

# Remotely Triggered Liquefaction of Hydrogel

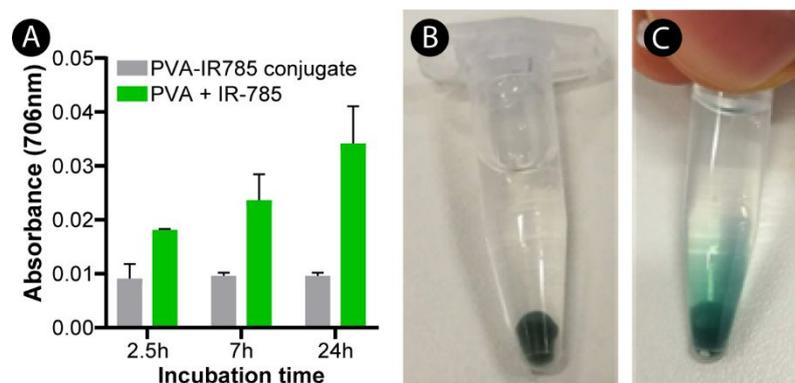
## Materials

*Søren L. Pedersen,<sup>1</sup> Tin H. Huynh,<sup>1</sup> Philipp Pöschko,<sup>1</sup> Anne Sofie Fruergaard,<sup>1</sup>  
Morten T. Jarlstad Olesen,<sup>1</sup> Yaqing Chen,<sup>1,2</sup> Henrik Birkedal,<sup>1,2</sup> Guruprakash Subbiahdoss,<sup>3</sup>  
Erik Reimhult,<sup>3</sup> Jan Thøgersen,<sup>1</sup> Alexander N. Zelikin<sup>1,2</sup>\**

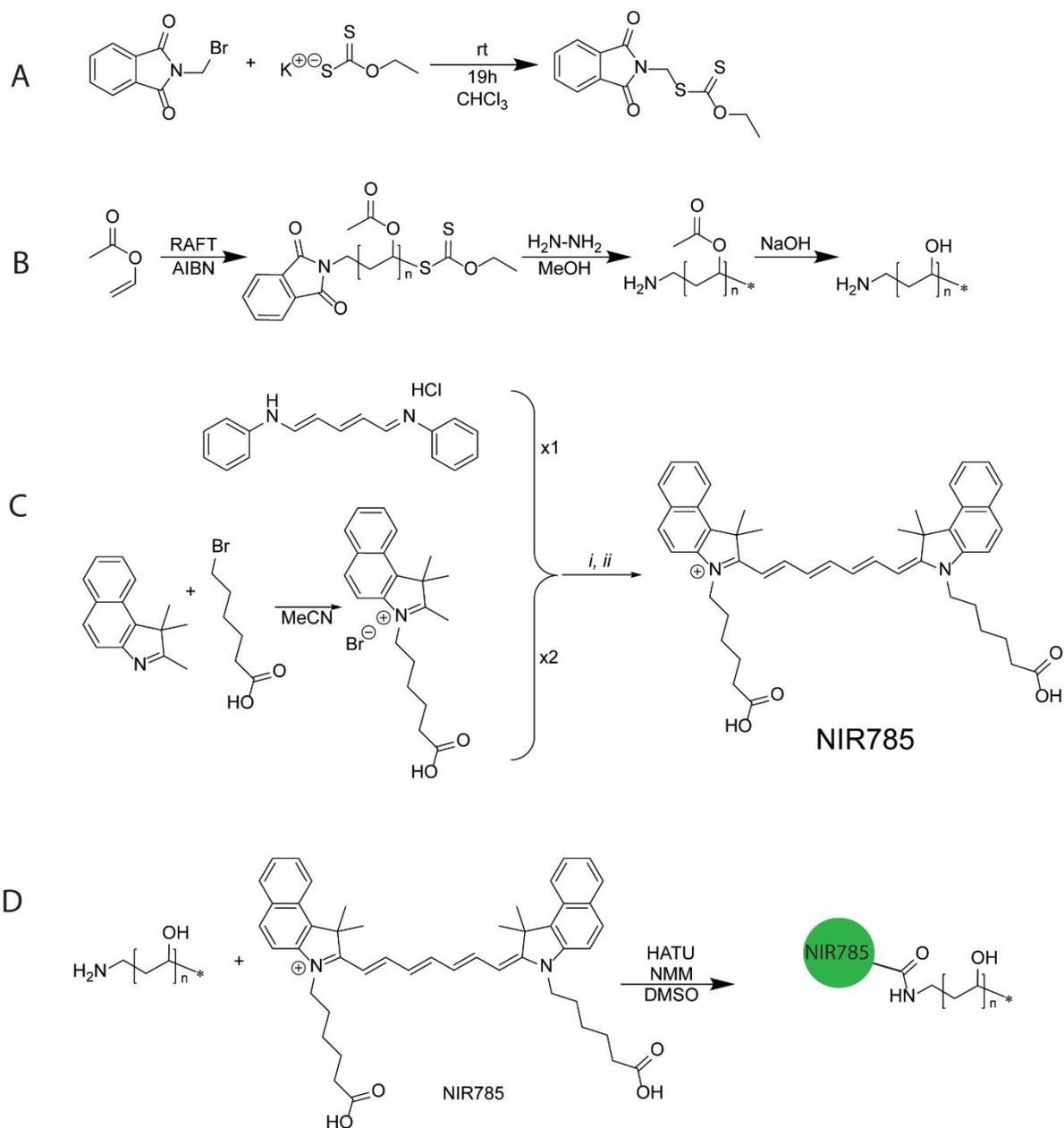
1. Department of Chemistry, Aarhus University, Aarhus 8000, Denmark.  
E-mail: [zelikin@chem.au.dk](mailto:zelikin@chem.au.dk)
2. iNano Interdisciplinary Nanoscience Centre, Aarhus University, Aarhus 8000, Denmark
3. Department of Nanobiotechnology, University of Natural Resources and Life Sciences, A-1190 Vienna, Austria

## SUPPORTING INFORMATION

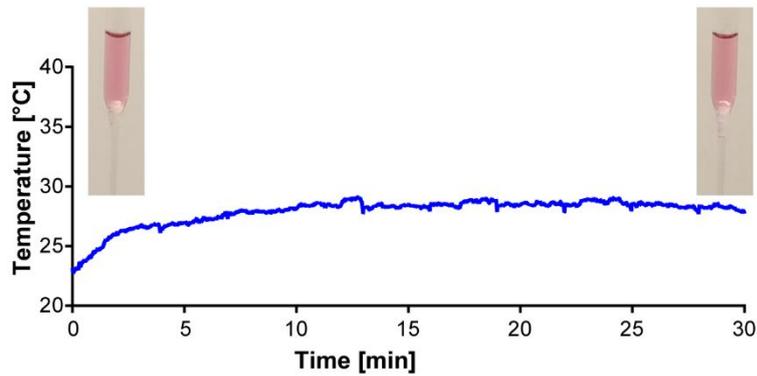
## Supporting figures



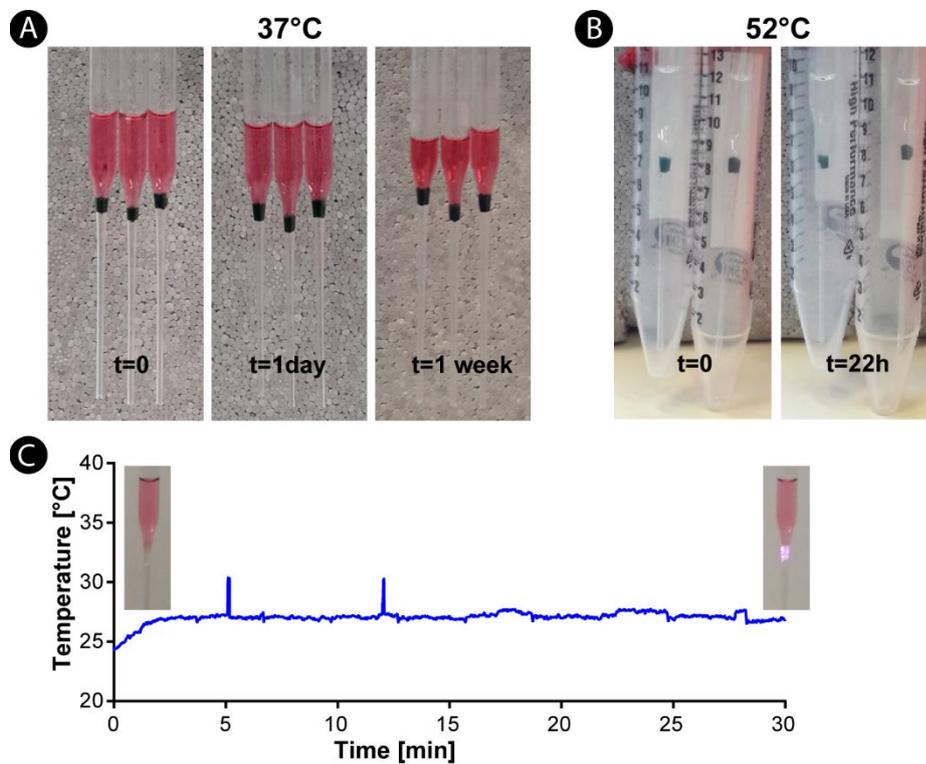
**Figure S1:** Spontaneous release of the non-conjugated NIR785. Hydrogels, 20 $\mu$ L volume, 5 cryocycles, 20wt% of PVA-NIR785 or PVA-NH<sub>2</sub> supplemented with equal amount of NIR785 in its free form. Hydrogels were incubated with 0.5mL PBS at 37°C. A) Absorbance of released NIR785 (free or as PVA-NIR785) to the supernatant over time. Results are plotted as mean + S.D., n=3 B) Picture of PVA-NIR785 hydrogel after 24h. C) Picture of PVA-NH<sub>2</sub>/NIR785 hydrogel after 24h.



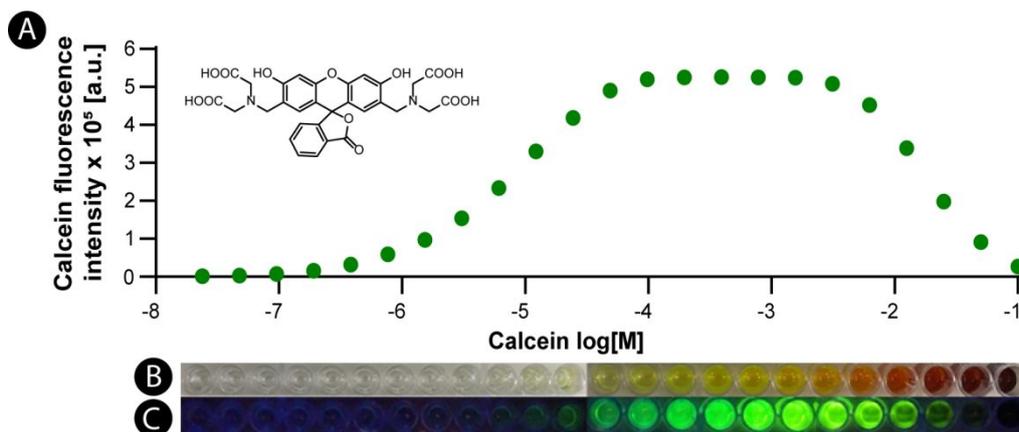
**Figure S2:** Schematic of the synthesis of PVA-NIR785. A) synthesis of phthalimide-containing chain transfer reagent. B) Synthesis of poly(vinyl acetate) followed by deprotection of acetate groups and the phthalimide functionality afforded PVA with one terminal amine group. C) Synthesis of NIR785. *i*: AcO<sub>2</sub>, DIPEA, DCM. *ii*: AcONa, MeOH. D) Conjugation of PVA with NIR785 yielding PVA-NIR785.



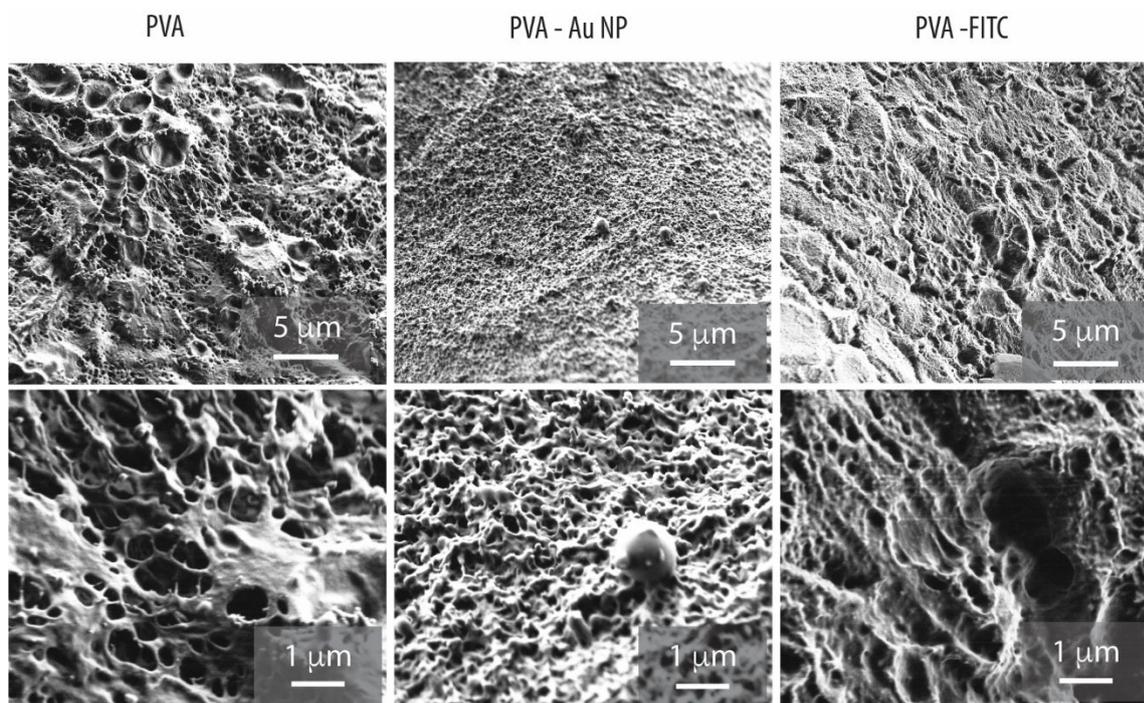
**Figure S3:** Stability of PVA hydrogels. PVA hydrogel (50 $\mu$ L, 8wt% PVA, 90kDa) without AuNP irradiated by NIR light at 1.5W for 30min. Temperature was recorded with an IR-camera. Inserts: picture at t=0 and t=30min.



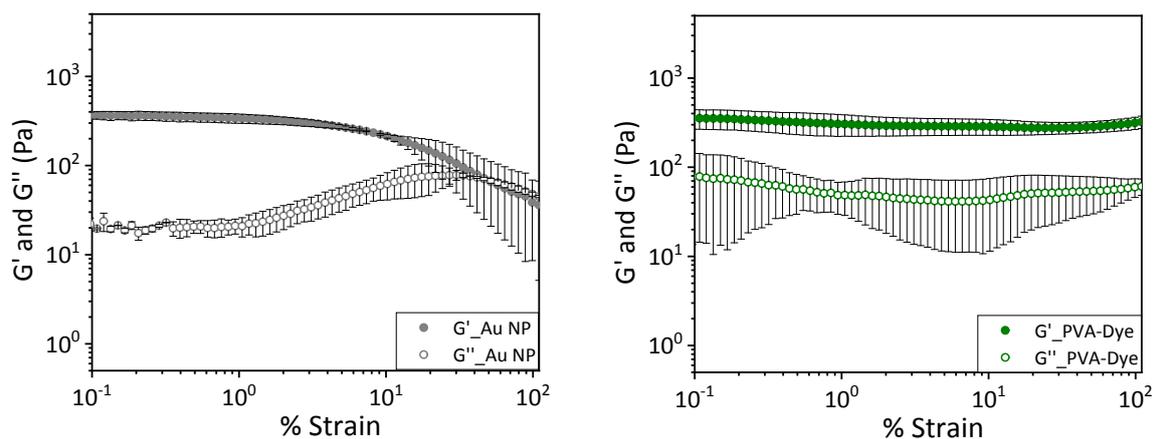
**Figure S4:** Stability of PVA-NIR785 hydrogels. Blocking setup containing PVA-NIR785 hydrogels (20 $\mu$ L volume, 20wt%) and 0.5mL PBS. A) Incubated at 37°C for 7days. B) Incubated at 52°C for 22h. C) PVA-NH<sub>2</sub> hydrogel (20 $\mu$ L volume, 20wt%, 20kDa) irradiated in the blocking setup by NIR light at 1.5W for 30min. Temperature was recorded with an IR-camera. The two spikes in temperature after 5 and 12min arise from inspection of the alignment of the sample within the laser beam. Inserts: picture at t=0 and t=30min.



**Figure S5:** Calcein. A) Self-quenching effect of calcein, shown from a serial dilution of calcein. Fluorescence measurements at  $\lambda_{ex}/\lambda_{em}$  498/515nm. B) Pictures of calcein solutions C) Pictures of calcein fluorescence under a UV lamp, 365nm.



**Figure S6.** Scanning electron microscopy of PVA hydrogels prepared *via* critical point drying.



**Figure S7:** Storage ( $G'$ , solid circles) and loss modulus ( $G''$ , open circles) of PVA hydrogels with AuNP (left) and PVA-NIR785 dye conjugate (right) as a function of strain-amplitude sweep at  $1 \text{ s}^{-1}$  radial frequency. Data are based on three independent experiments and presented as mean  $\pm$  st.dev.

## Super paramagnetic iron oxide nanoparticles and alternating electromagnetic field

X-ray diffraction was performed on a Rigaku SmartLab II diffractometer. Magnetization measurements were performed on a Physical Properties Measurement System (PPMS) from Quantum Design equipped with a vibrating sample magnetometer (VSM) operating at 300K and in the range of  $\pm 20$ kOe.

All magnetothermal experiments were performed with a MagneTherm™ system, NanoTherics, UK. The system consists of a high-power radio frequency amplifier connected to a solenoid coil. The radiofrequency amplifier was powered by an external DC power supply, and frequency was adjusted by an external function generator. The system was monitored by an oscilloscope. A double water cooling system with two Julabo bath circulating systems (F250 and ED) was used to cool down the coil and the magneTherm™ system. The temperature was recorded either with a FLIR C2 Compact Thermal Imaging System and FLIR Tools+ software or a thermocouple (EL-USB-TC-LCD data logger) controlled with EasyLog USB software.

**Nanoparticle synthesis by reduction of iron chloride salts** was performed as in An *et al.*<sup>45</sup>. In a three-necked flask equipped with a condenser, FeCl<sub>2</sub> (430mg, 2.15mmol, 1eq.) and FeCl<sub>3</sub> (1189mg, 4.35mmol, 2eq.) were dissolved in degassed MQ water (40mL) at r.t. under N<sub>2</sub> atmosphere. Under vigorous stirring NH<sub>4</sub>OH 28% (1.9mL, 12mmol, 5.6eq.) was added rapidly. Stirring rate was lowered and temperature was raised to 80°C. Oleic acid (150μL, 0.48mmol, 0.22eq.) was added at 50°C and the reaction was stirred for 1h at 80°C. Toluene (30mL) and NaCl (excess) were added and the two phases were separated. The organic phase was washed with water followed by addition of acetone, which facilitated precipitation and isolation by magnetic decantation. A second wash with toluene and acetone and magnetic decantation yielded 550 mg oleic acid-covered iron oxide particles.

### **Nanoparticle synthesis by thermal decomposition iron pentacarbonyl.**

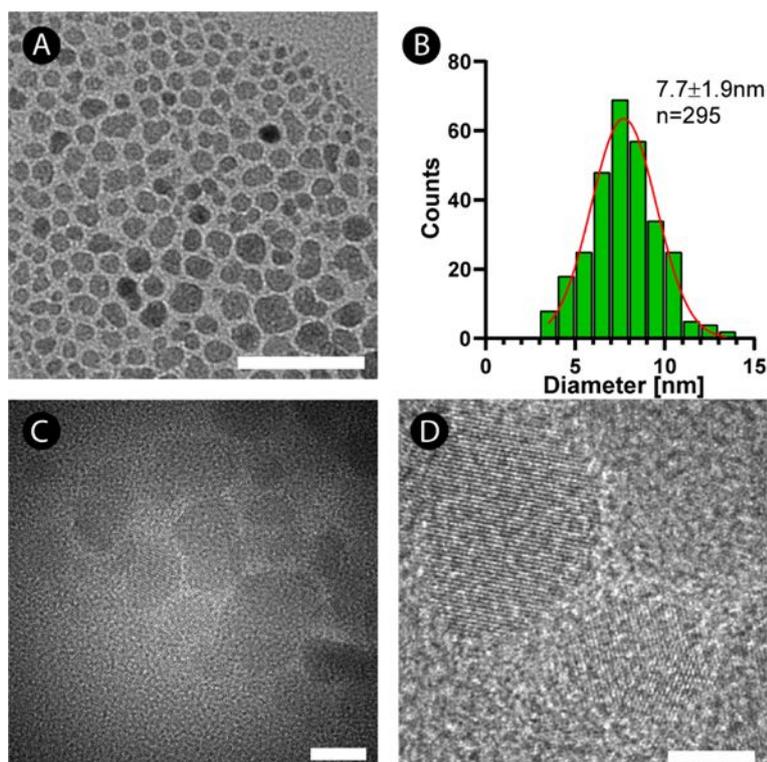
SPION were synthesized according to literature<sup>46</sup>. To a three necked 250mL round bottomed flask, equipped with a magnetic stirrer and a condenser, was added dioctyl ether (50mL) and oleic acid (6mL), the solution was heated to 100°C, degassed and dried of water under a nitrogen flow. Iron pentacarbonyl (1mL) was added and temperature was raised to 290°C with a ramp of 3°C/min. and held at that temperature for 1h before returning to r.t.. Reaction solution was poured into ethanol (250mL) to precipitate SPION which were isolated by magnetic decantation, followed by dispersion in toluene (6mL) and reprecipitation in ethanol. SPION were isolated by centrifugation.

### **Water dispersible SPION, ligand exchange of oleic acid for TMAOH**

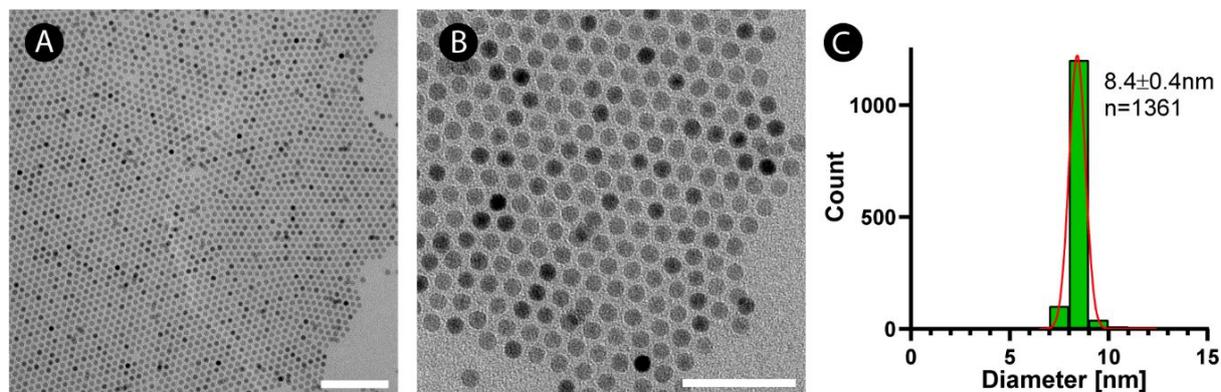
SPION (20mg) were washed (magnetic decantation) in ethanol/hexane (3:1), then mixed with TMAOH (2mL, 25wt% in H<sub>2</sub>O) and sonicated for 30min. followed by washes in water yielding (CH<sub>3</sub>)<sub>4</sub>N<sup>+</sup> coated SPION<sup>47-48</sup>. The SPION (15mg) were subsequently mixed with PVA (15mg, 90kDa) forming a homogeneous aqueous solution (8wt% SPION and 8wt% PVA).

### **SPION-hydrogel production and treatment in AMF.**

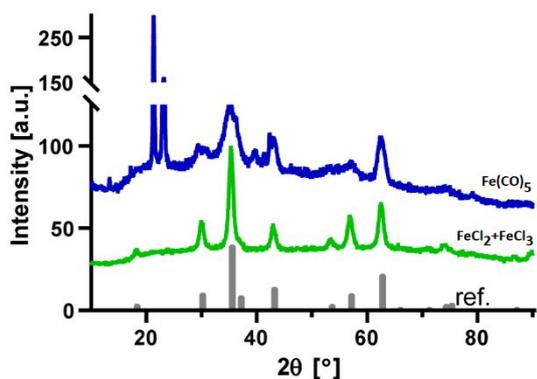
Solutions of PVA and SPION (as presented above with TMAOH) of 8wt% SPION and 8wt% PVA (90kDa) was cryogelated as 20μL volume gels using Eppendorfs tubes as molds, five rounds of freeze-thawing. A glass Pasteur pipettes, 150mm, with a hydrogel and 500μL of water on top was positioned within the AMF (MagneTherm system by NanoTherics) coil and treated up to 30min at 476kHz and 23mT.



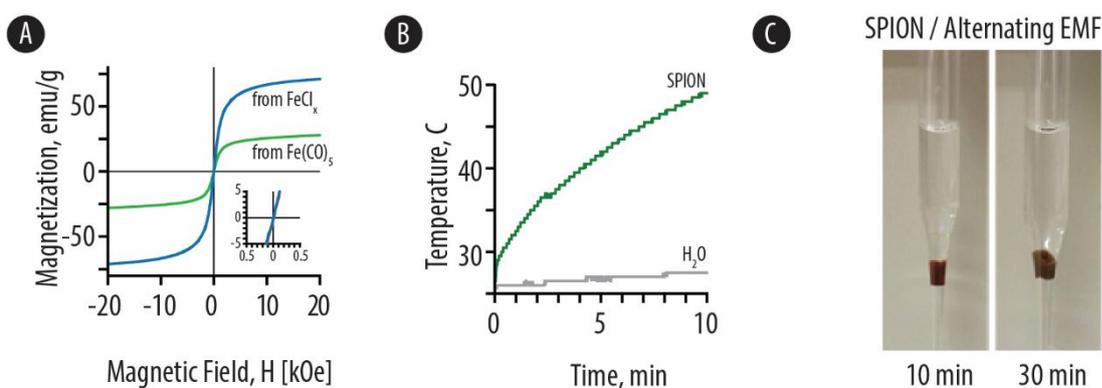
**Figure S8:** SPION by reduction of iron chloride salts. A) TEM of as synthesized SPION, scale bar: 50nm. B) Size distribution of SPION based on TEM picture. Diameter:  $7.7 \pm 1.9 \text{ nm}$  ( $n=295$ ). C) and D) High resolution TEM, scale bar: 10nm and 5nm, respectively.



**Figure S9:** SPION by thermal decomposition of iron pentacarbonyl. A) and B) TEM of as synthesized SPION, scale bar: 100nm and 50nm, respectively. C) Size distribution of SPION based on TEM picture. Diameter:  $8.4 \pm 0.4 \text{ nm}$  ( $n=1361$ ).



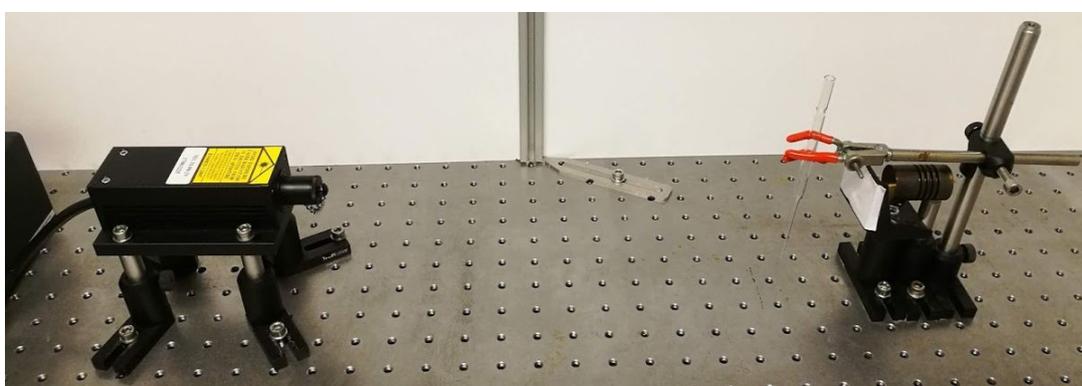
**Figure S10:** XRD diffractogram of SPION. SPION by reduction of iron chloride salts (green) and SPION by thermal decomposition of iron pentacarbonyl (blue). Reference angles for  $\text{Fe}_3\text{O}_4$  (grey).



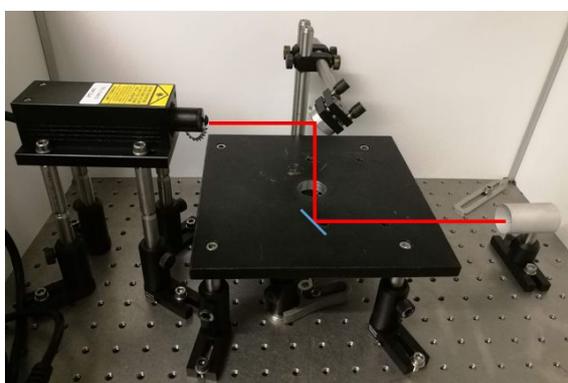
**Figure S11.** (A) SPION exhibited characteristic magnetisation profile confirming their added paramagnetism; (B). Heat evolution profile was recorded in aqueous suspensions of SPION, (C) Visualization of the PVA hydrogels containing SPION following stimulation with AMF (476 kHz, 23 mT).



**Figure S12:** MagneTherm™ setup. Top left: function generator; middle left: DC power supply; bottom left: oscilloscope; right: magneTherm™ system containing a solenoid coil (right).



**Figure S13:** Laser setup, horizontal. NIR light beam aimed for horizontal irradiation.



**Figure S14:** Laser setup, vertical. NIR light beam angled vertically downwards for top-down irradiation. Red line indicate the beam path.

# NMR spectra

