Conductive, physiologically responsive hydrogels
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Supporting Information

Experimental

Materials

Dimethylaminoethyl methacrylate (DMAEMA) and 2-hydroxyethyl methacrylate (HEMA) were purchased from Acros (Morris Plains, NJ, USA). Tetraethylene glycol dimethacrylate (TEGDMA) and hexylamine were obtained from Fluka (St. Louis, MO, USA). Monobasic and dibasic sodium phosphates, 2,2-dimethoxy-2-phenylacetophenone (DMPAP), KAuCl₄, NaBH₄, carbon tetrachloride, diethyl ether, hexane, 2,2’-azobisisobutyronitrile (AIBN), sodium bisulfate, dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF) were purchased from Sigma (St. Louis, MO, USA). For the synthesis of dT-DMAEMA, 1,4-diisopropenylbenzene was purchased from Tokyo Chemical Industry (TCI Co., LTD., Tokyo, Japan). All materials were used without further purification. Deionized water (18.2 MΩ) was obtained from a Milli-Q purification system (Millipore Corp., Billerica, MA, USA).

Synthesis of dT-DMAEMA

To synthesize dT-DMAEMA, a bifunctional RAFT agent 1,4-bis(2-(thiobenzoylthio)prop-2-yl)benzene was synthesized. Briefly, dithiobenzoic acid¹ (6.1 g) and 1,4-diisopropenylbenzene (3.0 g) in carbon tetrachloride (50 mL) was heated at 75°C
for 20 h as described previously. The solvent was removed under vacuum and a pink solid was obtained after filtration with 1:2 volume ratio of diethyl ether and hexane. Then, DMAEMA (1 g), AIBN, and 1,4-bis(2-(thiobenzoylthio)prop-2-yl)benzene were added into a 20 mL glass vial in an oil bath at 60°C for 48 h for RAFT polymerization. The obtained α,ω-dithioester-terminated DMAEMA was precipitated by hexane and filtered. Aqueous sodium bisulfate (0.5 mL) was added to α,ω-dithioester-terminated DMAEMA (1 g) in 10 mL THF and 0.5 mL hexylamine. The reaction mixture was stirred for 5 h under a nitrogen atmosphere. The mixture was washed in excess hexane and then filtered. One milliliter of DMSO was added to the product in deionized water and stirred for two weeks. Finally, oxidized dT-DMAEMA was obtained by removing water and precipitating in excess hexane.

Synthesis of Au nanoparticles within dT-DMAEMA/HEMA hydrogels

Different molar ratios of dT-DMAEMA and HEMA (10/90, 20/80, 30/70, 40/60, and 50/50) were used for the preparation of hydrogels crosslinked by either 3, 6, and 9 mol% TEGDMA. A dT-DMAEMA/HEMA solution was prepared at the desired molar ratio and mixed with 1:1 (mol: mol) ethylene glycol:deionized water. The molar ratio between the monomers and the solvent was 1. A predetermined mol% of TEGDMA as a crosslinker was added to the mixing solution. Three mol% DMPAP, a photoinitiator, was also added. The solution was degassed by bubbling with nitrogen gas and was put into a teflon mold immediately. UV light was allowed to pass through the mold for 90 s for photopolymerization. After polymerization, dT-DMAEMA/HEMA hydrogels were washed with deionized water in order to remove remaining monomers. dT-
DMAEMA/HEMA hydrogels were swollen in pH 5.5 phosphate buffer for 4 h and washed again with deionized water. To synthesize Au nanoparticles, dT-DMAEMA/HEMA hydrogels were transferred into 20 mL 5 mM KAuCl₄ overnight. Hydrogels were then placed into 20 mL 50 mM NaBH₄. Colloidal Au nanoparticles were obtained by reduction of Au salt at room temperature for 20 min. Finally, Au nanoparticle embedded dT-DMAEMA/HEMA hydrogels were washed with deionized water. Hydrogel dimensions were measured using a digital caliper (VWR, West Chester, PA, USA).

Equilibrium swelling studies

Equilibrium swelling of the hydrogels was performed in a buffered medium (0.2 M sodium phosphate monobasic, 0.2 M sodium phosphate dibasic) of known pH, composition, and temperature. The pH of the buffer was adjusted using 0.1 M NaOH and 0.1 M HCl to achieve pH 5.5, 6.0, 6.5, 7.0, and 7.4. Hydrogels were placed into a scintillation vial containing 20 mL of buffer at room temperature. The swelling ratio of the hydrogels as a function of pH was calculated by measuring the mass of the hydrogels at 0, 1, 2, 3, and 4 h as follows:

$$\text{Swelling ratio} = \frac{M_s}{M_i}$$

where $M_s$ is the mass of the swollen hydrogel in buffer and $M_i$ is the mass of the initial hydrogel before swelling.⁴

Mechanical properties

The elastic moduli of 10/90, 20/80, 30/70, 40/60, and 50/50 (mol/mol) Au
impregnated dT-DMAEMA/HEMA hydrogels crosslinked with 3 mol% TEGDMA were measured. For comparison, hydrogels were also tested without Au synthesis. Tensile tests of each hydrogel (30 × 10 × 1.9 mm) were carried out on an Instron BioPuls 5543 (Instron, Norwood, MA, USA) using a 500 N loading cell. Hydrogels were strained to failure at a rate of 2 mm/min. The Young’s modulus was calculated from the initial 40% strain. Five hydrogel samples of each formulation were tested.

Conductivity

The conductivity of hydrogels (30 × 10 × 1.9 mm) and microfabricated hydrogels (square type, 400 × 400 × 240 μm) was measured using a Keithley four-point probe measurement system (Model 6221; Keithley Instruments, Inc., Cleveland, OH, USA). To reduce the error from the contact conductivity between the probe and hydrogel surface, three different edges were selected for measurements and the average conductivity was determined. Each measurement was performed in triplicate.

UV-Vis spectroscopy

Au impregnated dT-DMAEMA/HEMA hydrogels (15 × 10 × 0.3 mm) were placed in a 1 cm polystyrene cuvette with 2 mL of deionized water and examined with an UV-Vis spectrophotometer (SpectraMax Plus384; Molecular Devices Corp., Sunnyvale, CA, USA) over an absorption wavelength range of 300-700 nm with background correction using deionized water.

Thermogravimetric analysis
Thermogravimetric analysis (TGA) of Au impregnated dT-DMAEMA/HEMA gel was performed on a TGA Q 5000 analyzer (TA Instrument-Waters LLC., New Castle, DE, USA). The samples, which were approximately 40 mg, were scanned with a heating range of 20 °C min\(^{-1}\) from 20 to 600 °C under continuous argon flow.

References