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Magnetic GMI sensor for detection of biomolecules

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Abstract

A magnetic sensor based on the giant magnetoimpedance (GMI) effect for the detection of biomolecules was made with a CoFeSiB amorphous magnetic microwire as sensing element. Using soft ferromagnetic cobalt microparticles and field sensitivities of the impedance of about 2.5%/A m^{-1} in the very low field region (less than 200 A m^{-1}) at frequencies close to 10 MHz, a highly sensitive response was measured, appropriate for the detection of low biomolecule concentrations.

Keywords: Magnetic sensor; Giant magnetoimpedance; Detection of biomolecules; Cobalt microspheres; CoFeSiB wire; Polystyrene

1. Introduction

Fast identification and diminution of the detection threshold of the pathogens or other targeted biomolecules (e.g. DNA, RNA, antibodies, metabolites, etc.) represent a biomedical requirement and a scientific challenge.

Although the classical detection methods (electrical, electrochemical, optical) were improved, they still present some important disadvantages such as high cost, time-consuming, high detection threshold. Magnetic methods have several advantages over the classical detection methods, such as rapid results, multi-analyte detection, low cost and reduced waste handling. Recently, giant magnetoresistance (GMR) biosensors that use magnetic beads and magnetic fields for biomolecules detection were reported [1,2]. These sensors have the advantage to be extremely sensitive and to process only electronic signals. Also, the magnetic beads used as markers in such biosensors present some superior characteristics in comparison with other labels (fluorescent molecules, radioisotopes, enzymes). Magnetic beads are very stable, easy to handle and can be used with a large spectrum of molecules. The biological samples usually contain no magnetic background that could interfere with magnetic particles.

The increase of the sensitivity and of the reliability of the biosensor is an important condition of the detection of small concentration of biomolecules (like RNA).

In this paper we propose a new magnetic biosensor based on the giant magnetic impedance

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(GMI) effect found in magnetic amorphous wires. The principle of such a sensor is described. Results are given on sensor design, the materials used to obtain a high sensitivity, and the magnetic markers specially prepared to be used in such type of sensor. Furthermore, results are discussed in terms of using this biosensor for the identification of different biomolecules.

2. GMI sensor

The giant magneto-impedance (GMI) effect consists of significant change of the impedance value of a magnetic conductor (wire, ribbon, thin layers) passed by a high frequency current, when it is subjected to a DC magnetic field.

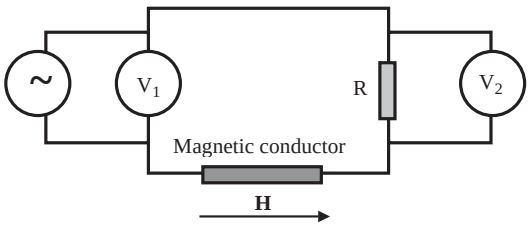

Fig. 1. Principle of GMI effect and impedance ($|Z|$) for a magnetic conductor.

The AC circular magnetic field, H_φ, generated by the driving current flowing through the magnetic conductor determines changes of the circular component of the magnetization, M_φ. The applied magnetic field affects the circumferential permeability of the magnetic conductor, determining modifications of the AC current penetration depth, which are closely related to the impedance value at a given frequency.

$|Z|$ (impedance modulus of the magnetic conductor) is measured by the so-called four-points method (Fig. 1), by which a given AC current flows along the magnetic conductor and a voltage is picked up at the ends. The impedance of the magnetic conductor is calculated from the measured voltage, V_1, and the current value, I, calculated using the voltage measurement across an accurately known low value resistor, R:

$$|Z| = V_1/I = R(V_1/V_2)$$

Co-rich wire-shaped amorphous alloys show the strongest GMI response (Fig. 2) because of their specific magnetic domain structure consisting of an

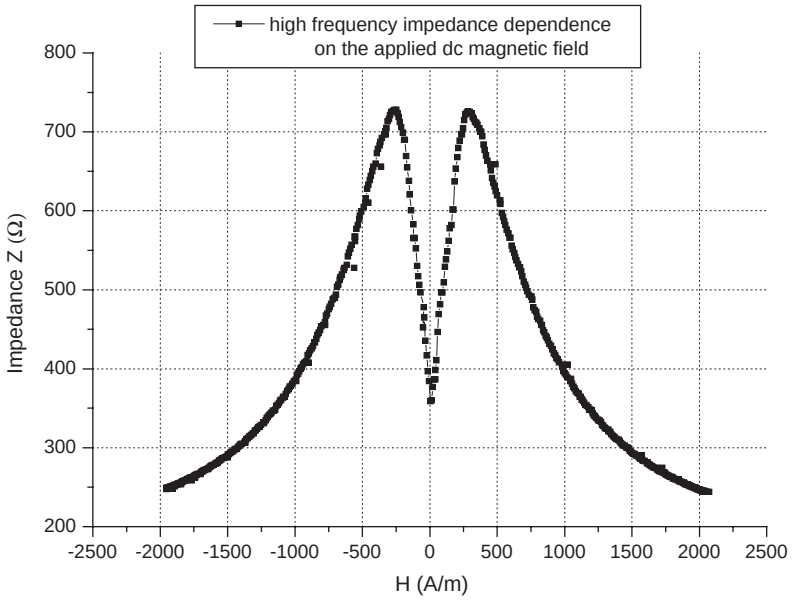

Fig. 2. Field dependence of the high-frequency impedance for the Co-rich wire-shaped amorphous alloys.

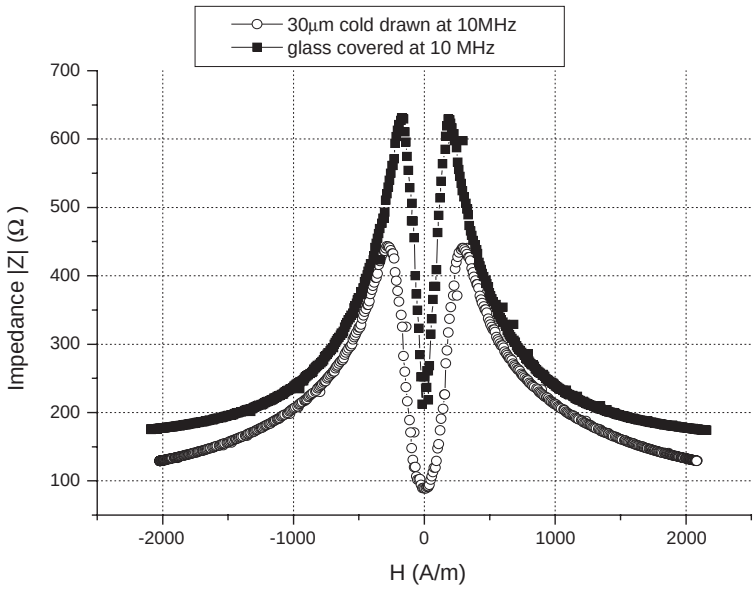

Fig. 3. Field dependence of the impedance for the CoFeSiB glass covered amorphous wires and 30 μm cold drawn wires at 10 MHz.

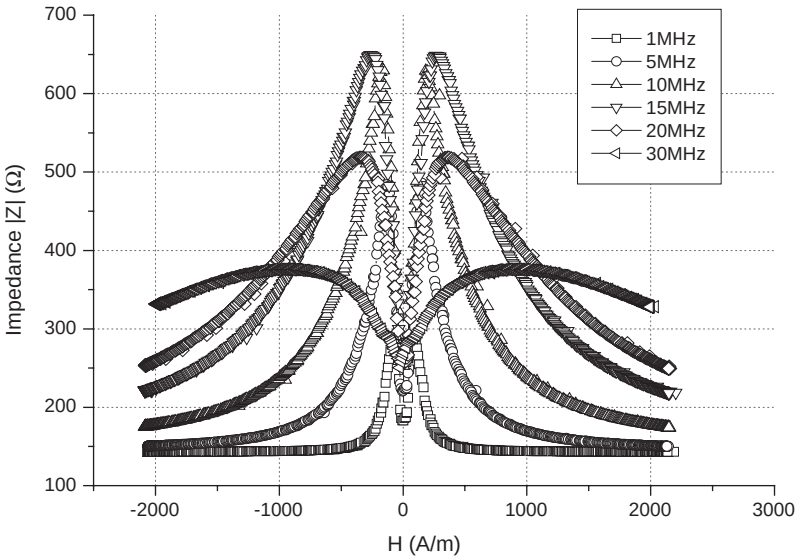

Fig. 4. Field dependence of the impedance for the CoFeSiB glass covered amorphous wires in 1–30 MHz frequency range.

axially magnetized inner core and a circumferentially magnetized outer shell.

The circumferential magnetic permeability plays an important role in this effect, being closely related to the domain structure mentioned above. GMI effect is characterized by GMI ratio usually defined as $\Delta Z/Z\,(\%) = 100 \times \{|Z(H)| - |Z(H_{\max})|\}/|Z(H_{\max})|$, where $|Z|$ is the impedance modulus and $H_{\max}$ is the maximum applied field at which the sample is considered to be magnetically

saturated. High GMI ratio, upto 600%, was found for CoFeSiB amorphous glass covered microwires at frequencies close to 10 MHz [3].

Two types of materials have been considered for the sensing element of the sensor, CoFeSiB glass covered amorphous wires and CoFeSiB conventional amorphous wires with diameters reduced from 120 to 30 μm by cold drawing in several steps [4] (Fig. 3).

We found that the glass covered amorphous wires present a higher sensitivity of the GMI effect (especially in the very low field region) and better linear dependence of the impedance with low applied magnetic field (Fig. 4).

Maximum field sensitivity of the impedance of $2.5\%/\mathrm{A\,m^{-1}}$ can be achieved in the very low field region (less than $200\,\mathrm{A\,m^{-1}}$) at frequencies close to 10 MHz. Resolution is below $10\,\mathrm{mA\,m^{-1}}$ at a full scale of $160\,\mathrm{A\,m^{-1}}$ with maximum sensitivity of about 50 nT. This shows that the magnetic microwire is extremely sensitive to very low magnetic fields.

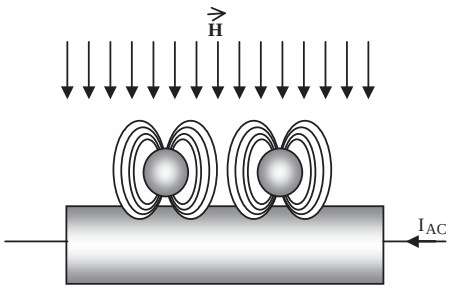

Fig. 5. Image of the magnetic microparticles under an applied magnetic field.

The possibility to use the GMI effect, which occurs in a glass-covered amorphous microwire, for a biodetection device is based on the microwire capability to detect the magnetic microparticles settled on and near the surface. Actually, in a magnetic field, the glass covered amorphous wire detects the magnetic fields arising from microparticles present on and near the surface (Fig. 5).

In this context, biomolecule detection is possible only if functionalized magnetic particles can bind to the target biomolecules previously caught on the sensing element surface.

In practice, such target biomolecules which have been previously specifically labeled, are intercepted on the sensing element surface by fixed specific natural or artificial bioreceptors such as ssDNA (single stranded DNA), antibodies, proteins, enzymes (Fig. 6). Thereafter, the functionalized magnetic microparticles (e.g. streptavidin magnetic beads) are introduced to mark the formed structures on the sensing element surface. The magnetic microparticles with high affinity for target biomolecules (e.g. biotinylated biomolecules) are designed to be attached to each target biomolecule. Subsequently, under an external magnetic field influence, the magnetic microparticles, bound to the sensing element active surface, will develop a dipole field that will be detected by the GMI sensor. Consequently, the amplitude of

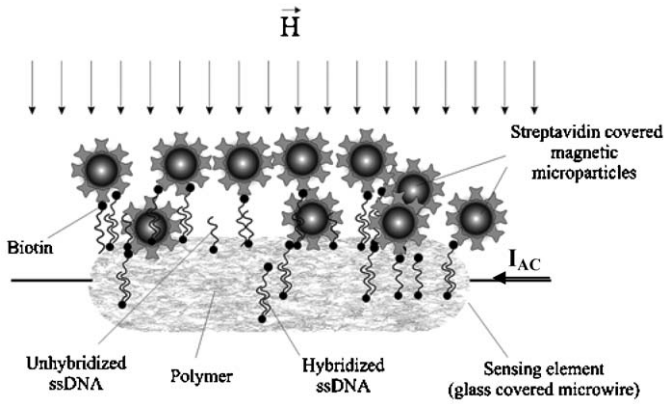

Fig. 6. The principle of a GMI-based magnetic biosensor, using the ssDNA hybridization phenomenon as example.

the sensor impedance will be modified proportionally with the magnetic microparticle concentration. Therefore, the target biomolecules will be detected and quantitatively evaluated.

In the biosensor, the magnetic microparticles must have a uniform spatial distribution over the sensing element to be able to obtain a reproducible response of the sensor. However, there is never a perfect uniform spatial distribution, but a certain probability to obtain it.

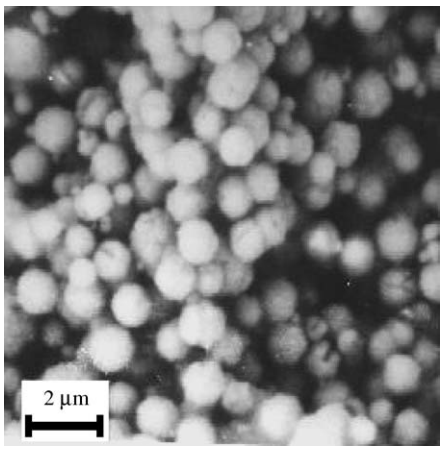

Fig. 7. Electronic microscopy of the cobalt magnetic microparticles.

3. Results and discussions

Taking into account that the biosensor sensitivity relates to both the magnetic marker size and magnetic marker characteristic [5], we realized that magnetic microparticles were specially intended for this type of sensor.

Therefore, using a chemical method (“polyol process”) [6] we prepared Co magnetic microparticles having 0.9–2 μm in diameter range with perfectly spherical shape (Fig. 7) and the magnetization saturation 160 emu/g (Fig. 8).

These Co magnetic microparticles were covered with polystyrene using an emulsion polymerization method. The magnetic microparticles size was of 10–15 μm in diameter. They were covered both to prevent their agglomeration and to facilitate their further combination with different organic molecules that work as coupling agents for target biomolecules.

Because the response of the sensor can be improved if the magnetic particles dimensions are comparable with the sensor sensing element, these magnetic particles (Fig. 9) could be very suitable for our GMI-based sensor because the sensing element is 25 μm in diameter and approximately 1000 μm in length.

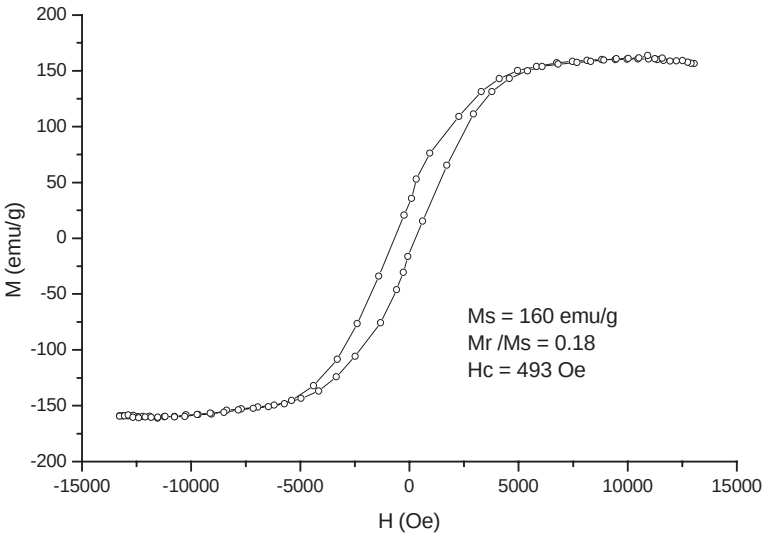

Fig. 8. The magnetization variation of the Co magnetic microparticles against applied magnetic field.

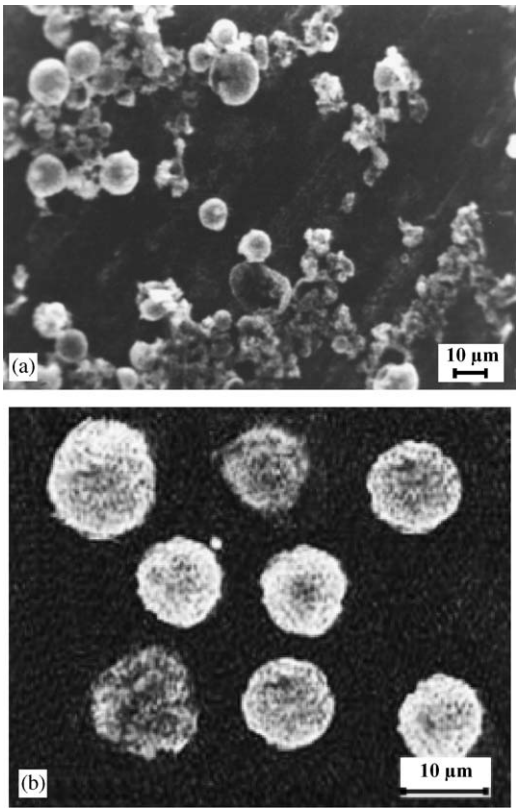

Fig. 9. Covered magnetic particles before (a), and after washing (b).

To verify the sensitivity of the GMI-based magnetic sensor, we measured the magnetic impedance variation, ΔZ, against different concentrations of magnetic particles dispersed in sodium dodecil sulphate (1% in distilled water). We used styrene-covered Co soft ferromagnetic microparticles with 10–15 μm in diameter. In Fig. 10 is presented the variation of the magnetic impedance, ΔZ, versus magnetic particle concentrations.

Considering the results, we can appreciate this sensor sensitivity, which is very suitable for different biomolecules detection. Also, we appreciate that concentrations of 25–30 magnetic particles/μl can be detected.

This GMI-based sensor presents a very high sensitivity, a good thermal stability, offering at the same time, due to its three-dimensional representation, a high detection surface. In addition,

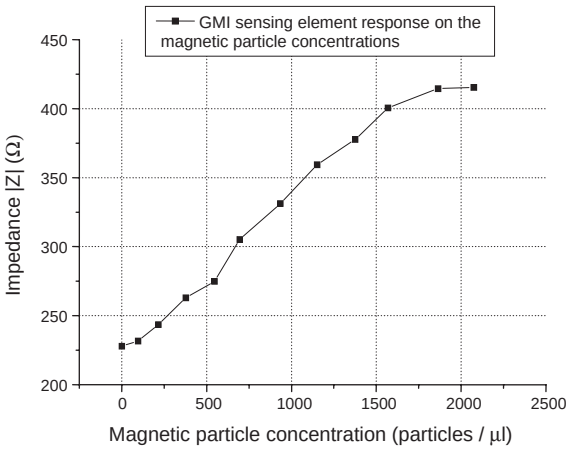

Fig. 10. Impedance response of the sensing element on the magnetic particles concentration.

structures of magnetic microwires arrays, even superposed, with high density are possible.

To effectively work as biosensor, the sensing element of the sensor must be functionalized with specific bioreceptors. For this purpose, the glass-covered amorphous microwire will be covered with a polymer using a procedure for binding polymers on glass [7] or other appropriate procedure [8]. This will be accomplished in our further work.

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