MethodsX 3 (2016) 297–306

Contents lists available at ScienceDirect

MethodsX

journal homepage: www.elsevier.com/locate/mex

# Nanometric resolution magnetic resonance imaging methods for mapping functional activity in neuronal networks

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## HIGHLIGHTS

- NV in diamond acts as an atomic size optically detectable spin probe.
- The probe combines high magnetic field sensitivity and nanometric resolution.
- Non-invasive mapping of functional activity in neuronal networks is one application.
- Synapse scale resolution ~10 nm but circuit scale FoV > 1 mm is possible.

## ABSTRACT

This contribution highlights and compares some recent achievements in the use of k-space and real space imaging (scanning probe and wide-filed microscope techniques), when applied to a luminescent color center in diamond, known as nitrogen vacancy (NV) center. These techniques combined with the optically detected magnetic resonance of NV, provide a unique platform to achieve nanometric magnetic resonance imaging (MRI) resolution of nearby nuclear spins (known as nanoMRI), and nanometric NV real space localization.

- Atomic size optically detectable spin probe.
- High magnetic field sensitivity and nanometric resolution.
- Non-invasive mapping of functional activity in neuronal networks.



## ARTICLE INFO

*Method name:* Nano Fourier magnetic resonance imaging
*Keywords:* Nitrogen vacancy in diamond, Optical detection, Magnetic resonance imaging, Neuronal networks, Nano scale, Super-resolution microscopy
*Article history:* Received 10 October 2015; Accepted 11 April 2016; Available online 16 April 2016

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http://dx.doi.org/10.1016/j.mex.2016.04.003

## Methods details

A nitrogen vacancy (NV) center in diamond [1–3] acts as an atomic size optically detectable electron spin probe with the ability to sense local small magnetic fields due to other electrons or nuclear spins at nanometric distance. Owed to the NV spin dependent fluorescence, its electronic spin state can be both readout and initialized optically. The application of microwave frequency pulses on its optically initialized state then permits the coherent control of its spin state at the single defect level, when weakly coupled with its surrounding nanometric environment. Thus the NV can be used directly as a sensor. Microwave sequences adapted from nuclear magnetic resonance (NMR) methods allow detecting alteration in NV spin dephasing time originated from a dilute concentration of nuclear spins producing small magnetic field around the probe. Compared to other probes, this defect allows a wide bandwidth sensing of nuclear magnetic Larmor frequency spins resonance.

NV can achieve very high magnetic field sensitivity down to single electron spin sensitivity [4] and the current best magnetic field sensitivity is of 0.9 $pT\,Hz^{-1/2}$ [5]. Some of these magnetometer techniques have direct sensing applications within biological samples [6]. A nanoMRI method using a single NV center has been successfully applied to achieve the 2D imaging of $^1H$ NMR signal with a spatial resolution of 12 nm [7]. These results can be achieved by combining conventional confocal or wide field optical microscopy in conjunction with specifically adapted Nuclear Magnetic Resonance (NMR) methods such as Hanh-echo sequence and universal dynamical decoupling [5,7].

Optical conventional imaging microscopic techniques based on confocal microscopy and wide field microscopy are however intrinsically diffraction limited (resolution ~half optical excitation wavelength). To achieve nanometric resolution in the localization of NV with purely optical methods, super-resolution methods based on Stimulated Depletion Emission Microscopy (STED) [8] and Stochastic Optical Reconstruction Microscopy (STORM) [9,10] must be employed. Therefore alternative methods combining STED and STORM with spin resonance techniques (spin echo sequences) have also been implemented. However, still some hurdles exist for the full deployment of nanoMRI technology [11].

This manuscript provides a summary of the latest works [1–3] showing nanoscale resolution in localizing NV in diamond with potential applications in magnetic resonance imaging of nuclear and electron spins. One of these methods, FMI, uses the Fourier (or k-space) phase-encoding of the NV electronic spins in a diamond sensor and it has been applied to magnetic field sensing. We will describe the implementation to neural field detection and discusses the potential extensions of these imaging techniques to quantum spin defects in other, possibly more practical material such as silicon carbide (SiC).

We also report on two main methods to achieve this. Fourier Magnetic Imaging (FMI) [1] of NV in diamond and optical super-resolution microscopy methods combined with Nuclear Magnetic Resonance (NMR) methods [2,3]. FMI acquisition and processing method applied to NV in diamond achieves imaging in the k-vector space providing a 3.5 nm resolution. STED and STORM imaging methods are achieving nanometric localization directly in real space, based on deterministic and stochastic localization of fluorophores.

These methods combined with NMR techniques have also been applied to NV and potentially could provide nanoMRI capabilities and magnetic field sensitivity. NV localization with resolution of 2.4 nm and 27 nm have been demonstrated, respectively. These last two methods have not yet been fully applied to magnetic sensing to assess their potential ultimate sensitivity to resolve other nearby spins. They are however expected to be relevant for direct spin-spin interaction studies.

This manuscript delivers an introduction to this rapidly advancing area and illustrates the case of advanced methods for the plausible and potentially significant applications to neural pathways. This contribution highlights the present advantages and relative performance of these methods. The non-invasive mapping of functional activity in neuronal networks is one possible application of these techniques and we will discuss its current status.

The contribution also discusses the further improvements of the technique including the use of atomic defects in a more probe fabrication friendly material such as SiC and concludes that the subject area is now sufficiently mature to engineering a probe and developing a protocol for practical medical applications especially in neuroimaging.