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Review

Nanostructured materials for magnetic biosensing

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ABSTRACT

Background: Magnetic nanoparticles (MNPs) are at the leading edge of the field of biomedical applications and magnetic biosensing.
Methods: MNPs were fabricated by electrophysical methods of the laser target evaporation (LTE) and spark discharge with electrodynamic acceleration of plasma jumpers (SD). Synthesis of polyacrylamide hydrogel was done in the presence of Fe_2O_3 MNPs in different concentrations obtained by LTE. $[FeNi/Ti]_3/Cu/[Ti/FeNi]_3/Ti$ multilayers for giant magnetoimpedance (GMI) based sensitive elements were prepared by rf-sputtering for testing a biosensor prototype.
Results: Iron oxide MNPs, ferrofluids, ferrofluids contacting with biological systems, synthetic ferrogels mimicking natural tissues – are the steps of the discussed in this work development of bionanomaterials. Thorough the structural and magnetic studies of a multilayered sensitive element, MNPs and ferrogels insure the complete characterization of biosensor prototype. The GMI responses were carefully evaluated in initial state and in the presence of ferrogel with known concentration of MNPs. SD MNPs had the smallest 5–8 nm size. This nanomaterial was characterized by large internal strains of the order of 25×10^{-3}, which can play an important role for the interaction with different biosystems.
Conclusions: Iron oxide MNPs were fabricated by LTE and SD methods. SD MNPs had the smallest 5–8 nm size and large internal strains of the order of 25×10^{-3}. Designed GMI biosensor prototype allowed precise evaluation of the stray field of the MNPs present in the ferrogel by evaluating the systematic changes of the GMI in a 20–400 MHz frequency range.
General significance: This work summarizes recent developments in the field of nanomaterials potentially applicable in magnetic biosensing.

1. Introduction

Biocompatible iron oxide magnetic nanoparticles (MNPs) are a subject of special interest for biomedical applications [1,2]. For biological tasks, it is important to ensure a well-controlled shape and a large single batch. The fabrication techniques providing enhanced batch sizes [3,4] attract special attention as the properties of MNPs can vary from batch to batch. One of the fabrication methods of MNP synthesis providing a high production rate is the electrophysical technique of the electric explosion of wire (EEW) [5]. It ensures fabrication of spherical MNPs with an average size of 20 to 100 nm. Another electrophysical method is the laser target evaporation (LTE): it provides 10 to 50 nm MNPs [6,7].

MNPs can enter the interior of a living system through the air, the gastrointestinal tract, as nanosized wears of implants or endoprosthesis. MNPs with a diameter below 50 nm penetrate tissue barriers and can be toxic. Their accumulation and their degradation products in the tissues and biofluids is a still poorly understood potential health hazard [8]. MNPs are widely studied as nanomaterials for hyperthermia and thermal ablation (promising forms of cancer therapies), drug delivery and magnetic biosensing [2,8–10]. The latter is especially requested in medicine and environmental control. A magnetic biosensor is a compact analytical device with a magnetic transducer that converts a magnetic field variation into a change of frequency, current, voltage, etc. Different magnetic effects are capable of creating sufficiently sensitive magnetic biosensors: magnetoelastic, Hall, inductive effects, anisotropic

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magnetoresistance, giant magnetoresistance, spin-valves and giant magnetoimpedance (GMI) [11]. The magnetoimpedance phenomenon consists in the change of the total impedance of a ferromagnetic conductor, $Z = R + jX$ (where R is a real and X is an imaginary components), in an external magnetic field, H, when a high-frequency alternating current $I = I_0 e^{-i\omega t}$ flows through it (t is the time and ω is the angular frequency) [12,13]. In a magnetic biosensor the magnetic field plays the role of a transducer.

GMI provides the highest sensitivity (change of the impedance or its components per unit of the field) with respect to the external applied field. The principle of magnetic label detection in a biosensing system is simple: the stray fields induced by the magnetic markers are employed as biomolecular labels providing a means to transfer information about the concentration of magnetic labels and the bicomponent of interest [14]. The sensitivity of a magnetic biosensor is related to the type of MNPs used as biomarkers because the magnetic moment of an individual particle in the external magnetic field creates the stray fields and changes of the sensitive element response. As MNP properties can vary from batch to batch, special attention is paid to fabrication techniques with enhanced batches of spherical nanoparticles like LTE.

Among other special demands for biomedical applications of magnetic MNPs is that they can be most efficiently employed in the form of water-based ferrofluids (FF) or ferrogels [15,16]. In our previous works, we analysed specific conditions for the formation of water-based FF on the basis of EEW and LTE MNPs [2,5]. There are two main strategies for obtaining colloidal suspensions of de-aggregated magnetic nanoparticles: electrostatic or steric stabilization [15]. All living systems rely on chemical reactions in water solutions characterized by a large concentration of salts. Therefore, the parameter of major importance for biomedicine is the stability of ferrofluids in physiological solutions. An increase of the ionic strength of the biological medium makes the electrostatic stabilization of the FF less favourable. In several recent studies, a natural polymer chitosan has been discussed as an effective electrosteric stabilizer [17]. The presence of amino and hydroxyl groups in its elementary unit provides the specific interaction between macromolecules of chitosan with the MNPs surface and leading to a suspension stabilization at low polymer concentrations [18]. The analysis of the morphofunctional response of living cells to the presence of different kinds of suspensions is missing in the literature with some exceptions [18] but a better understanding of the interactions of the living system and MNPs would be beneficial for the hyperthermia, biosensing and drug delivery.

Another interesting case requested for cancer therapies, which has not yet been properly addressed is the detection by a magnetic biosensor of the MNPs incorporated into biological tissues. The development of such a compact device is impossible without reliable samples. Biological tissues present a huge variety of individual morphologies depending on many parameters and conditions. It is especially true for the cancer tissues affected by the irregular accelerated growth of blood vessels with formation of defectively large pores [3]. In the previous studies, we proposed to substitute biological samples at the first stage of the development of GMI-based biosensor prototype by the adequate model material – synthetic gel. Hydra- /ferro-gels are capable of mimicking the main properties of the living tissues [19,20]. The capability of a GMI biosensor prototype in to measure the change of GMI of a FeNi/Ti-based thin film sensitive element in the presence of ferrogels with different concentration of iron oxide MNPs has been demonstrated. However, this is still an underdeveloped area with high potential for multidisciplinary research and applications.

Progress in fabrication of water-based EEW and LTE ferrofluids and ferrogels on the one hand offered the opportunity of advanced characterization of such materials but on the other hand it revealed the need to develop techniques for fabrication of large batches of MNPs with an average size below 10 nm. One of the candidates is the spark discharge (SD) electrophysical technique [21,22]. It the case of the SD method, researchers usually use microsecond generators with charging voltages equal or below 5 kV. The distances between electrodes were typically under a few millimeters and the energy stored by the capacitor around tens of mJ [22]. Small inter-electrode distances limited the volume where the condensation of MNPs took place from the vapor phase. The consequence was the formation of rather large MNPs. We propose the approach for substantial diminishment of the MNP size by using much wider discharge gaps and electrodynamic acceleration of plasma jumpers, arising in the discharge gap. The directed motion of the plasma jumper gives an additional momentum to the evaporation products of the material of the electrode, leading to a more rapid decrease in the concentration of vapors and the formation of small MNPs.

In this work, we describe, on the one hand, our experience preparing iron oxide MNPs with an average particle size of the order of 15 nm by the electrophysical LTE method. On the other hand, we describe the development of a preparation method of colloidal suspensions of de-aggregated MNPs and ferrogels on their basis. Well-adjusted spark discharge conditions with electrodynamic acceleration of plasma jumpers allows stable production of MNPs with an average size below 10 nm.

2. Materials and methods

2.1. Electrophysical methods of iron oxide nanoparticle fabrication

Laser target evaporation technique and spark discharge with electrodynamic acceleration of plasma jumper's technique will be discussed.

2.1.1. Laser target evaporation technique

Iron oxide MNPs were synthesized by laser target evaporation (LTE) – the method of high temperature physical dispersion based on the evaporation of a solid pellet by the laser beam with the consequent condensation of vapors in the gas phase [6,7,23,24]. LTE was performed using laboratory installation with Ytterbium (Yb) fiber laser with 1.07 μm wavelength (Fig. 1). The target pellet of 65 mm in diameter, 20 mm in height was pressed from commercial magnetite (Fe_3O_4) (Alfa Aesar, Ward Hill, MA, USA) powder (specific surface area 6.9 m^2/g). The pellet was mounted in the evaporation chamber upon a driving mechanism, which provided the rotation and horizontal movement of the pellet. The laser beam was focused onto the target pellet surface by the optical Optoscand d25 f60/200 system with 200 mm focal length. The diameter of the focal spot was 0.45 mm. The driving mechanism provided 20 cm/s beam scan rate on the target surface, which ensured a uniform wear-out of the target surface. The laser operated in a pulsed regime with a pulse frequency of 4.85 kHz and pulse duration 60 μs. The average output power of irradiation was about 212 W. The working gas (a mixture of N_2 and O_2 in the volume ratio 0.79:0.21) was blown into the evaporation chamber by the fan. The gas flow rate was 58 L/min at normal pressure. The linear flow rate at the target surface was approximately 12 m/sec. The oxide vapors were driven away from the focal spot and condensed in spherical nanoparticles, which were carried by the working gas into the cyclone and the fine filter where the powder was gathered.

2.1.2. Spark discharge with electrodynamic acceleration of plasma jumpers technique

The spark discharge method was developed a long time ago and the first results related to nanoparticle synthesis by spark discharge were introduced in the late 80's [25]. Currently, most researchers use microsecond spark generators, with charging voltages of a storage capacitor not exceeding 5 kV, the distance between electrodes being less than 3 mm, and the energy stored by the capacitor amounting to tens of mJ [26,27]. Such short inter-electrode distances limit the volume in which the condensation of particles from the vapor phase proceeds, which leads to the formation of large particles. In order to reduce the size of the particles, the energy released in the discharge gap must be reduced,

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