SPRING 2021

GIANT REVIEW

— *Exploring Science in Grenoble* —

10th ISSUE

ESRF: From fossils to the future of biomedical imaging

UGA: Hope for a first neuroprotective treatment for Huntington's disease

CEA: Hydrogen for a cleaner, greener Europe

ILL: Magnetism and neutrons: a powerful combination

Grenoble: a GIANT success

PARTENAIRE OFFICIEL GRENOBLE ALPES

GIANT (Grenoble Innovation for Advanced New Technologies) unites research, higher education and industry on a unique campus to overcome the major challenges of tomorrow.

Founding members: CEA, CNRS, EMBL, ESRF, GEM, ILL, Grenoble INP and UGA.

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Applied research and new business creation as well as innovation and industrial performance training for managers.

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Welcome to the spring 2021 GIANT Review

10th ISSUE

It is with great pleasure that I welcome you to the Spring 2021 issue of the GIANT Review. The milestone that this 10th issue marks for the magazine is rendered all the more meaningful by the noteworthy anniversaries with which it coincides: the passage of 50 years since Louis Néel was awarded the Nobel Prize in Physics and the construction of the ILL was completed, the 45 year anniversary of EMBL Grenoble. We also recognize important events that are happening now such as the inauguration of the EBS making the ESRF the first fourth-generation synchrotron light source in the world. These events, in combination with the planned opening of an exhibition on the history of the UGA at the Ancien-Évêché museum this year, inspire us to look back on the history of GIANT to better appreciate just how Grenoble has come to be synonymous with innovative research and industry.

GIANT demonstrates the power of bringing together research, higher education and industry and since the 1890's, Grenoble INP has adapted and continues to adapt to guarantee the education of engineers that are needed to support the industrial activity of Grenoble. The unification of Grenoble INP and UGA in 2020, was the opportunity for the institute to reaffirm its distinct identity. Combining internationally-renowned research with an education across all the domains of engineering, complemented by training in management, the defining vocation of Grenoble INP is to address industry. This identity and ambition has been strengthened by the recent integration of Polytech Grenoble and Grenoble IAE within our institute.

The commonly defined ambition of the GIANT partnership is to respond to major societal challenges in health, information and energy through fundamental and applied research. I invite you to discover within this magazine the latest advances that address these challenges, from game-changing new technology for the production of carbon-free hydrogen or to achieve the energy autonomy of connected objects, to the development of transformational biomedical imaging technology and fundamental magnetism research whose insights will impact the next generation of digital devices. These articles highlight not only the ecosystem's strength in transferring research to concrete application, but also the strong spirit of collaboration that GIANT strives to promote at the local, national and international level.

On behalf of all the directors of the GIANT partnership, it is my pleasure and honor to share with you this latest issue of the GIANT Review.

Pierre Benech
President Grenoble INP - UGA

AWARDS & HONORS

François Andrieu
CEA LETI – DCOS

ERC Consolidator: "My-Cube: 3D integration of a logic/memory CUBE for In-Memory-Computing"

Olga Matsarskaia
ILL

Award from the Condensed Matter Section of the German Physical Society (Deutsche Physikalische Gesellschaft, DPG)

Valentin Borshchevskiy
MOSCOW INSTITUTE OF PHYSICS AND TECHNOLOGY

ESRF Young Scientist Award for his outstanding contribution to the understanding of structure-based functional properties of membrane proteins - 2021 ESRF's User Meeting

Nora Dempsey
INSTITUT NÉEL – CNRS

Médaille de l'innovation 2021

GRENOBLE ECOLE DE MANAGEMENT
BUSINESS LAB FOR SOCIETY
CCI GRENOBLE

Grenoble Ecole de Management

Rewarded in the "Driving innovation in Higher Education" category for its 2020 Virtual Reality Back-to-School Challenge, by AACSB 2021 "Innovations That Inspire"

Houssame Boujjat
CEA LITEN

Student Award for excellent research work in the field of Biomass of the 28th European Biomass Conference and Exhibition

It is with great sadness that we have learned of the accidental death of **Cécile Renault**, astrophysicist at the LPSC. Cécile was not only an expert in observational cosmology but also an extremely talented science communicator, who tirelessly shared her passion for science with a wide range of audiences. Her intelligence and generosity will be sorely missed.

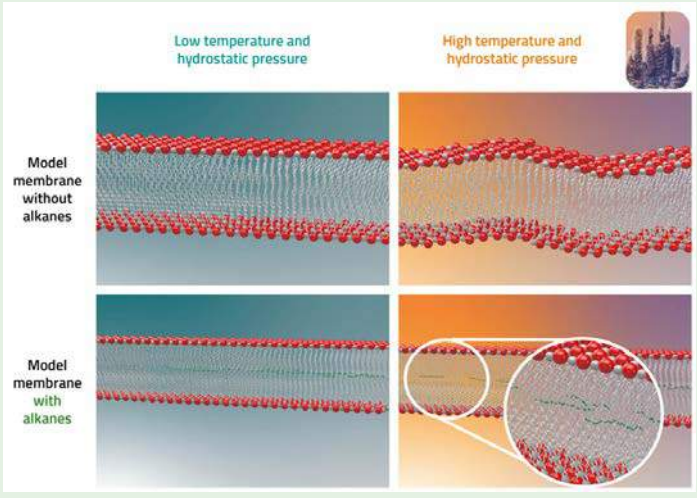
Commissariat à l'énergie atomique et aux énergies alternatives (CEA) · Centre National de la Recherche Scientifique (CNRS)
Grenoble Ecole de Management (GEM) · European Synchrotron Radiation Facility (ESRF) · Institut Laue-Langevin (ILL)

Lighting the way **WITH A NEW GENERATION OF SCIENTISTS**

The European Synchrotron (ESRF) launched its Extremely Brilliant Light Source (EBS) in 2020, the first of a new generation of synchrotrons, providing scientists with unprecedented tools to unveil the secrets of materials and living matter. A new generation of young scientists, that includes approximately 60 PhD students and post-doctoral scientists, has been recruited and recently joined the ESRF–EBS adventure. The curiosity and enthusiasm they bring will help push the boundaries in all scientific fields and thus address the complex global challenges facing our society such as health, the environment, and energy.
This new generation of scientists can be discovered through a series of portraits at https://humans.esrf.fr/.

Seeking **THE KEY TO EARLY LIFE** on Earth

A recent study at the Institut Laue-Langevin (ILL) has helped to uncover the role of alkane molecules in the emergence of early life. The energy required by early cells was available around deep-sea hydrothermal vents. As membranes could only be formed by simple molecules available at that time, a key question is how these early cells managed to form membranes that could survive the intense heat and pressures of that environment. The scientists discovered that the incorporation of alkanes into a model of cell protomembranes made it significantly more stable under conditions similar to those around a hydrothermal vent, thereby uncovering a previously unknown possible strategy that could have helped the appearance of life.



Molecules to ecosystem: EMBL and IAB sign memorandum of understanding

The European Molecular Biology Laboratory (EMBL) and the Institute for Advanced Biosciences (IAB) - a research center jointly supported by the CNRS, UGA and Inserm - have signed a memorandum of understanding, formalising a 15-year collaboration. EMBL's site in Grenoble and IAB share common interests across a range of biomedical science: RNA biology, epigenetics and cancer, host-pathogen interactions and translational research. Joint research activities in these fields, which are very much aligned with the next EMBL Scientific Program *"Molecules to ecosystem"*, will strengthen Grenoble as a European research centre in the life sciences. The collaboration has been exemplified for several years by the Grenoble Epigenetics Club which was created in 2012 by EMBL, IAB, and the Institute of Structural Biology (IBS). This successful model has been complemented by both the Grenoble Host-Pathogen Interactions Club, launched in December 2020 with a COVID-19 focussed meeting, and the newly formed Grenoble Drug Discovery Club, whose kick-off meeting is planned for this year.

MT180 Alps final won by a **Grenoble INP – UGA** graduate

The Grenoble INP - Phelma, UGA graduate Clara Aimar was recently awarded first prize by the jury at the Alps final of the competition 'My Thesis in 180 Seconds' (MT180). Her PhD, carried out at the 3SR research laboratory (CNRS, Grenoble INP - UGA, UGA) in collaboration with Decathlon, focuses on increasing the resistance of polymer foams that are used to make soles for sports shoes.

GEM: a *"Société à Mission"*

Grenoble Ecole de Management (GEM) is the first French business school to become a 'société à mission', the French equivalent of a benefit corporation. The framework supports organizations in achieving their social and environmental objectives in alignment with their 'raison d'être'. The fundamental purpose of GEM has been co-constructed with the 2020-2025 strategy and is as follows, *"Through education and research, to provide responses to the major challenges related to the ecological, societal and economic transition, and to contribute to a world that is more resilient, more just, more peaceful and more responsible."*

UGA on the way up in the **QS Subject Rankings**

QS World University Rankings by Subject is an annual publication that ranks the world's top universities across a total of 51 disciplines, grouped into five broad subject areas. The 2021 results class the Université Grenoble Alpes (UGA) within each of the five subject areas, with a higher position achieved compared to last year in four of them. In particular, the UGA is now placed in 99th position for the subject area of Natural Sciences, up from 120th in 2020. The UGA has also been ranked as the 51st top university in the world for three different disciplines: Earth and marine sciences, Geology and Geophysics.

An 'all-in-one' technique **TO FACILITATE AND ACCELERATE phage-therapy diagnosis**

The universal decline in the effectiveness of antibiotics and the increasing number of drug-resistant bacterial infections has generated renewed interest in phage therapy, whereby bacterial viruses (phages) are used to treat bacterial infections. Current research suggests that the technique has the potential to be used as either an alternative or a supplement to antibiotic treatments. However, phage therapy currently relies on a range of culture-based techniques which are then interpreted through direct visual observation. An 'all-in-one' method that could facilitate and accelerate phage-therapy diagnosis has recently been developed and demonstrated by scientists from CEA-Leti, CEA-Irig, CNRS-LTM and the phage-therapy team from Lausanne University Hospital, Switzerland. The custom-designed, wide-field lensless imaging system could easily be implemented in cost-effective and compact devices in phage laboratories.

Hydrogen for **a cleaner, greener Europe**

EU leaders have endorsed the objective of achieving EU climate neutrality by 2050 with the strategy through which to achieve it detailed in the European Green Deal. Hydrogen is considered a major potential solution and figures prominently within both the EU strategy and French stimulus package announced in response to the current health crisis. A clean, efficient and cost-effective technology for hydrogen production has been developed at CEA-Liten and the recent creation of Genvia – uniting CEA with a number of industrial partners – will accelerate the industrial deployment of this innovative technology.

#TECHNOLOGICAL RESEARCH #ENERGY

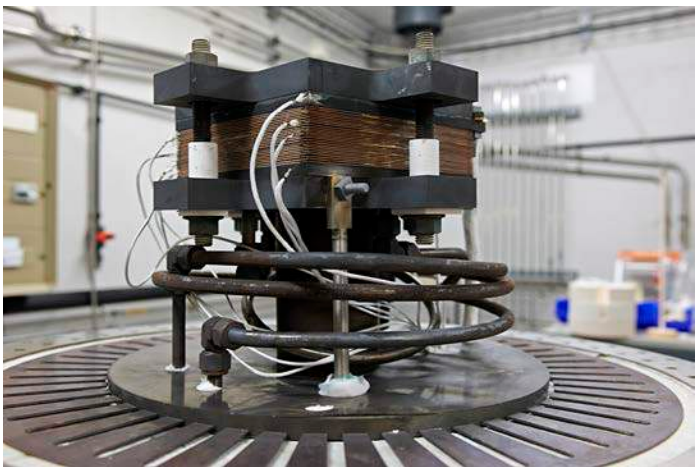
François Legalland
Director of CEA-Liten

Julie Mougin
Head of the Hydrogen Technologies Department at CEA-Liten

The versatility of hydrogen makes it a technically viable option as both a sustainable fuel and energy carrier across a range of sectors that include industry, transport, heat and electricity. As the only by-product of hydrogen fuel is water vapor, direct emissions are free of pollutants and greenhouse gases. The catch, however, is that the vast majority of hydrogen production is currently dependent on fossil fuels through processes that emit significant quantities of carbon dioxide (CO_2). Clean hydrogen, on the other hand, describes hydrogen that is produced using low carbon or fully decarbonized energy and the electrolysis of water.

Research carried out at CEA-Liten – one of the major European research institutes dedicated to the energy transition – supports the entire hydrogen sector, from production to usages through transport and storage. Indeed, the institute owns the world's second-largest portfolio of patents on high temperature electrolysis (HTE), a hydrogen production technology that is based on the dissociation of steam rather than liquid water into hydrogen and oxygen at high temperatures. The HTE technology developed over the last 15 years at CEA-Liten has now reached a point of maturity enabling its emergence as potentially the cleanest, most efficient and cost-effective method of hydrogen production.

One of the key aspects of hydrogen production concerns the yield, measured in terms of the lower heating value (LHV). While the electrolyzer technologies currently on the market – alkaline and proton exchange membrane (PEM) – can achieve yields of 60-70%, the CEA-Liten HTE technology is remarkably higher at 84%. This impressive efficiency has been obtained due to a sophisticated design of the system. *"The system requires a heat source of approximately 150°C, which is commonly found on industrial, incinerator or geothermal sites,"* explains Julie Mougin, head of the Hydrogen Technologies Department at CEA-Liten.



← Solid Oxide Cell stack

↑
Equipment for Stack Performance Validation, manufactured by ECM

"The input steam is then brought up from 150°C to 700°C by the recuperation of the thermal energy produced by the system. That means that although significant energy is required to start the process, the electrolyzer is thermally auto-sufficient once the nominal operating point has been reached."

The HTE technology developed by CEA-Liten is fully reversible providing the flexibility to switch from electrolysis mode for the production of hydrogen, to fuel cell mode for the production of electricity and heat using either hydrogen or a different fuel. *"The reversibility is an important and innovative feature of the technology, for example, if solar panels are installed on the roof of a building, when there is sunshine the electricity generated can fuel electrolysis to produce hydrogen. During periods without sunlight, electricity can be produced by switching to fuel cell mode. The mode can be changed in less than ten minutes and according to the use and needs of the application,"* explains J. Mougin.

Though clean hydrogen could supply up to 25% of the world's energy needs by 2050, one of the key challenges is lowering production costs to a level that is financially competitive with other energy sources. *"The associated investment and operating costs are major determining factors when considering the potential impact of the technology,"* explains François Legalland, director of CEA-Liten. *"That is why techno-economic analysis is systematically integrated into all research carried out at Liten to ensure that projects demonstrate not only scientific and technological potential but also performance that is financially competitive."*

Recognition of the performance of the technology has led to the recent creation of Genvia, a public-private partnership that unites CEA with Schlumberger New Energy, VINCI Construction, Vicat and the Regional Agency for Energy and Climate (AREC) of the French region Occitanie. Headed by Florence Lambert, former director of CEA-Liten, Genvia will enable an acceleration of the development by a joint R&D effort focused on improving the performance, durability and reliability of the technology. Further progress will be achieved by the scaling up of the technology at the first manufacturing pilot line, due to be established in Béziers in 2021. *"An extremely clear roadmap has been established for the achievement of a number of key milestones: demonstrators in the range of hundreds of kW in 2023 followed by demonstrators in the MW range in 2024. The objective being that by 2030, the cost of hydrogen produced with this technology has been reduced to less than €2 per kilogram, making the technology financially competitive,"* explains F. Legalland.

GIANT EFFECT

The developed technology has benefitted from collaboration with a number of GIANT partners: PhDs carried out jointly with research laboratories at Grenoble INP - UGA (Graduate Schools of Engineering and Management, Université Grenoble Alpes) and collaboration with the European Synchrotron (ESRF) have enabled advanced characterization of the microstructures at nanoscale and the degradation mechanisms of some of the technology components to be better understood. More generally, the development of the technology has been supported through the co-funding of buildings and strategic equipment by the Auvergne-Rhône-Alpes region and the Grenoble-Alpes Metropole, in addition to a number of national and European initiatives.

A nano-sized solution for a gigantic problem

Fundamental physics research dedicated to the quantification of heat transfer at low temperatures at the French National Centre for Scientific Research (CNRS) Institut Néel has led to the development of autonomous micro generators. Industrialized by the recently created start-up MOÏZ, the technology provides not only a sustainable energy solution for some of the billions of connected devices now in existence, but also demonstrates the co-existence of fundamental research and applications.

#FUNDAMENTAL RESEARCH #ENERGY

Dimitri Taïnoff
CEO of the start-up MOÏZ, senior lecturer at the UGA

Olivier Bourgeois
CNRS research director at the Institut Néel, scientific adviser of the start-up MOÏZ

"Understanding the mechanisms of heat transfer at low temperature interests a small community of specialists," admits Olivier Bourgeois, research director at the CNRS. *"But it is because we acquired such a good understanding of the physics at the micro and nano scale that we saw the opportunity to develop these very sensitive devices capable of harvesting ambient heat and converting it into electricity."* The resultant micro generators are made up of hundreds of nano-sized membranes integrated onto silicon using standard microelectronic techniques. The membranes absorb small quantities of thermal energy from their surrounding environment and a thin thermo-electric system converts the resultant temperature gradient into electricity by means of the thermoelectric effect. *"What distinguishes our technology is its size: thermoelectric generators have existed for decades but they've never been adapted to work at the micro or nano scale before,"* explains Bourgeois. *"Because the membranes are so small, they are very sensitive and that means that even a small amount of heat energy creates a temperature difference."*

The miniature scale of the developed technology makes it perfectly adapted for the market of connected devices. The incredible explosion in the number of which is associated with an equally dramatic increase in demand for the energy required for their operation.

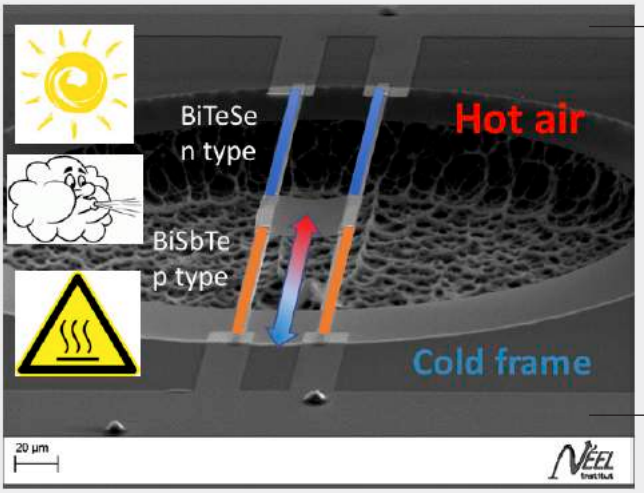
The resulting strain on grids and rise in global emissions hamper the ever more urgent attempts to meet climate change targets. *"We talk a lot about energy at the megawatt and gigawatt scale but it is also a huge issue at the very small scale. We don't have the means to produce or recycle the amount of batteries required for the predicted number of connected devices in 2030,"* explains Dimitri Tainoff, CEO of MOÏZ. *"The recycling rate of lithium-ion batteries is very low due to technical constraints, economic barriers and logistic issues. In addition to this environmental risk, there is also an ethical aspect in the sourcing of the raw materials required for producing batteries."*

GIANT EFFECT

The developed technology originated within the European project 'Merging' that included, in Grenoble, the CNRS and the French Alternative Energies and Atomic Energy Commission (CEA). The resultant start-up created, MOÏZ, was helped by the SATT Linksium incubator which is dedicated to the acceleration of technology transfer and the creation of start-ups and whose shareholders include a number of the GIANT partners: the CEA, CNRS, UGA and Grenoble INP - UGA.

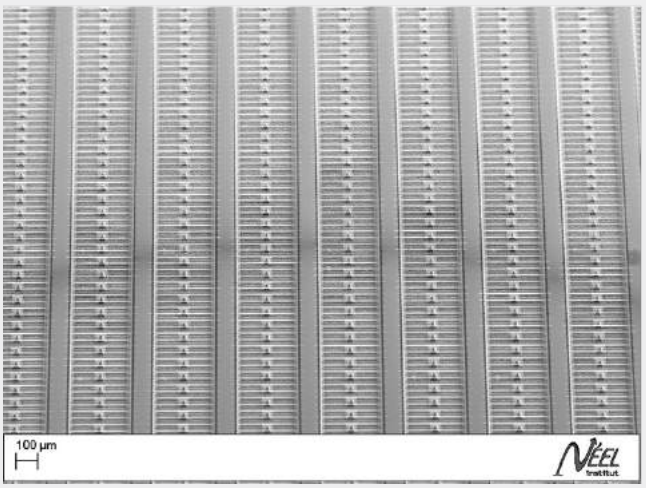
The solution proposed by MOÏZ is to employ the developed technology such that these smaller objects can be rendered energy autonomous. The solution is particularly applicable for powering connected industrial sensors, a number of which transmit information only a few times a day and are currently often produced with an integrated battery, meaning that once the battery is depleted, the entire sensor is discarded. *"The idea is to create autonomous connected sensors that can be used wherever they're needed. With an infinite source of energy and no battery to change, it constitutes a definitive and sustainable solution,"* explains Taïnoff.

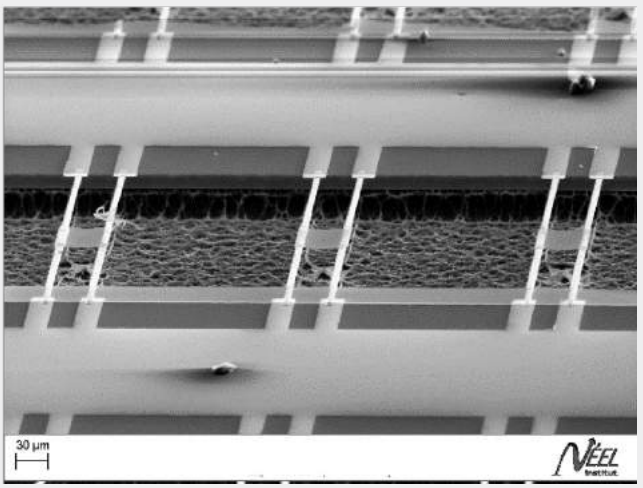
The potential applications of fundamental research are not always immediately evident and the support provided by the CNRS was crucial for the creation of MOÏZ. *"The technology transfer program within the CNRS is relatively recent,"* explains Bourgeois. *"Researchers, who want to, are now encouraged and supported if the possibility exists to transfer technology from research to industry."* Tainoff further explains that *"Fundamental science tends to be deep tech, so although there might not be hundreds of start-ups that emerge from the Institut Néel, the ones that do, tend to succeed because the technology really changes something: it's disruptive technology rather than an incremental development."*



Scanning Electron Microscope (SEM) image and operating principle of a single membrane based nanoTEG cell; the SiN membrane is suspended by four arms. Each SiN arm supports a n or p-type Bi2Te3 thin films: the p-type in orange is Bi2-xSbxTe3 and the n-type (blue) is Bi2-xTe3Sex. As an example, the hot thermoelectric junction is located on the membrane and the cold junction is on the bulk silicon frame. The temperature of the membrane is free to vary under an external source of heat like circulating air, radiation or solid conduction. The thermoelectric voltage V generated by the temperature gradient between the membrane and the silicon frame is collected by the two external contacts.

(Left) SEM pictures of an array of thousands of membrane cells as shown in the above figure. The nano-TEGs is assembled in series and parallel for adapting the internal electrical resistance to the impedance of the load (sensor to be fed). (Right) A close view of several membranes of the array shown in the left figure.





Neglected diseases in the spotlight

More than one billion people are currently infected with at least one Neglected Tropical Disease (NTD). Though that represents one-sixth of the world's population, it is low-income and marginalized populations that are disproportionately affected. Research into RNA editing and modification processes at the European Molecular Biology Laboratory (EMBL) in Grenoble provides key information for the future development of targeted drugs that are applicable to at least three of these diseases.

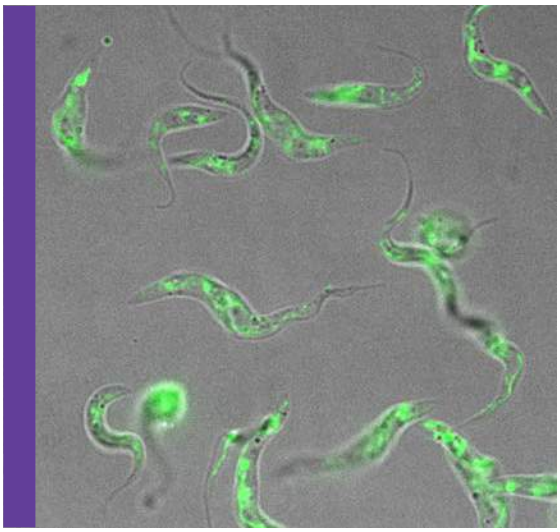
#EUROPEAN LARGE SCALE FACILITIES #HEALTH

Eva Kowalinski and one of her PhD students, Harald Bernhard

Eva Kowalinski
Group leader
at EMBL Grenoble

The World Health Organization (WHO) currently classifies 20 diseases and conditions as neglected tropical diseases. Though NTDs are largely preventable and treatable, there exists a lack of effective tools due to the historically limited attention and funding that these diseases have received. Furthermore, the impact of NTDs on health and life expectancy is compounded by an immense social and economic burden which perpetuates the cycles of poverty in the disadvantaged populations in which these diseases are concentrated.

African Trypanosomiasis, also known as '*sleeping sickness*', is an NTD caused by parasites of the species *Trypanosoma brucei* and transmitted through the bite of an infected tsetse fly. The first stage of the disease is long and relatively asymptomatic with more obvious signs and symptoms only appearing in the second stage after parasitic infection of the central nervous system. The disease is fatal if left untreated and, though curable with medication, diagnosis and treatment is complex. With no vaccine in existence, the disease represents a severe health threat in sub-Saharan Africa. Moreover, the presence of the disease in animals - called nagana in cattle - is a major obstacle to the economic development of the affected rural areas.



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Micrograph of Trypanosoma brucei.

Research carried out by Eva Kowalinski, group leader at EMBL Grenoble, focuses on studying RNA editing and modification processes of *Trypanosoma brucei* to understand how the genetic information is processed, modified, or even re-written. RNA processing is very complicated in trypanosomes and involves many proteins that together form large cellular machines. The function of the different proteins and protein complexes involved - how they work and interact with each other - can be better understood by studying their structure in atomic detail through the use of X-ray crystallography and cryo-electron microscopy (cryo-EM) techniques. *"Which technique we use depends on the questions we're asking, but also on the size of the protein complex, how easy it is to grow crystals of it or how well the complex can be embedded in the very thin layer of ice required for cryo-EM measurements. Each technique has advantages and disadvantages so the possibility to combine both methods is invaluable, together they are perfectly complementary,"* explains Kowalinski.

The future potential of this work is tremendous, recognized by a recently received grant from the French National Research Agency (ANR). *"The RNA processing of Trypanosoma brucei is very different to humans so from a fundamental research aspect, it's really interesting to first understand how it works,"* says Kowalinski. *"But there are also huge potential applications because targeting these pathways with drugs could prevent the parasite from reproducing."* Detailed protein structures enable the future development of tailor-made drugs that efficiently sabotage a distinct metabolic pathway of the parasite, thereby impairing the parasite and not the human host that it has infected.

While the Kowalinski group uses a laboratory-safe strain of *Trypanosoma brucei* for their research, any findings obtained can be more widely applied. *"Studying processes in this parasite advances our understanding of the molecular biology of organisms and life in general,"* explains Kowalinski. The work is also directly extendable to the *Leishmania* and *Trypanosoma cruzi* parasites, which are respectively responsible for Leishmaniasis and Chagas disease, both of which are also classified as neglected tropical diseases. *"These related parasites process RNA in a similar way to Trypanosoma brucei so it is highly probable that our findings will help fight these two diseases as well,"* explains Kowalinski.

These three diseases are all examples of vector-borne infectious diseases, meaning that the parasite is dependent on the insect vector for transmission of the pathogen. *"The transmission vector is entirely specific, sleeping sickness is transmitted by the tsetse fly and leishmaniasis by certain types of sandflies"* explains Kowalinski. The impact of climate change and global warming on tropical and infectious diseases is hard to predict. The insect vectors might migrate, together with their preferred climate, to different territories and altitudes. As insects invade new regions that have been previously untouched, the likelihood increases that many vector-borne diseases will spread. *"If this happens, it will cause huge problems because the health systems and vector control infrastructure of so far untouched zones are not prepared for it,"* warns Kowalinski.

GIANT EFFECT

X-ray crystallography beamlines jointly operated by EMBL Grenoble and the European Synchrotron (ESRF) and the cryo-EM beamline shared between EMBL Grenoble, ESRF, the Institut Laue-Langevin (ILL) and the Institute of Structural Biology (IBS) were used for structural analysis. The IBS also provided mass spectrometry measurements and the Partnership for Structural Biology (PSB) biophysics platform was used to characterize samples.

Grenoble: a GIANT success

Grenoble with its surrounding area, Grenoble Alpes, is one of the most important research, technology and innovation hubs in Europe and has been ranked as the 5th most innovative city in the world (Forbes, 2013).

Cutting-edge research associated with world-class higher education has enabled Grenoble Alpes to develop as one of the most dynamic industrial areas in France with the highest concentration of R&D jobs.

From laboratories to international research centers and from start-ups to established industry leaders, the vast and collaborative infrastructure of state-of-the-art facilities and technology ensures that the exceptional concentration of engineers and researchers have the necessary tools available to create and innovate.

But just how did Grenoble Alpes become synonymous with innovation?


EUROPEAN GREEN CAPITAL 2022
ESRF
HEALTH
ENERGY & DIGITAL
LOUIS NÉÉL - NOBEL PRIZE 1970
CEA
UGA
GEM
MINATEC

A powerful landscape

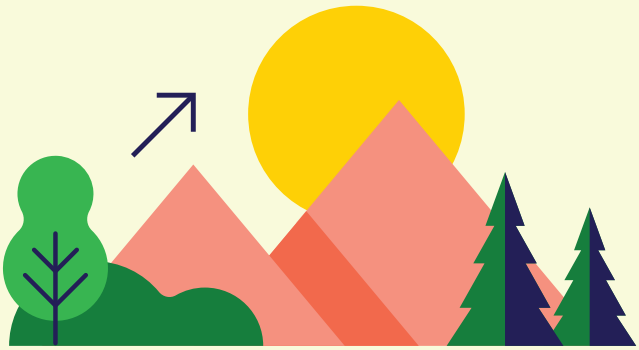
Grenoble, surrounded by mountains and at the confluence of two rivers, is recognized as the capital of the French Alps. This impressive landscape is intimately associated with the long and shared history of collaboration between higher education, research and industry in Grenoble that formed the solid foundation on which the success of GIANT has been built.

The ability to harness the energy of Alpine water to power factories was discovered in Grenoble in 1870 by Aristide Bergès. The invention of hydroelectricity, referred to as 'white coal' due to its ability to generate electricity second only to the primary source of energy at the time, was to have a tremendous and long-lasting impact on Grenoble. Indeed, the 38 hydroelectricity stations located in Grenoble Alpes today supply one third of French hydropower, making the region the leading producer of hydroelectricity in France.

At the time, the booming hydroelectricity industry caused a demand for technicians and engineers that far exceeded availability. Classes, schools and institutes were established to educate the workforce needed and thereby support the local industry. The first courses in industrial electricity and hydraulics were held, respectively, in 1892 and 1906. Developed in close partnership with local industrialists, the courses were an immediate success and led to the creation of the Institute of Electrical Engineering in 1898 and the Hydraulic Engineering School in 1928.

These first courses constitute the beginning of what is now known as Grenoble INP – UGA (Graduate Schools of Engineering and Management, Université Grenoble Alpes). *"The creation of Grenoble INP was driven by industry,"* explains Pierre Benech, president of Grenoble INP – UGA. *"Engineers were lacking pretty much everywhere and right from the beginning, in the 1890s, the courses were developed in synergy with the industrial sector. And that is still relevant today! New schools have been established as industry has developed and our courses are continuously adapted with respect to industrial activity. The objective of Grenoble INP has always been to meet the requirements of industry and to ensure that our students arrive in industry equipped with the necessary knowledge and techniques combined with management expertise."*

With an abundance of hydroelectricity produced and available, the hydroelectricity applications sector was booming. Innovation was supported by the introduction of training in the field of electrochemistry (1907), that was soon broadened to include electrometallurgy. The relevance of these disciplines was soon demonstrated by the First World War. The extensive use of chemical weapons and the strategic importance of metals such as aluminum and magnesium, created an unprecedented demand for industrial chemical and metal production. Close collaboration between research, higher education and industry accelerated development in these fields and the significant contribution to the war effort by Grenoble was recognized by the creation of the Grenoble Institute of Electrochemistry and Electrometallurgy in 1921. The aluminum production industry still in existence in the region today is testament to the continued relevance of the institute as it celebrates 100 years of existence.



A visionary orchestra conductor

A number of academics and scientists arrived in Grenoble from 1940 seeking refuge from the Second World War. Amongst the arrivals was Louis Néel, a physicist whose research transformed the understanding of magnetism. Beyond the undeniable excellence of his work, recognized by the award of the Nobel Prize in Physics in 1970, Néel was to have an immense and profound impact on Grenoble. *"Without Néel, Grenoble would not be as we know it now,"* explains Aurélien Masseboeuf, research scientist at Spintec, a laboratory jointly supported by the French National Centre for Scientific Research

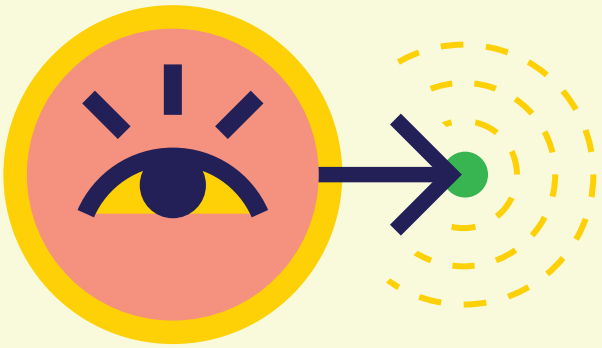
(CNRS), the French Alternative Energies and Atomic Energy Commission (CEA) and the Université Grenoble Alpes (UGA).

Indeed, it was under the leadership of Néel that a CNRS laboratory was created in Grenoble in 1946, followed in 1956 by the establishment of the Grenoble Nuclear Research Centre (CENG), now known as CEA-Grenoble. The installation of these structures in Grenoble was remarkable not only because the direction of both was undertaken by Néel, but that they were the first CNRS laboratory and CEA facility to be established outside of Paris.

Under the guidance of Néel, Grenoble was becoming an important university and experimental research center and the academic and industrial standing of the town made it an attractive and credible location for the installation of the Institut Laue-Langevin (ILL). This world-leading neutron research facility was originally an ambitious OECD project, however, when the idea was abandoned, France decided to continue alone, drawing on the considerable reactor expertise and experience centralized within the CEA. The huge scientific potential of the project was immediately recognized by Germany and the project was launched as a Franco-German bilateral endeavor in 1965. *"One should not forget the powerful political significance of the ILL, the bilateral agreement was signed only 20 years after the end of World War II, at a time when scientific collaboration was basically non-existent. The ILL really demonstrates the potential of science as a diplomatic tool,"* explains Helmut Schober, director of the ILL.

The ILL is a resolutely European project: the UK joined France and Germany as an associate in 1973 and from the 1980's an increasing number of countries joined as scientific members, such that 90% of neutron users in Europe are represented at the ILL today. This major European institute brought an international dimension to Grenoble and paved the way for the establishment of the European Molecular Biology Laboratory's site in France (EMBL Grenoble) in 1975, the Institute for Millimetric Radio Astronomy (IRAM) in 1979 and the European Synchrotron (ESRF) in 1988. *"There are 7 European intergovernmental institutes in France, it is remarkable that 4 of them are in Grenoble,"* remarks Schober.

The establishment of these institutes in Grenoble created an unfulfillable demand for scientists, engineers and technicians. As in the 1890's, new courses, departments and schools were



established, this time in the fields of radio engineering, nuclear engineering, information technology and applied mathematics. The objective was to train the engineers required not only today but also tomorrow. The Grenoble Engineering school in Applied mathematics and Computer Science (Grenoble INP – Ensimag, UGA) was one such precursor. *"Grenoble INP – Ensimag was created in 1960, at a time when there were only 10 or 20 computers on the planet and the term computer science had only just been created. We asked ourselves whether there would be enough work for all these engineers with so few computers!"* explains Benech.

In parallel to the development of the Presqu'île, the creation of a second and quite distinct campus was taking place on the eastern side of Grenoble. The university of Grenoble, now known as the UGA, has a long history that dates back to 1339 and its development over the years resulted in buildings scattered around Grenoble. The university campus was created with the purpose of bringing these different buildings together, while allowing for the necessary expansion of the university, on one campus dedicated to higher education and research. *"The two campuses developed in parallel and though there exists a very close relationship between the structures and individuals of the two sites, the mission of each site is very different. The majority of students in Grenoble and PhDs carried out in Grenoble are still based on the university campus,"* explains René Favier, historian at the UGA.

"Without Néel, Grenoble would not be as we know it now"

What linked these many different structures together at the time was Néel. He was responsible for the merging of six engineering schools in 1970 to form what is known today as Grenoble INP – UGA. He held the first presidency of that institute concurrently with a professorship at the UGA as well as the directorship of both CEA-Grenoble and the CNRS Magnetism

laboratory (now combined with a number of other laboratories into the Institut Néel). *"He was an exceptional character, equivalent to an orchestra conductor in his ability to unify Grenoble,"* explains Masseboeuf. *"But he was also immensely humble, he considered that his work on antiferromagnetism and ferrimagnetism, for which he was awarded a Nobel prize, was beautiful but without an application. Hard disks would not exist today without his work, he was simply too modest to imagine an application. Similarly, he couldn't accept that his work alone justified the prize, he believed that it was also in recognition of his role in the transformation of Grenoble."*

The decision to build the ESRF in Grenoble, and not in Strasbourg as also initially considered, is linked to this transformation of Grenoble and its establishment as a world-class center of advanced scientific research. *"The ESRF is in Grenoble because of the ecosystem,"* explains Francesco Sette, director general of the ESRF. *"Strasbourg is a large, international city, that is home to the European parliament and excels in many activities, but the ecosystem of Grenoble made the difference."* From the beginning of construction, the advantages of the Grenoble ecosystem were vital. *"The ESRF was the world's first third generation synchrotron. It was an incredibly challenging job and skepticism was very high that it would be possible to build,"* explains Sette. *"The presence of ILL and CENG in Grenoble meant that excellent engineers and expert companies were available to rapidly find solutions and successfully achieve the project, on time and within budget."*

A successful prototype

It was around this time that CEA-Grenoble profoundly changed. Historically, the center had concentrated on nuclear energy, with a limited number of opportunities for scientific or technological collaboration with the other institutes and facilities based in Grenoble. However, an ever greater proportion of work began to focus on the development of new and innovative high technology activities related to electronics, energy and health. This change led to a number of realizations, firstly, the evident necessity to increase collaboration, both with academic research and industry and secondly, the critical importance of the transfer and commercialization of technology.

Grenoble Ecole de Management (GEM) was originally created in 1984 to meet the needs of regional actors by uniting business, an international perspective and advanced technologies. The first French business school to include technology management within the curriculum, the unique expertise of GEM in the management of technology and innovation is now internationally recognized. Within CEA, innovation marketing is specifically addressed by the marketing research unit (BEM), created in 1993, the expertise of the unit includes the analysis of competition and the potential applications of a technology. Technology transfer in Grenoble is further supported by incubators whose objective is to help new technology start-ups succeed; Grenoble Alpes Incubation (Grain) was created in 1999 and has since become SATT Linksium Grenoble.

The MINATEC concept was a continuation of this dynamic, electronics based researchers, students and industry professionals were brought together on a single campus furnished with state-of-the-art equipment with the objective of encouraging collaboration and accelerating innovation. Buildings were constructed and attributed to higher education and academic research (CNRS, Grenoble INP, UGA, CEA), while applied research is carried out at CEA-Leti and MINATEC Entreprises is dedicated to the support of new technology companies. *"MINATEC formalized the collaboration between higher education, research and industry that has always existed in Grenoble,"* explains Jean-Charles Guibert, director of MINATEC. *"It is now an internationally recognized innovation campus but when MINATEC was launched in 2002, it was one of the first innovation campuses created in Europe."* MINATEC also plays an important role as a

central meeting point within Grenoble, welcoming visitors and international delegations while hosting hundreds of discussions, conferences and seminars each year.

The success of MINATEC greatly increased the international visibility of Grenoble and motivated a number of multinational corporations to develop R&D centers in the area, including Orange and bioMérieux. It also inspired Grenoble to look at what existed in other countries. *"Big, multi-thematic innovation campuses that unite higher education, research and industry were developing around the world, such as MIT in the US or Fusionopolis in Singapore,"* explains Guibert. *"The vision in Grenoble was to widen the MINATEC model to include all structures and institutes on both the Presqu'île and university campus and bring everybody together into the same project. MINATEC, as a highly successful monothematic innovation campus, served as the proof of concept."*

The creation of GIANT in 2009 marked the achievement of this vision. The 8 partner alliance enabled a critical mass of knowledge, competence, unique research infrastructure and high-level scientific and technological components to aggregate behind the commonly defined ambition to respond to major societal challenges in health, information and energy. Examples of recent progress in each of these domains can be found within this magazine, from the development of green hydrogen technology (page 8-9) and autonomous micro-generators (page 10-11) to the development of transformational X-ray tomography (page 22-23) and a potential first neuroprotective treatment for Huntington's disease (page 30-31). *"GIANT creates opportunities and promotes collaborative societal research in Grenoble: the ILL can work with the CEA on fuel cells and batteries and this pandemic has really demonstrated the huge possibilities for biology research in Grenoble,"* explains Schober. *"It also provides visibility on a different level in that the ILL is very well known in the scientific world, but GIANT improves the connection with the general public and with industry and that's very valuable."* The visibility provided by GIANT is similarly recognized by the CEA, Guibert explains that *"GIANT is not just about a change of name, or better advertising, GIANT is about being visible and attractive internationally, and that brings in high caliber scientists and industry, as well as funding, all of which enable further progress and development."*

Though GIANT may appear to represent the logical continuation of MINATEC, Sylvie Blanco, director of Innovation at GEM, considers that this is singular to Grenoble. *"People who have spent time living in the Grenoble ecosystem have an innate comprehension of technology-based progress. Disruption is in their DNA, they don't even realize it! So yes, it seems like a natural progression, it seems evident and this creates an instinctive adhesion to the next vision."*

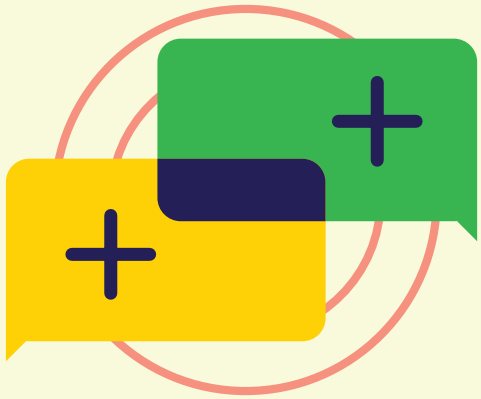
An ability to communicate, collaborate and innovate together

MINATEC originated from discussions and agreements that took place around a table, between people who knew each other well and trusted each other. *"The scientific project had been decided, buildings were constructed and we had already moved in before any convention or contract was signed. The prefect was certainly surprised when he discovered that!"* recalls Benech. *"That doesn't mean that negotiations were easy, but we speak to each other and when we give our word, we stick to it."*

This ability to communicate is key to the success of GIANT and a particularity of the Grenoble ecosystem. Blanco recalls that *"a representative from an innovation ecosystem project in San Diego came to visit Grenoble and I organized for him to meet a number of different people from GIANT. He couldn't believe it! He found incredible the number of meetings with highly placed people that I'd managed to organize, and not only that, but how generously and freely those people spoke. That's one of our strengths, we know each other well and we speak openly and transparently."*

The power of communication is at the heart of the recent formalization of the collaboration between EMBL Grenoble and the Institute for Advanced Biosciences (IAB), a research center jointly supported by the CNRS, UGA and the French National Institute of Health and Medical Research (Inserm). Exploration of the huge potential for collaboration between the two institutes will be achieved by increasing the number of joint scientific meetings and seminars organized in shared research areas, such as

the Grenoble Epigenetics Club, or the recently created Grenoble Host-Pathogen Interactions Club. *"You can't underestimate the potential value of bringing people together,"* explains Marco Marcia, group leader at EMBL Grenoble. *"By listening to talks and exchanging about work, you increase the probability that matches are made between research interests and ideas are found on how to share infrastructure or how to exploit the complementary scientific approaches and techniques of the two institutes. It may seem counter-intuitive, but if these local meetings don't happen, you're more likely to collaborate with a scientist that you meet at an event abroad."*



"You can't underestimate the potential value of bringing people together"

Arinax, based in Grenoble, is the company that sells by far the most synchrotron instruments in the world and the majority of those instruments were invented and developed by the instrumentation team at EMBL Grenoble in collaboration with the ESRF. *"Everything that was achieved was due to the desire of the ESRF scientists and EMBL instrumentation team to work together,"* explains Florent Cipriani, head of the Instrumentation Team at EMBL Grenoble until his recent retirement. *"The instruments were developed in response to the needs of scientists,"* explains Cipriani. *"For example, the first big project was with Stephen Cusack (head of EMBL Grenoble) at the ESRF: he had very small, micro-crystals and an enormous amount of time was wasted trying to put the crystals in the very small synchrotron beam. That's why the first microdiffractometer was developed."* Many scientists were interested in the developed instrument and realizing the potential to commercialize it, Cipriani contacted Maatel, a local company that was capable of producing it, which later led to the creation of Arinax. *"At the time, technology transfer was pioneering at EMBL,"* recalls Cipriani. *"Now with EMBLEM, the technology and knowledge transfer partner of the EMBL, it's an integrated aspect of research, like at all laboratories, to ensure the better transfer of research results to industry."*

The results of this technology transfer and the resultant creation of industry are visible throughout Grenoble today. Néel was a great believer in the importance of connecting industry with academic research and was intimately involved in the creation of the company SAMES in 1946, which remains present locally within the multinational SAMES-Kremlin. A more modern example is Soitec, created as a start-up in 1992 by two engineers from CEA-Grenoble, the company is now a world-leader in the design and manufacture of innovative semiconductor materials.

A bright future

The motivation of Néel behind the development of Grenoble was to *"measure things that nobody has measured before"*. That objective is as relevant today with the recent completion of the Extremely Brilliant Source (EBS) at the ESRF, the world's most brilliant light source. *"With the EBS, you can zoom from the sub-cellular scale all the way to the macroscopic scale - that has never been done before and it will enable spectacular results to be obtained in life sciences and medicine,"* explains Sette. The first of these spectacular results have enabled the clogged micro vascularization of COVID-19 infected lungs to be visualized, a tremendous contribution that supports the clinical observation that the administration of anti-coagulants improves the ability of patients to breathe. The unique coherence of the X-ray beam is also being used to image the neuronal network. *"The resolution is being pushed to such a limit that synaptic connections between the neuron cells should be visible, something that has never been seen before and that hopefully will lead to a new understanding of neuronal architectures!"* explains Sette.

Grenoble is also well-placed for understanding things that have never been understood before. The collaboration between EMBL Grenoble and IAB creates not only a bridge from the Presqu'île

to the university-hospital campus, bringing Grenoble one step closer to becoming a single scientific community but also from the nano to the cellular scale. *"The expertise of EMBL Grenoble is in structural biology, which involves zooming in at the atomic level to see how molecules work mechanistically,"* explains Marcia. *"Although enormous progress has been made in the last 50 years, there is a need now in structural biology to move to a broader scale because molecules work in the context of a cell or tissue. For example, if one protein is not working properly, it can translate into a pathology."* The collaboration with IAB, who use their expertise at the cellular tissue level to study the medical relevance of processes, will enable structural biology knowledge to be translated into information relevant to medicine and human well-being and reinforce the position of Grenoble as a leading center for research in life science.

"GIANT is located in an environment that is extremely exciting and stimulating"

The bright future of Grenoble extends beyond spectacular science and incredible discoveries. GIANT is also a major urban and architectural redevelopment project, with the objective to provide a quality living environment in the Presqu'île through the sustainable development of residential housing, shops and services, accompanied by ambitious environmental targets in alignment with Grenoble's title of European Green Capital 2022. *"The town of Grenoble and everything that it has to offer has played an important role in making ESRF one of the most attractive and successful synchrotron sources in the world,"* explains Sette. *"It is located in an environment that is extremely exciting and stimulating, of course professionally in terms of science and technology, but also in terms of culture and leisure. Grenoble is an attractive town, in close proximity to nature and with an important and increasing environmental awareness. The development of the GIANT campus has made the local area far more urban and attractive, while the extension of the tram line has created a direct link between the Presqu'île, Grenoble downtown and the university campus."* This perspective is shared by Schober who considers that *"Grenoble has it all! Affordable housing, international schools, a university whose standing has continuously improved, a fantastic landscape - it all helps to attract staff as well as the 1500 scientists who come to the ILL to carry out experiments every year."*

Grenoble is one of the most dynamic industrial areas in France and the development of the Presqu'île supports the increasing population. Indeed, roughly 1000 engineering graduates (approximately one third of Grenoble INP – UGA graduates) remain in Grenoble Alpes each year. This constant irrigation of the GIANT ecosystem maintains the industrial activity and has led to the on-site presence of companies such as Credit Agricole and Schneider Electric and the creation of factories and offices of a number of major companies in Grenoble-Alpes, such as Alstom, Thales and STMicroelectronics. *"The development of STMicroelectronics is particularly linked to the university. It is now one of the leading employers in the region but it wouldn't have happened without the university campus,"* explains Favier.

World-class higher education, cutting-edge research and innovative industry, combined with the desire to communicate and collaborate and the development of a vast and collaborative infrastructure of state-of-the-art facilities and technology have created a bright future for Grenoble. *"The field of potential applications within GIANT is enormous and that makes Grenoble very well positioned going into the future,"* explains Blanco. Indeed, Masseboeuf considers that *"the huge diversification that we see today is the heritage of Néel, it comes from having all this different knowledge, instruments and structures in one location."* The bright future of Grenoble will surely create a brighter future for society, *"every day there are new challenges, new expectations from society, new industrial needs,"* explains Benech. *"GIANT is a story without an end: we mustn't think that the last page has been turned, the book can be closed and the story is over. No! We need to keep developing the dynamic, we need to keep writing this story!"*

From fossils to the future of **biomedical imaging**

The pandemic created an urgent need for improved imaging ability to enable physicians to understand the damage caused to human organs by COVID-19. When the request was transferred to all those involved in imaging at the European Synchrotron (ESRF), it was – perhaps improbably – a paleontologist who responded positively. Paul Tafforeau, paleontologist and beamline scientist at the ESRF, is now working to adapt imaging techniques originally developed to examine fossils into a transformational X-ray tomography technology with funding from a $1 million Chan Zuckerberg Initiative (CZI) grant obtained jointly with UCL (University College London).

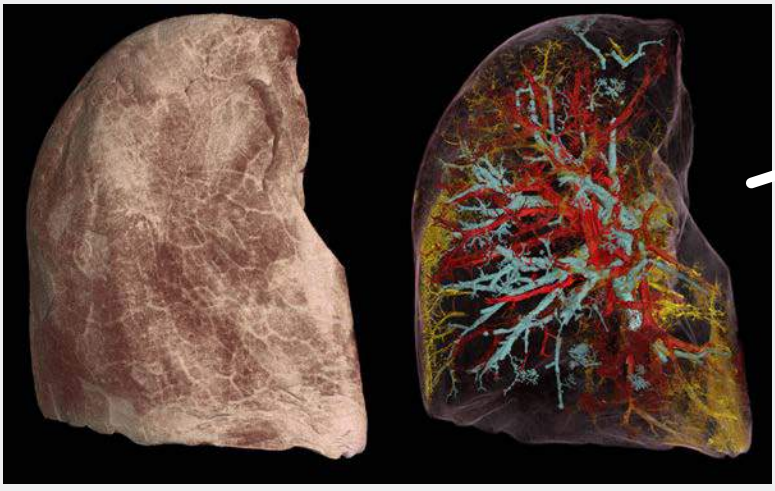
#EUROPEAN LARGE SCALE FACILITIES #HEALTH

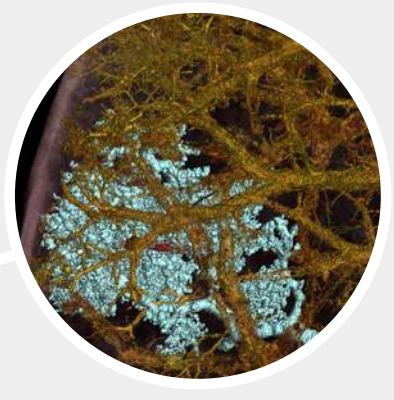
Paul Tafforeau
Scientist at the ESRF

Paleontology and biomedical imaging may not immediately appear to be the most complementary areas of research but in fact a number of correlations exist. *"As a paleo-anthropologist I have a solid training in general biology,"* explains Tafforeau. *"I've even worked on humans before, it's just that they were always fossils until now!"*

The key connection though is that paleontology regularly involves the imaging of large objects with the necessity to zoom in to see small details. This experience, combined with the unprecedented brilliance and coherence of the X-ray beams provided by the ESRF's recent Extremely Brilliant Source (EBS) upgrade, is what made Tafforeau realize that techniques developed for imaging fossils could be adapted to achieve the imaging of complete human organs with unparalleled precision.

The beamline BM05, usually dedicated to instrumentation, industrial experiments and paleontology research and the only line presently capable of accommodating entire human organs, was thus partially redirected to biomedical research. The first experiments carried out demonstrated the feasibility of the technique to image whole human organs at a resolution of 25 microns with the ability to zoom into local areas with a resolution approaching 1 micron. The unprecedented detail obtained enabled the complex vascular system of the lung, down to the smallest capillaries involved in the alveolar gas exchange, to be assessed both non-destructively and in 3D, revealing the damage caused by COVID-19 to human lungs.





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ESRF-EBS images a whole lung lobe of a 54 year-old male COVID-19 victim. It can be viewed in its entirety at 25µm voxel resolution, or zoomed in at up to 2µm resolution – 100 times better than the resolution of clinical CT imagery. The detail is such that even individual red blood cells can be resolved.

Paul Tafforeau, ESRF scientist, preparing a whole lobe of lung and brain from a control patient for imaging using new deep imaging technology with micron resolution at the European Synchrotron.

Work is now underway to transform these promising preliminary results into a biomedical imaging breakthrough through the development of new X-ray tomography techniques called Hierarchical Phase-Contrast Tomography (HiP-CT). *"We achieved a pixel size of 2.5 microns for COVID-infected lungs. Now, the objective is to go below 1 micron to visualize structures at the cellular level,"* explains Tafforeau. *"That requires a bit of work though because each time you increase the resolution by a factor of two, the X-ray dose increases by a factor of 8. The current dose is extremely high and performing too many high resolution scans leads to the sample becoming damaged."*

The project, 'Anatomical to cellular synchrotron imaging of the whole human body', led by Peter Lee and Rebecca Shipley at UCL, together with Paul Tafforeau at the ESRF, brings together an international multidisciplinary team of X-ray imaging researchers, mathematicians, biologists and physicians from across Europe. The potential impact of the imaging technology was recognized by the award of a $1 million CZI grant. The Chan Zuckerberg Initiative was founded in December 2015 by Dr. Priscilla Chan, a pediatrician, and her husband Mark Zuckerberg, founder of Facebook. CZI leverages technology and collaboration to support basic biomedical research.

Demonstration of the feasibility of sub-micron resolution imaging of entire organs within the 2.5 year duration of this first phase of the project could open the possibility of CZI funding for a second phase. *"The second stage of the project would change everything,"* explains Tafforeau. *"It would enable us to progress from scanning entire organs to imaging whole human corpses, meaning that not only can individual organs anywhere in the body be studied non-destructively in 3D, but also the relationship between organs."* Tafforeau is confident that the planned results will be achieved, *"We know how to do it, we are developing the necessary technology and we have 2.5 years to put everything in place and show that it works. We've also made enormous progress since we submitted the project."*

Both stages of the project will be greatly advanced by the availability of a new beamline, BM18, which is currently under construction and due to start mid 2022. *"BM18 is similar to BM05 but much bigger and more powerful and sensitive so we can do everything better. I'd imagined we could use it for more difficult paleontology research, but in addition to large human fossils, we'll be using it to scan whole human corpses,"* explains Tafforeau. The planned research has certainly changed for BM05, BM18 and Tafforeau himself. *"The current context has relativized a number of things,"* reflects Tafforeau. *"I've decided to stop my paleontology research for at least the duration of the project because I consider that I can contribute more by working on this biomedical topic than by scanning fossils myself. Paleontology remains an important topic at the ESRF though and other experts in the field will continue the work, fully benefitting from both the BM18 beamline and the techniques we're developing for biomedical imaging."*

GIANT EFFECT

The imaging techniques were developed from experiments carried out on control organs from bodies donated to science by individuals not infected with COVID-19, provided in the framework of a collaboration between the ESRF and the French Alps Anatomy Laboratory (LADAF), a joint Université Grenoble Alpes (UGA) and Grenoble-Alpes University Hospital (CHU-GA) structure.

Summer in Grenoble: hot, hotter, hottest

The Grenoble Ecole de Management (GEM) research panel was created to study current issues that are local to the Grenoble Alpes Metropole. The initiative, which is unique in France, enables researchers at GEM to identify and promote solutions that take into account the particularities of Grenoble. The most recent panel study focused on heat waves in Grenoble and revealed significant heterogeneity in how their effects are distributed.

#INNOVATION MANAGEMENT #SOCIETY

Corinne Faure
Professor of Marketing at GEM

"Our objective is to research topics that particularly affect people in the Metropole," explains Corinne Faure, Professor of Marketing at GEM. *"Grenoble has a reputation as being one of the hottest towns in France during the summer so this is certainly a problem that really affects people."* The study, carried out in September 2020, aimed to understand how people view, live with and manage the intense heat of the summer. The questions addressed solutions linked to technology, such as ventilation and air-conditioning which through their energy consumption further contribute to climate change, as well as solutions based on behavioral change.

The study also considered the particular location of Grenoble, not only the unique geographical formation that encloses the town and contributes to the high temperatures, but also the potential respite that is offered by the close mountain proximity. *"The research panel is supported by the Chair for Inclusive Sustainability: Territorial Ecosystems in Transition and one of their partners is Cluster Montagne, so we were able to integrate questions on how people view the mountains during periods of intense heat, as well as propose different suggestions on how the potential of the mountains could be better exploited, for example would people be interested in the possibility of remote working there?"* explains Faure.

Scientists predict that summers will become hotter across Europe in the years ahead and it appears that the majority of the local population surveyed have heard the message: 80% believe that summers will get hotter, with higher temperatures and longer periods of drought. *"We read a lot about the prevalence of climate skepticism and denial so we weren't sure of what response we would get,"* says Faure, *"But it appears that people are certainly realistic, or pessimistic depending on your opinion, about the future of summers in Grenoble."*

The results of the study highlighted the significant difference between urban and rural areas. Concrete and asphalt absorb heat during the day and then release it at night, keeping urban areas hotter than surrounding rural areas. Unsurprisingly, therefore, the survey found widespread support for increased vegetation and trees. Indeed, half of those surveyed living in the city of Grenoble considered that their home became unbearably hot during a heat wave, while the number was only 17% for those living in the countryside or at a slightly higher altitude. Though incentives aimed at encouraging home renovations that improve energy efficiency exist both nationally and locally, the study found that only 7% of respondents consider such an option. *"The impression that we got, is that people are more inclined at the moment to escape the situation, by moving to a better*

insulated home or to somewhere cooler in the Metropole, rather than face the situation by investing in insulation upgrades," explains Faure.

The second major difference that the study highlighted was the varying impact of the intense heat according to financial situation. While half of those surveyed considered that the last summer was particularly difficult, that number rose to 71% for people in a precarious financial situation. Similarly, the percentage of unbearably hot homes in the Metropole increased from one-third to two-thirds for those with a limited income. *"Though the heat problem is concentrated in the center of town, those who are financially comfortable can escape for weekends or holidays, but those living in the most inadequately insulated apartments can't afford to leave,"* explains Faure. The heterogeneity was further demonstrated by the answers provided to a question on the most bothersome aspect of the heat. *"We found that wasps and mosquitoes only register as a major bother for people who don't really suffer from the heat,"* explains Faure. *"For those with limited resources, the problems are notably different, for example not being able to leave the windows open at night because it's too noisy or dangerous."*

The insights obtained will direct the development of a follow-up study, planned for this summer, that will focus on the different choices and solutions possible, as well as on the trade-offs that people make between different solutions. *"The intense summer heat of Grenoble is a subject that remains relevant!"* remarks Faure. The panel will then move on to studies on waste management, addressing in particular the numerous local initiatives to reduce or reuse packaging, with a particular analysis on whether people are more willing to adopt something that has been developed locally.

GIANT EFFECT

Representatives from Grenoble Alpes Metropole were invited to participate in the development phase of the panel questionnaire to ensure that the questions were pertinent and that the results are valuable for the Metropole.

Think What **Matters**

As a climate and environmental emergency was declared by the European parliament at the end of 2019, a new collective dedicated to the ecological transition was created in Grenoble. Think What Matters (TWM) distinguishes itself in a number of ways from the other collectives that exist, most importantly by replacing the apportioning of blame with the proposition of collectively developed solutions. After barely more than a year of existence, TWM has achieved encouraging results and concrete progress.

#CLIMATE #ENGINEERING

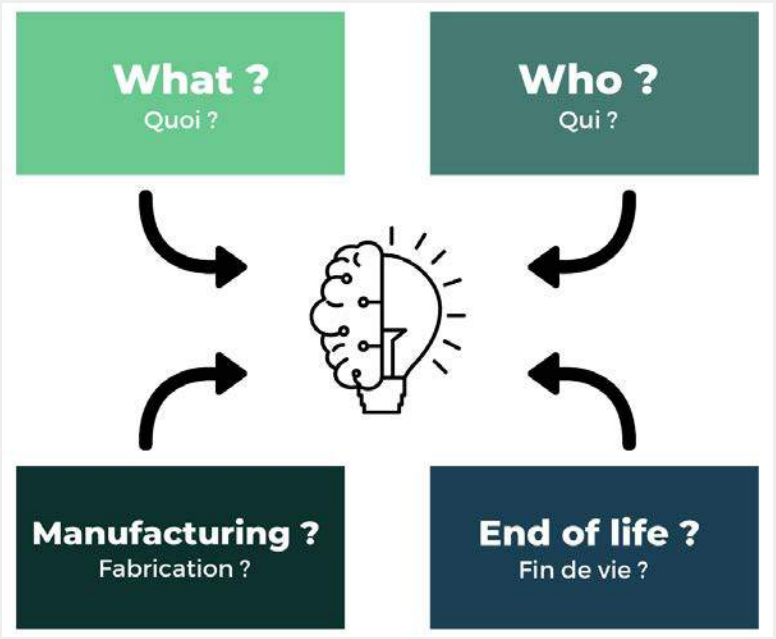
David Martin-Chevalier
Student at Grenoble INP - UGA and co-founder of TWM

Juliette Cassagne
Student at Grenoble INP - UGA and co-founder of TWM

The collective was inspired from the realization that although engineering students are provided with an excellent level of knowledge (savoir-faire), how this knowledge should be used (savoir-être) is less addressed. *"As engineers, we will create and develop new products, so it is crucial that knowledge about social and climate issues forms an integral part of the school's educational model, so that it can be incorporated into the design of these future products,"* reasons David Martin-Chevalier, student at Grenoble INP – UGA (Graduate Schools of Engineering and Management, Université Grenoble Alpes) and co-founder of the collective TWM. In order to encourage schools to better address these subjects, the collective TWM was created. The idea was to bring students together, first, to study the challenges of the ecological transition and the potential solutions for a more sustainable society and then, through the sharing of ideas, collectively develop new solutions. *"We shared the knowledge of the collective through conferences and some teachers from the school contacted us to start working on adapting the pedagogy,"* says Martin-Chevalier.

Despite the progress achieved, the collective is adamant that simply ensuring that engineering students are completely informed of all the relevant climate issues will not suffice. *"Eco-design alone is not the solution, as the ecological transition concerns everyone, we need everybody included and working together,"* explains Juliette Cassagne, student at Grenoble INP - UGA and co-founder of TWM. *"Innovation must be co-constructed for it to become a sustainable and responsible aspect of our society."* TWM has therefore made diversity a key characteristic of the collective and engineering students from a number of different specialties (materials, electronics, renewable energy) are joined by political science, international law and behavioral psychology students. *"The multidisciplinarity of our collective is a really important aspect because each profile contributes*

← Members of the collective Think What Matters



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2Q2F method developed by the collective to help engineers and innovation managers evaluate whether a project has meaning with respect to the ecological transition.

a unique set of skills and knowledge and that enables us to explore the subject much more easily and deeply," observes Cassagne.

Though the Fridays For Future climate movement may give the impression that all young people are convinced of the importance and urgency of the transition, TWM has found that the reality is somewhat different. *"There are many students who don't feel concerned by the ecological transition. By making the transition as understandable as possible and demonstrating that working on it is simple and can be done at every level, we hope to include as many people as possible in the movement,"* explains Martin-Chevalier. *"But even people who understand the climate urgency can become overwhelmed by the enormity of the challenge. The level of globalization makes everything seem so huge and complex that a certain level of fatalism and disillusionment can appear. We are determined to combat that."*

In the face of globalization, the collective believes in the power of local actions: working locally to make small changes that can then grow and spread, eventually inspiring a larger movement. *"At the moment, we are working locally in Grenoble but we hope to develop more widely through our conferences on different themes linked to the transition, our interviews with politicians and people from industry and the sustainable innovation method we've developed,"* explains Martin-Chevalier.

One solution developed by the collective is a new toolkit to help engineers and innovation managers evaluate whether a project has meaning with respect to the ecological transition. *"The 2Q2F method that we propose is based on four main questions: what, who, manufacture and end of life. The idea is to first question the context of the product – what are the needs it meets and how can it be made accessible. Then the manufacturing must be considered, including aspects such as the materials and processes that will be used – are they new or recycled, can they be sourced locally, etc.? Finally, but equally important, how much of the product can be repaired, replaced and recycled?"* explains Martin-Chevalier. The method will soon be evaluated using a low technology, portable LED lamp developed by Schenider Electric for emerging countries. *"The Mobiya lamp is a socially interesting model and the opportunity to question the engineers and designers involved in its development will allow us to test the method, but also to ask their advice and continuously improve the toolbox,"* explains Estelle Cotton, the member of TWM in charge of the 2Q2F method.

GIANT EFFECT

The collective Think What Matters brings together students from Grenoble INP, UGA, Sciences-Po Grenoble, INSA-Lyon and the Université de Poitiers.

Magnetism and neutrons: a powerful combination

Louis Néel was awarded a Nobel Prize in Physics for his research into antiferromagnetism and ferrimagnetism. Though leading theorists at the time refused to accept his work, it was experimentally proven to be correct through the use of neutrons. The legacy of Néel in Grenoble today includes not only magnetism expertise but also the Institut Laue-Langevin (ILL) – the world's leading neutron source. This powerful combination has recently enabled the complex magnetic behavior of a well-established technological material – yttrium iron garnet (YIG) – to be fully revealed for the first time.

#EUROPEAN LARGE SCALE FACILITIES #MATERIAL

Timothy Ziman,
Theory College,
Institut Laue Langevin

YIG is magnetic due to the presence of charged iron atoms that are caged within two structurally different types of interlocking crystal subunits. The magnetic moments of the iron atoms in each type of subunit collectively align but in opposite directions. *"Because the two subunit types exist in a 2:3 ratio, there are more moments pointing up than down and that creates an overall net magnetization called ferrimagnetism,"* explains Timothy Ziman, research director at the French National Centre for Scientific Research (CNRS). Each collective disturbance of the aligned magnetic moments (spins) in their lowest quantum energy state is referred to as a magnetic 'quantum wave' or magnon. Due to the spin of magnons, the application of a magnetic field causes these magnons to slowly 'precess' like a spinning top. Theory has furthermore indicated that the magnons propagating through a structurally complex ferrimagnet like YIG split into two branches with opposite polarizations and different energies.

"Neutrons provide valuable insights into many different areas but magnetism is where they are really dominant," explains Ziman. The intrinsic spin of neutrons provides them with the unique ability to directly measure magnetism with nanometer precision. Nevertheless, magnon polarization measurements are recognized as being among the most difficult neutron experiments to carry out. Though the experiment was attempted at Oak Ridge National Laboratory (ORNL) in the United States, it has so far only successfully been carried out at the ILL. *"The ILL is not only the most powerful steady state source of neutrons in the world but the instruments available enable experiments to be carried out that can't be done anywhere else in the world,"* explains Ziman. *"The instrument that was used for this experiment, IN20, is an outstanding instrument and people come from all over the world to use it."* The difficulty of the research means that 1-2 weeks usage of the instrument may be required, making the experiments expensive. But as Ziman explains, *"The exploration of some parts of science is just more difficult and expensive than others; seeing a black hole is more difficult than looking at the sun but nobody says we should stop studying astrophysics."*

Though the experiment was successfully carried out in Grenoble, the achievement was made possible by a truly global effort that united researchers from France, Japan, the United Kingdom, the United States and the Netherlands. *"This work would not have been possible without the contribution from each of the partners coupled with the tradition of collaborating together,"* explains Ziman. *"World class science depends on openness and collaboration and anything that hinders that is really a disaster for science."*

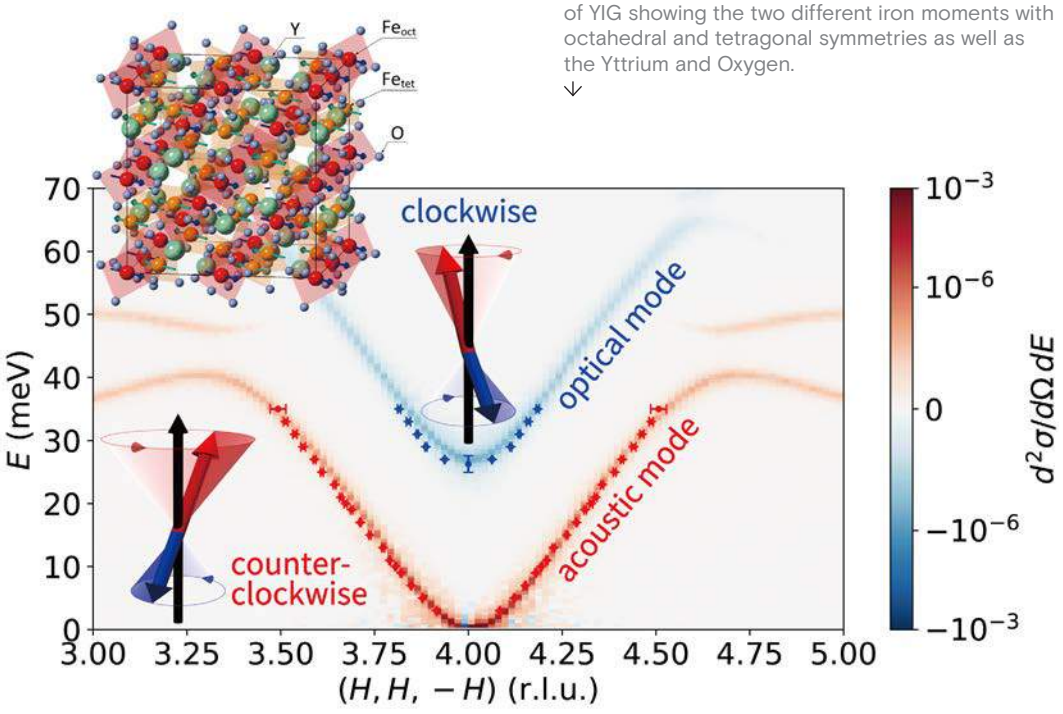
GIANT EFFECT

The close collaboration within GIANT is demonstrated by Timothy Ziman; CNRS research director at the Physics and Models in Condensed Media laboratory (LPMMC), which is jointly supported by the CNRS and the Université Grenoble Alpes (UGA), experimental validation of his work has been made possible by research carried out at the ILL.

Though the experiment validated the theory for the first time, it had already been widely accepted amongst theorists. The more surprising aspect of the experiment was the demonstration that the quantum properties persist at room temperature. *"It had been predicted theoretically but everybody was skeptical so it was a real surprise for both theorists and experimentalists,"* explains Ziman. The fact that these quantum effects exist at room temperature is very important for future potential applications, in particular spintronics.

The demand for increasingly fast and small devices is limited by the number of transistors that can fit on a chip. Though most current devices only utilize the charge of the electron, spintronics encode information using both the spin and charge, thereby enabling more to be done in the same space. With the potential to improve energy efficiency, processing speed and memory storage density, spintronics is key to the next generation of advanced digital devices. Continued development, however, is dependent on the identification of appropriate materials. YIG, one of the most widely used industrial ferrimagnets, represents a promising material for spintronics. The demonstration that quantum properties persist in YIG at room temperature increases that potential because, as Ziman observes, *"Nobody wants to operate their device at a temperature close to absolute zero (-273.15°C, -459.67°F)!"*

Experiments and theory show clearly the different polarizations - red for counter-clockwise rotation of the larger sub lattice moment, blue for clockwise - of the acoustic and optical modes with experimental points and calculations (shaded coloring). The insert illustrates the crystal structure of YIG showing the two different iron moments with octahedral and tetragonal symmetries as well as the Yttrium and Oxygen.



Hope for a first **neuroprotective treatment** for **Huntington's disease**

Huntington's disease (HD) is a devastating and incurable neurodegenerative condition that causes motor, cognitive and psychiatric disorders. While medications are available to help alleviate some of the symptoms, no treatment exists to prevent or slow the disease which is ultimately fatal. Research carried out at the Grenoble Institute of Neuroscience (GIN) provides hope for the development of what would be the very first neuroprotective treatment.

#FUNDAMENTAL RESEARCH #HEALTH

Frédéric Saudou
director of the Grenoble Institut Neurosciences (GIN), professor at the Université Grenoble Alpes (UGA) and practitioner at Grenoble-Alpes University Hospital (CHU-GA)

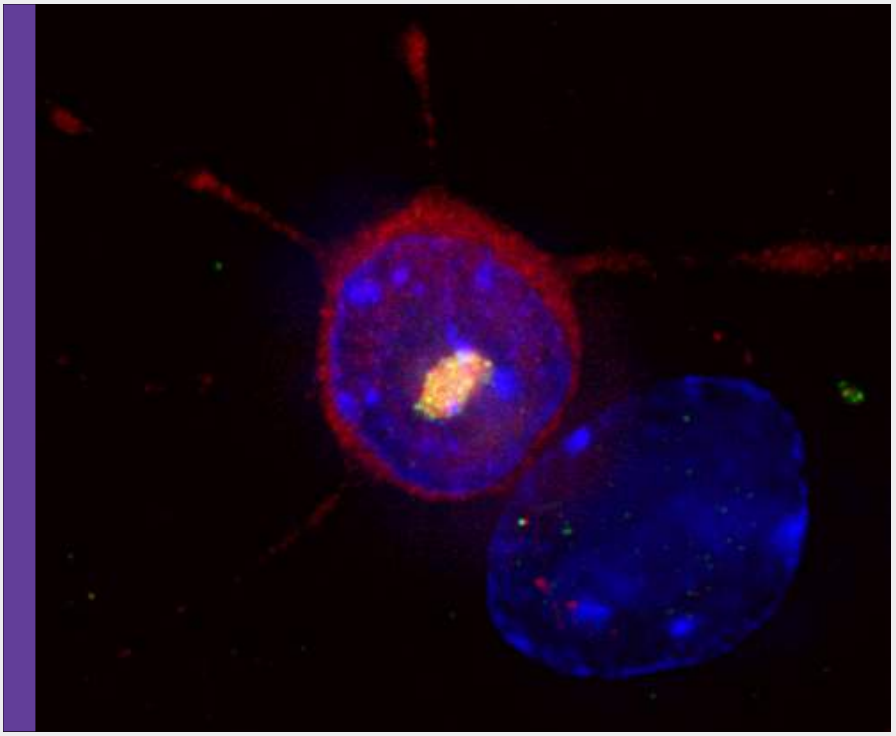
HD is caused by an inherited defect in the HTT gene that provides instructions for making a protein called huntingtin. The HTT gene contains a segment where the trinucleotide CAG is normally repeated 10 to 35 times, but people with HD have an increased number of repeats. As the defect is dominant, the child of an affected parent has a 50% risk of inheriting the defective version of the gene and thus developing the disease. Though HD is a relatively rare disorder, affecting 5-10 per 100,000 people in Europe, it was the first disease-associated gene to be mapped to a human chromosome, with the pathogenic mutation identified 10 years later in 1993.

"Huntington's disease is completely due to this genetic mutation in the HTT gene and if someone has the defective gene, it is practically certain that they will develop the disease," explains Frédéric Saudou, director of GIN, professor at the Université Grenoble Alpes (UGA) and practitioner at Grenoble-Alpes University Hospital (CHU-GA). *"That is an immense piece of knowledge that we don't have for other neurodegenerative diseases such as Alzheimer's or Parkinson's that affect far more people. Familial Alzheimer's disease is caused by a genetic mutation but it only accounts for about 5% of cases, the other 95% don't have the mutation and we do not know why they develop Alzheimer's."*

The identification of the mutation in the HTT gene finally provided a means to understand the cause of neuron death in neurodegenerative diseases. Research directed by Saudou at GIN has demonstrated that the cellular process palmitoylation contributes to the transport of brain-derived neurotrophic factor (BDNF) - a molecule that plays a central role in the development and survival of neurons.

The level of palmitoylation, and thus the level of transport of BDNF, is reduced in HD models and the work carried out at GIN has shown that this is due to an overactivation of the enzyme that inhibits palmitoylation. Remarkably, the researchers have not only managed to identify the source of the problem but also a potential solution. Their research, published in the March 2021 edition of Science Advances, demonstrates that the molecule ML348 is capable of blocking the overactivated enzyme. *"The notion of equilibrium is very important in neurodegenerative diseases and what we have managed to do here is find a molecule that enables the equilibrium in terms of palmitoylation to be reestablished which in turn reestablishes the transport of BDNF,"* explains Saudou.

Significant results were observed from the administration of the molecule to Huntington-affected mice. *"The symptoms were reversed in the mice that we treated, in comparison, the untreated mice continued to develop symptoms and their condition*



Huntington's disease (HD) is a rare and hereditary neurodegenerative condition. This image shows, within a brain striatal neuron, the presence of the mutant huntingtin protein (red) which is responsible for HD, that accumulates in the nucleus (blue), forming an aggregate composed of huntingtin and other proteins, including ubiquitin (yellow).

deteriorated," explains Saudou. *"In this case, we started treatment when the mice began to show symptoms. Now we want to evaluate the effectiveness of the treatment when it is started much later, when the symptoms are significant. We also want to investigate whether starting the treatment before the appearance of symptoms delays the onset of symptoms."*

Treatment before the appearance of symptoms is a unique possibility for HD, as the genetic defect in the HTT gene is entirely responsible for the disease, a blood sample can determine whether a person will develop the condition. *"This is a terrible aspect of Huntington's but it creates the opportunity to treat the disease much earlier,"* explains Saudou. *"This isn't possible for other neurodegenerative diseases like Alzheimer's or Parkinson's because, for the vast majority of cases, we currently have no way of knowing who will develop the disease."*

Research carried out by Sandrine Humbert, French National Institute of Health and Medical Research (Inserm) research director at GIN, demonstrating that neurodevelopmental effects due to HD are detectable in human embryos, has further convinced Saudou of the importance of treating the disease as early as possible. *"The symptoms begin right from the beginning, it's just that they're hidden for a long time. The brain is an incredible organ and it adapts to try and compensate for the reduced number of neurons or faulty connections, but little by little the level of dysfunction will increase and the symptoms become apparent. Treatment during this long phase of neuronal dysfunction before neuron death opens the potential to recuperate functions that have been lost to the disease,"* explains Saudou.

Support from the SATT Linksium, the incubator dedicated to technology transfer in Grenoble, will assist the preclinical validation of the molecule that is required before it can be administered to patients affected by HD. If the results achieved in the animal model can be successfully transferred to humans, the molecule would constitute the very first neuroprotective treatment for HD.

GIANT EFFECT

GIN brings together researchers from Inserm, UGA, CHU-GA, the French Alternative Energies and Atomic Energy Commission (CEA) and the French National Centre for Scientific Research (CNRS). Their research into neurodegenerative diseases is further supported by the collaborative network Grenoble Excellence in Neurodegeneration (GREEN) that includes the European Synchrotron (ESRF), the European Molecular Biology Laboratory's site in France (EMBL Grenoble), the Institute of Structural Biology (IBS) and the MINATEC campus.

People of GIANT

Sylvie BLANCO

Links technology to innovation, management and value creation across GIANT

Sylvie Blanco, Director of Innovation at Grenoble Ecole de Management (GEM) has been involved in the local ecosystem for over 25 years. Her roles have varied from student to researcher, entrepreneur, consultant and teacher and she is now the representative of GEM on the executive board of GIANT. She discusses here the different ways in which she has learned from and contributed to the ecosystem and the insights gained along the way.

Q How did your involvement with GIANT begin?

It started in 1993 at the CEA marketing research unit (BEM). I was a student at what is now known as Grenoble IAE – the Graduate School of Management at the Université Grenoble Alpes (UGA) – and it was at BEM that I carried out my final year project on the strategic monitoring of emerging innovations in the field of microsystems. BEM was a place that was really ahead of its time and I met a number of extraordinary people there whose desire to promote Grenoble made a deep impression on me. I enjoyed the job and the team I was working with so much that I ended up staying for 6 years, during which time I completed a PhD on a subject which is very close to my heart and extremely relevant today: the strategic anticipation of disruption from weak signals, i.e. early warning signs of change.

Q What other roles have you taken on within the ecosystem?

After finishing my PhD at BEM, I accepted the opportunity of managing the Grenoble office of Yole Développement that had just been created by one of the former heads of BEM, Jean-Christophe Eloy. It just so happened that my office was right in the middle of all the start-ups created from CEA (French Alternative Energies and Atomic Energy Commission) so I met a lot of people during this time. I was also, in parallel, teaching Management Information Systems at GEM so it was a busy period! In 1999, I was offered the role of managing a start-up project hosted within the new incubator Grain (Grenoble Alpes Incubation), on behalf of my former research team at the UGA. I worked there, discovering the world of valorization until I joined GEM full-time as a professor in 2001.

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Inauguration of GEM Labs
(January 2020)

Q How has your connection with GIANT evolved since joining GEM?

When I joined GEM, they straight away gave me responsibility for THE course most associated with GIANT - the Master in Technology Management and Innovation. They also very quickly realized my level of association with the local ecosystem. The Dean and Director of GEM at the time, Thierry Grange, was even more involved and played a big role in the dynamic to create GIANT. I worked very closely with him during this period and when he retired in 2012, I took on the role of representing GEM on the executive board of GIANT, on behalf of our new Dean and Director, Loïck Roche

Q How have your experiences formed your vision of GIANT?

I've met a lot of people involved in the Grenoble ecosystem, either through the master that I teach, my previous work at BEM or proximity to and direct involvement in a number start-ups and big collaborative projects like IRT Nanoelec. I've known some of these people now for nearly 30 years and that's one of GIANT's real strengths: people know each other well and that makes it much easier to talk, collaborate and work together. GIANT is unique and I think that the impressive environment in which it is located plays a part. There is a very real ability to anticipate in Grenoble, coupled with a research and experimentation mindset, and the surrounding mountains may be at the root of that: not only as the origin of extraordinary resources but by always blocking our view, we've been forced to develop this extra ability to see further, further and further ahead! Similarly, the extremes within which we live - the heatwaves in summer and the avalanches in winter – have contributed to the development of a strong resilience in Grenoble. I'm very positive about the future of GIANT which has reached a level of maturity, with the infrastructure, resources and people, that opens up an infinite field of opportunities, provided that the people and their relationships of trust and confidence are taken care of.

Higher Level Forum
(HLF 2020)
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GIANT

AT A GLANCE

40
COMPANIES
on-site

More than **7,000**
SCIENTIFIC PUBLICATIONS
per year

More than **10,000**
INDUSTRIAL JOBS

More than
10,000
RESEARCH JOBS

More than
10,000
STUDENTS

More than **700**
PATENTS filed per year

Annual direct and indirect
ECONOMIC IMPACT:
€4,1 BILLION

About **10,000**
INHABITANTS ON CAMPUS

More than **9,000**
INTERNATIONAL VISITORS

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