Journal of Magnetic Resonance Open 23 (2025) 100202

Contents lists available at ScienceDirect

Journal of Magnetic Resonance Open

journal homepage: www.sciencedirect.com/journal/journal-of-magnetic-resonance-open

Hyperpolarization: From toy to tool, and back to toy

April 2025

Little over two decades ago, the landscapes of solution, solid state and *in vivo* NMR and MRI were tectonically shaken by the advent of nuclear spin hyperpolarization. Nuclear hyperpolarization promised to introduce dramatic enhancements of both NMR and MRI signals, and triggered a plethora of investigations focused on maximizing and utilizing this potential. Much progress in the field ensued – a progress that would not have happened without significant synergistic inputs from the EPR, the spin-physics, the synthetic chemistry, the biophysical, and the microwave/RF engineering communities. In short: hyperpolarization would not have matured without world-wide, collegial, mutually-supporting efforts from all the disciplines that have traditionally contributed to the Science of Magnetic Resonance. With the passing of the years, one could have expected a plateauing in these efforts; however, as we appreciated from the overwhelming response from the community when preparing this *Special Issue on Hyperpolarization at The Journal of Magnetic Resonance – Open*, it is clear that the field remains as vibrant as ever. The quality of the submissions received for this special issue, bringing together close to thirty peer-reviewed publications, evidences the excitement still elicited by hyperpolarization.

All contributions serve the common goal of enhancing NMR and MRI's sensitivity, yet propose doing so by putting forward a wide variety of approaches and experimental conditions. This diversity is illustrated in the pie charts below, which summarize certain aspects of the contributions making up this Special Issue, and which include several of the main actors currently playing in the hyperpolarized magnetic resonance arena. From examining these charts, it is clear that some methods are indeed reaching "hyperpolarized equilibrium" – mature and well-established – while others continue to evolve with relentless creativity, unexpected innovations, and new directions. This is reflected in the profusion of hyperpolarization techniques featured in this Special Issue, which include Overhauser DNP, dissolution DNP, para-hydrogen-induced polarization, spin-exchange optical pumping (SEOP), and magic-angle spinning (MAS) DNP. Also broad is the spectrum of hyperpolarized applications presented by the convened articles, ranging from metabolic imaging in animals and humans via MRI, to materials science and chemical analysis – without skipping metabolomics and small-molecule analyses.

Relying on SEOP, the Meersman and Mitschang groups explore coupling hyperpolarized xenon gas with standardized MRI phantoms, as well as with benchtop NMR. The Wild group also demonstrates the potential of hyperpolarized xenon, assessing blood-brain barrier function by tracking how xenon reaches the brain. Other hyperpolarization methods based on optical excitation are also well featured: The group of Jain provides an analytical framework for NV ^{13}C systems, exploring how magnetic field strength, hyperfine interactions, and microwave parameters influence DNP efficiency, while Matysik et al. observe unexpected hyperpolarized ^{15}N signals due to photo-CIDNP in phototropin LOV1 and the bacterial photosynthetic reaction center. New insight is reported into the properties of hypervalent phosphorus(V) porphyrins, which provide high electron spin polarization upon photo-excitation, by Di Valentin's group. Laser excitation can even enable microwave-free polarization transfer to nuclear spins in solution, as here demonstrated by the Yanai group.

Particularly well-established in terms of applications is MAS DNP, as is also reflected in this Issue's contributions on the topic. Solid-state NMR studies employing MAS DNP are presented here on surfaces of organo-platinum complexes by Lesage et al., on microporous

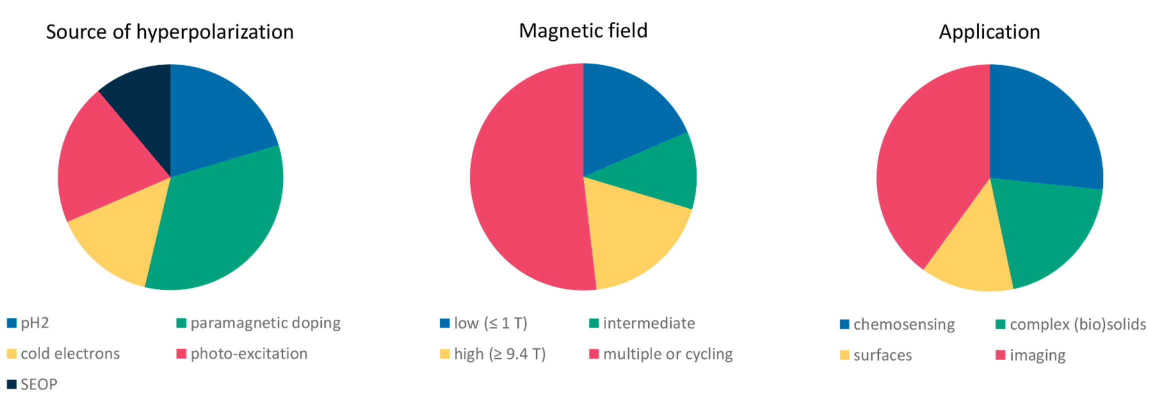

Fig. 1.

https://doi.org/10.1016/j.jmro.2025.100202

Available online 24 April 2025

aluminophosphates and fibrous nanosilica/alumina by Amoureux et al., and on cellulose by the Gutmann group. An approach to use MAS DNP to study dynamics in amyloid fibrils is presented by the Corzilius group, while the search for improved biradical polarizing agents is pursued by the Gutmann group.

Dissolution DNP has also confidently established itself as a critical tool for metabolic imaging. This is illustrated by the work of Lerche et al., which focuses on novel hyperpolarization agents and instrumentation designed to bridge the gap between preclinical studies and clinical applications. The Aggarwal group pushes this further with a dual molecular agent system for prostate cancer imaging.

Meanwhile, para-hydrogen-induced polarization (pH_2) has emerged as a new tool for chemosensing, as demonstrated by the groups of Tessari and of Reile, here applying this method to urine metabolome analysis. Interestingly, pH_2 is becoming a serious competitor to dissolution DNP for metabolic imaging, getting closer to clinical applications. The groups of Koptyug, Theis and their collaborators present efforts to optimize hyperpolarization for relevant imaging agents such as formate and pyruvate, while the group of Glöggler introduces a novel imaging agent derived from an endogenous metabolic end product. Another emerging, promising approach is Overhauser DNP, which is here explored by Van der Ham for maximizing signal-to-noise ratios per unit time, by the Anders group by coupling with miniaturized, chip-based platforms integrating NMR and microwave electronics, and by the Münneman and Dumez groups by combining ultrafast 2D under flow for process monitoring with increased resolution and sensitivity.

Several papers focus on establishing best practices, reflecting the field's growing sophistication. Elliott et al., as well as Kouřil and Meier, propose improved methods for estimating polarization and enhancement. Leskes and coworkers offer a practical guide for implementing metal-ion-based MAS DNP in materials science. Hautle and Wenckebach describe the state of the art in creating ultra-high, portable polarization by triplet DNP. Finally, Sheberstov and Barskiy demonstrate the use of an automated robotic arm system coupled with photo-CIDNP and pH_2-hyperpolarization to accelerate experiments and improve reproducibility.

The above-summarized contributions to this Special Issue, reflect the maturity as well as the exciting new developments happening in hyperpolarization nowadays. We hope that the open-access articles will give our readers an informative snapshot of the state of research in hyperpolarization, while also inspiring new ideas and discoveries. Please go ahead, and enjoy!

Guinevere Mathies[a,*], Sami Jannin[b], Lucio Frydman[c]

[a] *Department of Chemistry, University of Konstanz, Universitätsstrasse 10, 78464 Konstanz, Germany*

[b] *Université Claude Bernard Lyon 1, CNRS, ENS Lyon, UCBL, CRMN UMR 5082, 69100 Villeurbanne, France*

[c] *Department of Chemical and Biological Physics, Weizmann Institute of Science, Rehovot 7610001, Israel*

[*] Corresponding author.

E-mail addresses: guinevere.mathies@uni-konstanz.de (G. Mathies), sami.jannin@univ-lyon1.fr (S. Jannin), lucio.frydman@weizmann.ac.il (L. Frydman).