

Supporting Information

Near-Infrared photothermal activation of microgels incorporating polypyrrole nanotransducers through droplet microfluidics

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1. Synthesis and characterization of polypyrrole (PPy) nanoparticles

Synthesis: PPy nanoparticles were prepared in an aqueous solution that contained poly (vinyl alcohol) (PVA) (M_w 9000~10,000, Sigma-Aldrich, Singapore), $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (97%, Sigma-Aldrich, Singapore) and pyrrole monomer (98%, Sigma-Aldrich, Singapore). First, 0.75 g of PVA was dissolved in 10 ml of deionized water by being stirred on a 60 °C hotplate for 20 min. After the mixture cooled, 0.63 g of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ was added to the PVA solution and stirred for 1 h to fully dissolve the $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$. Subsequently, 69 μl of pyrrole monomer was added dropwise to the reaction mixture. The reaction mixture was maintained at 4 °C while being stirred for 24 h for the polymerization reaction. The resulting black PPy nanoparticle solution was centrifuged at $13,000\times g$ and 4 °C for 40 min to separate the PPy nanoparticles. The obtained PPy nanoparticles were then washed twice with deionized water. The centrifugation and washing processes were repeated three times to remove the excess PVA.¹

Characterization: Scanning electron microscopy (SEM, JEOLJSM-6430F, JEOL, Japan) was used to investigate the morphology of the PPy nanoparticles. One drop of the PPy nanoparticle suspension was placed onto a clean silicon wafer, dried, coated with Pt, and then observed under an accelerating voltage of 5 keV. To determine the hydrodynamic diameter and polydispersity index of the PPy nanoparticles, dynamic light scattering (DLS) measurements were performed using a Malvern Zeta-sizer (Malvern Zetasizer Nano, UK). First, 1 ml of a dilute PPy nanoparticle aqueous solution was placed in a disposable cuvette and was tested three times. The absorption spectrum of the PPy nanoparticle suspension in a quartz cuvette was measured using a UV-Vis spectrometer (UV-2401PC, Shimadzu, Japan). The wavelength range was set from 250 to 1000 nm. To investigate the ability of PPy nanoparticles to convert NIR light into heat, the PPy nanoparticle suspension was heated using NIR irradiation. 2ml of PPy nanoparticles with three different concentrations (0, 125, and 250 $\mu\text{g}/\text{ml}$) were placed into a 4ml cuvette (1cm path-length) which was put onto magnetic stirrer plate and kept stirring. The thermocouple of a digital thermometer with a precision of 0.1 °C (Fluke 51-II) was immersed into the solution. The PPy nanoparticle solution was then

irradiated with a 980 nm laser for 10 min at intensity of $2.2\text{w}/\text{cm}^2$. The laser intensity was calculated using the following equation provide by the Power Meter supplier; $(250/d^2) \times \text{Power}$, where d is the diameter of the laser beam in millimeters. Laser beam diameter was determined by using IR indication card. Power is determined by power/energy meter Model 841-PE (Newport Opto-Electronics Technologies, Singapore) and the temperature changes were recorded every 10 seconds.

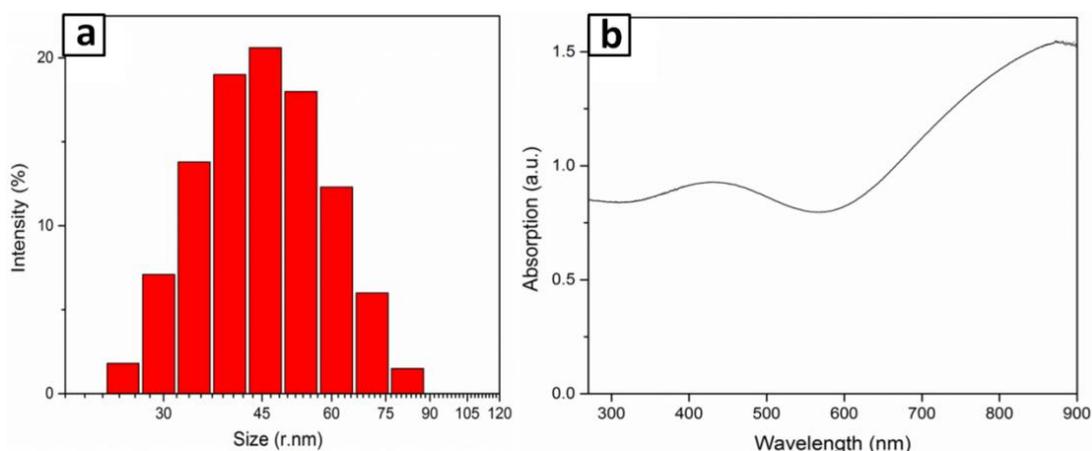


Fig.S1: (a) DLS results showing the hydrodynamic diameters of the PPy nanoparticles; (b) UV-vis-NIR absorption spectrum of the PPy nanoparticles at a concentration of $10\ \mu\text{g}/\text{ml}$.

2. Fabrication and light-response behaviors of a pNIPAM microgel device: The microchip was formed using poly(dimethylsiloxane) (PDMS) (Sylgard 184, Dow Corning). The fabrication primarily consists of three steps: (1) master fabrication, (2) PDMS curing, and (3) irreversible bonding of the PDMS microchannels onto the glass slides. First, an SU8 photoresist (SU8-2050, MicroChem) was patterned onto a silicon wafer to construct a positive master based on a photo-mask designed in AutoCAD. The master mold for the device contained channels that were $50\ \mu\text{m}$ wide and $50\ \mu\text{m}$ tall. The SU-8 master was further treated with hexamethyldisilane (Sigma-Aldrich, Singapore) for 20 min to prevent PDMS from adhering to the master. The hexamethyldisilane was evaporated and deposited onto the master in desiccators under a ~ 5 psi vacuum. Subsequently, PDMS with the curing agent (10:1) was thoroughly mixed and degassed in desiccators under a ~ 5 psi vacuum and was

subsequently poured onto the master mold and degassed again. The PDMS-covered mold was then cured in an oven at 65 °C overnight, and the PDMS layer was subsequently cut and peeled from the master. Holes were punched through the end of the channel using a punch with an outer diameter of 1 mm. To form the hydrophobic surface for creating the droplet, a glass slide was coated with a thin layer of PDMS. The PDMS was diluted by the addition of hexane (1:1) and was coated onto the glass slide using a spin-coater. The coated glass was then placed into an oven at 65 °C to dry. Finally, the PDMS channel and glass were treated with oxygen plasma in a plasma cleaner for 3 min and immediately bonded with each other. After being plasma bonded, the device was placed into an oven at 70 °C for more than 20 h.

Synthesis and characterization of pNIPAM microgels: An aqueous solution containing monomer *N*-isopropylacrylamide (NIPAM), crosslinker *N,N'*-methylenebisacrylamide (BIS), and initiator ammonium persulfate (APS) (Sigma-Aldrich, Singapore) with a w/v value of 9.4%, 0.7%, and 0.64%, respectively, was injected into the right channel (Figure S1) at a rate of 12 µl/min using a syringe pump (Parkland Scientific Lab & Research Equipment, Singapore). The left channel of the Y-junction was injected with an aqueous solution of the PPy nanoparticles (250 µg/ml) at a rate of 2 µl/min. For preparation of the pNIPAM microgels without PPy nanoparticles, the PPy nanoparticle solution for the left channel was replaced with pure water. The continuous phase was fluorocarbon oil (HFE 7500, 3M Novec Engineered Fluids) containing 2% (w/w) perfluorinated polyethers–polyethyleneglycol block copolymer (PFPE–PEG) surfactant² and 7% (v/v) TEMED as the accelerator. TEMED could dissolve in both the aqueous and oil phases. It diffused from the oil phase into the aqueous droplets to initiate a redox reaction that polymerized the NIPAM. After the NIPAM solidified, the composite microgels were separated from the oil phase by centrifugation at 4000×g for 5 min. Because of the higher density of the HFE7500 oil (1614 kg/m³), the microgels were collected in the upper portion of the centrifuge tubes. The collected composite microgels were then washed with IPA and water. The washed microgels were maintained in water for 1 day, during which time the water was frequently changed to remove the residual IPA.³

The composite microgels suspended in water were placed onto a slide, which was placed on a microscope equipped with a NIR laser to examine the response behavior of the microgels to the NIR laser. The sizes of the microgels before and after being irradiated with the laser were recorded. To test the site-specific controllability of the microgels irradiated by NIR light at different locations, the composite microgels were fixed and then irradiated with the NIR laser at different positions. FITC-albumin ($M_w = 66$ kDa, Sigma-Aldrich, Singapore) was used as a model compound to characterize the NIR-laser-triggered release profile of the composite microgels. Four milligrams of FITC-albumin was dissolved in 1 ml of 10 mM pH 7.0 Tris buffer, into which the same amounts of pNIPAM microgels with or without PPy nanoparticles (obtained from 0.2 ml of the pre-gel solution) were added. The entire suspension was incubated at 4 °C for 48 h. Subsequently, the microgels were separated by centrifugation and washed with water to remove the unloaded FITC-albumin. These FITC-albumin-loaded microgels were dispersed in 1 ml of H₂O and irradiated with the NIR laser. A 0.4 ml aliquot of the supernatant was removed for the fluorescence spectroscopy analysis, and equivalent amounts of fresh H₂O were added at designated time intervals. The concentration of the released FITC-albumin was analyzed using excitation light with a wavelength of 490 nm and emission light with a wavelength of 520 nm.

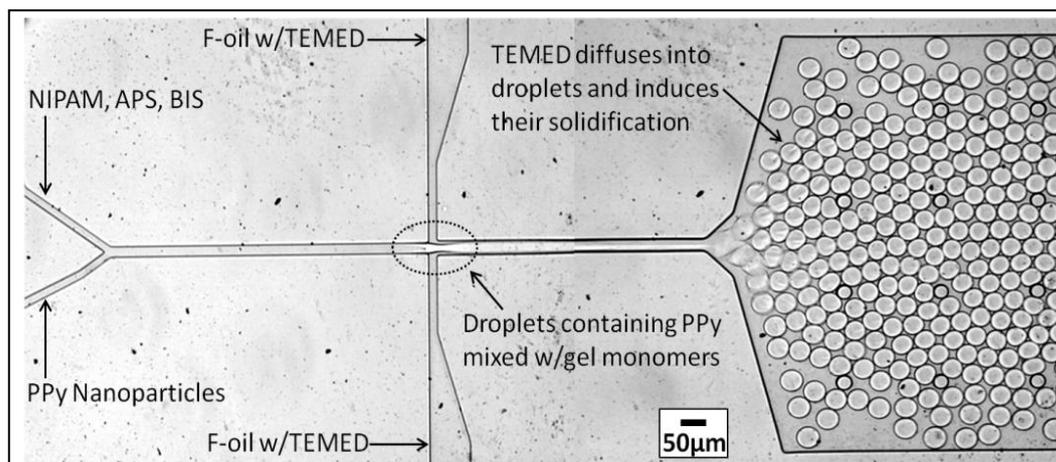


Fig.S2: Y-shaped droplet microfluidic device for forming the pre-gel droplets and their solidification.

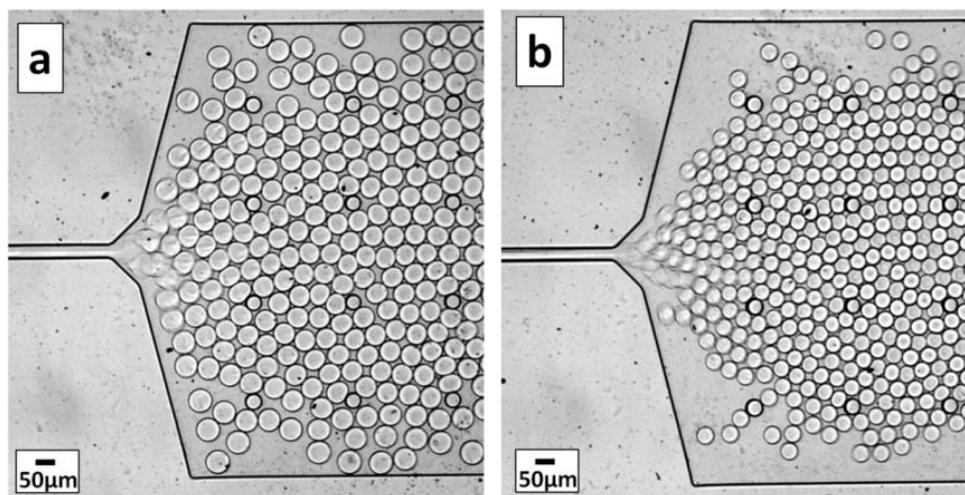


Fig. S3: Through tuning of the flow rate, microgels with different sizes were obtained: (a) pNIPAM composite microgels produced with an oil phase flow rate of 12 $\mu\text{l/ml}$; (b) pNIPAM composite microgels produced with an oil phase flow rate of 25 $\mu\text{l/ml}$.

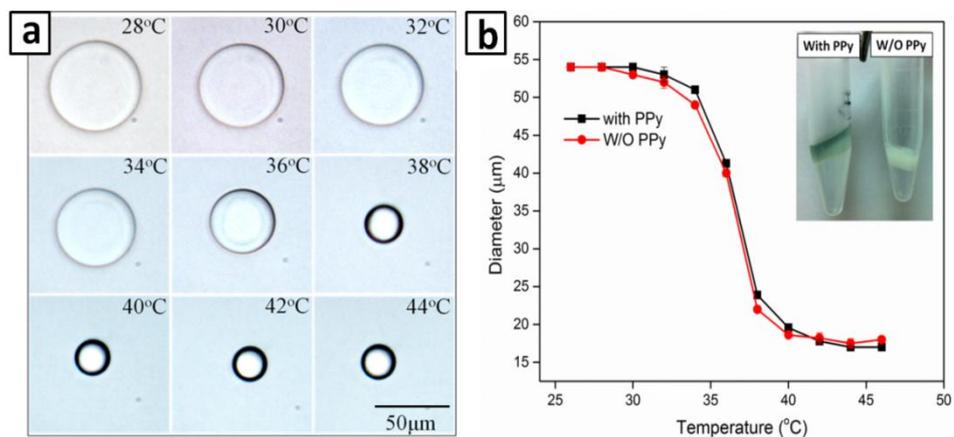


Fig. S4: (a) A series of optical microscopy images showing the size-reduction process of the composite pNIPAM microgels as the temperature increases, where the microgels are maintained for 5 min at each temperature. (b) Size changes of the pNIPAM microgels with and without PPy nanoparticles at different temperatures; the inset indicates the color difference of the pure pNIPAM microgels (W/O PPy) and the composite pNIPAM microgels (With PPy).

Reference

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