Supporting Information

pH- and Ligand-Induced Release of Loads from DNA-Acrylamide Hydrogel Microcapsules

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‡These authors contributed equally to this work.
Table S1. The nucleic acid sequences used in this study.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sequence (5’→3’)</th>
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<tbody>
<tr>
<td>1a</td>
<td>/5AmMC6/TTTTTTAGCTGACCTGGGGGAG</td>
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<tr>
<td>1b</td>
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<td>2</td>
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Determination of Molecular Weight and Ratio of Acrylamide/Acrydite-Nucleic Acids

Figure S1. Calibration curve of the diffusion coefficients against known molecular weights of poly(acrylic acid) (30,000, 450,000, and 1,250,000 Da). The linear equation is $y = -0.6751x - 7.325$ ($R^2 = 0.9835$). The diffusion coefficient is derived from the diffusion-ordered spectroscopy (DOSY) spectrum. Circles represent the known polymers utilized to form standard line, and squares represent the polymers measured for experimental studies.

Figure S2. Determination of the ratio between nucleic acid units and acrylamide monomer units on the hairpin (2) conjugated copolymer $P_A$. (A) Absorbance spectra corresponding to various concentrations of polyacrylamide (5000 kDa, ca. 70343 monomers) in the presence of constant concentration of the acrydite-modified nucleic acid (2), 1.6 μM: (a) 2.3, (b) 4.5, (c) 8.9, (d) 17.8, and (e) 35.6 nM. (B) Calibration curve between the molar ratio of acrylamide monomer/(2) and the ratio of absorbance
at wavelength of 200 nm and 260 nm.

**Figure S3.** Determination of the ratio between nucleic acid units and acrylamide monomer units on the nucleic acid (3) conjugated copolymer P_B or P_D. (A) Absorbance spectra corresponding to various concentrations of polyacrylamide (5000 kDa, ca. 70343 monomers) in the presence of constant concentration of the acrydite-modified nucleic acid (3), 5.6 µM: (a) 2.3, (b) 4.5, (c) 8.9, and (d) 17.8 nM. (B) Calibration curve between the molar ratio of acrylamide monomer/(3) and the ratio of absorbance at wavelength of 200 nm and 260 nm.

**Figure S4.** Determination of the ratio between nucleic acid units and acrylamide monomer units on the hairpin (5) conjugated copolymer P_C. (A) Absorbance spectra corresponding to various concentrations of polyacrylamide (5000 kDa, ca. 70343 monomers) in the presence of constant concentration of the acrydite-modified nucleic acid (5), 1.0 µM: (a) 2.3, (b) 4.5, (c) 8.9, and (d) 17.8 nM. (B) Calibration curve between the molar ratio of acrylamide monomer/(5) and the ratio of absorbance at wavelength of 200 nm and 260 nm.
Figure S5. Determination of the ratio between nucleic acid units and acrylamide monomer units on the hairpin (8) and tether (11) conjugated copolymer P_E. (A) Absorbance spectra corresponding to various concentrations of polyacrylamide (5000 kDa, ca. 70343 monomers) in the presence of constant concentration of the acrydite-modified nucleic acid (8), 0.75 μM and (11), 1.5 μM: (a) 4.5, (b) 8.9, (c) 17.9, and (d) 35.7 nM. (B) Calibration curve between the molar ratio of acrylamide monomer/(8)+(11) and the ratio of absorbance at wavelength of 200 nm and 260 nm.

Figure S6. Determination of the ratio between nucleic acid units and acrylamide monomer units on the hairpin (9) and tether (12) conjugated copolymer P_F. (A) Absorbance spectra corresponding to various concentrations of polyacrylamide (5000 kDa, ca. 70343 monomers) in the presence of constant concentration of the acrydite-modified nucleic acid (9), 0.75 μM and (12), 1.5 μM: (a) 4.5, (b) 8.9, (c) 17.9, and (d) 35.7 nM. (B) Calibration curve between the molar ratio of acrylamide monomer/(9)+(12) and the ratio of absorbance at wavelength of 200 nm and 260 nm.
Figure S7. (A) SEM images of uncoated TR-D-loaded CaCO$_3$ microparticles (panel I), cocaine aptamer-bridged hydrogel CaCO$_3$ microparticles (panel II), and TR-D-loaded cocaine-responsive hydrogel microcapsules after the dissolution of the CaCO$_3$ core (panel III). Scale bars, 2 $\mu$m (panels I and II) and 1 $\mu$m (panel III). (B) Confocal fluorescence microscopy images and bright-field microscopy images of cocaine aptamer-bridged hydrogel microparticles before (panel I) and after (panel II) the dissolution of the core. Scale bar is 10 $\mu$m.

Figure S8. (A) SEM images of uncoated DOX-D-loaded CaCO$_3$ microparticles (panel I), ATP aptamer-bridged hydrogel CaCO$_3$ microparticles (panel II), and DOX-D-loaded ATP-responsive hydrogel microcapsules after the dissolution of the CaCO$_3$ core (panel III). Scale bars, 2 $\mu$m (panels I and II) and 1 $\mu$m (panel III). (B) Confocal fluorescence microscopy images and bright-field microscopy images of ATP aptamer-bridged hydrogel microparticles before (panel I) and after (panel II) the dissolution of the core. Scale bar is 10 $\mu$m.
Figure S9. Calibration curves corresponding to (A) tetramethylrhodamine-modified dextran, TMR-D, (B) Texas Red-modified dextran, TR-D, and (C) doxorubicin, DOX. The fluorescence of DOX-D was measured after the acidification that allows for the cleavage of doxorubicin from the dextran.
Figure S10. The preparation of doxorubicin-conjugated dextran, DOX-D.
**Figure S11.** Confocal fluorescence microscopy images and bright-field microscopy images of i-motif-bridged hydrogel microparticles before (panel I) and after (panel II) the dissolution of the core, and subjecting the microcapsules to pH = 5.0 (panel III). Scale bar is 30 μm.

**Figure S12.** SEM images of uncoated DOX-D-loaded CaCO$_3$ microparticles (panel I), i-motif-bridged hydrogel CaCO$_3$ microparticles (panel II), and DOX-D-loaded pH-responsive hydrogel microcapsules after the dissolution of the CaCO$_3$ core (panel III). Scale bar is 2 μm.
Figure S13. Circular dichroism spectra corresponding to: (a) The pH-responsive acrylamide hydrogel at pH = 7.2. (b) The pH-responsive acrylamide hydrogel at pH = 5.0.

Figure S14. (A) Time-dependent release of TR-D from the cocaine-responsive hydrogel matrix in the absence of cocaine (curve a) and in the presence of 20 mM cocaine (curve b). (B) Schematic illustration of the preparation of the hydrogel membranes on a gold-coated surface and the separation of the hydrogel matrix by the cocaine-trigger. The Young’s module of the cocaine-responsive hydrogel corresponded to 123 ± 4 Pa. After treatment of the film with cocaine, 20 mM, the value of the Young’s module decreased to 44 ± 18 Pa.
Figure S15. (A) Time-dependent release of TMR-D from the pH-responsive hydrogel matrix subjecting to pH = 7.2 (curve a) and pH = 5.0 (curve b). (B) Schematic illustration of the preparation of the hydrogel membranes on a gold-coated surface and the separation of the hydrogel matrix by the pH-trigger.