Supporting Information

Engineering Cellular Degradation of Multilayered Capsules through Controlled Crosslinking

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Table S1. Crosslinker Amounts and Concentrations in Each Silica Particle Suspension

Sample	Amount of crosslinker for planar surfaces, mol	Concentration of crosslinker for planar surfaces, M	Amount of crosslinker for silica particle templates[a], mol	Concentration of crosslinker for silica particle templates, M
A	5.0×10^{-13}	5×10^{-10}	3.1×10^{-8}	2.1×10^{-5}
B	5.0×10^{-12}	5×10^{-9}	3.1×10^{-7}	2.1×10^{-4}
C	1.3×10^{-11}	1.3×10^{-8}	7.7×10^{-7}	5.1×10^{-4}
D	2.5×10^{-11}	2.5×10^{-8}	1.5×10^{-6}	1.0×10^{-3}

[a]The same amount of crosslinker per unit surface area as the planar films was calculated to achieve the same degree of crosslinking.

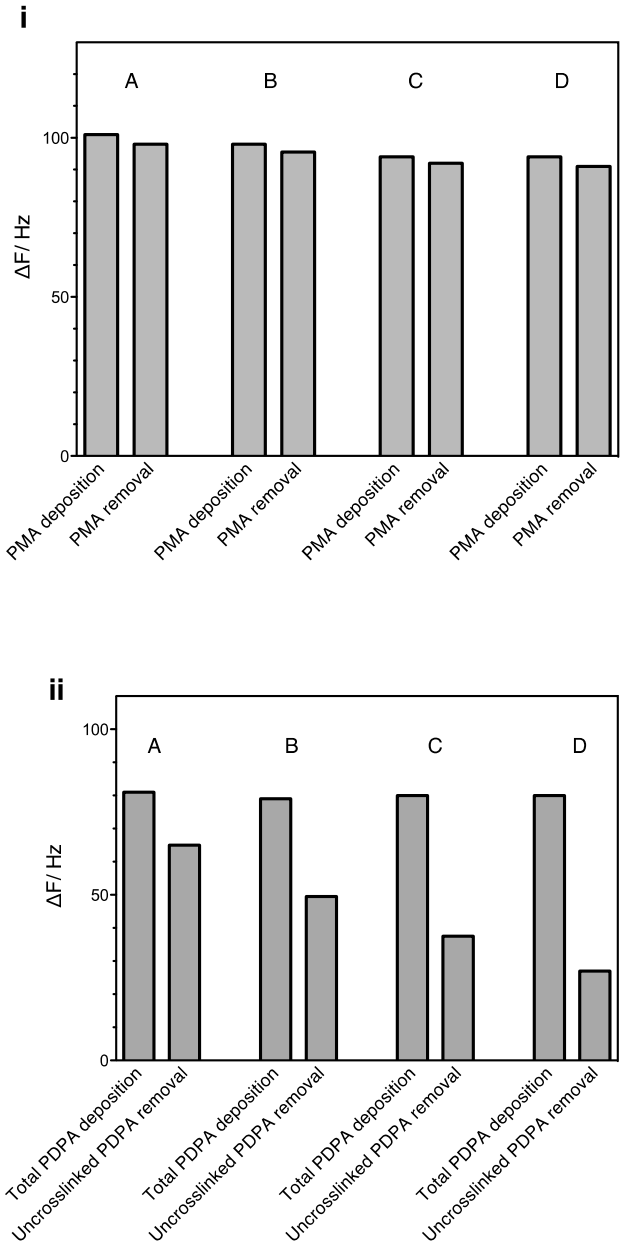


Figure S1. QCM analysis of five-layer $PDPA_{Alk}$ films crosslinked with (A) 5.0×10^{-13}, (B) 5.0×10^{-12}, (C) 1.3×10^{-11}, and (D) 2.5×10^{-11} mol of a redox-responsive linker. i) Frequency change for the deposition of five layers of PMA at pH 4 and PMA removal at pH 7.4; ii) Frequency change for the deposition of five layers of PDPA at pH 4 and removal of noncrosslinked PDPA after crosslinking (of PDPA) and PMA removal.

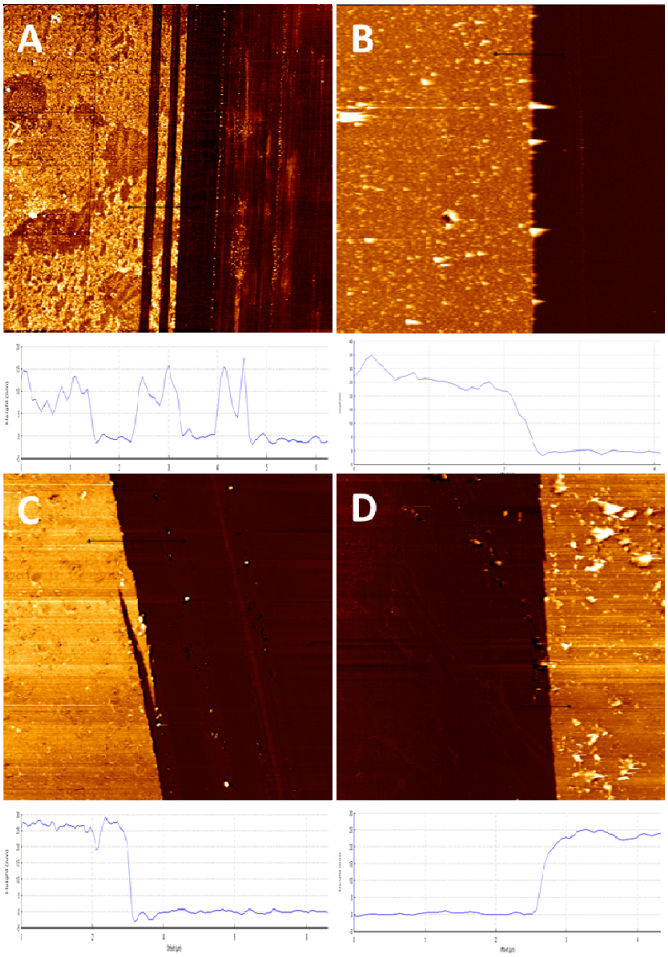


Figure S2. Aqueous AFM thickness analysis of five-layer $PDPA_{Alk}$ films crosslinked with (A) 5.0×10^{-13}, (B) 5.0×10^{-12}, (C) 1.3×10^{-11}, and (D) 2.5×10^{-11} mol of a redox-responsive linker.

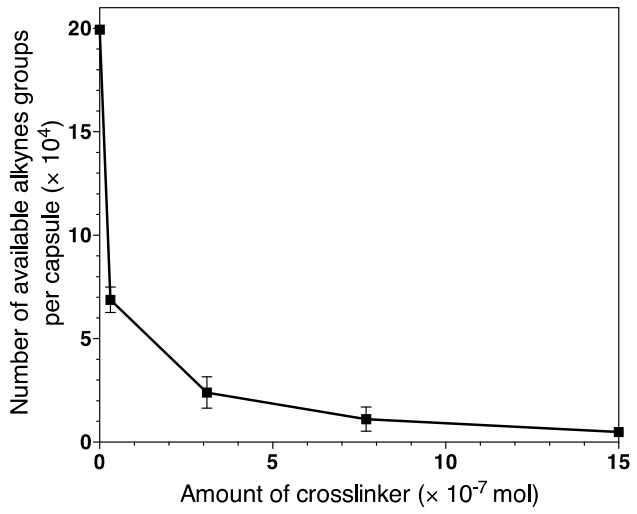


Figure S3. Available alkyne moieties in each PDPA capsule resulting from varying the crosslinker concentration, assessed from the specific radioactivity of 2×10^8 capsules.

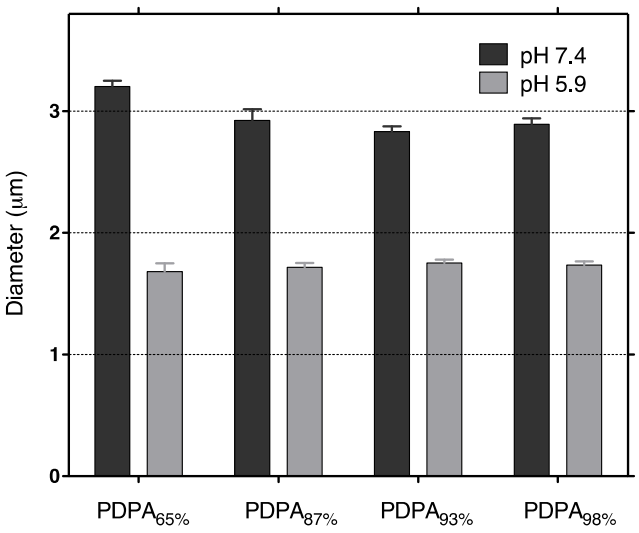


Figure S4. Average diameters of $PDPA_{65\%}$, $PDPA_{87\%}$, $PDPA_{93\%}$, and $PDPA_{98\%}$ capsules prepared from 2.6 μm-diameter silica templates and dispersed in PBS. The diameters of 20 capsules were measured at each pH using a fluorescence microscope.

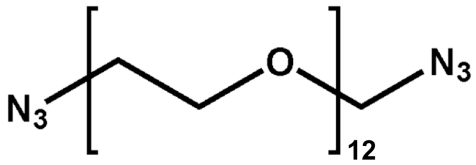


Figure S5. Structure of the nonreducible bisazide crosslinker, bisazido dodecaethylineneglycol.

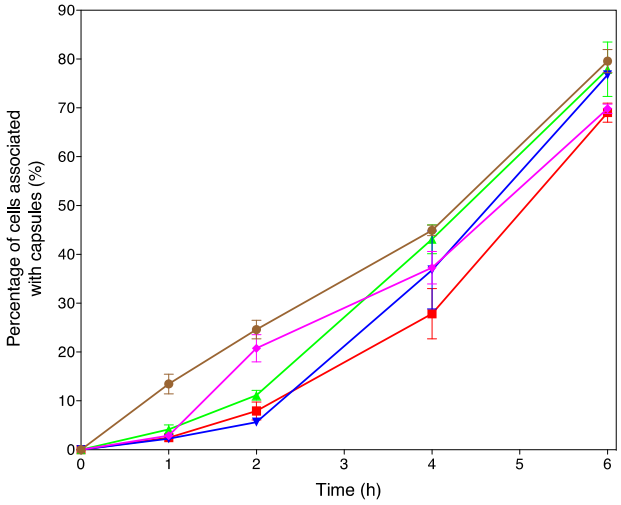
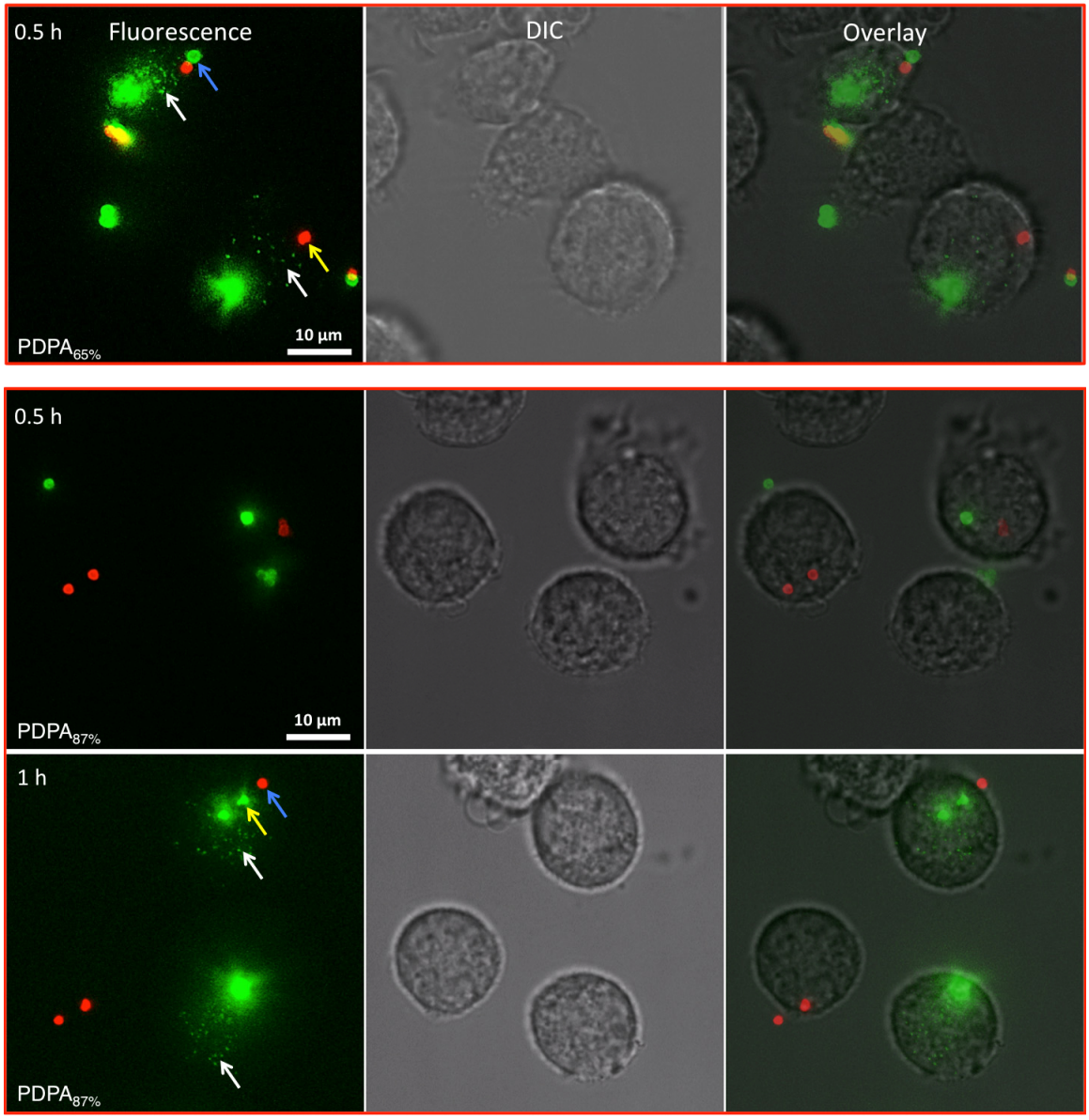
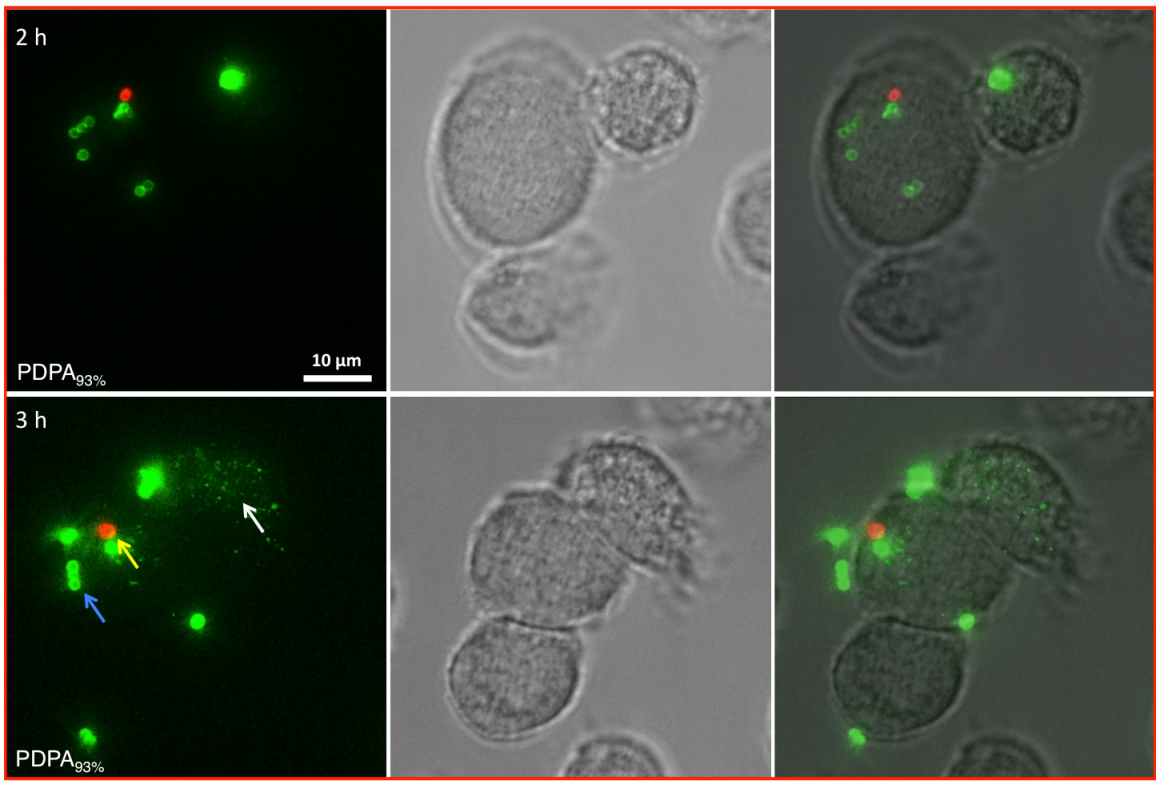


Figure S6. Capsule-cell association kinetics as a function of time at 37 °C, as monitored by flow cytometry. Capsules were crosslinked at 65% ($PDPA_{65\%}$, red squares), 87% ($PDPA_{87\%}$, green triangles), 93% ($PDPA_{93\%}$, blue triangles), and 98% ($PDPA_{98\%}$, purple diamonds) degrees using a redox-responsive linker. A control sample of capsules was crosslinked with a nondegradable crosslinker (brown circles). Experiments were performed in triplicate.


0.5 h
Fluorescence
DIC
Overlay
PDPA65%
10 µm
0.5 h
PDPA87%
10 µm
1 h
PDPA87%


2 h
10 µm
PDPA93%
3 h
PDPA93%

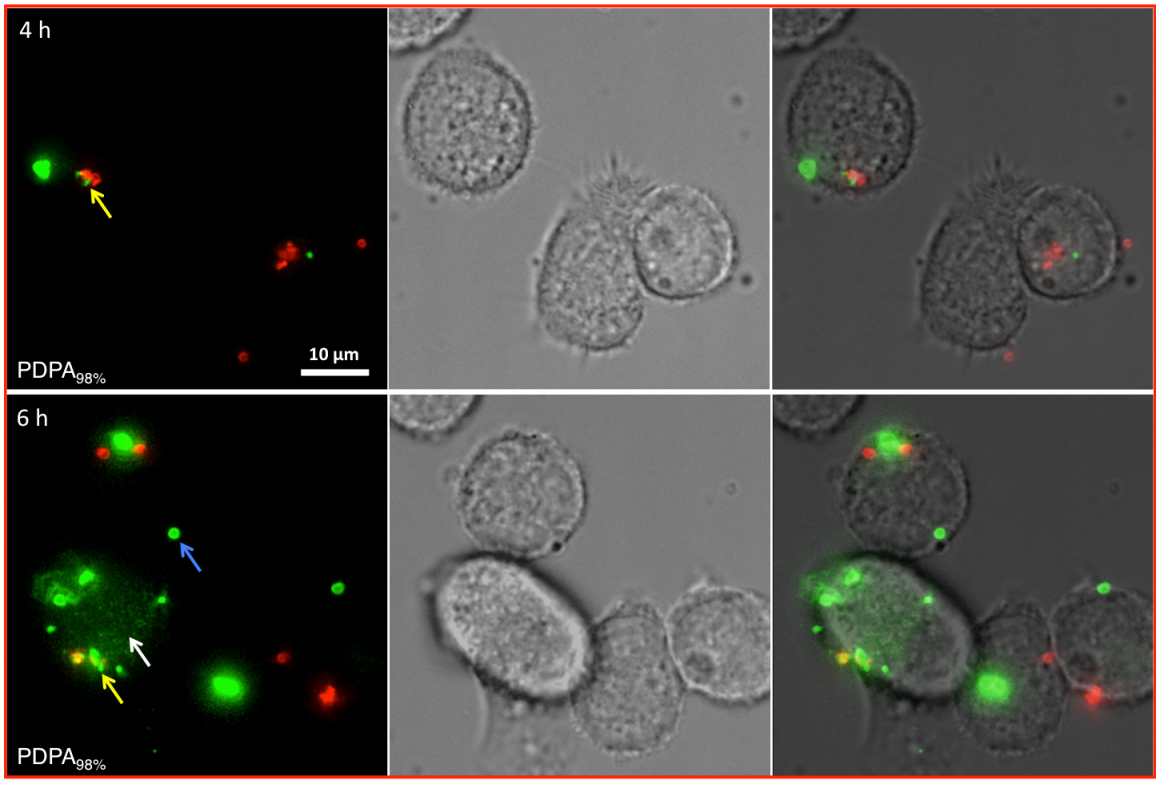

4 h
10 µm
PDPA98%
6 h
PDPA98%

Figure S7. Enlarged images of live deconvolution microscopy (maximum intensity projection) of JAWS II cells incubated with degradable $PDPA_{65\%}$, $PDPA_{87\%}$, $PDPA_{93\%}$, and $PDPA_{98\%}$ capsules (green) using a bisazide redox-responsive linker and non-degradable capsules (red). Time frames just before and after capsule degradation are shown. White arrows indicate degraded capsules, yellow arrows indicate distorted capsules inside cells, and blue arrows indicate capsules outside cells. Scale bars are 10 μm.

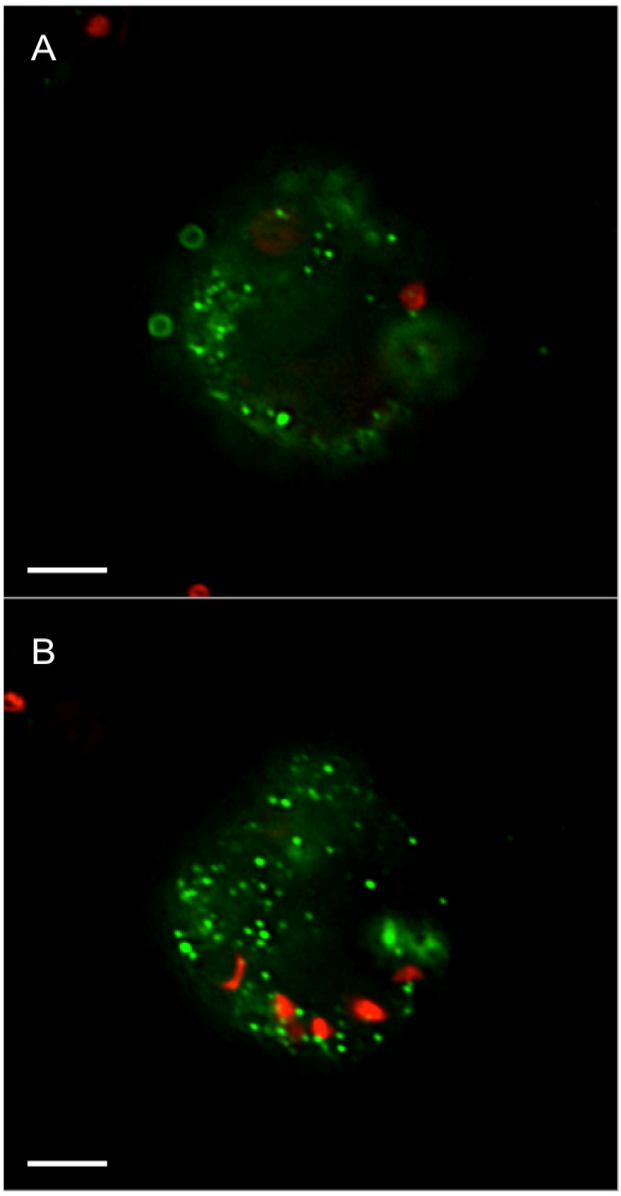


Figure S8. Deconvolution microscopy images of JAWS II cells incubated with degradable PDPA capsules (green) and non-degradable PDPA capsules (red). Image A and image B indicate different z-sections from the same cell.