Sub-millimetric ultra-low-field MRI detected in situ by a dressed atomic magnetometer

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Magnetic Resonance Imaging (MRI) is universally acknowledged as an excellent tool to extract detailed spatial information with minimally invasive measurements. Efforts toward ultra-low-field (ULF) MRI are made to simplify the scanners and to reduce artefacts and incompatibilities. Optical Atomic Magnetometers (OAMs) are among the sensitive magnetic detectors eligible for ULF operation, however they are not compatible with the strong field gradients used in MRI. We show that a magnetic-dressing technique restores the OAMs operability despite the gradient, and we demonstrate sub-millimetric resolution MRI with a compact experimental setup based on an in situ detection. The proof-of-concept experiment produces unidimensional imaging of remotely magnetized samples with a dual sensor, but the approach is suited to be adapted for 3-D imaging of samples magnetized in loco. An extension to multi-sensor architectures is also possible.

Isidor Rabi was awarded the Nobel Prize in Physics in 1944 for his seminal research, which, in 1938, demonstrated the phenomenon of nuclear magnetic resonance (NMR) in a molecular beam [1]. Felix Bloch and Edward Purcell were awarded the Noble Prize for their independent contributions to NMR (dated 1946) [2, 3] in 1952, the same year in which Robert Gabillard, in his PhD thesis, studied the NMR in the presence of magnetic field gradients (a crucial step in view of encoding spatial information in the precessing nuclei). It took two additional decades to realize that the potential of NMR to record spatial distribution of precessing nuclei could be exploited as a medical diagnostic tool [4]. The applicability of the idea of Raymond Damadian was demonstrated by Peter Mansfield and Paul Lauterbur [5], which thirty years after were awarded the Nobel Prize.

The attractiveness of MRI in medicine relies on its accurateness and on its substantially non-invasive nature. The latter feature is shared with ultrasonography [6], whose development occurred almost simultaneously with MRI. Both methodologies are spreadly used and constitute favourite choices with respect to more invasive imaging techniques based on ionizing radiation.

The great impulse impressed to the development of the MRI technology, led to fast and impressive progresses in the methodologies used to generate, detect, and analyze MRI signals. These advances were facilitated by the parallel progresses achieved in some related technologies, such as electronics, computer science and cryogenics.

Most of MRI and, more generally, NMR advances followed the straightforward direction of enhancing strength and homogeneity of the magnetic field (or accurate control of its gradients) as well as increasing the signal-to-noise ratio (SNR) of the detection stage. Cryogenics and superconductor technologies constituted an obvious opportunity for this evolution.

At the same time, cryogenics—allowing the development of innovative detectors (superconducting quantum interference devices, SQUIDs) with unrivaled sensitivity—made available alternative (non inductive) sensors, and opened the perspective of performing NMR and MRI at much lower precession frequencies, that is at low and ultra-low field strengths [7].

The ULF-NMR dates about three decades, similarly to ULF-MRI [8], for which intense progresses started, however, less than two decades ago [9, 10].

MRI in the ULF regime comes with several valuable advantages [7]. The ultimate spatial resolution of MRI is determined by the NMR spectral resolution, that depends on the absolute field inhomogeneity. At ULF, a modest relative field homogeneity turns out to be excellent on an absolute scale: very narrow NMR lines with a high SNR can be recorded in ULF regime, using relatively simple and unexpensive field generators [11-13]. The encoding gradients necessary for MRI can be generated by simple and low-power coil systems, as well [9, 13]. Further important advantages brought to MRI by ULF regime include the minimization of susceptibility [15] and conductance [12, 16] artefacts. Other delicate instrumentation (not compatible with strong and/or fast-varying magnetic fields) can be used in conjunction with ULF-MRI in more complex setups. In addition, the non-conventional magnetic detectors used in ULF-MRI can be used to record low-frequency magnetic signals originating not only from the precessing nuclei, but also from other (e.g. biomagnetic) sources. Hybrid instrumentation enabling multimodal MRI and magneto-encephalographic measurements in medical applications has been
demonstrated \cite{17} (see also Chap. 5 in Ref. \cite{7}).

While in conventional NMR and MRI, the premagnetization and precession are typically induced by one field, the two functions are often distinguished in ULF apparatuses. Here, the precession field can be extremely weak, and the homogeneity of the (strong) premagnetization field is not a critical parameter. It is worth mentioning that schemes of no-magnet NMR, with zero precession field and alternative premagnetization methods have been proposed \cite{18}.

There exists some incompatibility of SQUID sensors with strong fields (such as those used for premagnetization or spin manipulation), and this problem can be overcome using atomic magnetometers (OAMs) as alternative, robust high-sensitivity detectors \cite{19}. Beside robustness, OAMs bring the advantage of not requiring cryogenics, so to be a favourite choice whenever ULF systems are designed in view of building up simpler and low-cost apparatuses. Despite their simplicity, OAMs – in some implementations – may compete with SQUIDs in terms of sensitivity. In facts, the literature reports successful ULF-MRI experiments using both SQUIDs and OAMs as highly sensitive, non-inductive sensors \cite{20, 21}.

OAMs operate on the basis of paramagnetic atoms in which an atomic magnetic resonance (AMR) is induced using resonant light as a polarization tool (modern laser spectroscopy methodologies provide very effective instrumentation to this end) \cite{22}. The sensitivity of OAMs relies on the narrow spectral width of the AMR. The important field gradients necessary for MRI applications would broaden severely the AMR. As matter of fact, the ULF-MRI results obtained so far with OAM detection are based on ex-situ measurements: the magnetic signal produced by the precessing nuclei is coupled to the sensor via flux transformers \cite{23}, eventually resulting in remote-detection techniques \cite{24}.

In this letter we demonstrate that an approach based on an inhomogeneous magnetic dressing of the precessing atoms \cite{23} can be used to record in situ MRI signals by means of OAM, achieving sub-millimetric resolution. The described proof-of-concept experiment makes use of a dual sensor, but paves the way to multi-sensor detection, with the potential of improving the spatial resolution, enhancing the allowed sample size, and speeding up the acquisition.

The described setup performs MRI of samples premagnetized in strong field and subsequently transferred to the detection region, however the robustness of OAMs to strong magnetic fields would enable MRI of samples premagnetized in the same position where the NMR signal is detected, so to obtain a fully static operation. The core of the setup (see Fig. 1) is a dual channel OAM working in a Bell and Bloom configuration \cite{26}.

The strength and the first-order gradient of the field in which the OAM operates are numerically controlled and optimized. Namely, eight numerically controlled current terms and guarantee the field alignment along a fixed direction.

Sources \cite{27} supply the field and field-gradient coils. Automated procedures enable the nulling of the gradient terms and guarantee the field alignment along a fixed direction.

The dual sensor detector produces two magnetometric signals which contain the measurement of field variations due to both far-located and close-located sources. The first contribution is dominant and appears with the same sign on the two sensors. The second term appears with opposite signs, provided that the close-located source is opportunely displaced with respect to the sensors.

The two signals are recombined to extract their common mode (CM) term and difference-mode (DM) term: far-located sources (which in our measurement constitute a disturbance) contribute to the CM only, while the MRI signal appears in the DM one. Compensating the CM term has a twofold advantage: (i) the disturbances and drifts of the field which would affect the nuclear precession are removed; (ii) unavoidable imperfections of the differential system (a limited CM-rejection ratio) let the CM appear residually with the DM term, thus a preliminary reduction of the CM term improves the DM signal-to-noise ratio.

To this aim, while extracting the MRI signal from the DM term, the CM term is used to feed a self-optimized closed loop system \cite{28} to actively compensate the exter-

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**FIG. 1.** The laser beams (in red) propagate along the $x$ direction and cross parallelly two atomic cells (in blue). A static magnetic field is oriented along $z$ and varies with the position $x$ to the purpose of performing frequency encoding. Electromagnets (in yellow) produce a strong dressing field oscillating along $x$ much faster than the atomic Larmor frequency. The dressing field has a position-dependent intensity, such to restore the AMR width. The NMR sample cartridge (in dark and light grey) is represented sectioned to show the internal structure. Both the cartridge and the cells are merged in the inhomogeneous field required for the MRI frequency encoding (typical values are $B_z = 4 \mu T$ and $\partial B_z / \partial x = 40 \text{ nT/cm}$), and the magnetometer sensitivity is restored by the inhomogeneous dressing.
nal disturbances, which are strongly present due to the unshielded nature of the set-up.

As represented in Fig. 1, both the Cs atoms and the sample protons precess around a static (stabilized) field $B_x$ oriented transversely with respect to the beam propagation axis ($x$). The field $B_x$ is made dependent on the position $x$ to the purpose of performing MRI frequency-encoding. Its gradient $G = \partial B_x / \partial x$ is set by permanent magnets arranged in a quadrupolar configuration: $B_x = B_0 + Gx$, where $B_0$ is the field at the center of the cell. The proton and Cs Larmor frequencies set by the dressing field oscillating along $x$, degrading and eventually destroying the OAM operativity.

To this end, each sensor is coupled to an electromagnetic $B_D$ source (a coil wound on a hollow-cylinder ferrite, with the laser beams passing across the hole).

In a dipole at a distance $x$ from the center of the cell, the dressing field $B_D$ is

$$B_D(x,t) = \frac{\mu_0}{2\pi} \frac{m(t)}{(x_0 + x)^3} = B_{D0}(x) \cos(2\pi ft),$$

where $\mu_0$ is the vacuum permittivity, $m(t) = m_0 \cos(2\pi ft)$ is the oscillating dipole momentum, and $x_0$ is the distance of the dipole from the cell center.

Taking into account the dependence on $x$ of both the static and the dressing fields, $M_x$ oscillates harmonically at a frequency

$$\nu_D(x) = \frac{\gamma_{Cs}}{2\pi} (B_0 + Gx) J_0 \left( \frac{\gamma_{Ds}B_D(x)}{2\pi f} \right),$$

in a first-order Taylor approximation,

$$\nu_D(x) = \nu_D(0) + \nu_D'(0)x + O(x^2) 
\approx \frac{\gamma_{Cs}}{2\pi} \left( B_0 J_0(\alpha) + \frac{3B_0 x_0 J_1(\alpha)}{x_0} + GJ_0(\alpha) \right) x,$$

where $\alpha = (\mu_0/4\pi^2)(\gamma_{Cs}m_0)/(fx_0^3)$, so that the condition for compensating the effect of the gradient $G$ reduces to

$$- 3 \frac{B_0 x_0 J_1(\alpha)}{J_0(\alpha)} = G.$$ 

Under this condition, the OAM performance is recovered, so to guarantee the sensitivity necessary to detect MRI signals. It is worth noting that the dressing effect is negligible for protons, because of their much smaller gyromagnetic factor: $\gamma_H \ll \gamma_{Cs}$, which makes $J_0(\gamma_H B_D/2\pi f) \approx 1$.

Differing from the case studied in Ref. [25], here two distinct Cs cells are used, each of them equipped with a dressing dipole: an arrangement that increases the NMR signal improving the MRI performance. With this feature, the present results demonstrate that a multiplet sensor arrangement can be built, with one oscillating IDEA dipole for each sensor. It is possible to maintain cross-talking between dressed sensors at a negligible level.

The NMR sample is made of water protons contained in a polymeric cartridge having the structured shape shown in Figs. 1 and 2: it is a cylinder –19 mm in diameter, 32 mm in length— that contains three disks –2 mm in thickness— separated by 5 mm from each other, the water (in hydrogel) is confined in the four complementary disks. Care is taken to avoid ferromagnetic contamination of the container.

The setup includes an Halbach permanent-magnet assembly to premagnetize the sample at 1 T and a pneumatic shuttle system [32] to move it cyclically to the measurement region (see Refs. [33, 34] for additional details).

The cartridge position along $x$ slightly changes shot-by-shot. At each measurement, a camera monitors such sample positioning with respect to the sensors. An automated image analysis provides a localization $x_C$ (with respect to a fixed origin of the camera abscissa) with an uncertainty of 0.08 mm. The $x_C$ data are registered together with the corresponding NMR traces to be used in post processing.

Correspondingly to the cartridge internal structure shown in Fig. 2(a), a 1-D MRI profile is reported in Fig. 2
situ detection of the NMR signal, despite the presence of sensors are integrated by IDEA coils, which enable the OAM detector operated in unshielded environment. The millimetric ULF-MRI setups with a dual Bell and Bloom conclusion, this work demonstrates the feasibility of sub-
time-traces that finally result in the MRI profiles shown in Fig. 2. The panel a shows a photograph of the open cartridge with its internal structure. In the panel b an unidimensional image is shown as reconstructed from an average trace corresponding to tight (0.08 mm interval) positioning of the sample. Both a and b are in the same scale, blue lines associate MRI peaks to their origin in cartridge volume.

That profile is obtained by averaging over 300 traces. The latter are selected on the basis of the measured values, which in this case fall within a 0.08 mm interval. The 1-D image clearly shows the four peaks corresponding to the hydrogel disks. Such plot is directly obtained in-loco magnetization, i.e. in full-static experiments. The spatial resolution is set by the NMR intrinsic and instrumental linewidth, which –in absence of field gradient– amounts to 1.5 Hz: its effect is only partially compensated in the spectral analyses used in this paper.

For an alternative evaluation of the MRI spatial resolution, we use a set of traces collected in more than 2000 shots. Subsets of traces corresponding to narrow intervals in the statistic distribution of values are averaged to produce MRI profiles. The profile displacements are then compared with the variations.

In Fig. 3 the panel b shows the histogram of positions and five subsets extracted to produce the average time-traces that finally result in the MRI profiles shown in a. The four-peaks profile shifts progressively in accordance with the , with submillimetric accuracy. In conclusion, this work demonstrates the feasibility of sub-millimetric ULF-MRI setups with a dual Bell and Bloom OAM detector operated in unshielded environment. The sensors are integrated by IDEA coils, which enable the in situ detection of the NMR signal, despite the presence of the strong gradient necessary to the frequency encoding. The methodology can be applied in setups contemplating in-loco magnetization, i.e. in full-static experiments. Multi-sensor setups can be designed on the same bases, which would improve the sensitivity and/or enable ULF-MRI of large-size samples.

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FIG. 3. a The histogram shows the distribution of $x_C$ over a large set of measurements. Five subsets of measurements corresponding to narrow intervals of $x_C$ have been selected to reconstruct the MRI traces shown in the panel a. To this end, the selected time traces are averaged and analysed by FFT: the real part of the Fourier transform is shown. The inclined blue line guides the eyes to localize the leftmost peak position of each image as it varies along the histogram (3.5 mm from the upper to the lower plot). The maxima displacements match the corresponding camera estimations $x_C$ with submillimetric precision.

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