Alternating magnetic field and NIR energy conversion on magneto-plasmonic Fe$_3$O$_4$@APTES–Ag heterostructures with SERS detection capability and antimicrobial activity

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Multipurpose Fe$_3$O$_4$@APTES–Ag heterostructures for mutual heat generation, SERS probing, and antimicrobial activity were fabricated using a three-step process. Silver metallic particles were precipitated on a thin silica shell that served as an interlayer with Fe$_3$O$_4$ nanocubes. The structural properties were studied by means of the powder X-ray diffraction technique, and selected area electron diffraction. Particle size, distribution, and morphology were evaluated using transmission electron microscopy, while element mapping was performed using the STEM-EDS technique. The presence of the silica shell and the effectiveness of the Ag reduction were checked by FTIR-ATR spectroscopy. The heat generation ability was studied by using AMF and NIR contactless external stimulations working separately and simultaneously. We demonstrated that the dual mode stimulation leads to a SAR (specific absorption rate) of 1000 W g$^{-1}$ with the predominant role of the mechanism associated with the light interaction. The SERS effect was recorded with the use of the R6G standard molecule showing high capability of the heterostructures for Raman signal augmentation. Fe$_3$O$_4$ nanocubes decorated with Ag particles have shown antibacterial activity against $P$. aeruginosa. The Fe$_3$O$_4$@APTES–Ag presents promising potential as a multipurpose platform for biological applications ranging from photomagnetic therapies, to analytical probes exploiting the SERS effect and antibacterial activity.

1. Introduction

The ability of magnetite nanoparticles (MNPs, Fe$_3$O$_4$) to induce heat under the action of external stimulants is a basis for the biological application of hyperthermia that can support modern therapeutic approaches to cancer treatment.$^1$ This particular material attribute is directly related to the magnetic properties of Fe$_3$O$_4$ and is driven by the general mechanism of power loss that incorporates three main contributions being a consequence to the alternating magnetic field (AMF) exposure.$^2$ The first one is associated with hysteresis losses that depend on the coercive field and are characteristic of the particles with domain/multidomain structure, the second with generation of eddy currents whose strength is affected by the magnetic field frequency and intensity and their induction changes in the following material classification manner: metals > semiconductors > insulators. The last is connected with the residual losses that can be subdivided into Néel (internal) and Brownian (external) relaxations. Internal relaxation represents fluctuations in MNP magnetic moments, while the external mechanism is due to fluctuations in magnetic moments that cause rotation of the entire particle.$^3$–$^7$ The presence or absence of one of the power loss mechanisms is strongly dependent on many parameters like particle size, composition, shape, anisotropy, stability, presence of ligands, etc.$^8$

Laser exposure with wavelengths within the therapeutic optical biological window maximized tissue light penetration (650–1300 nm) is used to heat nanoparticles of different kinds to induce temperature effects.$^9$ The rule of thumb is to find a highly absorbing material that will dissipate the collected energy non-radiatively (net phonons) to heat a given system to achieve a biologically relevant temperature effect.$^{10,11}$ Among many materials exploited, magnetite is a very promising candidate to achieve this goal,$^{12–18}$ as its optical properties show reasonable absorption in the near-infrared range (NIR).$^{19}$
Recently, considerable interest has been faced towards exploitation of multimodal heat induction by the use of the simultaneous action of AMF and NIR. The trick is to take the advantage out of the two totally independent mechanisms of energy conversion into heat that allow to achieve much faster sample heating and reduce the development of thermodenial by cells that is characteristic of slow heating rates. It is also possible to go beyond the maximum temperature that can be achieved by using separate mode, to limit the concentration of MNPs if needed, or to reduce the overall exposure time. Therefore, the search for new materials with optimized properties and/or offering additional functions is of great importance.

The noble metal decorated magnetite particles, especially with silver and gold, are of special interest since combination of magnetic properties with plasmonic effect have interesting implications. For instance Fe3O4@Au heterostructures have been proposed for use as an opto-magnetic platforms, whereas Das et al. proposed reversed Ag@Fe3O4 composite structures. However, both materials did not show significant enhancement in SAR (specific absorption rate) compared to the commercially available Resovist®. In the case of the Fe3O4@Ag decorated hybrid material, not much was done in terms of temperature effects. The main direction was pushed towards surface-enhanced Raman scattering (SERS) for detection of analytes and effective catalysts or disinfectant with antibacterial activity. The role of the magnetic core in the latter examples was limited to separation agent facilitating collection of the heterostructures from the medium after use with a static magnetic field and particles recycle.

The purpose of the presented studies was to assess the efficiency of energy conversion using combined AMF and NIR (808 nm laser light) external contactless stimulation in the multipurpose heterostructure of Fe3O4@APTES–Ag. Except for the significant temperature response of the hybrid material, its multifunctional properties were tested towards the SERS probe for detection of analytes as well as antimicrobial activity estimated against Staphylococcus aureus ATCC 25923, Staphylococcus epidermidis ATCC 12228, Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27953 with pronounced effect against the last bacterial strain. Morphology-controlled Fe3O4 MNPs (nanocubes) were used as a core material, while (3-aminopropyl)triethoxysilane (APTES) served as an interconnector layer between Fe3O4 and Ag, a surface protection agent (prevention of MNP from oxidation and contact with outer media) and as a chelation enhancer due to increased affinity of amine APTES groups for silver cations.

2. Materials and methods

2.1. Three-step synthesis of MNPs core–shell structures decorated with Ag nanoparticles

The synthetic protocol for the fabrication of Fe3O4@APTES–Ag core–shell structures included three distinct steps, namely (I) preparation of the Fe3O4 nanocubes stock particles, (II) surface coverage of the stock MNPs with the APTES shell, and (III) reduction of silver cations to induce precipitation of metallic Ag nanoparticles.

2.1.1 Synthesis of Fe3O4 nanocubes. The stock Fe3O4 nanocubes were prepared by adopting the well-known thermal decomposition technique described by Kim et al. with slight amendments. Briefly, 2 mmol of iron(n) acetylacetonate precursor (Fe(acac)3; 99.7%, Thermo Fischer Scientific, Germany), 4 mmol (1.4 ml) of oleic acid (OA, 90%, Sigma Aldrich, Poland) and 10 ml of diyl ether (BE, 98%, Sigma Aldrich, Poland) were taken. The iron source was transferred to the three-neck glass flask and dissolved in BE solvent with the subsequent addition of the OA ligand under an inert N2 protective atmosphere (N2 99.999%, Linde, Poland) using an acrylic glove box (GS Glove Box Systemtechnik GMBH P10R250T2). The flask with mixed chemicals was attached to the setup combined with a mechanical stirrer, automatic temperature controller with Pt-100 sensor, reflux column, laboratory heater, and N2 line. Afterward, the reaction mixture was degassed for one hour at room temperature with a constant flow of N2. Finally, the solution was heated up to 285 °C and kept for 30 minutes. The resulting black product was separated from the mother liquor by centrifugation and washing cycles using portions of the solvent mixture hexane/acetone/ethanol (1 : 1 : 1 ratio, all pure for analysis from Chempur, Poland). The purified stock nanoparticle suspension is stored in an ethanol solution in a laboratory refrigerator. The concentration of Fe3O4 cubes was measured using the microbalance.

2.1.2 APTES silica shell formation. This step involved the following actions. First, 50 mg of well-dispersed Fe3O4 nanocubes are transferred to hexane and washed three times with this solvent to completely remove ethanol. If fresh particles are prepared from step (I), the MNPs can be kept directly in hexane after purification. A laboratory magnet can be used to facilitate cube separation if necessary. Finally, Fe3O4 particles are resuspended in 5 ml of hexane and sonicated for 2 hours at room temperature. The suspension is transferred to the flask and filled with an additional portion of hexane to 45 ml. After that, 2 ml of IGEPAL CO-520 (polyoxyethylene (5) nonylphenylether, Sigma Aldrich, Poland) was sonicated for an additional 15 minutes. Then, 0.4 ml of ammonia (25% solution, 99%, Honeywell, Poland) was kept in an ultrasound bath for an additional 15 minutes at room temperature. Subsequently, the mixture was placed in a glass flask in the set-up equipped with a mechanical stirrer and 100 μl of tetraethoxysilane (TEOS, 99.9%, Thermo Scientific, Poland) was added in constant mixing for one hour. Lastly, a mixture of 100 μl of TEOS and 100 μl of APTES ([3-aminopropyl]triethoxysilane, 99%, Sigma Aldrich, Poland) was added and left for 16 hours with stirring. The Fe3O4@APTES core–shell structures were separated using a laboratory magnet followed by washing cycles with an acetone and ethanol mixture. The concentration of particles was measured using the same technique as in the first step.

2.1.3 Fabrication of metallic Ag nanoparticles on Fe3O4@APTES surface. To induce Ag nanoparticle formation, 2 mg Fe3O4@APTES were dispersed in 20 ml of deionized water and sonicated for 15 minutes. Subsequently, four portions of 0.1 ml
of AgNO₃ solution (99%, POCH, Poland) (1 mg ml⁻¹) were added every 15 minutes. The sample was still placed in an ultrasonic bath during this stage. The entire suspension was then transferred to the glass flask and 0.76 ml of NaBH₄ solution (1 mg ml⁻¹, 99% Thermo Scientific, Poland) was added to induce a fast reduction of Ag⁺ and the formation of Ag metallic particles under mechanical stirring. The final Fe₃O₄@APTES–Ag product was purified separately with H₂O and ethanol (3 times each solution) and separated with a laboratory magnet. The core–shell material was resuspended in ethanol for storage and further use.

2.2. Characterization of nanoparticle physicochemical properties

Stock Fe₃O₄ nanoparticle structure was evaluated by means of the X-ray powder diffraction technique (XRD) using a Bruker D8 Advance diffractometer equipped with a Cu lamp as the X-ray source (1.54 Å) and K₂CO₃ nickel filter. The range of measured 2θ was between 15 and 70° with a step of 0.02° applying 0.8 s integration time. The recorded diffraction pattern was background corrected using Diffrac.Eva software (V.2) and compared with the ICDD diffraction database for structure identification and crystallographic plane assignment. Further data curation (including normalization and reference comparison) for the final presentation was performed using Origin Pro 2019 9.60 software (OriginLab, USA).

The particle size, morphology, additional structural data, and element mapping were performed using Tecnai Osiris X-FEG transmission electron microscope (TEM) operating at 200 kV using different techniques high-resolution TEM (HRTEM), high-angle annular dark-field (HAADF) imaging in scanning transmission electron microscopy (STEM) as well as energy dispersive analysis for confirmation of the presence of silica shell as well as the location of silver particles. Fourier transformation was applied to the HRTEM picture to measure the interplanar distance and identification of exposed crystallographic planes by Fe₃O₄ particles using DigitalMicrograph (v. 1.85.1535) software. The nanocube, silver particle size, and distribution together with silica shell thickness were evaluated in ImageJ software (v. 1.8.0_1720). The sample for TEM characterization was prepared by sonication cycles and further deposition of a droplet of MNPs ethanol suspension on a 200 mesh copper grid coated with a transparent layer of carbon (EM Resolutions, United Kingdom) and slow solvent overnight evaporation under dust protection.

The nanoparticle concentration was determined using the microbalance technique using a precise Radwag MYA 5.4Y scale. The measurement was made through three independent repetitions.

Fourier-transform infrared spectroscopy (FTIR) was used to carry out the measurements of the vibrational spectra of prepared materials utilizing a Thermo Scientific Nicolet iZ10 FTIR spectrometer equipped with Smart Orbit Diamond ATR (attenuated total reflection accessory). All materials were slowly dried and placed on a diamond surface. Spectra were recorded at room temperature within the 4000–500 cm⁻¹ wavenumber range.

2.3. AMF and NIR energy conversion on heterostructures

The behavior of the stock nanocubes and Fe₃O₄@APTES–Ag core–shell structures upon the action of the alternating magnetic field (AMF), near-infrared 808 nm laser radiation (NIR), and synergy of both external stimulants was measured with help of magnetic field generator G2 D5 Series Multimode 1500 W driver supplied by Nanoscale Biomagnetics (Spain) using calorimetric CAL1 coliset. The NIR radiation was delivered through 400 μm multimode optical fiber (CNI China). FLIR T660 Thermovision camera was used for a direct measure of sample temperature. The applied field frequency and intensity were within a range of 145–486 kHz and 23–33 kA m⁻¹ while laser power was between 0.3–1.7 W. The distance of the optical fiber from the suspension surface was 4 cm assured full top sample coverage (around 1 cm²). During the synergy of both contactless stimulants, optimized parameters were used (302 kHz, 28 kA m⁻¹, 900 mW). Before experiments, CAL1 was calibrated using manufacturer procedure whereas laser output power was checked using Ophir StarLite power meter with beam track thermal sensor 10A-PPS (Ophir, Israel). All data were recorded using ResearchIR software (FLIR, USA) and analyzed using Origin Pro software. The concentration of the prepared stock suspensions of Fe₃O₄ and Fe₃O₄@APTES–Ag core–shell structures used for energy conversion studies varied between 1–6 mg ml⁻¹.

2.4. Surface-enhanced Raman scattering (SERS) on heterostructures

The ability to generate the SERS effect was analyzed using an inVia Micro Raman Renishaw spectrometer combined with a Leica DM 2500M microscope (Renishaw, UK) equipped with a 488 nm laser as an excitation source. The measurements were taken with an exposure time of 10 s with triple scan accumulation and for the laser output power that ranged from 25 μW to 0.5 mW. As a reference material for testing, rhodamine 6G (R6G, Sigma-Aldrich, Poland) was chosen. Various ethanol dilutions of rhodamine were prepared (0.05–2.5 μM) and mixed with 0.75 mg ml⁻¹ of Fe₃O₄ nanocubes, Fe₃O₄@APTES and Fe₃O₄@APTES–Ag heterostructures, respectively. After a short incubation, samples were placed on quartz discs and slowly dried. The final SERS measurement was carried out with a 50× lens magnification and choosing three random positions for each material. Baseline correction was performed during data processing.

2.5. Antimicrobial activity tests with bacteria strains

Antibacterial activity of nanoparticles was evaluated by determination of minimum inhibitory concentration (MIC), on basis of the serial dilution method. As model bacteria, 4 reference strains were used: Staphylococcus aureus ATCC 25923, Staphylococcus epidermidis ATCC 12228, Escherichia coli ATCC 25922, and Pseudomonas aeruginosa ATCC 27953. Before the experiments, they were first cultured in Mueller–Hinton (M–H) broth (Biomaxima, Poland) at 37 °C to obtain inoculates of initial density equal to 0.1 McFarland (an equivalent of 3.0 × 10⁷ CFU
ml\(^{-1}\)). Suspension of each nanoparticle in ethanol was diluted in Mueller–Hinton (M–H) broth to obtain a series of concentrations: 50–500 \(\mu\)g ml\(^{-1}\) for Fe\(_3\)O\(_4\) nanoparticles and 1.56–50 \(\mu\)g ml\(^{-1}\) for Fe\(_3\)O\(_4\)@APTES and Fe\(_3\)O\(_4\)@APTES–Ag core–shell nanoparticles. As reference samples, ethanol was diluted in M–H broth to obtain analogous concentrations as in NPs dilutions. As a positive control of bacterial growth, pure M

late (to initial titer 0.6

\(\times\) 10^8 CFU ml\(^{-1}\)). Pure M–H broth without inoculation was used to control the initial medium sterility. Immediately after the inoculation (7 h), the absorbance of the wells was measured at 660 nm in Biotec Synergy H4 Hybrid multiplate reader (Fisher Scientific, USA). Then, the plates were incubated in Innova 42 incubator shaker (New Brunswick Scientific, USA) at 37 °C, 150 rpm, and 24 h. Finally, the turbidity in the wells was examined. MIC (minimum inhibitory concentration) was defined as the lowest concentration of NPs which prevented bacterial growth in the culture medium which was visualized by lack of turbidity in the wells.

Fig. 1 Indexed X-ray diffraction pattern as well as SAED image with FFT transformation of HRTEM for identification of exposed crystallographic plane of the stock Fe\(_3\)O\(_4\) nanocubes.

3. Results and discussion

3.1. Physicochemical characterization of materials

The structural properties of the core material, namely Fe\(_3\)O\(_4\) nanocubes, were evaluated using the XRD technique. The recorded diffraction pattern after background correction and normalization is presented in Fig. 1, and compared with the reference ICDD card (International Centre for Diffraction Data – PDF database) no. 019-0629 that is ascribed to the cubic \(Fd\bar{3}m\) magnetite structure. All the appearing reflections, within the measured 2\(\theta\) range, were assigned to the respective crystallographic planes showing a perfect match with the chosen standard card. In addition, selective area electron diffraction (SAED) was performed on a single particle together with identification of the exposed crystallographic fringes using Fourier transformation applied to the HRTEM image (Fig. 1 right panel). Both measurements confirmed that the stock material crystallized in a cubic symmetry that is characteristic of the ferrite family. The measured interplanar distance of the 0.149 nm (4 4 0) plane agrees with the reference data.

The size, distribution, and morphology of the Fe\(_3\)O\(_4\) nanocubes, Fe\(_3\)O\(_4\)@APTES–Ag, and Ag particles in the core–shell structures were defined using TEM imaging (Fig. 2). Non-modified Fe\(_3\)O\(_4\) particles have a predominant cubic morphology that is maintained during the APTES coverage and the Ag\(^+\) reduction step. The particle size and distribution for the stock cubes was 72 ± 13.9 nm, while Fe\(_3\)O\(_4\)@APTES–Ag was 94.7 ± 15.5 nm, and the Ag nanoparticles were 8.5 ± 3.7 nm. The shape of the Ag precipitate on the surface of Fe\(_3\)O\(_4\)@APTES is not well defined, and the particles tend to have a rather irregular morphology. In the case of silica modification using APTES, the thickness of the shell was measured giving the mean value of 12.8 ± 3.4 nm. As can be seen, the shell formed by the silica interlayer containing amine functional groups is rather thin. The choice of APTES as a shell-forming material was dictated by the fact that –NH\(_2\) functional groups bond Ag\(^+\) cations through chelation, not through sorption as –OH functionality, and ensures a higher affinity towards silver cations. All results have been collected and plotted in Fig. 3 for quick comparison. Interestingly, the particles tend to organize in chain-like structures.

According to Qiao et al., this behavior is characteristic of magnetic particles, where magnetic dipolar interactions between particles dominate (long-range) over van der Waals forces (short range). Usually, this kind of assemblies are observed for magnetite with a size greater than 40 nm. What can be potentially worth mentioning is that this type of self-organization is less pronounced for the Fe\(_3\)O\(_4\)@APTES–Ag

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core–shell since the thickness of the silica shell and Ag size probably reduce the possibility of effective magnetic interactions due that their diameters account for the separation of the magnetic cores between each other.

Element mapping was performed (Fig. 4) using the STEM-HAADF-EDS technique to check the effect of the surface coverage of APTES and silver reduction in terms of the presence of silicon and silver elements in the Fe₃O₄@APTES and

![Fig. 2 TEM images of the Fe₃O₄ stock nanocubes, nanocubes covered with a thin shell of APTES as well as Fe₃O₄ decorated Ag metallic nanoparticles on APTES shell.](image)

![Fig. 3 Particle size distribution curves for Fe₃O₄ stock cubes, APTES shell thickness, Fe₃O₄@APTES–Ag core–shell structures, and Ag particles.](image)
Fe₃O₄@APTES–Ag structures. It can be seen that the Fe₃O₄ nanocubes were covered with a rather uniform and thin APTES shell. The reduction of adsorbed Ag⁺ cations leads to the formation of separated islands of metallic silver, as confirmed by the overlap areas between the Ag element map and the HAADF image that are characteristic of the presence of individual Ag particles bounded to the Fe₃O₄ cubes through the APTES interlayer.

The FTIR-ATR spectroscopy was used to record vibrational spectra of Fe₃O₄ nanocubes, Fe₃O₄@APTES core–shell and Fe₃O₄@APTES–Ag heterostructures (see Fig. 5) and to assess the effect of silica surface coverage and silver attachment after the reduction process. The appearance of the Fe₃O₄ nanocubes IR spectra is characteristic of magnetite and consists of the band with a maximum intensity of around 550 cm⁻¹ that is generally ascribed to the Fe–O bond vibrations. The Fe₃O₄@APTES shows characteristic bands that are associated with the Si–O–Si modes at 1037, 763 cm⁻¹, Si–OH at 948 cm⁻¹, band at 1635 cm⁻¹ associated with NH₂ groups and 1542 cm⁻¹ mode of N–H, vibrations of C–H at 2979 and 2892 cm⁻¹, structural units –CH₂ and –CH₃ at 1488 and 1384 cm⁻¹ that give evidence of Fe₃O₄ surface coverage with APTES. In the case of the Fe₃O₄@APTES–Ag the attachment of the metallic particles after reduction is clear since most notable peaks are shifted toward lower energies, especially the ones associated with silica vibration modes.

3.2. AMF and NIR external contactless energy conversion on Fe₃O₄@APTES–Ag structures

Temperature generation was studied using three different modes of stimulation (1) alternating magnetic field followed by optimization of magnetic field frequency and intensity (145–486 kHz, 22–28 kA m⁻¹); (2) 808 nm NIR laser by applying a different output laser power; and (3) under the simultaneous action of both AMF and NIR (dual-mode) performed as a function of

Fig. 4 STEM-HAADF-EDS element mapping of the effect of Fe₃O₄ nanocubes surface modification with APTES and result of the reduction process leading to the formation of the Ag metallic islands.

Fig. 5 FTIR-ATR spectra of the stock Fe₃O₄ nanocubes, Fe₃O₄@APTES core–shell and Fe₃O₄@APTES–Ag heterostructures.
nanoparticle concentration (1–6 mg ml⁻¹) for altering heating effects. The choice of the 808 nm wavelength was motivated by the well-known spectral characteristic of Fe₃O₄ particles and its minimized absorption by water molecules and biological systems.\textsuperscript{9,15} Approaches (1) and (2) were used mainly to optimize both stimulant parameters and were carried out on colloids.

**Fig. 6** Heating curves of the Fe₃O₄@APTES–Ag under stimulation with (a) alternating magnetic field, (b) different field intensities for 302 kHz, and (c) 808 nm infrared laser radiation as a function of laser power. The solid black line represents reference Fe₃O₄ nanocubes behavior. The working particle concentration in each case was 1 mg ml⁻¹.

**Fig. 7** Concentration dependence of the induced heating effects on Fe₃O₄@APTES–Ag core–shell structures using different modes of external contactless stimulation. DUAL mode represents the simultaneous action of AMF and laser for optimized magnetic field and laser parameters.
with a concentration of 1 mg ml\(^{-1}\) exclusively. As reference material for comparison of the heating efficacy of Fe\(_3\)O\(_4\)@APTES–Ag structures, bare cubic MNPs colloid was taken. The heating curves for the optimization steps are presented in Fig. 6. As one can note, the best working set between all available field frequencies and intensities for AMF action was 302 kHz and 28 kA m\(^{-1}\) (compare Fig. 6a and b). Upon action of the 808 nm NIR light constant increase of the laser output power up to 1700 mW leads to a consecutive increase in the \(D_T\). Interestingly, during the comparison of Fe\(_3\)O\(_4\)@APTES–Ag structures with bare Fe\(_3\)O\(_4\) nanocubes, we observed that there is only a slight \(D_T\) difference for the best working AMF and NIR parameters applied. The effective concentration of magnetic material in the complex structure will be lower because of the presence of silica shell and silver particles. Another feature that could take place is that the silica shell and decorated silver particles can help reduce dipole–dipole magnetic interactions since their size accounts for the increase in distance between magnetic cores.  

This type of interaction between particles has already been shown to have a detrimental effect on heat generation.  

The heating mechanism induced by NIR radiation is not related to the heat losses generated by AMF. The temperature effect will depend on the absorption properties of the given material and the further dissipation of energy through non-radiative pathways.  

As one can see, the response of the core–shell sample to the 808 nm irradiation is strikingly greater than that of AMF and extreme \(D_T\) values can be achieved depending on the applied laser power (almost 50 °C). No saturation effect was observed within the laser power range studied, meaning that a further increase of this parameter will result in even higher \(D_T\).

Based on the behavior of the Fe\(_3\)O\(_4\)@APTES–Ag sample upon exposure to both stimulants, it was decided that the so-called dual-mode will be carried out to check if there will be any beneficial outcome that improves the heating efficiency. For dual-mode measurement, most optimal magnetic field parameters were applied, namely 302 kHz and 28 kA m\(^{-1}\), while for NIR laser it was decided that we will limit the laser power to 900 mW to not overcome the AMF heat induction mechanism, and to significantly reduce the laser optical density (around 1 W cm\(^{-2}\)).

All recorded heating curves were presented in Fig. 7 in a way that allows the comparison of the AMF, laser, and dual modes separately. Furthermore, the effect of particle concentration was studied as well. The values of \(dT/dt\) that define the speed of the temperature increase, \(D_T\), and \(T_{\text{max}}\) were extracted and presented in Fig. 8. In general, dual-mode heat induction results in improvement of \(D_T\) (Fig. 7) and the highest achievable \(T_{\text{max}}\) values (Fig. 8c). Separate AMF and NIR action gives in all cases a lower \(T_{\text{max}}\) than during dual exposure. The progressive increase of Fe\(_3\)O\(_4\)@APTES–Ag concentration increases \(T_{\text{max}}\) in an almost linear manner for AMF stimulation, which can be an indication of the absence of changes in particle state in suspensions.  

What is worth noting, is that the above concentration of 4 mg ml\(^{-1}\) AMF heat induction starts to dominate over laser exposure leading to the higher \(T_{\text{max}}\) while at this concentration the saturation is already achieved for NIR action though the further increase of the nanohoters does not change the \(T_{\text{max}}\) at all. The reason for that can be sought in the blocking of light penetration through the colloid due to the high number of NIR absorbers (critical concentration achieved) that are located at the proximal portion of dispersion. This fact can be supported by the data presented in Fig. 6c that showed a progressive temperature increase with laser power without achieving a saturation for the Fe\(_3\)O\(_4\)@APTES–Ag particles concentration of...
Table 1  Specific absorption rate (SAR), dT/dt, \( \Delta T \), and \( T_{\text{max}} \) parameters of the Fe\(_3\)O\(_4\) reference nanocubes and Fe\(_3\)O\(_4\)@APTES–Ag core–shell structures under contactless stimulation with AMF, laser, and synergic action. The corresponding magnetic field frequency was 302 kHz (optimal setting).

|          | AMF Field intensity (kA m\(^{-1}\)) | dT/dt (°C s\(^{-1}\)) | \( \Delta T \) (°C) | \( T_{\text{max}} \) (°C) | SAR (W g\(^{-1}\)) |
|----------|------------------------------------|------------------------|---------------------|-------------------------|------------------|
| Fe\(_3\)O\(_4\) | 28 | 0.023 | 13.3 | 37.1 | 96.2 |
| Fe\(_3\)O\(_4\)@APTES–Ag | 22 | 0.009 | 6.3 | 28.4 | 37.7 |
|          | 24 | 0.011 | 8.2 | 30.5 | 46.0 |
|          | 26 | 0.012 | 9.5 | 31.6 | 51.4 |
|          | 28 | 0.018 | 12.4 | 33.9 | 75.3 |

Table 2  Fe\(_3\)O\(_4\)@APTES–Ag particle concentration dependence of dT/dt, \( \Delta T \), and \( T_{\text{max}} \) values extracted for different external stimulations

| Concentration (mg ml\(^{-1}\)) | dT/dt (°C s\(^{-1}\)) | \( \Delta T \) (°C) | \( T_{\text{max}} \) (°C) |
|-------------------------------|----------------------|---------------------|-------------------------|
| **AMF 302 kHz 28 kA m\(^{-1}\)** | | | |
| 1 | 0.018 | 12.4 | 33.9 |
| 2 | 0.021 | 18.0 | 40.8 |
| 4 | 0.079 | 41.8 | 63.5 |
| 6 | 0.159 | 49.8 | 71.4 |
| **LASER 900 mW** | | | |
| 1 | 0.070 | 26.8 | 50.4 |
| 2 | 0.090 | 31.0 | 56.2 |
| 4 | 0.120 | 36.9 | 62.6 |
| 6 | 0.122 | 37.8 | 62.3 |
| **DUAL 302 kHz 28 kA m\(^{-1}\) 900 mW** | | | |
| 1 | 0.181 | 26.8 | 66.4 |
| 2 | 0.242 | 51.3 | 74.6 |
| 4 | 0.20 | 55.9 | 78.6 |
| 6 | 0.21 | 57.5 | 81.7 |

1 mg ml\(^{-1}\). The saturation forced by the core–shell concentration was also noticeable for dual-mode energy conversion. Utilization of the laser light leads to the observed saturation regime that depends on the particle number due to the same reason mentioned. However, one can note that the heating efficiency during simultaneous action of AMF and NIR can be strongly enhanced and this augmentation has an almost cumulative character.

The specific absorption rate (SAR), being a measure of the heating performance, was calculated using the following formula:

\[
\text{SAR} = \frac{C}{m} \frac{dT}{dt},
\]

where \( C \) is the specific heat capacity of the medium (\( C_{\text{H}_2\text{O}} = 4.185 \text{ J g}^{-1} \text{ °C}^{-1} \)), \( m \) is the particle mass in dispersion (g), and \( dT/dt \) is the slope of the linear fit of the heating curve for the first tens of seconds. The results of the fitting (dT/dt) and calculations (SAR) with additional parameters (\( \Delta T \) and \( T_{\text{max}} \)) were collected in Tables 1 and 2, while the chosen dependencies were presented in Fig. 8.

The SAR of the Fe\(_3\)O\(_4\)@APTES–Ag core–shell structures for the action of AMF was calculated for an optimized magnetic field frequency of 302 kHz as a function of field intensity and compared to bare Fe\(_3\)O\(_4\) nanocubes. In general, the obtained values are below 100 W g\(^{-1}\) meaning that the heating efficiency of both samples is not impressively high. However, due to their size (above 60 nm), and the presence of strong interparticle interactions, SAR for bare Fe\(_3\)O\(_4\) nanocubes (96 W g\(^{-1}\) calculated for the total Fe\(_3\)O\(_4\) mass) is comparable with reports in the literature about similar objects. It is worth mentioning that fabrication of the core–shell Fe\(_3\)O\(_4\)@APTES–Ag does not cause the loss of SAR. In our experiments, the values are very close to the uncovered cubes and we need to take into mind that within the same particle concentration the content of the iron will be lower than in a reference sample, though a drop in SAR was observed (75.3 instead of 96 W g\(^{-1}\)). Another reason can be sought in the presence of a silica insulating layer that can hinder heat dissipation, despite the thickness of about 10 nm. However, both samples at a particle concentration equal to 1 mg ml\(^{-1}\) cannot be heated above 40 °C and an increase of concentration (above 2 mg ml\(^{-1}\)) is necessary to achieve the biologically relevant temperature range when heated with AMF (see Table 2 and Fig. 7, 8c).

Significant heating with AMF can be achieved above 4 mg ml\(^{-1}\) of Fe\(_3\)O\(_4\)@APTES–Ag up to 71 °C. Upon analysis of the field intensity dependence of SAR and dT/dt (Fig. 8a), we found that both parameters change in a polynomial way (square). This trend should be expected by taking into account the Rosensweig formula on the dissipation of power losses under AMF. The heating effectiveness with NIR laser exposure is generally one order of magnitude greater in terms of SAR and dT/dt values,
pointing to a higher efficacy of the heating mechanism through photostimulation. For comparison, SAR for the AMF is 75.3 W g⁻¹ and above 500 W g⁻¹ for laser, while dT/dt changes from 0.018 °C s⁻¹ to 0.123 °C s⁻¹ when exposed to 808 nm wavelength at 1700 mW. As we can see, the SAR and dT/dt change linearly with laser output power as previously elucidated by others.¹⁹ The maximum temperature that was achieved was 72 °C at 1700 mW. The concentration dependence for laser radiation was measured for the 900 mW (to limit LOD) and saturation was observed above 2 mg ml⁻¹ meaning that in terms of NIR further increase of the nanoheaters number has no sense since no T_max is enhanced.

Interesting result has been achieved with dual-mode stimulation performed by using AMF with a field frequency of 302 kHz, 28 kA m⁻¹ intensity, as well as 900 mW of laser output power. The greater augmentation of dT/dt was observed up to 0.2 °C s⁻¹ while SAR was above 1000 W g⁻¹ for the Fe₃O₄@APTES–Ag concentration of 1 mg ml⁻¹. A further increase in the number of core–shell particles resulted in saturation similarly as for the laser mode alone. Comparison of the SAR values calculated for our heterostructures with the literature data is as for the laser mode alone. For comparison, SAR for the AMF is 75.3 W g⁻¹ and above 500 W g⁻¹ for laser, while dT/dt changes from 0.018 °C s⁻¹ to 0.123 °C s⁻¹ when exposed to 808 nm wavelength at 1700 mW. As we can see, the SAR and dT/dt change linearly with laser output power as previously elucidated by others.¹⁹ The maximum temperature that was achieved was 72 °C at 1700 mW. The concentration dependence for laser radiation was measured for the 900 mW (to limit LOD) and saturation was observed above 2 mg ml⁻¹ meaning that in terms of NIR further increase of the nanoheaters number has no sense since no T_max is enhanced.

3.3. Surface-enhanced Raman scattering on Fe₃O₄@APTES–Ag multipurpose platform

Verification of SERS augmentation on the prepared nanostructures was performed with the rhodamine 6G standard (R6G). As one can observe, only with presence of the Fe₃O₄@APTES–Ag characteristic Raman bands of the R6G dye were revealed at characteristic positions 611, 773, 1188, 1311, 1421, 1506, 1573, 1655 cm⁻¹, respectively (see Fig. 9a and inset). All other materials, including the R6G dye alone, did not generate any signal for 2.5 μM at 0.25 μW. Clearly, the presence of Ag metallic islands in Fe₃O₄@APTES–Ag promotes the SERS electromagnetic mechanism that results in a strong enhancement of the Raman signal that allows detection of the R6G analyte. The SERS sensitivity was tested using R6G standard solutions with the following concentrations 0.01, 0.05, 0.5, 1 and 2.5 μM (Fig. 9a). It should be noted that the R6G Raman bands can be detected down to 0.05 μM (50 nM) of the dye. Below that concentration no Raman modes were visible at 25 μW of laser power. The dependence of the 488 nm laser output power (25 μW–0.5 mW) on signal detectability was checked for the 0.5 μM R6G sample and shown in Fig. 9b. Approximately three-fold SERS signal improvement was observed meaning that the change in excitation power can be used for detection of lower R6G dye concentration, thus it can surpass the mention limit below 0.05 μM. Recently, it was shown that the excellent SERS probe was constructed based on purely Au snowflake NPs that is capable of detecting R6G at the level of 3 nM. However, it is hard to estimate what laser power was used in the experiments, since no data was provided. At the same time, one has to remember that SERS probe sensitivity depends strongly on the source laser output power and can be also detrimental on the stability of measured analyte (generated heat can damage molecules). Therefore, in the case of our Fe₃O₄@Ag heterostructures, we were able to detect the R6G at 50 nM and with the use of a low laser power that does not exceed 25 μW. As it was also shown by us, increase of the source power can enhance the signal intensity and as a consequence, increase the sensitivity of the probe significantly, as was presented by us in Fig. 9b. Another practical aspect can be found in the fact that the SERS

Fig. 9 SERS effect on Fe₃O₄@APTES–Ag heterostructures (a) as a function of R6G standard solution concentration recorded with 25 μW laser power (inset shows no signal recorded neither for R6G alone, R6G on Fe₃O₄ nor Fe₃O₄@APTES) as well as (b) as a function of the 488 nm laser power measured for 0.5 μM of R6G.
3.4. Antibacterial activity of Fe3O4@APTES–Ag heterostructures

Fe3O4 particles are recognized in general as inert for bacteria. However, after silver-nanostructures decoration, they are likely to exhibit antibacterial activity. For this purpose, the minimum inhibitory concentration of the nanocubes was determined against four bacterial strains prevalent in nosocomial and medical devices-related infections. The results revealed, as expected, that bare Fe3O4 nanocubes did not show any antibacterial activity in concentrations up to 500 μg ml\(^{-1}\). Fe3O4@APTES–Ag nanocubes were not effective against both tested Gram-positive strains as well as against E. coli (up to 50 μg ml\(^{-1}\)). However, they inhibited the growth of the P. aeruginosa strain at a concentration of 50 μg ml\(^{-1}\) (Table 3). This observation is particularly interesting because P. aeruginosa is a critically dangerous bacterial strain associated with nosocomial infections, causing morbidity and mortality in many patients and remarkably resistant to antibacterial agents, thus difficult to eradicate.\(^44\) Its mechanism of resistance to antibacterial factors is based on outer membrane permeability, efflux systems, antibiotic-inactivating enzymes, resistance by mutations and acquisition of resistance genes, biofilm-mediated resistance, and formation of persister cells.\(^45-48\) For this reason, the World Health Organization (WHO) has recently listed carbapenem-resistant P. aeruginosa as one of three bacterial species in which there is a critical need for the development of new antibiotics to treat infections.\(^49\) Therefore, the sensitivity of P. aeruginosa to Fe3O4@APTES–Ag nanocubes deserves particular interest and further studies, although the MIC value is relatively high (50 μg ml\(^{-1}\)). However, this is understandable in view of the low percentage of silver in the overall structure of the nanocubes.

Interestingly, Fe3O4@APTES (without silver) also showed notable activity against S. aureus and S. epidermidis strains (50 μg ml\(^{-1}\) and 25 μg ml\(^{-1}\), respectively; Table 3). S. aureus is usually reported as the most common nosocomial infection-causing bacteria.\(^51,52\) Whereas S. epidermidis, although being a natural skin colonizer, is nowadays regarded as the most frequent cause of nosocomial infections and indwelling medical device-associated infections, mainly due to its high ability to form biofilm on the surfaces of such devices.\(^52,53\) The reason of the antibacterial activity of APTES-capped Fe3O4 nanocubes is intriguing. APTES contains amino groups which can bring benefits in increasing of antibacterial activity of Fe3O4 particles. It was earlier reported\(^54\) that recombinant peptides with numerous amino acid residues showed antibacterial activity. Moreover, it was demonstrated that APTES-modified ZnO particles induced an antimicrobial effect, in particular against Gram-negative bacteria.\(^55\) APTES modification of TiO2 NPs enhanced the antibacterial efficiency against Escherichia coli under artificial solar light\(^56\) and APTES-functionalized zeolite shows evidence of antibacterial activity against both Gram-positive and Gram-negative strains.\(^57\) Thus, it seems that this phenomenon also deserves more attention in further studies because APTES-coating of nanostructures may form a platform for their further modifications, increasing their antimicrobial potential.

### Table 3 Minimum inhibitory concentrations (MICs) of tested nanocubes against 4 reference bacterial strains: Staphylococcus aureus ATCC 25923 (S.a.), Staphylococcus epidermidis ATCC 12228 (S.e.), Escherichia coli ATCC 25922 (E.c.) and Pseudomonas aeruginosa ATCC 27953 (P.a.)

| NPs                    | Concentration range (μg ml\(^{-1}\)) | MIC (μg ml\(^{-1}\)) |
|------------------------|-------------------------------------|-----------------------|
|                        | S.a.  | S.e. | E.c. | P.a. |                        |
| Fe3O4                  | 50–500       | >500 | >500 | >500 | >500                  |
| Fe3O4@APTES            | 1.562–50    | 50   | >25  | >50  | >50                   |
| Fe3O4@APTES–Ag         | 1.562–50    | >50  | >50  | >50  | 50                    |

4. Conclusions

The Fe3O4@APTES–Ag heterostructures were synthesized using a three-step process involving the synthesis of the magnetite nanocube core material, surface coverage with a thin silica shell, and chemisorption of Ag\(^{+}\) cations and their subsequent reduction resulting in the formation of silver metallic islands. The estimated size of the multipurpose composite was around 94.5 nm, while Ag silver particles were of 8.5 nm interconnected with the Fe3O4 surface through a silica shell with an average thickness of 12.8 nm. The effectiveness of heterostructure fabrication was evidenced by the TEM imaging and FTIR-ATR spectroscopy. The silica shell and silver particles are clearly distinguishable, as well as FTIR gave an indication of the Fe3O4 surface coverage and Ag attachment that manifested in the shift of the characteristic vibration bands and the appearance of new features.

The multifunctionality of Ag-decorated Fe3O4 nanoparticles was manifested in the ability to generate significant temperature effects under the action of AMF and NIR radiation, to use it as a SERS probe and antimicrobial activity. In the case of heat induction, Fe3O4 heterostructures showed exceptional responsiveness to synergic action of AMF and NIR (808 nm laser light) that resulted in a high SAR value of 1000 W g\(^{-1}\). The laser-induced energy conversion was more effective than AMF stimulation, with one order of magnitude higher d\(^{\text{max}}\)dt\(^{-1}\) in the first case. It was shown that even the AMF-based mechanism is not that efficient; the temperature effect can be enhanced by increasing the concentration of nanoheaters, leading to a \(T_{\text{max}}\) of 71 °C. Increase of the same particle concentration during laser exposure leads to saturation above 2 mg ml\(^{-1}\), and the same behavior was observed for dual mode stimulation.

The verification of the ability of Fe3O4@APTES–Ag to enhance the Raman signal of the R6G molecule was confirmed. The detection limit of R6G can be augmented by modulating the
incident laser power and can be increased below 0.01 μM of the dye.

The antimicrobial activity of the heterostructures was tested against four bacterial strains, Staphylococcus aureus ATCC 25923, Staphylococcus epidermidis ATCC 12228, Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27953. The Fe₃O₄@APTES–Ag showed the highest activity for inhibition of P. aeruginosa at 50 μg ml⁻¹. This is a very interesting effect from the application point of view, since P. aeruginosa is an extremely dangerous bacteria that causes high mortality in patients and is very resistant to antibacterial agents.

Author contributions

M. K.-G., D.S. and A.T. synthesis of particles, heterostructures, and their characterization, M. K.-G., D. S. energy conversion measurements, R. P. and M. K.-G. data analysis and figures preparation, A. D. particle imaging, and element mapping, A. M. and A. B. antimicrobial activity tests, data analysis, R. W.-N. SERS experiments and data analysis, R. P., A. T., M. K.-G., A. T, D. S., A. D., A. M., A. B., R. W.-N., writing manuscript, editing and corrections. R. P., M. K.-G., A. B. idea, methodology, conceptualization. All authors read the manuscript and agreed with its content.

Conflicts of interest

There are no conflicts to declare.

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