Supporting Information

Development of an In-line Magnetometer for Flow Chemistry and its Demonstration for Magnetic Nanoparticle Synthesis

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Contents

1 Calculation of Magnetic Properties

1.1 Derivation of Voltage Difference Induced in Sample and Reference Pick-Up Coils

The time dependent voltage difference induced by an alternating magnetic field (B) in the sample ($V_{\mathrm{PU\ sample}}$) and reference ($V_{\mathrm{PU\ ref}}$) pick-up coil depending on the sample's volumetric magnetic susceptibility ($\chi_{\mathrm{sample}} = \mu_{\mathrm{r\ sample}} - 1$) in equation 5 is obtaned as follows:

$$V_{\mathrm{PU\ sample}}(t) - V_{\mathrm{PU\ ref}}(t) = -N_{\mathrm{PU}} \cdot A_{\mathrm{PU\ sample}} \cdot \frac{\partial B_{\mathrm{sample}}}{\partial t} + N_{\mathrm{PU}} \cdot A_{\mathrm{PU\ ref}} \cdot \frac{\partial B_{\mathrm{ref}}}{\partial t}$$

$$= N_{\mathrm{PU}} \cdot A_{\mathrm{PU}} \cdot \left(\frac{\partial B_{\mathrm{ref}}}{\partial t} - \frac{\partial B_{\mathrm{sample}}}{\partial t} \right)$$

$$= N_{\mathrm{PU}} \cdot A_{\mathrm{PU}} \cdot \left(\frac{\partial B_{\mathrm{ref}}}{\partial t} - \frac{\partial \left(B_{\mathrm{ref}} \cdot \mu_{\mathrm{r\ sample}} \right)}{\partial t} \right) \qquad \text{Assuming } \mu_{\mathrm{r\ sample}} > 1 \text{ and } \mu_r = \frac{B_{\mathrm{sample}}}{B_{\mathrm{ref}}}$$

$$= N_{\mathrm{PU}} \cdot A_{\mathrm{PU}} \cdot \left(\frac{\partial B_{\mathrm{ref}}}{\partial t} - \mu_{\mathrm{r\ sample}} \cdot \frac{\partial B_{\mathrm{ref}}}{\partial t} \right)$$

$$= -N_{\mathrm{PU}} \cdot A_{\mathrm{PU}} \cdot \frac{\partial B_{\mathrm{ref}}}{\partial t} \left(\mu_{\mathrm{r\ sample}} - 1 \right)$$

$$= -N_{\mathrm{PU}} \cdot A_{\mathrm{PU}} \cdot \frac{\partial B_{\mathrm{ref}}}{\partial t} \cdot \chi_{\mathrm{sample}} \qquad \text{= equation 5}$$

$$= -N \cdot A \cdot \omega \cdot B_0 \cdot \cos(\omega \cdot t) \cdot \chi_{\mathrm{sample}} \qquad \text{Assuming sinusoidal B field, see equation 2}$$

$V_{\mathrm{PU\ sample}}(t) - V_{\mathrm{PU\ ref}}(t) = \Delta V_{\mathrm{PU}}(t)$ … Difference in voltage induced by sample and reference pick-up coil

N_{PU} …Turns of pick-up coil

A_{PU} … Area/cross section of pick-up coil

B … Magnetic flux density in sample (B_{sample}) or reference (B_{ref}) pick-up coil

μ_{r} … Relative permeability of sample

χ_{sample}… magnetic susceptibility of sample ($= \mu_{\mathrm{r}} - 1$)

B_0 ·… Amplitude of magnetic flux density inside the induction coils covering the pick-up coils

1.2 Estimation of Change in Magnetisation during Co-Precipitation Synthesis

The monitoring of iron oxide nanoparticles syntheses via co-precipitation was chosen to showcase the flow magneotmeter. Most co-precipitation protocols use Fe concentrations between 0.01 and 1 M, usually with a 1:2 ratio of ferrous and ferric (Fe^{2+} + Fe^{3+}). Assuming a saturation magnetisation of the co-precipitated iron oxide nanoparticles of ~80 emu/g for magnetite (Fe_3O_4) and ~60 emu/g for maghemite (Fe_2O_3), *i.e.*, the iron oxide structures of the highest magetisation, the sample magnetisations at saturation can be estimated as shown in Table 1. The inline magnetometer must therefore be able to monitor changes of $\Delta M_{\mathrm{sample}} < 10\ \mathrm{A\ m^{-1}}$. The calculations are summarised in the Matlab file *estimate_change_magnetic_moment.m* provided as electronic supplementary material. It should be noted that saturation is not reached for the magneitc field strenghts applied, hence, even smaller changes ($\Delta M_{\mathrm{sample}}$) must be detected. Hence, for further calculations we assume $\Delta M_{\mathrm{sample}} = 10\ \mathrm{A\ m^{-1}}$.

Table S1: Expected volumetric magnetisations of iron oxide nanoparticles

Fe ion concentration [M]	Magnetite in solution [g/ml]	Saturation magnetisation assuming magnetite [A/m]	Maghemite in solution [g/ml]	Saturation magnetisation assuming maghemite [A/m]
0.01	7.7167e-04	61.73	7.9850e-04	47.91
1	0.0772	6173	0.0798	4791

1.3 Estimation of Change of Magnetic Susceptibility during Co-Precipitation Synthesis

The (volumetric) magnetic susceptibility ($\chi = \partial M / \partial H$) does not only depend on the applied magnetic field, but also the particle properties. When comparing with typical iron oxide nanoparticle magnetisation curves from literature, the change of χ at $\Delta M_{\mathrm{sample}} = 10\ \mathrm{A\ m^{-1}}$ is estimated as

$$\Delta\chi \approx 2 \cdot \frac{10}{6000}\left[\frac{\mathrm{A}}{\mathrm{m\ Oe}}\right] = 2 \cdot \frac{4\pi \cdot 10}{6000 \cdot 1000}\left[(\mathrm{A\ m^{-1}})/(\mathrm{A\ m^{-1}})\right] = 1.0167 \cdot 10^{-5}\ [-].$$

1.4 Estimation of Sensitivity Required in Terms of Induced Voltages Difference(ΔV_{PU})

The difference in induced voltage amplitude at the pick-up coil can be estimated using equation 5. Assuming a pick-up coil with 500 turns like the ones used, and that a spherical cross section of 1 mm in diameter is filled with sample, a magnetisation of $\Delta M_{\mathrm{sample}} < 10\ \mathrm{A\ m^{-1}}$ results in a difference in induced voltage (amplitudes) of

$$V_{\mathrm{PU\ sample}} - V_{\mathrm{PU\ ref}} \sim 0.5\ \mathrm{mV}$$

This difference is small and is below what can be measured accurately by standard laboratory oscillometers. Therefore, a lock-in amplifier was used.

2 Chemicals and Components Used

All chemicals used for the iron oxide nanoparticle synthesis are listed in Table S2. All components and equipment used for the development and operation of flow magnetometer are listed in Table S3.

Table S2: Details of chemicals used for iron oxide nanoparticle syntheses

Compound	Purchased from	Manufacturer	Product Nr.	Lot Nr(s).
Iron(II) chloride tetrahydrate, $FeCl_2 \cdot 4H_2O$, ≥ 99%	Sigma Aldrich UK	Honeywell Fluka	44939	BCBT2444
Iron(III) chloride hexahydrate, $FeCl_3 \cdot 6H_2O$, ≥ 99%	Sigma Aldrich UK	Honeywell Fluka	31232	STBH0744
NaOH 2 M solution	Fischer Scientific Ltd	Honeywell Fluka	35254	H2980
Sodium carbonate decahydrate	Sigma Aldrich UK	Honeywell Fluka	71360	BCBR7637V

Table S3: Details of components used for flow magnetometer development and operation

Compound	Brand - Model	Comment
Signal generator	*TTi - TG2511*	Arbitrary/Pulse, 1 Channel, 25 MHz, TGxx11 Series
Lock in amplifier	*Jupiter Microsystems-LA9060*	Two phase digital lock-in amplifier
Power amplifier	*CleverLittleBox- CIE.CA9.2* 12W	Mini stereo amplifier with a 20 Hz - 20 kHz Range (product discontinued)
Oscilloscope	*Tektronox-TDS 2004B*	Used for development and current/magnetic field measurements
Potentiometers	*Vishay-Precision Potentiometer 1911 MEX*	10 turn potentiometer
Inductors	*Power Inductor-SDR0805 Series*	
Resistors	*Ohmite-20J10R series* and *Visaton- cement resistors* (or similar)	Rated for 10-20 W
Counting dials	*Vishay- 11A11B10 Satin Chrome*	For 10 turn potentiometers
Pick-up coil wiring	*Vero Technologies-79-19038*	0.15 mm copper wire enamelled
Induction coil wiring	*Rowan cable-1230981*	0.50 mm copper wire enamelled
Solderable breadboard	*SparkFun PRT-12699*	

3 Details of the Flow Magnetometer: Construction and Operation

3.1 Coil Construction and Flow Magnetometer Set-Up

Details of the coil construction and flow magentometer operation are shown below. Figure S1 shows the induction and pick-up coil generation and Figure S2 an overview of the flow magnetometer set-up.

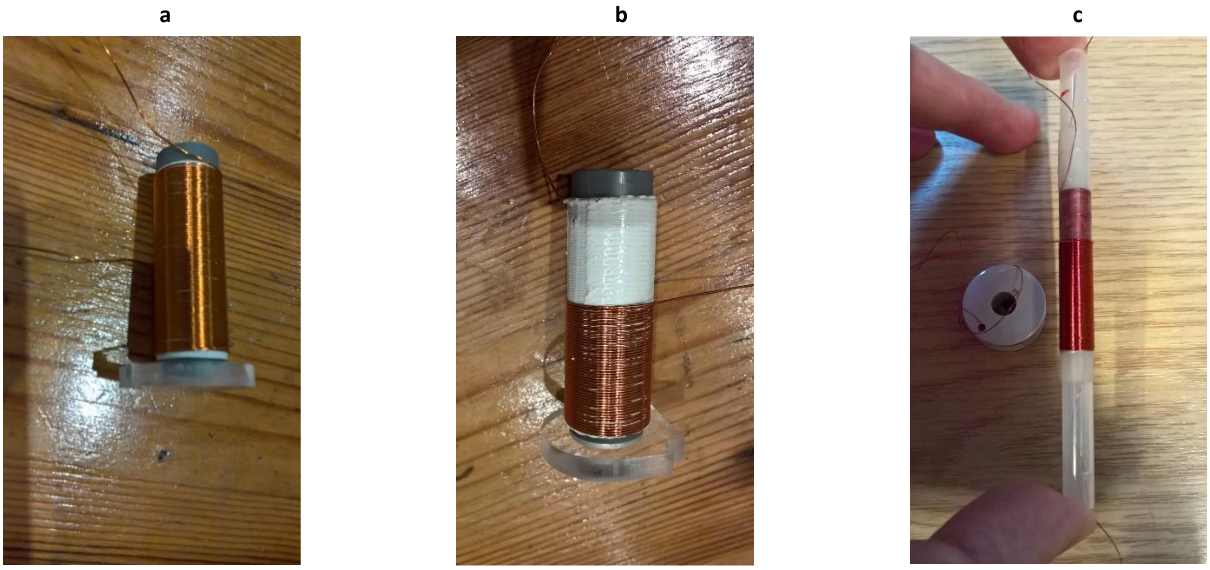

Figure S1: Photographs during the generation of Photograph of the (**a** & **b**) induction coil and (**c**) pick-up coil

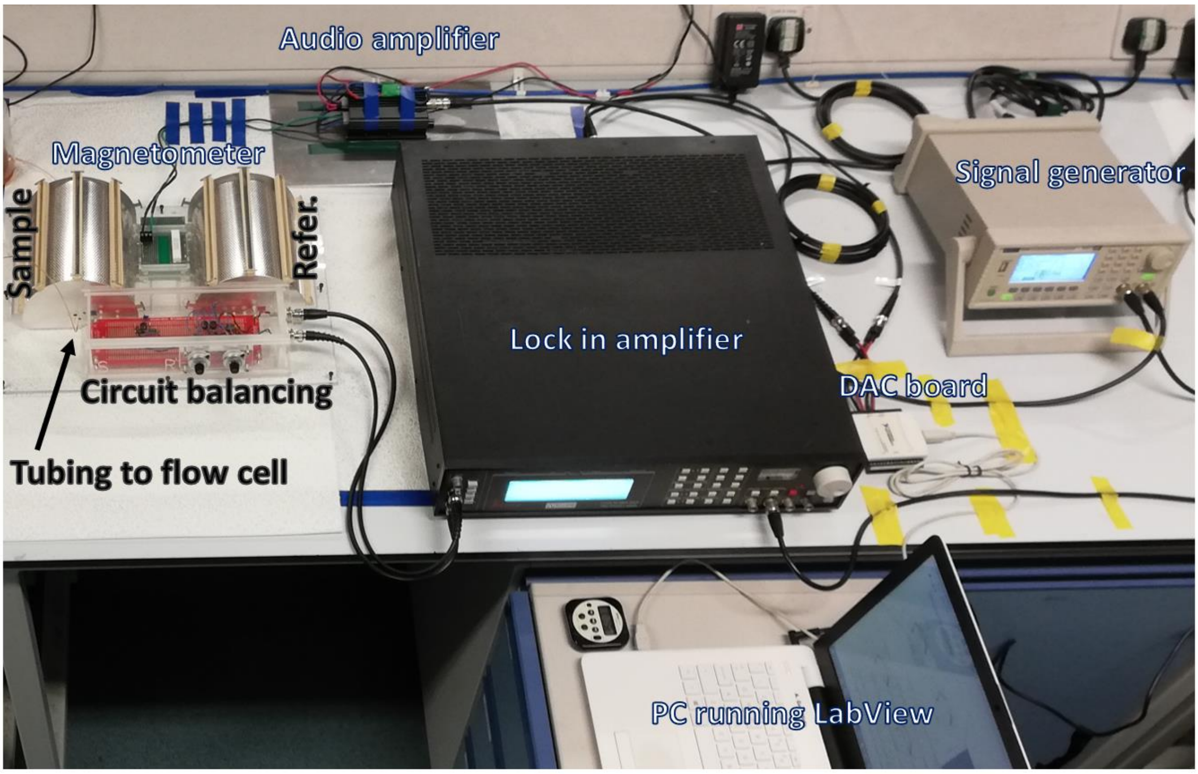

Figure S2: Overview of flow magnetometer set-up including data recording *via* digital analogue converter (DAC).

3.2 Determination of Magnetic Field Strengths in Induction Coils

The amplitude of the magnetic field strength inside the induction-coil (H_0) was determined *via* the voltage drop across a $4.7\ \Omega$ resistor in series with both induction coils at frequencies between 1 and $30\ \text{kHz}$. All settings, such as power amplifier gain, signal generator voltage ($5\ \text{V}$ peak to peak) resembled the settings during operation. Figure S3 shows, the voltage (amplitude) across and the current (amplitude, I_0) through the $4.7\ \Omega$ resistor, as well as the magnetic field induced in a solenoid with $N = 400$ turns over $l = 8$ cm long solenoid with a diameter of $d = 2.2$ cm approximated by the equation for infinitely long solenoids

$$H_0 = N \cdot I_0 / l$$

This analysis indicates that the magnetic field strengths during the operation at $12\ \text{kHz}$ is approximately $20\ \text{Oe}$ (or in SI units $\sim 1600\ \text{A m}^{-1}$).

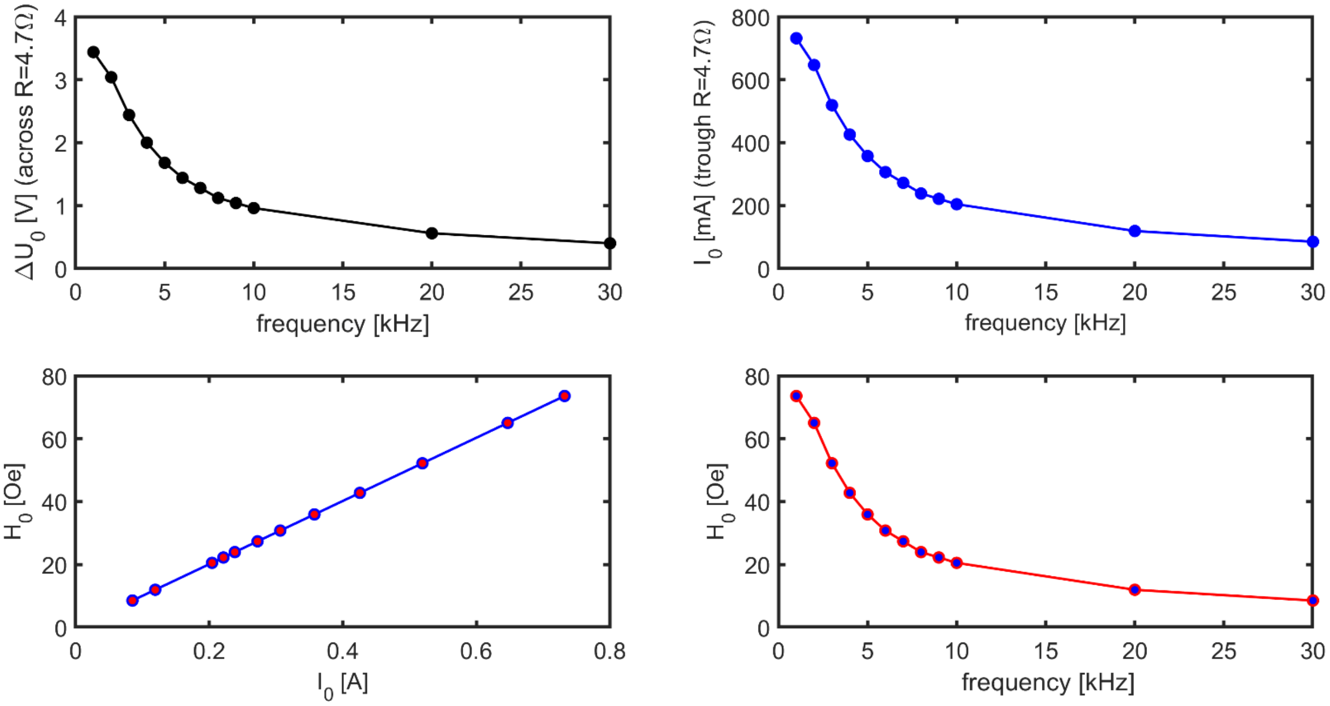

Figure S3: (*top*) Voltage across and current through 4.7 Ω resistor in series with both induction coils; (*bottom*) Magnetic field strengths amplitudes in induction coils.

4 Details of Set-ups Used for Iron Oxide Nanoparticle Synthesis Monitoring

4.1 On-Line Monitoring of Batch Co-Precipitation Synthesis Using Sodium Carbonate

The batch co-precipitation synthesis of iron oxide nanoparticles using sodium carbonate (Na_2CO_3) as base was monitored on-line using the set-up shown in Figure S4.

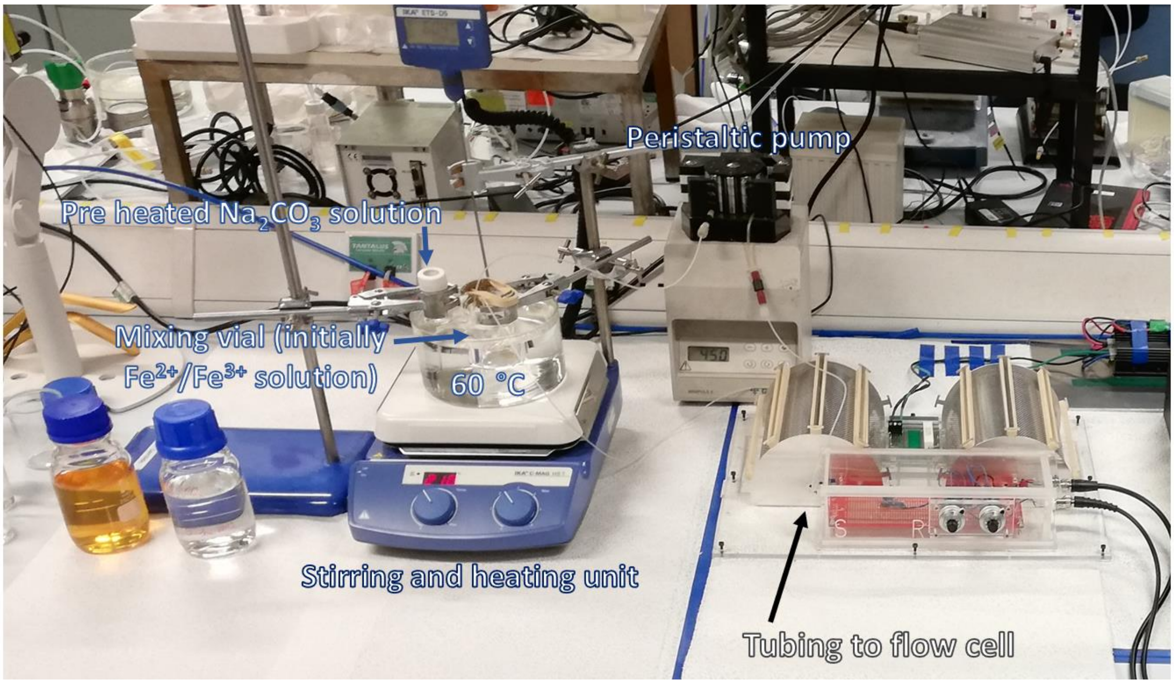

Figure S4: Overview of set-up used for on-line monitoring of Na_2CO_3 co-precipitation synthesis of IONP at temperatures from 30-90 °C

The magnetometer signal during a synthesis at 60 °C and subsequent flow cell cleaning is shown in Figure S5. As described in the main article, the flow magnetometer signal reached the lock-in amplifiers overload region, after which the lock-in amplifier's sensitivity had to be decreased. The magnetometer signal up to this overload point for 5 repeated experiments is shown in Figure 4a. Afterwards the synthesis monitoring was stopped, the flow cell was flushed with air (simply by lifting the tubing between the mixing vial (= the batch reactor) and the peristaltic pump out of the solution) causing the signal drop as expected. Since a change to the original sensitivity settings indicated residuals of magnetic material in the magnetometer flow cell (either due to sediments or fouling), it was rinsed with a 1 M HCl solution untill the signal dropped again below the noise level.

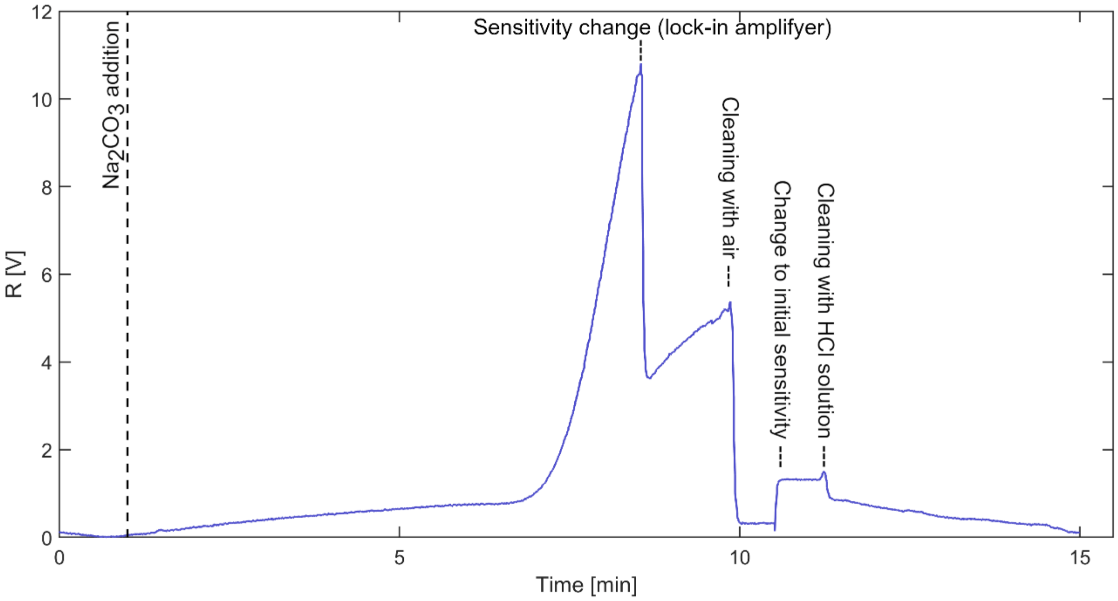

Figure S5: Magnetometer signal during one of the five sodium carbonate co-precipitation synthesis at 60 °C and subsequent flow cell cleaning procedure.

The Na_2CO_3 co-precipitation performed at 30 °C showed no indication of magnetite formation over the first 25 min after synthesis initiation. The sodium carbonate solution turned the mixture into a black-greenish solution as observed before, the magnetometer signal remained constant (and below the noise level). After ~25 min the temperature of the water bath in which the vial was immersed was set to 60 °C and the formation of magnetite was observed after the temperature exceeded 40 °C. The magnetometer signal during sodium carbonate co-precipitation synthesis initiated at 30 °C (first 8 min shown in Figure4a) and heated subsequently is shown in Figure S6.

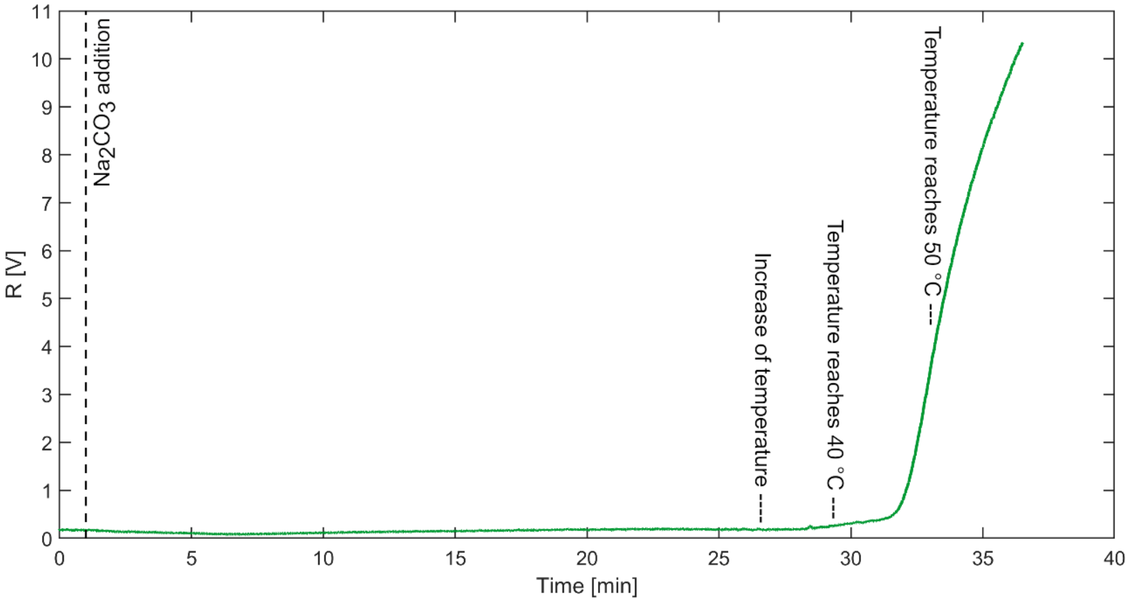

Figure S6: Magnetometer signal during sodium carbonate co-precipitation synthesis initiated at 30 °C and heated subsequently.

4.2 Semi-Batch Co-Precipitation Synthesis Using Sodium Carbonate at Different Temperatures

The influence of the temperature for the magnetite/maghemite transition was studied using the set-up shown in Figure S7. The sodium carbonate base solution was mixed continuously with the iron precursor solution in a T-mixer (P-632 from *IDEX Health Science*) immersed in the 1st water bath heated to 30 °C. This mixing stage comprising preheating of the solutions before mixing to guarantee that mixing occurs at the 30 °C (= the temperature of the 1st water bath) and small coiled flow inverter after the T-mixer is identical to that described in Besenhard *et al.* (*Chemical Engineering Journal, Vol. 399, 2020, 125740*). After mixing, *i.e.*, after the colloidal solution exitted the mixing stage, the just precipitated solution was collected in a vial and stirred magnetically. After 20 ml have been collected (corresponding to 2 min for the used total flow rate of 10 ml/min) the collection vial was transferred to the second water bath, heated to temperatures from 30-55 °C, while stirring was continued. The vial was removed from the 2nd water bath after 20 min and sample preparation was started, *i.e.*, washing via magnetic decantation and drying.

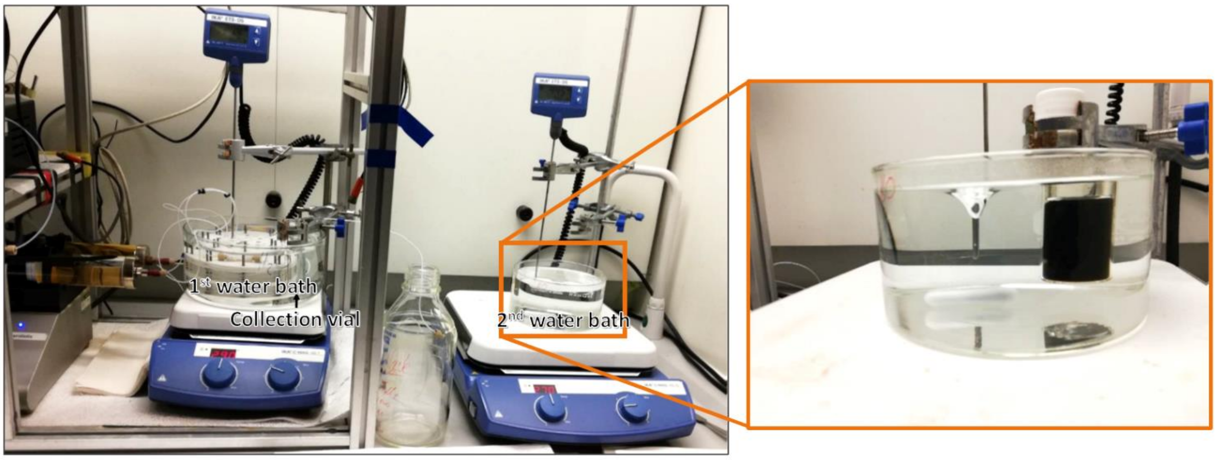

Figure S7: Overview of semi-batch set-up used for temperature studies of sodium carbonate co-precipitation synthesis. Left, the set-up before initiating the semi-batch synthesis (collection vial in 1st water bath); right/magnified, collected mixture immersed in 2nd water bath.

The importance of the temperature for this sodium carbonate co-precipitation synthesis is obvious from Figure S8, showing the solutions after removal from the 2nd water bath beside a magnet. For the solution processed entirely at 30 °C, the nanoparticles could not be separated with the magnet. It should be mentioned that also after several days, this sample showed no attraction of the nanoparticles to the magnet. However, for the sample processed at 35 °C in the second water bath, the nanoparticles could be separated easily with the magnet and the supernatant remained slightly yellowish (indicating some unreacted iron species or particulate phases that cannot be withdrawn by the magnet). At 40 °C, also the supernatant appeared clear.

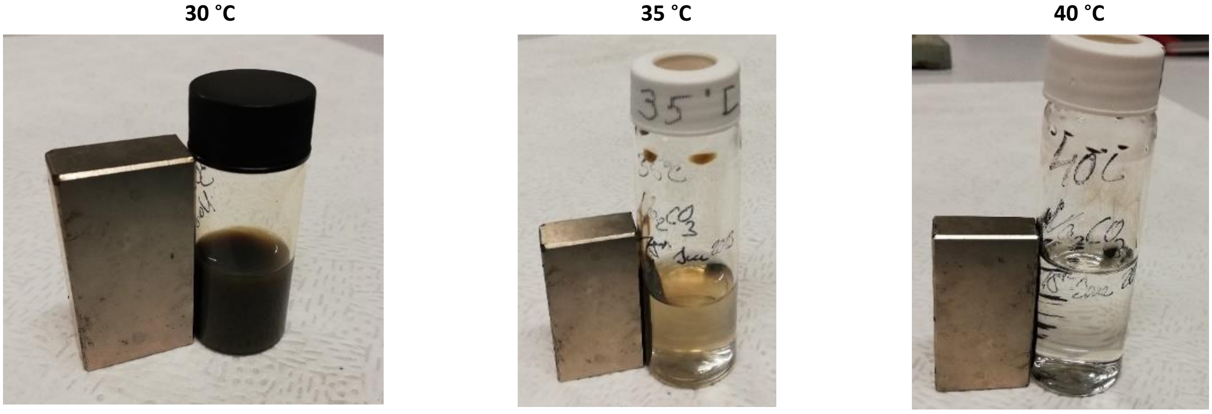
30 °C **35 °C** **40 °C**

Figure S8: Samples synthesised *via* co-precipitation using Na_2CO_3 at 30 °C, 35 °C and 40 °C beside a magnet.

4.3 In-Line Monitoring of Flow Co-Precipitation Synthesis Using Sodium Hydroxide

The flow synthesis of IONPs using a flow co-precipitation method with sodium hydroxide (NaOH) as base was monitored in-line using the set-up shown in Figure S9. Two syringe pumps were used to perform synthesis with different sodium hydroxide solution flow rates. The ferrous/ferric ion precursor solution was always fed at 5 ml/min.

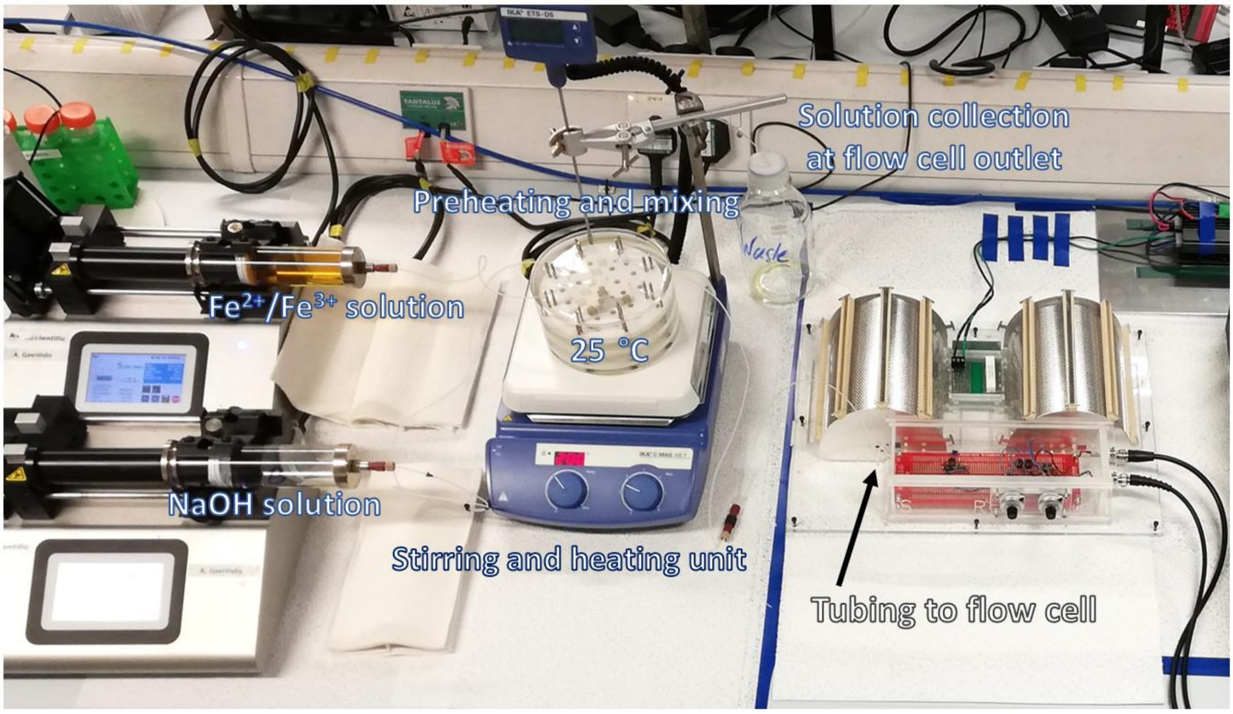

Figure S9: Overview of set-up used for on-line monitoring of NaOH flow co-precipitation synthesis of IONPs at different pH values

For the experiments shown in Figure 9, the NaOH was fed at 5 ml/min too but the NaOH concentration in the feed solution was changed. Figure S10 shows the coiled flow inverter used to increase the time after which the reactor effluent entered the magnetometer flow cell by 20 s.

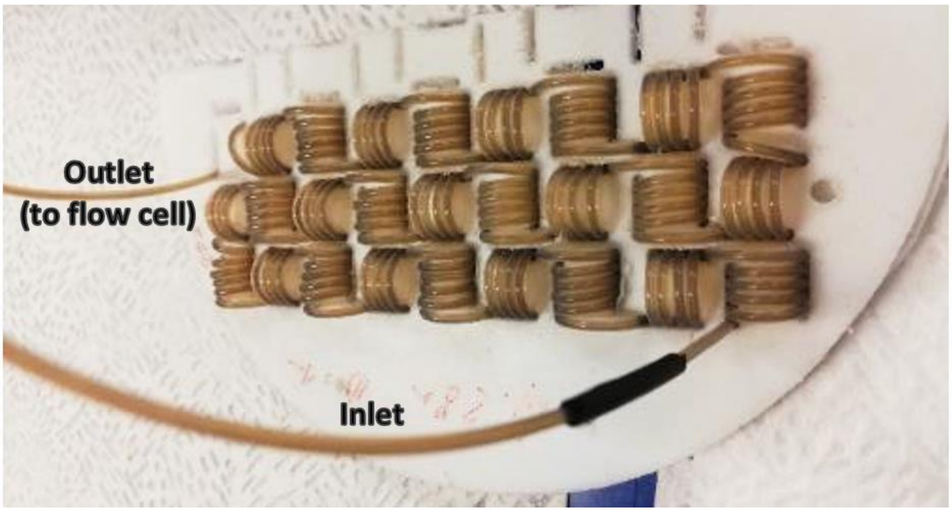

Figure S10: Picture of the coiled flow inverter made of 1/16'' tubing (with an inner diameter of 1 mm) and used to extend the residence time between T-mixer and magnetometer flow cell. The picture was taken during a synthesis, and hence the dark colour is due to the IONP solution passing through