Electronic Supplementary Information
for

Janus molecularly imprinted polymer particles

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1. Materials

Methacrylic acid (MAA, 98.5%) was purchased from ACROS (Geel, Belgium). Azobisisobutyronitrile (AIBN, 98%) was purchased from Merck (Darmstadt, Germany). Allylamine (98%) and divinylbenzene (DVB, technical grade, 80%, mixture of isomers) were purchased from Sigma-Aldrich (Steinheim, Germany). *N*-isopropylacrylamide (NIPA) and *N,N'*-methylene-bis-acrylamide (MBAAm) were purchased from Monomer-Polymer Laboratories (Windham, USA). Acrylamide and (*R,S*)-propranolol hydrochloride (99%) were supplied by Fluka (Dorset, UK). Atenolol (98%) was purchased from Sigma-Aldrich (Gillingham, UK). [^{3}H]-(*S*)-propranolol (specific activity 555 GBq mmol^{-1}, 66.7 μM in ethanol solution) was purchased from NEN Life Science Products, Inc. (Boston, MA). The scintillation liquid Ecoscint A was obtained from National Diagnostics (Atlanta, GA). To remove the polymerization inhibitor, DVB was passed through an aluminum oxide column. AIBN was recrystallized from methanol before use. Other solvents were of analytical reagent grade and were used without further purification.

2. Syntheses of MIP-core and MIP-NH_2 microspheres

Molecularly imprinted microspheres were synthesized using precipitation polymerization described by Yoshimatsu et al.[1] Briefly, 0.53 mmol of (*R,S*)-propranolol was dissolved in 40 mL of acetonitrile in a borosilicate glass tube equipped with a screw cap. The functional monomer (MAA, 1.31 mmol), the crosslinker (DVB, 5.25 mmol) and the initiator (AIBN, 28 mg) were added into the tube. The solution was purged with a gentle flow of N_2 for 5 min. The glass tube was fixed horizontally in a Stovall HO-10 Hybridization Oven (Greensboro, NC, USA). Polymerization was carried out at 60 ℃ for 24 h with a rotation speed of 20 rpm. After polymerization, the particles were separated from the solution by centrifugation. To extract the templates, the particles were washed using a mixture solvent (methanol containing 10% acetic acid). When no template could be detected from the washing solvent by spectrometric measurement, the MIP-core particles were washed with acetonitrile and dried in a vacuum chamber. As reference polymers, non-imprinted polymer (NIP-core) particles were also prepared under an identical condition except that no template was added during the synthesis.

It is noted that, to make specific and rigid cavities, the cross-linkers were 80% of the total monomers when we synthesized the MIP-core particles. However, the cross-linkers were only 6% of the total monomers when we introduced a hydrophilic shell on the MIP-core particles. In previous works, the

grafting of a polymer layer onto MIP-core with low crosslinking had been proved to have no effects on the template migration and the MIP-core binding ability.[2]

To graft amino groups on the MIP-core (or NIP-core) particles, 40 mL of acetonitrile, 188 μL of allylamine, 566 mg of NIPA, 77.2 mg of MBAAm, 24 mg of AIBN, and 1000 mg of the MIP-core (or NIP-core) particles were added into a borosilicate glass tube and sonicated for 3 min. The solution was purged with a gentle flow of N_2 for 5 min. The glass tube was fixed horizontally in a Stovall HO-10 Hybridization Oven. Polymerization was carried out at 60 ℃ for 48 h with a rotation speed of 20 rpm. After polymerization, the MIP-NH_2 (or NIP-NH_2) particles with hydrophilic shell were separated from the mixture by centrifugation. The MIP-NH_2 (or NIP-NH_2) particles were washed with methanol and acetone, and dried in a vacuum chamber.

3. Synthesis of Janus MIP particles

20 mg of MIP-NH_2 (or NIP-NH_2) particles and 1 mL of acetonitrile were added into a borosilicate glass tube equipped with a screw cap. After a sonication for 2 min, 2 mL of water and 200 μL of NaOH (3 mol L^{-1}) were added into the borosilicate glass tube. In this way, the water phase containing solid particles for the Pickering emulsion was obtained. To synthesize a stable Pickering emulsion, 1.5 mL of molten wax was selected as oil phase. After mixing the water phase containing solid particles and oil phase, the borosilicate glass tube was then inserted into a water bath pre-set to 80 ℃. When the wax was completely melt, the hot mixture was shaken vigorously for ~ 1 min by hand to obtain a stable Pickering emulsion. After cooling down to room temperature, the polymer particles in wax colloidosomes were obtained. The colloidosomes containing MIP-NH_2 (or NIP-NH_2) particles were gently washed with water (until the washing solution showed a pH value of 7), and dried in a vacuum chamber.

To fabricate the Janus MIP (or NIP) particles, 1 mL of $AgNO_3$ (2 mg mL^{-1}) solution and 200 mg of wax colloidosomes were added into 9 mL of water. After an agitation for 2 h, 5 mL of $NaBH_4$ solution (2 mg mL^{-1}) was added to the above mixture dropwise. The suspended mixture immediately turned yellow indicating the formation of the Ag nanoparticles. The reaction system was rocked for 5 h at room temperature. The colloidosomes were washed with water for three times. After washing with methanol, the colloidosomes were dried in a vacuum chamber. The wax of the colloidosomes was dissolved using chloroform. The Janus particles were separated by centrifugation and were washed with methanol and dried in a vacuum chamber.

4. Characterization

4.1 FT-IR analysis

To confirm the synthesis of Janus MIP particles, the surface groups of the particles were studied by FT-IR analysis using a Perkin-Elmer FTIR instrument (Perkin-Elmer Instruments). All spectra were recorded at 25 °C in the 4000-375 cm^{-1} region with a resolution of 4 cm^{-1} using 32 scans. The FT-IR spectra of the MIP-core, MIP-NH_2, and the Janus MIP particles are presented in Fig. S1. In comparison with MIP-core

particles, the MIP-NH_2 particles containing a NIPA-allylamine-MBAAm copolymer shell showed several obvious changes: i) the amide I band (1650 cm^{-1}, C=O stretching), amide II band (1550 cm^{-1}, N–H stretching) and the amino group (3340 cm^{-1}, N–H asymmetric stretching)[3] were clearly observed; ii) the intensity ratio between the presence bands at 1353 cm^{-1} and 1367 cm^{-1} (which are associated with the deformation mode of two methyl groups on isopropyl of NIPAM[4]) was increased; iii) a new peak was emerged at 3175 cm^{-1}, which is assigned to the C–H stretching vibration. These changes indicate that the copolymer had been successfully coated onto the MIP-core particles. When MIP-NH_2 particles were deposited with Ag nanoparticle, three new peaks were found on the Janus MIP particles. These three peaks at around 1218 cm^{-1}, 1360 cm^{-1} and 1711 cm^{-1} are attributed to the C–O stretching, deformation vibration of CH_3, and C=O stretching, respectively.[5] Simultaneously, the intensity of amino group at 3340 cm^{-1} decreased on the Janus MIP particles. These indicate that the Ag nanoparticles were tightly coated onto MIP-NH_2 particles through hydrogen bond.

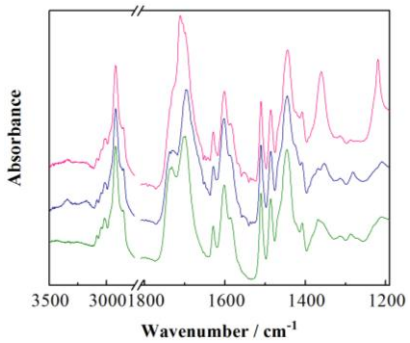

Fig. S1 FT-IR spectra of the MIP-core (green), MIP-NH_2 (blue) and Janus MIP (pink) particles.

4.2 UV-vis analysis

To further verify the coating of Ag nanoparticles, the UV-vis spectra were recorded for the MIP-NH_2 particles and the Janus MIP particles, as shown in Fig. S2a. The UV–vis analysis of the particles was performed using a Beckman Coulter DU 800 spectrophotometer. Typically, 1 mg of particles were dispersed into 500 μL of acetonitrile. After addition of 1.5 mL of water, the suspension was measured using the spectrophotometer.It can be seen that the Janus MIP particles displayed an obvious surface plasmon resonance absorption band (which is centered at 409 nm), further indicating that the MIP-NH_2 particles were perfect carriers for the formation of Ag nanoparticles.[6]

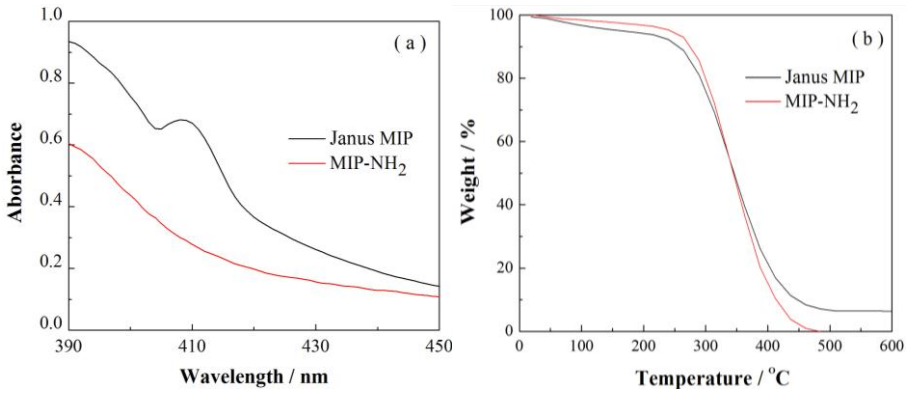

Fig. S2 (a) UV-vis spectra and (b) TGA curves of the MIP-NH_2 particles and the Janus MIP particles.

4.3 Thermogravimetric analysis

Thermogravimetric analysis (TGA) of the particles was conducted through thermogravimetric measurement using a Q500 Thermogravimetric Analyzer (TA Instruments, New Castle, USA). Samples were heated from 25 °C to 600 °C in air with a heating rate of 10 °C min^{-1}. In order to evaluate the loading amount of Ag nanoparticles within the Janus MIP particles, TGA measurements were performed for both the MIP-NH_2 particles and the Janus MIP particles. Based on the analysis of Fig. S2b, the weight proportion of Ag nanoparticles on the Janus particles was determined to be 8.6%.

4.4 SEM analysis

The surface morphology of the particles was observed using a Thermal Field Emission scanning electron microscope (SEM LEO 1560, Zeiss, Oberkochen, Germany). Fig. S3a and Fig. S3b are the SEM images of the MIP-NH_2 particles. From these figures, it is seen that the MIP-NH_2 particles were monodisperse with a size of 2.0 μm.

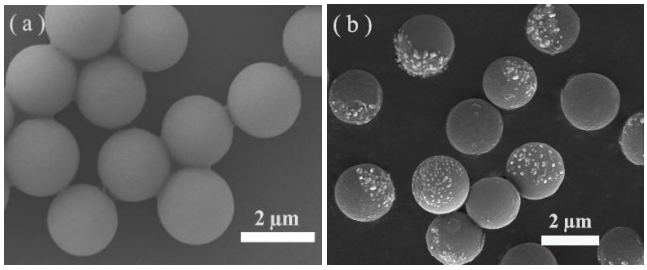

Fig. S3 SEM images of MIP-NH_2 (a) and Janus MIP (b) particles.

5. Radioligand binding analysis

Polymer microspheres and [^{3}H]-(*S*)-propranolol (246 fmol) were added into 1 mL of 25 mM citrate buffer (pH 6.0)/acetonitrile (50/50, v/v). For displacement experiments, an excess amount of competing compound (propranolol or atenolol) was also added. The mixture was gently stirred at room temperature

for 12 h. After centrifugation, 500 μL of the supernatant was collected and mixed with 10 mL of scintillation liquid (Ecoscint A). The radioactivity of the samples was measured using a Tri-Carb 2800TR liquid scintillation analyzer (PerkinElmer). The amount of [^{3}H]-(*S*)-propranolol bound to the polymer particles was calculated by subtracting the amount of free radioligand from the total radioligand added.

6. Path of Janus MIP particle in H_2O_2 and UV light

In order to observe the movement of the Janus MIP particle, experiments were performed in H_2O_2 with or without UV light. The suspension of the Janus MIP particle in 2.5% H_2O_2 was prepared by mixing 300 μL of particle suspension (10 μg mL^{-1}) with 50 μL of 30% H_2O_2 and 250 μL of water. The movement of the Janus MIP particle in H_2O_2 and UV light was recorded under a Pro AM413T5 500X Digital Microscope.

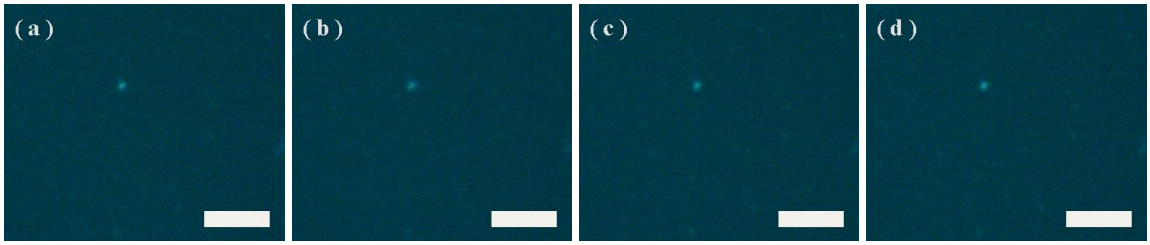

Fig. S4 Real-time optical microscopy images of a single MIP-NH_2 particle in 2.5% H_2O_2 with UV light, showing the trajectory at: (a) t=0 s, (b) t=2 s, (c) t=4 s and (d) t=6 s. Scale bar=10 μm.

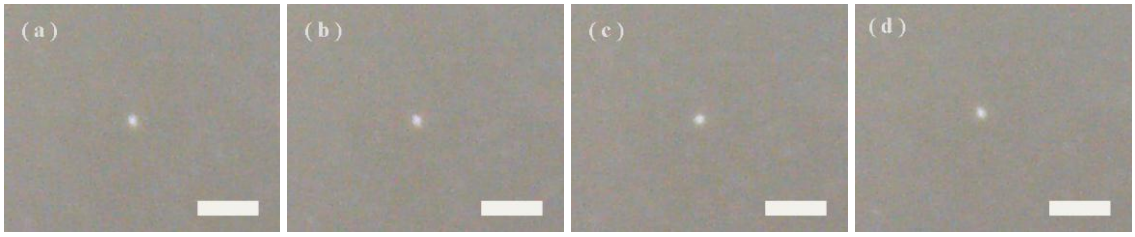

Fig. S5 Real-time optical microscopy images of a single Janus MIP particle in 2.5% H_2O_2 without UV light, showing the trajectory at: (a) t=0 s, (b) t=2 s, (c) t=4 s and (d) t=6 s. Scale bar=10 μm.

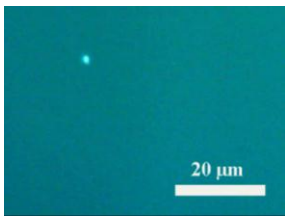

Fig. S6 Real-time optical microscopy images of a Janus MIP particle in 2.5% H_2O_2 with UV light (254 nm), showing the trajectory at t=6 s. Scale bar=10 μm.

Janus Uv.rmvb

Video S1. Path of a single Janus MIP particle in 2.5% H_2O_2 solution. 0-30s, without UV light; 31-40s, without UV light; 41-70s, with UV light.

7. Controlled drug release from the Janus MIP particles

[^{3}H]-(*S*)-propranolol was selected as probe to study the controlled drug release feature from the polymer particles. The loading procedure was conducted as follows: 2 mg of polymer microspheres and [^{3}H]-(*S*)-propranolol (246 fmol) were added into 1 mL of 25 mM citrate buffer (pH 6.0)/acetonitrile (50/50, v/v). The mixture was gently stirred at room temperature for 12 h. The solution containing the remained propranolol was removed by centrifugation.

1 mL of water containing 5% acetic acid and 2.5% H_2O_2 was added into the polymer particles (2 mg) with or without UV light (254 nm). The solution was sampled at different time. After centrifugation, 500 μL of the supernatant was collected and mixed with 10 mL of scintillation liquid (Ecoscint A). The radioactivity of the samples was measured using a Tri-Carb 2800TR liquid scintillation analyzer (PerkinElmer).

8. References

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