Determination of Monomer Reactivity Ratios for Copolymerizations of Methacrylic Acid with Poly(ethylene glycol)Monomethacrylate

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ABSTRACT: Self-associating copolymers of methacrylic acid (MAA) with poly(ethylene glycol)monomethacrylate (PEGMA) were prepared by free radical copolymerization of MAA with PEGMA using dispersion polymerization in D_2O, or solution polymerization in a 50/50 ethanol–D_2O mixture. These copolymers have been studied as components of reversible hydrogels[1] and in medical applications.[2] In order to understand the relationship between the copolymer structure and its performance, it is important to determine the sequence distribution of the copolymer. The copolymer architecture is determined by the reactivity ratios and integrated instantaneous feed compositions. The reactivity ratios were determined using the first-order Markov method[3] by running a series of reactions at various initial monomer ratios and determining the monomer incorporation into the copolymer as a function of time, via ^1H nuclear magnetic resonance. The reactivity ratios for dispersion copolymerizations of MAA with PEGMA in water were determined to be $r_1 = 1.03$ and $r_2 = 1.02$, whereas solution copolymerization in 50/50 EtOH–H_2O gave reactivity ratios of $r_1 = 2.0$ and $r_2 = 3.6$. These results show that the reactivity ratios and copolymer architecture are influenced by the solvent system. © 1998 John Wiley & Sons, Inc. J Appl Polym Sci 68: 1019–1025, 1998

Key words: reactivity ratios; methacrylic acid; poly(ethylene glycol)monomethacrylate; sequence length distributions

INTRODUCTION

Copolymers prepared by free radical polymerization can form in four commonly accepted structures,[3] including a statistical, or random, copolymer; an alternating copolymer; a block copolymer; or a graft copolymer. The structure of a copolymer is largely determined by the reactivity ratios of the two monomers, r_1 and r_2, which relate the preference of a monomer to reacting with itself or with the second monomer. The reactivity ratios can be calculated using the integrated method.[3–8]

During copolymerization the monomers, M_1 and M_2, can either add to themselves or to the other propagating species. The monomer addition equations, in the case where there are only two monomers, are as follows.

$$M_1^* + M_1 \overset{k_{11}}{\Rightarrow} M_1^* \quad (1)$$

$$M_1^* + M_2 \overset{k_{12}}{\Rightarrow} M_2^* \quad (2)$$

$$M_2^* + M_1 \overset{k_{21}}{\Rightarrow} M_1^* \quad (3)$$

$$M_2^* + M_2 \overset{k_{22}}{\Rightarrow} M_2^* \quad (4)$$

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According to the method of Fineman and Ross,[4] at steady state, the relationship between consumption of monomers 1 and 2 is

$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1](r_1[M_1] + [M_2])}{[M_2]([M_1] + r_2[M_2])} \quad (5)$$

Where the following assumptions were made,

$$\text{Steady state: } k_{21}[M_2^*][M_1] = k_{12}[M_1^*][M_2]$$

and

$$\frac{d[M_i^*]}{dt} = 0$$

The type of copolymer formed can be determined from the reactivity ratios. If $r_1 = r_2 = 1$, then the two monomers will have equal reactivities towards either propagating species and the copolymer will have the same overall composition as that of the feed, but the distribution of each monomer in the backbone will be random. If r_1 is much larger than r_2 but their product is 1, then a copolymer rich in monomer one, but with random placement of the monomer, will be formed. If $r_1 = r_2 = 0$, then the monomers will enter the copolymer in an alternating arrangement, irrespective of the initial monomer feed. If $r_1 \gg r_2$, or vice versa, and their product larger than 1, then the reaction will proceed as the homopolymerization of monomer one until it is consumed and then the homopolymerization of monomer two. Finally, if both r_1 and r_2 are greater than 1, the copolymer formed tends to be a block copolymer.

The copolymers of methacrylic acid with poly(ethylene glycol)monomethacrylate (PEGMA) can form intramolecular hydrogen bonded complexes, which exhibit reversible precipitation in water.[1,2] Intramolecular complexes allow for a stable collapsed colloidal copolymer at acidic pH, which exhibits latex-like viscosity. The complexes can be disrupted by increasing the pH to give a viscous solution. This pH-dependent viscosity is desired so that the copolymer can be handled easily during formulation then thickened by increasing the pH.

The use of this approach is dependent on the ability to form one to one intramolecular complexes between the acid backbone and the ethylene oxide side chains in the copolymer. Ideally, in order to do this, the average poly(methacrylic acid) (PMAA) block length should roughly correlate to the average poly(ethylene glycol) (PEG) block. A more random copolymer would be expected to allow for the above conditions to be more readily met. Block copolymers (especially PEGMA blocks) would reduce the efficiency of intramolecular complex formation. Homopolymers of PEGMA may form complexes with PMAA but would not form intramolecular complexes. The relative propensity for random versus block copolymer formation can be determined from the reactivity ratios.

Additional information can be obtained by knowing the sequence length distributions for the copolymer. The sequence length distributions allow one to determine if intramolecular bonding can readily occur between the ethylene oxide side chains and the acid. Ideally, the best copolymer would be one such that the length between the PEGMA units would allow room for the PEGMA side chain to hydrogen bond to the adjacent acid block in the copolymer chain. The sequence length distribution is a statistical representation of the probability of monomer one being attached to monomer one and monomer two being attached to monomer two. The distribution of the sequence lengths are determined by using the r_1 and r_2 information along with the following equations.

$$(N_1)_j = (p_{11})^{(j-1)}p_{12} \quad (6)$$

$$p_{11} = \frac{r_1}{r_1 + ([M_2]/[M_1])} \quad (7)$$

$$p_{12} = \frac{[M_2]}{r_1[M_1] + [M_2]} \quad (8)$$

where $(N_1)_j$ is the sequence length of monomer one, p_{11} is the probability of monomer one being attached to monomer one, and p_{12} is the probability of monomer one being attached to monomer two. The sequence length distributions allow for the determination of the probability of uninterrupted intramolecular complexes, compared to interrupted intramolecular or intermolecular complexes.

For each copolymerization condition, it was necessary to determine the r values independently because reactivity ratios are dependent on numerous reaction conditions, such as temperature, pH, solvent, and the instantaneous concentration of each of the monomers.[3]

EXPERIMENTAL PROCEDURE

The copolymers were prepared by solution or precipitation polymerization techniques. The polymerizations were done by placing all components in a sealed glass walled reaction vessel. The reaction vessel was then placed in a water bath at 60°C. The vessel remained in the bath the desired time for each copolymerization. Copolymerizations were done with 17% solids and 1% initiator, in either D_2O or a 50/50 wt/wt ethanol–D_2O solution.

The reactivity ratios were determined in the following manner. Initially, a series of runs were done wherein the initial monomer ratios (here represented in moles of acid versus moles of ethylene oxide) were varied. Samples were taken at known time intervals during the reactions. The samples were inhibited with methylhydroquione and neutralized with sodium carbonate. Nuclear magnetic resonance (NMR) samples were prepared from each by diluting the polymer solution with deuterium oxide and adding trace amounts of tetramethyl silyl propane sulfonate (TMS). The spectra were then obtained on a 300 MHz Gemini Varian Fourier transform NMR at 21°C. Using the ^{1}H-NMR integration data, plots were generated of concentration versus time for each monomer by looking at the change in peak areas as a function of time. The fit line for each plot was used to determine $\frac{d[M_1]}{dt}$ and $\frac{d[M_2]}{dt}$ for each copolymerization. Since the initial monomer ratios and the change in monomer concentration versus time was known, r_1 was related to r_2 by rearranging eq. (5) to the following:

$$r_2 = \frac{[M_1]}{[M_2]}\left[\frac{d[M_2]}{d[M_1]}\left\{1 + \frac{r_1[M_1]}{[M_2]}\right\} - 1\right] \quad (9)$$

where $[M_1]$ and $[M_2]$ are the initial concentrations of monomers 1 and 2, respectively.

A plot of r_1 versus r_2 lines for each initial monomer concentration ratio was then generated. The area where the lines intersect contains the true r values. The average values from the plots are then used to determine the sequence length distributions for each monomer in the copolymer.

The sequence length distribution for the ethylene oxide groups in the PEGMA polymer were determined using supercritical fluid chromotography (SFC). The capillary SFC was obtained on a Dionex/Lee Scientific Model 501 SFC equipped with a Valco injector (internal loop volume of 0.2 μL), a SB-Phenyl-50 capillary column (10 m $\times$ 50 μm i.d., 0.25 μm film) fitted with a frit restrictor, a flame ionization detector (375°C), and a PE Nelson Access Chrom 6000 integrator. The mobile phase was carbon dioxide and a linear velocity of

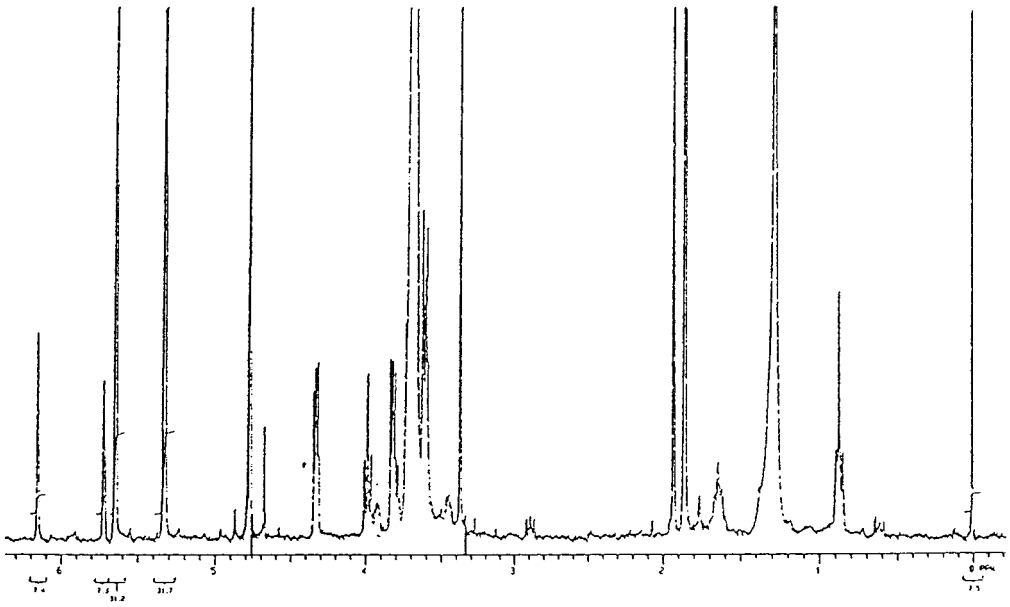

Figure 1 ^{1}H-NMR plot for *co*-PEGMA.

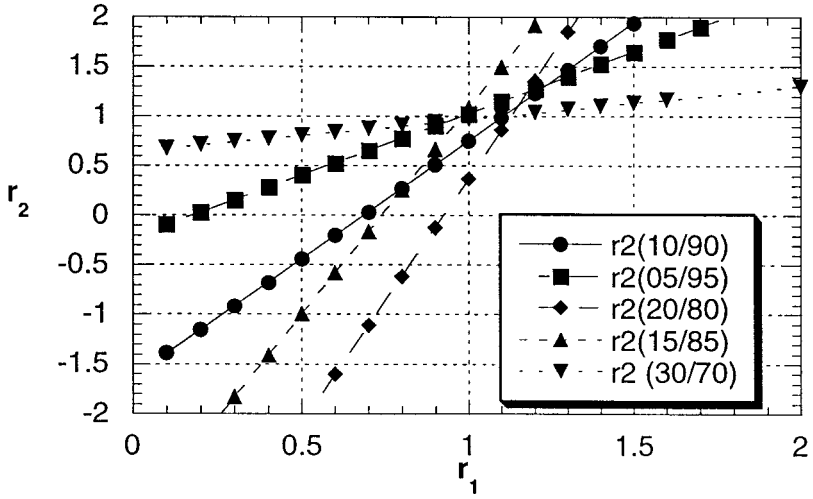

Figure 2 r_2 as a function of r_1 for copolymerizations of MAA and PEGMA in the D_2O system.

2 cm/s was used at an oven temperature of 100°C. A linear density pressure program was used according to the following program: 0.2 g/mL for 10 min, followed by increased pressure at 0.021 g mL^{-1} min^{-1} to 0.76 g/mL, held for 10 min.

RESULTS AND DISCUSSION

The copolymerization of PEGMA with MAA was completed under both aqueous solution and aqueous alcohol solution polymerization conditions to determine the effects of solvent on the reactivity ratios for the copolymerization. Since the peaks found for the acid monomer were in the same region as those for the PEGMA, the samples were neutralized by addition of Na_2CO_3 to the TMS/D_2O solution to enhance resolution in the NMR spectra.

Figure 1 is a representative ^{1}H-NMR spectra for the copolymerization of MAA with PEGMA. TMS was used as a calibration standard and is set to 0 ppm. The MAA peaks are found at 5.3 and 5.65 ppm while the PEGMA peaks are found at 5.75 and 6.15 ppm. These peaks decrease in intensity as the copolymer is formed such that they were not visible after 30 min into the copolymerization.

Figure 2 shows the calculated r_2 values as a function of given r_1 values for varying initial mole ratios of acid to ethylene oxide in the solution copolymerization of MAA and PEGMA. These values were calculated using eq. (9) and the change in monomer concentrations versus time was determined by NMR analysis. The area bounded by the intersection of all of the lines contains the true r values for these reaction conditions. The reactivity ratios are then determined to be $0.98 < r_1 < 1.18$ and $0.97 < r_2 < 1.25$. These values agree well with the values reported in literature for similar copolymerizations.[9,10]

The r values were also determined for the MAA–PEGMA copolymerization with a 50/50 EtOH–D_2O system (Fig. 3). In this case, the r values were determined to be in the range of $1.9 < r_1 < 2.1$ and $3.3 < r_2 < 3.9$. These values are significantly higher than those determined for the pure aqueous system. These reactivity ratios indi-

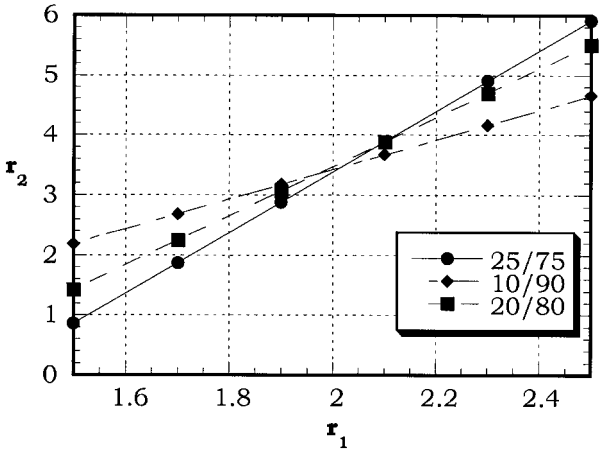

Figure 3 r_2 as a function of r_1 for copolymerizations of MAA and PEGMA in the ethanol–D_2O system.

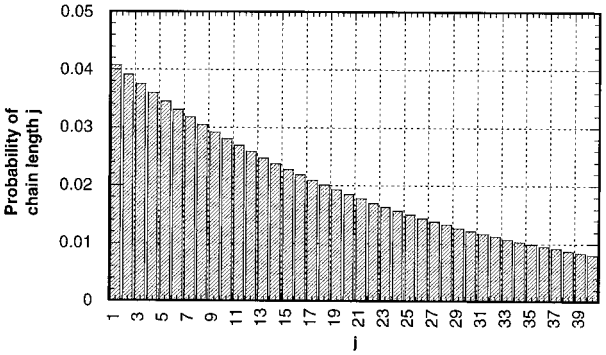

Figure 4 Sequence length distribution for MAA units in the copolymerization of MAA and PEGMA.

cate that in EtOH–D_2O, the reaction essentially proceeds more as a "blocky" copolymerization rather than as a random copolymerization. These solvent effects have been noted for other polymerization systems.[11]

To calculate the sequence length distributions for the MAA–PEGMA copolymerization, we used the values of 1.03 and 1.02 for r_1 and r_2, respectively. These values were chosen as they fell in the middle of the region bounded by curves in Figure 2. These values are approaching the values for an ideal random copolymerization, that is, $r_1 = r_2 = 1$. In this case, the copolymer formed would have the same overall composition as the feed, but the distribution of each monomer in the backbone would be random. This is an advantage because it allows for the tailoring of the copolymer by adjustments in the monomer ratios in the initial feed solutions. For example, to produce a copolymer that is random in nature, but which has a backbone more concentrated in M_1, then the initial feed could be adjusted to yield the desired concentration.

Figure 4 shows the number-average sequence length for MAA if copolymerized with PEGMA, under solution conditions, initial mole ratios of 95/05 MAA–PEGMA, and with $r_1 = 1.03$ and $r_2 = 1.02$. The bars show the probability of having MAA segments of the given monomer unit length carried to a unit length of 40 MAA segments.

Figure 5 shows the number-average sequence length distribution for the ethylene oxide groups in the PEGMA ($n = 1000$). This shows the average length of the EO groups $(—CH_2—CH_2—O)_n—$ in the PEGMA polymer. This is determined from the PEGMA itself and is not dependent on the copolymerization of the PEGMA with any other monomer. Note that the EO chain lengths range from 14 to 32 units long.

Figure 6 shows the number-average sequence length distributions for both MAA and EO when copolymerizing MAA and PEGMA 1000 with an initial mole ratio of 1 mol MAA to 1 mol EO and using the reactivity ratios previously determined. This distribution shows that the probability of the EO having a length of 16 to 29 units is much higher than that of the MAA. This will lead to a high probability of interrupted intramolecular or intermolecular complexes because many of the EO sequences are longer than those of the MAA and the EO will not have sufficient room to form intramolecular complexes.

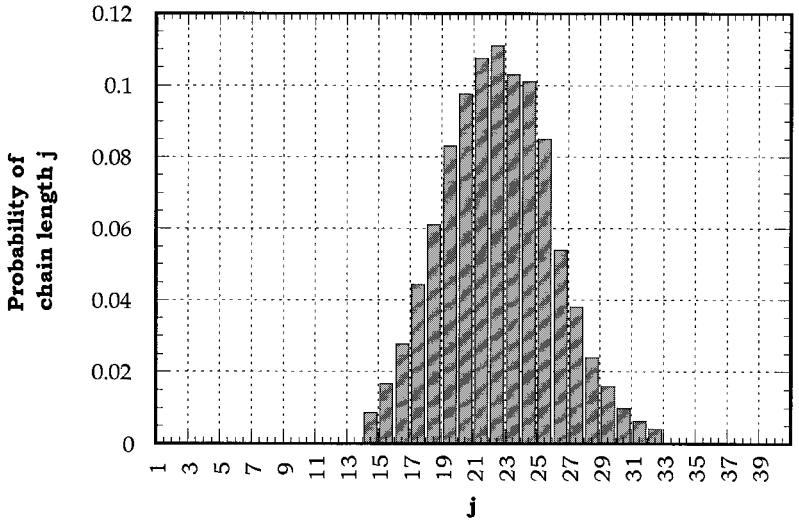

Figure 5 Sequence length distribution for PEGMA (1000).

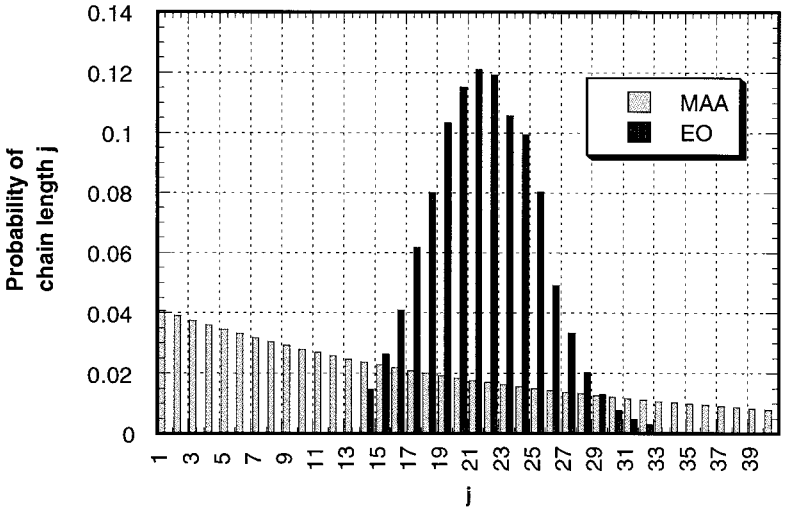

Figure 6 Sequence length distribution for MAA and EO in the copolymerization of MAA and PEGMA.

In Figure 7, the probability of forming a given length of MAA monomer units is shown. Additionally, the EO curve shows the summation of all EO probabilities up to and including that length, normalized to the acid probabilities. The area under the curve formed by the acid, minus the area covered by the EO, is the total probability that the copolymer formed has too short of acid chain lengths to accommodate the uninterrupted intramolecular complexation with the EO groups. However, the area where the probabilities are equal (total EO probabilities and acid chain length probabilities) is where there would be adequate room in the copolymer backbone for the EO to form all one-to-one, uninterrupted intramolecular complexes with the acids. The area of the plots where the EO totals are present, but where they are less than the probability of the acid chain length formation, is where the copolymer will form a mixture of uninterrupted and interrupted intramolecular complexations as well as intermolecular complexations.

Therefore, there could not be uninterrupted intramolecular complexation in the copolymer chain segments where the MAA segments were less than 15 units long. When the MAA segments are

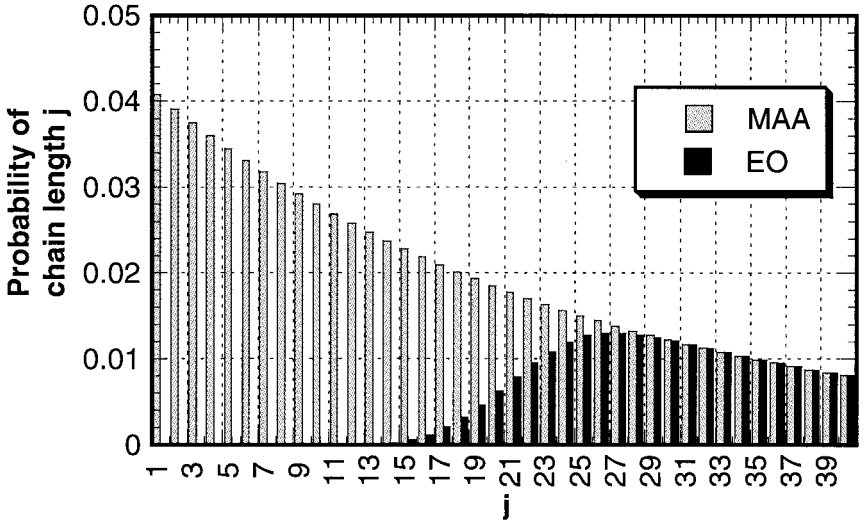

Figure 7 Sequence length distribution for MAA and PEGMA (1000).

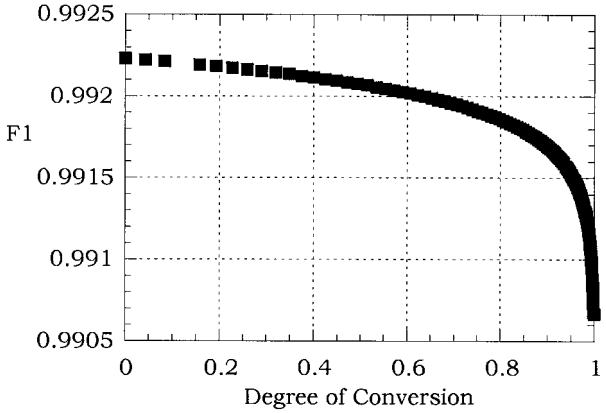

Figure 8 Mole concentration of MAA as a function of total copolymer.

between 15 and approximately 28 units long, a fraction of the complexations could be uninterrupted intramolecular complexations, but the remaining EO groups would have to complex with neighboring copolymer chains or distant sequences in the copolymer chain. In the region where the acid segments are longer than 27 units, the acid segments are available to the entire length of the PEGMA chain, and there is the highest probability for uninterrupted intramolecular complexations.

Figure 8 shows the concentration of monomer 1 in the polymer as a function of the degree of conversion during the solution copolymerization of MAA and PEGMA. These values were calculated using the method of Dionisio and O'Driscoll[12] and the reactivity ratios previously reported. This shows that the copolymer formed with MAA–PEGMA is a uniform copolymer with a high concentration of MAA.

CONCLUSION

Self-associating copolymers of MAA with PEGMA were prepared by free radical copolymerization of MAA with PEGMA. The copolymers were prepared using dispersion polymerization in D_2O, or solution polymerization in a 50/50 ethanol–D_2O mixture. The reactivity ratios for these copolymerizations were determined by running a series of reactions at various initial monomer ratios and determining the monomer incorporation into the copolymer as a function of time, via ^{1}H-NMR. The reactivity ratios for dispersion copolymerizations of MAA with PEGMA in D_2O were determined to be $r_1 = 1.03$ and $r_2 = 1.02$. Solution copolymerization of MAA with PEGMA in 50/50 EtOH–D_2O gave reactivity ratios of $r_1 = 2.0$ and $r_2 = 3.6$. These results show that the reactivity ratios and copolymer architecture are influenced by the solvent system.

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