REVISTA DE QUÍMICA PUCP

Imanes pequeños, grandes impactos: una breve perspectiva sobre la madurez analítica de la RMN de bajo campo en el dominio del tiempo

SMALL MAGNETS, BIG IMPACTS: A BRIEF PERSPECTIVE ON THE ANALYTICAL MATURITY OF LOW FIELD TIME-DOMAIN NMR

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This brief perspective explores the growing trajectory of low-field Time-Domain Nuclear Magnetic Resonance (TD-NMR), tracing its transition from a specialised domain in agriculture, food, and the petroleum industries to a foundational component of modern analytical chemistry. While high-field NMR systems remain the gold standard for structural elucidation, the "small magnets" powering TD-NMR have matured sufficiently to enable high-impact applications in many scientific fields, from cultural heritage to polymer characterisation and pharmaceutical research. This shift stems from key hardware milestones, specifically the development of highly stable permanent magnets and sophisticated digital electronics. These advancements allow benchtop and portable instruments to deliver laboratory-certified (ASTM, ISO, and IUPAC) results without the need for cryogenics or expensive maintenance. Furthermore, the establishment of international benchmarks and validated protocols has addressed previous concerns regarding cross-instrument reproducibility, grounding the reliability of the method. Despite these advances, hurdles remain regarding signal-to-noise optimisation, which is essential for miniaturised devices in resource-limited settings. Ultimately, the true value of TD-NMR lies in its democratising potential, shifting analytical power from centralised facilities directly to the production line and the field.

Keywords: Time-Domain NMR; Benchtop; Small Magnets; Portable spectrometers; Relaxometry; Analytical Chemistry.

Esta breve perspectiva explora la evolución de la Resonancia Magnética Nuclear en el Dominio del Tiempo (RMN-DT) de bajo campo, trazando su transición de un dominio especializado en las industrias de los alimentos, petróleo y agricultura a una componente fundamental de la química analítica moderna. Aunque los sistemas de RMN de alto campo siguen siendo el estándar de oro para la elucidación estructural, los "imanes pequeños" presentes en los espectrómetros de RMN en el dominio del tiempo (RMN-TD) han madurado lo suficiente. Esto permite aplicaciones de gran impacto en muchos campos científicos, desde el patrimonio cultural hasta la caracterización de polímeros y la investigación farmacéutica. Este cambio surge de hitos clave en el hardware, específicamente el desarrollo de imanes permanentes altamente estables y electrónica digital sofisticada. Estos avances permiten que instrumentos de mesa y portátiles ofrezcan resultados certificados de laboratorio sin necesidad de criogenia ni mantenimientos costosos. Además, la creación de estándares internacionales y protocolos aprobados por ASTM, ISO e IUPAC ha resuelto preocupaciones previas sobre la consistencia entre distintos instrumentos, aumentando la confianza en el método. A pesar de estos avances, persisten obstáculos respecto a la optimización de la relación señal-ruido en entornos de recursos limitados. Por lo tanto, el verdadero valor de la RMN-DT reside en su potencial democratizador, trasladando el poder analítico directamente a la línea de producción y al campo.

Palabras clave: RMN en el dominio del tiempo; Equipos de mesa; Pequeños imanes; Espectrómetros portátiles; Relaxometría; Química analítica.

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BRIEF PERSPECTIVE

For decades, Nuclear Magnetic Resonance (NMR) was synonymous with high-maintenance superconducting magnets, liquid helium cooling, and restricted access facilities. While high-field systems remain essential for mapping complex molecular structures and dynamics, compact benchtop systems have expanded the reach of the technology. Specifically, low-field Time-Domain NMR (TD-NMR) based on permanent magnets has evolved beyond its origins as a simple tool for industrial quality control into a sophisticated analytical method capable of providing straightforward, reliable and rapid data across complex, real-world matrices.

This transition reflects an analytical maturity where the focus moves from frequency-domain chemical shifts to the time-resolved physics of relaxation dynamics. By measuring how nuclear spins return to equilibrium, via longitudinal (T_1), transverse (T_2), and rotating-frame ($T_{1\rho}$) relaxation time constants, as well as self-diffusion coefficient measurements, these compact systems provide an immediate window into the physical state and compartmentalisation of matter (**Figure 1**).

The journey of NMR spectroscopy, which began as a physics phenomenon, has evolved into an indispensable scientific tool, marked by five distinct Nobel Prizes that have significantly changed the fields of chemistry and biology. The groundwork was laid by Isidor Isaac Rabi, who received the 1944 Nobel Prize in Physics for his 1938 discovery measuring NMR in atomic beams, proving that atomic nuclei reveal their magnetic properties[1]. Felix Bloch and Edward Purcell expanded upon Rabi's work, adapting the technique to liquids and solids in 1946, an achievement that earned them the 1952 Nobel Prize in Physics[2,3]. This grounded knowledge transitioned NMR from isolated atomic beams into a practical tool for studying the physical and chemical environments of bulk matter.

As the technique matured, it shifted from pure physics into molecular analysis. Richard R. Ernst was awarded the 1991 Nobel Prize in Chemistry for introducing Fourier Transform (FT) NMR and multidimensional techniques, replacing slow, continuous-wave scanning with rapid radiofrequency pulses to increase sensitivity and resolution[4]. This allowed chemists to map molecular structures quickly. This structural capability was pushed further by Kurt Wüthrich, who won the 2002 Nobel Prize in Chemistry for developing methods to determine the three-dimensional structures of biological macromolecules, such as proteins and nucleic acids, in their native liquid solutions[5,6]. Finally, translating these same quantum principles to medicine, Paul Lauterbur and Peter Mansfield utilised magnetic field gradients to spatially map signals, earning the 2003 Nobel Prize in Physiology or Medicine for developing Magnetic Resonance Imaging (MRI), turning laboratory spectroscopy into a non-invasive diagnostic tool[7].

While high-field applications historically prioritised frequency-domain analysis to map chemical structures, modern developments have also embraced Time-Domain NMR (TD-NMR)[8–11]. Rather than chasing high-resolution chemical shifts, TD-NMR uses time-domain relaxation phenomena to probe the physical and chemical environment of nuclei non-destructively. Today, this scientific achievement has practical utility across diverse sectors, such as food science, where it distinguishes between bound, entrapped, and free water in food matrices[9,10,12–14], and materials science, where

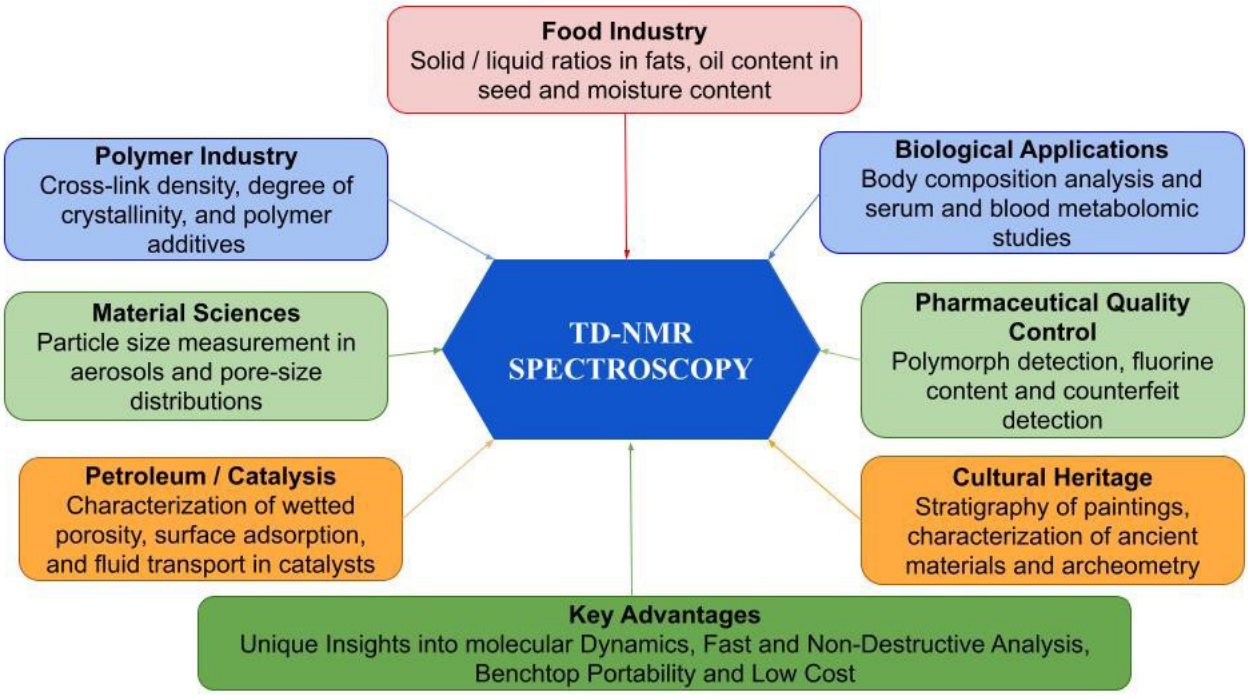

Figure 1. Overview of TD-NMR applications in complex real-world matrices.

it quantifies cross-link density in polymers[15–18]. In the end, these modern benchtop advancements realise the original vision of NMR: a universal, non-invasive probe of matter, now accessible outside of centralised, resource-intensive facilities.

THE QUANTUM AND CLASSICAL ORIGIN OF THE NMR SIGNAL

To understand the sensitivity of relaxation parameters to the local structural environment in TD-NMR, it is necessary to consider the two main relaxation processes that govern the return of nuclear magnetization to equilibrium. The longitudinal relaxation time, T_1, describes the recovery of the magnetization component parallel to the static magnetic field after excitation and reflects the rate at which nuclear spins exchange energy with their surrounding molecular environment (the lattice)[19,20]. In contrast, the transverse relaxation time, T_2, characterizes the decay of magnetization in the plane perpendicular to the static magnetic field and is primarily determined by the loss of phase coherence among neighboring spins[19,20] (**Figure 2**). Both parameters depend strongly on molecular motion, intermolecular interactions, and the degree of restriction experienced by the nuclei[19]. Consequently, changes in water mobility, viscosity, molecular association, or confinement within a heterogeneous matrix produce measurable changes in T_1 and T_2. In many food, polymeric, and porous materials, T_2 is particularly sensitive to changes in molecular mobility and interactions with the surrounding matrix, making it a useful parameter for distinguishing mobile and restricted populations of hydrogen nuclei.

These relaxation processes originate from the magnetic properties of nuclei possessing non-zero spin angular momentum, $\boldsymbol{I}$, such as ^{1}H, ^{13}C, and ^{19}F, which are associated with a nuclear magnetic dipole moment, $\boldsymbol{\mu}$, given the equation 1, defined as[19]:

$$\mu = \gamma \times I \qquad (1)$$

where γ is the gyromagnetic ratio, a constant unique to each nuclear isotope.

In the absence of an external magnetic field, these nuclear magnetic dipoles are randomly orientated. However, when the sample is placed within a static magnetic field, $\boldsymbol{B_0}$ (directed along the z-axis), the Zeeman effect causes the nuclear energy levels to split. For a spin-1/2 nucleus like the hydrogen proton (^{1}H), two distinct energy states emerge: a lower energy state parallel to the field (m = +1/2) and a higher

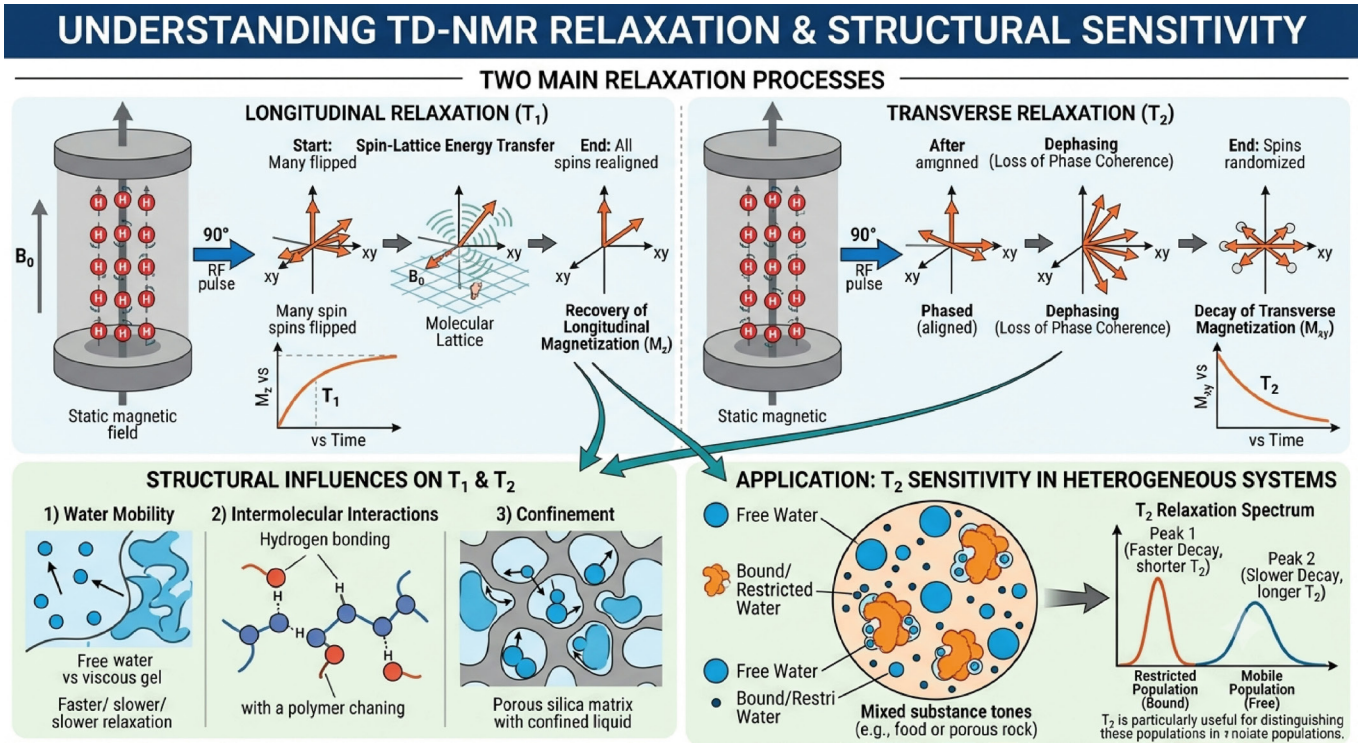

Figure 2. This diagram illustrates the physical principles of time-domain nuclear magnetic resonance (TD-NMR) relaxation and its application to structural characterization in complex and real-world matrices. Following a 900 radiofrequency pulse within a static magnetic field ($\boldsymbol{B_0}$), two fundamental processes drive the system back toward equilibrium: longitudinal relaxation (T_1), where nuclear spins exchange energy with the surrounding molecular lattice to recover z-axis magnetization ($\boldsymbol{M_z}$), and transverse relaxation (T_2), where spin-spin phase coherence degrades in the transverse plane ($\boldsymbol{M_{xy}}$). Both parameters depend directly on local molecular dynamics, including water mobility, hydrogen-bonding interactions with polymer networks, and physical confinement inside porous networks. In heterogeneous environments such as food or porous rock, T_2 spectral distribution effectively differentiates distinct hydrogen populations, mapping shorter T_2 values to restricted or matrix-bound molecules and longer T_2 values to unrestricted bulk liquid. Image created by the authors using Gemini AI tool from Google.

energy state antiparallel to the field (m = −1/2). The energy differential ΔE between these states is expressed as:

$$\Delta E = \hbar \gamma B_0 \qquad (2)$$

where ħ is the reduced Planck constant. This energy split dictates the characteristic Larmor frequency (ω_0) at which the nuclear spins precess around $\boldsymbol{B_0}$:

$$\omega_0 = \gamma B_0 \qquad (3)$$

At thermal equilibrium, the population distribution of spins between these two levels strictly obeys the Boltzmann distribution[19]:

$$\frac{N_{antiparallel}}{N_{parallel}} = exp\left(-\frac{\Delta E}{k_B T}\right) \qquad (4)$$

Because ΔE is remarkably small relative to the thermal energy (k_BT), there is only a minuscule fractional excess of spins in the lower energy state (on the order of parts per million)[20]. Despite its size, this net population bias creates a macroscopic net magnetisation vector, $\boldsymbol{M_0}$, pointing parallel to $\boldsymbol{B_0}$ along the longitudinal (z) axis.

The observable NMR signal is generated when an alternating radiofrequency (RF) magnetic field, $\boldsymbol{B_1}$, is applied perpendicular to the static magnetic field $\boldsymbol{B_0}$ at the Larmor frequency. The RF pulse rotates the net magnetisation from the z-axis into the transverse (*xy*) plane, and, after the pulse is terminated, the coherent precession of the transverse magnetisation induces a decaying voltage in the receiver coil[19]. This time-dependent signal is the Free Induction Decay (FID), which constitutes the primary time-domain signal acquired in TD-NMR. The FID reflects the loss of transverse coherence and is therefore directly related to T_2*, defined as the observed or effective transverse relaxation time, which includes both intrinsic transverse relaxation and magnetic-field inhomogeneity effects.

In contrast, T_2 is obtained by removing or minimizing the contribution of field inhomogeneities, typically through spin-echo or CPMG-based measurements, whereas T_1 is determined from the recovery of the longitudinal magnetisation using inversion- or saturation-recovery experiments[19]. Thus, FID, T_1, and T_2 are not interchangeable quantities: the FID is the raw time-domain signal from which relaxation information is obtained, while T_1 and T_2 are relaxation times derived from specific experimental measurements of longitudinal and transverse magnetisation, respectively (**Figure 3**). Their relationship is central to TD-NMR because changes in molecular mobility, interactions, and local environment modify the relaxation behaviour observed in the acquired time-domain signal.

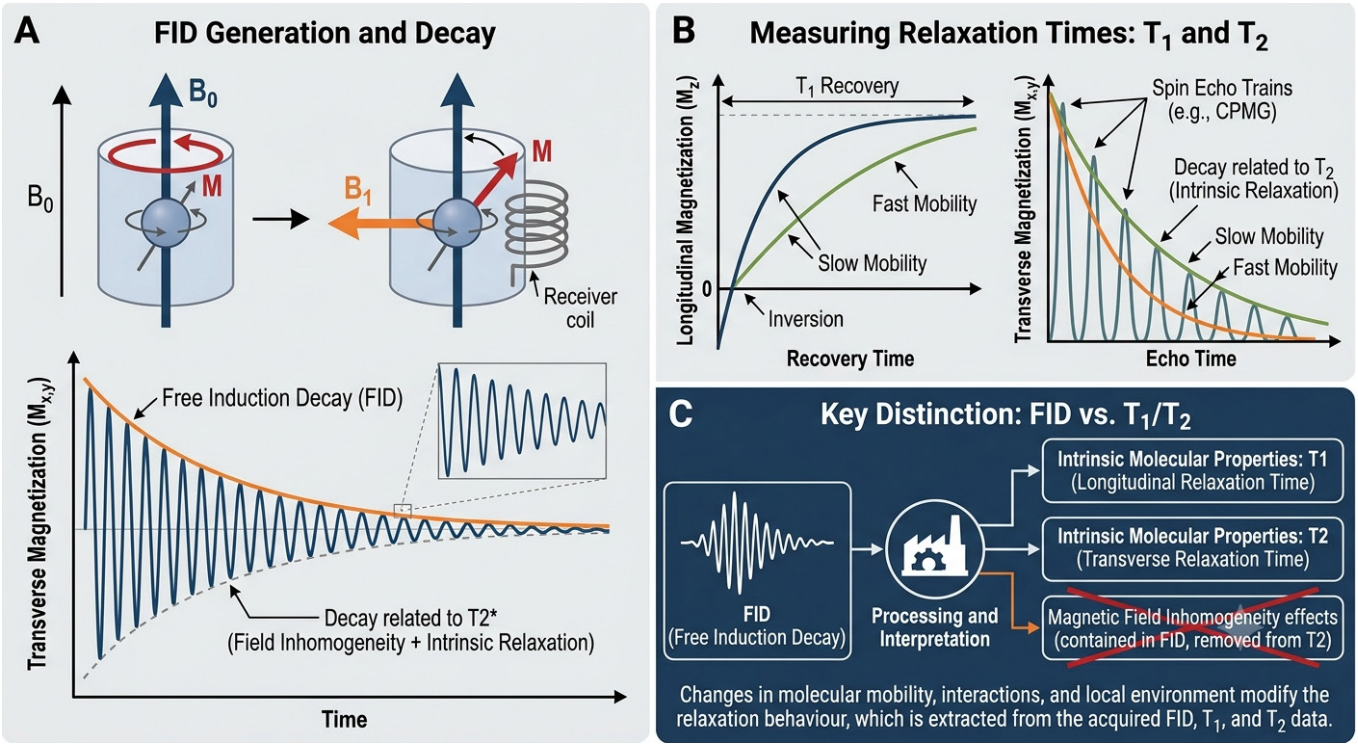

Figure 3. (A) An RF pulse rotates the magnetization into the xy-plane, where it then undergoes free induction decay (FID). The decay of the FID is characterized by T_2*. (B) Different pulse sequences are used to isolate specific relaxation times: spin-echo/CPMG for T_2 and inversion- or saturation-recovery for T_1. Image created by the authors using Gemini AI tool from Google.

FIELD INHOMOGENEITY: CHALLENGES AND APPLICATIONS

Although traditional NMR instrumentation prioritises highly homogeneous magnetic fields to ensure sharp resonance lines and precise quantitative measurements, valuable applications utilise inhomogeneous magnetic fields, particularly in portable or single-sided NMR devices[8,21]. In these compact systems, the static magnetic field $\boldsymbol{B_0}$) varies spatially, causing a spread in resonance frequencies ($\omega_0 = \gamma B_0$) across the sample. The resulting line broadening and accelerated dephasing are quantified by the effective transverse relaxation time (T_2^*), defined:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \Delta B_0 \qquad (5)$$

where ΔB0 represents the distribution of local field strengths.

Consequently, T_2^* is always shorter than the intrinsic T_2, reflecting the combined effects of molecular relaxation and field inhomogeneity[19].

Despite these limitations, inhomogeneous fields can be exploited for spatial encoding and depth profiling, as demonstrated by single-sided NMR[8,22]. Unlike conventional NMR, in which the sample is positioned within a highly homogeneous $\boldsymbol{B_0}$ field and spatial information is introduced through controlled magnetic-field gradients, single-sided NMR employs a unilateral magnet geometry that produces a strong and deliberately inhomogeneous $\boldsymbol{B_0(z)}$ field above the magnet surface[8]. This field configuration enables measurements outside the magnet and provides depth-dependent resonance frequencies, allowing spatially resolved measurements without requiring the sample to be enclosed within the magnet bore[8], as visualized in the comparative representation in **Figure 4**.

Consequently, the spatial dependence of $\boldsymbol{B_0(z)}$ can be used for depth profiling and position-sensitive measurements through gradient-echo or spin-echo sequences[8,21,22]. The echo amplitude, $\boldsymbol{M_{echo}(t)}$, in an inhomogeneous field can be modeled as:

$$M_{echo}(t) = M_0 exp\left(-\frac{t}{T_2^*}\right) \qquad (6)$$

where $\boldsymbol{M_0}$ is the initial magnetization[9].

APPLICATIONS AND FUTURE DIRECTIONS

Therefore, in low-field portable NMR, field inhomogeneity represents an inherent trade-off for instrument

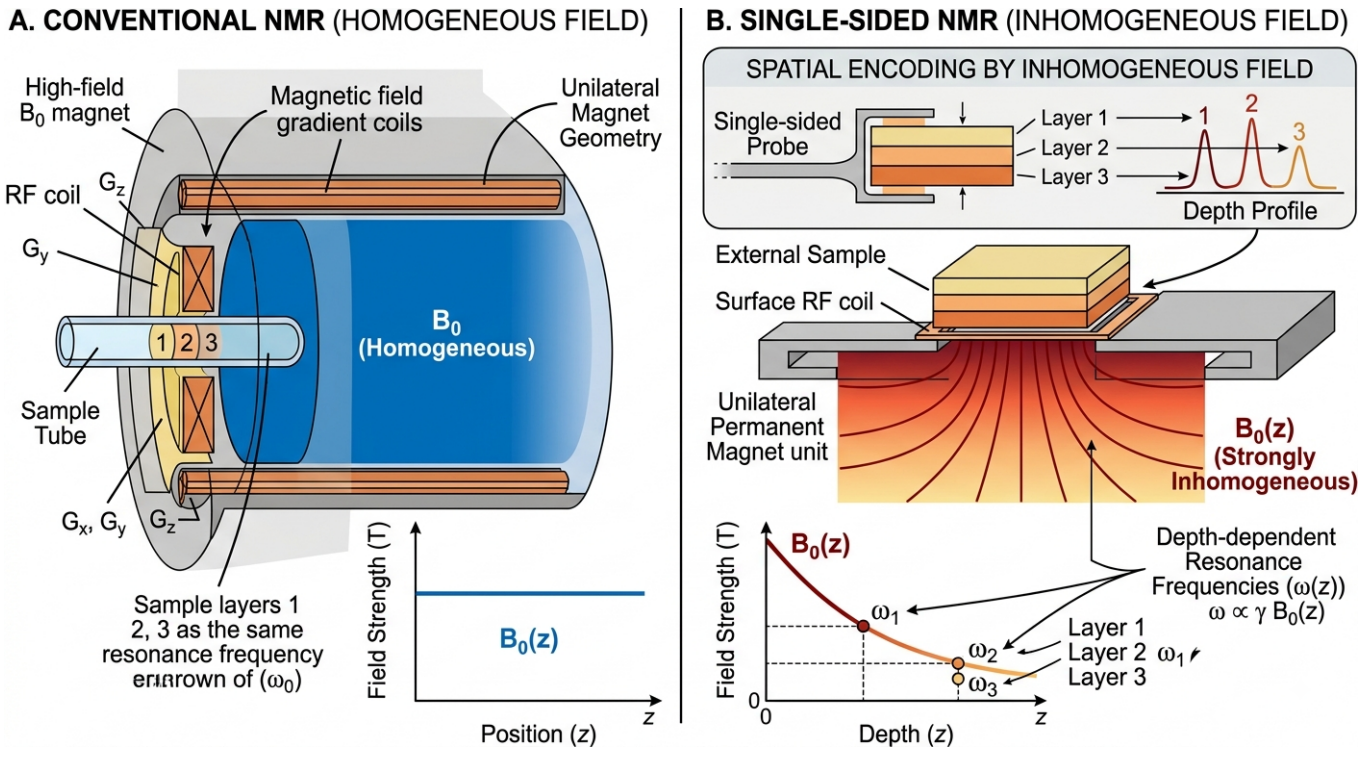

Figure 4. (A) Standard NMR utilizes a highly uniform main magnetic field ($\boldsymbol{B_0}$) where spatial information relies on active magnetic field gradient coils (G_x,G_y,G_z). (B) Single-sided NMR employs an open-geometry permanent magnet that generates an intentionally non-uniform field $\boldsymbol{B_0(z)}$ extending outside the unit. This steep field gradient directly links depth (z) to unique resonance frequencies ($\omega(z)=\gamma B_0(z)$), enabling precise spatial profiling of external samples without requiring an enclosed magnet bore. Image created by the authors using Gemini AI tool from Google.

simplicity and lower cost. Nevertheless, advances in pulse sequence design, such as the Carr-Purcell-Meiboom-Gill (CPMG) sequence, and signal processing methods like inverse Laplace transforms (ILT) enable the robust extraction of relaxation distributions even under non-ideal conditions[9,23]. Therefore, while homogeneous fields yield optimal spectral resolution, engineering solutions for inhomogeneous fields expand the practical reach of NMR, establishing these benchtop advancements as universal, non-invasive probes accessible outside of centralised, resource-intensive facilities.

The impact of this maturity is most visible in the food industry, where TD-NMR has become a primary method for non-destructive analysis. Recent studies[9,10] demonstrate that, unlike traditional wet chemistry, which destroys samples using hazardous solvents, low-field NMR distinguishes between bound, entrapped, and free water fractions in real time, even in packaged foods **(Figure 5**). Consequently, this capability allows for the precise quantification of moisture migration in meat and dairy, providing critical data for shelf-life prediction. Furthermore, the formal adoption of peer-verified methods, such as the Association of Official Analytical Chemists (AOAC) Performed Verified Methods (PVM) 1:2003[24], underscores a broader, consistent, and necessary movement toward sustainable, solvent-free industrial quality control that prioritises sample integrity over destructive extraction.

Additionally, in the field of polymer characterisation, this technique is indispensable for quantifying cross-link density and crystallinity[25]. Through the analysis of the relaxation behaviour of ^1H nuclei, the technique effectively differentiates between rigid domains (e.g., crystalline or highly cross-linked regions) and mobile phases (amorphous or sol fractions) by the measurement of T_1 and T_2 relaxation times[15]. Similarly, in catalysis, TD-NMR has proved highly effective for probing liquid-phase behaviour within porous structures. As discussed by Suekuni et al. (2025)[26], this approach excels at characterising surface adsorption and wetting, allowing researchers to quantify how reactants and products interact with catalyst surfaces via measurements of adsorption energy and liquid distribution across porous beds. Thus, these small magnets fill a significant analytical gap by providing insights into length scales ranging from nanometres to micrometres, data that is fundamentally complementary to molecular-level spectroscopy.

For instance, in Cultural Heritage (**Figure 6**), researchers can characterise the porosity of ancient scrolls, ceramic fragments, documents, and paintings to better understand ancestral techniques[27]. Simultaneously, in engineering, the equipment facilitates the development of sustainable construction materials[28], while in food science, it allows for the precise monitoring of the oxidative stability of oils and fats[12,29], paving the way for groundbreaking research into native Andean oils and fats. Consequently, these instruments hold the potential to foster multidisciplinary projects that rely on rapid, non-destructive, and highly reproducible physical-chemical data.

This robustness further extends into the highly regulated world of biopharmaceuticals. As reported by Almeida et al. (2025)[11], the main benefit of TD-NMR in pharmaceuticals (**Figure 7**) is that it can tell different forms of a substance apart and measure the amount of non-crystalline material in complicated mixtures, usually without needing a lot of sample preparation or calibration curves. Thus, by utilising compact benchtop equipment equipped with permanent magnets, TD-NMR bridges the gap between sophisticated laboratory R&D and at-line industrial quality control. This accessibility enables the continuous monitoring of Active Pharmaceutical Ingredient (API) stability and hydration behaviour, ensuring the safety and efficacy of final dosage forms. Furthermore, this technology significantly reduces both measurement time and operational costs compared to traditional methods.

Simultaneously, miniaturisation has catalysed a move towards point-of-care medical diagnostics. The development of ultra-low-field spectrometers operating in the

a) **b)**

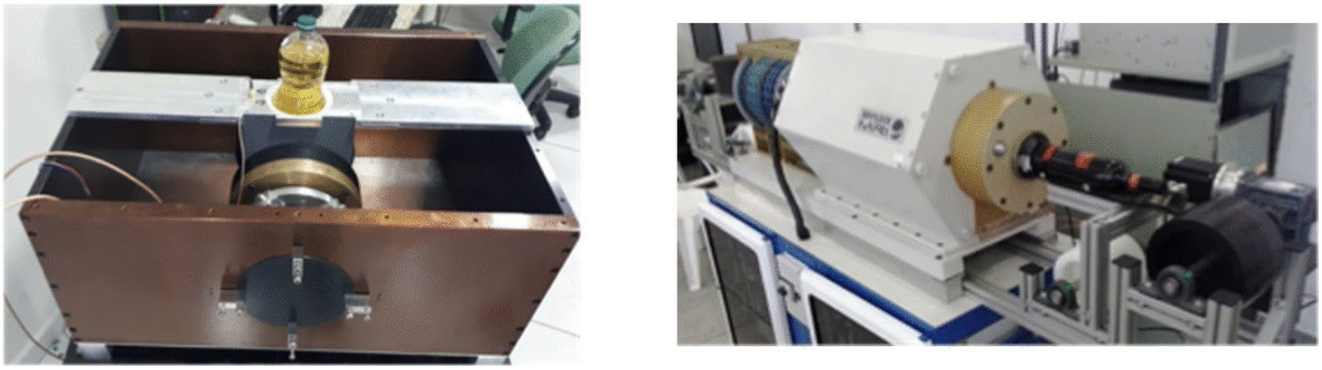

Figure 5. TD-NMR instruments equipped with a Halbach magnet array are utilized to analyze packaged commercial products. These devices feature a closed magnetic structure, positioning samples within a coil region that maintains a consistent and homogenous magnetic field. A) A TD-NMR spectrometer model Specfit HR 100 with resonance frequency of 4.2 MHz for ^1H. B) A TD-NMR Halbach Spinlock spectrometer, model SKL-IF-1399 operating at a resonance frequency of 9 MHz for ^1H. Image taken by the authors at the NMR lab at Embrapa Instrumentação, São Carlos, Brazil.

Figure 6. Applications of the TD-NMR for cultural heritage study: Examples include scrolls and documents (top left: Dead Sea Scrolls); ancient mummies and bones (top right: Rameses II); paintings (left: Fra Bartolomeo's Madonna and Child); frescoes and mosaics (right: Herculaneum wall painting); and musical instruments (bottom: Stradivarius violin). Reproduced from Baias, M. Mobile NMR: An Essential Tool for Protecting Our Cultural Heritage. *Magnetic Resonance in Chemistry* **2017**, *55* (1), 33–37. Licencia CC BY 4.0.

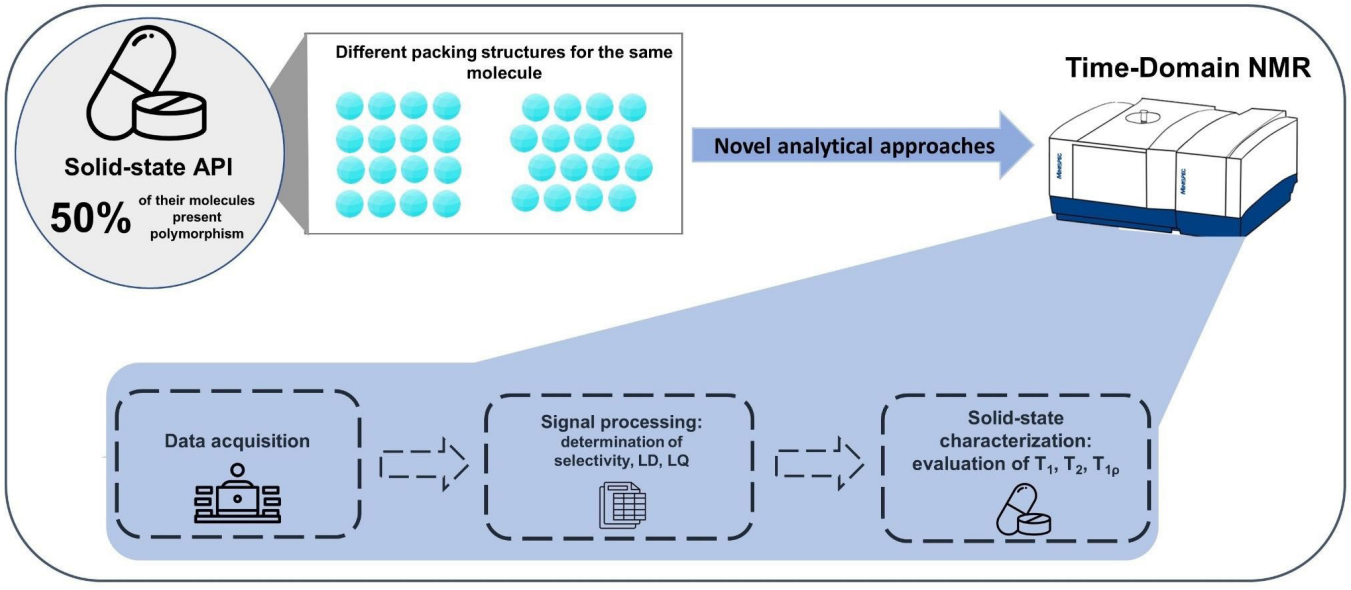

Figure 7. Workflow for characterisation of API polymorphism using TD-NMR. The process integrates data acquisition and signal processing to evaluate relaxation times (T_1, T_2, and $T_{1\rho}$), enabling the differentiation of distinct crystal packing structures in solid-state pharmaceuticals. . Figure adapted by Luisa Souza Almeida, with permission, from Almeida, L. S.; Carneiro, J.; Colnago, L. A. Time Domain NMR for Polymorphism Characterization: Current Status and Future Perspectives. *Int. J. Pharm.* **2025**, *669*, 125027.

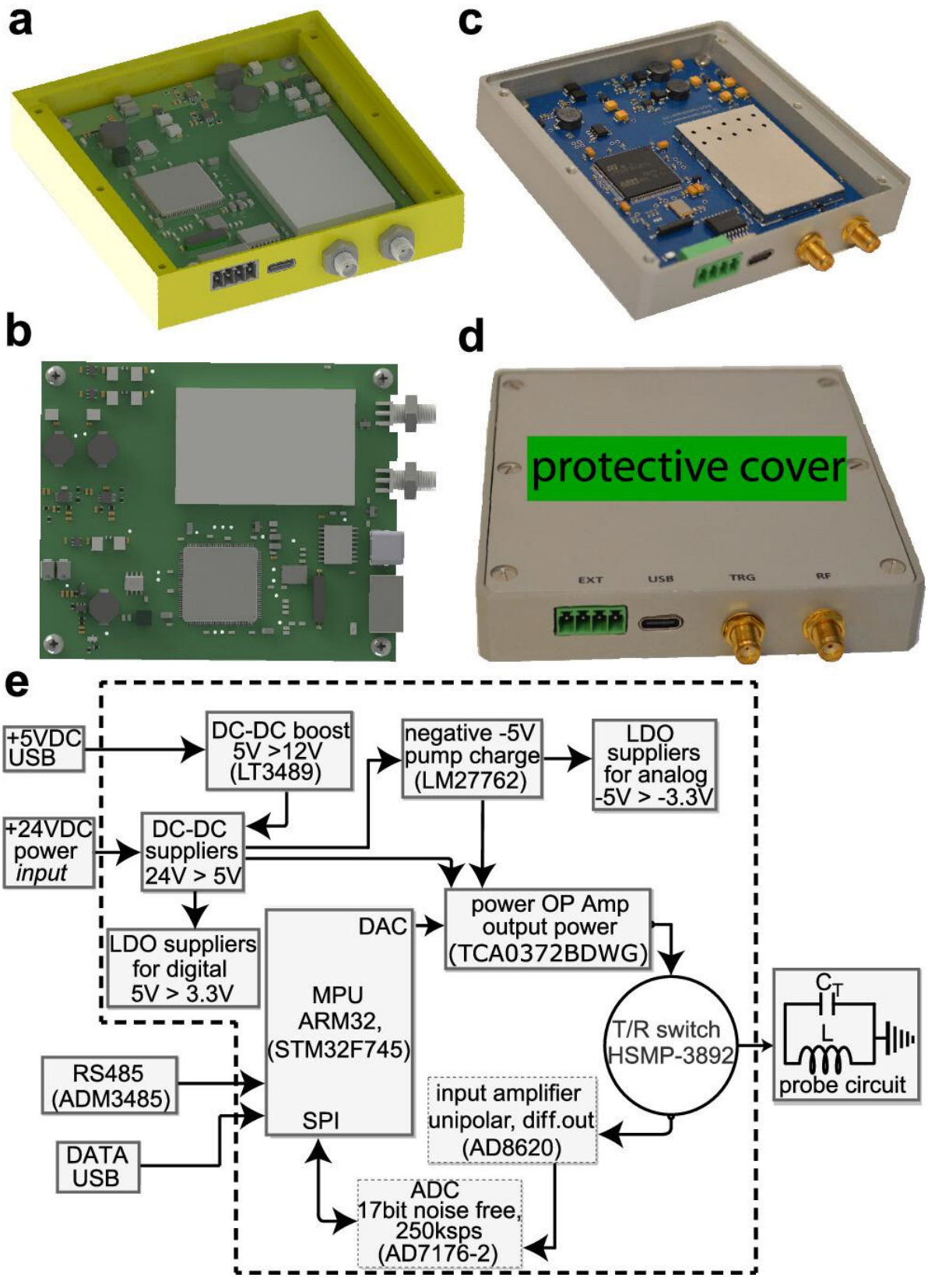

Figure 8. (a) 3D model and **(b)** internal photograph of the device with the top cover removed. **(c)** 3D rendering of the printed circuit board (PCB) layout. **(d)** External view of the fully assembled device; dimensions are 10 cm × 10 cm × 2.0 cm. **(e)** Functional block diagram of the system. Image reprinted with permission from Chowdhury, M. R. H.; Ahmed, F.; Oladun, C.; Adelabu, I.; Abdurraheem, A.; Nantogma, S.; Birchall, J. R.; Gafar, T. A.; Chekmenev, Y. A.; Nikolaou, P.; Barlow, M. J.; Goodson, B. M.; Shcherbakov, A.; Chekmenev, E. Y. Low-Cost Purpose-Built Ultra-Low-Field NMR Spectrometer. *Anal. Chem.* **2024**, *96* (42), 16724–16734. © 2026 American Chemical Society.

kilohertz range has produced NMR devices weighing as little as 370 grams (**Figure 8**)[30]. Powered via USB-C and paired with hyperpolarised contrast media, such as [^{13}C] pyruvate or ^{129}Xe gas, these portable spectrometers analyse standard sample volumes that typically range from 0.5 to 1 mL. This system employs an automated "pulse-wait-acquire-recover" sequence, enabling the direct acquisition of high-level magnetic resonance data at a patient's bedside without the need for specialised operators. This advancement effectively moves cutting-edge metabolic profiling studies from the centralized laboratory to the point of care by removing the financial and logistical barriers associated with traditional NMR.

Finally, a digital movement toward software democratisation consolidates the analytical maturity of TD-NMR (**Figure 9**). The historical "black box" nature of NMR data has been overcome by online platforms, such as the https://nmr-ilt.esalq.usp.br/processing, that automate the processing of Inverse Laplace Transforms (ILT)[23]. These advancements make complex mathematical tools, such as Tikhonov regularisation[31], accessible to the broader scientific community, ensuring that relaxation distributions remain reproducible and transparent.

Ultimately, this convergence of hardware and software indicates that the narrative of magnetic resonance is no longer defined by the strength of the field, but by the intelligence and the accessibility of the application. The most significant breakthroughs are no longer confined to specialised basements; they are happening wherever a small magnet can be placed.

LIMITATIONS AND CHALLENGES

Despite the substantial progress in TD-NMR technology, several critical limitations persist that constrain its broader adoption and performance. One of the most significant challenges arises from the inherently lower sensitivity associated with low magnetic field strengths. The net magnetisation, and thus the signal-to-noise ratio (SNR), is directly proportional to the strength of the static magnetic field ($\boldsymbol{B_0}$), which limits the detection of analytes at low concentrations and diminishes spectral resolution compared to high-field instruments[8,19].

Field inhomogeneity is not an intrinsic limitation of TD-NMR spectroscopy but rather an instrumental factor that depends on the magnet design and the specific configuration of the NMR system. In conventional high-field NMR spectrometers, extensive magnetic-field homogeneity is maintained through careful magnet design and shimming, whereas compact and portable TD-NMR instruments based on permanent magnets may exhibit larger spatial variations in $\boldsymbol{B_0}$. Such variations can broaden resonance signals and contribute to differences between (T_2*) and the intrinsic (T_2), potentially affecting measurements that depend on spectral resolution or accurate characterization of relaxation components[8,21,22]. However, most TD-NMR applications rely on time-domain relaxation measurements, particularly CPMG-based (T_2) determination, which uses refocusing pulses to reduce the effect of static field inhomogeneity. Consequently, the impact of ($\boldsymbol{B_0}$) inhomogeneity depends on the instrument and measurement being performed rather than representing

Figure 9. Image capture of a NMR data processing performed using the online platform available at https://nmr-ilt.esalq.usp.br/processing

a fundamental limitation of TD-NMR itself. In instruments specifically designed for relaxation measurements, including systems with a sufficiently homogeneous field over the sample volume, this effect can be minimized and does not necessarily compromise quantitative (T_2) analysis[8].

Moreover, reproducibility and standardization also remain areas of concern. Although the adoption of international protocols (e.g., ASTM, ISO, and AOAC methods) has improved cross-instrument comparability, discrepancies can still arise from differences in magnet configuration, sample positioning, and temperature control[9,32]. Such factors complicate the establishment of universally accepted calibration standards, particularly for complex or heterogeneous samples.

Efforts to miniaturize and reduce the cost of TD-NMR devices, while expanding accessibility, introduce further technical challenges. Reduced sample volumes and simplified hardware can exacerbate SNR limitations and increase susceptibility to external electromagnetic interference[33]. Moreover, miniaturized devices often lack advanced temperature stabilization, contributing to baseline drift and measurement variability.

Another significant challenge lies in the interpretation of relaxation data, especially in systems with overlapping relaxation distributions, which relies on sophisticated mathematical post-processing, such as the ILT. These analyses are sensitive to noise and regularization parameters, sometimes leading to ambiguous or non-unique solutions[23,34]. The "black box" nature of some analytical pipelines may further challenge transparency and reproducibility.

Finally, addressing these collective challenges will require coordinated advances across hardware design, electronics, calibration methodology, and open-source data analysis tools. Continued development of standardized protocols and inter-laboratory benchmarking will be essential to fully consolidate the potential of TD-NMR as a robust and widely adopted spectroscopy method for addressing the modern challenges in analytical chemistry.

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