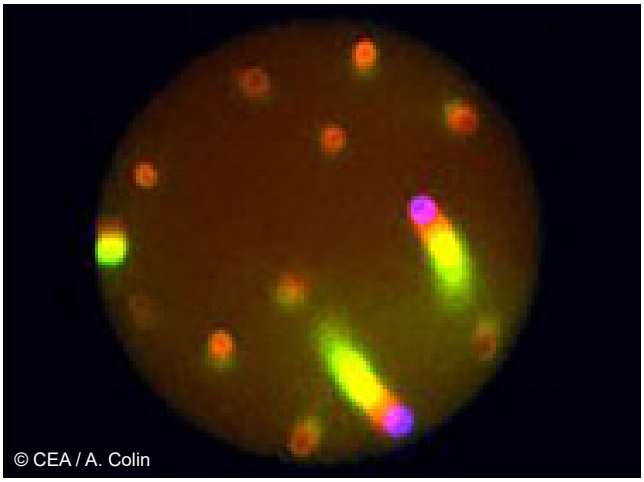
Scientific Newsletter

SPRING 2025

Cellular architectures at the heart of a competition

Alexandra Colin - Cell & Plant Physiology Laboratory

Inside cells, dynamic actin networks coexist, while competing for a limited amount of resources. Using a biomimetic system, researchers from IRIG/LPCV have highlighted the importance of protein recycling for the coexistence of these different networks within the cell.



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Actin is a constitutive protein of the cytoskeleton, regulating cell shape, movement and division. Actin polymerizes into filaments that form dynamic networks in the presence of specific proteins. Within the cell, as access to resources is limited, there is competition for their use: networks have to share the same resources in order to coexist and perform their respective functions. Some of these sub-networks are located at the periphery, others more towards the center of the cell. Some are very dense and homogeneous, while in others filaments forming the sub-networks create architectures that are more heterogeneous. They are also more or less extensive and more or less rigid. How do these networks coexist in this competitive, resource-constrained environment?

Authors of this study analyzed how resources are shared between different cell architectures. To do this, they reconstituted the competition between several actin networks using purified proteins, in order to grow these networks in micro-wells from small beads. This biomimetic system made it possible to control the number of competing networks, as well as the available quantity of resources (actin and associated proteins).

As expected, they observed that if one network consumed more resources than the others, it prevented its neighbors from growing. On the other hand, if these networks are dynamic and renew themselves by constantly disassembling and reassembling their filaments, they release the resources they have used and allow the other networks to use them in turn.

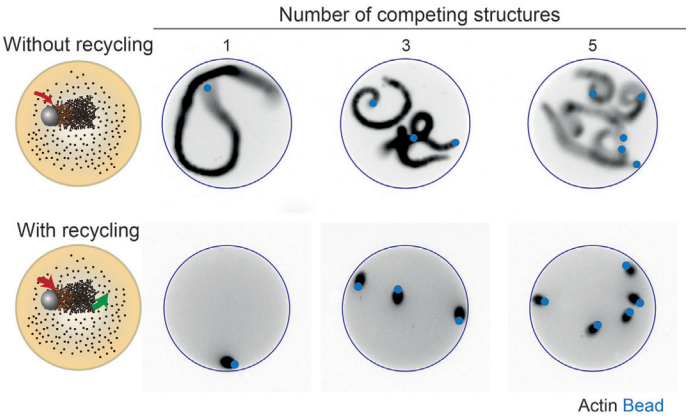
The constant renewal of structures is an essential signature of living systems, and it is this fundamental mechanism that enables the coexistence of different networks, with different sizes and levels of consumption.

This study shows how the renewal of a dynamic system enables the sharing of resources and thus the coexistence of the strongest elements with the weakest. More generally, this study echoes the competition for available resources that exists at all levels of life, between different species in nature, between different organs in an organism or between different cells in a tissue.

Collaboration
Alex Mogilner (Courant Institute, New York)

Fundings
ANR SCALING (Alexandra Colin)
ANR MOVING (Laurent Blanchoin)
ERC AAA (Laurent Blanchoin)
ERC ICEBERG (Manuel Théry)
ANR GRAL (plateforme mulife)

Reference
Guerin C, N'diaye A-B, Gressin L, Mogilner A, Thery M, Blanchoin L Et Colin A.
Balancing limited resources in actin network competition
Current Biology 2025



Left: schematic diagram of experimental system (red arrow indicates actin assembly site, green arrow indicates disassembly site).
Top: use of available proteins without actin filament polymerization/depolymerization as a function of the number of beads with their respective actin comets.
Bottom: use of available proteins with actin filament polymerization/depolymerization (actin recycling phenomenon), based on the same number of beads with their respective actin comets.

When resources are recycled, the size of the comets is independent of the number of beads present, enabling the coexistence of several dynamic networks, whereas in the absence of recycling the size of the comets is function of the available amount of actin monomers.

Resurrection of heat-stable, gamma-resistant prehistoric proteins

Dominique Madern - Institut de Biologie Structurale

Researchers at Irig/IBS have been able to resurrect 500 million-year-old proteins and show that they can survive high temperatures and very high doses of radioactivity.

Enzymes are responsible for the chemical reactions that provide energy and transform various constituents during cellular metabolism. How they acquired their specific functions during evolution is a fundamental question. Indeed, the way they function today has evolved over very long periods of time. As part of a collaborative project, researchers at Irig/IBS have characterized very ancient enzymes, from extremophiles (micro-organisms capable of living in extreme conditions of temperature, pressure, etc.), using a paleo-enzymological approach to understand how some of today's enzymes have evolved.

Some micro-organisms, such as methanogenic archaea (unicellular prokaryotic micro-organisms that produce methane), have colonized a wide range of environments with very different temperature conditions. For example, growth temperatures approach 100°C for species isolated in deep hydrothermal vents. Their enzymes are therefore adapted to operate in these conditions.

Using malate dehydrogenase, an enzyme involved in metabolism, and using an evolutionary biochemistry approach coupled to a previously described biophysical approach, it has been possible to identify mutations responsible for the adaptation to various modern enzyme lineages from an ancestral form capable of withstanding conditions of radioactivity and temperature considered extremely deleterious. Until now, the ability to resist radioactivity had only been shown for some cells, in particular via DNA protection/repair mechanisms.

For the first time, researchers at Irig/IBS have demonstrated the existence of a favorable capacity to resist a strong radioactive dose, which seems to be quite ancient.

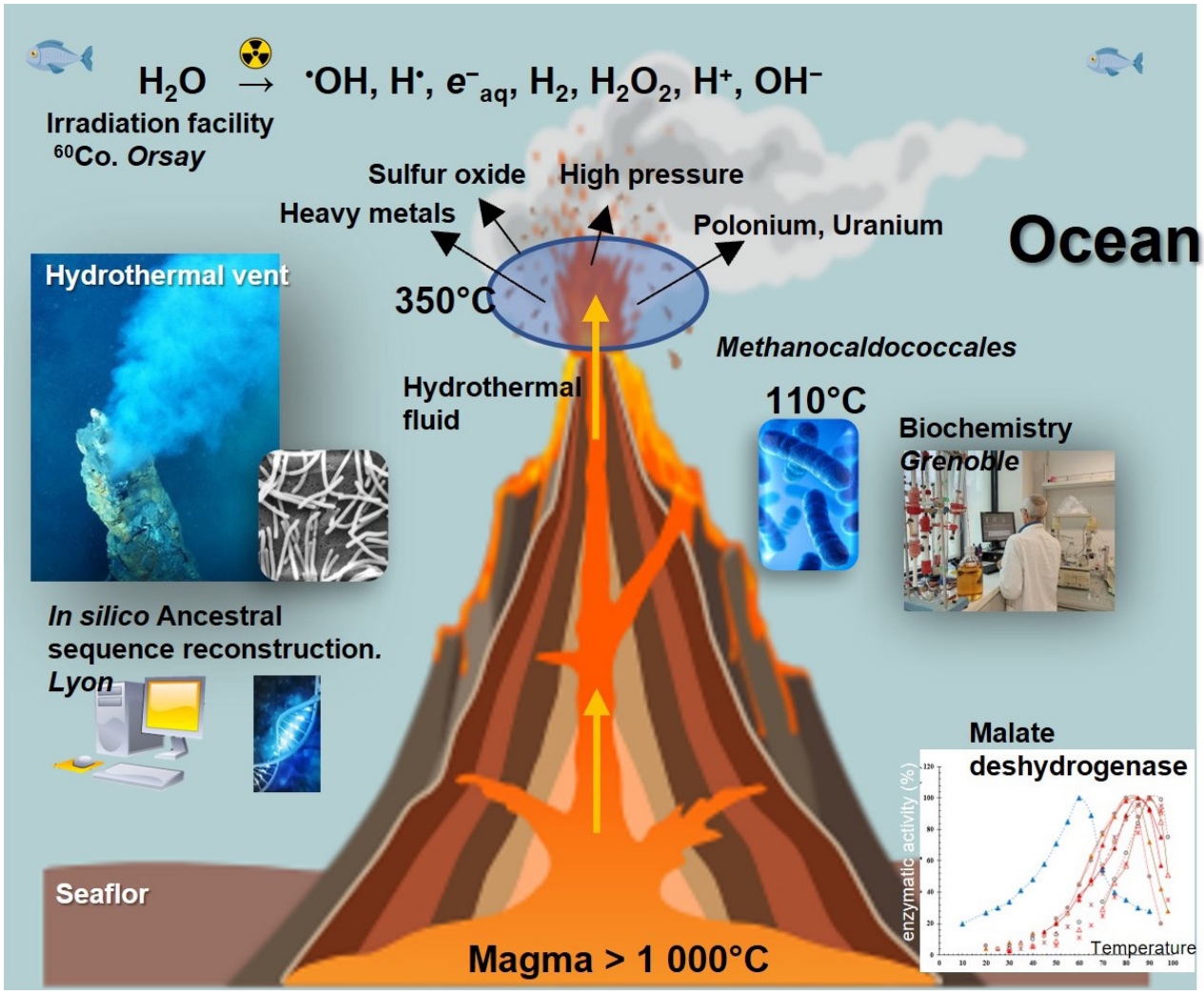
The discovery of a link between the thermal stability of an enzyme and its ability to survive intense radioactive stress opens up new prospects for studying the conditions of emergence of ancient cells under radioactive environmental conditions previously prevalent on Earth or found on other planets. This study also contributes to a better understanding of the process of rational engineering of enzymes useful for cleaning up radioactive sites.

Additional information
The resurrection of ancient proteins is based on a bioinformatic method for reconstructing ancestral sequences. The calculated coding sequences are then fully chemically synthesized. The genes thus obtained are introduced into bacteria, which then "manufacture" the corresponding proteins. These proteins are then characterized in the laboratory using a variety of techniques.

Collaborations
Laboratoire de Biométrie et Biologie Evolutive, Lyon
Institut de Physico Chimie, Orsay

Fundings
ANR Allospace & Thermadapt projects

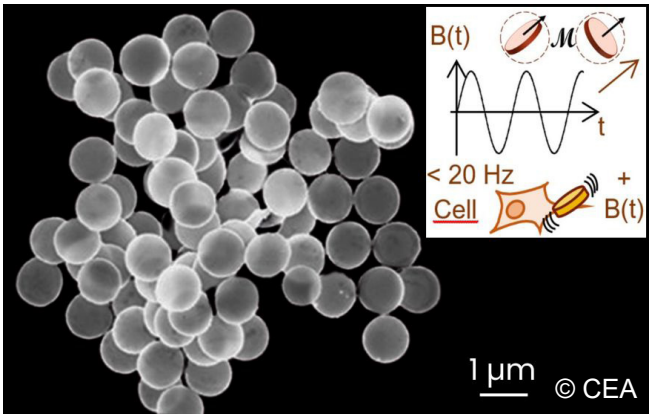
Reference
Madern D, Halgand F, Houe-Levin C, Dufour A-B, Coquille S, Ansanay-Alex S, Sacquin-Mora S Et Brochier-Armanet C. The Characterization of Ancient Methanococcales Malate Dehydrogenases Reveals That Strong Thermal Stability Prevents Unfolding Under Intense γ-Irradiation. *Mol Biol Evol.* 2024



Ancient methanogenic Archaea living in hot and/or radioactive environment. © CEA / D. Mardern)

Magnetism and biology join forces against cancer

Bernard Diény - Spintronics and Technology of Components laboratory



Thanks to magnetism, it is possible to exert controlled mechanical forces on cells and selectively generate physiological reactions such as the death of cancer cells.

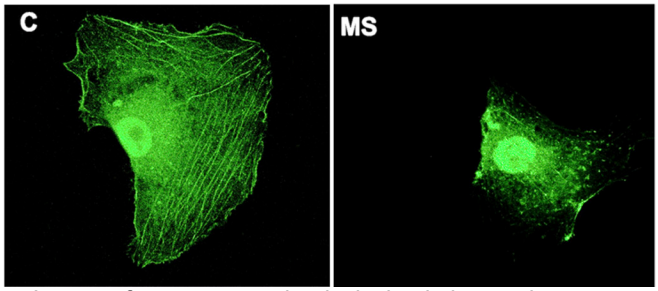
Magnetism offers extremely interesting prospects in biology, particularly in mechanobiology and for various biomedical applications, including cancer. *In vitro* studies on three-dimensional cell assemblies have shown that the death of different types of cancer cells (pancreatic, brain, kidney, melanomas) can be triggered by magnetic stimulation of the cells. The effect is mechanically induced by exerting mechanical stress on the cells through magnetic particles dispersed among them.

Researchers from our Institute have conducted initial research on glioma cells (brain cancer) cultured in 2D at the bottom of culture dishes. However, these results vary significantly depending on the cellular microenvironment, which differs between 2D cultures and actual biological tissues.
Today, the researchers have taken a new step by reproducing these effects on tumoroids, 3D assemblies of cancer cells that are much closer to biological tissues. To maximize efficacy, it is crucial to readjust the magnetic field conditions to lower frequencies (2 to 5Hz instead of 20Hz) to adapt to the different texture of 3D environments. A very strong impact of magneto-mechanical stimulation on the cellular cytoskeleton has been demonstrated, leading to cell death.

This study paves the way for *in vivo* testing of innovative cancer treatments using magneto-mechanical stimulation of cells. This approach could be used alone or in synergy with chemotherapy.

Fundings
Exploratory Project CEA : CELLSTIM, NANOVIBER contract (Joint Transnational Call EURONANOMED2)

Collaboration
Irig/Spintec, Irig/BGE/Biomics and Irig/SyMMES, CNRS/Laboratory of Microelectronics Technologies
INSERM/Braintech
Grenoble Institute of Neurosciences



Impact of magneto-mechanical stimulation on the cytoskeleton of glioma cancer cells (left=control, right=after magnetic stimulation). The actin fibers constituting the cytoskeleton are clearly visible in the control. These fibers are destroyed after magnetic stimulation, leading to cell death.© CEA

Reference

B. Dieny, R. Morel, H. Joisten, C. Naud, A. Nicolas, A. Visonà, P. Obeïd, S. Belin and F. Berger
Magnetism for mechanobiology and related biomedical applications
Physical Review Applied 2025

A hopping point defect in silicon

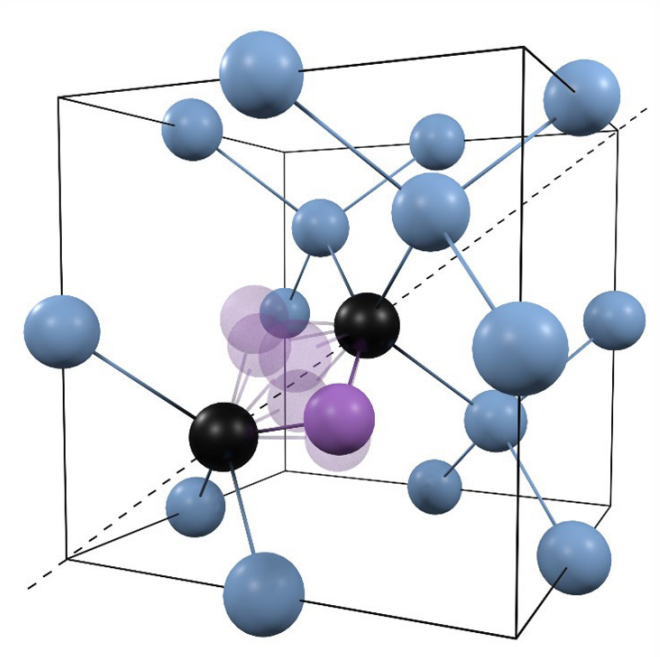
Jean-Michel Gérard - Quantum Photonics, Electronics and Engineering laboratory

In a semiconductor material fluorescent defects atoms are quantum systems that behave like optically addressable artificial atoms. Researchers at IRIG are shedding new light on a silicon defect, known since the 1970s as the G centre, in which one of the constituent atoms can explore several crystalline sites.

Fluorescent point defects in semiconductors are fascinating quantum systems as they behave as optically-addressable embedded artificial atoms. Usually, these defects have a static microscopic structure where atoms are only allowed to vibrate around well-defined equilibrium positions. Here, researchers shed new light on an old defect in silicon, known since the 70's as the G center, for which one of the constituent atoms can explore several crystal sites. Using low-temperature microspectroscopy at single-defect scale, they detected a fine structure in the emission line, signature of the motion of that atom inside the silicon crystal.

By analyzing the emission properties of individual G centers, they showed that their motion dynamics is strongly sensitive to perturbations in the crystal environment. Especially, the silicon-on-insulator structure commonly used in microelectronics and nanophotonics induces a strain acting on the defects. As a consequence, the mobile atom of the G center, which is perfectly delocalized between 6 sites in the unperturbed case, jumps randomly between the different positions under optical excitation, like a ball in a 6-slot roulette wheel. By combining spectral and polarization analysis, we can link the G center emission lines to specific crystal sites.

The next challenge will be to control the reconfiguration dynamics of single G centers in silicon. Exploration paths include strain engineering and the development of resonant excitation protocols to lock the mobile atom at a specific crystal site. Another promising research direction will be to investigate how the atomic reconfiguration of the G center influences its spin quantum degree of freedom.



Artist view of a hopping G center. Blue balls represent Si atoms and black balls carbon atoms in substitutional position. The violet ball is a Si interstitial atom that jumps between six different lattice sites. © CEA

Collaboration

Charles Coulomb Laboratory (Montpellier)
CEA léti (Grenoble)
IM2NP Marseille
Leipzig University
Budapest University

Reference

Durand A. et al.
Hopping of the Center-of-Mass of Single G Centers in Silicon-on-Insulator
Physical Review X 2025

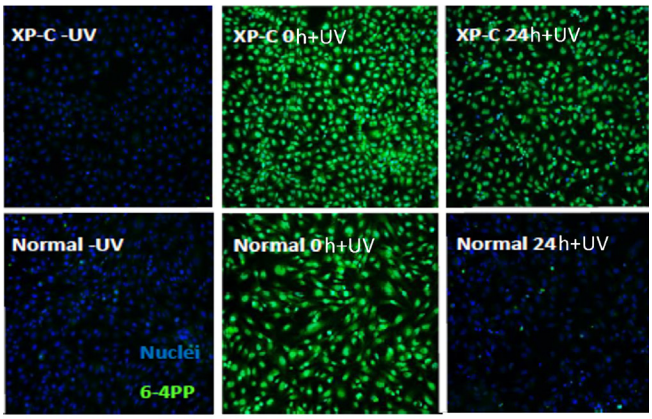
Potential new therapeutic target for moon children

Xavier Gidrol - Biosciences and bioengineering for health Laboratory

Xeroderma pigmentosum (XP) is a rare genetic disease that affects young children. These young sufferers, known as moon children, are extremely sensitive to ultraviolet (UV) rays and have an increased risk of skin cancer. Forced to avoid sunlight, they can only go out at night. Their disease is due to a «loss of function» mutation in the gene encoding the XPC protein, a key protein in the repair of DNA damage induced by the UV rays of natural light.

In this study, the researchers inhibited 646 different genes, one by one, in patient cells where the XPC protein no longer functions. They showed that inhibition of the gene encoding PIK3C3 partially restored the cellular damage caused by UV rays and enabled XP-C cells to survive better. These results suggest that the use of PIK3C3 inhibitors could be a promising therapeutic avenue for reducing symptoms and slowing the progression of the disease. Although further validation is required before clinical trials can be envisaged, this discovery offers a potential treatment for these patients.

More generally, this study shows that the genetic context in which a mutation is expressed should be systematically considered, particularly in oncology.



XP-C or healthy human skin cells
6-4PP in green = DNA damage. © CEA

Fundings
CEA "plan de couplage"
ANR PG2HEAL
Programme "Investissements d'avenir" (ANR NANB-0002) et (ANR IDEX-02)

Reference
Kobaisi F, Sulpice E, Nasrallah A, Obeïd P, Fayyad-Kazan H, Rachidi W and Gidrol X.
Synthetic rescue of Xeroderma Pigmentosum C phenotype via PIK3C3 downregulation.
Cell Death & Disease 2024

Spintronics nano-oscillators for cryptography

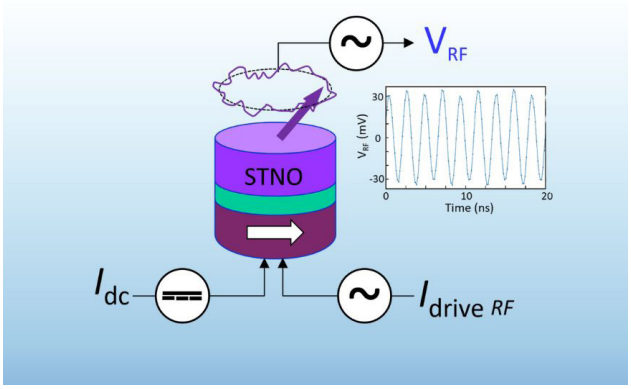
Ursula Ebels - Spintronics and Technology of Components laboratory

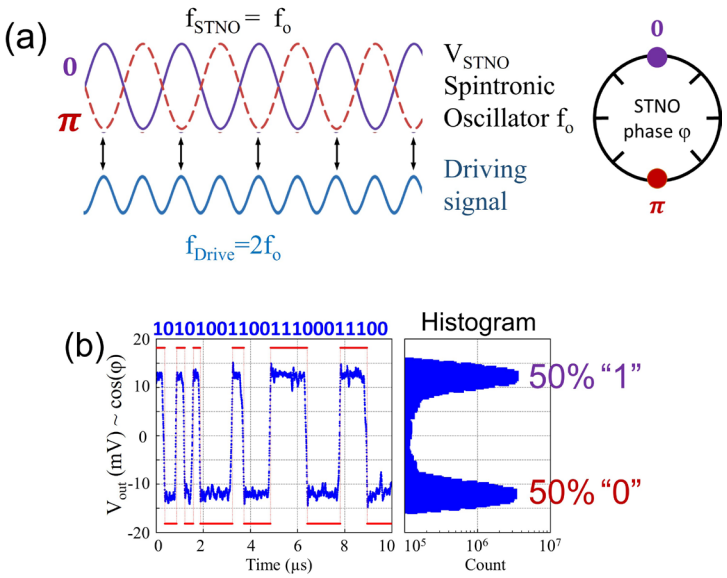
The generation of unbiased, true random numbers is essential for data encryption, secure communication and unconventional computing. IRIG/SPINTEC and collaborators have demonstrated a simple physical implementation based on spintronic nano-oscillators.

Encryption of data and communication protocols requires unbiased, true random numbers. However, in most cases, they are actually pseudo-random because they are generated from deterministic and therefore predictable digital hardware.
Active research is underway to explore intrinsically random and non-deterministic processes in physical devices. Among these, thermal fluctuations provide an efficient and virtually cost-free means to generate a random bit stream (0 and 1) from a physical system characterized by two energy minima. However, these hardware implementations often suffer from an intrinsic bias, leading to unequal energy minima and energy barriers. This leads to significant deviations from a fully balanced distribution of the binary levels 0 and 1. In order to make the two levels equivalent, additional signal processing is needed.

Researchers at CEA-IRIG/SPINTEC have validated a concept for generating true random and intrinsically unbiased bit streams, based on the stochastic phase dynamics of spintronic nano-oscillators. When the oscillator is synchronized to an external signal, whose frequency is twice its own frequency, then its phase stabilizes on one out of two discrete values with equal probability, in multiples of π. (cf. **figure a**). Thus, a π-periodic potential for the phase appears whose minima and maxima are intrinsically identical. In the presence of thermal noise, stochastic transitions of the phase between the minima, such as from a state 0 to π and from π to 2π, have exactly equal probability, allowing the generation of an unbiased bit stream (cf. **figure b**). Validation using the National Institute of Standards and Technology statistical test suite confirmed the suitability of the generated bit stream for secure encryption applications.

Compared to other concepts, the spintronic nano-oscillator-based implementation does not require additional signal processing to make the bit stream unbiased. The researchers are currently exploring an innovative magnetic tunnel junction configuration to reach a bit-stream-fluctuation-rate in the GHz range. These results are exploited in collaboration with CEA-LETI to implement an Ising machine based on the stochastic phase dynamics of spintronic nano-oscillators.





(a) Illustration of phase binarization by synchronization to an external source signal (Drive). The phase of the oscillator locks to that of the external signal.
(b) The two values of the binarized phase are converted into a binary voltage signal, using an electronic circuit specifically developed for this purpose. The generation of an unbiased bit stream is confirmed by the perfectly balanced histogram.

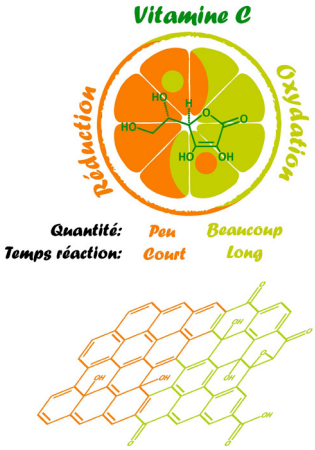
Collaboration
Iberian Nanotechnology Laboratory (INL)
National Institute of Standards and Technology (NIST)
University of Maryland

Fundings
ANR-NSF Stochnet
Grenoble INP Bourse Présidence
ANR MIAI@Grenoble Alpes
Bourse de these CEA Focus Numérique Frugal

Reference
Nhat-Tan Phan et al.
Unbiased random bitstream generation using injection-locked spin-torque nano-oscillators
Physical Review Applied 2024

Vitamin C: To be, or not to be a reducing agent ?

Florence Duclairoir - [Molecular Systems and nanoMaterials for Energy and Health laboratory]



Vitamin C is used to reduce graphene oxide. But unexpectedly, it has two faces: a bright side leading to GO efficient reduction, and a dark side, under certain conditions, leading to concomitant reoxidation.

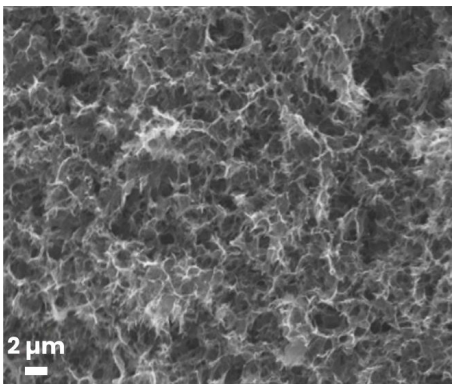
At CEA-Irig we synthesize graphene using a chemical exfoliation method of graphite. Graphene oxide (GO) is produced during the first oxidation/exfoliation step, and it must be reduced to obtain partially reduced graphene oxide (rGO). Hydrazine hydrate is the most commonly used GO reducing agent, but it is toxic and explosive.

Therefore, many other reducers are tested in the literature. Vitamin C (or L-ascorbic acid) is among the less hazardous and more eco-friendly reducers. Numerous examples of its use exist, and we aimed to rationalize the operating conditions to compare the reduction degrees of different rGO samples.

In this study, we were surprised to find that longer reaction times led to a less reduced graphene oxide than that obtained from shorter reaction times (see **chart**). This phenomenon is even more pronounced when the vitamin C concentration is higher. This observation suggests that, under these reaction conditions, both the reduction of the initial graphene oxide and its re-oxidation occur simultaneously. The proposed explanation is that, at high temperatures and vitamin C concentrations, vitamin C undergoes auto-oxidation, leading to graphene re-oxidation. Mechanistic studies could confirm the involvement of reactive species, such as H_2O_2 or radicals from its degradation, in this process.

By rationalizing the reduction conditions with vitamin C, we identified those leading to the production of highly reduced rGO, an important result for the design of efficient supercapacitor electrodes.

Fundings
ANR SPICS (ANR-19-CE05-0035)
PEPR HiPoHyBat (ANR-22-PEBA-003)



Scanning electron microscopy SEM image of rGO sample. © CEA

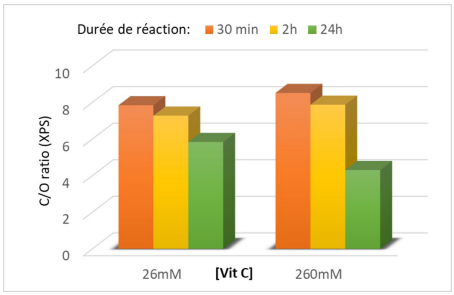
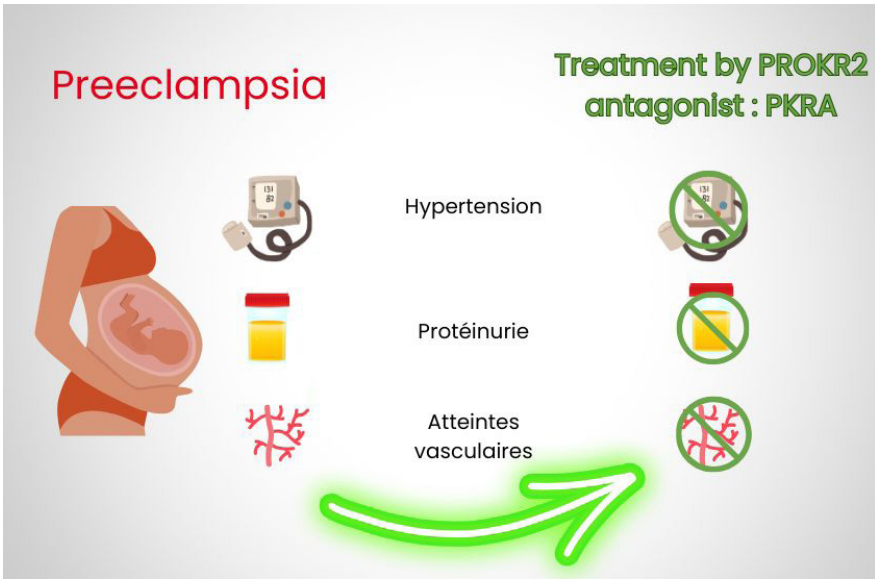


Chart: evolution of rGO reduction degree (C/O ratio determined by X-ray photoelectron spectroscopy XPS) depending on Vitamin C concentration (26 mM or 260 mM) and reaction time (30 min, 1h or 24h).

Reference
Omar El-Basha Hassan, Yves Chenavier, Vincent Maurel, Julien Pérard, Adnane Bouzina, Lionel Dubois et Florence Duclairoir
Vitamin C: friend or foe! A synopsis of ascorbic acid's reduction and oxidation of graphene oxide
Material Advances 2025

New therapeutic approach for preeclampsia

Nadia Alfaidy - Biology and Biotechnology for Health Laboratory



Preeclampsia affects 2% to 8% of pregnancies. It manifests itself through the appearance of symptoms in the mother as early as 20 weeks' amenorrhea, including hypertension, proteinuria (presence of protein in the urine) and damage to the maternal vascular system affecting various organs, including the heart and brain.

To date, there is no treatment to alleviate these symptoms or cure the condition, with the exception of termination of pregnancy, which can lead to premature delivery. Among the causes of preeclampsia, the genetic mutation of the STOX1 transcription factor has been identified.
In this context, our research team used a gravid mouse model carrying this mutation to study the mechanisms of the pathology and explore new therapeutic avenues based on inhibition of the PROKR2 receptor for prokineticins, a family of proteins involved in the development of the placenta.

The STOX1 heterozygous pregnant mouse model was used to generate two distinct forms of preeclampsia. The first, representative of preeclampsia of placenta origin (STOX1 heterozygous fetus), and the second representative of preeclampsia of maternal origin (normal fetus growing in a preeclamptic environment). The researchers tested the effects of PKRA, a PROKR2 antagonist, on the alleviation of symptoms in both forms of preeclampsia. They observed that this treatment reduced hypertension and proteinuria in both forms. Moreover, its efficacy was more marked when preeclampsia was of maternal origin. Finally, they demonstrated in vitro that treatment with PKRA attenuated the damage to vascular integrity induced by overexpression of the STOX1 gene.

This study proposes a new treatment for preeclampsia based on inhibition of the PROKR2 receptor, offering prospects for treating the vascular alterations associated with this pathology.

Fundings
Inserm Transfert

Collaborations
Cochin Institute
CEA Saclay
University of Melbourne

Reference
Sergent F. et al.
Antagonisation of Prokineticin Receptor-2 Attenuates Preeclampsia Symptoms
Journal of Cellular and Molecular Medicine 2025

Lanthanides illuminate cells observed under the microscope

Olivier Sénèque - Chemistry and Biology of Metals Laboratory

In the context of cell microscopy, researchers at CEA-IRIG have succeeded in introducing lanthanide complexes into the cytosol of living cells so that they can be better detected by fluorescence microscopy.

Lanthanides are chemical elements in the rare earth family that have formidable luminescence properties. For this reason, they are essential components in many of today's technologies (lasers, lighting devices, screens, anti-counterfeiting inks for banknotes, etc). Their luminescence properties are very specific compared with those of fluorescent organic molecules and could be of interest for applications in biological or medical microscopy imaging.

In this article, researchers at LCBM [**Collaboration**] describe a new step towards this goal. Lanthanide emission is distinguished from that of fluorescent organic molecules by very fine emission lines, at fixed wavelengths characteristic of each lanthanide, and by very long light emission, of the order of microseconds to milliseconds instead of nanoseconds for natural luminescence from cells or biological fluids. Their emission can therefore be easily distinguished from endogenous biological luminescence during microscopy experiments, which is of major interest. Lanthanides, in the form of cations, are toxic and must be encapsulated in a molecule – this is referred to as a metal complex or lanthanide complex - if they are to be used in living organisms. Until now, the difficulty with lanthanide complexes has been the lack of control over their penetration into cells and their distribution within them, with most of the lanthanide complexes described in the scientific literature as capable of penetrating cells ending up in the lysosomes, which is the cells' dustbin.

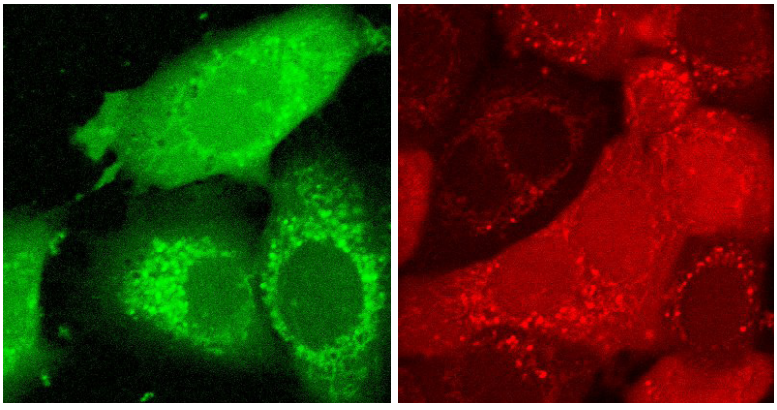
Researchers at LCBM have grafted lanthanide complexes onto peptides that are capable of entering living cells and reaching the cytosol to distribute themselves uniformly throughout them. Microscopic images were thus obtained, showing the distribution of the lanthanide throughout the cell.

This study is a first step towards the creation and use by biologists of intelligent probes for microscopy, based on lanthanides and capable of detecting and locating molecules of interest present in cells and better understanding their metabolism.

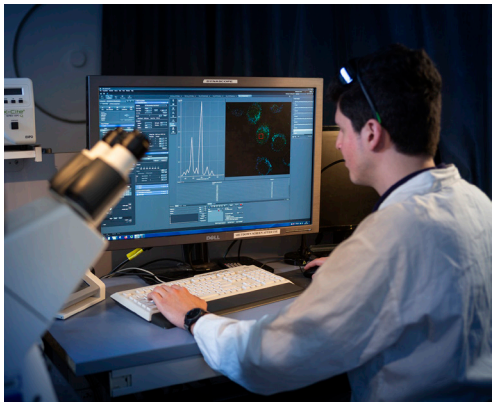
Fundings
Aviesan : programme ITMO Cancer PCSI
Projet ANR RECODNA
CEA : programme FOCUS Biomarqueurs

Collaboration
École Normale Supérieure, Lyon
Institut pour l'Avancée des Biosciences, Grenoble

Reference
Malikidogo K P. et al.
Efficient cytosolic delivery of luminescent lanthanide bioprobes in live cells for two-photon microscopy
Chemical Science 2024



Microscopic images: cells containing terbium emitting green light ; cells containing europium emitting red light. © CEA



Microscope study of cells and identification of the characteristic emission of terbium, one of the 15 lanthanides.

© Christian Morel / LCBM / CNRS

Press releases – Prizes – Others

CEA-Irig Annual General Meeting

IRIG website

Tech & Fest 2025

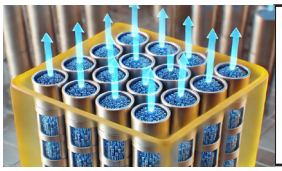
IRIG website

Celebrating 30 years of French beamlines at ESRF

IRIG website

Bernard Diény promoted Chevalier in the National Order of the Legion of Honor

IRIG website

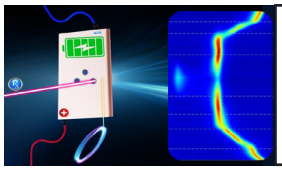


Improving solid-state batteries through one-dimensional (1D) electrolyte confinement

IRIG website

PFAS can affect the health of the placenta during pregnancy

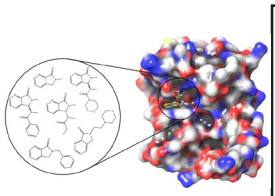
IRIG website



Placing sensors inside Li-ion battery cell impacts anode lithiation

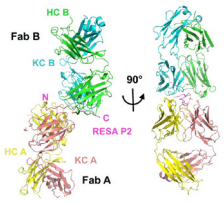
IRIG website

Other scientific news of the laboratories



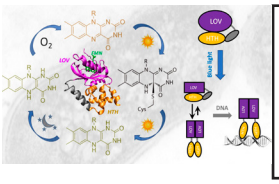
Fragment Discovery by X-Ray Crystallographic Screening Targeting the CTP Binding Site of *Pseudomonas Aeruginosa* IspD

IBS website



A new method for the agnostic isolation of human monoclonal antibodies (mAbs) reveals a mode of recognition of *Plasmodium falciparum* repetitive motif proteins

IBS website



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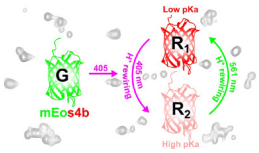

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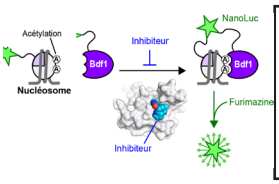

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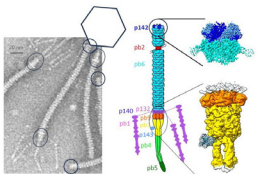

The structure makes it possible to localise a previously untraceable protein

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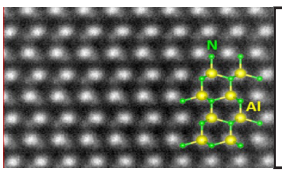

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Interdisciplinary Research Institute of Grenoble

CEA
17 Avenue des Martyrs
38054 Grenoble Cedex 9

Publishing Director
Pascale Bayle Guillemaud
Editor
Alain Farchi