Scientific Newsletter

Fall 2025

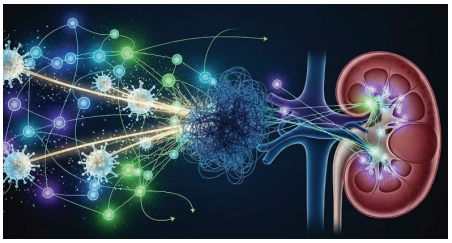
© Photo: A. Aubert / CEA

Summary

Highlights

Prediction of therapeutic response in kidney cancer using gene network analysis

Christophe Battail
Biology and Biotechnology for Health Laboratory



In silico approaches to predict therapeutic response in kidney cancer. Patient-specific gene network analysis indicates that enhanced connectivity and negative interactions between genes are hallmarks of resistance to immunotherapy.

Immunotherapies have become a reference treatment for advanced cancers, leading to improved overall survival. Nevertheless, only a limited proportion of patients benefit, primarily because reliable molecular biomarkers for identifying responders are still lacking. Here, we introduce an in silico approach based on gene co-expression network analysis to derive predictive signatures of immunotherapy response in renal cancer patients.

We constructed gene co-expression networks and analyzed their topological properties to assess their utility in predicting therapeutic response in renal cancer patients. Based on a cohort of over 300 renal tumor transcriptomes, we generated patient-specific gene networks (**Figure, panel A**) and evaluated their connectivity, gene-gene associations, network similarity, and pathway deregulation (**Figure, panel B**). This analysis uncovered gene co-expression signatures and enhanced the predictive performance of machine learning models for immunotherapy response (**Figure, panel C**).

Our study highlights the utility of gene co-expression networks as an alternative to single-gene markers for improving the prediction of therapeutic response in cancer patients.

Fundings

- the KATY and CANVAS projects under the European Union's Horizon 2020 Research and Innovation programme
- the DIGPHAT project through the France 2030 initiative, within the PEPR Digital Health programme of the French National Research Agency (ANR)

REFERENCE
Yin L et al.
Sample-specific network analysis identifies gene co-expression patterns of immunotherapy response in clear cell renal cell carcinoma.
IScience 2025

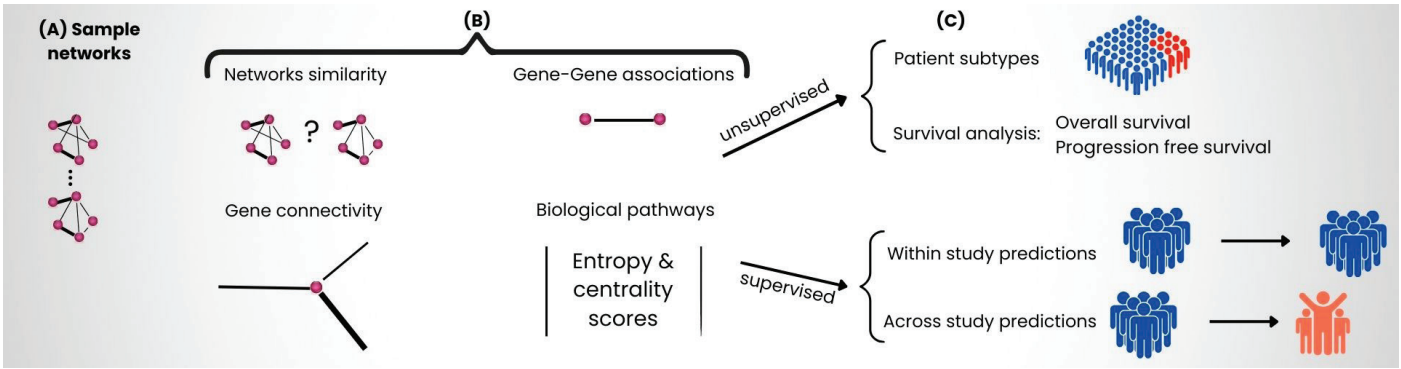


Figure: Overview of the in silico methodology: (**A**) patient-specific gene network modeling, (**B**) computation of four classes of topological features, and (**C**) evaluation for patient classification, survival analysis, and therapeutic response prediction. © CEA

Optimisation of solar cells assisted by a combined design of experiments/artificial intelligence approach

Cyril Aumaître
Molecular Systems and nanoMaterials for Energy and Health laboratory

Optimising a process influenced by multiple parameters is a common problem in research. This generally requires numerous time-consuming experiments. For instance, optimising a process with four variables would require 44 (256) experiments, which would take a considerable amount of time. Furthermore, this method carries a risk of failing to identify the optimal conditions if certain parameters have combined effects.

Researchers at **CEA-IRIG/SyMMES** (UMR UGA, CEA, CNRS, Grenoble INP UGA) have developed a methodology based on a combined approach involving design of experiments and artificial intelligence. By exploring different parameters with a reduced design of experiments, they have produced a dataset that can be easily exploited by an artificial intelligence algorithm. This approach enables the creation of a visual map of the different areas of interest and the identification of the optimal testing conditions. It accelerates the visual optimisation process by enabling researchers to focus on areas or conditions that have been identified as optimal.

As part of their research into dye-sensitised solar cells, SyMMES researchers used this strategy to optimise an electrolyte solution containing numerous additives. Electrolytes are often complex formulations in which the components and additives can interact with each other in favourable or unfavourable ways. With so many interrelated parameters, it can be challenging to interpret experimental results and optimise formulations.

In a study published in the journal Materials Horizons, the SyMMES team sought to maximise the energy conversion of these cells while maintaining high transparency — a challenging balancing act. This methodology enabled the researchers to understand the influence of each parameter and identify the optimal composition to achieve the best possible balance between solar energy conversion and transparency. The team quickly optimised a new electrolyte with four variables, conducting only 32 experiments and succeeding in simultaneously improving the efficiency and transparency of the solar cells.

This versatile new optimisation method has numerous applications. At SyMMES, it is currently being used to optimise the synthesis of quantum dots by exploring their composition. It is also being used to improve the deposition and composition of active layers in the latest generation of solar cells.

To achieve this objective, SyMMES will acquire a deposition robot as part of the AMARIA project, which receives financial support from the French programme France 2030's PEPR DIADEM and the CEA's Transversal Skills-Materials Programme (PTC-Matériaux). Using robotics to develop this methodology will speed up experimentation and reproducibility, significantly accelerating the development of active layer materials and solar cells.

Collaboration
CEA-Irig, CEA-Liten, CEA Tech-Bordeaux and Institut Courtois de Montréal, Canada.

Fundings
- ERC PISCO
- Bourse CFR

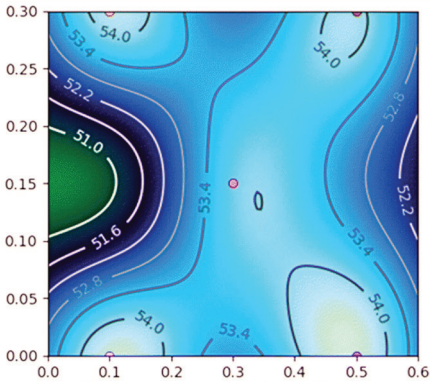


Figure: Map created by artificial intelligence representing the optimisation of dye-sensitised solar cell transparency based on electrolyte components. Four local optima were identified using this approach. © CEA

REFERENCE
Liotier J et al.
Data-driven modelling for electrolyte optimisation in dye-sensitised solar cells and photochromic solar cells
Materials Horizons 2025

Impact of nanoplastics on immune cells

Thierry Rabilloud
Chemistry and Biology of Metals Laboratory

The world has never used so much plastic, with an annual production of 500 million tons. Unfortunately, due to poor management of plastic waste at the global level, 10 million tons of plastics are released into the seas every year. This plastic waste, which takes decades or even centuries to fully degrade, first breaks down into microplastics (less than 1mm in size), then into nanoplastics (less than 1 micrometer in size). These micro- and nanoplastics are found everywhere on earth, from the abyss to mountain tops and polar ice caps. Living beings are constantly exposed to them, and humans are no exception.

To better understand the effects of these plastic particles on our cells, researchers at **CEA-Irig/LCBM** have studied the effects of plastic particles on the immune cells responsible in the body for removing particles (including biological particles such as bacteria and viruses), the macrophages. Macrophages also play a pivotal role in immunity, particularly via inflammatory reactions. What are the effects of plastics on these immune cells?

To answer this question, the researchers studied the effects of two different plastic particles on macrophages. On the one hand, they studied particles of poly (ethylene terephthalate) or PET, which is used in beverage bottles and is known to release particles into the liquids it contains. On the other hand, particles of polycaprolactone (PCL), a biodegradable plastic currently being studied as a replacement for conventional polyethylene-polypropylene-type plastics, which are poorly biodegradable, in applications such as packaging.

The researchers showed that these two particles induce very different effects in macrophages. PET particles induce cellular stress, in particular oxidative stress, and also induce a pro-inflammatory response in macrophages exposed to PET (see Figure). In addition, PET-exposed macrophages have a perturbed response to microorganisms, and would be less effective in their defensive role.

Macrophages exposed to PCL show no signs of cellular stress. Oppositely, they show a marked inhibition of their specialized functions, either phagocytosis (the ability to remove particles from the organism) or the establishment of an inflammatory reaction in the presence of a bacterial stimulus (see Figure). Therefore, they are overall, less effective in combating external aggression.

In conclusion, plastic particles are not without consequences for the functions of our immune cells. While these consequences differ from one plastic to another, plastic particles can alter the delicate balance of the immune system.

Collaborations

- Chemistry and Biology of Metals, CNRS UMR5249, CEA, IRIG-LCBM, Univ. Grenoble Alpes, France
- Univ. Grenoble-Alpes, CEA, CNRS, Grenoble-INP, IRIG, SyMMES, CIBEST, Grenoble, France
- Institut de Biologie Structurale, Université Grenoble Alpes, CEA, CNRS, Grenoble, France
- Group of Mutagenesis, Department of Genetics and Microbiology, Faculty of Biosciences, Universitat Autonoma de Barcelona, Cerdanyola del Valles, Barcelona, Spain
- Facultad de Recursos Naturales Renovables, Universidad Arturo Prat, Iquique, Chile
- Laboratoire de Spectrométrie de Masse BioOrganique (LSMBO), IPHC UMR 7178, CNRS, Université de Strasbourg, 67087 Strasbourg, France
- Infrastructure Nationale de Protéomique ProFI – UAR 2048, 67087 Strasbourg, France

Fundings

- European project PlasticHeal (Horizon 2020).
- Plastox project (ANR)

REFERENCES
[1] Collin-Faure V et al.
About the effects of true-to-life polyethylene terephthalate...
Environmental Science: Nano 2025
[2] Collin-Faure V et al.
A comparison of the effects of polystyrene and polycaprolactone nanoplastics on macrophages
Environmental Science: Nano 2025

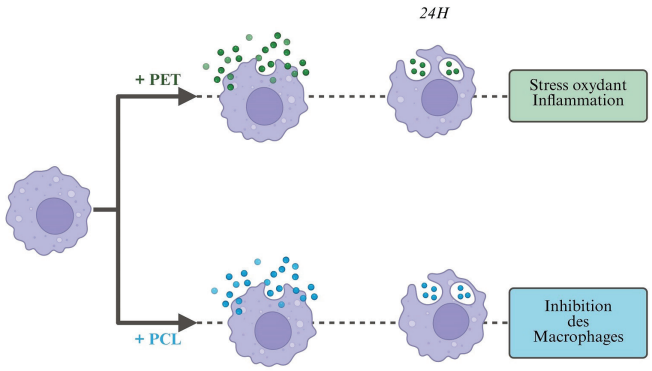
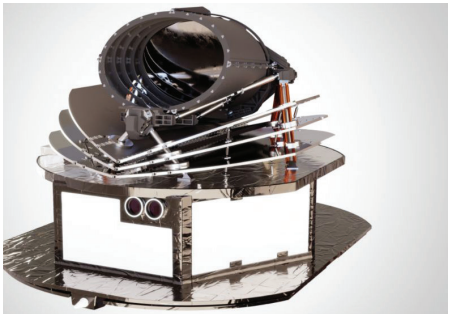


Figure: schematic diagram for studying the effects of nanoplastics on macrophages: macrophages (in violet) are exposed in culture to a non-lethal concentration of nanoplastics (green beads 200 nm in diameter) for 24 h. At the end of this exposure, the cells were harvested and tested for various parameters.

Grenoble at the heart of European space cryogenics

Sylvain Martin
Low Temperature Systems Department



The **CEA-Irig/DSBT** Laboratory hosted the 9th European Space Cryogenics Days in Grenoble from June 24 to 26, 2025, reaffirming its central role in this high-tech field.

Held in Grenoble from June 24 to 26, 2025, the 9th European Space Cryogenics Workshop was organized by CEA-Irig/DSBT in partnership with the European Space Agency (ESA). The event gathered over 70 European experts to discuss cutting-edge advancements in space cryogenics.

As a flagship scientific conference, it provided a comprehensive overview of the latest breakthroughs in cryogenic technologies. It is a major field for space exploration including refrigeration techniques, thermal design for ultra-high-sensitivity onboard instruments, cryogenic systems for quantum applications, and orbital fluid transfer technologies.

This seminar highlighted the important activity of Grenoble-based teams in the field of cryogenics, particularly with the participation of major local partners such as Air Liquide, Absolut System, Lynred, and the Néel Institute. The CEA-Irig/DSBT demonstrated its commitment through multiple presentations covering a wide range of topics and temperature scales, including closed-cycle space dilution refrigeration at ~40 mK (millikelvin), five-stage adiabatic demagnetization for the Athena mission, achieving cooling down to 50 mK, compact pulse tube coolers targeting 15 Kelvin, and thermal architecture for the European instrument developed for NASA's PRIMA mission.

A highly positive in-flight performance review of the LPTC (Large Pulse Tube Cooler), developed by Air Liquide Advanced Technologies (Sassenage) under DSBT license for the MTG (Meteosat Third Generation) satellite, underscored the robustness of these technologies after years of orbital operation.

The six presentations dedicated to the Athena mission—ESA's future X-ray astrophysics flagship—emphasized its central role in space exploration. These discussions highlighted the extreme cooling requirements of the mission, in which DSBT is deeply involved, showcasing ongoing technological solutions under development.

Other presentations focused on ESA's ARIEL exoplanet mission, particularly the Joule-Thomson coolers currently in development. These contributions demonstrated that certain European institutions retain strong in-house expertise in cryogenic manufacturing and assembly, reinforcing the importance of maintaining production capabilities within the region.

The event brought together European industrial and academic stakeholders to explore concrete collaboration opportunities, while reaffirming Grenoble's scientific and technical hub — including CEA-Irig/DSBT — as a leading platform in space cryogenics.

With broad community engagement, the workshop strengthened the visibility of national expertise in this strategic technological sector.

Fundings
UGA, Grenoble Alpes Métropole, Air Liquide, Cryogenic Society of Europe, Labex FOCUS and CEA-Irig.

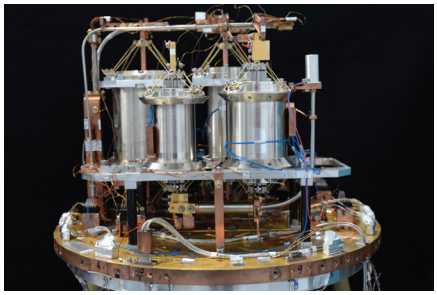
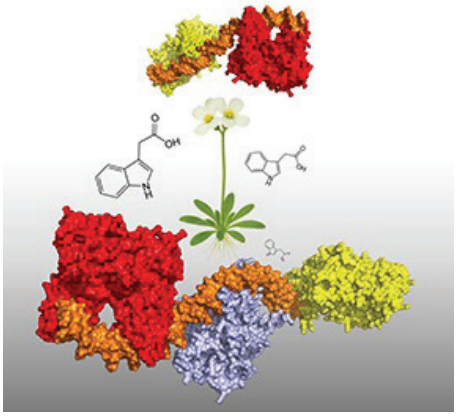


Photo: A four-stage adiabatic demagnetization refrigerator (ADR) demonstrator for Athena, capable of reaching 320 mK. © CEA.

REFERENCE
J-M Duval et al.
5-stage ADR cooler for the Athena space mission: design and preliminary characterization
Cryocoolers 2024

Auxin, the master regulator of plant development

Renaud Dumas
Cell & Plant Physiology Laboratory



In a paper published in Cell, a team from **CEA-Irig/LPCV**, in collaboration with a team from the Plant Reproduction and Development Laboratory (RDP), proposed a model to understand how auxin, a plant hormone, is responsible for a wide variety of transcriptional responses depending on the cellular context.

Caption: Auxin is involved in most developmental mechanisms in plants, including the formation of flowers, stems, leaves, and roots. This figure illustrates a two-level model to explain the diversity of responses to auxin. It is based on the combination of ARFs expressed in each cell and the arrangement of DNA sequences to which ARFs bind in the genes they regulate. © CEA-Irig/LPCV/Flo_RE/R. Dumas

The development of any multicellular organism (plant or animal) depends on genes that must be activated in the right tissue at the right time. The activation of these genes is controlled by proteins called **transcription factors***. Auxin Response Factors (ARFs) are among these factors: by activating or inhibiting a multitude of genes, they enable auxin, a plant hormone, to play roles that are always important but differ depending on the plant tissue (for example, guiding root growth according to gravity, causing a flower to emerge, or helping the stem to grow toward the light).

How does the same "auxin" signal enable this multiplicity of responses: activation and inhibition of genes specific to each tissue ?

Together with their collaborators, researchers at **CEA-Irig/LPCV-Flo_Re** have attempted to understand how auxin and ARFs control gene activity in *Arabidopsis* in space and time..

In *Arabidopsis*, there are 23 ARF proteins, some considered activators and others inhibitors. Until now, it was assumed that the response to auxin depended on the ARFs present in a given tissue, which competed to activate or repress each gene.

But the solution is more complex. ARFs act by binding to DNA motifs located near the genes they control. By combining biochemical approaches, single-cell sequencing, and "*in planta*" studies, the study reveals that the diversity of responses to auxin also depends heavily on the combinations of motifs present near each gene.

Using synthetic sequences consisting of different motif configurations, the researchers discovered that each ARF has a preference for certain configurations, and that its activity—as an activator or repressor—varies depending on the arrangement of the motifs. The action of auxin therefore involves two levels: on the one hand, the combination of ARFs present in each cell and, on the other hand, the configuration of motifs present in each gene. This combination generates a complex "two-layer" ARF/motif regulatory code.

This two-level code allows each gene to respond "in its own way" and according to the tissue, and plays a major role in the diversification of responses to auxin in plant tissue development.

Transcription factors* : proteins capable of binding to DNA and regulating genes by activating or inhibiting mRNA synthesis.

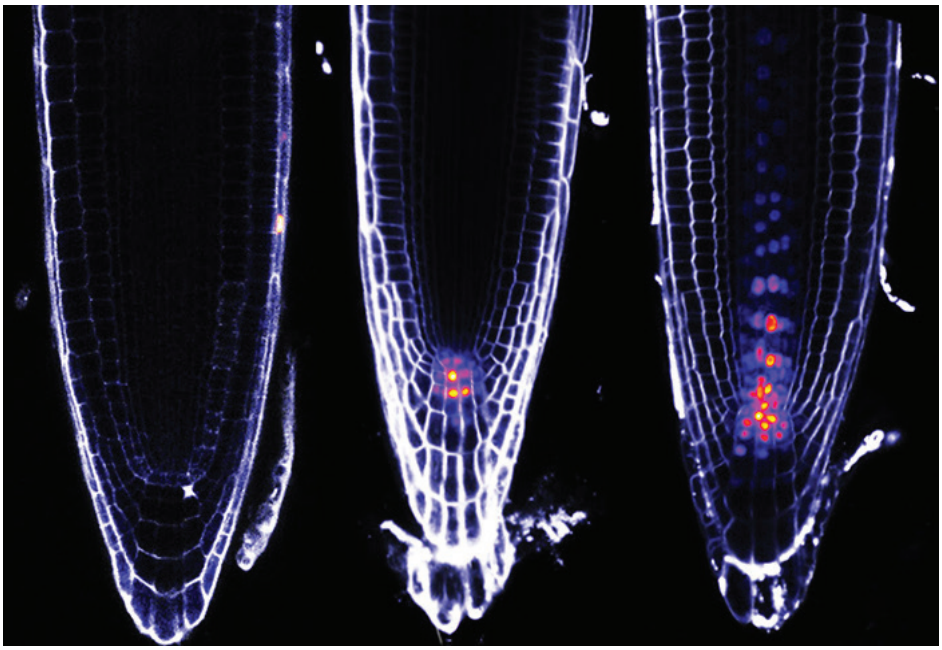


Figure: Activity in Arabidopsis roots of three synthetic DNA sequences constructed from three different configurations bound by ARFs and controlling the expression of a fluorescent protein (mTurquoise). This figure illustrates that varied expression profiles give rise to a double-layer code based on the composition of ARFs in each cell and on the binding of ARFs to different DNA motif configurations. The images were obtained by confocal microscopy. Fluorescence is visualized in a color range from violet to yellow-orange. Images from Raquel Martin-Arevalillo..

Understanding how, within an organism, information from a developmental signal is translated into a multitude of cellular responses in space and time is a key factor in understanding the development of that organism. Thanks to this study, it is now possible to understand how auxin can induce a multitude of transcriptional responses, despite the complexity of the molecular interactions involved. This breakthrough opens up new prospects for agriculture and medicine, by enabling better control and prediction of organisms' responses to developmental signals.

Collaborations

- Laboratoire Reproduction et Développement des Plantes, Université de Lyon, ENS de Lyon, CNRS, INRAE, INRIA, 69342 Lyon, France
- Institute of Synthetic Biology, University of Düsseldorf, 40225 Düsseldorf, Germany
- CEPLAS – Cluster of Excellence on Plant Sciences, University of Düsseldorf, 40225 Düsseldorf, Germany
- Center for Genomics and Systems Biology, New York University, New York, NY, USA
- Center for Genomics and Systems Biology, New York University Abu Dhabi, Abu Dhabi, United Arab Emirates

Fundings

- ANR ChromAuxi
- ERC TEMPO Project
- GRAL/CBH-EUR-GS (ANR-17-EURE-0003)

REFERENCE
Raquel Martin et al.
Synthetic deconvolution of an auxin-dependent transcriptional code
Cell 2025

Superconductivity of UTe_2 under extreme conditions

Jean-Pascal Brison
Quantum Photonics, Electronics and Engineering laboratory

The so-called **conventional superconductivity*** characterised by the vanishing of electrical resistance at low temperature (T) has been well described since the 50's. However, some superconductors, deemed **unconventional*** exhibit some intriguing, exotic properties such as robustness against magnetic field (H) or the emergence of several distinct superconducting phases under various conditions for T, H or external pressure (P)..

One of the most striking examples of such materials is UTe_2 whose singular phase diagram is showed in **Figure 1**.

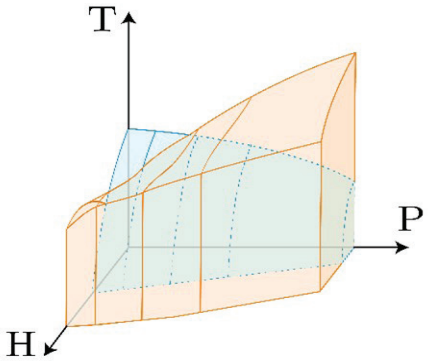


Figure 1: Pressure-field-temperature phase diagram of UTe2. The blue and orange regions depict two distinct superconducting phases.

The results that helped to build this figure are detailed in **Figure 2**.

Since the discovery of its superconductivity in 2018, the researchers from around the world have been unveiling more and more of its astounding properties. When cooled to temperatures below 2 K, a first, single superconducting phase (SC1) appears. Surprisingly, a second superconducting phase is stabilised and reinforced when a strong magnetic field is applied to the sample. Finally, a third superconducting phase emerges under strong pressure (approximately 0.2 GPa, i.e. 2 000 times the atmospheric pressure). The researchers from **CEA-IRIG/PHELIQS** recently sought to study the behaviour of UTe_2 under even more extreme conditions, by applying at the same time both strong magnetic fields and pressure. To this end, specific heat measurements have been carried out at the Laboratoire National des Champs Magnétiques Intenses (LNCMI) in Grenoble, in collaboration with researchers from LNCMI and Tohoku university, in Sendai, Japan.

The results unambiguously show that both the field-induced and pressure-induced superconducting phases are in reality only one single phase: SC2 (**Figure 2**).

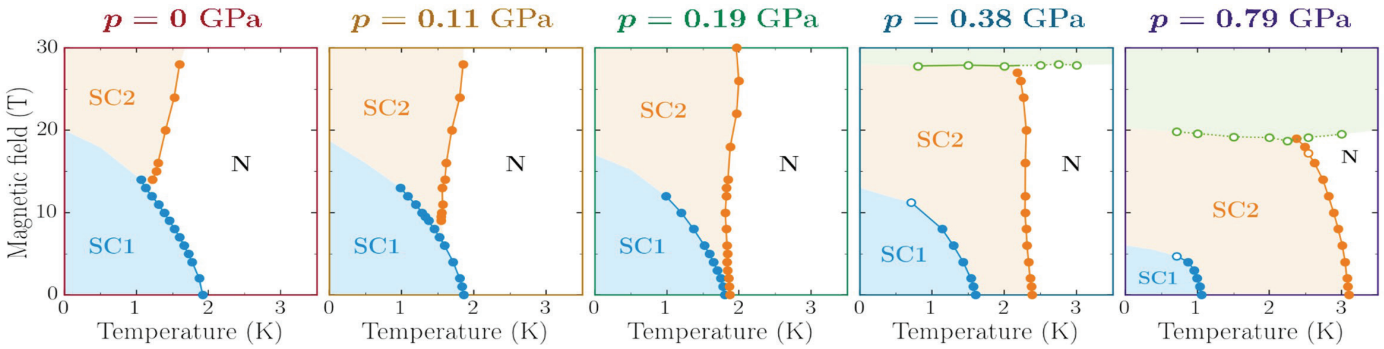


Figure 2 : Critical field of UTe_2 as a function of temperature, for different values of pressure. Without pressure nor field, UTe2 undergoes a transition from a normal state N to a superconducting phase SC1 at around 2 K. The second superconducting phase SC2 occurs either under field (15 T) at ambient pressure, or under pressure (0.2 GPa) at zero field, while evolving in a continuous manner. Thus, SC2 really constitutes a single "high-pressure / high-field" superconducting phase ».

This rather "simple" result actually raises a very complex question: what kind of pairing mechanism, responsible for this particularly robust superconducting phase, could be reinforced either by applying a strong magnetic field, or pressure?

In the first case, the magnetic field favours spin alignment until achieving a meta-magnetic transition into a ferromagnetic-like, spin-polarised state. On the contrary, pressure seems to promote an antiferromagnetic state, which makes it very tough to conciliate the two scenarios. Exotic superconductors such as UTe2 often reveal puzzling properties when subjected to extreme conditions of field or pressure.

Today, characterising the microscopic properties of the interactions that make superconductivity possible in UTe2 is a major fundamental challenge, and these recent results draw yet another target for future theoretical models and experiments that are currently working towards a better understanding of this **unconventional superconductivity***.

REFERENCE
Vasina T *et al.*
Connecting High-Field and High-Pressure Superconductivity in UTe_2
Phys. Rev Lett 2025

Conventional superconductors* : They have been well described since the elaboration of the BCS theory (Nobel Prize 1972). The mechanism allowing superconductivity to appear has been identified as the vibrations of the atomic lattice (phonons). Among them are found most of the pure elements (e.g. mercury), some alloys such as niobium-titanium (used in most MRIs) but also the recently found pressure-induced hydrides.

Unconventional superconductors* : In unconventional superconductors, the mechanism underlying superconductivity does not emerge from an electron-phonon interaction, but rather from more direct electron-electron interactions (those involving magnetic properties for instance). Unconventional superconductors are often found among several families in which electrons states are strongly entangled. Examples of such strongly-correlated electron compounds are the high-temperature cuprates, iron-based pnictides, or even uranium-based heavy-fermion compounds such as UTe_2.

When AI and cryo-electron microscopy reveal the structure of complex biological objects...

Grégory Effantin
Institute of Structural Biology

Baculoviruses are viruses with a circular double-stranded DNA (dsDNA) genome that specifically infect insect cells, playing an important role in regulating their populations. They are therefore widely used as biological agents in agriculture. In addition, they are used as expression systems, constituting a biotechnological tool of choice for the production of recombinant proteins in insect cell cultures.

Although commonly used, structural studies on the assembly of the **nucleocapsid*** of baculoviruses at the molecular level remain limited. A better understanding of its organization would provide clearer insight into how it functions, especially regarding its effectiveness as an expression system.

In this study, researchers investigated the Baculovirus "*Autographa californica* multiple nucleopolyhedrovirus" (AcMNPV). This virus consists of a nucleocapsid surrounded by a lipid membrane in which viral glycoproteins are inserted. The nucleocapsid forms an elongated structure that is 50 nm wide and approximately 300 nm long on average, with two distinct terminal parts, the "apical" cap and the "basal" structure, which are connected to each other by the capsid. At the start of this study, many of the structural proteins that make up the nucleocapsid had not yet been localized or even identified.

Using cryo-ME, researchers focused particularly on the "basal" and "apical" structures of the nucleocapsid. They obtained several 3D maps ranging from high to medium resolution, allowing to identify and position proteins building each of these 3D maps. The AcMNPV nucleocapsid can be described by several distinct protein sub-assemblies, each with its own symmetry. By elucidating these different symmetries within these sub-assemblies for the first time, a pseudo-atomic model representing all the symmetrical parts of the AcMNPV nucleocapsid was obtained. To achieve this, at the highest resolutions of the 3D maps (below 4 Å), they were able to assign densities of unknown nature using "**Modelangelo***". For 3D maps with lower resolution (above 4 Å), they identified and positioned several proteins based on structures predicted by "**Alphafold***".

AlphaFold was used not only to predict the structures of individual proteins among the 155 encoded by the AcMNPV genome, but also to suggest possible interaction partners, thus facilitating the interpretation of complex assemblies.

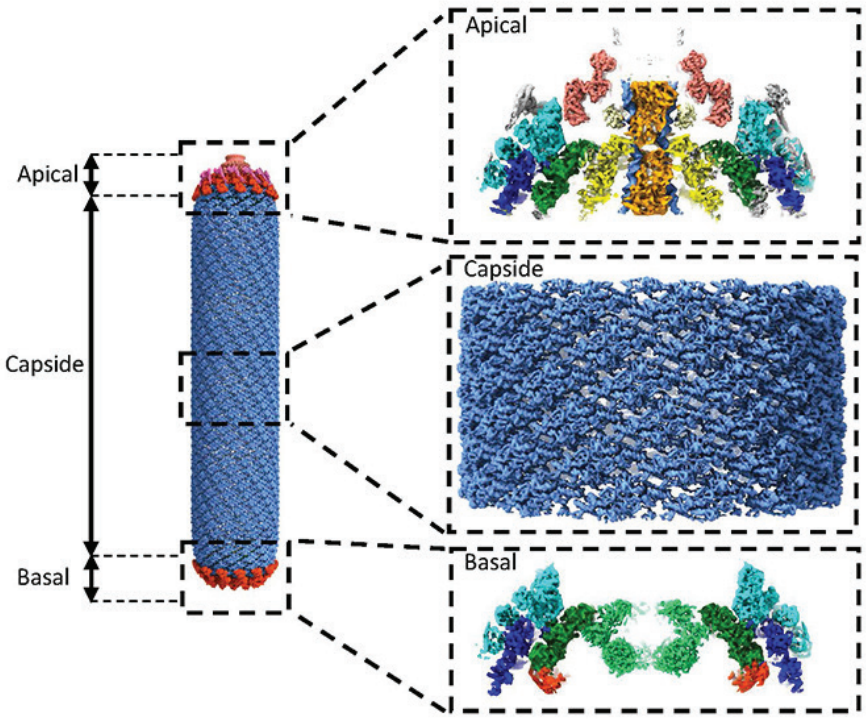


Figure: Structure of the whole nucleocapsid of AcMNPV obtained by cryo-EM. On the right, from top to bottom: zoom on a side view of the "apical" cap (the "entry point" for viral DNA), the capsid, and a side view of the "basal" structure. © CEA-Irig/IBS/G. Effantin

These results ultimately led to the identification of eight new proteins and a short segment of the viral genome in the "apical" domain of the nucleocapsid, providing experimental evidence for the proposed role of viral DNA entry and exit points.

Using high-resolution cryo-EM combined with AI algorithms, the authors of this study determined for the first time the entire structure—at near-atomic resolution—of the nucleocapsid of the Baculovirus AcMNPV. This work provides an in-depth understanding of how baculoviruses function by enriching the structural database of the virus, and will certainly contribute to a more rational development of biotechnological tools based on baculoviruses.

Collaborations

- European Synchrotron Radiation Facility (ESRF), Grenoble, France
- European Molecular Biology Laboratory (EMBL), Grenoble, France

Nucléocapside*: a complex consisting of the virus capsid and its nucleic acid (DNA or RNA), the viral genome.

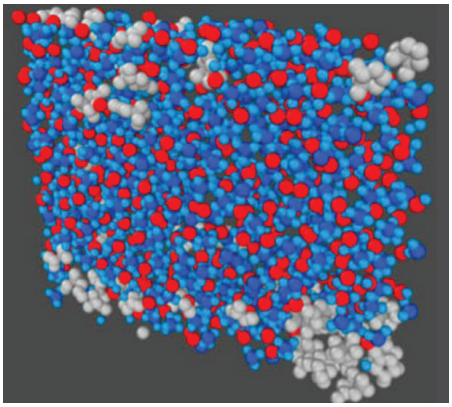
Modelangelo*: machine learning program designed to build atomic models of proteins (with known or unknown amino acid sequences) from cryo-EM maps.

Alphafold*: machine learning program that predicts the 3D structure of proteins based on their amino acid sequence. In 2024, Alphafold offered free access to more than 200 million protein structure predictions.

REFERENCE
Effantin G, Kandiah E & Pelosse M. Structure of AcMNPV nucleocapsid reveals DNA portal organization and packaging apparatus of circular dsDNA baculovirus. ***Nature Communications*** 2025

Unveiling Hidden Length Scales in Concentrated Electrolytes

Stefano Mossa
Modeling and Exploration of Materials laboratory



An international collaboration involving a researcher from **CEA-IRIG/MEM** has directly compared simulations to Surface Force Balance experiments, resolving the origin of anomalous screening in concentrated electrolytes.

Electrolytes are central to technologies such as batteries, supercapacitors, and biosensors. At low concentrations, Debye–Hückel theory predicts that ions screen each other's charges over a characteristic distance—the Debye length—which decreases as concentration increases. However, at high concentrations, Surface Force Balance (SFB) experiments have reported screening lengths unexpectedly growing with concentration, spanning tens or hundreds of ion diameters. This surprising result conflicts with simulations and theory, raising fundamental questions about electrostatic interactions in complex electrolytes.

Using large-scale molecular dynamics simulations of lithium tetrafluoroborate in ethylene carbonate, the authors systematically explored structural, dielectric, and transport properties across a broad concentration range. Direct comparison with SFB experiments revealed two distinct scales: a decreasing electrostatic screening length and a growing scale associated with the size of ionic clusters. The anomalous long-range decay observed experimentally is linked to these growing clusters, not to extended electrostatic forces, providing a consistent, parameter-free explanation.

This work reconciles a long-standing discrepancy between theory, simulations, and experiments by showing that anomalous screening reflects collective ionic clustering. Beyond solving a fundamental puzzle, these insights may guide the design of advanced electrolytes for next-generation energy storage and sensing technolgies.

This research was carried out in collaboration with the University of Ioannina, Greece. It was supported by the French National Research Agency through the France 2030 program (Grant ANR-22-PEBA-0002) and the MoveYourIon project (projet ANR-22-PEBA-0002).

REFERENCE
Skarmoutsos I. and Mossa S.
Length scales in electrolytes
J. Chem. Phys 2025

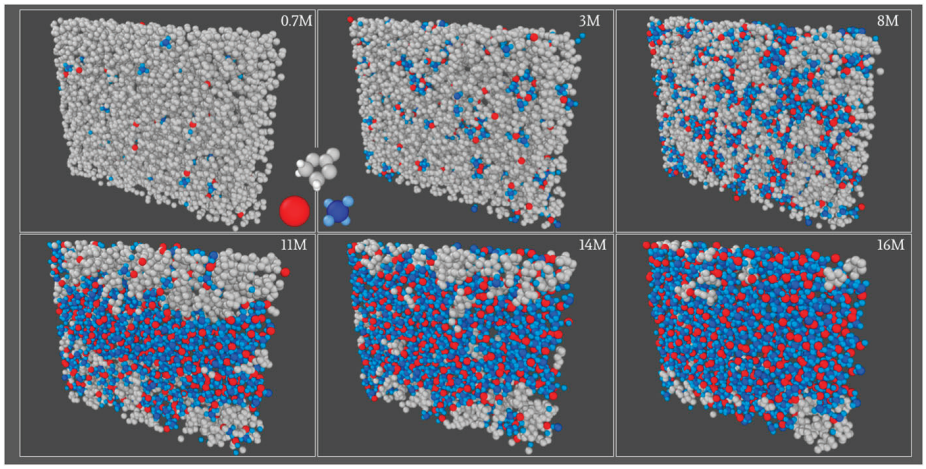
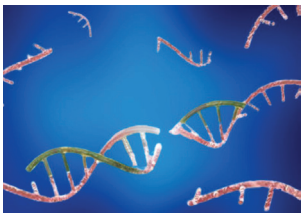


Figure: Representative MD snapshots show Li⁺ cations in red, BF₄⁻ anions in blue, and ethylene carbonate molecules in gray. As salt concentration increases, isolated ions merge into larger clusters, forming a percolated network and eventually phase-separating. © CEA

Rigorous analysis of single-cell microRNA co-sequencing to better understand their interactions

Laurent Guyon
Biology and Biotechnology for Health Laboratory



Single-cell co-sequencing techniques (miRNA + messenger RNA) offer a unique opportunity to explore, cell by cell, the relationships between a miRNA and its target genes. But their statistical interpretation requires methodological precautions..

The regulation of gene expression by **microRNAs*** (miRNAs) is a major field of research in biology and medicine. These small non-coding molecules finely control protein production, and their deregulation is implicated in numerous pathologies. However, understanding their precise mode of action remains a scientific challenge.

In a study published in Nature Communications 2025, a **CEA-IRIG/Biosante** team has conducted a new critical analysis of pioneering data published in 2019. While these initial analyses concluded that several abundant miRNAs regulated the expression of a large number of their targets, the researchers demonstrate that this was an artifact linked to methodological biases.

By applying a systemic strategy and publicly sharing their analysis codes, they show that:

- only one miRNA, miR-92a-3p, shows robust anti-correlation with many predicted target genes,
- the majority of miRNAs, including highly expressed ones, do not exert a detectable generalized effect,
- the choice of analysis parameters (expression thresholds, evolutionary conservation of targets, prediction scores) influences results, and must therefore be standardized.

Beyond this critical review, the work establishes best practices for the exploitation of single-cell co-sequencing data.

It stresses the need to assess the quality of target prediction software and experimental methods, and suggests using these data as reference tools to improve bioinformatics algorithms.

These advances reinforce the reliability of the conclusions that can be drawn from single-cell co-sequencing, a rapidly expanding technology. They will contribute to a better understanding of the role of miRNAs in complex diseases, and open up prospects for personalized medicine, where miRNAs are emerging as promising biomarkers and therapeutic levers.
This work confers on the team a recognized and rare competence in the analysis of co-sequencing datasets at the single-cell level, reinforcing its position as a reference in this emerging field.

microRNAs* play a key role in regulating gene expression by degrading one or several messenger RNA (mRNA) targets. Yet, precisely identifying their modes of action remains a challenge, as their effects are often subtle and context-dependent. Single-cell co-sequencing, which simultaneously measures microRNA and mRNA expression in each cell, provides a unique and physiological way to explore these interactions.

REFERENCE
Velut L, Fancello L, Cherradi N & Guyon L.
Single-cell microRNA-mRNA co-sequencing techniques convey large potential...
Nature Communications 2025

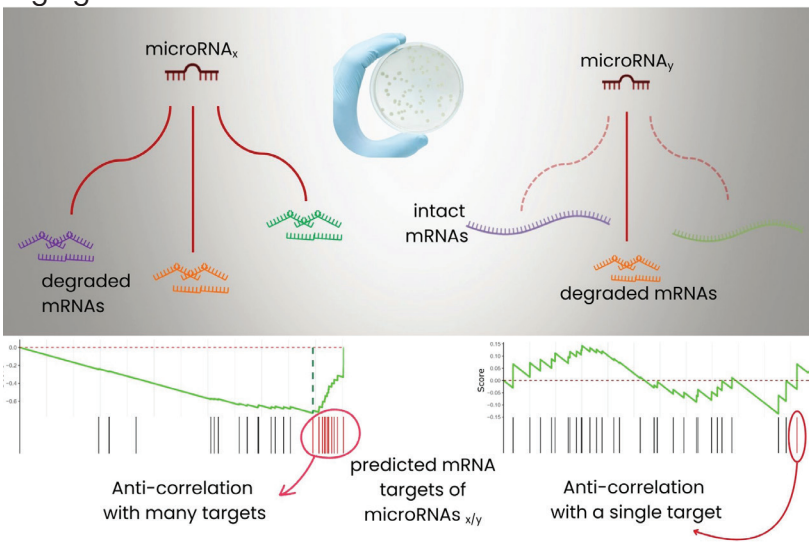
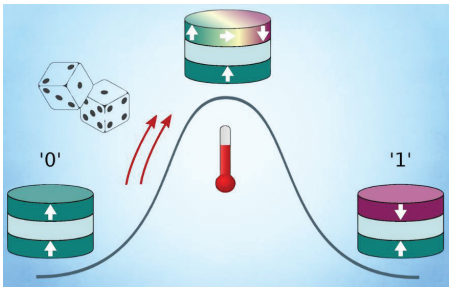


Figure: Statistical analysis of Single-Cell co-sequencing of microRNA-mRNA Left, a microRNA degrading multiple mRNA targets, predicted both by an algorithm and by strong anticorrelation of expression. Right, a microRNA acting on a single target only, highlighting the diversity of regulatory mechanisms.

Stochastic magnetic nanoneurons operate in a few nanoseconds

Philippe Talatchian
Spintronics and Technology of Components laboratory



Researchers from **CEA-Irig/SPINTEC** are the first to measure ultrashort mean waiting times between thermally-activated magnetization reversals in superparamagnetic tunnel junctions. These low-power components are being envisioned as nanoneurons in ultralow power calculators dedicated to a more frugal artificial intelligence.

In an era where the rapid rise of artificial intelligence is accompanied by exponentially increasing energy costs, a promising avenue is to exploit thermal noise at room temperature as an ultralow-power computing resource. This strategy, which biology already appears to be exploiting in the brain—where noise helps neurons explore and decide—has prompted researchers to design noisy nanocomponents capable of emulating neurons within electronic chips dedicated to computing. To this end, magnetic memory-type nanoneurons have been developed: **superparamagnetic tunnel junctions** (SMTJs).

SMTJs consist of a free magnetic layer and a fixed magnetic layer, separated by an insulator. The relative orientation of the magnetization in these layers, parallel or antiparallel, corresponds to two metastable states separated by an energy barrier.

In this study, the specific design allows SMTJs to be very sensitive to ambient thermal noise, unlike in usual applications (memory and sensors). Indeed, thermal fluctuations alone can randomly reverse the magnetization of the free layer. In that way, these SMTJs react like binary stochastic neurons, while consuming very little energy. The shorter the mean waiting time between magnetic reversals, the higher the computing speed.

A team from **CEA-Irig/SPINTEC** has experimentally measured mean waiting times between magnetization reversals in perpendicularly magnetized superparamagnetic tunnel junctions miniaturized to 50 nm in diameter, purely induced by thermal fluctuations. The measurement requires very low applied currents, in order to observe changes in the orientation of the free magnetic layer on a scale of a few nanoseconds, a timescale never before observed in these systems.

The measured mean waiting times are found to be much lower than those predicted by conventional models, which the researchers theoretically interpret as a significant contribution from Entropy, increasing the probability of overcoming the energy barrier separating the magnetic states of the SMTJ.

Entropy reflects the number of magnetic configurations accessible to the system. In perpendicularly magnetized SMTJs, there are many intermediate states where the magnetization gradually switches from the parallel to the antiparallel orientation (and vice versa). This contributes to a large Entropy, by increasing the number of different ways to transition between states.

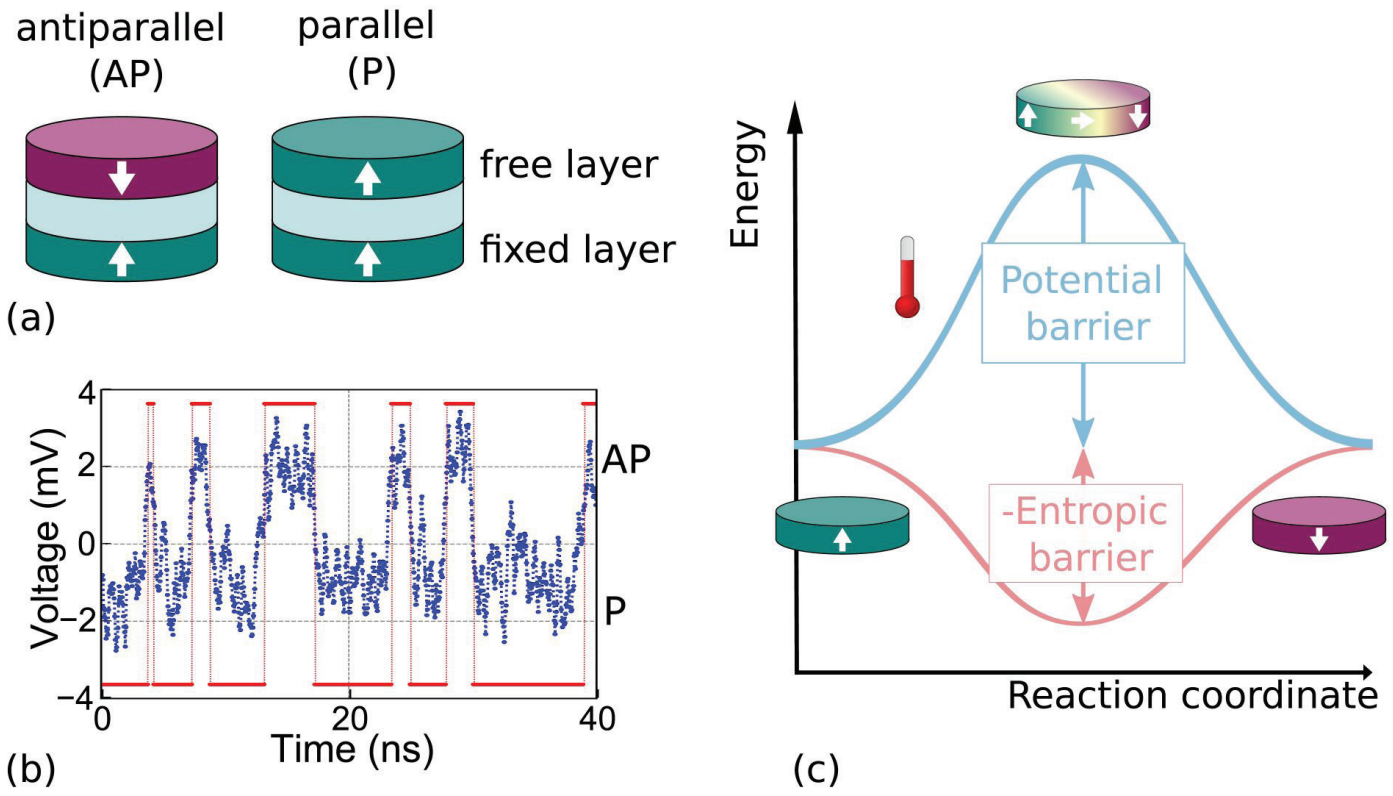


Figure © CEA
(a) Schematic of a magnetic tunnel junction. The free layer can be parallel (P) to the fixed layer (green), or anti-parallel (AP) (purple).
(b) Time evolution of the voltage in an SMTJ showing the waiting times between reversals on the scale of a few nanoseconds between the P (-2 mV) and AP (+2 mV) states.
(c) Schematic of the energy landscape associated with the magnetization reversal.

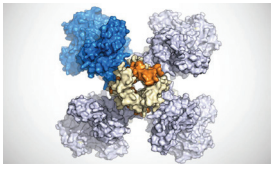
Under the effect of thermal energy alone, perpendicular magnetic tunnel junctions with a diameter of only a few tens of nanometers randomly switch from one state to another, with ultra-short mean waiting times between reversals on the order of nanoseconds. By capitalizing on these fluctuations as a magnetization reversal mechanism, this work paves the way for the implementation of stochastic elements for neuromorphic computing with ultralow energy consumption.

Fundings
- ANR (StochNet PRIME SPOT)
- NSF (CCF-CISE-ANR-FET-2121957)
- The French RENATECH network
- The University of Liège (Special Funds for Research, IPD-STEMA Programme)

Collaboration
- National Institute of Standards and Technology
- Gaithersburg, Maryland
- USA University of Maryland
- College Park, Maryland, USA

REFERENCE
Soumah L et al.
Entropy-assisted nanosecond stochastic operation in perpendicular superparamagnetic tunnel junctions
Physical Review Applied 2025

Press releases - Prizes- Media

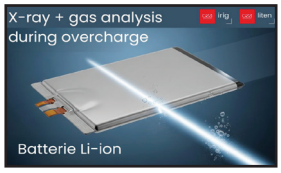


Discovery of a new protein structure providing a better understanding of bacterial energy metabolism

Read more

PEPR MED-OOC kick-off

Read more



Ever wanted to see an overcharged battery deteriorate in real time? Well, now you can!

Read more

Clemens Winkelmann appointed to the Institut Universitaire de France

Read more

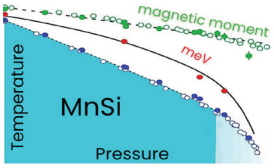
Laura Alvaro Gomez prix SFP Claudine Hermann 2024

Read more

Geneviève Blondin honored with the Luigi Sacconi Medal in Inorganic Chemistry

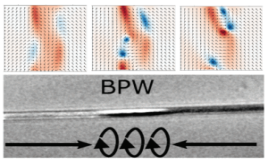
Read more

Other scientific results from the laboratories



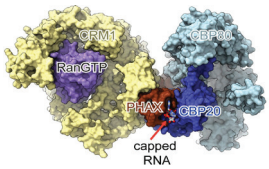
Origin of the Suppression of Magnetic Order in MnSi under Hydrostatic Pressure

PHELIQS website



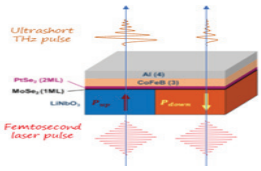
Topological analysis and experimental control of DW transformations in cylindrical wires

SPINTEC website



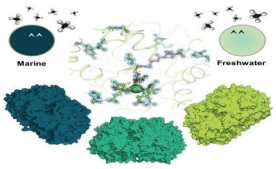
How Cells Export Small Nuclear RNAs to the Cytoplasm

IBS website



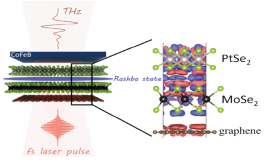
Modulating TeraHertz emission using 2D materials and ferroelectricity

SPINTEC website



Atomic resolution snapshots of the methane capturing machine from native microbes

IBS website



Monolayer control of spin-charge conversion in van der Waals Heterostructures

SPINTEC website

Quantum Photonics, Electronics and Engineering laboratory
CEA-UGA
www.Pheliqs.fr

Biology and Biotechnology for Health Laborator
CEA-Inserm-UGA
www.Biosante-lab.fr

Spintronics and Technology of Components laboratory
CEA-CNRS-UGA
www.Spintec.fr

Molecular Systems and nanoMaterials for Energy and Health laboratory
CEA-CNRS-UGA
www.Symmes.fr

Institute of Structural Biology
CEA-CNRS-UGA
www.IBS.fr

Modeling and Exploration of Materials laboratory
CEA-UGA
www.MEM-lab.fr

Chemistry and Biology of Metals Laboratory
CEA-CNRS-UGA
www.CBM-lab.fr

Biosciences and bioengineering for health Laboratory
CEA-Inserm-UGA
www.BGE-lab.fr

Cell & Plant Physiology Laboratory
CEA-CNRS-UGA-INRAE
www.LPCV.fr

Low Temperature Systems Department
CEA-UGA
www.d-SBT.fr

cea irig

Interdisciplinary Research Institute of Grenoble

Follow us on LinkedIn

CEA
17 Avenue des Martyrs
38054 Grenoble Cedex 9

Publishing Director
Pascale Bayle Guillemaud
Editor
Alain Farchi

cea cnrs Inserm UGA Université Grenoble Alpes INRAE