

## Supporting Information

Crosslinked hydrogels formed through Diels-Alder coupling of Furan- and Maleimide-modified Poly(methyl vinyl ether-*alt*-maleic acid)

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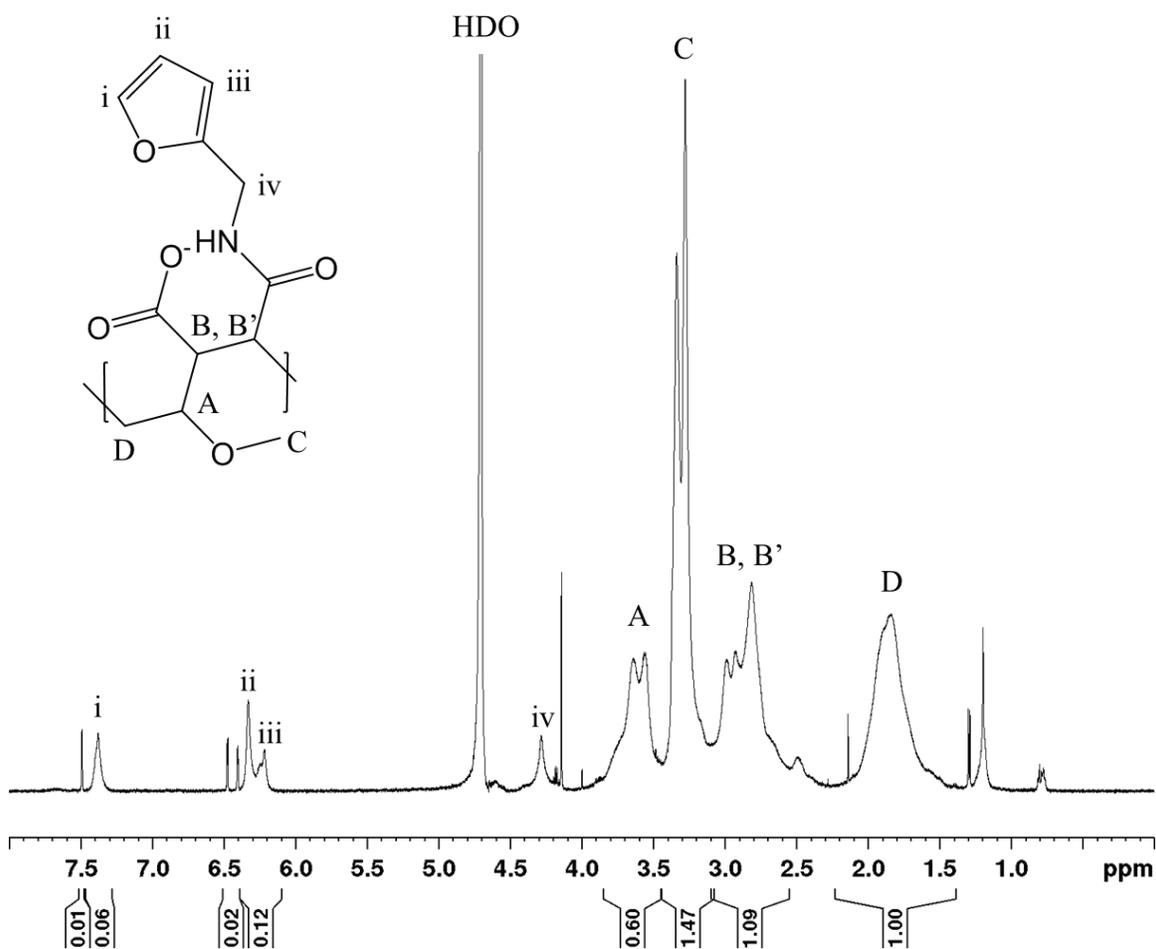


Figure S-1. <sup>1</sup>H-NMR of PMM-FFA12 in D<sub>2</sub>O. The ratio of the furan vinyl signals (at 6.25 (iii), 6.35 (ii), and 7.40 (i) ppm) to the backbone methylene signal (D), was used to determine the percent functionalization with FFA.

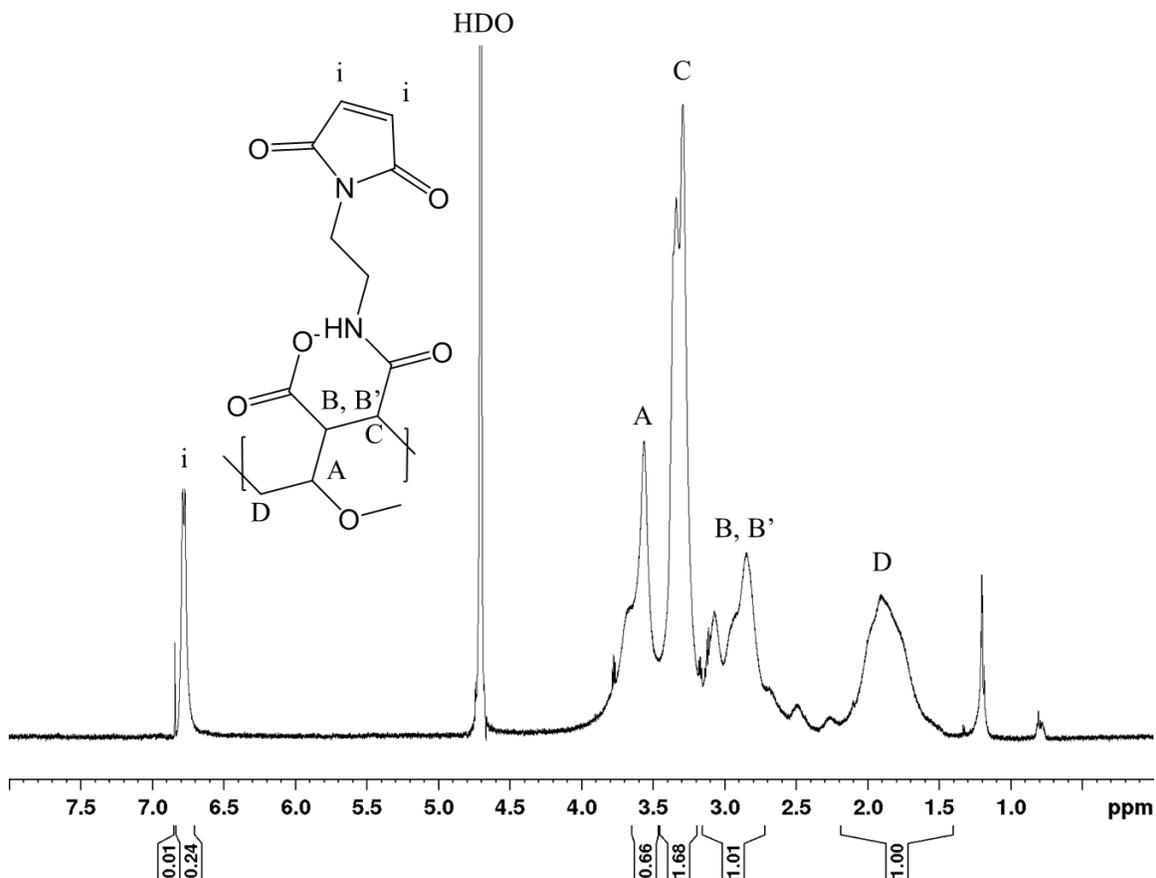


Figure S-2.  $^1\text{H-NMR}$  of PMM-MAL24 in  $\text{D}_2\text{O}$ . The ratio of the maleimide vinyl signal at 6.75ppm (i) to the backbone methylene signal (D) was used to determine the percent functionalization with MAL.

About 1-5 % of the furfurylamine and aminoethyl maleimide in the final samples are present as free small molecules, as indicated by small sharp peaks in the corresponding NMR spectra, just downfield from the corresponding signals for the polymer-bound FFA and MAL. This is attributed to electrostatic retention of some of the protonated amines by the polyanionic PMM backbone, even after dialysis. Future experiments will explore the use of added salts during dialysis to facilitate removal of these low molecular weight amines. Amide hydrolysis, occurring either during polymer dialysis or NMR sample preparation, may also be responsible for a small portion of the free FFA and MAL.

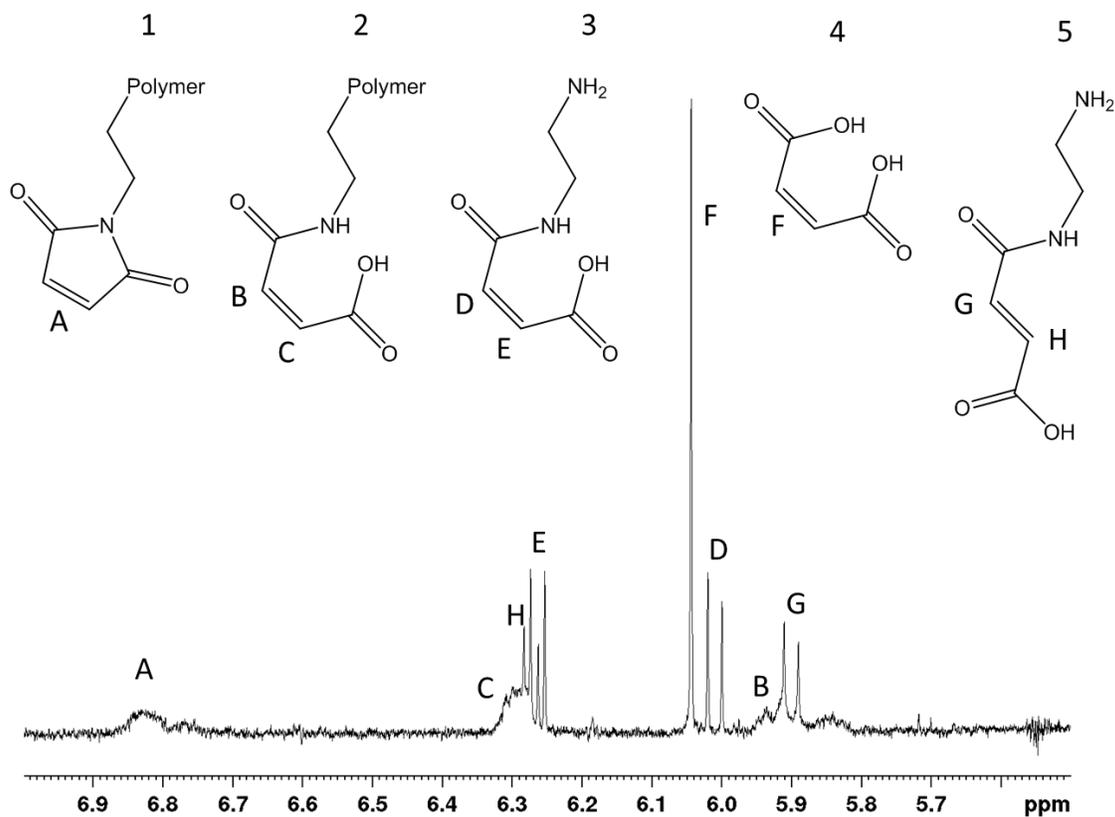


Figure S-3.  $^1\text{H-NMR}$  spectrum of a solution of PMM-MAL24 kept at pH 6 in MES buffer for 7 days at  $37^\circ\text{C}$ .

Fig. S-3 shows a representative  $^1\text{H-NMR}$  spectrum after 7 days of hydrolysis at  $37^\circ\text{C}$  and pH 6. At this point about 80% of the initial maleimide has hydrolyzed to a mixture comprising polymer-bound maleamic acid 2 (broad signals B and C), aminoethyl maleamic acid 3 (two sharp doublets: D, E), aminoethyl fumaric acid<sup>1,2</sup> 5 (two sharp doublets: G, H) and maleic acid 4 (sharp singlet, F).

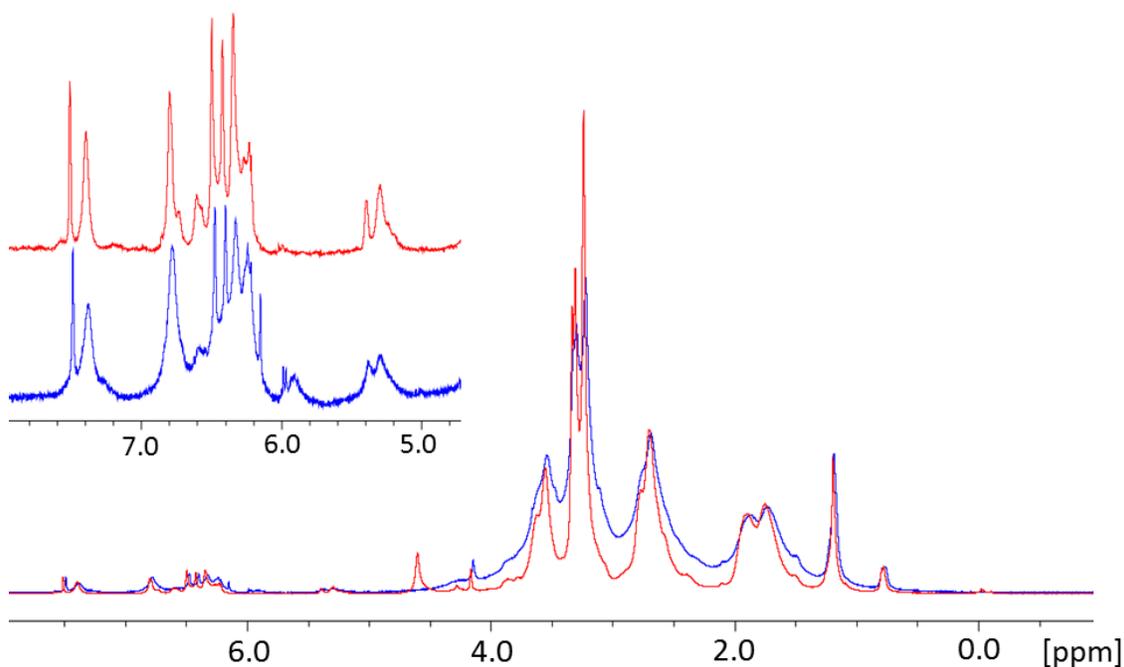


Figure S-4. Comparison between solution-state (blue) and HR-MAS (red) spectra of crosslinked PMM-FFA25/MAL24 gels cured at  $\text{pH } 5.1 \pm 1$  at  $37^\circ\text{C}$  for 18 hrs. MAS rate = 3500 Hz.

Figure S-4 compares the HR-MAS spectrum (red, top trace in insert) with the broader solution-state  $^1\text{H-NMR}$  spectrum (blue, bottom trace in insert), for a PMM-FFA25/PMM-MAL24 mixture with a total polymer concentration of 10% w/v (5% of each polymer) at pH 5.1 in  $\text{D}_2\text{O}$ , cured for 18 hrs at  $37^\circ\text{C}$ .

The MAS spectrum shows significantly narrower signals compared to the conventionally acquired spectrum. The inset shows the vinyl protons for polymer-bound furan at 7.4 ppm (1H) and at 6.1-6.3 ppm (2H), and for polymer-bound maleimide at 6.8 ppm (2H). The Diels-Alder adduct shows a vinyl signal at 6.6 ppm, and a bridgehead proton signal at 5.2-5.3 ppm. There are also sharper vinyl signals for free furfurylamine at 7.5, 6.5 and 6.4 ppm (1H each), and a sharper peak attributed to the bridgehead proton of the free FFA / PMM-MAL Diels-Alder adduct at 5.4 ppm. The solution-state sample also shows small amounts of free and polymer-bound maleamic acid at 5.9-6.0 ppm.

Figure S-5 compares in detail the above PMM-FFA25/MAL24 MAS spectrum taken at 18 hours after mixing (red, top spectrum), with the corresponding MAS spectrum of the same sample taken 36 minutes after mixing (blue, bottom spectrum).

The lower spectrum (36 minutes) shows very little evidence of the Diels-Alder adduct. The upper spectrum (18h) shows the appearance of Diels-Alder adduct signals at 5.1-5.2 (bridgehead) and 6.5 (vinyl), as well as decreases in furan (6.1, 6.2 and 7.3ppm) and maleimide (6.7ppm) intensity.

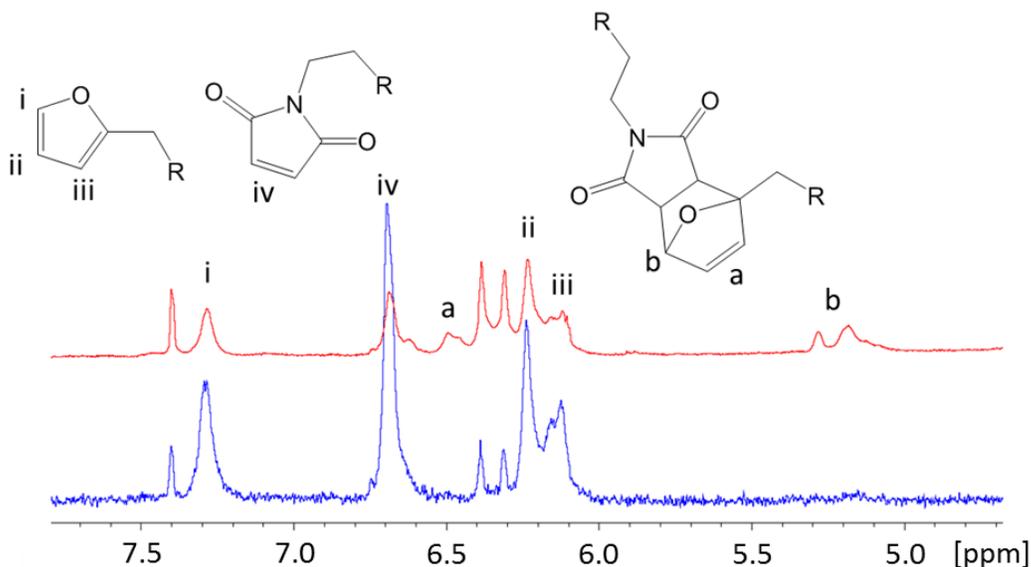


Figure S-5.  $^1\text{H-NMR}$  HR MAS spectrum of mixture containing 5% PMM-MAL24 and 5% PMM-FFA25 at pH 5.2 after 36 mins (bottom spectrum) and 18h (top spectrum) at  $37^\circ\text{C}$ . The polymer-polymer Diels-Alder adduct peaks appear between 6.4 and 6.5 ppm (vinyl protons) and at 5.1-5.3 ppm (bridgehead proton). The bridge head proton of the Diels-Alder adduct at 5.1 – 5.3 ppm becomes visible in the bottom spectrum, after 36 min of reaction. The sharp signals at 7.4 and 6.3-6.4 ppm correspond to free furfurylamine, while the signal at 5.3ppm is attributed to the Diels-Alder adduct formed between PMM-MAL and free FFA. MAS rate  $\sim 3500$  Hz.

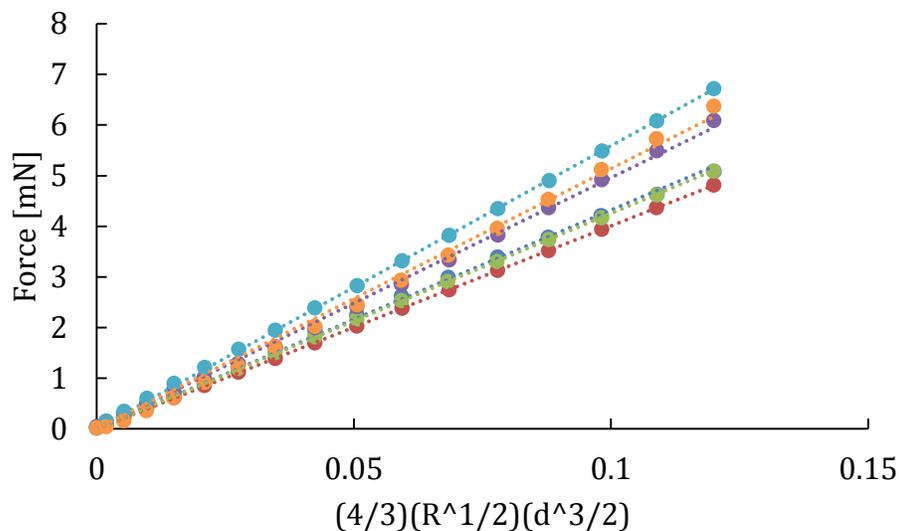


Figure S-6. Force strain curve for PMM-FFA18/MAL24 hydrogel (10 w/v% total polymer concentration). The measured forces are plotted as a function of strain ( $d^{3/2}$ ) and fitted to the equation:  $F = \frac{4ER^{1/2}}{3(1-\nu^2)} d^{3/2}$ . The slope of the above strain curve are given as  $E^*$ . The elastic modulus can then be found from the average  $E^*$  as  $\frac{1}{E^*} = \frac{1-\nu}{E}$ , where  $\nu$  is the Poisson's ratio (assumed to be 0.5) and  $E$  is the Young's modulus.

#### References:

- 1) Choi, W.; Kang, S.; Mok, Y.; Park, E.; Song, Y.; Choi, S.J.; Lee, Y. Unlocking the pH-Responsive Degradability of Fumaramic Aic Derivatives Using Photoisomerization. *Chem. Eur. J.* **2014**, *20*, 15715-15718.
- 2) Sánchez, A.; Pedroso, E., Grandas, A. Esterification of Maleamic Acids without Double Bond Isomerization. *Eur. J. Org. Chem.* **2010**, *13*, 2600-2606.