Supplementary Information for:

Unequal Stoichiometry Between Crosslinking Moieties Affects the Properties of Transient Networks Formed by Dynamic Covalent Crosslinks

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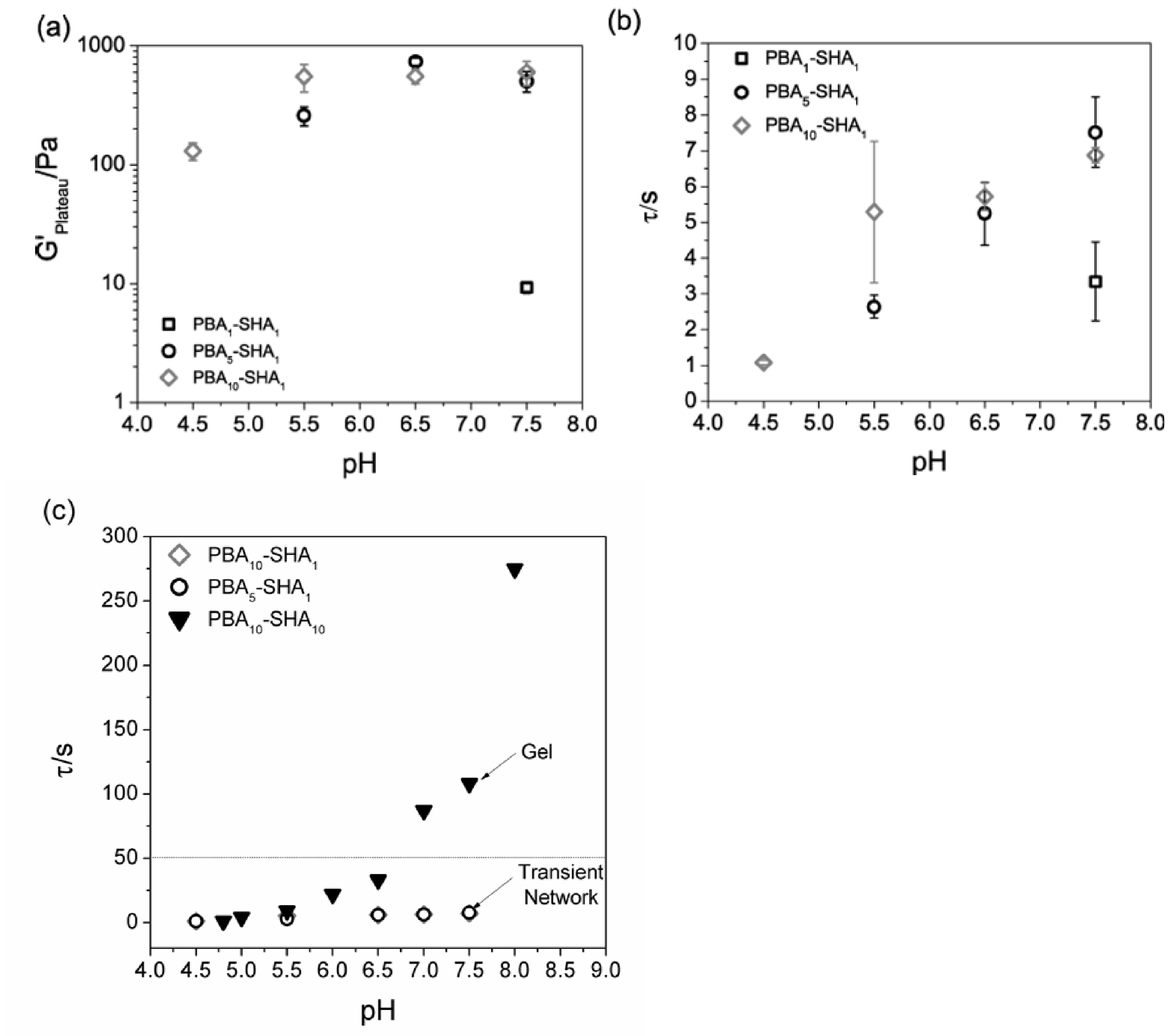

Figure S1. Effect of pH and disproportional PBA to SHA ratio on time-dependent viscoelastic behaviour at 37°C. a) Dynamic gel strength ($G'_{Plateau}$, Pa) and b) characteristic relaxation time, τ, s. N = 3, Mean ± SD. c) characteristic relaxation time versus pH for the unequal stoichiometry between PBA and SHA and equal stoichiometry PBA_{10}-SHA_{10} (data from Ref . 10 closed triangles) showing that the unequal stoichiometry maintains the transient gel network at pH 7 whereas PBA_{10}-SHA_{10} is a crosslinked gel network. Standard errors have been eliminated.

One of the interesting outcomes of this paper is that the stoichiometry between PBA and SHA moieties can modulate the pH at which a transient network to gel transition occurs. This effect can be clearly seen in Supplementary Figure S1. The low characteristic relaxation times on the order of a few seconds for PBA_5-SHA_1 and PBA_{10}-SHA_1 transient networks remains relatively unchanged as a function of pH from pH 4 to 7.5 (**Figure S1b**). The characteristic relaxation time for symmetrically crosslinked PBA_{10}-SHA_{10} polymers shows a dramatic increase between pH 4 and 7, as can be seen in **Figure S1c**. From pH 4 to 8, τ ranged from 1 to 300 s and 10 to 1000 s for PBA_5-SHA_5 and PBA_{10}-SHA_{10} gels respectively. [17, 38] Both the PBA_5-SHA_5 and PBA_{10}-SHA_{10} mixtures are gel networks at pH 7. In the symmetrically crosslinked PBA-SHA gels the ratio of PBA to SHA remains constant as the pH decreased; thus the characteristic relaxation time and number of crosslinks correlated with the dissociation and association of the pH sensitive PBA-SHA complex. The rapid rate of hydrolysis of the PBA-SHA complex at pH 4.5 likely resulted in very few crosslinks forming, while the increase in pH dramatically shifted the PBA-SHA equilibrium to the bound state. Due to the higher degree of functionality in the PBA_5-SHA_5 and PBA_{10}-SHA_{10} gels, the stabilized PBA-SHA complex at pH 7.5 likely resulted in larger number of crosslinks compared to the PBA_1-SHA_1 and the PBA_5-SHA_1 and PBA_{10}-SHA_1 transient networks described here, thus accounting for the order of magnitude higher characteristic relaxation times. In total these data imply that the increase in the ratio of PBA to SHA moieties reduces τ's dependence on the state of the PBA-SHA equilibrium by increasing the probability for crosslink formation at acidic pH and constraining the density of crosslinking above neutral pH, thus stabilizing the total number of crosslinks capable of forming across the pH 4.5 to 7.5 range. These results reveal the importance the number of associations between PBA and SHA moieties has in determining the characteristic relaxation time.

The stabilization in the extent of crosslinks formed in the disproportionally crosslinked gels is also revealed in the dynamic gel strength. At pH 4.5 where the fewest crosslinks would form, PBA_{10}-SHA_1 had a G'Plateau of 130 Pa and rose to 600 Pa at pH 7.5. This increase, like that for the characteristic relaxation time, is much more gradual than that exhibited by the symmetrically crosslinked PBA_5-SHA_5 and the PBA10-SHA10 gels.17 The dynamic gel strength leveled off for both unequally crosslinked gels suggesting the extent of crosslinking reached a maximum quantity in the PBA_{10}-SHA_1 gel at pH 5.5 and the PBA_5-SHA_1 gel at pH 6.5. By increasing the probability for crosslink formation at slightly acidic pH, but constraining the maximum number of crosslinks formed at pH 7.5, the PBA_{10}-SHA_1 gel maintains a more stable level of associations between the polymer-bound PBA and SHA, thus decreasing the impact pH has on this material's viscoelastic properties.

Table S1. Determined shift factors for PBA-SHA gels as a function of pH (reference = PBA_{10}-SHA_1 gels at 200 mg mL^{-1}, pH7.5, 37°C).

	PBA_1-SHA_1		**PBA_5-SHA_1**		**PBA_{10}-SHA_1**	
pH	***a***	***b***	***a***	***b***	***A***	***b***
7.5	1.57	73.49	1.06	1.23	1	1
6.5			1.12	0.71	0.93	0.81
5.5			0.41	1.91	1.38	1.45
4.5					0.16	3.21

Table S2. Determined shift factors for PBA-SHA gels at pH 7.5 as a function of temperature (reference = PBA_{10}-SHA_1 gels at 200 mg mL^{-1}, pH7.5, 37°C).

	PBA_1-SHA_1		**PBA_5-SHA_1**		**PBA_{10}-SHA_1**	
Temperature	***a***	***b***	***a***	***b***	***A***	***b***
55°C			0.313	1.53	0.24	1.11
45°C			0.47	1.20	0.53	0.98
37°C	1.57	73.49	1.06	1.23	1	1
25°C	2.52	31.75	2.30	1.07	2.50	0.93
10°C	32.38	13.06			10.56	0.936

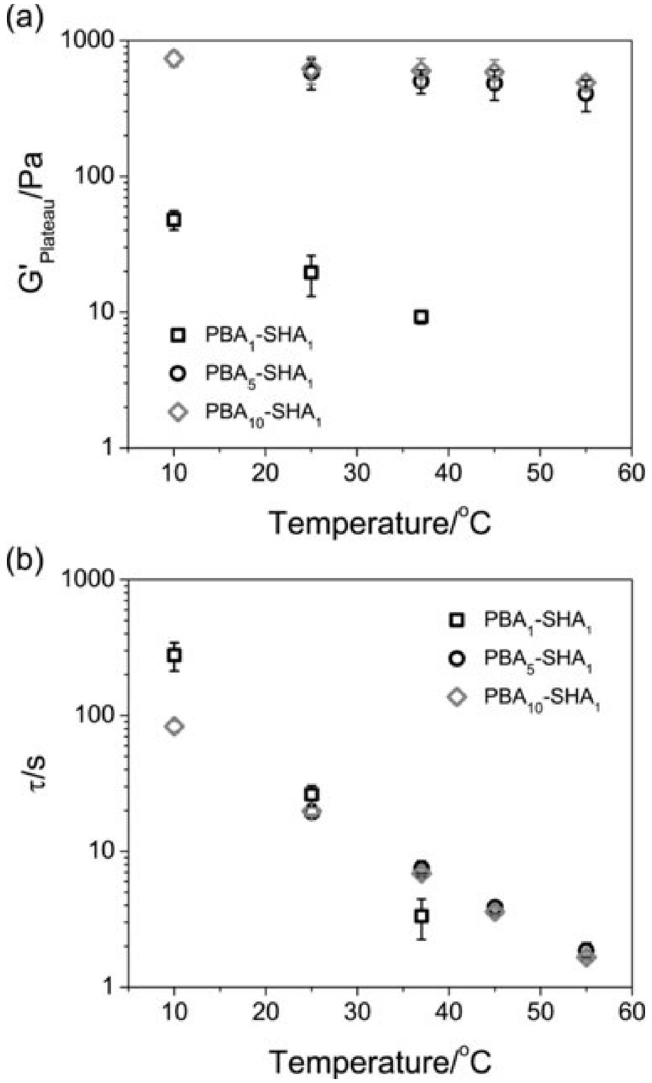

Figure S2. Effect of temperature and PBA to SHA ratio on time-dependent viscoelastic behavior at pH 7.5. a) Dynamic network strength ($G'_{Plateau}$, Pa) and b) characteristic relaxation time. For the PBA_5-SHA_1 and PBA_{10}-SHA_1 temperature change of 40 K changed the dynamic network strength as much as 50%. However, the strength of the PBA_1-SHA_1 transient network dropped by almost an order of magnitude in the same temperature range. The characteristic relaxation time showed a continual decrease as temperature rose for all crosslink conditions. N = 3, mean ± SD.

The individual frequency sweep curves as a function of temperature were used to experimentally determine $G'_{Plateau}$ and τ (**Figure 7**). The PBA_5-SHA_1 and PBA_{10}-SHA_1 networks demonstrated similar behavior. An increase of temperature of 40 K resulted in an approximate 50 % decrease on the $G'_{Plateau}$. The higher ratio of PBA to SHA stabilized the number of crosslinks formed resulting in less of a decrease $G'_{Plateau}$ across the $\Delta T=40$ K temperature range tested. The characteristic relaxation time for both systems decreased revealing that temperature impacted the ensemble lifetime of the crosslinks significantly, but not the overall number of crosslinks as suggested by the shift factors used to create the superposition of the frequency sweep curves. Both the G'$_{\text{Plateau}}$ and τ for PBA_1-SHA_1 network displayed a more rapid decrease with increasing temperature likely due to the small number of crosslinks present in this particular system. .

NMR Spectra

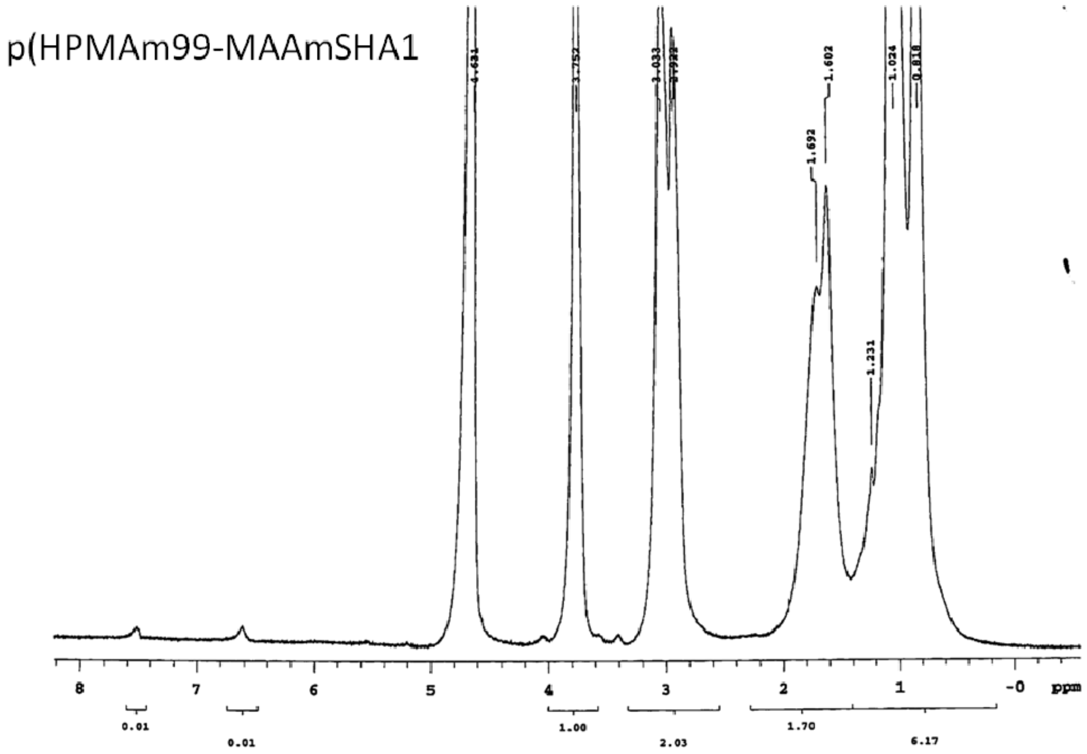

Figure S3 NMR Spectra for p($HPMA_{99}$-MAAm SHA_1)

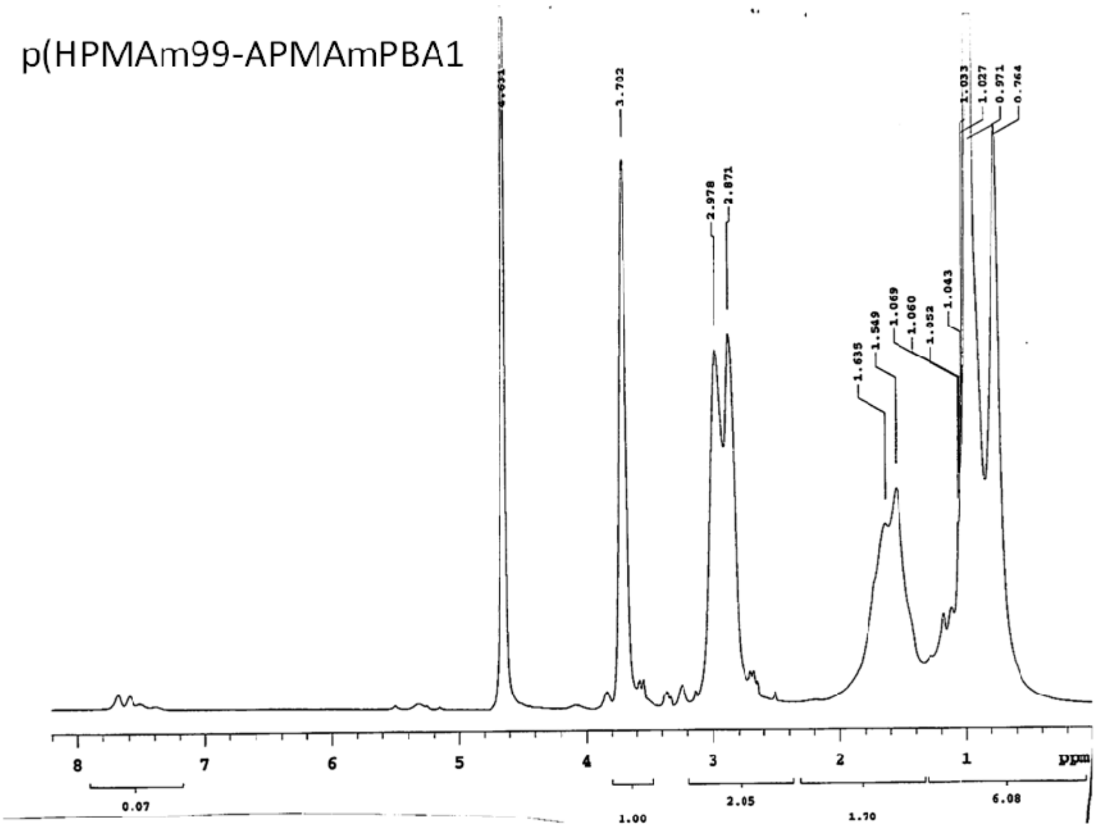

Figure S4 NMR Spectra for p($HPMA_{99}$-APMAm PBA_1)

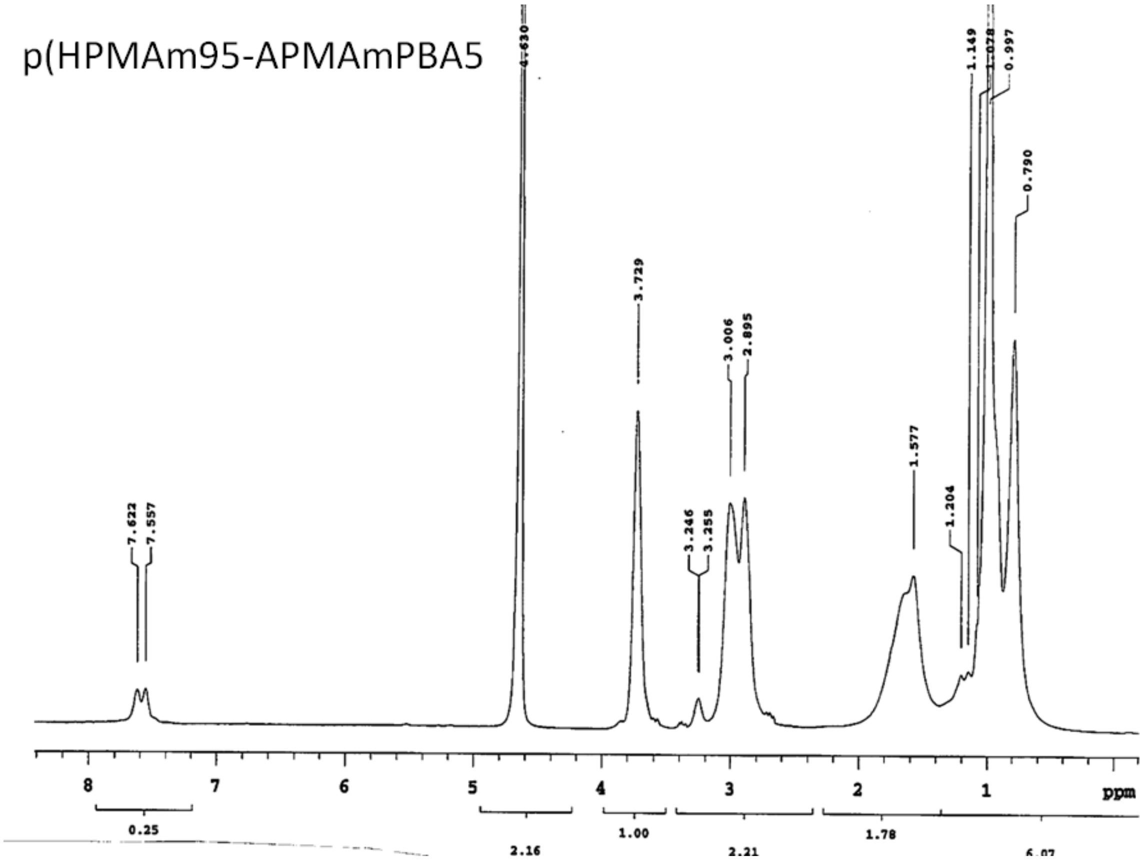

Figure S5 NMR Spectra for p($HPMA_{95}$-APMAm PBA_5)

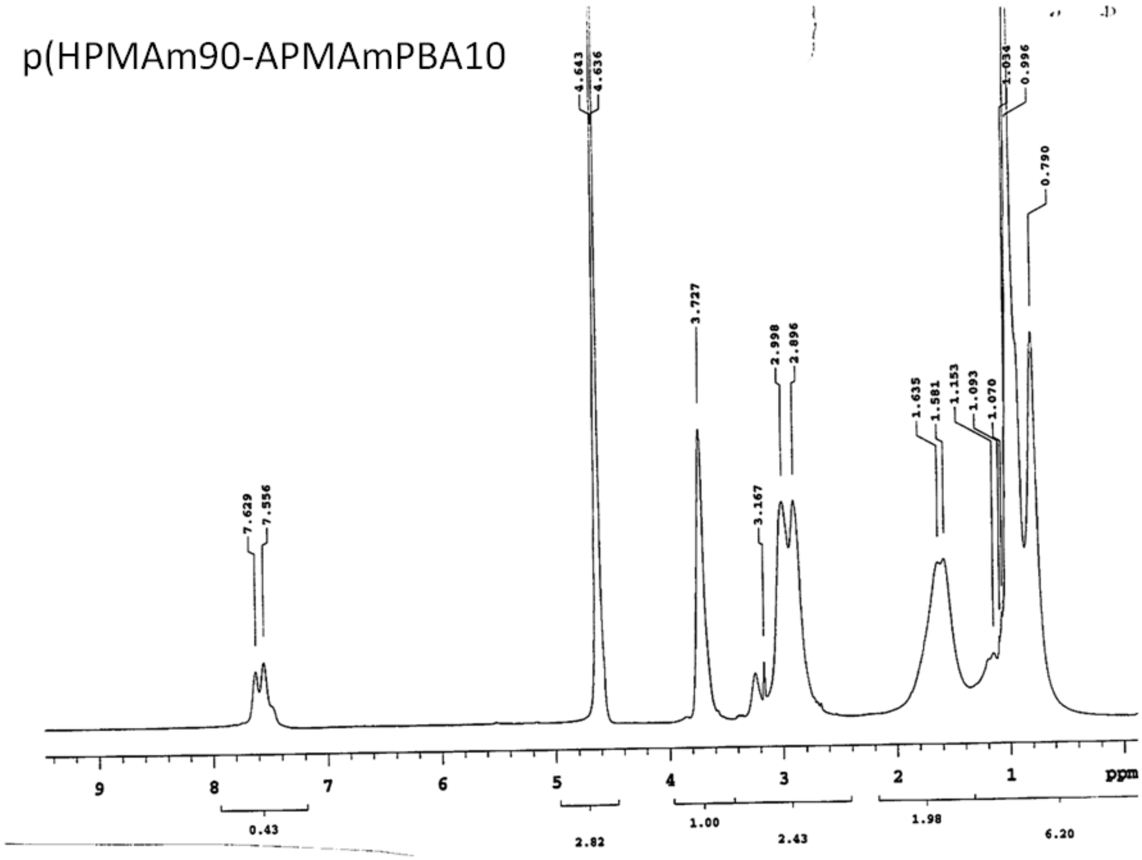

Figure S6 NMR Spectra for p(HPMA$_{90}$-APMAm PBA$_{10}$)