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Tough hydrophilic polyurethane-based hydrogels with mechanical properties similar to human soft tissues

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Supplementary Information

Synthesis of F-127 dimethacrylate (XL)

As described in our previous publication,[1] F-127 dimethacrylate (FDMA) (a.k.a. XL in this study) was synthesised by adding 1.25 g Pluronic® F-127 (MW=12,500 Da) to 8.5 ml dichloromethane and 56 µL trimethylamine (MW=101.19 Da). Methylacryloyl chloride (MAC) (MW=104.53 Da) was then added to the solution, and the whole batch was stirred at room temperature under nitrogen for three hours. The reaction proceeded for 72 h. The side product of this reaction was TEA.HCl that formed in DCM. Hence, samples were purified by diluting 60 times with Milli-Q water and dialysed with 1000 Da membrane (Spectrumlab, USA). Eventually, the functionalised Pluronic® was freeze-dried at –35 °C for 48 h. The product of this stage, which was a fine white powder, named FDMA hereafter.

To confirm the successful reaction between Pluronic® F-127 and MAC, the dried FDMA was dissolved in D_2O for ^{1}H-NMR measurements. Spectrum was acquired at 298 K using Bruker Avance III 600 MHz NMR spectrometer. The obtained spectrum was processed using TOPSPIN3 (Bruker, Karlsruhe, Germany). The ^{1}H-NMR spectrum confirmed the formation of dimethacrylate end-capped Pluronic® F-127 via incorporating the methacryloyl groups (Figure S1). The chemical shifts at 5.62 and 6.18 ppm (doublet, one proton, peak “a” in Figure S1) correspond to unsaturated bonds of the hydrogen atoms at each tail of FDMA. The spectrum also shows the binding of the methacryloyl moieties, the last methylene group of polyethylene oxide block by the generated ester group, indicated as a signal at 4.3 ppm (triplet, two protons, peak “c” in Figure S1).

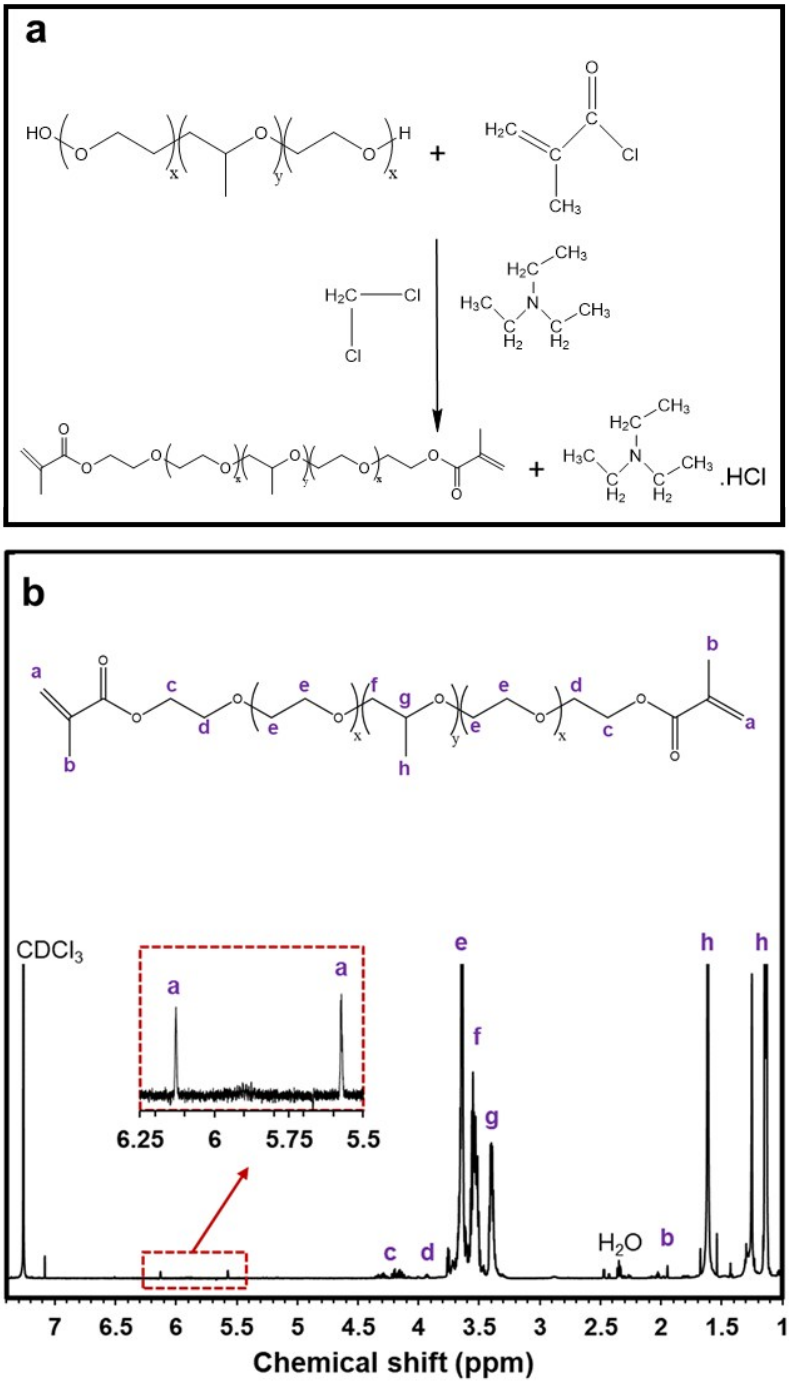

Figure S1. Reaction scheme for synthesis of Pluronic® F127 dimethacrylate (FDMA) (a), and ^{1}H NMR spectrum (b) of FDMA (x = 99 and y = 67).

Hydrophilic polyurethane (HPU)

Three grades of HPU were used in this study. Gel Permeation Chromatography (GPC) was performed using a Shimadzu LC20A HPLC system at room temperature, flow rate of 1 ml min^{-1} with ELSD Sedex 60LT detector (Sedere) and tetrahydrofuran as solvent in a Shodex high performance KF803, 300 x 8 mm column (Phenomenex). Polystyrene

standards ranging from 1320-156000 were used for calibration standards (Figure S2). ^{1}H-NMR spectra were obtained at 400 MHz using a Bruker Avance III 400 spectrometer and $CDCl_3$ as solvent, 30 ^{o}C. Data is expressed in ppm, with all peaks shifted in reference to tetramethylsilane as the internal standard (Figure S3).

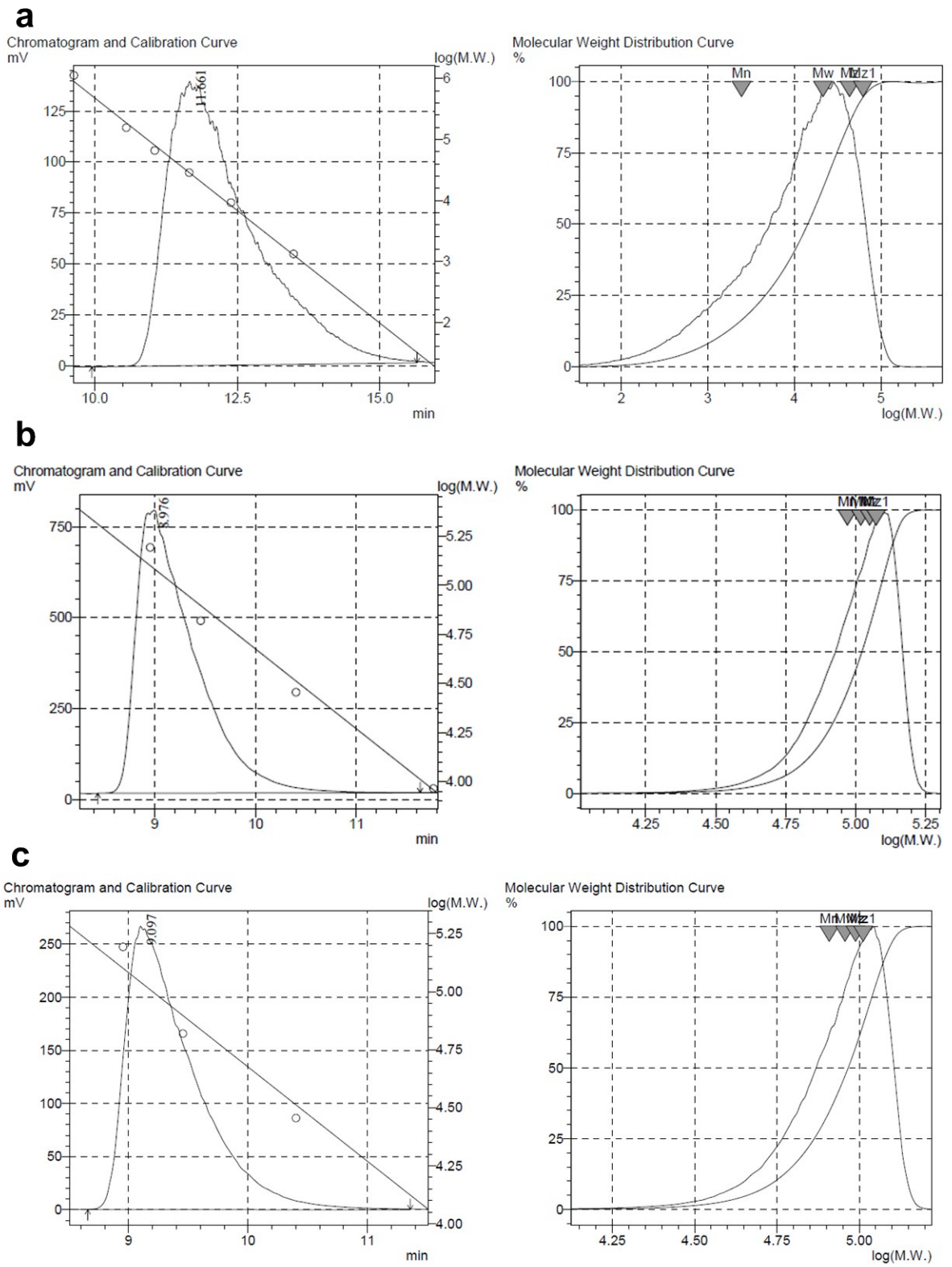

Figure S2. Calibration curves and molecular weight distribution curves of HPU1(a), HPU2(b), and HPU3(c).

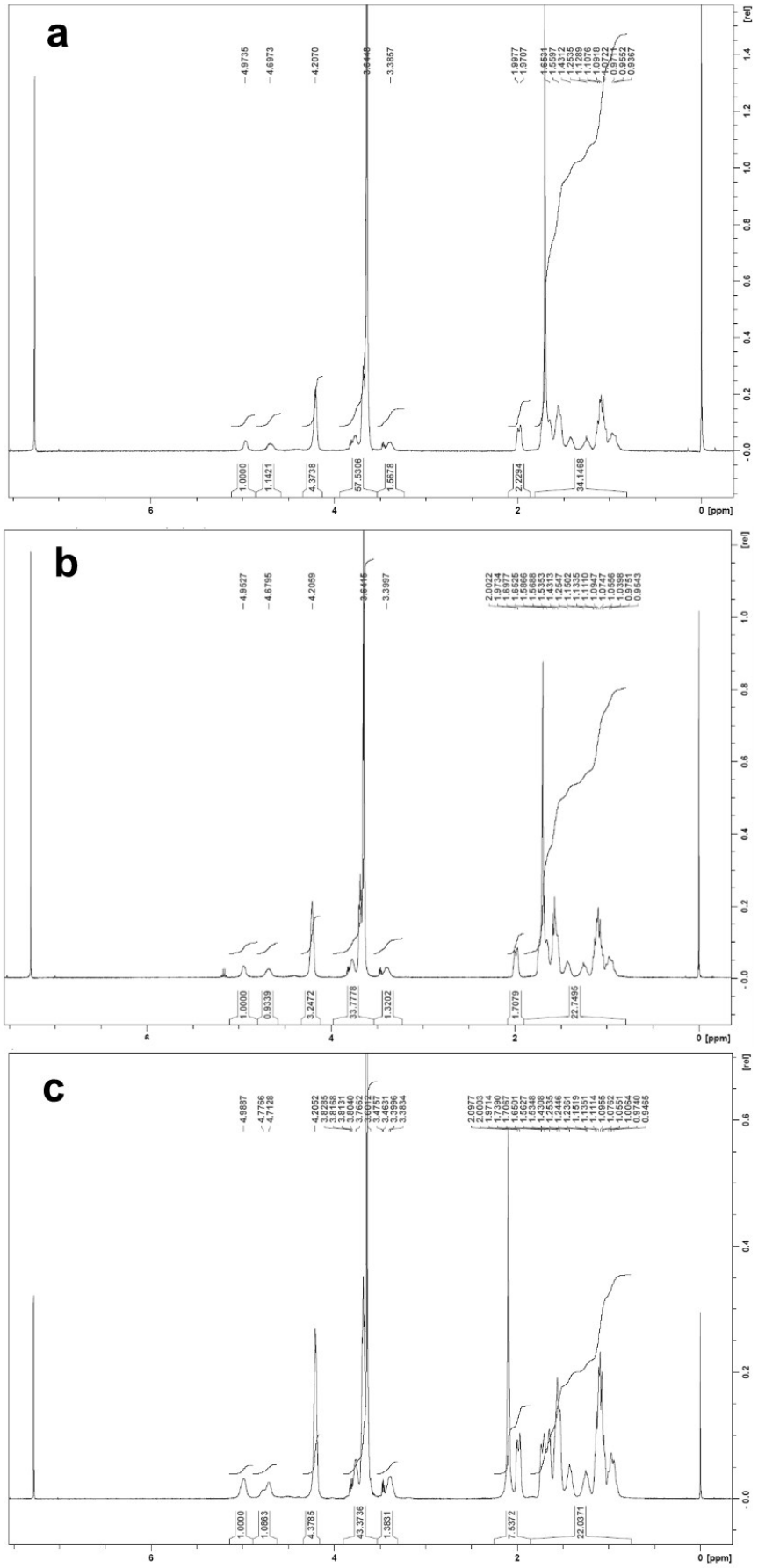

Figure S3. HNMR spectra of HPU1(a), HPU2(b), and HPU3(c).

Synthesis of PPHUN

The interpenetrating hydrogels were made by incorporating a chemically crosslinkable copolymer into the network of the hydrogen-bonded HPU. The copolymer network consisted of HEMA, NAS, and a crosslinking agent. Crosslinkers used in this study alone are biocompatible block copolymer (poly(ethylene oxide)$_{99}$-poly(propylene oxide)$_{67}$-poly(ethylene oxide)$_{99}$) which cannot participate in radical polymerisation due to lacking vinyl carbons in its structure. Hence, Pluronic® F-127 dimethacrylate (FDMA) was synthesised by end-capping the OH-terminated F-127 with methacryloryl chloride) (see above). A 3 M solution of HEMA in DMF was prepared in which various combinations of NAS (0 to 1 mol.% per HEMA), HPU (0.005 to 0.021 mol.% per HEMA), and crosslinker (XS, XM, or XL) were added and stirred for 12 h until fully dissolved. The random polymerization and crosslinking of HEMA, NAS and crosslinker were then initiated by addition of 1.5 mol.% 4,4'-azobis (4-cyanovaleric acid) to the samples. All batch systems were fully sealed and stirred overnight at room temperature. The polymerisation solutions were then cast, wrapped with porous aluminium foils, and incubated at a 60 °C oven for three days. Eventually, all samples were washed with extensive amounts of water to eliminate the remaining DMF and unreacted reagents from the samples. The samples were then kept in Milli-Q water to reach the swelling equilibrium. These fully swollen poly((PEO-PPO-PEO)-HEMA-HPU-NAS), denoted as PPHUN subjected to further characterisation.

Chemical bonding of succinimide groups to the network (FTIR analysis)

The fabricated hydrogels with (PPHUN) and without NAS (PPHU) were characterised using FTIR (Nicolet 6700, ThermoFisher Scientific, USA). The FTIR signals were expressed as percentage transmittance (%Transmittance) over a range of 500–4000 wavenumbers (cm^{-1}). The occurrence of the peak at 1700 cm^{-1} in PPHUN spectrum confirmed the chemical bonds of succinimide groups with the network (Figure S4). Similar band was observed and reported as the ester group of NAS in previous studies.[2, 3] The peak at 1080 cm^{-1} referred to stretching of ether groups (-C-O-C-) in HEMA and FDMA.[4] The band between 1500 to 1600 cm^{-1} was due to the stretching of N-H from HPU. The band at 960 cm^{-1} occurred because of stretching the carbonyl group (C=O).[4] Finally, the obtained spectra demonstrated a peak at 1635 cm^{-1} indicating a stretch in alkenes (C=C) of FDMA and HEMA.[5]

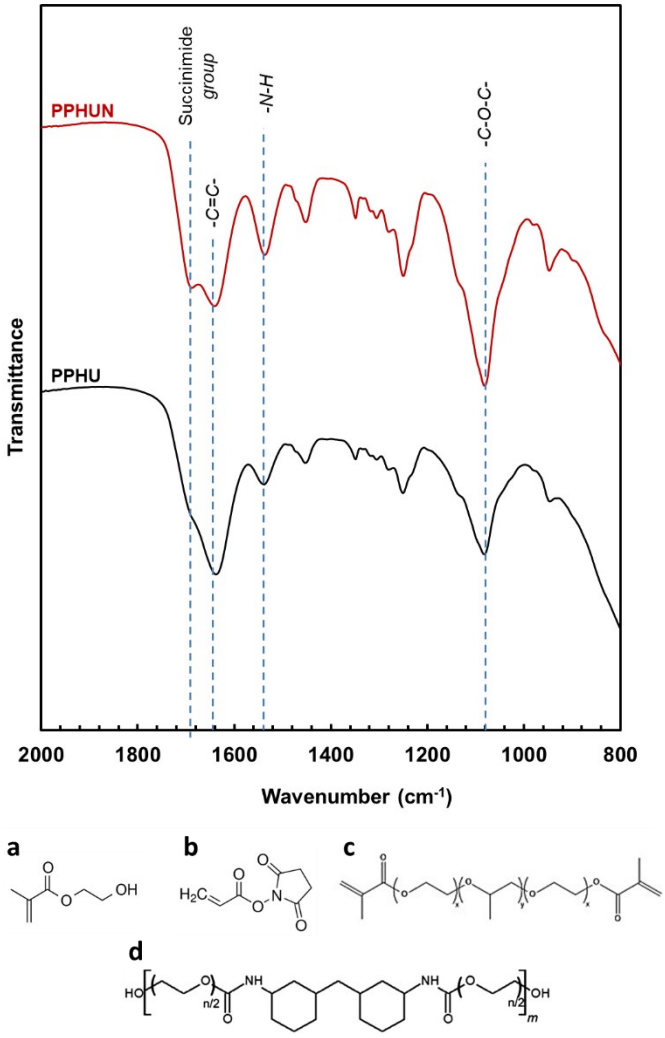

Figure S4. FTIR spectra of the fabricated hydrogel with NAS (PPHUN) and without NAS (PPHU) after synthesis from their building units: HEMA (a), NAS (b), FDMA crosslinker (c), and HPU(d).

Cyclic load-unload behaviour

Cyclic compression testing consisting of ten consecutive loading and unloading was performed to determine the dissipated work and elastic recovery of PPHUN. Hydrogel films were punched at 5 mm diameter by a standard biopsy punch prior to the measurements. The cyclic test was performed on fully swollen hydrogel discs to 60% strain using a 10 N load cell at displacement rate of 10 mm min^{-1}. The dissipated energy (work of cycle) was calculated as the difference between the work of unloading and the work of unloading.

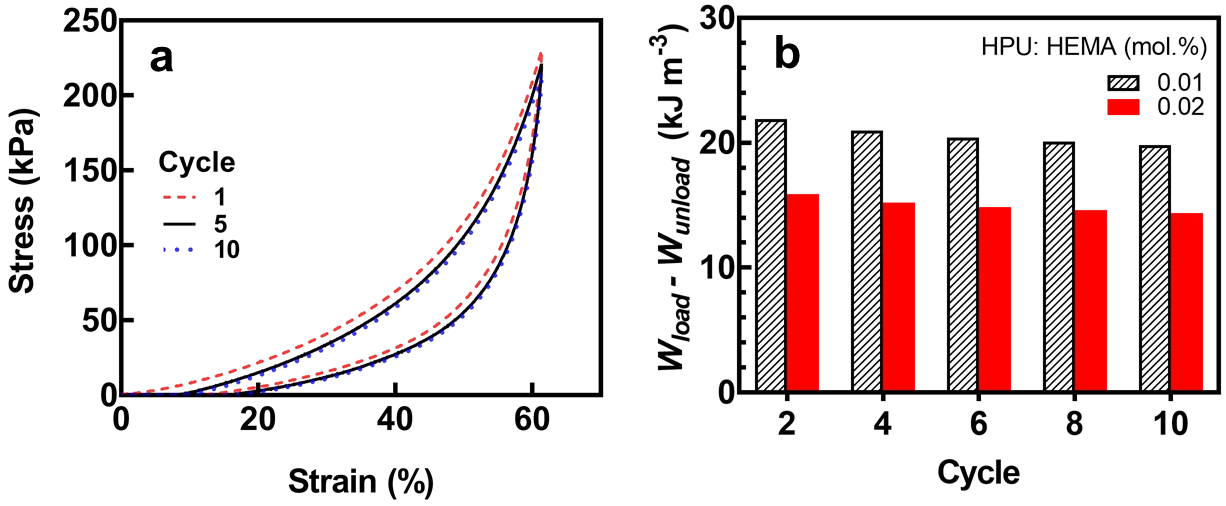

Figure S5. (a) an example of loading-unloading cycles for fully swollen PPHUN hydrogels; (b) energy dissipated between loading and unloading cycles, demonstrating no network damage in under consecutive loading cycles.

Referecences

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