## ---Electronic Supplementary Information---

## Time Programmable Hydrogels: Regulating the Onset Time of Network Dissociation by a Reaction Relay

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## **Experimental:**

**Materials.** All chemical reagents for synthesis and enzymes were purchased from Sigma-Aldrich. Solvents, inorganic salts were from Fisher Scientific.

Synthesis of Br-PEG<sub>455</sub>-Br ATRP Initiator. Bromine terminated polyethylene glycol (Mn=20000) was synthesized according to the published procedure in the literature.<sup>1</sup> Briefly, hydroxy terminated polyethylene glycol (Mn=20000, 15 g, 0.75 mmol) was dissolved in dichloromethane with triethylamine and deaerated for 30 minutes with nitrogen. 1.68 ml of  $\alpha$ -bromoisobutyryl bromide (13.5 mmol) was added dropwise into the solution at 0 °C over the course of 30 minutes and then stirred overnight. The mixture was then filtered and the filtrate was washed with water, NaHCO<sub>3</sub>/NaOH aqueous solution (pH=9-10), and water. The organic phase was dried over anhydrous MgSO<sub>4</sub> and filtered. The filtrate was concentrated and precipitated in n-hexane. The precipitates were vacuum dried overnight at room temperature to obtain a white solid. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$ : [1.93 (12H), 3.68 (1840H), 4.35 (4H)].

Synthesis of PDEA<sub>53</sub>-b-PEG<sub>455</sub>-b-PDEA<sub>53</sub>. Br-PEG<sub>455</sub>-Br (1.0 g,  $4.93 \times 10^{-5}$  mol) was dissolved in 8.6 mL anisole. Diethylaminoethylmethacrylate (DEA, 1.236 mL,  $6.16 \times 10^{-3}$  mol) and PMDETA (20.15  $\mu$ L,

 $1.08 \times 10^{-4}$  mol) were added to the solution and purged with nitrogen gas. After one hour of purging, under nitrogen gas protection, CuBr (0.016 g,  $1.08 \times 10^{-4}$  mol) was added and sealed with parafilm. The solution was then heated to 60 °C. Sampling was done periodically with NMR characterization to determine the conversion percentage. The reaction reached 80 % conversion after 6 hours and was quenched by opening the flask to air and dilution with THF. The diluted solution mixture was passed through a neutral alumina column to remove the catalyst and washed with THF. The resulting solution was rotavaped to almost dry and n-hexane was added to precipitate out the target polymer. The precipitates were recrystallized three times and vacuum dried at room temperature for three days. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$ : [0.8-1.3 (9H), 1.6-2.1 (2H), 2.6-3.1 (6H), 3.64 (17H), 4.0-4.3 (2H)]. DP=455/(17H/2H/2)/2=53. M<sub>p,SEC</sub>=53.0 kDa in DMF (Polystyrene as the standards), PDI=1.25.

**Dynamic Light Scattering (DLS).** DLS measurements were conducted on a Malvern Zetasizer Nano. The samples were in 1 cm path length polystyrene cuvette and kept at 21°C during measurements. The scattered light detection was at 90 degrees. The time dependent measurements were averaged for 600 seconds for satisfactory S/N particularly at faster relaxations. The time interval between each measurement was set at 10 minutes.

**Transmission Electron Microscopy (TEM).** TEM image was obtained on a JEOL 100CX II. The specimen was stained by 1% phosphotungstic acid and drop casted onto a carbon coated copper grid and washed by DI water. The sample was dried in air before sending to the microscopy chamber.

**Rheological Measurements.** Rheological measurements were performed on a TA Instruments Rheometer equipped with a Peltier plate for gel temperature control at 294 K. The hydrogel sample was mounted onto an 8 mm in diameter flat plate by a spatula. Drops of water was added to the outer layer of the Peltier plate to minimize solvent evaporation with a solvent trap cover on. The frequency dependent G' and G'' measurement was conducted by frequency sweep from 0.05 to 50 rad/s with a strain amplitude  $\gamma$  of 2 %. The time dependent modulus measurements were operated by oscillatory shear at a fixed frequency of 1 rad/s.



Figure S1. Plot of R<sub>h</sub> as a function of pH for 0.1 wt% PDEA-b-PEG-b-PDEA in PBS buffer.



**Figure S2.** Plot of  $R_h$  of the ABA triblock copolymer micelle solution as a function of time with variation of GOx concentration. GOx concentration lower than 0.05 mg/mL resulted in inconsistent deactivation of the enzyme that did not lead to full micelle disassembly while too high of a concentration larger than 0.5 mg/mL led to dormant time of stable micelle assembly too short to be accurately measured.



**Figure S3**. Micelle size changes at the transition time delays for PDEA-b-PEG-b-PDEA micelle solutions and the corresponding relaxation time distribution.



**Figure S4.** Time programmable degradation of PDEA-b-PEG-b-PDEA hydrogels by glucose concentrations. Storage modulus change as a function of time shows the programmed onset time of storage modulus decrease was not able to be tuned due to substrate saturation in the enzymatic reaction.

## **Reference:**

1 D. M. Henn, R. A. E. Wright, J. W. Woodcock, B. Hu and B. Zhao, *Langmuir*, 2014, **30**, 2541-2550.