

Electronic Supplementary Information

Materials and Methods

General

5 **Materials.** If not specified otherwise, chemicals of the highest purity available were obtained from Fluka (Buchs, Switzerland), Merck (Darmstadt, Germany) or Riedel-deHaen (Seelze, Germany).

Particle synthesis and characterisation

Materials. Iron (III) acetylacetonate and polyvinylpyrrolidone
10 58.000 for synthesis were purchased from Sigma-Aldrich (Munich, Germany), and diethyleneglycol (DEG, 99%) from Acros Organics (Geel, Belgium).

Dynamic light scattering (DLS) was measured using a Beckman-Coulter DelsaNanoC (Beckman Coulter, Krefeld, Germany). This
15 device features a diode laser (30 mW, $\lambda_0 = 658$ nm) and is able to measure the scattered light at scattering angles of 15° and 165° . The experiments were carried out at the backscattering angle 165° . The scattered light is detected using a photo multiplier tube and analysed with a digital correlator. A sample volume of 1.2 mL was filled in
20 Sarstedt fluorescence cuvettes (polystyrene, $d = 1$ cm, Sarstedt, Nümbrecht, Germany) and was thermostated at $t = 25$ °C in the device for 4 min before the measurement time of 140 s per repetition. For the evaluation of the correlation functions $g^{(2)}$ the properties of pure water for the refractive indices n (658 nm, 25 °C)
25 = 1.3328 and for the viscosity η (25 °C) = 0.8878 cP were used as given by the Beckman Coulter Software. The cumulants method was used to calculate the z-average of the hydrodynamic diameter d and the polydispersity index (PI).

Zetapotential measurements were also done using the Beckman
30 Coulter DelsaNanoC. A sample volume of 5 mL was filled in a Flow Cell and equilibrated with the same conditions mentioned in the DLS section. Here the measurement time was 130 s per repetition. For the evaluation additionally to refractive index and viscosity the dielectric constant of pure water was used $\epsilon = 78.3$ as
35 given by the Beckman Coulter software.

In vitro testing – Enzymes

Materials. Sodium hydrogen carbonate was purchased from Gibco (Eggenstein, Germany) and acetylthiocholine iodide was
40 provided by Fluka (Buchs, Switzerland). Acetylcholinesterase (AChE, EC 3.1.1.7) from the electric organ of the electric eel (*Electrophorus electricus*) type VI-S – suspended in a BSA containing phosphate buffer – was purchased from Sigma-Aldrich (Steinheim, Germany). Yeast glutathione reductase – suspended in a
45 BSA containing phosphate buffer –, bovine serum albumin, nicotinamide adenine dinucleotide phosphate (NADPH), glutathione (GSH), glutathione disulfide (GSSG) were from Sigma (Deisenhofen, Germany). All other chemicals of the highest purity available were obtained from Fluka (Buchs, Switzerland), Merck
50 (Darmstadt, Germany) or Riedel-deHaen (Seelze, Germany). 96-well microtitre plates were from Nunc (Roskilde, Denmark). The salts for the mineral salt medium and the trace element solution for the sewage sludge inhibition test were received from Merck

(Darmstadt, Germany). The activated sludge was obtained in April
55 2010 from an industrial wastewater treatment plant in Germany.

Glutathione reductase (GR) inhibition assay. The inhibition of yeast GR was determined using a modification of the microtiter plate assay described by ¹. The enzyme (0.04 U/mL) was incubated
60 with a 1:1 dilution series of the particles in 100 mM potassium phosphate buffer containing 1 mM ethylenediamine tetraacetic acid (EDTA) and 4 mM NADPH. Then the activity of the GR was measured in a total volume of 360 μ L by direct addition of 180 μ L of 2 mM GSSG in 100 mM potassium phosphate buffer (pH 7.0,
65 room temperature). The concentration response curves were calculated from the measured decrease in the absorbance at 340 nm. The data for the particle treated enzyme were normalised to those of untreated controls.

Acetylcholinesterase (AChE) inhibition assay. The inhibition of
70 the AChE was measured using a colorimetric assay based on the reduction of the dye 5,5'-dithio-bis-(2-nitrobenzoic acid) (DTNB) by the enzymatically formed thiocholine moiety from the AChE substrate acetylthiocholine iodide. The assay is described in detail in ². Briefly, a dilution series of the particles in phosphate buffer
75 (0.02 M, pH 8.0) was prepared directly in the wells of a 96-well microtiter plate. DTNB (2 mM, 0.185 mg/mL NaHCO₃ in phosphate buffer pH 8.0) and the enzyme (0.2 U/mL, 0.25 mg/mL bovine serum albumin in phosphate buffer pH 8.0) were added to each well. The reaction was started by the addition of
80 acetylthiocholine iodide (2 mM in phosphate buffer). The final test concentrations were 0.5 mM of DTNB and acetylthiocholine iodide and 0.05 U/mL AChE, respectively. Enzyme kinetics were measured at 405 nm in 30 seconds intervals in a microplate-reader (MRX TC Dynex Technologies, Denkendorf, Germany) for a time period of 5
85 min. The enzyme activity was expressed as OD/min from a linear regression. To avoid false positive results it was shown in preliminary tests that the particles themselves did not interact with the formed thiocholine during the assay (data not shown).

In vitro testing – OLN-93

Materials. Fetal calf serum (FCS), penicillin/streptomycin and trypsin solution were obtained from Biochrom (Berlin, Germany). Dulbecco's modified Eagle's medium (DMEM) was from Invitrogen (Karlsruhe, Germany). Deferoxamine (DFX),
95 neocuproine, sodium ascorbate, Tris, 5,5'-dithio-bis(2-nitrobenzoic acid), dihydrorhodamine 123 and sulfosalicylic acid were purchased from Sigma (Steinheim, Germany). Bovine serum albumin, NADH and NADPH were obtained from Applichem (Darmstadt, Germany). Glutathione reductase and glutathione disulfide (GSSG)
100 were purchased from Roche Diagnostics (Mannheim, Germany). 96-well microtitre plates were from Nunc (Roskilde, Denmark) and 12-well cell culture plates from Greiner Bio-one (Frickenhausen, Germany).

Cell cultures and experimental incubation. For experiments,
105 25,000 cells were seeded in wells of 12-well plates. After 16 to 18 h, the cells were washed with 1 mL pre-warmed (37°C) culture medium (90% DMEM, 10% FCS, 1 mM pyruvate, 20 U/mL of penicillin G and 20 μ g/mL of streptomycin sulphate) and incubated in 1 mL culture medium without or with the indicated
110 concentrations of IONP. The experimental incubations were stopped by washing the cells twice with 1 mL ice-cold phosphate

buffered saline (PBS; 10 mM potassium phosphate buffer, 150 mM NaCl, pH 7.4).

In vivo testing

5 Daphnia acute toxicity.

The water flea *Daphnia magna* was obtained from IBACON laboratories (Roßdorf, Germany) and cultured continuously in a climate controlled chamber at $20 \pm 1^\circ\text{C}$ and a 16:8 h (light:dark) photoperiod. Animals were cultured in Elenit M7 medium which was renewed twice a week. Animals were fed with the green algae *Pseudokirchneriella subcapitata* on a basis of 150 μg carbon/animal/day.

Sediment contact test. The bacteria *Arthobacter globiformis* (Type Strain: DSM 20124) were bought as a freeze-dried culture from the German Collection of Microorganisms (DSMZ) and stored as liquid cultures in DSM-medium with 4 Vol% DMSO at -20°C . For preparing the inoculum, 500 μL of carefully defrosted bacteria were added to 50 mL of DSM-medium and afterwards incubated for 16 hours in a horizontal shaker at 30°C , darkness and 150 rpm. In the beginning of the test the optical density (OD₆₂₀) of the bacteria culture was measured at 620 nm in a plate reader (Wallac; Victor² 1420 Multilabel Counter) and diluted to 0.15 in order to change the bacterial growth phase from static to exponential.

The tests were conducted on 24-well microplates. Each well was filled with 1 mL of inoculum (OD₆₂₀ of 0.15; for the blanks 1 mL of DSM medium) and 1 mL of the PVP-coated IONP dilutions or the controls. The plates were kept on a horizontal shaker at 30°C , darkness and 150 rpm. After the incubation time (2 h), 0.8 mL of resazurin was pipetted into each well and the plates were incubated again for 1.5 h on the horizontal shaker (30°C , darkness, 150 rpm). After this the plates were centrifuged for 10 min at 3000 rpm (G-) and 20°C to isolate the redox-active dye from the bacteria. The supernatant was pipetted, transferred to a 96-well microplate and the absorption was measured at 620 nm with the plate reader. The results were calculated with the formula according to DIN 38412 L48³.

Contents of DSM-Medium: 3.33 g/l peptone from casein, 1.67 g yeast, 1.67 g D(+)-glucose and 1.67 g sodium chloride (NaCl) per L distilled water. After stirring the Medium was autoclaved for 20 min at 120°C . The Medium was prepared according to DIN 38412 L48³.

Contents of the reductive dye resazurin: 45 mg/L resazurin were dissolved in phosphate buffer containing 50 mM KH_2PO_4 ; 70 mM K_2HPO_4 ; 0.2% $\text{C}_2\text{H}_3\text{NaO}_2$; 0.2% Glucose, adjusted to pH 7.0 and autoclaved 20 min at 120°C . The reductive dye resazurin was prepared according to DIN 38412 L48³.

Sewage sludge inhibition. Activated sludges samples were taken from a tank of an industrial waste water treatment plant and cultured under anaerobic laboratory conditions. The total solids for all performed inhibition tests (TS) amounted to 51.2 ± 12.7 mg/L, which is close to the natural density of activated sludge flocks in a wastewater treatment plant. To test the inhibitory potential of the PVP-coated IONP to the bacterial community present in these sludge samples, varying particle concentrations were added to the medium containing the activated sludge flocks. The inhibition was followed via the gas production of the bacteria over time, since

metabolically active bacteria produce N_2 and CO_2 under anaerobic conditions. The inhibition experiment was modified from OECD test guideline N^o 224 (2007)⁴ using conditions, which are applied for denitrifying biodegradation tests. The inhibitory potential of the PVP-coated IONP under denitrifying conditions on the used activated sludge was derived from the cumulative gas production of three replicate samples compared to three replicates of an untreated control. The samples were prepared with defined amounts of acetate and nitrate. Positive controls with 3,5-dichlorophenol as inhibiting agent and untreated negative controls as reference were additionally set up. The vessels were stored at 25°C in temperature controlled cabinets. The pressure increase was monitored after a 1 h equilibration time of the system and subsequently twice a day for up to 13 days. According to OECD guideline N^o 224⁴ the inhibitory effect depends on the total amount of solids in the sample. The total solids (TS) were determined by the help of an additional vessel which was set up equally to the control samples. After inoculation it was opened and 5 mL of the sample suspension were filtered through 0.45 μm cellulose nitrate with 25 mm in diameter (Sartorius AG, Göttingen, Germany) by a water jet pump. The filter was dried overnight at 80°C and then cooled down in a desiccator. The average of at least three replicates was taken to represent the total solid concentration. The concentration of the PVP-coated IONP is given as the ratio of the nominal iron concentration in mg to TS in mg.

The vessels were filled with 200 mL mineral salt medium, 20 mL activated sludge suspension, 20, 2 or 0.2 mL of PVP-coated IONP stock solution (1 g Fe/L), 6 mL sodium acetate solution (2.05 mol/L), 4 mL sodium nitrate solution (0.58 mol/L) and a nitrogen phase. The composition of the mineral salt medium was modified based on a conventional mineral salt media recipe (OECD guideline 301 1992)⁵ as it is typically practised for the growth of facultative anaerobic bacteria. The phosphate buffer concentration was increased to get a higher buffer capacity, since the amount of hydroxyl ions increases when the denitrification process occurs. The final mineral salt medium composition was as follows: phosphate-buffer (3.75 g/L KH_2PO_4 and 8.73 g/L $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$) and magnesium and calcium salts (22.5 mg/L $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, 36.4 mg/L $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$). The medium was supplemented with a trace element solution containing 0.2 g of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$, 100 mL of trace element solution SL-6, and 900 mL of water. Trace element solution SL-6 contained 0.1 g of $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, 0.03 g of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, 0.3 g of H_3BO_3 , 0.2 g of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, 0.01 g of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 0.02 g of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, 0.03 g of $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$, and 1.0 L of water. Anaerobic conditions were obtained by degasing the hot autoclaved medium with a nitrogen stream and further maintained by adding ascorbic acid (serving as reducing agent for molecular oxygen) in a non-inhibiting concentration of 0.5 g/L. The inoculum had a final concentration of 206 ± 45 mg/L TS. The inoculum was cultivated in anaerobic mineral salt medium and fed with acetate functioning as organic carbon source. Nitrate was added to act as terminal electron acceptor for the denitrifying bacteria. The volume of each sample was additionally adjusted with deionised water up to a volume of 236 mL. During the course of the experiment the pressure increase due to microbial activity was measured by a pressure measuring device with a precision of 0.1 Pa (V-D3, Schlee., Witten-Herbede, Germany).

Using different concentrations (0.1 mg/mg TS – 0.7 mg/mg TS) of 3,5-dichlorophenol as a positive reference the validity of the test

could be shown in accordance with OECD test guideline N°224⁴ (data not shown).

Data processing

The bacterial inhibition was calculated according to equation 1 as proposed by the OECD test guideline.

$$I = (1 - Pt / Pc) * 100 \quad \text{Equation 1}$$

where I is inhibition in %

Pt : cumulative pressure at a selected time

Pc : cumulative pressure of the untreated control at the same time

As time point for determining the inhibition of the treated samples, the end of the exponential growth phase of the untreated control was taken as proposed by⁶. This point was calculated from the point of intersection between the tangent of inflection of the pressure curve and the asymptote of the pressure after the control reaches the stationary phase.

The data are shown as means ± standard deviations that were obtained from at least three independent experiments. The fitting of the measurement data and the calculations were done with MATLAB 7.9.0 according to the formula given for a limited growth curve (logistic function) since the amount of acetate and nitrate is limited in the sewage sludge inhibition test. Significance of differences between two sets of data was analysed by the *t*-test and significances of differences between groups of data were analysed by ANOVA followed by the Bonferroni *post hoc* test using the open source “R” software for statistical computing.

Modelling and scenarios

Stability modelling using extended DLVO theory. According to Lim et al.⁷ the total interaction energy of spherical particles can be represented by the sum of four major interaction energies: The van der Waals U_{vdW} and magnetic U_{mag} attractions and the electrostatic double layer U_{elec} and steric U_{steric} repulsions.

$$U_{total} = U_{vdW} + U_{mag} + U_{elec} + U_{steric}$$

Equation 2

The classical DLVO theory considers just the van der Waals attraction U_{vdW} and the electrostatic double layer repulsion⁸ and⁹. Due to the magnetic properties of IONP and the polymer coating one has to take into account the two additional terms for magnetic attraction U_{mag} and steric repulsion U_{steric} .

The van der Waals attraction of two spheres with radii r_1 and r_2 depends on the Hamaker constant A and the surface-surface separation distance h .¹⁰ gives the following equation for the calculation of this term using the centre to centre distance

$$s = r_1 + r_2 + h;$$

Equation 3

In this work we use for magnetite in water $A = 33$ zJ calculated by Faure et al.¹¹. This work considers both dielectric and magnetic contributions to Hamaker constants of iron oxide NP.

The electrostatic repulsion originates from the surface underlying the adsorbed polymer layer and its term U_{elec} is calculated using the

equation given by Lim et al.⁷ for spherical particles with identical radii r :

$$U_{elec} = 2\pi r \epsilon_r \epsilon_0 \zeta^2 \ln [1 + \exp(-\kappa h)]$$

Equation 4

where ϵ_r is the relative dielectric constant of the medium and ϵ_0 the permittivity of the vacuum. The potential ζ is approximated by the zeta potential of the coated nanoparticles. The inverse of the Debye screening length $\kappa = 1/\lambda_D$ is calculated by¹²

$$\lambda_D = \sqrt{\frac{\epsilon_0 \epsilon_r k_B T}{2N_A I e_0^2}}$$

Equation 5

with the Boltzmann constant k_B , the absolute temperature T , the Avogadro constant N_A , the ionic strength I and the elementary charge e_0 .

The steric repulsion can be calculated by taking into account the contribution osmotic and elastic terms like Phenrat et al. did¹³. However in this work we followed an ansatz for one common steric term including both, osmotic and elastic steric repulsion, used by Lim et al.⁷. The steric repulsion term U_{steric} is set to infinity for $s < 2r$, which is obvious for hard spheres. For centre to centre distances $s > 2(r + L)$ with L the thickness of the polymer layer, U_{steric} is set to zero. In the intermediate range $2r < s < 2(r + L)$, where the adsorbed polymer layers overlap U_{steric} is described by the following series:

$$U_{steric} = U_0 \left[-\ln(y) - \frac{9}{5}(1-y) + \frac{1}{3}(1-y^3) - \frac{1}{30}(1-y^6) \right]$$

Equation 6

with

$$y = \frac{s - 2r}{2L}$$

and

$$U_0 = \left(\frac{\pi^3 L \sigma_p k_B T}{12 N_p l^2} \right) r L^2$$

N_p is the number of segments in the polymer chain, l is the segment length and σ_p the surface density of the adsorbed chains. The segment length for PVP, $l = 0.269$ nm, was estimated by using a HyperChem 7.5 (Hypercube, Inc., www.hyper.com) geometrical optimisation of a PVP oligomer in vacuum. Here we used the same value of $\sigma_p = 1$ nm⁻² as given by Lim et al.⁷. We estimated the number of chain segments $N_p = 43$ for data of primary particles in water (see Table S3 and S6) considering geometrically the volume of polymer layer, surface density σ_p , molecular weight of polymer $M_w = 58000$ g/mol and monomer $M_{mono} = 111.14$ g/mol and density of PVP, $\rho_{PVP} = 1.23$ g/cm³, given by MSDS of PVP (<http://www.sciencelab.com/msds.php?msdsId=9926650>, requested 2nd of May 2012),

$$N_p = \frac{1}{3} \frac{((r+L)^3 - r^3) N_A \rho_{PVP} M_w}{M_w r^2 \sigma_p M_{mono}} \quad \text{Equation 7}$$

The thickness of polymer layer L was estimated comparing DLS and TEM data of our IONP (data not shown here). It is assumed that the polymer layer thickness is 35% of the hydrodynamic radius.

The attractive magnetic interaction U_{mag} of IONP was calculated following Phenrat et al.¹³ assuming worst case, maximum magnetic attraction, which is the case for perfect alignment of magnetic spins of IONP

$$U_{mag} = -\frac{8\pi\mu_0 r_c^6 M_s^2}{9s^3} \quad \text{Equation 8}$$

where μ_0 is the permeability of free space and M_s is the saturation magnetisation of the IONP. Typically there is a spin-disordered surface layer on superparamagnetic NP which is about $l_m \approx 1$ nm thick¹⁴⁻¹⁶. This is accounted for by using the reduced particle radius $r_c = r - l_m$ in the calculation of the magnetic interaction U_{mag} . For the saturation magnetisation M_s of magnetite Utech et al.¹⁷ give $M_s = 92$ emu/g at 300 K. The parameters and physical constants¹⁸ as well as the experimental data used for the calculations are listed in Tables S4 - S6.

The extended theory was used to calculate the total interaction potential and contributing potentials for PVP-coated IONP in water, as shown in Fig. 5. The energies are normalized to $k_B T$. With decreasing surface to surface distance h the magnetic and van der Waals attractive forces increase. The magnetic interaction U_{mag} has a stronger contribution on the attractive forces than the van der Waals forces U_{vdW} (see Fig. 5). With h getting smaller than $2L$ the polymer layers of two particles start to overlap and the steric repulsion steeply increases. Due to the very low absolute value of the zeta potential the electrostatic repulsion is negligible (see Fig S1) and the curves in Fig. 5 of the other contributions U_{vdW} , U_{steric} , U_{mag} and most importantly the total interaction potential U_{total} apply for all test media in this work. The total interaction potential U_{total} is determined mostly by the steric repulsion and the magnetic attraction. Near $h \approx 2L$ the total interaction potential has a minimum of about $-1.4 k_B T$. Since the energy of Brownian motion is $1.5 k_B T$ the tendency of the IONP to aggregate is weak⁷.

Exposure assessment. For estimating the PEC in surface waters, we used an approach by EMEA^{19,20}

$$PEC_{SurfaceWater} = \frac{A \times (100 - R)}{365 \times P \times V \times D \times 100} \quad \text{Equation 9}$$

A represents the predicted amount of the substance and R is the removal rate for biodegradation or other loss through adsorption, volatilisation and hydro- or photo-lysis during the release to surface waters. P denotes the population of the region of interest. The population of Germany was estimated 82 Million in 2009²¹. The

estimated wastewater volume per capita ' V ' in Germany is 0.3 m^3 per day. The factor ' D ' is the dilution rate which covers the possible dilution of the substance within the fate and is always set to 10 as default as suggested in the EMEA draft.

The data on MRI use in Germany was taken from the health insurance report of Barmer-GEK in 2009²². Computer tomography and MRI amounted to overall 18 Million investigations in 2009. The collected data correspond quite well with the estimation of the Federal Statistic Agency²². MRI with contrast agents made up to 2.2 Million of 8 Million MRI investigations in total. Ambulant MRI investigations accounted to 1.5 Million as major emission source²². Therefore the release into sewage treatment plants as well as surface waters is likely to increase and to be more diffusive due to the longer blood half time. As in the years from 2004-2009, we expected an annual average growth of MRI investigations by 6%.

The standard dose of Gd-diethylene triamine pentaacetic acid (DTPA) is 0.0001 mol/kg body weight. The atomic mass of Gd is 157.25 g/mol. The Fe_3O_4 based contrast agent standard dose is assumed to be equal to ultrasmall superparamagnetic iron oxide (3Fe) contrast agent Sinerem® with 30 $\mu\text{mol/kg}$ body weight and an atomic mass of 167.535 g/mol. The average body weight of Germans was 75.5 kg in 2009²¹, resulting in a standard dose of 1.18 g for Gd-DTPA and of 0.379 g for Fe_3O_4 based contrast agents. Current market data of contrast agents are rare and only a few indications were found. The Nano Observatory Project reports of a high market penetration of Gd based contrast agents, which is why we assume a 97% market penetration in the business-as-usual scenario. In the future it could decrease to 50% in case of an adequate substitution of Gd based contrast agent by iron oxide based contrast agents.

We assumed Gd-DTPA to be persistent and set the removal rate R to zero percent in the business-as-usual scenario. The best-case scenario represents a Gd^{3+} removal rate of 15% due to transmetallation processes²³. The removal rate in the business-as-usual scenario is set to zero percent for IONP based contrast agents. On the other hand little is known about clearance and degradation of iron oxide contrast agents especially with PVP coating. PVP is usually excreted via kidneys and therefore would enter the sewage treatment plant²⁴. A possible alteration during the sewage treatment is unknown. For that reason it is assumed that iron oxide has a removal rate of zero percent in business as usual and ten percent in the best-case scenario.

Notes and references

1. J. M. Gutterer; Dringen, R.; Hirrlinger, J.; Hamprecht, B. *Journal of Neurochemistry* **1999**, 73(4), 1422-1430.
2. F. Stock; Hoffmann, J.; Ranke, J.; Stormann, R.; Ondruschka, B.; Jastorff, B. *Green Chemistry* **2004**, 6(6), 286-290.
3. DIN Deutsches Institut für Normung e.V. *Deutsches Einheitsverfahren zur Wasser-, Abwasser und Schlammuntersuchung - Testverfahren mit Wasserorganismen (Gruppe L) - Teil 48; Arthrobacter globiformis - Kontakttest für kontaminierte Feststoffe (L 48)*. DIN Deutsches Institut für Normung e.V. [38412-48], 1-15. 2002. Berlin, Beuth Verlag GmbH.

4. OECD; Allianz in *Opportunities and risks of nanotechnologies*, 2007; Chapter 6.4, pp. 30-35.
5. OECD . Ready Biodegradability. OECD Guidelines for the testing of chemicals. Test No. 301, 1-62. 1992.
- 5 6. R. P. H. Schmitz; Eisentrager, A.; Dott, W. *Journal of Microbiological Methods* **1998**, *31*(3), 159-166.
7. J. K. Lim; Majetich, S. A.; Tilton, R. D. *Langmuir* **2009**, *25*(23), 13384-13393.
8. Berg, J. C. An introduction to Interfaces and Colloids The Bridge to Nanoparticle science. World Scientific Publishing Co. Pte Ltd.
- 10 9. J. D. Hu; Zevi, Y.; Kou, X. M.; Xiao, J.; Wang, X. J.; Jin, Y. *SCIENCE OF THE TOTAL ENVIRONMENT* **2010**, *408*(16), 3477-3489.
10. Hunter, R. J. *Foundations of Colloid Science*; Clarendon Press: Oxford, 1987; Vol. 1.
- 15 11. B. Faure; Salazar-Alvarez, G.; Bergstrom, L. *Langmuir* **2011**, *27*(14), 8659-8664.
12. Elimelech, M.; Gregory, J.; Jia, X.; Williams, R. A. *Particle Deposition and Aggregation: measurement, modelling and simulation*; Butterworth-Heinemann Ltd.: 1995.
- 20 13. T. Phenrat; Saleh, N.; Sirk, K.; Kim, H. J.; Tilton, R.; Lowry, G. *Journal of Nanoparticle Research* **2008**, *10*(5), 795-814.
14. G. A. Held; Grinstein, G.; Doyle, H.; Sun, S.; Murray, C. B. *Physical Review B* **2001**, *64*(1), 012408-1-012408-4.
15. T. Kim; Shima, M. *Journal of Applied Physics* **2007**, *101*(9), 09M516-1-09M516-3.
- 25 16. M. Lévy; Gazeau, F.; Bacri, J. C.; Wilhelm, C.; Devaud, M. *Physical Review B* **2011**, *84*(7), 075480-1-075480-11.
17. S. Utech; Scherer, C.; Krohne, K.; Carrella, L.; Rentschler, E.; Gasi, T.; Ksenofontov, V.; Felser, C.; Maskos, M. *Journal of Magnetism and Magnetic Materials* **2010**, *322*(21), 3519-3526.
- 30 18. Lide, D. R. ed. *CRC Handbook of Chemistry and Physics 78th Edition*; 78th ed.; CRC Press, Inc.: Boca Raton New York, 1997.
19. Emea . Discussion paper on environmental risk assessment of non-genetically modified organisms containing medicinal products for human use. 1-22. 2001.
- 35 20. J. O. Straub *Toxicology letters* **2002**, *135*(3), 231-237.
21. Fsa *Federal Statistic Agency - Statistical Yearbook 2010 - For the Federal Republic of Germany Including International Tables*; Federal Statistical Office Germany: Wiesbaden, 2009.
- 40 22. Grobe, T. G.; Dörning, H.; Schwartz, F. W. Barmer GEK Arztreport 2011 - Schwerpunkt: Bildgebende Diagnostik - Computer- und Magnetresonanztomografie. 1-33. 2011. Schwäbisch Gemünd.
23. P. Möller; Knappe, A.; Dulski, P.; Pekdeger, A. *Applied Geochemistry* **2011**, *26*(1), 140-149.
- 45 24. R. Steele; Van Slyke, D. D.; Plazin, J. *Annals of the New York Academy of Sciences* **1952**, *55*(3), 479-484.