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# Settings of DiffMag handheld probe for maximal detection depth aiming perioperative lymph node harvesting

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**Abstract**

Magnetic nanoparticles (MNPs) are used in many biomedical applications, including sentinel lymph node biopsy (SLNB) and magnetic particle imaging (MPI). University of Twente has developed DiffMag handheld probe for a magnetic SLNB utilising MNPs. This probe is based upon differential magnetometry employing nonlinear magnetic response of superparamagnetic MNPs. The DiffMag handheld probe consists of an excitation coil to activate the MNPs, and a set of detection coils to acquire the signal generated by MNPs. The hydrodynamic size and surface properties of MNPs may change when introduced to a new environment. This alteration in mechanical properties will have an effect on their magnetic behaviour. In this study, the protocol settings for the nonlinear handheld detection probe during the SLNB procedure is optimized. The observed detection depth of DiffMag handheld probe decreases slightly by increasing the environment viscosity.

## I. Introduction

Sentinel lymph node (SLN) harvesting, facilitated by magnetic nanoparticles (MNPs), is an essential step in the surgical treatment of a growing number of malignancies. Nonlinear detection principle, referred to as differential magnetometry (DiffMag), allows for detection of small amounts of MNPs trapped in SLN without disruptions of surgical procedures[1]. A prototype DiffMag handheld system (DMH) has been developed by University of Twente and employs a patented DiffMag processing[2]. This study reports the optimal settings and investigates the detection depth of DiffMag handheld probe.

## II. Material and methods

DMH (schematic in Fig. 1 – upper panel) consists of a handheld probe, base unit, and a windows laptop with MATLAB-operated software employing DiffMag nonlinear detection principle[2].

The tip of DMH probe has a diameter of 22 mm and consists of an excitation coil, two detection coils and a set of compensation coil. The excitation coil generates an alternating magnetic field. A set of compensation coil is used for dynamic field compensation to eliminate the influence of the excitation field on the detection coils. Fig.2 illustrates an excitation sequence consisting of AC and DC components[2].

The detection coils, a polarity-reversed coil-pair functioning as a gradiometer, sense the voltage variations due to the changes in magnetic moment of the MNPs. The acquired signal is discretized into 100nV increments

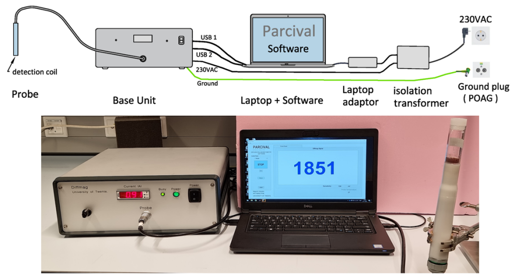

**Figure 1:** DiffMag handheld system diagram and MATLAB-operated software

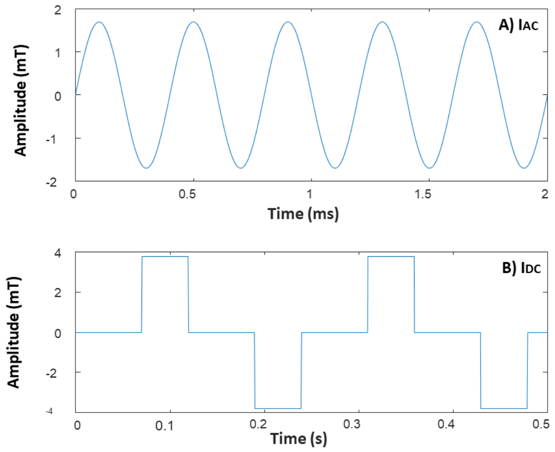

**Figure 2:** Generated magnetic field by the DMH probe: AC field (upper panel - A), and DC offset field (lower panel - B)

referred to as DMH counts.

The introduced excitation field along the axis of the DMH probe is illustrated in Fig.3 by simulations[3] and experimental confirmation for DC magnetic field (left) and for AC magnetic field (right). The generated magnetic field was measured by FM302 tesla meter (Projekt Elektronik GmbH, Germany).

Detected signal by DMH probe is influenced by property of the magnetic nano particles and depends on the frequency of AC field ($f_{AC}$), amplitude of AC field ($I_{AC}$) and amplitude of DC field ($I_{DC}$).

Magtrace® (Endomag, UK), CE-certified and FDA-approved[4] magnetic tracer, was used to illustrate the influence of excitation field and tracer viscosity on the detection depth of DMH probe. Magtrace®, the dark brown aqueous suspension, contains multiple iron-oxide cores (single-core diameter: 3.5–10 nm), agglomerated and encapsuled by a carboxydextran coating, with the hydrodynamic diameter of the 45–65 nm[5].

The experiment setup (shown in Fig.4) consists of DMH, phantom and MECA500 robotic arm to hold and move the DMH probe.

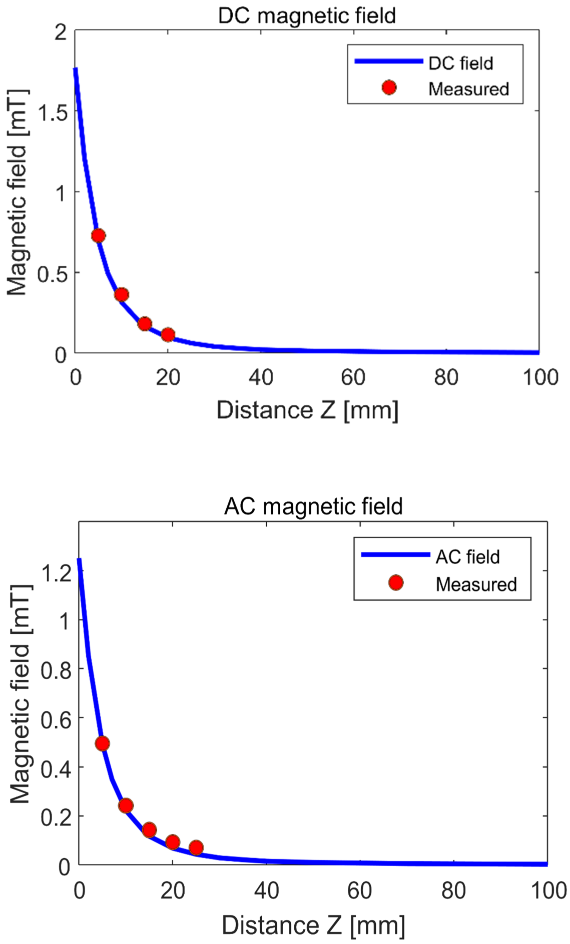

**Figure 3:** Measured and simulated magnetic field strength adjacent the probe.

### Experiment I – Optimal AC field frequency

In experiment I, we used an open Delrin® (polyoxymethylene) phantom (MD&I, University of Twente) consisting of 13 column-wise triplet pits. Total volume of 150 µl (containing 500 µg iron oxide diluted in water) was pipetted in to a pit with a total capacity of 500 µl (Φ8.92mm, 8mm depth). The probe surface was placed at 0 mm distance from the phantom. The amplitude of $I_{AC}$ = 0.25A and a pulse amplitude of $I_{DC}$ = 1.5A with a 30% duty cycle was used throughout this experiment[2]. Experiment I reported DMH counts as a function of field frequency in the range 1 to 10 kHz (step size 0.5 kHz).

### Experiment II – Optimal AC and DC amplitude

Same sample and phantom from experiment I was used in experiment II. The optimum range of AC field frequency obtained from experiment I was implemented in experiment II. A grid search involving all combinations of the following excitation parameters was used to optimize the DMH probe detection signal.

1. $f_{AC}$ from 5 to 7 kHz with a step size of 0.5 kHz

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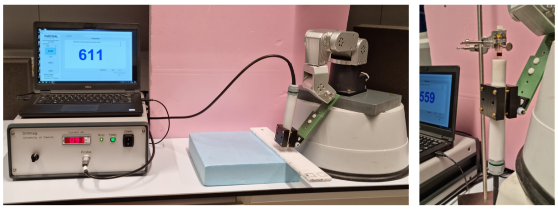

**Figure 4:** Experiment set up including DMH and MECA500 robotic arm

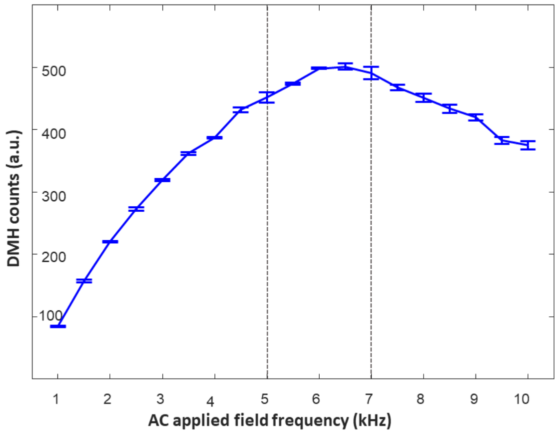

**Figure 5:** DMH counts, $I_{AC} = 0.25$ A, $I_{DC} = 1.5$ A for 19 applied field frequencies.

2. $I_{AC}$ from 0.1 to 0.8 A with a step size of 0.1 A
3. $I_{DC}$ from 0.25 to 2 A with a step size of 0.25 A.

### Experiment III – Detection depth

The optimum combination of excitation parameters obtained from Experiment II was used to assess the detection depth of DMH probe in Experiment III. The counts were collected for the two samples starting with probe tip at a distance of 1 mm. Two Magtrace® samples were diluted by water or glycerol to contain 500µg iron oxide in a total volume of 150µl, and were pipetted in glass tube with 1mm thickness. The estimated viscosities of samples[6] diluted with water and glycerol were 0.98 mPa.s and 218 mPa.s, respectively. The data was acquired with a step size of 1 mm in a downwards movements. The detection depth was established as a distance with the last measurable value above the detection threshold, i.e. 10% above the background noise level. The optimum combination of excitation parameters obtained from experiment II was used to assess the detection depth of DMH probe.

### Data analysis

The repeatability is assessed as a percentage of standard deviation over all data acquires for a specific distance.

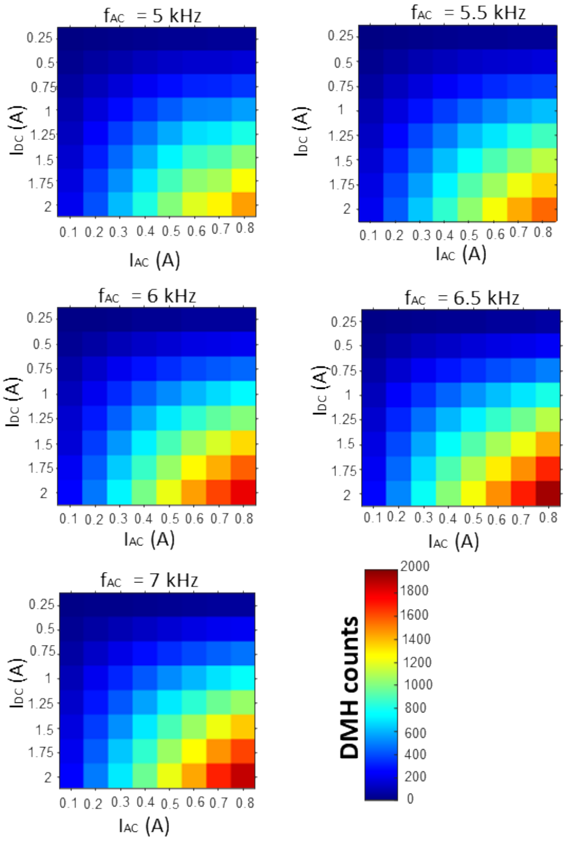

**Figure 6:** DMH Counts as function of $f_{AC}$, $I_{AC}$ and $I_{DC}$

## III. Results and discussion

### Experiment I – Optimal AC field frequency

Fig. 5 illustrates the DMH counts for water diluted sample as a function of applied field frequency. Maximum DMH probe readout is clearly in the range of 5 and 7 kHz. The count stability was not influenced by frequency as illustrated by standard deviation bars in the figure.

### Experiment II – Optimal AC and DC amplitude

Fig. 6 illustrates the DMH counts at different frequencies of applied field for the water diluted sample for combination of various amplitude of AC and DC current.

DMH counts increased by increasing $I_{AC}$ and $I_{DC}$. However for $I_{DC}$ larger than 1A, the probe temperature quickly increases to the fixed 38°C alert limit (See Fig.7).

### Experiment III – Detection depth

To estimate the effect of DC current on probe detection depth, $I_{DC}$ of 1A and 1.5A was used. Fig. 8 shows the detection depth of the DMH probe (operating parameters $f_{AC}$ = 6.5 kHz, $I_{AC}$ = 0.8A) for two DC applied field, $I_{DC}$= 1 and $I_{DC}$=1.5A. The thickness of sample tube container is 1 mm, which is minimum depth detectable in this exper-

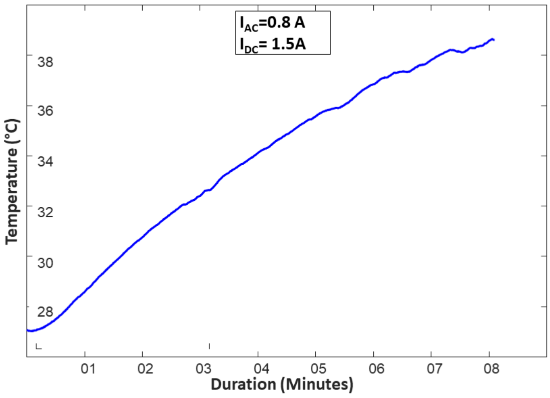

**Figure 7:** Probe surface temperature recorded with PT100 sensor, $f_{AC} = 6.5$ kHz, $I_{AC} = 0.8$ A and $I_{DC} = 1.5$ A.

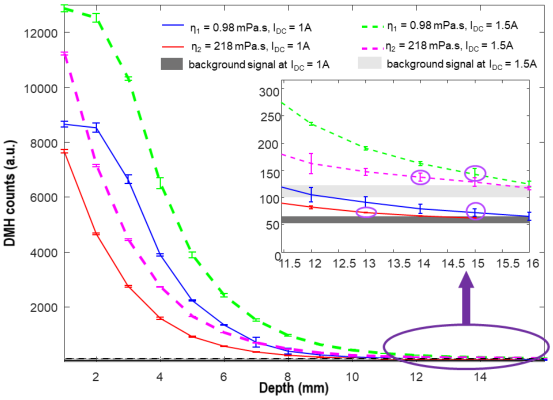

**Figure 8:** DMH probe detection depth, $f_{AC} = 6.5$ kHz, $I_{AC} = 0.8$ A, water and glycerol diluted Magtrace®

iment. Detection depth of DMH probe for Magtrace® (summarised in Table 1) ranged between 13 and 15 mm.

Even though higher $I_{DC}$ delivered higher initial DMH counts in close proximity of the probe, this had no influence on the detection depth. However, increasing the viscosity of the samples generally decreased the DMH counts which decreased the detection depth by 2 and 1 mm, respectively.

## IV. Conclusions

In conclusion, regardless the viscosity, the DiffMag handheld probe detects magnetic nanoparticles at a distance up to 15 mm.

**Table 1:** Average number of counts at a maximum depth for DMH probe operating at $f_{AC} = 6.5$kHz and $I_{AC} = 0.8$A for water diluted ($\mu = 0.98$ mPa.s ) and glycerin diluted ($\mu = 218$ mPa.s ) sample.

| $I_{DC}$ | **water diluted sample mean ± std** | **glycerol diluted sample mean ± std** |
|---|---|---|
| **1 A** | Depth 15 mm<br>72 ± 7 | Depth 13 mm<br>72 ± 1 |
| **1.5 A** | Depth 15mm<br>142 ± 27 | Depth 14mm<br>137 ±7 .63 |

Clinical applications of handheld probes would need to preserve the magnetic performance when particles are transferred from a laboratory to in vivo environment. Increasing viscosity (as a model for changing environment for in vivo applications) seems to decrease the detection depth slightly. Future investigate assessing DMH probe detection depth using different MNPs in environments with similar viscosity of human lymphatic fluid and realistic amount of iron trapped in SLN is necessary to grasp the clinical situation better.

## Author's statement

Conflict of interest: Authors state no conflict of interest.

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