confinement: the displacement of electrons or holes in a semiconductor material, limited in one or more dimensions; modifies the electronic properties of a material.

quantum numbers: in quantum mechanics, the electron is characterized by four numbers. The principal quantum number n, an integer ≥ 1, corresponds to the number of the electron layer and to a large extent indicates the energy of the electron and the size of the orbital, which increases with n. The secondary quantum number l, which take can any integer value between 0 and $n - 1$, primarily defines the form of the orbital – orbitals s ($l = 0$), p ($l = 1$), d ($l = 2$), f ($l = 3$)... The magnetic quantum number m, whose integer values range from $-l$ to $+l$, determines the orientation of the orbital followed by the electron. Finally, the spin quantum number s represents the electron's spin, that is ± ½.

quartz: a mineral species of the silicates group.

quencher: a chromophore specifically absorbing the energy emitted by a donor fluorochrome, leading to the expected signal being extinguished.

R

R7T7 glass: a type of borosilicate glass, intended for the confinement of waste resulting from the reprocessing of spent fuels, and so-called after the name of the R7 and T7 facilities in the La Hague plant in which it is produced.

radioactive decay: the process by which a nucleus or particle breaks down into several fragments (particles and nuclei, which constitute the decay products, photons) to achieve a lower energy state which is therefore more stable. The characteristics of this transformation only depend on the initial state of the nucleus (of the particle) and not on the process which produced it.

radioactive half-life: the time after which half of the radioactive atoms initially present in a sample of a radioactive nuclide have disappeared through natural decay.

radioactive waste: a radioactive substance for which no subsequent use is planned or envisaged. Ultimate radioactive waste is radioactive waste that can no longer be processed in current technical and economic conditions, in particular through extraction of its reusable part or by mitigation of its polluting or hazardous nature.

radioactivity: the property possessed by certain natural or artificial elements which, as they decay, spontaneously emit alpha particles (helium nuclei), beta particles (positrons [beta + or β^+ emission] or electrons [beta - or β^- emission]) and/or gamma radiation (high-energy photons). This term more generally refers to the emission of radiation accompanying the decay of an unstable element, or fission.

radioelement: an element of which all the isotopes are radioactive.

radiography: the set of techniques for taking pictures of the internal structures of a patient or mechanical component using X-rays.

radionuclide: an unstable nuclide of an element which spontaneously decays or disintegrates, emitting radiation.

radioprotective: refers to a substance which, if ingested by a living organism, attenuates the effects of any subsequent irradiation to which it may be exposed.

radiotherapy: a cancer treatment based on the administration of gamma rays or X-rays, designed to destroy or reduce the size of a clearly defined tumor volume.

radiotoxicology: a recent scientific discipline which studies the direct and/or indirect effects of radioactive chemical bodies on living organisms and ecosystems.

radiotracer: a radioactive substance whose path through a tissue, organ or living organism can be easily detected by an appropriate device.

Raman diffusion spectrometry: used to identify the chemical structure and molecular composition of a sample by subjecting it to laser radiation and analyzing the scattered light. This is a local measurement technique: by focusing the laser beam on a small part of the medium, it is possible to investigate it in volumes of a few cubic microns. This is then referred to as micro-Raman spectroscopy.

rare earths: a family of elements chiefly comprising the lanthanides as well as yttrium and scandium.

receptor: a membrane or soluble protein the activity of which is regulated by one or more "signal" molecules.

recoil nucleus: a nucleus which, as a result of a nuclear reaction or radioactive emission, is given kinetic energy.

recycling: the reutilization of reusable materials after a production process. In a nuclear reactor, the reuse of fissile material (generated plutonium, residual uranium 235, etc.) resulting from a previous cycle after reprocessing of the spent fuel.

redox (reduction/oxidation): a redox reaction is a chemical reaction during which a transfer of electrons occurs. The chemical species capturing the electrons is called the oxidant and that which releases them the reductant.

reduction: a reaction during which an atom or an ion gains electrons released by a reductant.

reforming: the chemical cracking of a molecule of a hydrocarbon or alcohol to transform it into its major components.

relaxivity: a measurement of the effectiveness of a paramagnetic complex to create a contrast; an increase in the speed of relaxation of the protons of the neighboring water molecules, when the concentration of contrast agents increases by one millimol/L.

resistance: the property of certain materials to oppose the passage of an electric current.

RFID (Radio Frequency IDentification): an electronic identification tag readable by radiowaves.

ribosome: a giant macromolecular complex present in cells, in which the RNA is converted into proteins.

rubrene: an organic crystal with semiconducting properties.

S

***S. cerevisiae* yeast:** used since the earliest days of mankind for making bread, wine and top-fermented beer.

saccharide: a term previously used to designate glucides.

salt: in chemistry, a salt is an ionic compound consisting of cations and anions forming a neutral product with no net charge.

SANEX (Selective ActiNides EXtraction): a process used to separate actinides(III) (americium + curium)/lanthanides(III).

sarin: an odorless, colorless, volatile substance of the organophosphorus family, extremely toxic for humans and animals, even in very small doses (0.01 ppm can be lethal); about 500 times more toxic than cyanide.

Scanning Electron Microscopy (SEM): in scanning microscopes, the image is built up point by point, by scanning a small probe of electrons over the object. For each probe position, a signal is recorded by one or more detectors and a software or acquisition board maps the signals detected.

Scanning Tunneling Microscopy (STM): a method of microscopy which, at the atomic scale, can be used to explore the surface topology of conducting solids by means of a probe so thin that its tip consists of only a few atoms, moving along the surface. The interaction between the tip and the surface is measured by the number of electrons circulating by tunnel effect between the metal probe and the conducting surface. Scanning tunneling microscopy is based on the fact that there is a non-nil probability that a particle with energy lower than the height of a potential barrier can cross it (tunneling effect). Scanning tunneling microscopy also allows the study of surfaces immersed in a liquid.

Schrödinger's equation: an equation which, when resolved, can determine the energy of the system as well as a function, the wavefunction, from which all the properties of this system can be deduced. It was proposed by Erwin Schrödinger in 1926.

Seldi-TOF (Surface Enhanced Laser Desorption Ionization – Time Of Flight) from Ciphergen: a method of ionization for Time Of Flight mass spectrometry, marketed by the Ciphergen company for analysis of protein samples.

selectivity (chemo- and regio-): chemoselectivity is characterized by the preferential attack of a functional group within a molecule from among other (different) groups; regioselectivity is defined by the preferential attack of a particular functional group within a molecule containing several copies of these groups (identical).

selenite: SeO_3^{2-} ion formed in oxidizing conditions.

semiconductor: a material in which the band of occupied electronic states (valence band) is separated from the band of unoccupied states (conduction band) by a relatively narrow inhibited energy band (gap). Such a material is an electrical insulator at absolute zero, but becomes moderately conducting when its temperature is high enough to excite electrons in the valence band towards the conduction band.

sequence: a succession of amino acids in a protein, or of DNA bases in a gene.

silica: a chemical compound of formula SiO_2 (silicon dioxide). It is used in the composition of numerous minerals.

silicon alkoxides: metallo-organic precursors containing Si-O-R functions ($R = CH_3$, CH_2CH_3...) that are easily hydrolysable in the presence of water to obtain silanol functions (Si-OH).

siloxanes: a class of silicon compounds, with formula R_2SiO, where R is a radical group which may be organic. These compounds may be organic and inorganic hybrids.

single-crystal: a crystal formed in a single block with no discontinuity, from an assembly of atoms, ions or molecules periodically and regularly distributed in the three spatial directions, contrary to a poly-crystal.

sintering: an operation consisting in fusing the grains of precursor powders (of metal and/or inorganic compounds) by performing a heat treatment at a temperature lower than the melting point of the main component, in order to produce a continuous solid.

sol-gel: a process which allows the production of vitreous materials without requiring fusion.

solvation: a chemical interaction of the molecules of a solvent with the ions of the solute.

solvent: a substance capable of dissolving a body; **solute:** a dissolved body.

speciation: the characterization of the chemical species of an element present in a substance and, more generally, in a given environment; by extension, the characterization of the method of binding an element or a molecule to particles. The speciation of an element or a molecule is essential in evaluating its possible toxicity.

specific capacity (of electrode materials): corresponds to the quantity of electricity used in these materials during oxidation or reduction reactions (exchange of lithium ions between the negative and positive electrodes in the case of a lithium-ion rechargeable battery). It is expressed in milliampere-hours per gram (mAh/g) or in ampere-hours per kilogram (Ah/kg).

specific energy and energy density: these respectively correspond to the energy output per unit of mass (Wh/kg) or volume (Wh/l) by an electrochemical generator.

specific power and power density: these respectively represent the energy per unit of time that can be produced by the unit of mass (W/kg) or volume (W/l) of an electrochemical generator.

specific surface area: the actual surface area of an object (taking account of its roughness for example) as opposed to its apparent surface area.

spectroscopy: the study of bodies according to the radiation they emit or the transformations they undergo because of other bodies placed in their path; **spectrometry:** the measurement and interpretation of spectra of quantities linked to the physical or chemical composition of a body, or to the analysis of a wave.

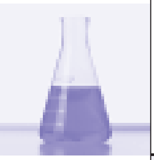
spin coating: a method for producing a thin film by deposition of a solution containing different molecules on a rotating substrate.

spinel structure (of oxides): a crystalline structure of oxides in which the oxygen ions (O^{2-}) form a compact face-centered cubic type stack (a structure in which the atoms occupy the eight summits of a cube and the centre of each of the faces of this cube), with the cations occupying the octahedral and tetrahedral sites of these assemblies. In the case of $LiMn_2O_4$, the arrangement of the MnO_6 octahedra bounds the lithium diffusion channels in the three orthogonal axes of the mesh.

spintronics: a discipline based on electron spin (angular momentum).

stainless steel: an alloy of iron and carbon to which is mainly added chromium which, at over 12 to 13%, produces the required resistance to oxidation.

steric: relative to the spatial configuration of a molecule.



stoichiometry: the study of the proportions, during a chemical reaction, in which reagents combine and products form. A reaction is said to be stoichiometric when the quantities of reagents are in molar proportions identical to those of the chemical equation.

sulfate: a salt formed by the combination of sulfuric acid with a base.

supercritical (fluid): a fluid which, when placed in temperature and pressure conditions higher than their critical values, exhibits a viscosity close to that of a gas, a density close to that of a liquid and a high diffusivity. Its solvent capacity evolves with the pressure and temperature conditions. Fluids most commonly used: carbon dioxide (CO_2) owing to its low critical temperature (31 °C) and water (H_2O) owing to its high oxidizing capacity.

superoxide dismutase: a metalloprotein with an enzymatic activity; an important part of the defense system against free radicals, it is to be found in nearly all aerobic organisms.

supramolecular: which associates, *via* non-covalent interactions, several molecules within the same structure. By extension, a compound is said to be supramolecular if it associates several distinct properties carried by different centers and clearly identified.

Surface Plasmon Resonance (SPR): a physical method able to quantify the bond between a ligand and a "receptor", fixed to a specific matrix, itself adsorbed on a metal layer (generally gold); the technique uses the measurement of the variations in the refraction indices caused by the formation of a ligand-receptor complex.

synapse: region of the interaction between two nerve cells, acting as a junction across which the chemical message passes from one neuron to another, leading to its excitation or inhibition.

synchrotron radiation: the electromagnetic radiation emitted by electrons which circulate in a storage ring; these electrons regularly change their path and their acceleration also changes regularly; when this change occurs, the electrons emit energy in the form of photons. This radiation is used to study the structure and electronic properties of matter.

T

tar: an organic compound (other than soot or coal) with a molar mass higher than that of benzene.

TCO (Transparent Conductive Oxide): a transparent and conducting oxide used to make electrodes, for example for flat screens or photovoltaic cells.

tellurite: TeO_3^{2-} ion formed in oxidizing conditions.

theranostics: arisen from the association of the two words "therapeutic" and "diagnostic", this practice will lead to personalized medicine by choosing a treatment according to the reaction by each individual.

thermobalance: a laboratory reactor for measuring the evolution of the mass of a sample versus time, according to the temperature and the gas atmosphere.

thermochemistry: the application of the laws of thermodynamics to isothermal and/or isobaric chemical reactions.

thermodynamics: the branch of physics describing energy transfers within matter.

thermodynamics (chemical): the branch of chemistry describing the evolution of chemical reactions and the associated exchanges.

thin layer: a coating, the thickness of which can vary from a few atomic layers to about ten micrometers, modifying the properties of the substrate on which it is deposited.

thiol: an organic compound comprising an —SH thiol group (sulfhydryl group) bonded to a carbon atom; owing to its strong odor, it is used in the manufacture of "stink bombs" or as an additive to domestic gas as a means of detecting leaks.

time-resolution: the smallest interval of time separating two successive productions of a time signal and enabling them to be perceived as separate.

Time-Resolved Laser Fluorescence Spectroscopy (TRLFS): a technique used to monitor the evolution versus time of the fluorescence emitted by a molecular system after short photo-excitation by a laser.

Time-Resolved Laser Spectroscopy (TRLS): an ultra-sensitive analytical technique for determining certain fluorescent actinides and lanthanides in solution. Its principle is based on pulsed laser excitation, followed by time resolution (positioning of a measurement gate of a few µs after the laser pulse) of the fluorescence signal thus eliminating stray short-lived fluorescences.

toxicology: a science studying toxic substances, their etiology, the circumstances of their contact with the organism, the effects of exposure on an organism, the effects of exposure on the environment, the means of detecting and combating them.

trace: an element present in small concentrations; there are no precise rules to define a threshold concentration as of which the term trace is to be used; this notion of trace varies with the changing sensitivity of the techniques used and does not have the same meaning for a geochemist, a biologist, a metallurgist, and so on. In practice, an analyst will talk of traces when the element to be assayed is present in concentrations varying from a few tens of mg/kg to a few tens of µg/kg and of ultra-traces for lesser concentrations.

trace elements: elements (metals, metalloids, vitamins) which exist in trace levels in living organisms and whose presence is essential to the life of animal or plant cells.

tracer: an element or chemical compound that can be easily identified by physico-chemical means; tracing consists in using a tracer to monitor the displacement of matter in a chemical reaction or in the environment.

transcriptomics: the study of all the RNA (ribonucleic acids) which are the messengers produced during the process of transcription of a genome.

transferrin: a beta globulin, synthesized by the liver, consisting of a single polypeptide chain carrying 2 iron binding sites, with 2 iron atoms per molecule of transferrin; the main participant in the homeostasis of iron, it allows transfer of this metal from the blood compartment to the intracellular medium.

transistor: an active electronic component that is fundamental to electronics, used as a switch, for amplification to stabilize a voltage, modulate a signal, etc.

Transmission Electron Microscopy (TEM): a beam of electrons is sent to the sample and passes through it before being detected. A system of lenses focuses the beam on the sample and another set of lenses then modifies the output beam to form a magnified image of the object.

transmutation: the transformation of one nuclide into another by a nuclear reaction. The transmutation envisaged for the management of radioactive waste aims to transform a nuclide with a long half-life into one with a shorter half-life or into a stable nuclide.

trichloramine: a volatile irritant substance, belonging to the family of chloramines, which develops when the chlorinated products used to disinfect waters combine with nitrogen pollution from organic derivatives (sweat, saliva, urine, etc.).

trientine: a polyamine type chemical molecule used as a chelating agent in the treatment of Wilson's disease.

tritiated water: in its chemically pure form, tritiated water (or super-heavy water) is a form of water in which all or some of the hydrogen atoms have been replaced by tritium; not to be confused with heavy water, which is deuterium oxide; as tritium is itself a radioisotope with a half-life of 12.32 years, pure tritiated water is highly radioactive.

trophic: relates to everything concerning the nutrition of a living tissue or an organ.

tryptophane: one of the 20 amino acids making up proteins; obtained from food, it is essential to humans.

U

ultraviolet and visible radiation absorption spectrometry: based on the absorption of light radiation by matter. This technique is mainly used to measure the concentrations of chemical species in aqueous or other solution.

ultraviolet radiation (UV): a region of the electromagnetic spectrum characterized by a wavelength of 100 to 400 nm.

uranium: chemical element of symbol U and atomic number 92, exists in the natural state in the form of a mixture of three isotopes: ^{238}U fertile (99.28%), ^{235}U fissile (0.71%) and ^{234}U (traces).

uranium dioxide: a mineral with formula UO_2, with a cubic crystal structure, in which the uranium has valence IV; in nature, its composition varies between UO_2 and UO_3, resulting from a more or less oxidized state of uranium.

uranyl ion (UO_2^{2+}): a cation in which the uranium is at its +6 oxidation state and forms salts with the acids; this is the most frequent form of uranium in its aqueous solution chemistry.

V

vacuole: an organelle present in plant and fungi cells.

valence: valence electrons are those of the external electronic subshells (not filled) of an ion. In coordination chemistry, this term is often used to indicate the degree of oxidation. A monovalent ion has charge +1, a divalent ion +2 and so on.

van der Waals (interaction or force): named after the physicist Johannes Diederik van der Waals, 1910 Nobel laureate in Physics; a low-intensity electrical interaction between atoms, or between a molecule and a crystal.

vectorization: the action consisting in modulating and controlling the distribution of an active ingredient to a target, by associating it with a vector.

vicinal position: in DNA, describes the relative position of two bases, situated side by side, on the same strand.

viscosity: the capacity of a fluid to flow.

visible radiation: the electromagnetic radiation stimulating the human optic nerve, with a wavelength approximately situated between the ultraviolet (380 nm) and the infrared (780 nm).

vitrification: the operation consisting in incorporating radioactive waste into glass providing it with stable packaging, in the form of a package compatible with storage or disposal.

VOC (volatile organic compounds): carbon and hydrogen compounds which can easily be found in gaseous form in the atmosphere; of anthropic origin (from refining, evaporation of organic solvents, unburned substances, etc.) or naturally occurring (emissions from plants or certain types of fermentation), they are biodegradable at various rates by bacteria and fungi, or even plants, or are degraded by UV or by ozone.

voltage: (*general definition*) the circulation of the electric field along a circuit; (*usual definition*) the electrical potential difference between two points on an electric circuit (positive electrode and negative electrode).

voltammetry: understanding the fundamental characteristics of an electrochemical reaction can be achieved by measuring current variations versus the potential applied to the terminals of an electrolysis cell; the general principle of voltammetry is thus to obtain a response (the current) from the system studied at the excitation (the potential) responsible for the desired chemical reaction.

W

water radiolysis: when water is irradiated with ionizing radiation, the first step is ionization. The ejected electron may have enough energy to ionize other water molecules in turn. This step is followed by extremely rapid reactions (primary events) which lead to the formation of stable molecular products, hydrogen H_2 and hydrogen peroxide H_2O_2, as well of free radicals $R^{\bullet}$ ($H^{\bullet}$, $HO^{\bullet}$, $HO_2^{\bullet}$, $e^{\bullet}_{aq}$). These latter exhibit an unpaired electron in a chemical bond, noted by a dot, which makes them highly reactive. The hydrated electron $e^{\bullet}_{aq}$ is not bound to any water molecule but is trapped in a cavity consisting of the neighboring water molecules. For its part, the oxygen O_2 is not a primary product of water radiolysis. It primarily forms by a reaction of the $HO^{\bullet}$ hydroxyl radicals with hydrogen peroxide.

watt (W): a unit of power corresponding to the consumption of one joule per second. Main multiples: kilowatt (1 kW = 10^3 watts), megawatt (1 MW = 10^6 watts), gigawatt (1 GW = 10^9 watts) and terawatt (1 TW = 10^{12} watts); watt-hour (Wh): the amount of energy consumed, or delivered by a system, corresponding to a power of 1 W for 1 hour.

weak acids: acids which do not completely dissociate in water. They are classified according to their acidity constant (pKa), which measures their ability to dissociate. The higher the pKa, the weaker the acid.

Wilson's protein (ATP7B): an ATPase type trans-membrane protein, called ATP7B, coded by the *ATP7B* gene. It takes part in the intra- and extra-cellular transport of copper, regulating the concentration of this metal and its excretion by the bile duct. If the protein is deficient, the metal builds up inside the cells. Mutations of this gene have been associated with Wilson's disease (WD).

X

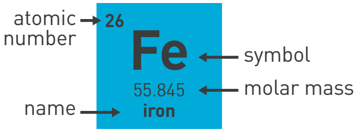
X-ray crystallography: a method for determining the structure of molecules using X-rays.

X-rays: an electromagnetic radiation with a wavelength comparable to the distances between atoms, between a few fractions of a nanometer (0.005 nm) and from 1 to 100 nm, and with an energy between a few keV and a few hundred keV.

Z

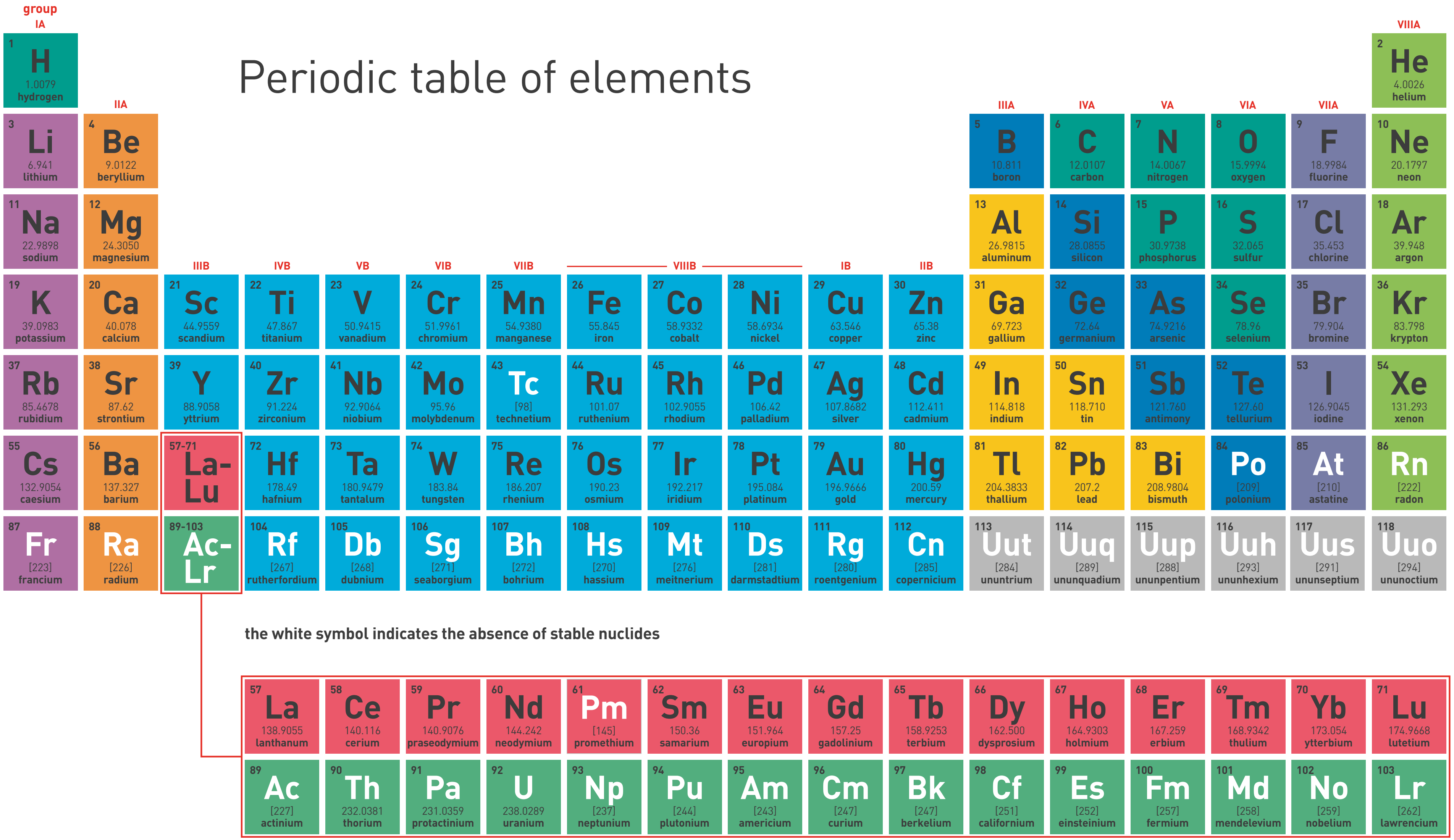
zinc selenide: a chemical compound with formula ZnSe, semiconducting.

zinc sulfide: a chemical compound of formula ZnS, semiconducting.



- 🟪 alkali metals
- 🟧 alkaline earth metals
- 🟦 transition metals
- 🟥 lanthanides
- 🟩 actinides
- 🟨 other metals
- 🟦 semi-metals (metalloids)
- 🟩 other non-metallic elements
- 🟪 halogens
- 🟩 noble gases

Periodic table of elements



group IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIIIB			IB	IIB	IIIA	IVA	VA	VIA	VIIA	VIIIA
1 **H** 1.0079 hydrogen																	2 **He** 4.0026 helium
3 **Li** 6.941 lithium	4 **Be** 9.0122 beryllium											5 **B** 10.811 boron	6 **C** 12.0107 carbon	7 **N** 14.0067 nitrogen	8 **O** 15.9994 oxygen	9 **F** 18.9984 fluorine	10 **Ne** 20.1797 neon
11 **Na** 22.9898 sodium	12 **Mg** 24.3050 magnesium											13 **Al** 26.9815 aluminum	14 **Si** 28.0855 silicon	15 **P** 30.9738 phosphorus	16 **S** 32.065 sulfur	17 **Cl** 35.453 chlorine	18 **Ar** 39.948 argon
19 **K** 39.0983 potassium	20 **Ca** 40.078 calcium	21 **Sc** 44.9559 scandium	22 **Ti** 47.867 titanium	23 **V** 50.9415 vanadium	24 **Cr** 51.9961 chromium	25 **Mn** 54.9380 manganese	26 **Fe** 55.845 iron	27 **Co** 58.9332 cobalt	28 **Ni** 58.6934 nickel	29 **Cu** 63.546 copper	30 **Zn** 65.38 zinc	31 **Ga** 69.723 gallium	32 **Ge** 72.64 germanium	33 **As** 74.9216 arsenic	34 **Se** 78.96 selenium	35 **Br** 79.904 bromine	36 **Kr** 83.798 krypton
37 **Rb** 85.4678 rubidium	38 **Sr** 87.62 strontium	39 **Y** 88.9058 yttrium	40 **Zr** 91.224 zirconium	41 **Nb** 92.9064 niobium	42 **Mo** 95.96 molybdenum	43 **Tc** [98] technetium	44 **Ru** 101.07 ruthenium	45 **Rh** 102.9055 rhodium	46 **Pd** 106.42 palladium	47 **Ag** 107.8682 silver	48 **Cd** 112.411 cadmium	49 **In** 114.818 indium	50 **Sn** 118.710 tin	51 **Sb** 121.760 antimony	52 **Te** 127.60 tellurium	53 **I** 126.9045 iodine	54 **Xe** 131.293 xenon
55 **Cs** 132.9054 caesium	56 **Ba** 137.327 barium	57-71 **La-** **Lu**	72 **Hf** 178.49 hafnium	73 **Ta** 180.9479 tantalum	74 **W** 183.84 tungsten	75 **Re** 186.207 rhenium	76 **Os** 190.23 osmium	77 **Ir** 192.217 iridium	78 **Pt** 195.084 platinum	79 **Au** 196.9666 gold	80 **Hg** 200.59 mercury	81 **Tl** 204.3833 thallium	82 **Pb** 207.2 lead	83 **Bi** 208.9804 bismuth	84 **Po** [209] polonium	85 **At** [210] astatine	86 **Rn** [222] radon
87 **Fr** [223] francium	88 **Ra** [226] radium	89-103 **Ac-** **Lr**	104 **Rf** [267] rutherfordium	105 **Db** [268] dubnium	106 **Sg** [271] seaborgium	107 **Bh** [272] bohrium	108 **Hs** [270] hassium	109 **Mt** [276] meitnerium	110 **Ds** [281] darmstadtium	111 **Rg** [280] roentgenium	112 **Cn** [285] copernicium	113 **Uut** [284] ununtrium	114 **Uuq** [289] ununquadium	115 **Uup** [288] ununpentium	116 **Uuh** [293] ununhexium	117 **Uus** [291] ununseptium	118 **Uuo** [294] ununoctium

the white symbol indicates the absence of stable nuclides

57 **La** 138.9055 lanthanum	58 **Ce** 140.116 cerium	59 **Pr** 140.9076 praseodymium	60 **Nd** 144.242 neodymium	61 **Pm** [145] promethium	62 **Sm** 150.36 samarium	63 **Eu** 151.964 europium	64 **Gd** 157.25 gadolinium	65 **Tb** 158.9253 terbium	66 **Dy** 162.500 dysprosium	67 **Ho** 164.9303 holmium	68 **Er** 167.259 erbium	69 **Tm** 168.9342 thulium	70 **Yb** 173.054 ytterbium	71 **Lu** 174.9668 lutetium
89 **Ac** [227] actinium	90 **Th** 232.0381 thorium	91 **Pa** 231.0359 protactinium	92 **U** 238.0289 uranium	93 **Np** [237] neptunium	94 **Pu** [244] plutonium	95 **Am** [243] americium	96 **Cm** [247] curium	97 **Bk** [247] berkelium	98 **Cf** [251] californium	99 **Es** [252] einsteinium	100 **Fm** [257] fermium	101 **Md** [258] mendelevium	102 **No** [259] nobelium	103 **Lr** [262] lawrencium