

Scientific Newsletter

SUMMER 2020

Watching Measles virus factories at work in liquid droplets

It has been demonstrated for several years that liquid-liquid phase separation, induced by weak interactions often involving intrinsically disordered proteins or RNA, provides a very effective means of spatially and temporally controlling cellular processes. The physicochemical properties of these microenvironments provide optimal conditions for enhancing specific molecular interactions, not only by protecting molecules from their environment, but also obviating the need to form membranes. The molecular basis for stabilizing these microenvironments remains poorly understood. IRIG researchers have characterized how these processes are used by measles virus proteins.

Many viruses form compartments in the cells they infect. In this study, researchers at our institute show that when measles virus nucleo-proteins (N) and phospho-proteins (P) are mixed *in vitro*, they form membraneless liquid organelles, like oil droplets in water. To understand this process, they use nuclear magnetic resonance (NMR) to identify weak interactions involving intrinsically disordered domains of N and P and show that one of these interactions are essential for phase separation. The researchers follow the modulation of N and P dynamics by fluorescence during droplet formation, and study the thermodynamics of this process by NMR.

They thus observe that when RNA is added to a suspension of droplets formed by MeV N and P proteins, it localizes to the droplets where it induces an *essential step* in the virus replication cycle: the assembly of viral nucleocapsids. They also measure that the rate at which this process takes place in these droplets is higher than in the dilute phase. As a result of this work, they are then able to rationalize why viruses form these droplets in infected cells, creating truly ephemeral and transient

factories, where they can synthesize nucleocapsids at high speed to ensure their replication, all in a favourable and protected environment.

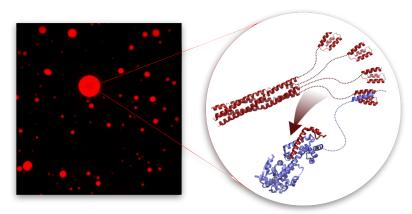
This study shows that viral replication could be reduced by inhibiting droplet formation, and that the formation of these phases could represent a novel pharmacological target for these viruses.

Intrinsically disordered proteins lack a stable threedimensional structure and are functional in their disordered state. Their high flexibility allows them to adapt easily to the surface of their partners and are able to fold up during interaction. This essential step is the assembly of N protomers into nucleocapsid particles that encapsulate RNA molecules.

REFERENCE

Guseva S, Milles S, Jensen MR, Salvi N, Kleman JP, Maurin D, Ruigrok RWH and Blackledge M. Measles virus nucleo- and phosphoproteins form liquid-like phase-separated compartments that promote nucleocapsid assembly. <u>Science Advances</u>, 2020

Contact: <u>Martin Blackledge</u> <u>IBS</u> Institut de Biologie Structurale



Fluorescence and nuclear magnetic resonance characterization of membraneless droplets formed by measles virus replication proteins.

MAP6, a neuronal protein in the lumen of microtubules

Microtubules, major components of the cytoskeleton, are 25 nm-wide hollow tubes composed of tubulin dimers. Microtubules are dynamic structures: they spontaneously alternate between phases of assembly and disassembly through gain and loss of tubulin dimers at their extremities. This unique property known as dynamic instability is crucial for cell plasticity and cellular events such as cell division and motility. In terminally differentiated cells such as neurons, dynamic microtubules co-exist with stable microtubules that exhibit a low turnover of tubulin and are resistant to external stresses like bending forces or load. Stable microtubules are crucial to maintain neuronal specific morphology and to accommodate morphological changes responsible for neuronal development and activity. In pathological conditions such as neurodegenerative diseases or brain injury, abnormal microtubule stability leads to an imbalance between dynamic and stable microtubule populations. To date, the molecular basis behind the stability of neuronal microtubules remain mysterious. Strikingly, protein densities called MIPs (Microtubule Inner Proteins) have been observed for a long time inside neuronal microtubules and proposed to confer neuronal microtubules their high stability. However, the molecular identity of these neuronal MIPs remained totally unknown until today.

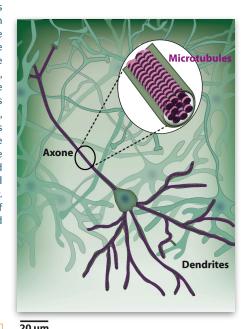
In that context, a collaborative work between Annie Andrieux's and Isabelle Arnal's teams recently allowed identifying MAP6 as the first neuronal MIP in mammals. MAP6 is a neuronal protein that stabilizes microtubules. MAP6-deficient mice suffer from severe cognitive and behavioral deficits related to schizophrenia, deficits due at least in part to an alteration in microtubule stability. The two teams have discovered that MAP6 can localize in the lumen of microtubules. MAP6 inside microtubules generates microtubules with remarkable properties including a helical growth and the formation of persistent holes in the lattice. What could be the role of such helical microtubules with persistent holes? One possibility is that apertures could facilitate the accessibility of other proteins to the lumen, for instance the enzyme aTAT1 known to acetylate the microtubule inner face, a modification associated with mechanical resistance of microtubules. The helical structure of microtubules generated by MAP6 exhibit a width equivalent to that of axons: they could therefore define the diameter of axons and/or confer to axons physical resistance to the compressive forces they encounter in brain tissues during development or regeneration.

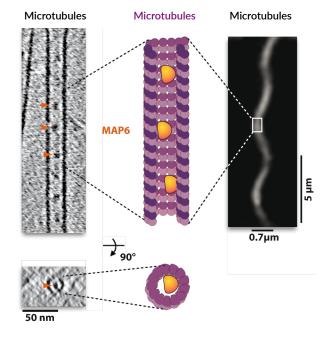
This pioneering discovery of the first MIP present in the lumen of neuronal microtubules opens up a completely new field of investigation to understand this hidden side of microtubules. Exploring the inner life of neuronal microtubules, hitherto unknown, should reveal new functions of these biopolymers.

Microtubules are rigid filaments that are part of the skeleton of cells. They are constantly being renewed and their average lifespan does not exceed a few minutes. Indeed, microtubules grow regularly from the centre of the cell to the periphery, but can disassemble completely and randomly at any time. The permanent reconstruction process allows the microtubule array to adapt its architecture and to accompany the morphological changes of the cells.

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Cuveillier C, Delaroche J, Seggio M, Gory-Fauré S, Bosc C, Denarier E, Bacia M, Schoehn G, Mohrbach H, Kulić I, Andrieux A, Arnal I and Delphin C. MAP6 is an intraluminal protein that induces neuronal microtubules to coil. *Science Advances*, 2020





Contact: Annie Andrieux
GPC
Physiopathologies of the Cytoskeleton
Group

μm

The neuronal protein MAP6 localizes inside microtubules (cryo-electron tomography) and induces their helical growth (Total Internal Reflection Fluorescence microscopy).

© Christophe Bosc, Camille Cuveillier and Julie Delaroche.

A "thermometer" protein that controls the flowering of plants

phenology of plants, their seasonal with the changing environment.

Seeing trees blooming in the middle The Evening Complex (EC) is a protein complex that acts of winter is not unusual anymore. as a repressor of gene expression. It is essential to the Plants are very sensitive to their plant's circadian clock and helps regulate the growth of environment and can sense changes the plant in a temperature-sensitive manner in a number in temperature of just a few degrees. of different species. The EC is made of three proteins, These slight elevations in LUX ARRHYTMO (LUX), EARLY FLOWERING 3 (ELF3) temperature due to global warming and EARLY FLOWERING 4 (ELF4). In this study, IRIG cause some of them to flower earlier researchers examined the role of these three proteins in and earlier in the season. This can vitro and their DNA binding activity with respect to lead to many negative effects in wild temperature. They showed that LUX binds to DNA and crop plants including reduced (Figure) with high specificity and recruits ELF3 and ELF4 seed production, smaller and fewer to the DNA. Ultimately, only the activity of ELF3 is fruits and decreased biomass. For directly dependent on temperature: when the these reasons, it is fundamental to temperature rises, ELF3 prevents the complex from understand how plants perceive and binding to the DNA; it then becomes less active and can respond to temperature as the no longer repress growth and flowering.

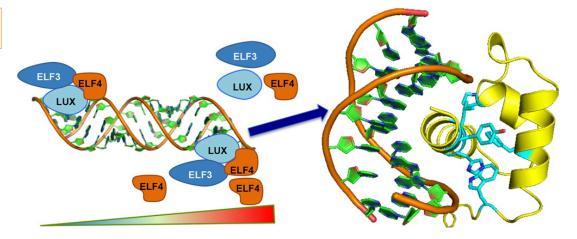
Based on the crystal structure of LUX, a mutation was growth and development, change designed that decreased EC binding to DNA. This mutation was introduced into the model plant Arabidopsis. As a result, plants grew faster and flowered earlier, even at lower temperatures. These data indicate that changes in the DNA-binding affinity of LUX can have an effect on the entire complex and result in plants that have changed sensitivity to warmer temperatures with respect to their growth and flowering time.

Understanding the molecular mechanisms underlying EC activity, in particular how different protein partners contribute to its DNA-binding activity, helps explain how small changes in temperature lead to profound changes in plant growth.

In plants, *phenology* is the study of their seasonal development phases: foliage, flowering, fruiting, autumn yellowing. These developments are linked to certain climatic parameters.

Silva CS, Nayak A, Lai X, Hutin S, Hugouvieux V, Jung JH, López-Vidriero I, Franco-Zorrilla JM, Panigrahi KCS, Nanao MH, Wigge PA and Zubieta C. Molecular mechanisms of Evening Complex activity in Arabidopsis. Proceedings of the National Academy of Sciences of the USA, 2020

Contact: Chloe Zubieta Cell & Plant Physiology Laboratory



The Evening Complex (EC) acts as a thermosensor by binding DNA at low temperatures and repressing its target genes. But when the temperature rises, the complex dissociates from the DNA and gene expression occurs, resulting in early flowering. The structure of the EC protein, LUX ARRYTHMO, linked to the DNA is shown above: on the left, EC is presented around the DNA. On the right the structure of the LUX protein is shown attached to the DNA double helix

Multi-omics for understanding the regulation of gene expression

Within a living organism, one cell type is differentiated from another by its own gene expression program. Genes are encoded by DNA that wraps around proteins called histones to form a structure called chromatin. Gene expression is closely controlled by the dynamic modification of histones through the addition of covalent chemical groups on certain amino acids. The most well-known modifications are methylation and acetylation of histone lysine. Their diversity has greatly increased over the last decade with the discovery of a wide range of acylations, structures that are fairly close to acetylation but which give to modified lysines different physico-chemical properties. These acylations are added to lysines from the corresponding Acyl-CoA small molecules (metabolites). A key question that has emerged from the discovery of these new modifications, known as epigenetic marks, is whether they provide redundant functions with acetylation or whether they have specific roles, particularly in the dynamics of chromatin structure (open or compacted) and the control of gene expression.

Among acylations, crotonylation is a modification of lysine residues which consists of the addition of a crotonyl group whose particularity is its rigid planar structure. To better understand the role of this epigenetic mark ignored until 2011, researchers at our institute have analyzed its dynamics during the process of cellular differentiation represented by murine spermatogenesis. By proteomic analysis, they observed in particular that the crotonylation of lysine 27 on histone H3 (H3K27cr) was similar in abundance to the acetylation of the same amino acid (H3K27ac). Lysine acetylation on histones has been explored for more than 50 years, and H3K27ac is known to mark the active expression of genes when present upstream of their sequence. Given the substantial abundance of H3K27cr, it seemed very opportune to finally highlight its cellular functions in relation to those of H3K27ac. The researchers then obtained the genomic location of this new histone mark and compared it to that of H3K27ac, as well as to that of proteins involved in the regulation of gene transcription. They observed that these two marks often functioned synergistically, inducing maximal gene expression. However, some regions of the genome carry more one mark than the other, which results in preferentially attracting different panels of transcriptional regulators.

This integrated analysis of omics data provides an unprecedented level of understanding of the regulation of gene expression of these two histone marks and reveals the synergistic and specific actions of each histone modification. Knowledge of all modified histone forms, as well as the proteins that bind to them, is essential for understanding the molecular mechanisms regulating gene transcription at work in normal developmental processes, but also in many pathologies.

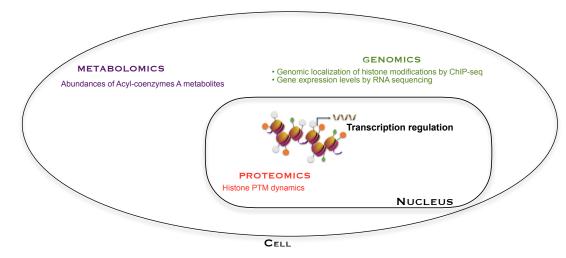
Histones are proteins located in the nucleus of eukaryotic cells. They are the main protein constituents of chromosomes and are closely associated with the DNA, and allow their compaction. The DNA is in fact wrapped around the histones like thread around a coil. Histones are very rich in the basic amino acids lysine and arginine.

Epigenetic marks are placed on the genome and are used to select the genes to be expressed. These are "post-it" notes that mark the RNA biomolecules to be synthesized.

Collaboration Institut Cochin and CEA-Saclay

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Contacts: <u>Delphine Pflieger</u>
<u>BGE</u>

Large Scale Biology laboratory
<u>Christophe Battail</u>
<u>BCI</u>

Cancer Biology and Infection Laboratory

Gene expression is analyzed by RNA-seq (a sequencing technique). It is regulated by histone modifications, in particular on lysines whose position on the histone sequence and level of modification can be apprehended by proteomic analysis. Lysine acylations are introduced from Acyl-CoA co-factors, whose abundances are quantified by metabolomic analysis. The position of a histone mark on the genome (such as H3K27cr) is obtained by another type of genomic analysis (ChIP-seq, a technique for studying DNA/protein interactions at the genome level). These various analyses have been combined in this work to better understand the mechanisms regulating gene expression.

Towards an energy disruption in microelectronics: controlling and detecting spin currents using ferroelectricity

Electron spin, a quantum property par excellence, is at the heart of the magnetism of materials as well as a technology called spintronics, which exploits spin currents in addition to the charge currents used in conventional electronics. After revolutionizing digital storage with magnetic hard disks, spintronics could play an important role in making new processors that surpass current silicon-based technology. To generate and detect spin currents, spintronics traditionally uses ferromagnetic materials in which the spins are all aligned in the same direction (spin up or spin down). Ferromagnetism has the advantage of giving spintronic devices a nonvolatile character, which can reduce the overall energy cost of the devices. However, the energy required to reverse the magnetization by application of a magnetic field or electric current remains significant.

Researchers from our institute have developed, in collaboration with the CNRS/Thales Joint Physics Unit, a new approach to generate and detect spin currents by exploiting the particular electronic properties present at the interface between two non-magnetic materials. In these systems, the injection of a charge current in a given direction generates spins in a transverse direction; reciprocally, the injection of spins in one direction gives rise to a charge current in the transverse direction. The way in which spin and charge currents are thus interconverted (and in particular their sign) is determined by the nature of the interface.

By giving these interfaces a ferroelectric character, the researchers were able to control the sign of interconversion *via* electrical polarization. To do this, they applied a strong electric field to induce a ferroelectric character to the oxide used, obtaining for the first time a *non-volatile* electrical control of the conversion between charge current and spin current. This opens up the possibility of encoding the information in the polarization of the ferroelectric element, and using spin-charge conversion to read this polarization state.

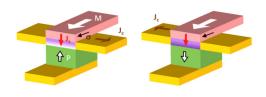
This work paves the way for spintronic devices in which the non-volatility would be provided not by ferromagnetism but by ferroelectricity, and for which the electrical consumption would thus typically be reduced by a factor of 1000.

Spin-polarized current: an electric current passing through a ferromagnetic material will see its proportion of spin down and spin up electrons changed. These electrons are said to be spin-polarized, like photons going through a polarizer. By this means, we can inscribe information in the spin of the electrons. In a non-magnetic material, a current can also be spin-polarized by the coupling of orbital and spin angular momentum, the spin-orbit coupling.

Non-volatility: conservation of data in the absence of a power supply.

REFERENCE

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Contacts: <u>Jean-Philippe Attané</u> and <u>Laurent Vila</u> <u>Spintec</u> Spintronics and Component Technology

Ferromagnetic
Interface material
Ferroelectric
Metal

Example of a device made possible thanks to the results obtained by the researchers.

A ferromagnetic material is used to generate a vertical spin current J_s and injecting it into an interface material in which it is converted into a lateral J_c charge current. The spins σ are represented by the small black arrow and their direction is fixed by the direction of magnetization of the ferromagnetic material M represented by the big white arrow. Traditionally, to change the sign of the charge current produced, the magnetization of the ferromagnetic must be reversed by applying a magnetic field or a strong current to it. Here, this is achieved by reversing the polarization P of the ferroelectric material acting on the interface by means of an electric field.

Artificial photosynthesis: Hybrid systems for visible light-driven hydrogen evolution

Hydrogen (H₂) is a promising green fuel and a good way to store renewable energy, which can be easily released by combustion with molecular oxygen (O2) producing just water (H_2O) as product of the reaction with zero-carbon footprint. Green Hydrogen can indeed be produced from water, using solar energy in a process mimicking photosynthesis. The sustainability of this upcoming technology however relies in the development of novel materials architectures that are together active, stable and based on Earth-abundant and cheap elements. Within the context of the "Make Our Planet Great Again" initiative, researchers at our Institute [collaboration] have been one step closer with the preparation of a cost-effective photoelectrode for H₂ evolution made of p-type light-harvesting semiconductor covalently interfaced with earthabundant molecular catalysts for hydrogen evolution.

> Contacts: <u>Cristina Tapia-Garcia</u> and <u>Vincent Artero</u> <u>CBM</u> Chemistry and Biology of Metals

Laboratory

Amorphous TiO₂ protective layer

2e
2H

Cobaloxime (CoHEC) grafted on TiO₂ to catalyze hydrogen

The strategy followed starts with the synthesis of a

copper-iron oxide light harvesting semiconductor

photocathode based only on Earth-abundant metals.

This material was protected with amorphous TiO₂ (green

circle in Figure 1) deposited by Atom Layer Deposition

(ALD). This thin film of TiO2 (<10 nm) prevents the

copper-iron oxide from corrosion while allowing the

transfer of electrons towards a molecular cobaloxime

catalyst (CoHEC) grafted at its surface (red circle in

Figure 1), following previous work from the team.

Figure 1: Scheme of electron pathway on $\text{CuFe}_x\text{O}_y|\text{TiO}_2\text{-CoHEC}$ hybrid photocathode.

cight-harvesting semiconductor CuFe_xO_y absorbent in the visible spectrum

The resulting Earth-abundant element-based photoelectrodes evolve hydrogen from near-neutral aqueous solutions with quite positive onset photocurrent potentials (> 700 mV vs RHE, Figure 2) and their performance compare well with other recently reported systems. The *collaboration* with IRIG and EPFL researchers allowed for a detailed characterization of this photoelectrode architecture and a better understanding of its performances.

Future work aims at enhancing the photocathode performance and to integrate it in a full photoelectrochemical system for self-sustained solar hydrogen evolution.

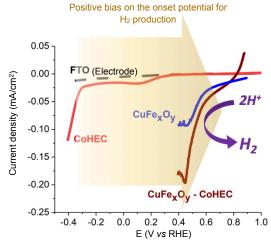


Figure 2: Linear Scan Voltammograms showing the positive bias on the onset potential when using the CuFexOy-CoHEC. (RHE: Reversible Hydrogen Electrode)

Collaboration: LCBM (Chemistry and Biology of Metals Laboratory, UGA, CNRS, CEA), Institut Neel (CNRS), PHELIQS (Quantum Photonics, Electronics and Engineering Laboratory, UGA, CNRS, CEA), SyMMES (Molecular Systems and nanoMaterials for Energy and Health, UGA, CNRS, CEA), LIMNO (Laboratory for Molecular Engineering of Optoelectronic Nanomaterials, EPFL). The Solar-Hybrid project is supported by the MOPGA postdoctoral program 2018 (Make our planet great again initiative) and DRF Impulsion 2018 program.

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New eyes for an optoelectronic nose

The monitoring of volatile organic compounds (VOCs) has become an important issue, particularly in the control of air quality, industrial processes, public safety, healthcare and so on. Electronic noses are promising candidates for analysis and monitoring of these ubiquitous compounds, some of which are harmful to the environment and sometimes even dangerous to human health. Surface Plasmon Resonance (SPR) is an optical technique widely used in the development of biosensors for the detection of chemical and biological compounds. The use of gas-phase SPR imaging is innovative and interesting because of its multiparameter detection capabilities, particularly suitable for the detection of VOCs.

In an effort to improve the performance of the optoelectronic nose, researchers at IRIG propose to study fundamental aspects related to optics such as wavelength, temperature and thickness of metallic film deposited on the SPR prism. To this end, they studied the influence of the wavelength of the light source (usually a LED) on the sensitivity of the system [1]. A comprehensive theoretical study has been corroborated by a related experimental study. In the 530 nm to 740 nm wavelength range, they showed an increase in sensitivity as the wavelength increased, with good consistency between the theoretical and experimental results. At the optimal wavelength of LEDs, the detection limits of their optoelectronic nose are in the order of ppb (parts per billion) for VOCs such as 1-butanol, limits that are similar to those of the human nose

To go further in optical characterization, the researchers analyzed the effect of the different metallic layers deposited on the SPR prisms in terms of optical performance [2]. They developed a theoretical model considering each thickness of the metallic layers measured during the deposition (carried out at the CEA Advanced Technology Platform) as well as the surface roughness as analyzed by atomic force microscopy (carried out at the CEA Nano-characterization Platform). In order to compare theory *versus* experiments, they established a new method for characterizing the optical

performance of gas-phase SPR imaging prisms. This method makes it possible to obtain a generic measure of sensitivity, independent of the nature of the carrier gases. The experimental sensitivities thus obtained are quantitatively comparable to the theoretical results without adjustable parameters over a temperature range from 5°C to 45°C.

These results are of importance for the use of optoelectronic noses in real conditions and especially on-field in order to consider corrective measures during seasonal or regional temperature variations.

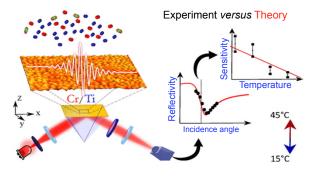
With the support of the Fondation Nanosciences (thesis of J. Weerakkody), the Labex Arcane (post-doc of F.-X. Gallat), the DGA and the CEA (thesis of S. Brenet) but also of BPI France (FUI WISE) and the company Aryballe Technologies.

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Contacts: <u>Yanxia Hou-Broutin</u> and <u>Arnaud Buhot</u> <u>SyMMES</u> Molecular Systems and nanoMaterials for Energy and Health



Schematic diagram of the optical device for SPR imaging

Chromium (Cr) and titanium (Ti) have been tested as metals for the adhesion layer of gold deposited on the SPR prism. Surface roughness information, analyzed by atomic force microscopy, is used in the model to predict the reflectivity versus incidence angle curve. Optical index sensitivity is obtained as a function of temperature between 5 °C and 45 °C. A quantitative agreement between theory (red curves) and experiments (black dots) is observed.

Towards efficient and mercury-free LEDs

The international Minamata Convention, which came into effect August 16, 2017, aims at eventually banning the use of mercury and mercury-based devices, due to the high toxicity of this element for the nervous system. This concerns mercury lamps which are the traditional sources of UV light for a wide range of applications including water and air treatment, disinfection, psoriasis bleaching, banknote counterfeiting detection, agriculture etc... This context favourably affects the fast-growing market of light-emitting diodes (LEDs) in the UV range and strongly stimulates research and development in this field. The recent emergence of Covid-19 and the likelihood of other highly pathogenic viruses emerging in the future make it particularly urgent to find effective and easy-to-use "mercuryfree" solutions for surface disinfection by UV-C irradiation.

UV LEDs are made from nitrides of element III (third column of the Periodic Table of the Elements), i.e. GaN, AIN and their alloy AIGaN. With the progressive ban of mercury, there is a growing, worldwide interest in this type of LED, illustrated by the rapidly increasing number of players in the field. However, the external quantum efficiency of most UV LEDs produced remains low. A very small number of players were able to demonstrate an efficiency of more than 10%, but most devices in the UV-C range used for sanitary applications (230-280 nm) exhibit an efficiency of less than 5%. The main causes of this reduction in efficiency for increasingly shorter wavelengths (achieved by increasing the molar fraction of AIN in the AIGaN alloy) are assigned to the presence of crystal defects such as "dislocations" and the associated non-radiative recombination, i.e. optical "losses", if the density of the dislocations exceeds 108/ cm2. This limitation is also related to light extraction limits and to the difficulties of p-type doping for an increasing molar fraction of AIN, which increase the electrical resistance and make the electrical contacting of the LED more and more difficult to achieve.

In this context, researchers from the IRIG and the Néel Institute recently obtained a spectacular result by demonstrating that the incorporation of a small fraction of indium in AIN together with magnesium (which is the

doping material) led to a considerable increase in the quantity of magnesium incorporated and therefore in the level of p-type doping of the AlN nanowires used. The use of nanowires, rather than thin films, also facilitates the relaxation of the stresses generated by the dopant. This result is a significant break with the state of the art. It was confirmed by the realization of a p-n junction with AlN nanowires and paves the way for the realization of a new type of UV-C LED whose process has been patented. It also opens the way to the realization of hybrid LEDs for UV-C, an approach also patented by the researchers.

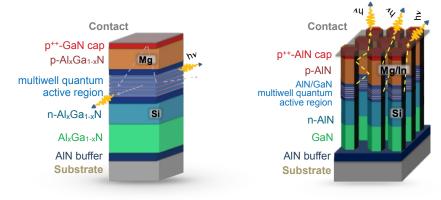
The external quantum efficiency is the ratio of the number of photons extracted from a LED to the number of charges injected.

Doping is the addition of impurities in small amounts to a semiconductor to modify its conductivity properties. There are two types of doping. n-type doping consists of increasing the electron density. p-type doping, on the other hand, reduces the electron density and creates missing electrons or "holes", which behave like positively charged particles.

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Contact: <u>Bruno Daudin</u>
<u>Pheliqs</u>
Quantum Photonics, Electronics and
Engineering



On the left, structure of a "standard" LED. On the right, structure of a nanowire LED (patented) taking advantage of the p-type doping achieved for AIN nanowires.

miRViz: Viewing and analyzing microRNA data

We know for more than 70 years that genes encoded by DNA are transcribed into messenger RNAs and then translated into proteins. But the way our cells functioned turned out to be much more complex. Participating in this complexity and discovered in many eukaryotic organisms in the early 2000s, microRNAs are RNAs that do not code for a protein. These microRNAs, about 22 nucleic acids long, repress and are therefore major regulators of gene expression. Their role has been demonstrated in many physiological and pathological mechanisms. In some cancers, for example, microRNAs are involved in tumor initiation and progression as well as metastasis formation. In humans, 2500 microRNAs are identified. Experimental measurements of their level of expression as well as their functional role generate large amounts of data that are difficult to analyze in the absence of dedicated bioinformatics In a previous study, IRIG researchers built *MicroRNA networks*. The objective was to reuse the mathematical theories developed with the rise of social networks in order to understand the complexity of the links between all human microRNAs. In these microRNA networks, each node (represented by a circle) corresponds to a microRNA; two nodes are linked if the corresponding microRNAs have similarities. The goal of miRViz is to provide an open access website for all biologists so they can use the power of networks to visually analyze their microRNA data. This new study presents several examples of use involving cancer cells, stem cells or data from cancer patients.

By means of this website, researchers have taken over public data from patients with cortico-adrenal carcinoma and analysed them from a new perspective. They were thus able to visually retrieve the results initially published, without the need for programming expertise. They were also able to demonstrate, for the first time, that the expression of miR-29, a microRNA expressed in these tumours, is a favourable prognostic factor for survival.

Among the properties of miRViz is its ability to visualize microRNA redundancy (Figure), *i.e.* whether microRNAs that have the same physiological or pathological role are co-expressed.

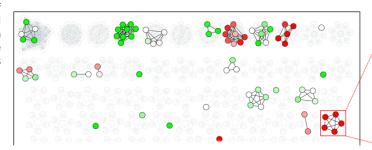
To date, miRViz is the only website to offer microRNA data analysis with pre-established networks for 11 different species species (human, mouse, drosophila, etc.)

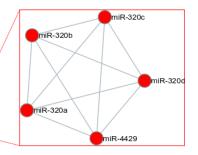
MicroRNA Network: Mathematical and graphical representation where each microRNA is represented by a circle. Two circles are connected if the corresponding microRNAs are neighbors on the DNA or repress similar genes, depending on the chosen

Exosomes: Nano-vesicles exported by cells to act as messengers for cell-to-cell communication, and also to evict cellular components from the cell.

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Contact: <u>Laurent Guyon</u>
<u>BCI</u>
Cancer Biology and Infection
Laboratory

Image extracted from microRNA analysis of cancer cell **exosomes** with miRViz. Each node (represented by a circle) corresponds to a microRNA. In this network, microRNA families can be identified at first glance, and it is noticeable that the expression of microRNAs is not randomly distributed. The miR-320 family, for example, is preferentially exported in the exosomes of colon cancer cells, a preferential export represented by the colour red.

Crystalline quality, ferroelasticity and performance of hybrid perovskitebased photovoltaic cells

In the context of an imperious energy transition that requires progress towards decarbonization of energy production, renewable energy sources are being developed, among which solar technologies. Each year, the sun provides the Earth with an amount of energy equivalent to more than 8,000 times the world's energy consumption. However, this energy is not very concentrated, hence the technological challenges involved in its efficient recovery. In 2018, solar (photovoltaic and thermal) accounted for 3 % of the world's electricity production. Over the last ten years, its growth rate has been close to 50 %, mainly due to the massive development of photovoltaics. The most commonly used semiconductor in photovoltaic technologies is silicon. But over the last ten years or so, important work has been conducted on other very promising materials such as halogenated hybrid perovskites. These, however, present challenges of stability and reproducibility.

MAPbI₃ (MA = CH₃NH₃) is the emblematic perovskite material for photovoltaic applications. But the low value of its formation energy leads to a strong dependence on the synthesis conditions, making the reproducibility of the chemical and structural properties of the synthesized thin films a challenge for the experimenters. However, mastering these properties is a prerequisite for optimizing the performance of photovoltaic cells.

Within the framework of a *collaboration*, teams from the IRIG and the National Institute of Solar Energy (INES) have studied the mechanisms of formation of thin layers of MAPbl₃. They highlighted the effects of the intrinsic instability of iodinated perovskite, which decomposes under the effect of strain. In this study, researchers elucidate, by *in situ* X-ray diffraction (XRD), the crystallization process of MAPbl₃ thin films in the presence of chlorine. Chlorine is known to have a beneficial effect on crystal quality, but the mechanisms are not yet clearly identified yet.

These teams demonstrate (*Figure* 1) that methyl ammonium iodide (MAI) and lead chloride PbCl₂ spontaneously form a MAPbCl₃ perovskite layer, which is gradually transformed into a MAPbl₃ layer by halogen substitution during thermal annealing at 100 °C. The MAPbl₃ layer thus formed is highly strained due to the difference in lattice parameter between the two perovskites, so that above a critical threshold MAPbl₃ decomposes to form, among other compounds, lead iodide Pbl₂.

Photovoltaic cells were made from thin layers of MAPbI₃ whose synthesis was stopped at different stages of the ion substitution process. The influence of the chemical composition (presence or not of PbI₂) and the crystalline properties (in particular the strain) of the active layer on the performance of the devices could thus be studied.

In addition, as frequently observed with compounds with a perovskite structure, MAPbl₃ is a *ferroelectric material*: it undergoes a *ferroelastic cubic/tetragonal phase transition* at around 57 °C (*Figure 2*). Researchers have highlighted an important consequence of this ferroelasticity which induces a variability in the crystalline properties: the strained state of MAPbl₃ reached during its formation at 100 °C, in the cubic phase, determines the crystalline orientation of the layer at room temperature, in the tetragonal phase.

This study confirms the intrinsic nature of the instability and structural variability of MAPbl $_3$ thin films. The introduction of different types of cations instead of MA alone is a promising way to improve stability. The study of such complex materials will benefit from the approach developed in this study, correlating crystallization mechanisms, structural properties and device efficiency.

REFERENCE

Medjahed AA, Dally P, Zhou T, Lemaitre N, Djurado D, Reiss P and Pouget S. Unraveling the formation mechanism and ferroelastic behavior of MAPbl $_3$ Perovskite thin films prepared in the presence of chloride. Chemistry of Materials, 2020

Contact: <u>Stéphanie Pouget MEM</u>
Modeling and Exploration of Materials

The *perovskite* crystal structure is common to many oxides of the general formula ABO₃. This type of material has long generated a great deal of interest, in particular because of its frequent ferroelectric properties. For photovoltaic applications, these are not oxides but materials in which A and B are organic and inorganic ions respectively, and the oxygen is replaced by halogens, as in the emblematic compound MAPbl₃ (MA = CH₃NH₃).

Collaboration: SGX and STEP teams, respectively from the MEM and SyMMES laboratories of IRIG, and the SMPV/LMPO team from the Institut National de l'Énergie Solaire.

A *ferroelectric material* has several energy-equivalent stable states. The transition from one stable state to another can be achieved by the temporary application of an external magnetic, electrical or mechanical force respectively in the case of ferromagnetic, ferroelectric and ferroelastic materials.

MAPbl₃ and ferroelasticity. During the structural phase transition that MAPbl₃ undergoes at 57 °C, the transformation of the highly symmetrical cubic lattice into a less symmetrical tetragonal lattice induces, for a specific orientation of the cubic lattice, several possible equivalent orientations of the tetragonal lattice, hence the existence of crystalline defects called twins. A ferroelastic material is characterized, among other things, by the fact that in the phase of low symmetry, the application of a constraint can transform the orientation of a crystalline domain into an equivalent different orientation.

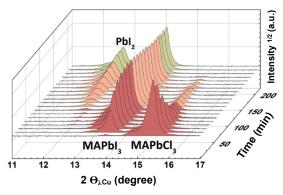


Figure 1: Evolution of diffractograms obtained during annealing at 100 °C.
The colors represent the successive stages during the

annealing process: starting from a MAPbCl₃ layer, the first stage (dark brown) is characterized by the coexistence of the two perovskites MAPbCl₃ and MAPbl₃; it is followed by a stage in which the Pbl₂ degradation phase is formed (light brown); the chlorinated perovskite then finally disappears in a third stage (green).

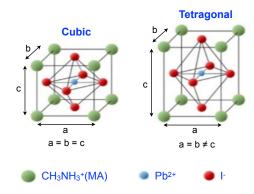


Figure 2: Around 57 °C the MAPbl₃ material undergoes a structural phase transition from high-temperature cubic symmetry to tetragonal symmetry.

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- Interdisciplinary Research Institute of Grenoble
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