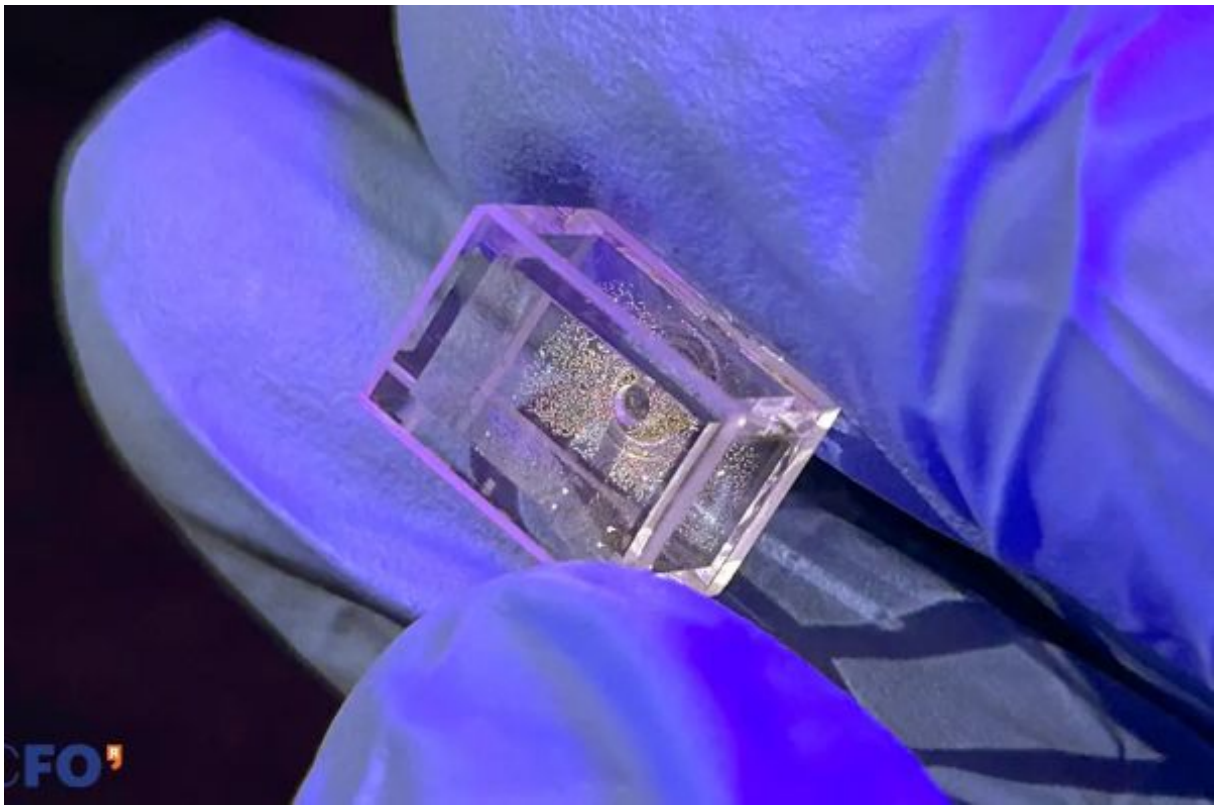


Atomic sensors unveil hidden dynamics of molecular polarization

Researchers from IBEC and ICFO demonstrate the ability of atomic sensors to non-destructively monitor, measure and optimize nuclear spin hyperpolarization of some clinically relevant molecules in real-time. These features, reported in PNAS, could enhance and reduce costs of quality controls used in clinical magnetic resonance imaging.

October 16, 2024

Magnetic resonance imaging (MRI) has long been a cornerstone of modern medicine, providing highly detailed images of internal organs and tissues. MRI machines, those large, tube-shaped magnets commonly found in hospitals, use powerful magnets to map the densities of water and fat molecules within the body. In addition to these molecules, other substances like metabolites can also be mapped, but their concentrations are often too low to produce clear images. To overcome this limitation, a technique known as **hyperpolarization** is employed to enhance the magnetic resonance signal of these substances, making them more visible during MRI scans.

Hyperpolarization involves preparing a substance outside the body in a state where its magnetization-key to creating MRI images-is near its maximum. This process can boost the signal by thousands of times compared to its natural state. Once hyperpolarized, the substance is injected into the patient and transported to the target organ or tissue. However, before this can happen, it is crucial to confirm that the substance is adequately hyperpolarized through rigorous quality control processes.

Current quality control techniques face two significant challenges. First, these methods often reduce the magnetization of the sample during the read-out process, thereby diminishing its ability to enhance the MRI scan. Second, the time required for measurement can be lengthy, during which the substance's magnetization naturally decays, limiting the opportunity for consecutive measurements. This results in a lack of critical data that could otherwise help maximize the efficiency of hyperpolarization. Furthermore, once the sample is hyperpolarized, there is a risk that it could lose its magnetization during transport to the MRI machine. Traditional quality control techniques, due to their time-consuming nature, may fail to detect this loss in time.

Now, a collaboration of IBEC researchers Dr. James Eills (now at Forschungszentrum Jülich Germany) and Dr. Irene Marco Rius and ICFO researchers**ICREA Prof. Morgan W. Mitchell** and **Dr. Michael C. D. Tayler** has demonstrated how **atomic sensor techniques** overcome the limitations of conventional sampling when measuring the magnetization of hyperpolarized materials. This breakthrough was recently reported in the journal PNAS.

In particular, the team used optically pumped atomic magnetometers (OPMs), whose operating principles differ fundamentally from traditional sensors, enabling **real-time detection of the fields produced by hyperpolarized molecules**. The nature of OPMs allowed these researchers to perform **continuous**, **high-resolution** and **non-destructive observations** throughout the entire experiment, including the hyperpolarization process itself.

According to the authors, if the field of hyperpolarization sensing was cinema, previous methods would be like a sequence of still photos, leaving the plot between frozen pictures open to the viewer's guess. i¿½Instead, our technique is more like a video, were you see t e whole story frame by frame. Essentially, you can observe continuously and without resoluti n limits, and this way you do not miss any details!i¿½, explains Dr. Michael Tayler, CFO researcher and co- author of the arti

Unveiled behaviors of chemical compounds during magnetization

The team tested their OPMs by monitoring hyperpolarization in clinically relevant molecules. The atomic sensors' unprecedented resolution and real-time tracking allowed them to witness how the polarization in a metabolite compound ([1-13C]-fumarate) evolved under the presence of a magnetic field.

The atomic sensors revealed ?hidden spin dynamics' that had gone unnoticed until now, offering a new path towards optimizing the hyperpolarization from the very start of the

process. i¿½Previous methods obscured subtle oscillations in the magnetization profil
, which previously went undetectedi¿½, remarks Tayler. i¿½Without the OPM, we woul
have achieved a suboptimal final polarization without even realizing.i¿½ Beyo
d simple observation, the method could be used to control the polarization process in real
time and stop it at the most convenient point, for instance when the maximum polarization is
ttained. The study revealed other unexpected behavior when the team applied a magnetic
field to repeatedly magnetize and demagnetize the hyperpolarized fumarate molec
le. They expected to see the magnetization increasing to a maximum and then going bac
to zero over and over, transitioning smoothly from one state to the other every time. Co
trary to these simple expectations, the molecule exhibited complex dynamics due
o hidden resonances at certain magnetization-demagnetization durations and magnetic fields
i¿½This understanding will help us detect when unwanted behavior occurs and adjust
parameters (like the duration of the cycle or the intensity of the magnetic field) to prevent iti?
½, exp
ains Tayler. The work represents an advancement in hyperpolarized MRI technology, thanks
n large part to the collaborative efforts of IBEC's Molecular Imaging for Precision Medicine group and
ICFO's Atomic Quantum Optics group. IBEC expertise in hyperpolarization methods and
ICFO's expertise in OPM sensing technologies were critical in achieving the results.
"This is a beautiful example of the new science that can be achieved when researchers from
different disciplines work together, and the proximity of IBEC and ICFO meant we were able
to collaborate closely and achieve something truly novel", acknowledges Dr. James Eills, IBEC
researcher and first author of the article.
Dr. Tayler reflects on the team's success: i¿½The OPM measurements worked beautifully fr
m the start. **The sensors' exquisite sensitivity revealed hidden dynamics we hadn't anticipated,
as if they were meant for this purpose. The ease of use and the wealth of new information
make them a powerful tool for hyperpolarization monitoring.**i¿

Benefits for MRI and other future applications

The immediate application of this study would be to integrate portable atomic sensors into
clinical sample quality control for MRI, something that is currently being implemented by the
ICFO team in the Spanish Ministry Project i¿½SEE-13-MRIi¿½. This way, **one could guide
molecules to the highest possible level of polarization during hyperpolarization and reliably
certify the polarization level before substances are injected into patients**.
The development could significantly reduce the cost and logistical challenges of metabolic
MRI. If so, this would expand its reach from the handful of specialized research centers where
it is currently used, to many hospitals worldwide.
However, the potential of atomic sensors extends far beyond medical imaging. The same
non-destructive, real-time tracking system using optically-pumped magnetometers (OPMs)
could be applied to monitor macromolecules in chemical processes, study high-energy

physics targets, or even optimize spin-based algorithms in quantum computing. According to Dr. Tayler: i¿½The method we've developed opens up new avenues not only for improvi g MRI but for various fields that rely on precise magnetic sensing, and we are excited about i s further development.i

Reference:

James Eills, Morgan W. Mitchell, Irene Marco Rius, and Michael C. D. Tayler, i¿½Live magnet c observation of parahydrogen hyperpolarization dynamicsi¿½, PNAS 121 (43) e241020 121 (2024). Dhttps://doi.org/10.1073/pnas.2410209121

Acknowledgments

The work described is funded by the Spanish Ministry of Science MCIN with funding from European Union NextGenerationEU (PRTR-C17.I1)- Plan Complementario de Comunicaciones Cuanticas - and by Generalitat de Catalunya i¿½Severo Ochoai¿½ Center of Excell nce CEX2019-000910-S; the Spanish Ministry of Science projects SAPON RIA (PID2021-123813NB-I00), MARICHAS (PID2021-126059OA-I00), SEE-13-MRI (CPP2022-009 71) plus RYC2020-029099-I and RYC2022-035450-I, funded by MCIN AEI /10.13039/501100011033; Generalitat de Catalunya through the CERCA program; Agenci de Gestio d'Ajuts Universitaris i de Recerca Grant Nos. 2017-SGR-1354 and 2021 FI_B_01 39; Fundacio Privada Cellex; Fundacio Mir-Puig; and the BIST-la Caixa initiative in Chem cal Biology; the Helmholtz Association (DB002399). The project has received funding from the European Unions Horizon 2020 Research and Innovation Programme under the M rie Sk?odowska-Curie Grant Agreement 101063517. We are also grateful to Andreas Trabesi ger and Sven Bodenstedt for discussions.

