Scientific Newsletter

SUMMER 2023

At the front page of IRIG

Indium phosphide quantum dots see red and infrared

Indium phosphide quantum dots are semiconductor nanostructures used to improve the color rendering of television screens, as they emit intense fluorescence throughout the visible spectrum. Beyond this, the near-infrared range is used for applications such as biomedical imaging, photodetectors and solar cells.
For in vivo imaging the use use of infrared enhances the signal-to-noise ratio, by minimizing absorption and scattering by the biological medium enabling more in-depth analysis of tissues (**Fig. left**).
Capturing photons over an extended range from the visible to the near infrared enhances the efficiency of solar cells. (**Fig. right**).

Contact: Peter REISS
SyMMES
Molecular Systems and nanoMaterials for Energy and Health

REFERENCE

Yadav R. Kwon Y. Rivaux C. Saint-Pierre C. Ling WL and Reiss P
Narrow Near-Infrared Emission from InP QDs Synthesized with Indium(I) Halides and Aminophosphine
Journal of the American Chemical Society 2023

The main advantage of quantum dots is that their optical properties can be adjusted down to a few nanometers in size. The band gap that separates the valence band from the conduction band in indium phosphide (InP) is 1.35 eV; this energy "gap" corresponds to a light wavelength of around 920 nm.
Until now processes enable InP quantum dots to be synthesized only to a maximum size of 6 nm limiting the emission wavelength to around 630 nm (red).

For the past fifteen years, researchers at IRIG [collaboration] have been working on the synthesis of new types of quantum dots free from toxic heavy metals. They have succeeded in synthesizing InP quantum dots largerer than 10 nm, in order to achieve infrared luminescence up to 730 nm (infrared). The process involves the use of a new indium precursor wich acts both as a source of indium and as a reductant for the precursor (of aminophosphine type). Another advantage is the narrower luminescence line width in the near infrared, as it is less sensitive to size variations.

Thanks to the development of their optical properties, indium phosphide quantum dots are becoming a promising material in the visible and infrared ranges. These heavy-metal-free nanoparticles are used in preference to cadmium selenide and lead sulfide which contain toxic elements restricted by the European RoHS (Restriction of Hazardous Substances) directive.

Collaboration
MEM for structural analysis. These results were obtained as part of an ANR project (18-CE09-0039-01 FLUO), involving the LPCNO Laboratory of Physics & Chemistry of Nano-Objects at INSA Toulouse, and the ALEDIA company in Grenoble.

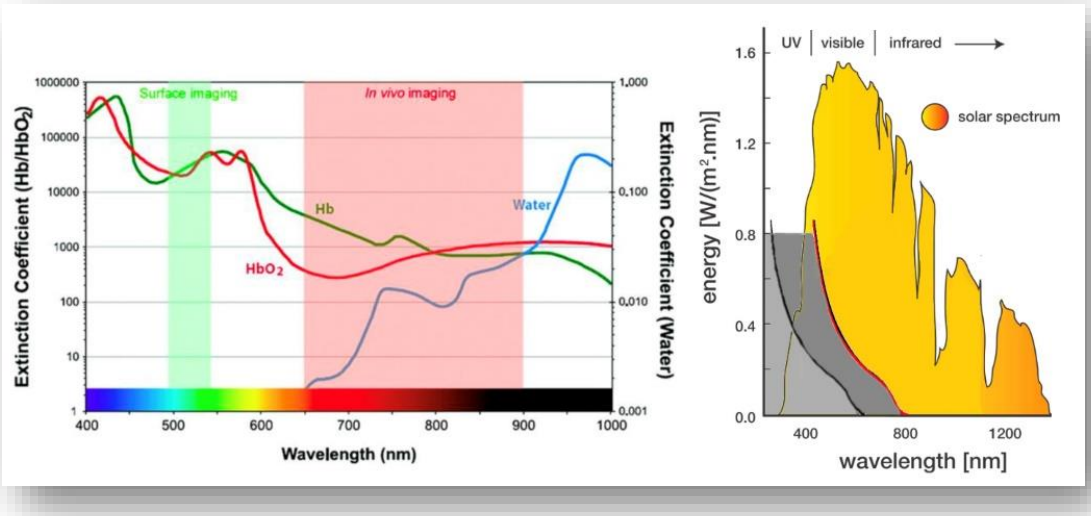

Figure on the left: for in vivo imaging, the reduced absorption between 650 and 900 nm makes this spectral range particularly suitable, notably due to the reduced absorption of hemoglobin (Hb, green), oxyhemoglobin (HbO2, red) and water (blue).
Figure on the right: overlap between the solar emission spectrum (yellow) and the absorption spectra of InP quantum dots: threshold at 630 nm for sizes up to 6 nm according to the classical synthesis (light grey) and according to the Irig synthesis, the threshold increases to 730 nm for 10 nm quantum dots (dark grey).

Elucidation of the trigger of infection of bacteria by their viruses

Pathogenic bacteria are becoming increasingly resistant to antibiotics. Alternatives must be found and validated to avoid falling back into the pre-antibiotic era. The use of bacteriophages, natural enemies of bacteria, is one of the most promising alternatives, both in agriculture/veterinary medicine and in human health. Sixty percent of known phages consist of a capsid protecting the viral DNA and a long flexible tail, which serves to recognise the host via one or more receptor binding proteins (RBPs) located at the tip of the tail. The RBP-receptor interaction triggers the infection: opening of the capsid, perforation of the bacterial wall and injection of the viral DNA into the host cytoplasm. Once injected, the viral DNA takes control of the bacterium and converts it into a phage factory; the cycle ends with the explosion of the bacterium and the release of hundreds of new virions.

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In this study, researchers at IRIG unveiled the infection of the bacterium *E. coli* by bacteriophage T5. This infection is initiated by the irreversible binding of T5 (RBP pb5) to its bacterial receptor FhuA, an E. coli outer membrane iron transporter. Thanks to advanced electron microscopy, both in terms of microscopes and cameras, as well as in software for the analysis of the images obtained, the scientists were able to determine the structure of T5 tail tip before and after interaction with FhuA reconstituted in a small membrane patch (nanodisc), as well as the structure of the FhuA-pb5 complex. These structures at atomic resolution allowed to understand how the interaction between pb5 and FhuA, i.e. the recognition of the host by the phage triggers the infection process. Moreover, it details the molecular mechanisms involved in the different steps, from the interaction between the phage and its bacterial receptor, to the perforation of the host's external membrane, including the opening of the phage tail and its anchoring to the membrane.

These studies will contribute to better control and use in health, biotechnology etc…, of these fascinating bacteriophage nanomachines.

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Structural basis of bacteriophage T5 infection trigger and *E. coli* cell wall perforation.
Science Advances 2023

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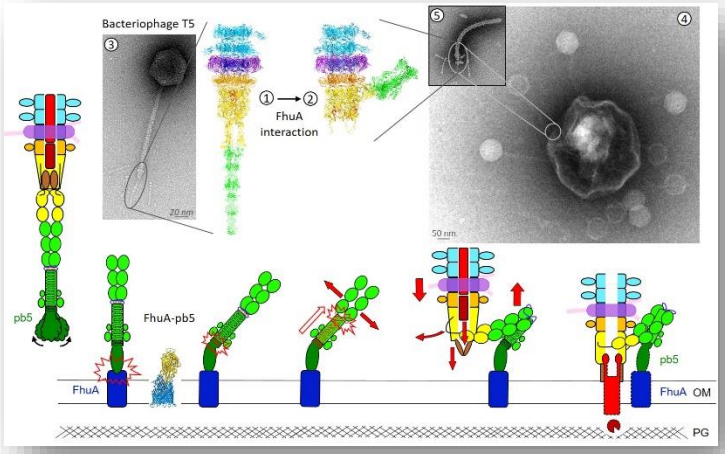
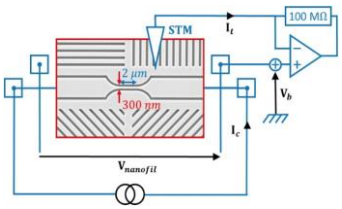
Deciphering Bacteriophage T5 Host Recognition Mechanism and Infection Trigger.
Journal of Virology 2023



Molecular mechanism of the trigger of infection of *E. coli* by bacteriophage T5
Structures of phage T5 tail tip before (1) and after (2) interaction with FhuA are shown in ribbon. On either side, negative stain images of phage T5 isolated (3) and interacting with a minicell (4). (5): T5 phage tail interacting with FhuA in a nanodisc.
Below are detailed the steps of the molecular mechanism, indicated in red or by arrows, from the recognition of the host by the phage to the opening of the phage tail, its anchorage to the membrane and the perforation of the latter.
OM: Outer-membrane,
PG: Peptidoglycan

Dynamics of electrons in a superconductor nanowire

In the ground state of a superconductor, electrons pair up to form so-called Cooper pairs. The temperature, a magnetic field, an electric current or an incident photon can break these pairs to restore single electrons also called quasi-particles. The presence of quasi-particles is therefore the sign of a weakening of superconducting properties, which can harm the proper functioning of superconducting circuits such as Qbits or, on the contrary, be used to make photon detectors.



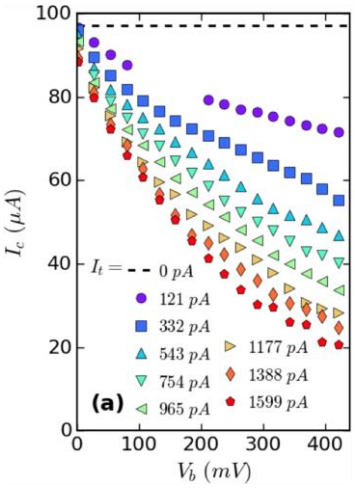
Sketch of the experimental set-up
The nanowire is in the center of the image (red box). The tip of the STM (blue triangle) is used to inject electrons without contact into the nanowire by tunnel effect. The critical current of the nanowire is detected simultaneously.

Researchers at IRIG have studied the dynamics of quasiparticles using a scanning tunneling microscope (STM) operating at very low temperature near absolut zero (0.050 K). The STM makes it possible to locally inject electrons into a device by controlling both their energy by the electrical voltage, and the flux of injection by the tunneling current. Each injected electron then transfers its energy to the superconductor either by Coulomb interaction with the Cooper pairs, or via a phonon, i.e. a vibration of the atomic lattice. Each broken Cooper pair thus releases two very energetic quasi-particles which will in turn break other Cooper pairs. This cascade leads to the formation of a cloud of quasi-particles, thus creating a hot spot which can limit the critical current that a superconducting device is able to transport by superconductivity.

The scientists studied the injection of quasi-particles into a niobium nanowire 300 nm wide and 2 µm long. They simultaneously measured the critical current of about a hundred micro-amperes that could have been greatly weakened by the tunneling current a million times weaker. The attenuation is proportional to the product current multiplied by the voltage. It is therefore mainly due to a heating effect well described by a thermal model.

Moreover, by examining small deviations from the thermal model measured for different values of the tunneling current, we were able to model the dynamics of formation of the cloud of quasi-particles and determine a relaxation time of their energy of the order of 40 ps.

This information is fundamental for optimizing the performance of photon detectors or protecting Qubits from quasiparticle poisoning.



Measurement of the critical current as a function of the injection voltage for different tunnel currents.
The dotted horizontal line indicates the value of the critical current without quasi-particles injected.

Contact: Claude CHAPELIER
Pheliqs
Quantum Photonics, Electronics and Engineering

REFERENCE

Jalabert T. Driessen EFC. Gustavo F. Thomassin JL. Levy-Bertrand F and Chapelier C
Thermalization and dynamics of high-energy quasiparticles in a superconducting nanowire probed by scanning critical current microscopy.
Nature Physics 2023.

How the facets of a platinum nanoparticle control catalytic properties

Nanoparticles offer a significant advantage over solid materials: their nanometric di-mension consid-erably increases contact surfaces, thus enhancing their catalytic activity and selectivity. This ena-bles chemical processes to be carried out using fewer reagents, reducing energy consumption and therefore costs. However, as these particles are highly complex, it has not been possible to charac-terize them individually until now. Average measurements were carried out on at least a hundred nanoparticles. Information on their structural properties and the respective contributions of their vari-ous catalytic sites was therefore only known on average.

Thanks to the extremely high resolution and brilliance of the ESRF synchrotron's X-rays, it has become possible to characterize a single platinum nanoparticle with a resolution of just a few nanometers. Researchers at IRIG, in collaboration with CNRS-LEPMI and ESRF, were able to determine the precise structure, shape and nature of the facets, as well as the distribution of deformations, via the displacement of atoms. What's more, the use of a brillant beam at ESRF enabled these measurements to be carried out during the catalytic activity of the nanoparticle, under electrochemical conditions, which had never been done before in a liquid medium. These studies revealed that, contrary to what was previously thought, the deformation induced by catalytic reactions propagates very heterogeneously throughout the volume of the platinum nanoparticle and not just on its surface, particularly at the edges, corners and facets. In fact, the deformation of a particle is closely linked to catalytic activity and has a positive influence on the reaction.

More generally, the feat of carrying out these operando measurements will enable us to understand how to improve the efficiency of nanocatalysts, particularly in fuel cells and water electrolyzers.
The researchers will complement their work with theoretical studies. The results could be applied to synthesize catalysts with optimized activity, selectivity and lifetime.

Contact : Marie-Ingrid RICHARD
Clément ATLAN
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Modeling and Exploration of Materials

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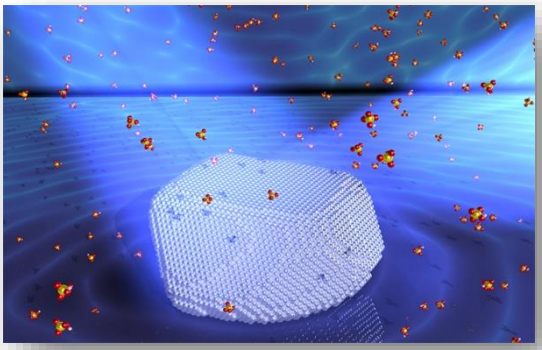

Artist view of the facets of a platinum nanopartcle
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New insights on the regulation of CO_2 fixation in microalgae

Quenching of energy (qE) and CO_2 Concentrating Mechanism (CCM) are crucial for the survival of microalgae. Mutants deficient in qE cannot survive exposure to intense light, and mutants deficient in CCM cannot grow photoautotrophically (i.e. using light as an energy source and carbon dioxide as a carbon source) unless they are supplemented with high levels of CO_2. While the two processes have traditionally been studied separately, researchers at IRIG [**collaboration**] have shown that they are largely co-regulated and **share common regulatory elements** (**Figure**).

While the presence of light was thought to be essential for the activation of qE and CMM, this study unexpectedly shows that the expression of genes involved in these processes is largely controlled by the availability of CO_2. This finding suggests that the effect of light on the regulation of gene expression is often indirect and reflects changes in intracellular CO_2 levels, which are determined by the balance between CO2 fixation in chloroplasts and CO_2 generation by mitochondrial respiration. These data add a new facet to the role of CO_2 in photosynthetic microalgae. In addition to being a substrate for photosynthesis, CO_2 is also a signalling molecule that regulates gene expression in response to changes in light and CO_2 availability.

These discoveries provide a better understanding of the molecular mechanisms governing photosynthetic CO_2 metabolism and can be used to enable the biosphere to respond more effectively to the regulation of atmospheric CO_2 concentrations, but also to progress towards a sustainable low-carbon economy by fully exploiting the biotechnological potential of microalgae.

Collaboration
International consortium of scientists led by Dimitris Petroutsos

Contact: Dimitris PETROUTSOS
LPCV
Cell & Plant Physiology Laboratory

The **shared transcriptional regulators**, between qE and CCM, identified in this study are:
- **CIA5**, initially established as a master regulator of CCM, has now been shown to be a crucial regulator of the expression of genes and proteins involved in photoprotection [1].
- The transcription factor **LCR1**, initially identified as a regulator of CCM, has also been shown to control the expression of photoprotection [2].
- **QER7**, a transcriptional factor whose function is as yet unknown in Chlamydomonas, acts as a repressor of the expression of genes linked to qE and CCM under the control of the blue light photoreceptor, phototropin [2].

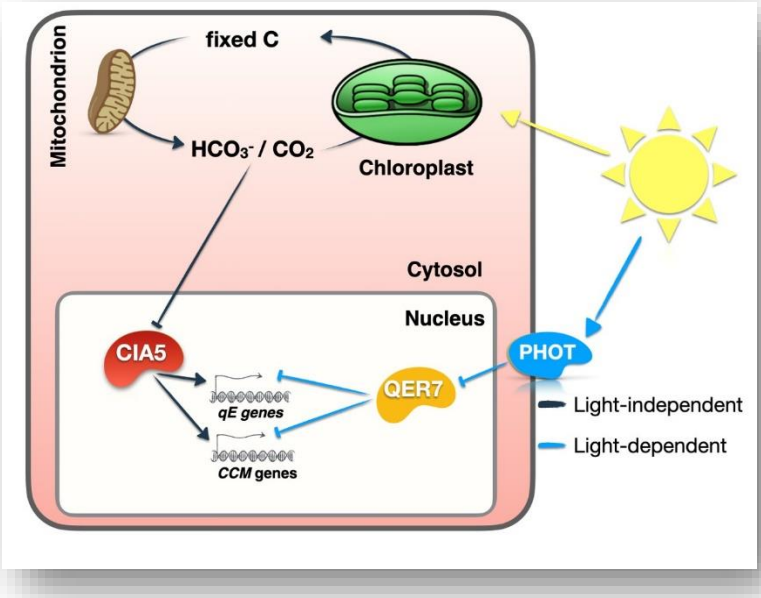

Figure: An increase in respiration or a decrease in photosynthesis leads to high levels of intracellular CO_2, which represses the CCM and qE genes by inactivating CIA5. Exposure to bright light increases the rate of CO_2 fixation, leading to CO_2 depletion and activation of CIA5, which activates the genes associated with qE and CCM. The CIA5-dependent pathway is independent of light. Light affects the expression of the qE and CCM genes via phototropin. This regulatory protein operates in a signal transduction cascade, by acting as a repressor of the transcription factor QER7, which in turn represses the CCM and qE genes. The PHOT-QER7 signalling pathway is independent of CIA5.

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Arend M, Yuan Y, Águila Ruiz-Sola M, Omranian N, Nikoloski Z and Petroutsos D. Widening the landscape of transcriptional regulation of green algal photoprotection.
Nature Communications 2023

The origin of the Universe will be unveiled by the LiteBIRD cryogenic satellite

The exploration of the distant and mysterious primordial universe is the focus of much astrophysical research into the complex dynamics of our universe. The satellite will be equipped with ultra-sensitive detectors that need to be cooled down to 0.1 K (absolute zero) using a single cryogenic chain for the entire assembly. Due to the accumulation of heat received from the sun, radiated energy and operation, the satellite's temperature finds its equilibrium at around 300 K. A specific cryogenic system must be implemented to cool the telescope and the detectors to their operating temperature. As a first step, radiative panels are used to provide an interface at 35 K. Then, a first refrigerator lowers the temperature of the instrument envelop to 4.8 K and a second system cools the first stage of the telescopes to 1.8 K.

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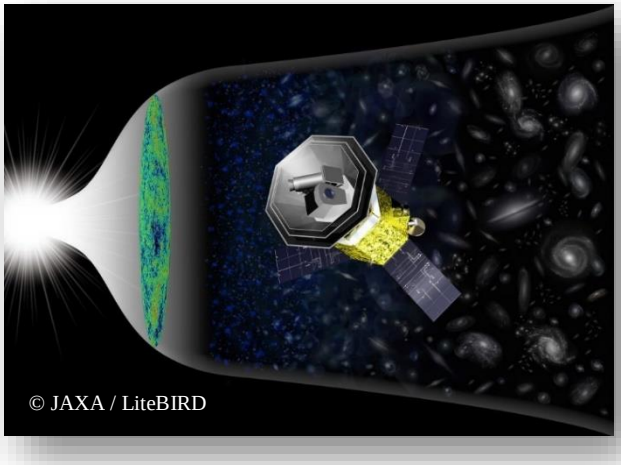
Low Temperature Systems Department

Researchers at IRIG [**collaboration**] will provide the cooling system for the last two stages at 0.35 K and 0.1 K. To achieve this, scientists are using new magnetocaloric materials, such as YBGG (Ytterbium Gallium Garnet) or CPA (chromium potassium alum), which change temperature under the effect of variations in the magnetic field according to the principle of adiabatic demagnetization. Technological challenges include the compactness of components such as superconducting magnetic coils, and the development of gas-gap or superconducting thermal switches. In addition, the Irig researchers will provide low-temperature multi-stage links between the refrigerator and the telescopes, optimizing thermal and mechanical performance, since a single cryogenic chain requires greater distances to link the various instruments.
In addition, the researchers specially developed the refrigeration system, the last two stages of which have to be maintained at very low temperatures of 0.35 k and 0.1 K respectively.
For the 0.35 K stage, the characteristics of each of the components were checked, and they were then meticulously assembled to form a highly compact integrable unit that functions perfectly. Further measurements will be carried out to determine the various cooling capacities.
For the last stage at 0.1 K, a high-performance superconducting thermal switch was designed and installed. Its operation has been validated by tests showing that it achieves the cut-off factor required for the desired cryocooler efficiency.
This work on the overall thermal architecture is being carried out in parallel with technological developments, in order to propose the best possible couplings between the various sub-systems.

The satellite is scheduled for launch in 2032, following on from the Planck satellite in 2009. The budget is estimated at 500 M€, which is comparable to ESA M-class missions. All the teams contributing to the LiteBIRD project are due to deliver study reports estimating the feasibility of the project by the end of 2023. They will then deliver an engineering model of the refrigerator and thermal links in 2025, followed by flight models in 2029.



Collaboration
The project is led by the Japanese space agency JAXA (Japan Aerospace Exploration Agency), responsible for the satellite and the low-frequency telescope (LFT). The Medium and High Frequency Telescope (MHFT) is a European project, under the responsibility of CNES. Canada and the USA are involved in both projects for the detectors.

REFERENCE

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Probing Cosmic Inflation with the LiteBIRD Cosmic Microwave Background Polarization Survey,
PTEP 2023

Solubilization of TiO_2 nanoparticles by a bacterial siderophore

With the emergence of nanotechnology, the nanoparticulate forms of TiO_2 are found in an increasing number of daily-life products such as adhesives, paints, sunscreens, toothpastes, cosmetics as well as in the food industry. For example, the TiO_2 food additive E171, contains a variable portion of TiO_2 nanoparticles depending on the source, is now forbidden by the European community since August 7th 2022 but still used in many countries to make foods whiter and brighter,. The average of ingested amount of titanium has been estimated at about 10-50 mg per person and per day. TiO_2 is considered as robust, chemically stable, and by common belief, insoluble.

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Chemistry and Biology of Metals Laboratory

Commonly, robust and chemically stable TiO_2 nanparticle was considered insoluble, while its dissolution could have an impact on antimicrobial properties, toxicity, health, and the environment. Size is considered the main physicochemical property affecting nanoparticle solubility; but various other parameters such as surface area, morphology and crystallinity must also be considered. The presence of organic ligands can also affect suspension stability, leading to nanoparticle dissolution.

Researchers at IRIG [**collaboration**] have taken an interest in organic siderophore ligands interaction with TiO_2. Bacteria synthesize and secrete siderophores to capture the iron essential for their development. They have an extremely high affinity for iron (III) and exhibit a wide structural diversity: in particular, enterobactin (ent) forms the most stable complex with iron. The structure of enterobactin is composed of 3 catechol groups linked to a central lactone macrocycle (Figure). Its affinity for Fe(III) is so high that enterobactin is able to solubilize iron present in minerals such as olivine.

For the first time, studies have revealed that enterobactin binds covalently and forms complexes with Ti(IV), whose ionic radius is almost identical to that of Fe(III). In addition, Ti(IV) has a particular affinity for oxygenated ligands and could compete with hexacoordinated oxygenated metalloproteins or biomolecules.
The researchers were therefore interested in the binding of enterobactin to TiO_2 nanoparticles, which could then dissolve. They showed that enterobactin, by binding to the surface of TiO_2 nanoparticles, promotes Ti(IV) solubilization through the formation of Ti-ent complexes. This dissolution depends on intrinsic properties such as the size, surface defects and crystallographic shape of the nanoparticles.

In addition, the dissolution of the food additive TiO_2 (E171) and the entry of the Ti-ent complex into Escherichia coli bacteria were also demonstrated. All these results raise questions about the possible impact, in terms of health or ecosystems, of the interaction between a powerful iron chelator such as enterobactin secreted by bacteria and TiO_2 nanoparticles.

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Ligand-Promoted Surface Solubilization of TiO2 Nanoparticles by the Enterobactin Siderophore in Biological Medium
Biomolecules 2022

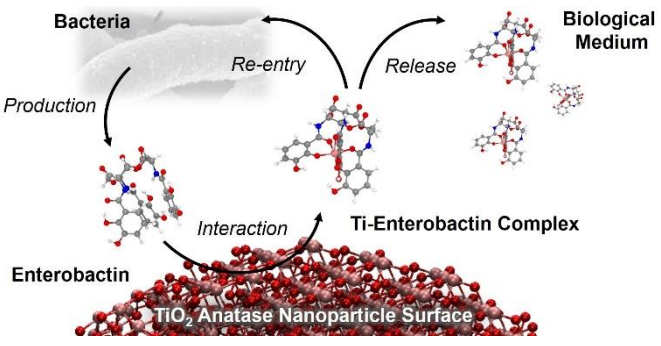


Figure: titanium atoms are represented by pink spheres, oxygens in red and nitrogens in blue, carbons in grey and hydrogens in white.

Collaboration
LCBM, SyMMES, CEA Saclay, National Institute of Materials Physics in Romania.

Financial support
LabEx SERENADE (acronyme of Laboratory of Excellence for Safe(r) Ecodesign Research and Education applied to NAnomaterial

Spin-transfer tunnel junctions to miniaturize magnetic sensors

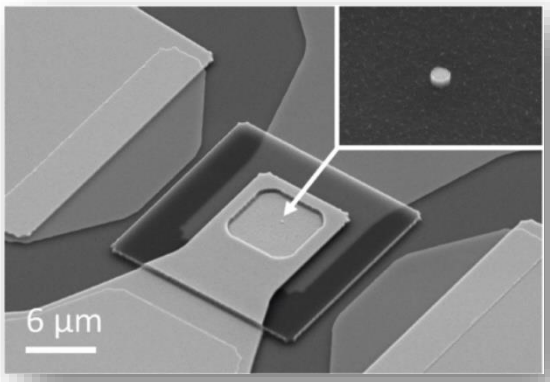
The principle of this electronic devices is of particular interest to the consumer market, the automotive industry and industry in general. Field measurement is based on the detection of periodic transitions between two resistor states, either by direct time measurement or pulse-width modulation conversion. It is an alternative to conventional hall-effect or magnetoresistive magnetic sensors. The magnetic sensor is based on a tunnel junction using the spin transfer effect, an elementary component developed for a non-volatile memory, but ingeniously put to good use here in another context. Its nanometric dimension is several thousand times smaller than that of other hall-effect or magnetoresistance sensors. In a first iteration, the sensor is already showing comparable performance: a detection range of 80 mT, a frequency bandwidth of 30 kHz, and a very low noise level. All the electronic components used are standard to facilitate integration into an integrated circuit.

A disadvantage of conventional magnetic sensors is that their operation involves a compromise between signal amplitude and the strength of the magnetic field to be measured, so high-sensitivity sensors have a limited measurement range. As a reminder, sensor sensitivity depends on the variation in resistance per unit of magnetic field; and sensor range is the resistance range where the magnetic field measurement remains linear.
Researchers at IRIG [**collaboration**] have developed a sensor based on a magnetic tunnel junction with spin transfer torque. Thanks to its physical principle, detection is no longer limited by the accuracy of resistance measurement. Resistance changes between the junction's high and low values are measured by applying a periodic sinusoidal or triangular voltage. The voltage at which the junction changes state therefore varies linearly with the applied field.

Two modes of magnetic field detection are possible: time conversion to find switching voltages, or modulation of a signal by resistance transitions. The modulation mode results in lower noise and better measurement resolution, thanks to more powerful detection electronics. The main advantages of the proposed sensor are its small size, hence low power consumption, and reduced packaging electronics footprint. The detection range can be wider than that of other magnetic sensors, as detectivity is no longer limited by field range. What's more, this sensor is insensitive to the intense fields that cause irreversible damage to magnetoresistive sensors. The design of this sensor is similar to STT MRAM magnetic tunnel junction memory cells, whose technology is already mature, enabling the sensor to be integrated into CMOS circuits. As a result, mass production can be carried out in MRAM foundries with few changes.

Sensor performance has not yet reached the level of commercially available magnetic sensors. But simple improvements to the sensing element and conditioning electronics are underway to further reduce noise levels. This type of sensor could find applications in a variety of fields, from industrial applications to the medical field, integrated on a chip, or in an array of detectors to produce 2D images.

Contact: Ricardo SOUSA
SPINTEC
Spintronics and Component Technology



Electronic microscopy of 50 nm diameter magnetic tunnel junction

Collaboration
University of Applied Sciences Northwestern, Suisse, et ICube (Université de Strasbourg)

REFERENCE

Nicolas H. Sousa R. Mora-Hernández A. Prejbeanu I-L. Hebrard L. Kammerer J-B and Pascal J
Conditioning circuits for nanoscale perpendicular spin transfer torque magnetic tunnel junctions as magnetic sensors. *IEEE Sensors Journal* 2023

Using genetics to identify kidney cancers most at risk

Sometimes diagnosed at an advanced stage, cancer can progress, spread to distant organs (metastasis) and/or reappear after treatment. Assessing patients' chances of survival would therefore help clinicians to improve disease management. Researchers at IRIG investigated the prognostic potential of each gene to identify new biomarkers for predicting patient survival in clear cell renal cell carcinoma, the seventh most common type of cancer in the Western world. Their research revealed that increased expression of the *COL7A1* gene, encoding a specific form of collagen, correlates with the advancement of this cancer and therefore with the risk of death (Figure A). Moreover, this high expression also makes it possible to identify patients most at risk among patients of the same stage, such as stage II (generally with a good prognosis) (Figure B). This new method of survival assessment is complementary to, and more precise than some of the methods (such as the stage) used today in the clinic. Since the COL7A1 biomarker is robust, it can be applied to patients of different genetic/ethnic origins or who have undergone different therapies.

Preliminary experiments on cultured kidney cancer cells have led researchers to hypothesize that this correlation with risk is causal: *COL7A1* may play a role in cancer cell migration, a key step in the development of metastasis in patients (Figure C). Furthermore, the presence of *COL7A1* is also correlated with high expression of genes involved in important molecular mechanisms of carcinogenesis: cell division, inflammatory response and epithelial-mesenchymal transition.

In conclusion, researchers at IRIG have developed a method for identifying kidney cancer patients most at risk, with the aim of improving their management. To further improve predictions, researchers are currently using artificial intelligence (AI) methods, using the expression of several genes. In the longer term, if *COL7A1*'s role in cancer cell migration/invasion is confirmed, it could be a therapeutic target to reduce the onset of metastasis.

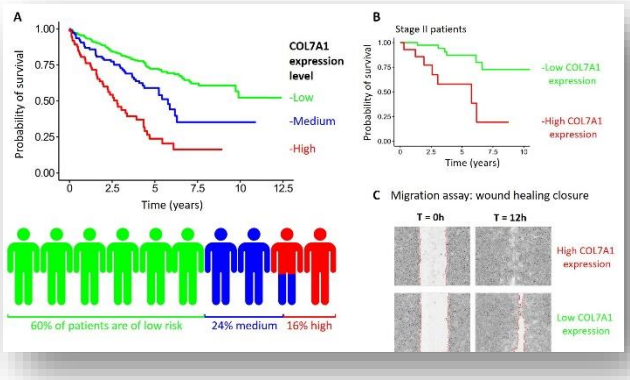


Figure A. Probability of survival for kidney cancer patients as a function of time after surgery. In green, the 60% of patients with low COL7A1 expression in the tumor - these patients have the best chance of survival (over 10 years for more than half of the patients). In blue, 24% of patients with medium *COL7A1* expression have an intermediate chance of survival (over 5 years for half of the patients). In red, 16% of patients with high *COL7A1* expression have a reduced chance of survival (less than 2.5 years for half of the patients).
Figure B. Identical to Figure A, but restricted to stage II patients (early stage). These patients are not considered "at risk" using current methods. Measurement of *COL7A1* expression identifies the 15 patients (out of 57) most at risk.
Figure C. In vitro cell migration experiment. After removing the cells from the center of the petri dish (clear vertical zone or wound, i.e. devoid of cells, at time T = 0h), cells expressing a high level of *COL7A1* (top) migrate faster: in 12h, they have "filled in" the wound, which is not the case for cells with low *COL7A1* expression.

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COL7A1 expression improves prognosis prediction for aatients with clear cell renal cell carcinoma atop of stage.
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Prognosis of lasso-like penalized Cox models with tumor profiling improves prediction over clinical data alone and benefits from bi-dimensional pre-screening.
BMC Cancer 2022

Contact: Laurent GUYON
Biosante
Biology and Biotechnology for Health

Deregulation of autophagy alters tumor progression

Gene expression is the process by which genetic information is translated into functional macromolecules. Transcription is the first step in this process, which involves the synthesis of messenger RNAs (mRNAs) from the corresponding gene DNA template. Over the past few decades, genome-wide transcriptional profiling approaches have made it possible to assess the expression levels of thousands of genes in parallel in various biological contexts. In statistical analyses, the expression of a gene is estimated by counting the number of occurrences of the corresponding mRNA sequences over a set of samples and is defined by two dimensions: the mean and the variance.

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The overwhelming majority of transcriptomic analyses based on the study of expression profiles focus on the identification of genes whose mean expression changes significantly when comparing samples from different conditions, corresponding to biological processes of interest, such as developmental biology, disease etiology, therapeutic target discovery, etc. In this classical approach, variance is usually considered only as a noise parameter to be estimated before comparing expression means.. Yet, the estimation of expression variance can be relevant from a physiological point of view, since a change in this parameter can reflect a biological change in the regulation of gene expression. Fluctuations in gene expression may indeed be due to various sources intrinsic to cellular life, such as the stochastic nature of gene transcription, the phase of cell cycle, chromatin changes or mRNA degradation.
Researchers at IRIG propose to compare the performance of statistical methods that identify such differentially variant genes. They demonstrated the potential of this approach by analyzing expression datasets in various cancers, which identified key cellular functions in tumor progression that could not have been identified by comparing average expression.
The researchers evaluated four recent methods that detect differences in the mean and dispersion of RNA-seq data. By applying these methods on simulated data, they have characterized reliable parameters to detect genes with expression variance between two conditions. The Cancer Genome Atlas data were then subjected to these methods. Among the genes showing increased expression variance in tumors and no change in average expression, some key cellular functions were identified, the majority of which are related to catabolism and are overrepresented in most of the cancers analyzed.

It may be biologically and physiologically relevant to consider differential variance in gene expression. These results highlight autophagy in carcinogenesis, illustrating the potential of the differential variance approach to gain new insights into biological processes and to discover new biomarkers.

REFERENCE

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Detection of genes with differential expression dispersion unravels the role of autophagy in cancer progression
PLOS Computational Biology 2023

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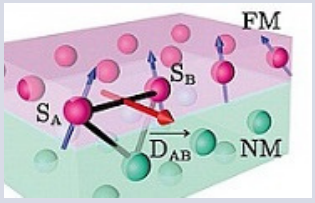

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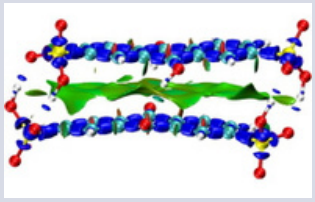

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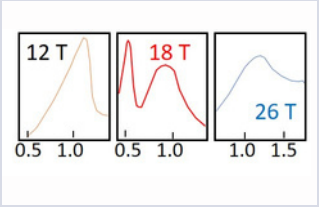

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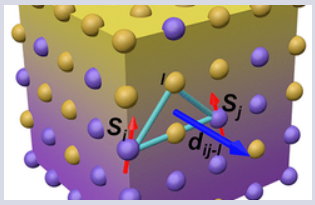

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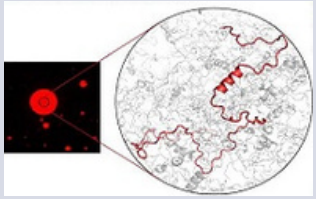

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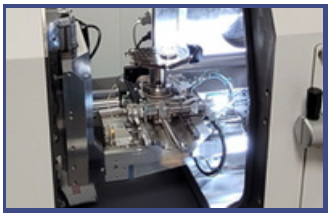

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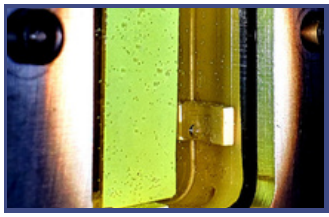

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