

## OPTIMIZATION OF A NOVEL MAGNETIC NANOPARTICLE SENSOR

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**Abstract:** This paper represents an experimental iteration of a novel magnetic nanoparticle (MNP) sensor. MNPs can be used as labels in quantitative diagnostic. Planar microcoils in an impedance bridge are used to measure the amount of the particles. Particles change the inductance of the coil due to their permeability. The shape and size of the coil are critical to the sensitivity and robustness. Experimental measurements supported by numerical simulations have been used in sensor designing, improving and optimization.

**Keywords:** magnetic nanoparticle, microcoil, sensitivity

### 1. INTRODUCTION

The need for point-of-care (POC) testing made at home or doctor's office has increased rapidly during the last years. Aging of population, threat of pandemic and need for doping tests, for example, create new demands for quantitative clinical diagnostics. Expensive and time-consuming laboratory tests can be reduced without losing reliability and accuracy of a diagnosis. The POC tests make the diagnosis faster, simpler, and more affordable.[1]

These tests use sophisticated immunodiagnostic assays based on specific binding and immunocomplex formation between two molecules, antibody and antigen (also known as analyte). The most common principle utilizes a special labeling technique. Instead of measuring analyte molecules directly, special particles used as labels are detected. The number of label particles is proportional to the amount of target substance. The use of label typically increases the sensitivity and decreases the detection limit. [2,3]

Magnetic nanoparticles (MNP) are small ferrite oxides (such as magnetite, Fe<sub>3</sub>O<sub>4</sub>) typically ranging from few nanometers to few micrometers in diameter. Magnetic particles can be used in immunodiagnostic as magnetic labels. The MNP label can be a single bead or bead cluster closed in a polymer matrix. The measurement of the magnetic label is substantially safer compared to radioactive labels and more affordable when compared to optical measurement methods using fluorescent labels.[4]

In section 2 the basic sensing principle and studied sensor structures are introduced. Section 3 describes measurement setups and Section 4 presents the results. The results are analyzed in Section 5 and final conclusions are made in Section 6.

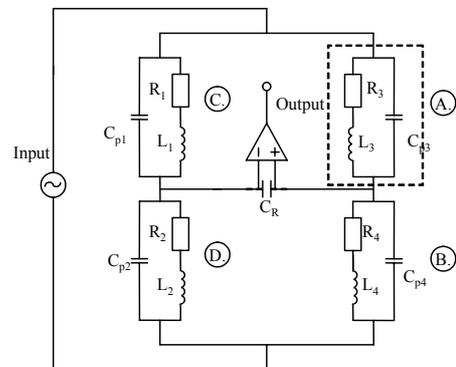
### 2. DESCRIPTION

#### 2.1. Sensing Principle

A set of planar micro coils symmetrically aligned in an impedance bridge are used for quantitative measurement of magnetic nanoparticles. Sample MNPs are placed on one of the identical coils. The inductance of the coil is changed due to the relative permeability of the particles. This unbalances the bridge at high frequencies and an output signal (Eq. 1) proportional to the amount of the particles can be measured.

$$\Delta U = \frac{U}{4Z} \Delta Z_A, \quad (1)$$

where  $U$  is voltage,  $Z$  is impedance and  $\Delta U$  and  $\Delta Z$  are voltage change and impedance change (relative to the amount of the particles) respectively. Equation is derived from the voltage division of the bridge.



**Fig. 1. Equivalent circuit of an impedance bridge with sensing coil (A), reference coil (B) and compensation coils (C and D).**

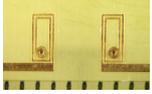
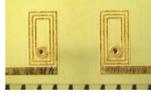
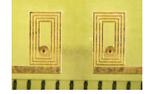
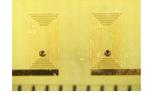
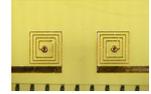
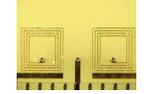
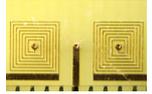
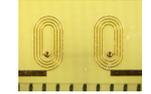
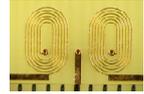
#### 2.1. Studied Structures

Studied macro scale sensor structures (bridges) contain four identical spiral coils. Two of the coils (A and B) are used for measurement and reference purposes. The other two coils (C and D) are used for compensation.

Different bridges have coils with different amount of turns. Also spacing and width of the coil conductor differ. All structures are made of copper on FR-4 substrate. The copper layer is about 36 μm thick and is coated with gold to prevent oxidation.

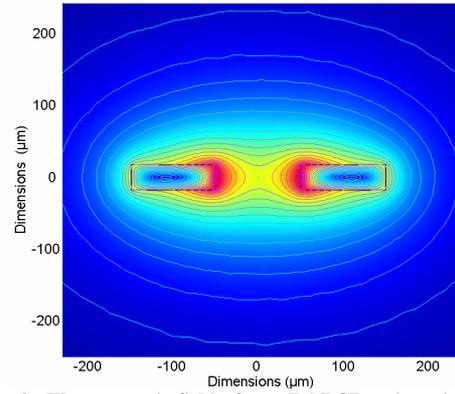
Layout and parameters of the coils are presented in Table 1. Figures (a.-i.) present symmetrically aligned measurement and reference coils. Compensation coils (not seen in the figures) are similar and they locate about 10 mm below the measurement and reference coil pair. The spacing of the scale shown in the figures is one millimeter. Typically X-direct (in these figures horizontal direction) cross-section of the coil and Y-direct (in these figures vertical direction) cross-section of the coil varies from 2-3 mm. Electrical parameters of the separate coils were measured using probe station and Agilent 4396B impedance analyzer (measurement results are shown for each coil) [5].

**Table 1. Studied bridges. Spacing of the scale is 1 mm. Measured inductance, resistance and impedance for one coil are presented below each picture.**

<p>a.</p>  <p>R = 0.12 <math>\Omega</math> L = 11.2 nH Z = 0.50 <math>\Omega</math></p>	<p>b.</p>  <p>R = 0.12 <math>\Omega</math> L = 26.8 nH Z = 1.18 <math>\Omega</math></p>	<p>c.</p>  <p>R = 0.20 <math>\Omega</math> L = 49.4 nH Z = 2.18 <math>\Omega</math></p>
<p>d.</p>  <p>R = 0.98 <math>\Omega</math> L = 104 nH Z = 4.66 <math>\Omega</math></p>	<p>e.</p>  <p>R = 0.28 <math>\Omega</math> L = 29.8 nH Z = 1.34 <math>\Omega</math></p>	<p>f.</p>  <p>R = 0.43 <math>\Omega</math> L = 75.9 nH Z = 3.36 <math>\Omega</math></p>
<p>g.</p>  <p>R = 0.61 <math>\Omega</math> L = 116 nH Z = 5.14 <math>\Omega</math></p>	<p>h.</p>  <p>R = 0.38 <math>\Omega</math> L = 50.2 nH Z = 2.24 <math>\Omega</math></p>	<p>i.</p>  <p>R = 0.54 <math>\Omega</math> L = 117 nH Z = 5.16 <math>\Omega</math></p>

### 2.3. Numerical and Analytical Model

The sensing elements have been designed and further improved and optimized using numerical and analytical simulations. Numerical method like FEM (Finite Element Method) has been used to describe the interactions between sensing coil and magnetic nanoparticles (Fig. 2.). Simulations are also used for early stage optimization of frequency, spacing, width etc.



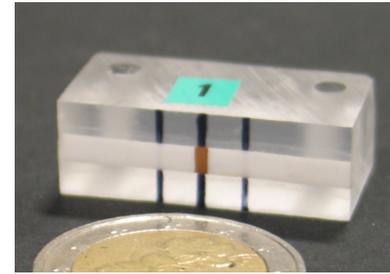
**Fig. 2. The magnetic field of parallel PCB strips with magnetic nanoparticle in the center.**

## 3. MEASUREMENT

### 3.1. Sample

Measurements were done by aligning the sample (containing about half billions of particles, diameter ~250 nm) close to the surface and center of the sensor coil with XYZ-stage. Optimum aligning was checked visually.

The sample is made by absorbing magnetic nano particles in a porous strip. The size of the sample area is 1 mm x 3 mm. The strip is 100  $\mu\text{m}$  thick and it is attach in the bottom of a blastic rectangle. Strip and MNPs are covered with a tape layer (60  $\mu\text{m}$  thick).



**Fig. 3. Sample rectangle with magnetic nanoparticles. Scale is two euros coin.**

### 3.2. Sensitivity Measurement

First the sample was aligned on coil A and bridge was calibrated at 7 MHz. Particle free reference zone of the sample was simultaneously aligned on the coil B. After measuring the calibrated value the sample was pulled up and the difference was measured. Both coils (A and B) were used alternately for measurement and reference purposes when the procedure was repeated totally 10 times (5 times for coil A and 5 times for coil B) for each bridge.

### 3.3 Robustness Measurement

The place dependency of the sensor was measured adjusting the place of the sample from visually aligned origin. Displacement was done with 100  $\mu\text{m}$  increments in X- and Y- directions (from -2000  $\mu\text{m}$  to +2000  $\mu\text{m}$ , Fig 3.) and with 20  $\mu\text{m}$  increments in Z-direction (from 0 to 200  $\mu\text{m}$ , Fig. 3). Each direction was measured separately. Calibration (at 7 MHz) was made before sample aligning.

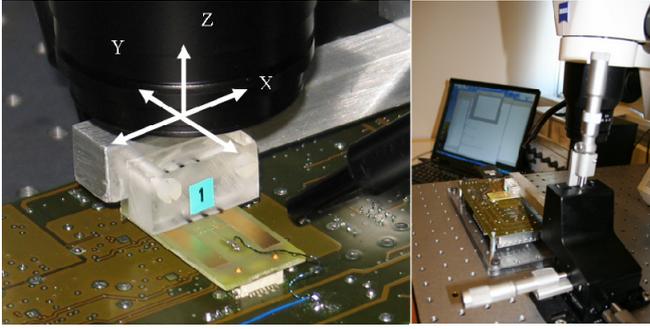


Fig. 4. Measurement setup. Sample (plastic rectangle with number 1) can be displaced accurately using XYZ – stage.

## 4. RESULTS

### 4.1. Sensitivity Measurement

Output signals of the different impedance bridges are presented in Table 2. Both A and B coils are used as measurement coil while other is used as reference. Results are presented in  $\mu\text{V}$ . Standard deviation of each measurement (repeatability was tested by repeating each measurement 5 times) is presented. Measurement data has been analyzed with Matlab<sup>®</sup>. Drifting was removed and noise averaged.

Table 2. Measured output signals for different bridges. Both A and B coils are measured. Each measurement has been repeated 5 times.

	a	b	c	d	e	f	g	h	i
$U_A$ [ $\mu\text{V}$ ]	173	230	237	229	227	87.5	232	187	189
$\sigma_A$ [ $\mu\text{V}$ ]	0.2	0.4	1.2	1.8	0.2	0.1	0.5	0.6	0.4
$U_B$ [ $\mu\text{V}$ ]	157	222	236	273	260	80.2	234	167	173
$\sigma_B$ [ $\mu\text{V}$ ]	0.6	2.4	0.2	0.2	0.6	0.4	2.8	2.8	1.9

### 4.2. Robustness Measurement

The robustness of the sensing system was tested by misaligning the sample with XYZ-stage. Results are presented in Figures 4. – 6.

Most of the curves in Fig. 4. seem to be almost equal. Small drifting of the highest peak shows that the optimum placement of the sample is not at the center of coil but about  $150 \mu\text{m}$  off the origin.

Bridges a and f cause the greatest difference to the output signal. That is because the coils in the bridge a have less turns than other coils. It has also slightly smaller coils in X-direction than the other bridges. This appears as narrower peak and broader “stairs”. Coils in bridge f are special because they have the widest empty gap at the center of the coil (about 2 mm). For this kind of structure the magnetic field is stronger near to the surface of the coil wire than at the origin. Strong magnetic field magnetize particles stronger [1] causing higher output signal.

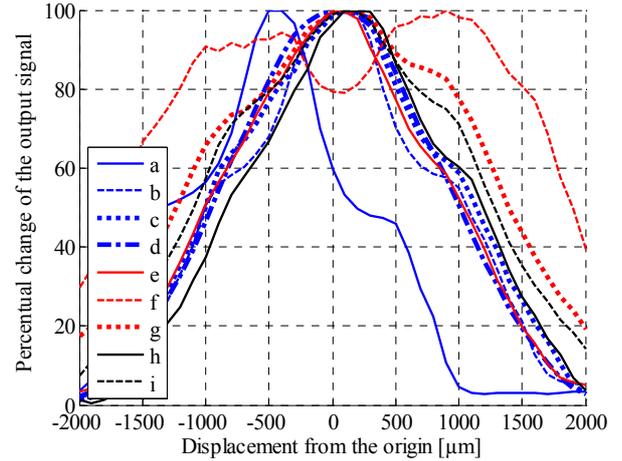


Fig. 5. Percentual change of the output signal when sample is displaced along the X-axis.

According to the results presented in Fig. 5. Y-dicect displacement has similar effect on most of the coils. Only the bridge e differs from this trend. The reason is that it has the smallest cross-section in Y- direction compared to the other bridges (about 2 mm ~ 3 mm).

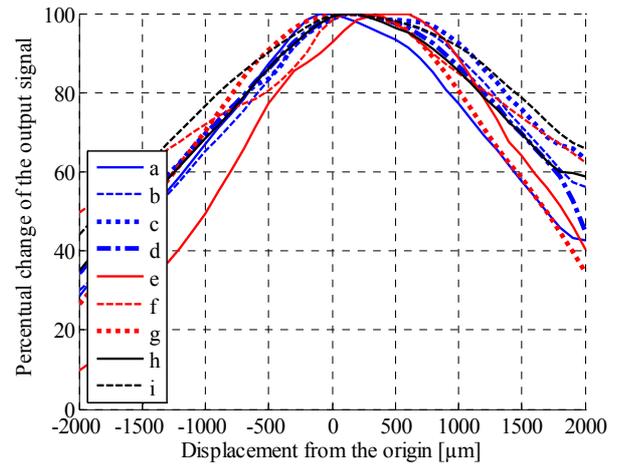


Fig. 6. Percentual change of the output signal when sample is displaced along the Y-axis.

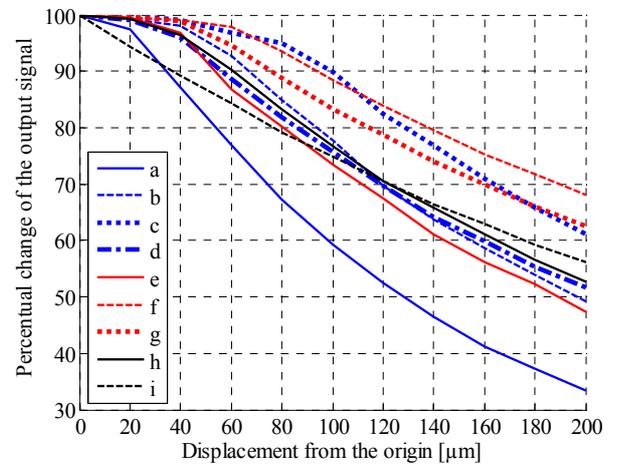


Fig. 7. Percentual change of the output signal when sample is displaced along the Z-axis.

The vertical misalignment (Z-direction in Fig. 6) is most critical to the sensitivity. It can be seen that even small error of 100  $\mu\text{m}$  causes drop of signal from 100 % to 80 % (average). As reference X-direct displacement can be about 500  $\mu\text{m}$  and Y-direct displacement over 1000  $\mu\text{m}$  to gain same scale of drop in the signal level.

A common trend is that bridges having narrower coils loose sensitivity earlier than bridges that have wider coils (e.g. bridge a  $\sim$  1.2 mm and bridge c  $\sim$  2.1 mm).

The most interesting range for the vertical misalignment is from 0 to 100  $\mu\text{m}$ . Some of the measured values below 100  $\mu\text{m}$  misalignment have been gathered in Table 3.

**Table 3. Percentual signal when the sample has been displaced along the Z – axis.**

	a	b	c	d	e	f	g	h	i
<b>20 <math>\mu\text{m}</math></b>	97	99	100	99	99	100	100	99	94
<b>60 <math>\mu\text{m}</math></b>	77	93	97	89	87	98	95	90	84
<b>100 <math>\mu\text{m}</math></b>	59	78	90	76	73	88	83	77	75

## 5. DISCUSSION

The different bridges can be compared by using their key figures. The most important key figure is the sensitivity. After the sensitivity the second important key figure is the robustness (tolerance to the misalignment especially in X- and Z-directions). Also other aspects like high self-inductance (potential for higher Q-value and in this way to higher sensitivity) must be taken into account.

According to the Table 2 bridges c, d and g have the highest output signal. On the other hand the bridge c and g are also quite tolerant to the misalignment in X- and Z-directions. Coils in the bridge g have higher inductance than coils in the bridge c and slightly better tolerance to the X-direct misalignment.

The most interesting result appears in Fig. 4 for the bridge f. It can be speculated that if a coil design which produces signal like the bridges f and g can be found, there could be a structure that has high and steady output signal when the sample is misaligned in X-direction. On the other words with certain shape of the coil and number of turns robustness for X-direct misalignment can be increased.

## 6. CONCLUSION

The measurement method based on a micro coil and high-frequency impedance measurement of magnetic nanoparticle labels has been studied. It has been shown that the shape and size of the sensing element is critical to the sensitivity and robustness. Measurement results create a base for the further research of the more sensitive and robust coil design.

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