Supplementary Information

A pH-Driven DNA Nanoswitch for Responsive Controlled Release

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I. Materials.

Tetraethoxysilane (TEOS, 28%), n-cetyltrimethylammonium bromide (CTAB, ≥99%), ammonium hydroxide solution (25%), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC, 99%), N-Hydroxysuccinimide (NHS, 98%), 3-Aminopropyltriethoxy-silane (APTES, 99%), succinic anhydride (99%), sodium citrate tribasic dihydrate, tannic acid, and Rhodamine B were purchased from Sigma Company. Hydrogen tetrachloroaurate(Ⅲ) was purchased from Jinke reagent company, China. All DNAs were purchased from TaKaRa Biotech (Dalian, China) and used as received. All buffers were prepared with ultra-pure MilliQ water (resistance > 18 MΩ cm^{-1}).

DNA Sequences

1: 5'- (H_2NC_3)-ATTGCAGGGTTAGTG -3'

2: 5'- T CCC TAA CCC TAA CCC TAA CCC TGCAAT- (C_6SH)-3'

1': 5'- (Dabcyl)-ATTGCAGGGTTAGTG -3'

2': 5'- T CCC TAA CCC TAA CCC TAA CCC TGCAAT-(Rhodamine green)-3'

II. General Methods.

Scanning electron microscope (SEM) was performed with a JEOL-6700FE instrument. Transmission electron microscopy (TEM) images were obtained using a Philips CM 200 kV electron microscope. Powder X-ray diffraction (XRD) patterns were collected using a Rigaku D/max 2500 equipped with Cu Kα radiation. UV-Vis spectra were collected using a Hitachi U-4100

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spectrophotometer. Fourier transform infrared (FT-IR) spectra were taken on a Bruker-EQUINOX55 spectrometer. All spectra were taken with an instrument resolution of 4 cm^{-1}. All fluorescence spectra were recorded on a Hitachi F-4500 FL Spectrophotometer in PBS buffer. N_2 adsorption-desorption isotherms were obtained at 77 K on a Micromeritics ASAP2020 automated sorption analyzer. The BET model was applied to evaluate the specific surface areas. Pore size and pore volume were determined from the adsorption data by BJH method. X-ray photoelectron spectroscopy (XPS) data were obtained with an ESCALab220i-XL electron spectrometer from VG Scientific using 300 W Al Kα radiation. The base pressure was about 3×10^{-9} mbar. The binding energies were referenced to the C1s line at 284.6 eV from adventitious carbon.

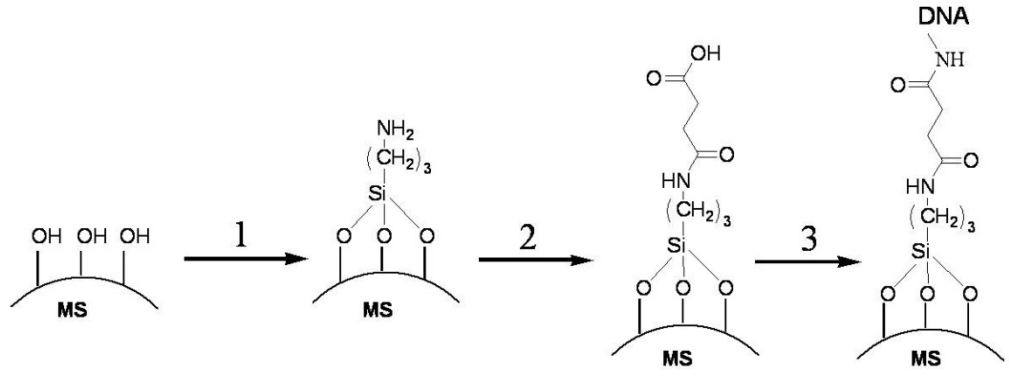
III. Preparation and Characterization of the Controlled Release System

Gold colloids with mean diameters of 3.6 nm were synthesized by the citrate/tannic acid method. [S1] DNA-AuNP conjugates were prepared by mixing AuNPs with the modified ssDNA 2 in 1:3 molar ratio and incubated for 12 h in PBS buffer (20 mM, 50 mM NaCl, pH 7.2). The sample was then centrifuged to remove the unattached free DNAs. The modified AuNP-DNA conjugates were further mixed with MS-DNA 1 to create the controlled release system.

Porous silica particle was prepared according to a modified literature procedure.[S2] In a typical synthesis, 0.40 g of CTAB was mixed with 17.0 mL water, 7.0 mL ethanol and 0.7 mL ammonium hydroxide under stirring for 30 min. To this solution, 2.0 g of tetraethoxysilane (TEOS) was added dropwise. The whole mixture was stirred at room temperature for 12 h and the product was repeatedly washed and separated by centrifugation. Finally, the obtained nanoparticles were washed with ethanol, and dried in the oven (60 ºC) overnight. The mean diameter of the nanoparticles was about 350 nm based on SEM observations. Amino-modification of the silica surface was performed by suspending 200 mg nanoparticles in a solution of 3-aminopropyltriethoxysilane (1 mM) in 20 mL dry toluene for 30 min.[5b] Toluene was get rid off by a rotary evaporator at 60 °C for 1 h. 90 mg of amine-

functionalized MS was added into 50 mL dimethyl sulfoxide (DMSO) solution containing succinic anhydride (60 mg) and triethylamine (60 mg) and stirred at 40 °C for 48 h. The particle was recovered by centrifugation, washed with ethanol and dried under vacuum to obtain MS-COOH. 50 mg of MS-COOH was well suspended in 30 mL H_2O containing 50 mg 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and 20 mg N-Hydroxysuccinimide (NHS), and stirred at room temperature for 8h to get NHS ester. The amine-modified oligonucleotides with a solution concentration of 3.3 μM were then added to react overnight to get the DNA modified MS. [S3]

The pores of DNA 1-modified MS were diffusion-filled with cargo molecules by immersing the articles in a 0.6 mM solution for 6 h. The loaded particles were then dispersed in the PBS buffer (pH = 7.2) and the AuNP-DNA 2 conjugates were added to cap the openings of pores on the MS particles. The excess AuNPs were removed by centrifugation. The controlled release experiments were performed by sequential adjustment of pH between 8.0 and 5.0 through alternating additions of the required amount of 1 M HCl or 1 M NaOH. Luminescence spectroscopy was used to monitor the amount of released cargo molecules in aqueous solution.



1. 3-aminopropyltriethoxysilane; 2. succinic anhydride and triethylamine;

3. N-hydroxysuccinimide (NHS), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide-HCl (EDC), and DNA b

MS : Mesoporous Silica

Scheme S1. Synthesis of DNA modified MS

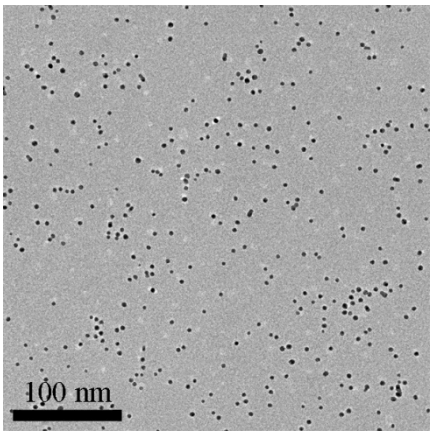


Fig. S1. Representative TEM photograph of AuNPs.

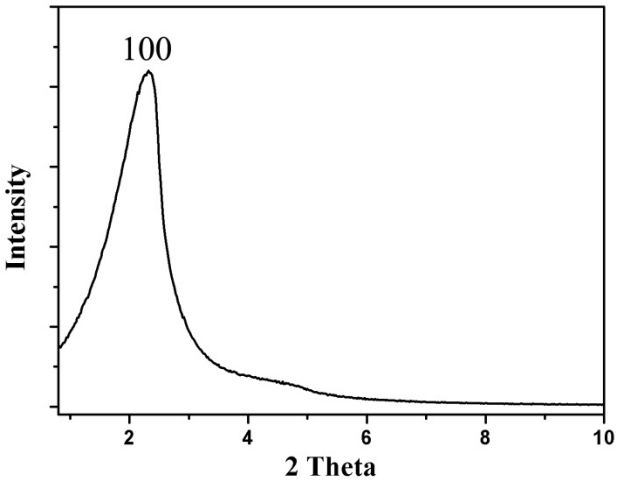


Fig. S2. XRD pattern of MS as-synthesized, which confirms the presence of a 2d-hexagonal mesostructure with about 3.8 nm lattice spacing.

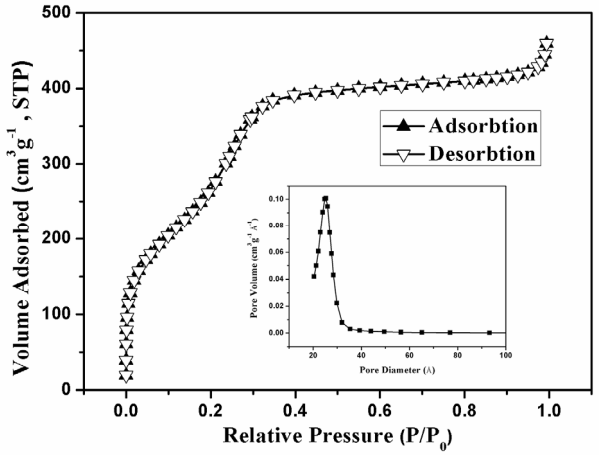


Fig. S3. Nitrogen adsorption-desorption isotherms for the MS material. Inset: Pore size distribution of MS material.

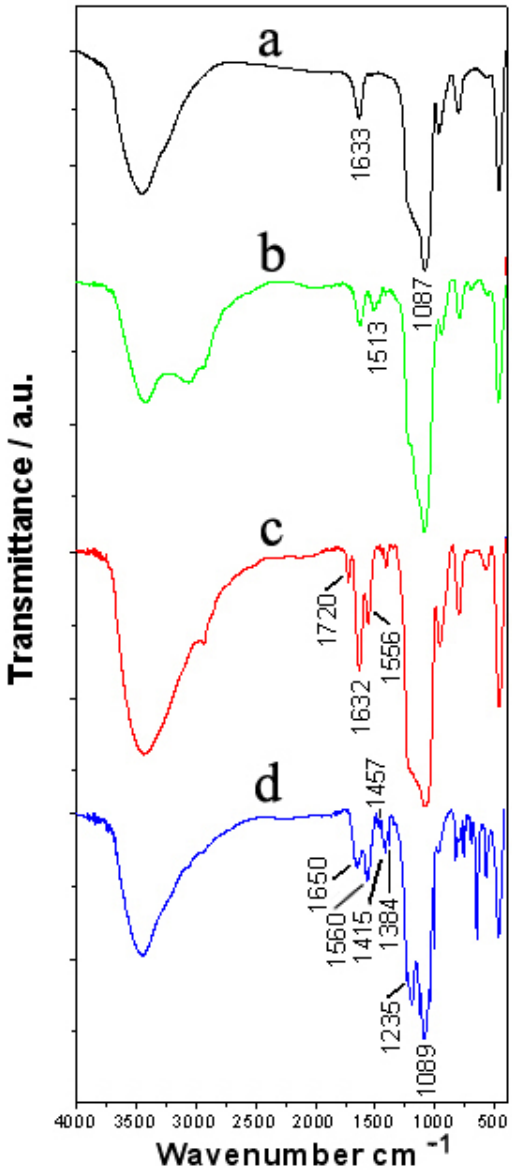


Fig. S4. FT-IR spectra of monolayers formed on MS surface after each modification step.

Fig. S4 compares the FT-IR spectra of monolayer formed on MS surface after each modification step. In the spectrum of MS materials (curve a), the dominant bands are those due to the silica matrix (1087 and 803 cm^{-1}) and those related to the vibrations of water molecules (1633 cm^{-1}).[5g] For the amine-terminated MS (MS-NH_2) (curve b), the presence of amine groups was confirmed with the N-H vibrations at 1513 cm^{-1}. The spectrum of MS-COOH (curve c) exhibits absorption bands in the regions of amide I (1632 cm^{-1}), amide II (1556 cm^{-1}), and at 1720 cm^{-1}, which arise from the carbonyl stretching modes.[S4] In the case of the DNA-modified MS (MS-DNA), bands related to the DNA

moieties can be observed.[S5] As seen from curve d in Figure S6, two strong absorption bands, assigned to the phosphate vibrations (antisymmetric PO_2^- stretching vibrations at 1235 cm^{-1} and symmetric stretching vibrations at 1089 cm^{-1}) can been clearly identified on the spectrum, which are the specific fingerprints of the DNA. The new features at 1457, 1415 and 1384 cm^{-1} can be attributed to sugar vibrations. The bands at 1650 and 1560 cm^{-1} related to amide I and amide II are clearly observed.[S5, S6a] The drop in relative intensity of the band I and II indicates that there exist substantial amine groups on the functionalized MS particles.

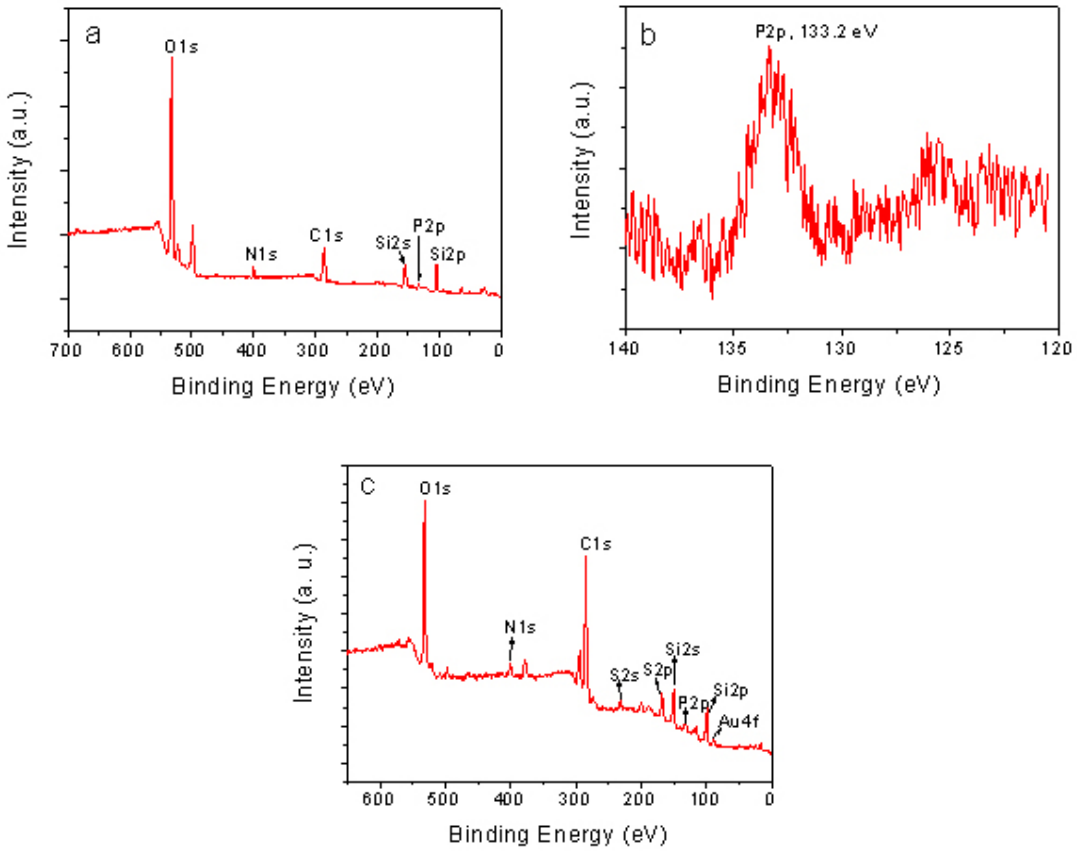


Fig. S5. (a) XPS survey spectra of the DNA monolayer attached to MS. (b) High-resolution XPS spectrum of the P_{2p} region. (c) XPS survey spectra of the DNA-AuNP capped MS.

The modified MS surface was examined by XPS to determine the surface characteristics. Figure S5 shows a representative XPS survey spectrum of as-prepared DNA-modified MS and the AuNP-capped MS. As shown in Figure S5 (a), (b), in addition to the substrate Si signal (Si_{2p} (99.0 eV), O_{1s} (532.2

eV)), the presence of C_{1s} (284.8 eV), N_{1s} (401.6 eV), and P_{2p} (133.2 eV) signals indicates that a DNA monolayer is formed on the MS surface. In Figure S5 (c), the XPS survey spectrum of acid- treated MS shows a peak at 88.2 eV, indicating that the AuNPs attched on the DNA 2 are capped on the pore openings on the MS surface through the hybrizition of DNA at the acidic conditions.[S6]

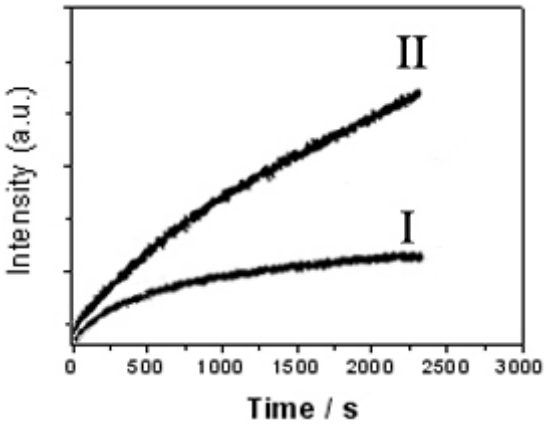


Fig. S6. A control experiment to prove the effect of AuNPs in the controlled release system. The release behavior of DNA nanomachine at pH = 8.0 (curve I) and 5.0 (curve II). Here, the same sequences as DNA 1 and 2 have been used, but no AuNPs have been attached to the ends of DNA 2.

A control experiment was performed to prove the effect of AuNPs in the controlled release system. As shown in Figure S6, when no AuNPs are attached at the end of DNA 2, the DNA nanomachine-modified MS has a slow release rate at pH = 8.0 (curve I) and a fast release rate at pH 5.0.

The UV-Vis spectra changes of the controlled nanoswitch system were measured. As shown in Figure S7, when the nanoswitch system at pH = 5.0, the UV-Vis spectrum shows a clear AuNP absorption peak at about 515 nm (curve I), but when the pH is changed to 8.0, the absorption intensity greatly reduces and there is a red-shift of the absorption peak (curve II). This indicates that the AuNPs dispersed in the solution are adsorbed on the surface of MS particles because of the hybridization effect and the AuNPs are in a state of aggregation.

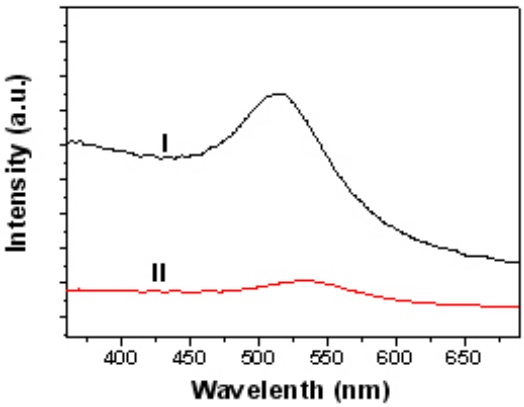


Fig. S7. UV-Vis spectra changes of the controlled nanoswitch system. The UV-Vis spectrum of DNA nanomachine at pH = 5.0 (curve I) and 8.0 (curve II). In this experiment, no cargo molecules were loaded in the pore of MS particles.

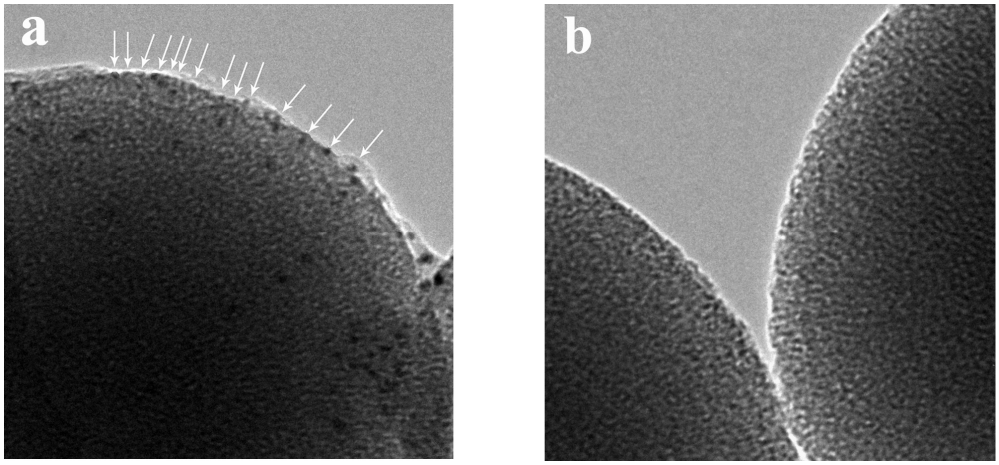


Fig. S8. TEM images of the controlled nanoswitch system at pH = 8.0 (a) and pH = 5.0 (b). At neutral or alkalic, the AuNPs were adsorbed on the surface of MS particles (indicted by small arrows in Fig. S8 (a)) because of the hybridization effect. When the pH was changed to 5.0, the AuNPs departed from the surface of MS and dispersed in the solution. In such condition, no AuNPs were observed on the surface of MS (Fig. S8 b).

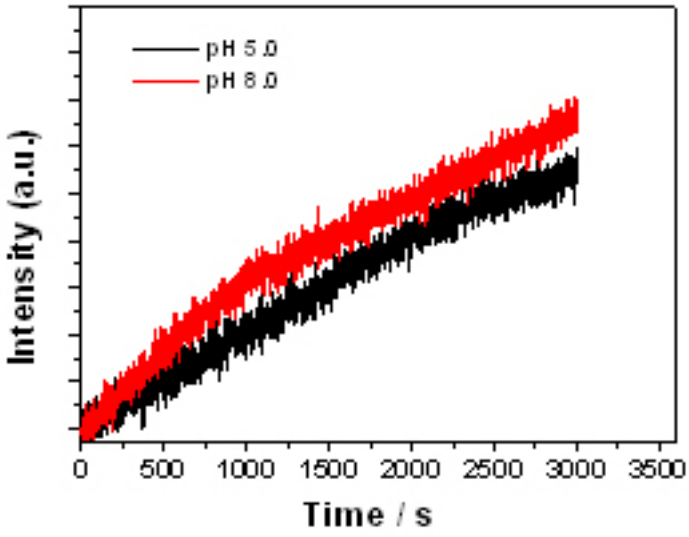


Fig. S9. A control experiment to prove the trapping and releasing property of MS particles without the AuNPs caps. The release behavior of DNA nanomachine at pH = 8.0 (red curve) and 5.0 (black curve). Here, no DNA sequence has been attached onto the surfaces of MS particles. This result can help to exclude the possibility that pH itself influence the encapsulating property of MS.

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