LOCAL CHARACTERISATION OF BIOMAGNETIC MATERIALS

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▴ Albatross using the Earth magnetic field for orientation

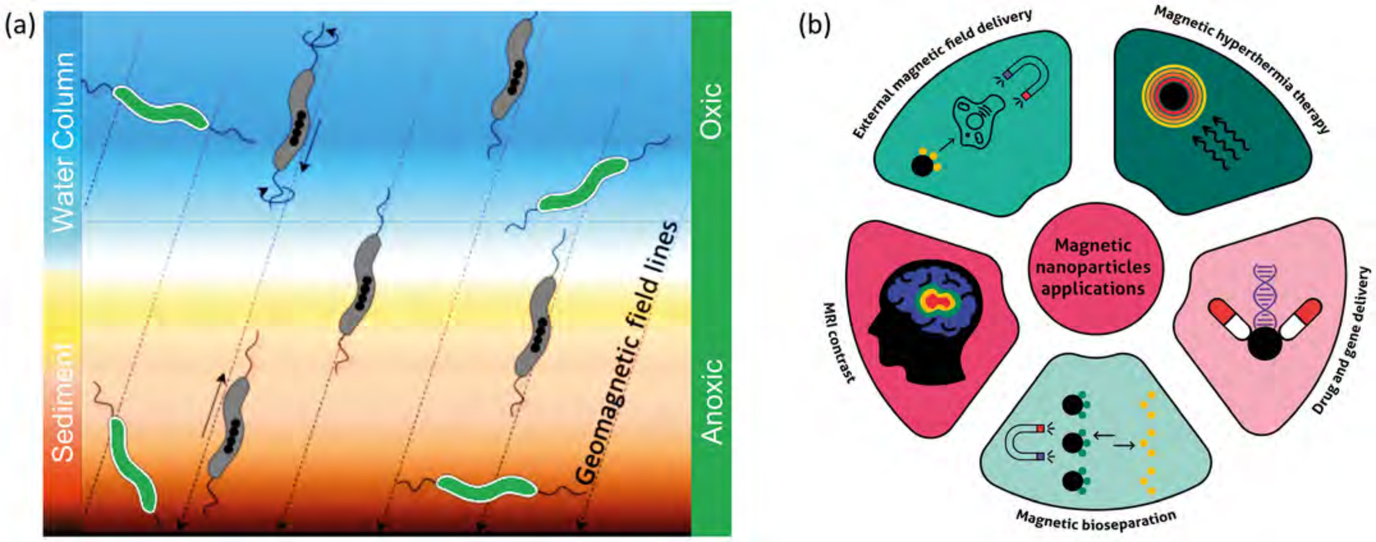
Magnetic materials offer attractive applications in biomedicine with a variety of applications from sensors to diagnosis and treatment. Special attention deserves the nanofeature elements as the nanostructured surfaces or the nanoparticles that have been proposed as alternatives for drug delivery vectors, bactericide treatments, lab-on-a-chip sensors, hyperthermia-based cancer therapy, magnetic bio-separation or emerging magnetic resonance imaging (MRI) contrast agents.

Despite the numerous advances in the synthesis of biomagnetic nanomaterials, challenges remain in its local characterisation and in particular, in the study of isolated elements at the nanoscale. In this work, we will give an overview of the most promising techniques to characterise magnetic nanostructures of importance in bioapplications.

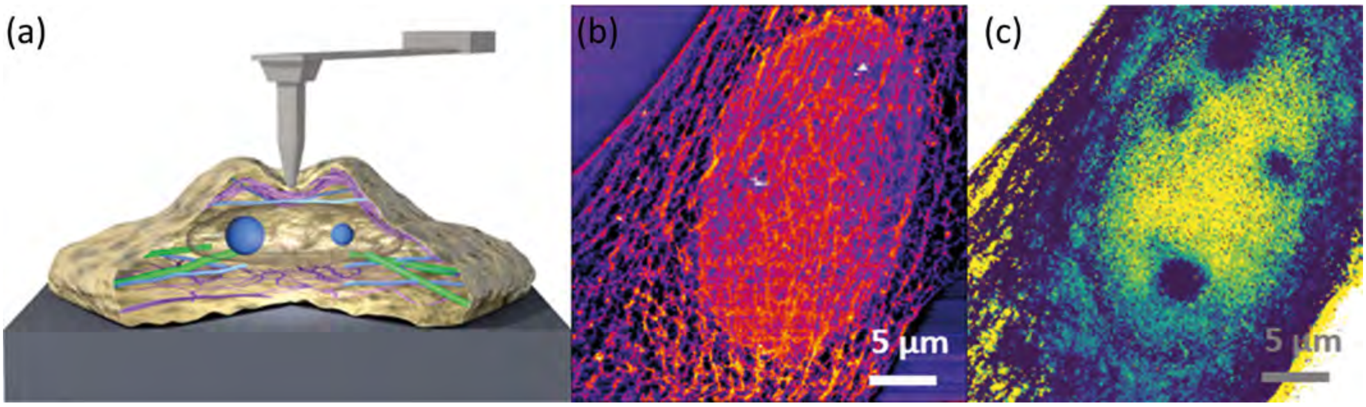
State of the art

The field of Biomagnetism encompasses a broad range of topics in magnetism associated to life elements. This includes the mechanism employed by various living organisms for navigation based on the Earth's magnetic field [1, 2]. Additionally, Biomagnetism investigates the magnetic properties of biomaterials and the effect of the magnetic fields in those elements. Biomaterials with magnetic properties have gained significant attention in recent years due to their unique properties and potential applications in various fields, including biomedicine, biotechnology, sensing and environmental science. Special attention deserves the magnetic nanoparticles [3], their characterisation is key for unravelling the underlying the physical principles that inspire some current biomedical applications.

Despite the numerous advances and promising vistas that biomagnetic materials unveil, challenges persist on multiple fronts. These challenges cover the study of stability, improved magnetic properties, compatibility or long-term safety. Further dedicated research is needed to surmount these obstacles and



▾ **FIG. 1:** (a) Sketch of the magnetotaxis process used by magnetotactic bacteria for swimming along the Earth's field lines. (b) Courtesy of M.L. Fdez-Gubieda. Overview of different applications of Magnetic Nanoparticles in biomedicine. Adapted from [4].



▲ **FIG. 2:** (a) Schematic layered structure of a eukaryotic cell with its different components. b) Topography and (c) Viscosity map of the actin cytoskeleton. Adapted from [10].

thereby, effectuate a full comprehensive understanding of these materials.

Apart from the structural characterisation via electron microscopy techniques, mainly Scanning Electron Microscopy (SEM) and High-Resolution Transmission Electron Microscopy (HRTEM), the most extended characterisation methods are based on optical microscopy techniques. These techniques furnish a non-invasive alternative for morphological and functional characterisation of the living specimen under observation. From well-established methods such as phase contrast microscopy, differential interference contrast microscopy, digital holography and fluorescence microscopy, to the more contemporary nonlinear optical multi-photon microscopy, the spectrum is rich and diverse [5].

Focusing towards magnetic properties, it is imperative to highlight that the investigation of magnetic fields generated by biomagnetic entities requires high-sensitivity magnetometers. These instruments must exhibit resolutions up to $1\ fT/\sqrt{Hz}$ all within a frequency range between 0.1 and 1000 Hz. These high demanding requirements magnifies when the size of the materials or the working area are reduced to the nanoscale. The study of tissues, cells, nanoparticles or molecules and the discernment of the intricate relationship between structure and function, stand as formidable tasks, demanding advancements in sample preparation, sensing methodologies, advanced measurements and sophisticated data management. Intriguingly, the topic of biomagnetic sensing also involves the exploration of diverse magnetic phenomena, such as giant magneto-resistance effect, nuclear magnetic resonance, superconducting quantum interference or giant magnetoimpedance effect [6].

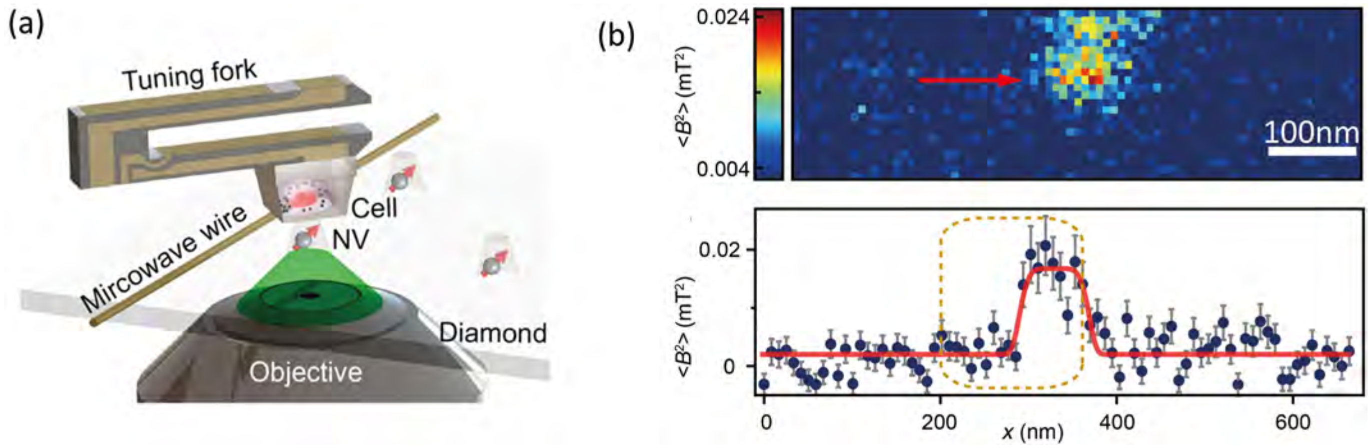
However, it's worth noting that the majority of prevailing techniques for characterizing magnetic biomaterials tend to provide an averaged collective behaviour rather than insights into the properties of individual nanoelements. Although these techniques enlighten useful empiric information about its functionality as the hyperthermia efficiency of magnetic nanoparticles [7], or the bactericide properties of the surfaces [8], in some cases, there remains unclear mechanism underlying certain processes. Further experimental effort is needed to reach the successful individual characterisation. The advent of the scanning probe microscopy (SPM) leads to new opportunity for the exploration of biomagnetic materials. SPM techniques offer the capacity to probe different set of properties such as structural, mechanical, chemical, electrical, magnetic or functional properties [9] at the nanoscale (see Figure 2).

Current and Future Challenges

In the last years, several techniques have showcased their capacity for imaging the intricate magnetic configuration of biospecimens at the nanoscale. Notably, Scanning SQUID microscopy and particularly the innovation of nanoSQUID growth at the apex of a sharp element, (SQUID-on-tip) has emerged as a technique of high sensitivity, less than $0.5\ \mu\phi_0/\sqrt{\mathrm{Hz}}$ at temperatures below 1 K [11]. However, this technique has to face challenges posed by the spatial resolution (determined by the tip-sample distance) and the necessity of cryogenic operational conditions.

Elucidating the magnetic configuration of isolated magnetic nanoparticles can be achieved through techniques like Electron Holography imaging in ultra-high vacuum settings and Magnetic Force Microscopy in ambient conditions. Additionally, Electron Spin Resonance in combination with Scanning Tunneling Microscope (ESR-STM) has been demonstrated its capability in studying single atoms and molecules. Yet, the investigation of biomaterials under physiological conditions persists as an ongoing challenge. While some successful results are obtained by MFM [12], the influence of the tip stray fields poses complications when measuring the remanence states of the magnetically soft samples.

A recent breakthrough in scanning techniques presents a promising alternative for characterising biological systems, harmonising the strengths of previously mentioned methodologies. This innovation is •••



▲**FIG. 3:** (a) Sketch of the setup and experimental principle of the NV center technique use to characterize a biospecimen. A copper wire is used to deliver the microwave pulse. A cell, embedded in resin is attached to a tuning fork and scans above the diamond nanopillar that contains a shallow NV center (b) Ferritin cluster imaged by the NV-SPM technique and the profile corresponding to the line directed by the red arrow. Adapted from [13]

• • • based on the Nitrogen Vacancy center in diamond (NV) sensor combined with Scanning Probe Microscopy, as depicted in Figure 3 [13]. This technique includes the advantage of the high-sensitivity of SQUID, the high-resolution of Electron Holography, the versatility of the MFM for working under diverse environment and the specificity of the ESR-STM. Remarkably, it's read-out mechanism is non-invasive. The NV center in diamond sensor, a color center possessing a non-zero spin in its ground state with long coherence time, even under ambient conditions, serves as an excellent high-resolution and high-sensitivity magnetometer.

Recent advances employing optically-addressable NV centers have culminated in the achievement of high-resolution NMR spectroscopy and imaging (MRI) under ambient conditions. This breakthrough scales down to the level of individual biological cells and in very small liquid samples [14] with good resolution.

Nonetheless, the pursuit of characterizing biomagnetic materials introduces further complexities, including the three-dimensional imaging challenge. Addressing this challenge, Magnetic Resonance Force Microscopy emerges, taking advantage of its chemical specificity and sub-surface imaging capabilities, thereby enabling the detection of proton spins in virus [15]. Evidently, the evolution of scanning probe techniques necessitates continued development toward an easy to use system. Those systems should encompass spectroscopic capabilities, accommodate diverse working conditions (including in situ magnetic fields and physiological environmental) and offer versatility for integration with complementary methodologies. ■

About the Author

Agustina Asenjo is Senior Researcher at the Institute of Material Science of Madrid-CSIC. Her research focuses on the development of Advanced Magnetic Force Microscopy modes and the study of materials for spitronics, biomagnetic materials and materials for energy.

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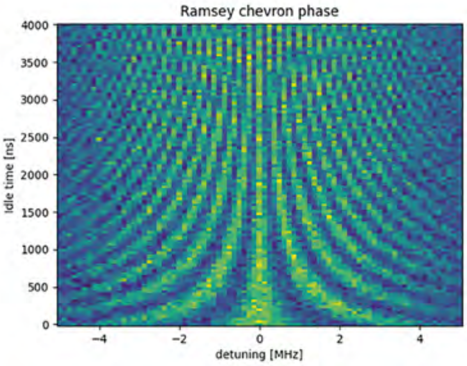
Proteox and OPX:
Enabling technologies, working together

The first installation of a ProteoxMX Cryofree© dilution refrigerator in a university research lab was made back in December of 2020 at the University of Glasgow. Since then, and after winning an InnovateUK grant to commercialise quantum technologies, the university's quantum circuits group has been pioneering research in commercialising superconducting qubit hardware.

The **Proteox**MX, the first to be launched in the Proteox family, is a dilution refrigerator that was fully re-developed to provide an interchangeable, experimental unit that can support multiple users and a variety of experiments from a single system. The system provides less than 10 mK base temperature and can hold hundreds of superconducting cables and signal conditioning components, perfect for superconducting qubits and research in quantum computing.



▲ Gate frequency optimisation.

The **Proteox**MX has since been the heart of the Quantum Measurement as a Service (QMS) user facility provided by Oxford Instruments NanoScience in the lab of Professor Martin Weides. A variety of researchers and commercial companies have been using the leading cooling technology and instrumentation in the facility to test their components and access low temperatures.

▲ ProteoxMX and OPX+ in the QMS facility.

The most recent addition to the lab was a Quantum Machines' OPX+. The room temperature control hardware from Quantum Machines is connected seamlessly to the low temperature environment for superconducting qubits from Oxford Instruments.

With its specially designed Pulse Processing Unit (PPU) technology the OPX+ is a state-of-the-art quantum control platform. It uniquely combines real-time processing and ultra-fast parametric (not Boolean) feedback at the heart of quantum control with advanced control flow. OPX+ is an extremely powerful and easy-to-use control solution that allows running complex experiments with best performance and fastest runtimes.

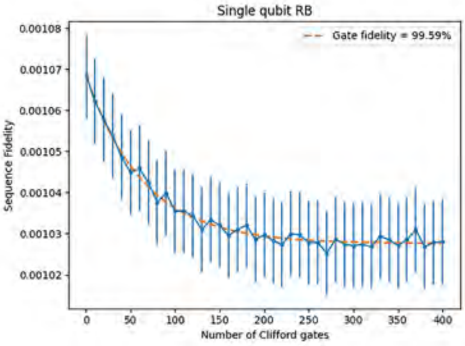
With the superconducting qubit device mounted inside the Proteox and the Proteox at base temperature, the OPX+ could be set up and programmed from a python environment to run experiments. Using QUA, OPX's pulse-level programming language for quantum devices, Rabi oscillation, T1 and T2 measurements, active reset and randomised benchmarking were all completed.

"The OPX is very straightforward and self-explanatory to use. Compared to other room temperature control electronics, it was great to not have to download multiple drivers or take lots of time reconfiguring the system," mentioned Muhammad Ali, measurement scientist working in the QMS facility.

Very quickly the team were able to get one qubit working well, showing the compatibility between the Proteox and the OPX. The interesting physics may be limited for a one qubit device, but they were able to get the system set up quickly, and reach advanced single qubit characterisation within a couple of days of unboxing the Quantum Machines OPX.

Itamar Sivan, CEO of Quantum Machines: "The OPX and Oxford Instruments NanoScience fridge are definitely a good match!"

Stay tuned for more!



▲ Randomised benchmarking for a single qubit.