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Perspective of zero-field ODMR to study nano-biological systems

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Abstract. This work presents an introduction, a short literature review as well as our recent optical and high field magnetic resonance experiments with regard to the applications of nitrogen paramagnetic defects in (nano)diamonds for biomedical related research. The perspectives of combination of optical and magnetic resonance (high field electron paramagnetic resonance) spectroscopic methods for the sensitive spatially resolved screening of electrical and magnetic gradients in biological tissues on the nanoscale level are discussed.

1. Introduction

Advancements in magnetic resonance (MR) have contributed immensely to a wide range of scientific areas from fundamental physics and chemistry to practical applications such as medical sciences, for example [1, 2]. Even though, MR methods have two inherent features that under some circumstances could be regarded as their disadvantages, e.g. low sensitivity and broad spectral lines. To overcome these obstacles, so called “brute-force” approach which utilizes low temperatures and extremely high magnetic fields is in use [3–5]. Alternative and complementing to the brute-force approach are the methods of double resonances. Though such popular methods as an electron-nuclear double resonance (ENDOR), electron-electron double resonance (DEER or ELDOR), and dynamic nuclear polarization (DNP) have proven their efficiency to study biological systems [6–8], none of the state of the art MR detection techniques combines high sensitivity, nanoscale spatial resolution and life sustaining working conditions, therefore limiting applications in life sciences. An illustration of the importance of nanoscale spatial resolution in the studies of biological substances – a part of the results of our micromorphological study of the aorta wall deposit from the male patient – is presented in figure 1 (see also an accompanying paper [9] for details). The corresponding microanalysis shows that the sample on the 10 μm scale is highly inhomogeneous. While section #1 and #4 of the investigated organomineralic matrix contain a detectable amount of Na and Cl, none of their traces were found in other sections. Nitrogen and iron in section #2 were revealed, while high calcification levels in sections #3 and #5 with the Ca content up to 6 wt. % were measured.

It is clear enough that for the research of inhomogeneous samples (biological or of any other kind) it is vital to have an experimental device with high spatial resolution as well as with high sensitivity. Let us have a look over the optically detected MR methods that could be capable to satisfy these two criteria.


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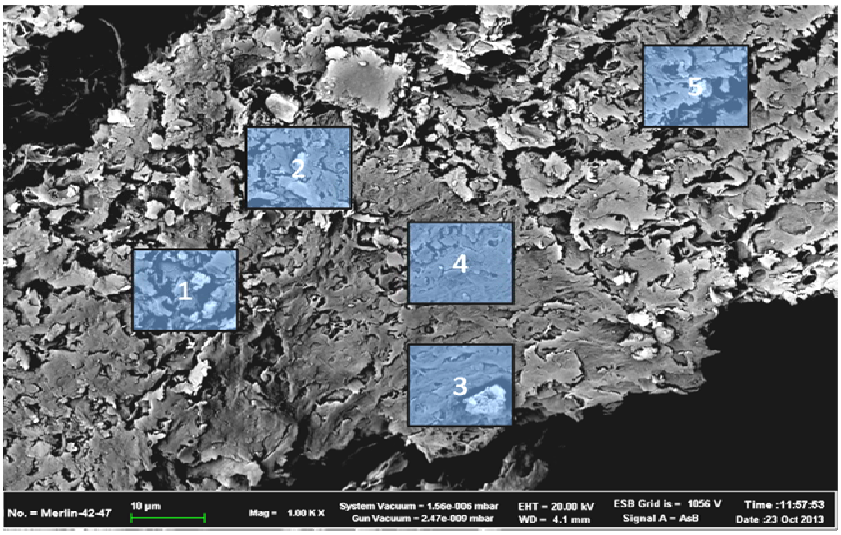


Figure 1. Electron microscopy of the part of the fatty deposit of the aorta wall of male patient gathered during the surgical operation. The squares mark the sections which were analyzed by elemental EDS.

2. ODMR: short history and basic concepts

ODMR (optically detected magnetic resonance) is a double resonance technique combining optical measurements (fluorescence, phosphorescence, absorption etc) with EPR. Bitter was the first who in 1949 theoretically showed that the resonance pumping of the EPR transitions should lead to the perceptible changes in polarization scheme of emission spectrum of mercury vapor [10]. Since that time the main area of the ODMR application is an investigation of different paramagnetic centers (often denoted as point defects) in semiconductors, layered structures and low-dimensional systems [11]. Schmidt and Van der Waals demonstrated that in some cases the ODMR signal could be detected in the vanishing magnetic fields if the paramagnetic system possesses zero-field splitting (ZFS) [12]. Resolution of the transition frequencies in zero-field ODMR is determined mainly by local environment of paramagnetic species, whereas EPR linewidths are much wider due to additional contribution of magnetic-field dependent interactions. A fruitful area of application of ZFS singlet-triplet states concerning biology has proven to be photosynthesis [13].

Due to the fact that the energies of optical quanta are much higher than the energies of microwaves quanta, ODMR is a quite sensitive technique compared to conventional EPR. For the same reason optical waves could be focused onto the much smaller spot on the sample. Therefore, ODMR studies could be done locally with high spatial resolution. Anisimov with his co-workers demonstrated that just 20 short-lived radical pairs could be detected by ODMR [14] while the amount of 10^9 spins are considered to be the lower detection limit for the commercial conventional EPR spectrometers. In 1993 two groups independently reported single spin detection on a single pentacene molecule in a p-terphenyl crystal [15, 16]. The experiments were done at T = 1.5 K - usual for the most ODMR experiments temperature to overcome the short relaxation times (lifetimes) of the centers studied.

Nobody could expect that the ODMR methods would be applied for the physiologically relevant investigations. Breakthrough was done in 1997 with the idea to use nitrogen-vancancy defects in diamonds for these purposes [17].

3. NV defects in (nano)diamonds

The nitrogen-vancancy (NV) center has recently become a high profile candidate for many different solid state applications, ranging from solid state quantum computing to magnetometry. NV centre in diamond consists of a nearest-neighbor pair of a nitrogen atom, which substitutes for a carbon atom and a lattice vacancy (figure 2). The center exists in two charge states: neutrally charged state NV^0 with electron spin S=1/2 and negatively charged state NV^- with electron spin S=1 (denoted as NV in this paper) [18–21].

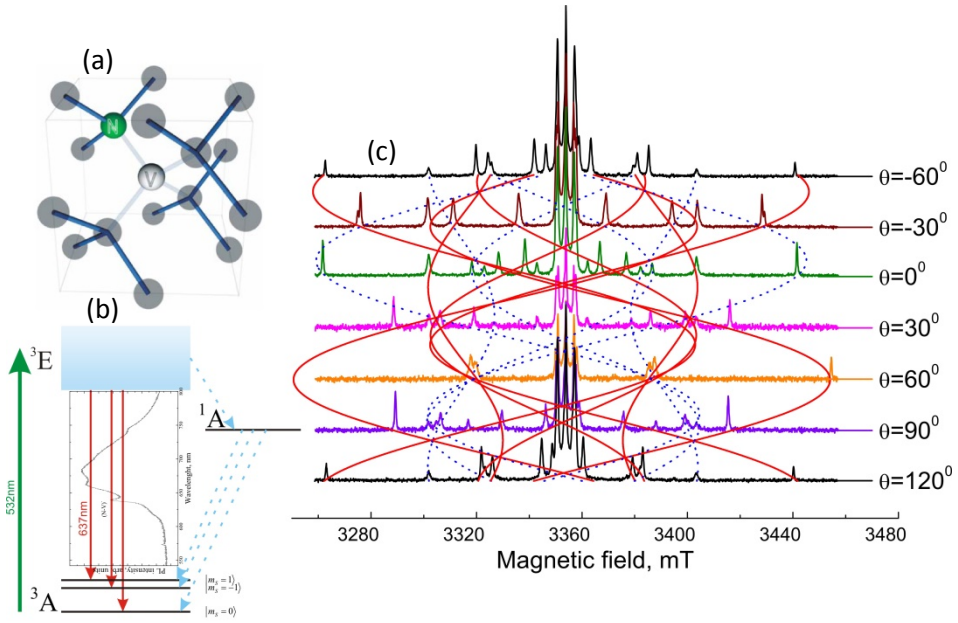


Figure 2. a) Schematic structure of NV center in diamond. b) Energy level structure and an example of the photoluminescence spectrum with ZPL lines shown at 637nm. (c) Example of the orientation dependence of 94 GHz electron-spin echo detected EPR spectra of N^0_S donor at RT (group of the central lines) and NV centers (highly anisotropic) in a detonation nanodiamond. Roadmap simulation for NV centers is shown by solid and dotted lines.

Among others, biological applications demand very bright and photostable fluorescence. The NV defects transform nanodiamonds into sensitive optical probes. The fluorescence spectrum of the NV is presented in figure 2. ZFS parameter of NV center is quite sensitive to the local magnetic [22] and electric fields [23] as well as to the temperature changes [24]. Moreover, since NV centers are atomic-sized point defects and can be localized in direct proximity to a diamond surface, they can be brought to within a few nanometers of samples, allowing for nanometric spatial resolution [25]. Nowadays, there are two main concepts of the zero-filed ODMR experiments at ambient conditions that exploit diamond thin film or functionalized nanodiamonds correspondingly.

First approach utilizes a diamond thin film with shallowly implanted nitrogen atoms converted afterwards to NV centers by using different procedures [26]. The lasts could be located very close to the film surface. That surface is covered by biological (or any other) material for investigation. The advantage of this method is high sensitivity because of the relatively high and controllable NV centers concentration. Disadvantage is a limited spatial resolution due to the finite minimal distance between the sensing NV center and area of interest in the material studied.

Second approach uses nanodiamond particles with NV centers inside. By the methods of chemical functionalization these nanoparticles could be directly bound to the desirable place in the biological tissue, so the distance between the NV center and measuring point could be small. This approach has a few disadvantages: decreased sensitivity due to the low NV concentration in nanodiamonds which depends on the nanoparticle size and functionalization procedure [27], and lower resolution because of physical motion of the nanoparticles in the biological tissues under physiological conditions [28].

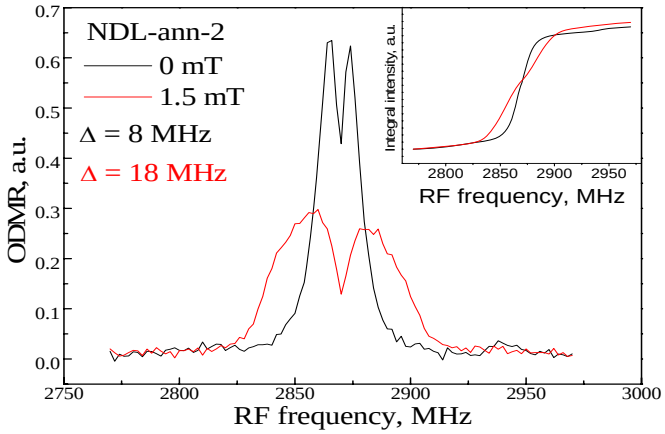


Figure 3. Low-frequency ODMR of NV centers in nanodiamonds, registered at RT in zero and low (1.5 mT) magnetic fields. Inset shows that integral intensity of lines in both cases are practically the same

Figure 3 presents the ODMR spectra of NV centers in the weak magnetic fields. The observed feature could be used for the mapping/screening of the distribution of the magnetic and electric fields caused by the inhomogeneities of the biological tissues. There are already a few promising attempts are done to combine the optical "single molecular" spectroscopy with ODMR [16] and their effectiveness is shown.

4. Materials and methods

For the details of EPR and microscopy experiments please have a look at the accompanying paper [9].

ODMR experiments in zero-field was done in continuous wave (CW) regime with simultaneous frequency sweep and modulation, using Rohde&Schwarz SMC 100A RF synthesizer as a source of microwave signal at frequencies of 2.87 GHz with maximal power of 0.5 W; laser illumination at 532 nm wavelength with power up to 150 mW in CW was provided by Nd:YAG laser from Wicked Lasers.

5. Conclusion

We are sure that ODMR approach combined with the modern techniques of the optical confocal microscopy would be effective for studying the wide range of biological objects at physiologically relevant conditions and would allow one to obtain new information about the objects and processes studied. Moreover, it should open a perspective to search for new materials which properties could be even more profitable for using them as nanosensors comparing to the NV-based sensors [29, 30].

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