Proton magnetization relaxation in aqueous suspensions of composite silicon-iron nanoparticles for biomedical applications

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Abstract. Silicon-iron composite nanoparticles produced by arc-discharge plasma ablation method were characterized by scanning electron microscopy, dynamic light scattering, X-ray fluorescence diffractometry, and the effect of iron content and size of the nanoparticles on hydrogen nuclei magnetization relaxation were investigated by nuclear magnetic resonance relaxometry. It was shown that increasing in iron content during the synthesis leads to distortion of the spherical shape of the nanoparticles and increasing of their mean sizes from 140 nm to 350 nm. Nonlinear dependence of the longitudinal and transverse relaxivities from iron content was demonstrated. Increase in the iron concentration above 2.5 at. % leads to reduction of the both relaxivities, which can be explained by nonuniform distribution of iron and formation of iron containing agglomerates. It was shown that transverse and longitudinal relaxivities of the nanoparticles in their aqueous solutions inversely proportional from their hydrodynamic diameters in the range of 100 – 300 nm. The possibilities of using composite silicon-iron nanoparticles for biomedical applications are discussed.

1. Introduction

The application of nanoparticles (NPs) in biomedicine is one of the priority areas of research. A large number of different NPs have been developed for targeted drug delivery, cell labeling, gene delivery, diagnostics, and treatment of diseases [1-5].

Silicon NPs are the object of growing interest and intensive research due to their high biocompatibility and biodegradability, which are confirmed by numerous in vitro and in vivo experiments [6,7]. Intravenously injected silicon NPs of a dose of 20 mg/kg in mice were completely removed from the body through renal clearance within four weeks. It was shown that silicon NPs can be used as sensitizers of external electromagnetic fields, light, ultrasound, and used as agents for therapy and diagnostics [8-12]. The possibility of using porous silicon NPs as contrast agents for magnetic resonance imaging (MRI) was investigated [13,14]. To increase the contrasting properties of the silicon
NPs, composite silicon-iron (Si-Fe) NPs were synthesized with an iron content less than 0.2 at. % [15,16]. Such NPs showed low toxicity and high efficiency in MRI as contrast agents. In this work, NPs with an increased iron content of up to 10 at. % were obtained and the effect of iron content and size of the NPs on the T1 and T2 relaxation times of the hydrogen nuclei in aqueous suspensions was studied.

2. Materials and methods
Si-Fe NPs were prepared by using an arc-discharge plasma ablative synthesis, where polycrystalline Si powder was mixed with 2.5, 5, and 10 at. % of Fe powder, evaporated at 5500 °C in an arc-discharge reactor and then cooled down for condensation of the Si-Fe NPs [16,17].

NPs were investigated using a scanning electron microscope (SEM) obtained by Tescan Maia 3 at an accelerated voltage of 15-20 kV. X-ray fluorescence (XRF) analysis of the elemental composition of the NPs was carried by RADIANT apparatus using SmartXRF software. Sizes of the prepared NPs in water solutions were studied using dynamic light scattering (DLS) with a Malvern Zetasizer Nano ZS size analyzer. The proton relaxation times T1 and T2 were measured by a Bruker Minispec NMR Relaxometer with 20 MHz probe and magnetic field 0.5 T at 40 °C.

3. Results and discussion
Figure 1 shows SEM images of the Si-Fe NPs with 2.5, 5, and 10 at. % of iron content. One can see that part of the NPs are non-spherical and the fraction of such NPs increases with increasing iron content. The mean sizes of NPs increase with an increase in the iron concentration, and the size distribution mode shifts from 140 nm to 350 nm.

![Figure 1. SEM images of Si-Fe NPs with different iron content.](image)

XRF comparative analysis of the prepared NPs showed that NPs consist of silicon and iron in different ratios. Figure 2 (a) shows peaks associated with K a and K b lines of iron. It can be seen that intensity of the iron peaks increases with increasing of the iron content. Figure 2 (b) shows energy-dispersive spectroscopy (EDS) spectra obtained from two regions of individual NP. It can be seen that an increase in the concentration of iron above 2.5 at. % leads to the formation of iron enriched agglomerates on the surface on NP. It should be noted that we have not seen any iron agglomeration in samples with less than 0.2 at. % iron content [14,15].
Figure 2. (a) XRF comparative analysis of iron content in the obtained Si-Fe NPs, (b) EDS spectra obtained from two regions of a Si-Fe NP with 10 at. % of iron.

To quantify the effect of Si-Fe NPs on the proton relaxation one can calculate the longitudinal, $r_1$, and transverse, $r_2$, relaxivities as follows:

$$r_{1,2} = \frac{R_{1,2}}{C},$$

where $C$ is the mass concentration of NPs in suspension, $R_1$ and $R_2$ are longitudinal and transverse relaxation rates. The relaxation rates are estimated as:

$$R_{1,2} = \left(\frac{T_{1,2}}{T_{1,2}^w}\right)^{-1} - \left(\frac{T_{1,2}^w}{T_{1,2}^w}\right)^{-1},$$

where $T_{1,2}^w$ and $T_{1,2}^w$ are the corresponding times for pure water, $T_1$ and $T_2$ are the measured times for the NP suspension.

Figure 3 shows the dependence of the transverse and longitudinal relaxivities of the Si-Fe NPs in their aqueous solutions from iron content. It can be seen that there is almost linear dependence of relaxivity values from the iron content in the range of $10^{-4} - 0.2$ at. %. The increase of the relaxation rate in presence of Si-Fe NPs is caused by the silicon dangling bonds and iron ions on the surface of the NPs. However, further increase in the concentration of iron leads to a reduction of both transverse and longitudinal relaxivities and only for the sample with the highest iron content an increase in both relaxivities is observed. Such effect can be due to formation of iron-enriched agglomerates in NPs with more than 2.5 at. % of iron content, which leads to a decrease in the number of active iron ions.

Figure 3. (a) Transverse and (b) longitudinal relaxivities of the Si-Fe NPs in their aqueous suspensions from iron content.
Since the obtained Si-Fe NPs have a large variation in size the suspensions were subjected to multiple centrifugations at different speed. As a result, a set of Si-Fe NPs with a narrow size distribution was obtained and the influence of NP’s size on the relaxation of the proton magnetization was investigated. Figure 4 shows that a decrease in the hydrodynamic size of NPs leads to an increase of both the transverse and the longitudinal relaxivities, which can be explained by an increase of the total surface area. The value of relaxation is normalized to the concentration of iron left in sample after centrifugation.

![Figure 4](image)

**Figure 4.** (a) Longitudinal and (b) transverse relaxivities of Si-Fe NPs in their aqueous solutions from hydrodynamic diameter of the NPs.

### 4. Conclusions

Silicon nanoparticles with 2.5, 5, and 10 at. % of iron were prepared by an arc-discharge plasma ablative synthesis and characterized by a number of physical methods, including scanning electron microscopy, dynamic light scattering, X-ray fluorescence diffractometry. It was shown that increasing in iron content during the synthesis leads to distortion of the spherical shape of the nanoparticles and formation of composite particles with iron-enriched and iron-depleted regions. The mean sizes of the nanoparticles increase with an increase in the iron concentration, and the size distribution mode shifts from 140 nm to 350 nm. Influence of the NPs on proton magnetization relaxation in their aqueous suspensions were investigated by the nuclear magnetic resonance relaxometry. The obtained results demonstrate nonlinear dependences of the transverse and longitudinal relaxivities from iron content that can be explained by nonuniform distribution of iron in case of relatively high iron contents. It was shown that transverse and longitudinal relaxivities of the nanoparticles in their aqueous solutions inversely proportional from their hydrodynamic diameters in the range of 100 – 300 nm. High relaxivity values of the prepared nanoparticles demonstrate the potential for their applications in MRI diagnostics.

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