Supporting Information

A Robotic Approach to Polymerisation Kinetics: A Case Study on Copolymerisation Parameter Estimation

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1. Experimental Section

Materials

Butyl methacrylate (99%), Butyl acrylate (99%), Styrene (99%), Methyl methacrylate (99%), and Glycidyl methacrylate (97%) were purchased from Sigma-Aldrich and passed through a column of Aluminium oxide to remove inhibitors before use. 2,2′-Azobis(2-methylpropionitrile) (AIBN, 12 wt. % in acetone, Sigma-Aldrich) was recrystallized twice and used. Toluene (Merck), N,N-Dimethylformamide (Univar) and Chloroform-D (D, 99.8%, Cambridge Isotope Laboratories) were used as received.

Equipment

HTP Reactor Method:

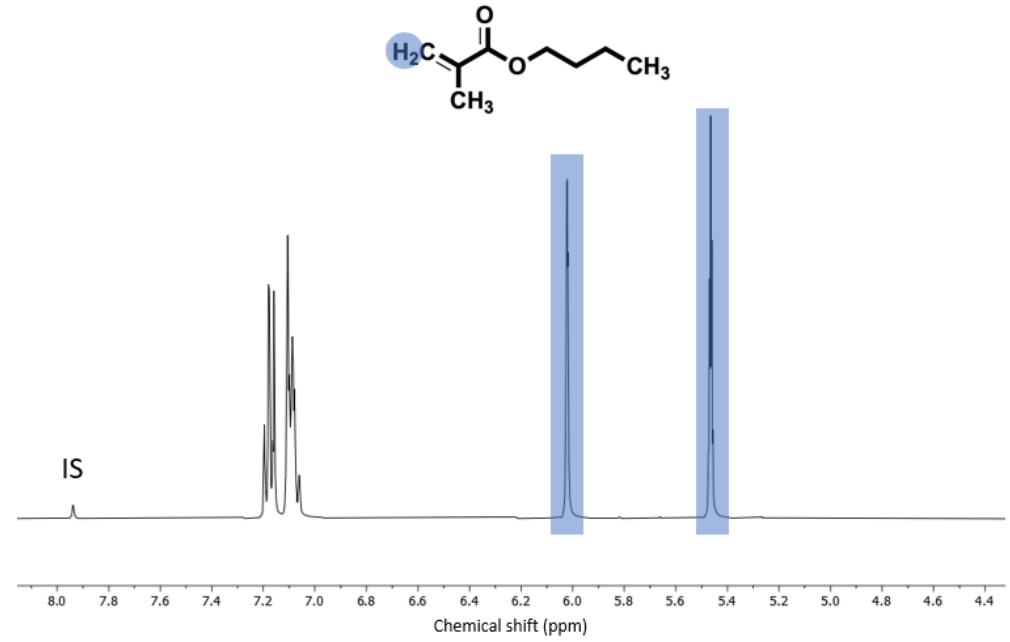
A Para-Dox Temperature Controlled Reactor (TCR) (Analytical Sales and Services, Inc.) was used for polymerisation experiments. A heater circulator (VEVOR) containing water heated to 75 ℃ was used to circulate hot water through the TCR. A Biosan PST-100HL Plate Shaker-Thermostat was used for agitation during polymerisation with shaking at 400 rpm. An Opentrons OT-2 liquid handling robot equipped with 11 deck slots was used for all liquid transfers and automation workflows, via Python code executed in PyCharm IDE Community Edition.

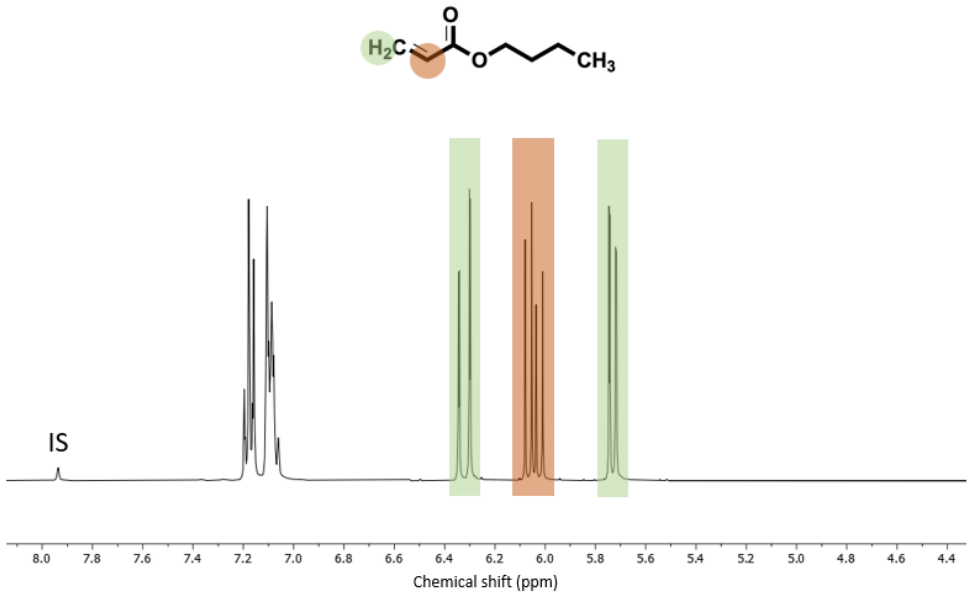
96-Well Plate Method:

A Greiner polypropylene 96-well plate was used for polymerization experiments. Nunc™ Aluminium Seal from Thermo Fisher was used to cover and seal well-plates. A Biosan PST-100HL Plate Shaker-Thermostat was used for polymerization at 70 ℃ with shaking at 250 rpm. An Opentrons OT-2 liquid handling robot equipped with 11 deck slots was used for all liquid transfers and automation workflows via Python code executed in PyCharm IDE Community Edition.

Characterization:

A 400 MHz Bruker Avance III Nuclear Magnetic Resonance Spectrometer was used for NMR analysis. To determine monomer conversion, 30 µL of crude polymer aliquots were automatically dispensed and mixed with 600 µL Chloroform-D. Total monomer conversion (X) was calculated by comparing the integration of the vinyl monomer peaks (BMA: δ ~5.40-5.50 ppm, BA: δ ~6.20-6.40 ppm, St: δ ~5.10-5.20 ppm, MMA: δ ~5.40-5.50 ppm, GMA: δ ~5.55-5.65 ppm) for t_0 and t_1 samples, using DMF as internal standard. As an example, vinyl peaks of monomers BMA and BA are shown below.





To calculate monomer conversion for mixtures of BMA and BA, vinyl peaks at δ ~5.40-5.50 ppm (BMA) and δ ~6.20-6.40 ppm (BA) are integrated with respect to the internal standard for two samples at t_0 and t_{2h}. Values obtained at this stage are subsequently used in the excel file provided by IUPAC to prepare datasets for reactivity ratio measurement.

General synthesis protocol:

For copolymerisation of given monomers M_1 and M_2, a total monomer concentration of 4 M was used with a 400 µL total reaction volume. Copolymerisation reaction mixtures were prepared and performed at different comonomer ratio and varying AIBN initiator wt. % with respect to total monomer mass. For example, for a copolymerisation reaction of BMA and BA with equal molar ratio and 1 wt. % AIBN

with a total reaction volume of 400 μL, the following were added to the reaction mixture: 0.8 mmol BMA, 0.8 mmol BA, 0.016 mmol AIBN, and 158 μL reaction solvent (constituting 5 vol.% DMF in Toluene, with DMF added in as an internal standard for NMR analysis).

Use of Contour for the prediction of reactivity ratios:

In order to perform calculations using the Contour program,[1] a *csv* file was prepared for each monomer pair, including four columns of data including initial monomer-1 fraction (f_{10}), total monomer conversion (X), cumulative copolymer composition (F_1), and the calculated error in F_1. An excel spreadsheet provided by the IUPAC working group was used to prepare the datapoints for the .csv file, which is also provided in the supporting information of this work. (Monomer composition values at t_1 (f_1) were calculated using the integration values for both monomers at t_1.)

2. Supporting Figures

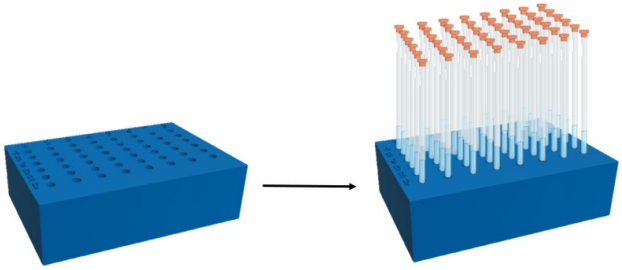


Figure S 1. 3D design of the NMR tube holder.

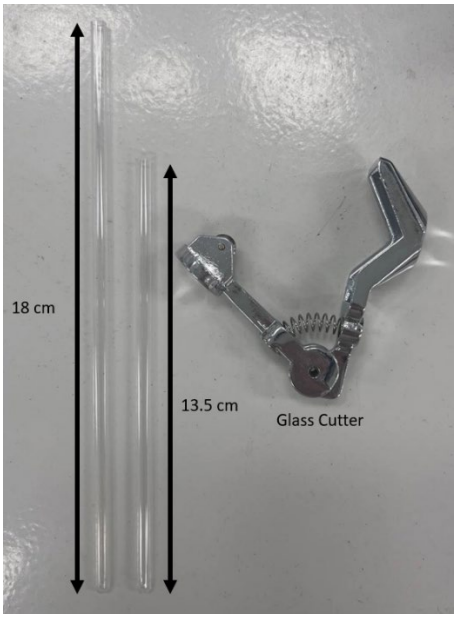


Figure S 2. Comparison between the length of an original NMR tube (left) and the altered NMR tube (centre) when a glass cutter (right) is used to cut excess length to ensure that NMR tubes fit inside the OT-2 robot when loaded onto the NMR tube holder (Figure S1).

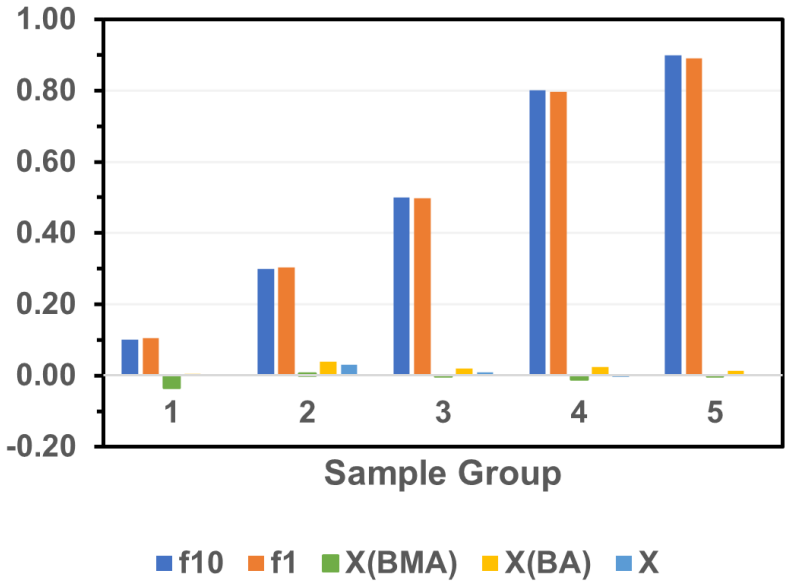


Figure S 3. Visual assessment of the evaporation of BMA and BA monomers from the reactor when exposed to 75 °C in a plate shaker. Monomers were mixed at the ratios and scale used for copolymerisation experiments as set out in Table 1, while no AIBN was added. The change in monomer fraction as well as conversion are negligible for all groups, indicating no evaporation of monomers.

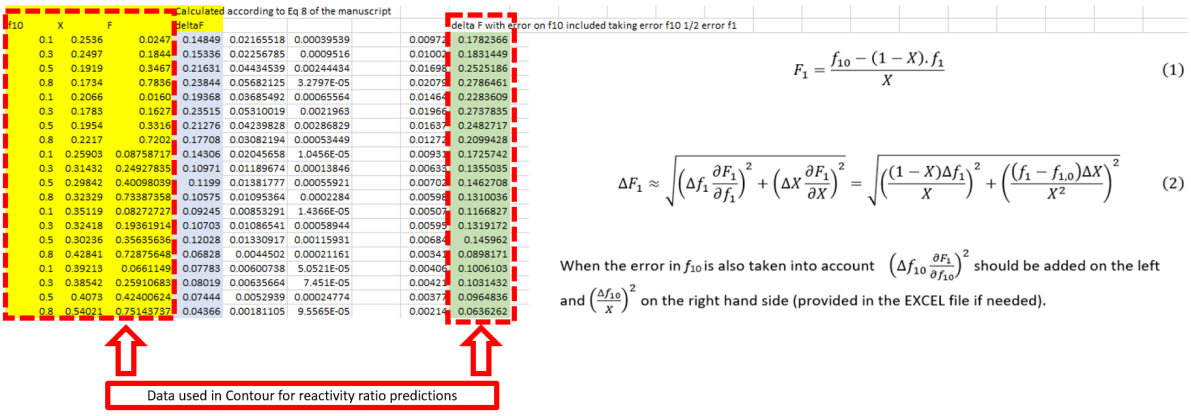


Figure S 4. Snapshot of the excel worksheet provided by the IUPAC working group which was used in this work to calculate input data for the Contour program. The highlighted columns are used as input data saved as a .csv file in Contour for the prediction of reactivity ratios.

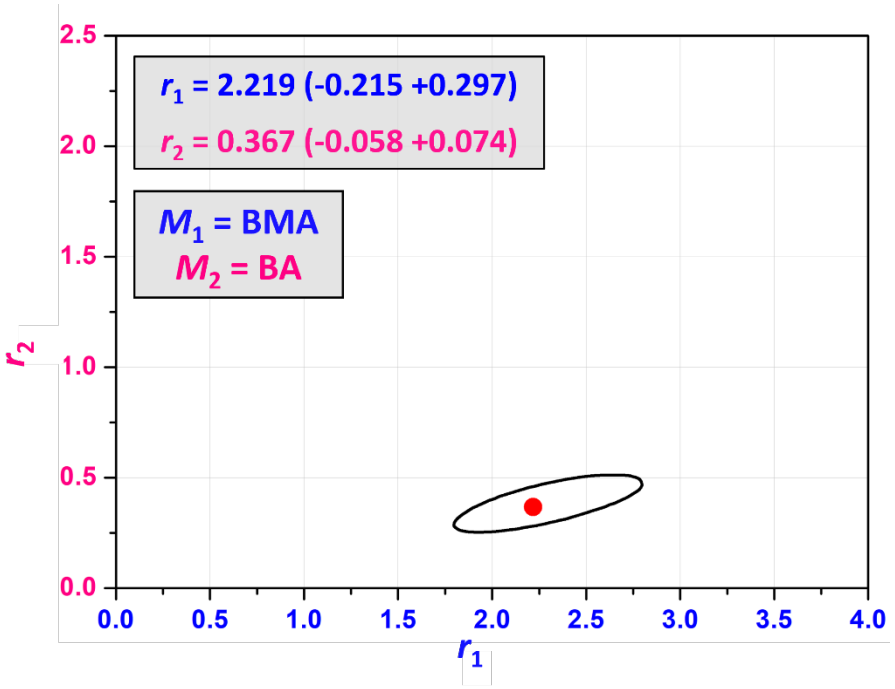


Figure S 5. 95% JCI plot obtained from Contour for BMA-BA with calculations conducted using given f_{10} values and an absolute error of 0.005 or 0.05 for X and f_1.

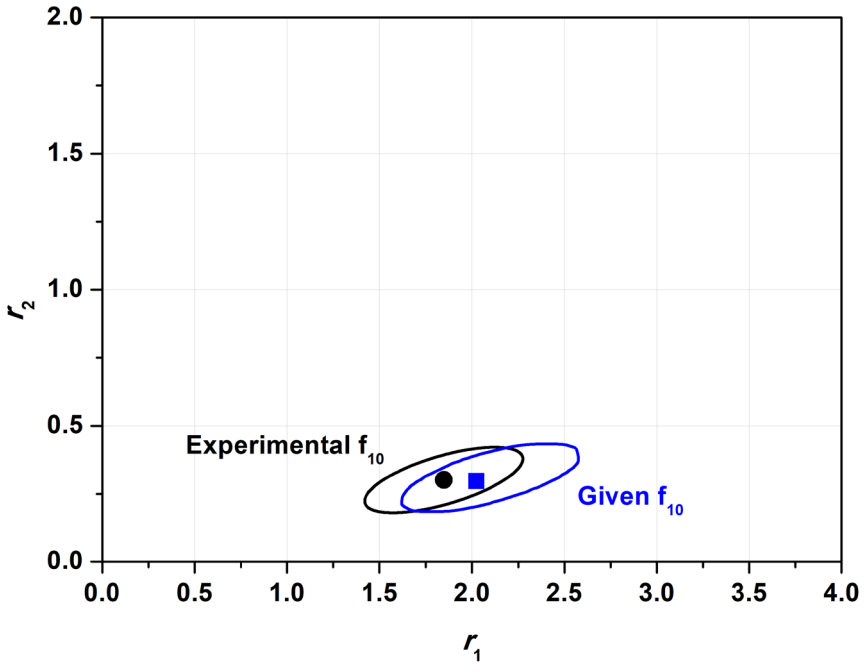


Figure S 6. Comparison between given and experimental f_{10} in the final prediction of reactivity ratios for BMA-BA in Contour for experiments shown in Table 1.

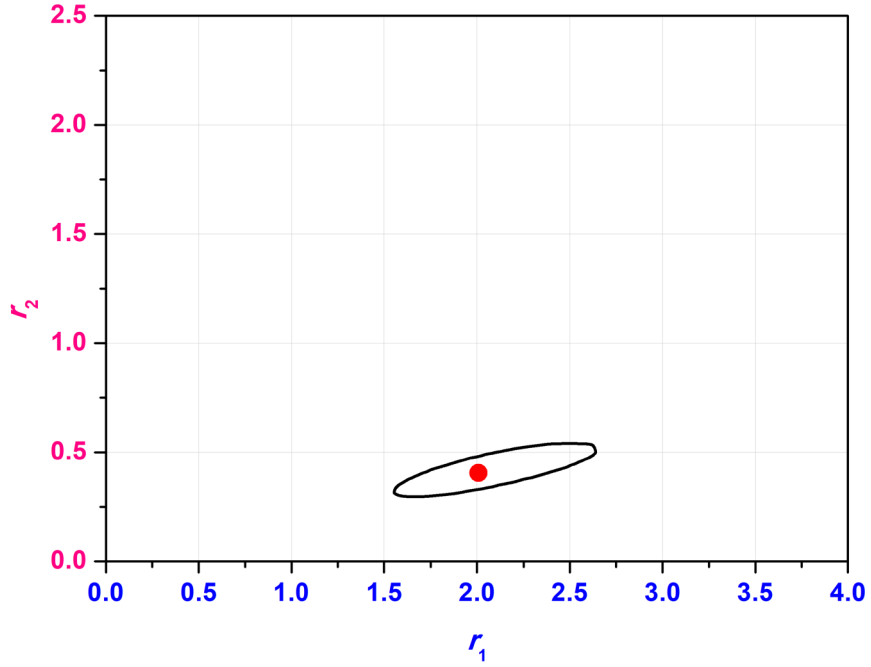


Figure S 7. 95% JCI for BMA-BA at 30 min.

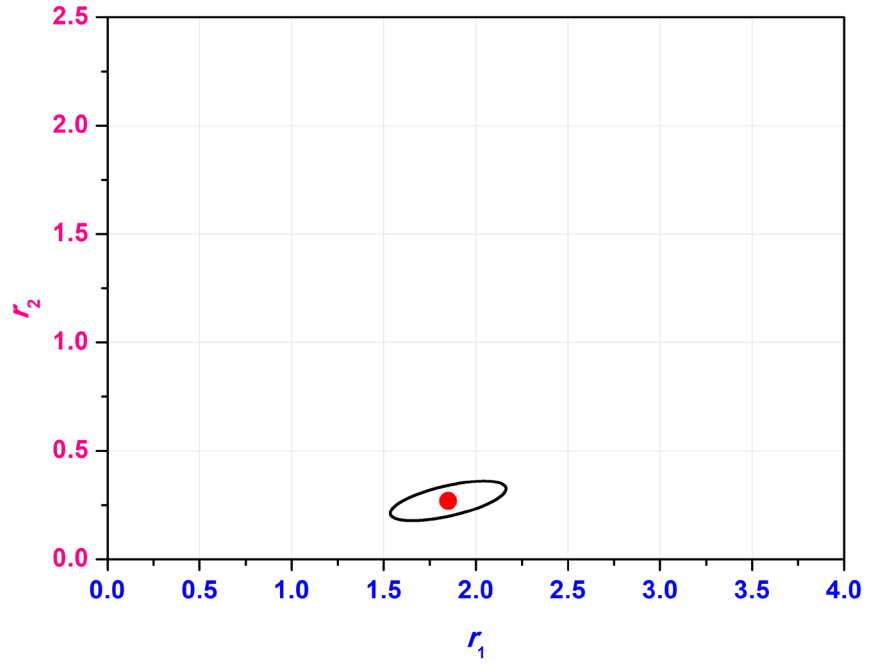


Figure S 8. 95% JCI for 45-datapoint set of BMA-BA at 2 h.

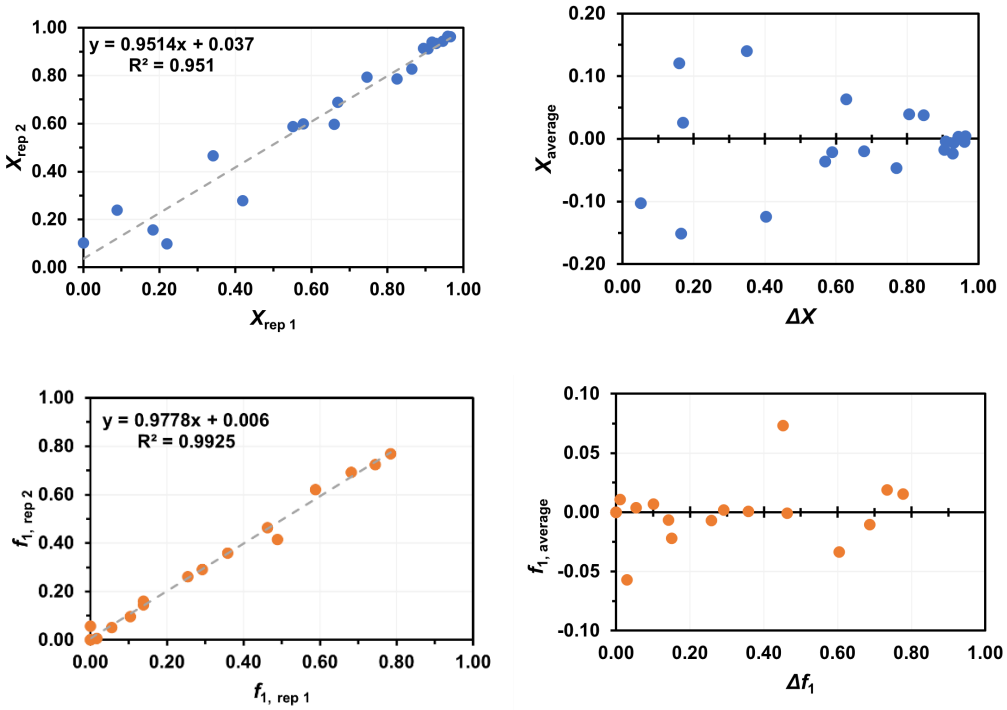


Figure S 9. Comparison of X and f_1 values between replicate BMA-BA polymerisations in randomised wells. Each experiment was conducted under the same reaction conditions on different days, in different and re-randomised wells identified by their unique index. Reactions were conducted for 2 h at 75 °C. Left panels: scatter plots of X (top) and f_1 (bottom) from rep 1 vs rep 2, with linear regression fits shown. Right panels: residual plots showing average X vs ΔX (top) and average f_1 vs Δf_1 (bottom).

3. Supporting Tables

Table S 1. Repeatability results for the copolymerisations of BMA-BA. Each row represents consecutive experiments conducted under the same reaction conditions, but in different and re-randomised wells identified by their unique index. Reactions were conducted for 2 h at 75 °C, each on different days.

$Index_1$	$Index_2$	AIBN wt.%[a]	f_{10}[b]	$f_{1,1}$[c]	$f_{1,2}$[c]	X_1[d]	X_2[d]
44	39	0.0005	0.1	0.10	0.10	0.00	0.10
0	23	0.0005	0.3	0.25	0.26	0.22	0.10
39	9	0.0005	0.5	0.46	0.46	0.18	0.16
35	7	0.0005	0.8	0.78	0.77	0.09	0.24
45	3	0.0025	0.1	0.02	0.01	0.67	0.69
1	25	0.0025	0.3	0.14	0.15	0.55	0.59
40	5	0.0025	0.5	0.36	0.36	0.34	0.47
46	40	0.0025	0.8	0.74	0.72	0.42	0.28
29	1	0.005	0.1	0.00	0.00	0.89	0.91
11	33	0.005	0.3	0.06	0.05	0.75	0.79
34	45	0.005	0.5	0.29	0.29	0.58	0.60
26	32	0.005	0.8	0.68	0.69	0.66	0.60
42	35	0.01	0.1	0.00	0.00	0.92	0.94
17	21	0.01	0.3	0.00	0.00	0.93	0.93
33	24	0.01	0.5	0.14	0.16	0.86	0.83
8	2	0.01	0.8	0.59	0.62	0.83	0.79
38	15	0.02	0.1	0.00	0.00	0.97	0.96
31	19	0.02	0.3	0.00	0.00	0.96	0.96
32	16	0.02	0.5	0.00	0.06	0.95	0.94
22	27	0.02	0.8	0.49	0.42	0.91	0.91

[a] AIBN wt.% with respect to total monomer mass, [b] initial molar ratio of BMA as given in the reaction recipe, [c] molar ratio of BMA at t_1 calculated from NMR, [d] overall monomer conversion calculated from NMR.

Table S 2. Compiled data of all BMA-BA experiments. Different cell shades represent different experiment sets conducted on different days. Values are reported as obtained from NMR analysis, and negative datapoints are deleted from the final dataset used in Contour for reactivity ratio calculations.

Variant	Reaction Time	AIBN wt%	$f_{10,\,given}$	f_1	X	F_1
01	2 h	0.05	0.10	0.10	0.00	-
02	2 h	0.05	0.30	0.25	0.22	0.46
03	2 h	0.05	0.50	0.46	0.18	0.67
04	2 h	0.05	0.80	0.78	0.09	0.96
05	2 h	0.25	0.10	0.02	0.67	0.14
06	2 h	0.25	0.30	0.14	0.55	0.43
07	2 h	0.25	0.50	0.36	0.34	0.77
08	2 h	0.25	0.80	0.74	0.42	0.88
09	2 h	0.50	0.10	0.00	0.89	0.11
10	2 h	0.50	0.30	0.06	0.75	0.38
11	2 h	0.50	0.50	0.29	0.58	0.65
12	2 h	0.50	0.80	0.68	0.66	0.86
13	2 h	1.00	0.10	0.00	0.92	0.11
14	2 h	1.00	0.30	0.00	0.93	0.32
15	2 h	1.00	0.50	0.14	0.86	0.56
16	2 h	1.00	0.80	0.59	0.83	0.84
17	2 h	2.00	0.10	0.00	0.97	0.10
18	2 h	2.00	0.30	0.00	0.96	0.31
19	2 h	2.00	0.50	0.00	0.95	0.54
20	2 h	2.00	0.80	0.49	0.91	0.83
21	2 h	0.05	0.10	0.10	0.10	0.13
22	2 h	0.05	0.30	0.26	0.10	0.65

23	2 h	0.05	0.50	0.46	0.16	0.70
24	2 h	0.05	0.80	0.77	0.24	0.90
25	2 h	0.25	0.10	0.01	0.69	0.14
26	2 h	0.25	0.30	0.15	0.59	0.41
27	2 h	0.25	0.50	0.36	0.47	0.66
28	2 h	0.25	0.80	0.72	0.28	1.00
29	2 h	0.50	0.10	0.00	0.91	0.11
30	2 h	0.50	0.30	0.05	0.79	0.36
31	2 h	0.50	0.50	0.29	0.60	0.64
32	2 h	0.50	0.80	0.69	0.60	0.87
33	2 h	1.00	0.10	0.00	0.94	0.11
34	2 h	1.00	0.30	0.00	0.93	0.32
35	2 h	1.00	0.50	0.16	0.83	0.57
36	2 h	1.00	0.80	0.62	0.79	0.85
37	2 h	2.00	0.10	0.00	0.96	0.10
38	2 h	2.00	0.30	0.00	0.96	0.31
39	2 h	2.00	0.50	0.06	0.94	0.53
40	2 h	2.00	0.80	0.42	0.91	0.84
41	30 min	0.05	0.10	0.10	0.00	-
42	30 min	0.05	0.30	0.29	0.00	-
43	30 min	0.05	0.50	0.48	0.00	-
44	30 min	0.05	0.80	0.79	0.05	0.98
45	30 min	0.25	0.10	0.09	0.08	0.21
46	30 min	0.25	0.30	0.27	0.13	0.50
47	30 min	0.25	0.50	0.46	0.13	0.78

48	30 min	0.25	0.80	0.77	0.16	0.95
49	30 min	0.50	0.10	0.06	0.48	0.15
50	30 min	0.50	0.30	0.25	0.29	0.43
51	30 min	0.50	0.50	0.44	0.24	0.67
52	30 min	0.50	0.80	0.77	0.25	0.90
53	30 min	1.00	0.10	0.04	0.58	0.14
54	30 min	1.00	0.30	0.17	0.45	0.46
55	30 min	1.00	0.50	0.40	0.50	0.61
56	30 min	1.00	0.80	0.76	0.32	0.89
57	30 min	2.00	0.10	0.03	0.71	0.13
58	30 min	2.00	0.30	0.13	0.61	0.40
59	30 min	2.00	0.50	0.34	0.57	0.62
60	30 min	2.00	0.80	0.74	0.45	0.87
61	2 h	0.05	0.20	0.20	0.00	-
62	2 h	0.05	0.40	0.37	0.02	-
63	2 h	0.05	0.60	0.56	0.16	0.80
64	2 h	0.05	0.70	0.69	0.04	0.90
65	2 h	0.05	0.90	0.90	0.07	0.94
66	2 h	0.25	0.20	0.05	0.69	0.27
67	2 h	0.25	0.40	0.21	0.60	0.53
68	2 h	0.25	0.60	0.48	0.47	0.74
69	2 h	0.25	0.70	0.59	0.52	0.80
70	2 h	0.25	0.90	0.88	0.48	0.92
71	2 h	0.50	0.20	0.03	0.85	0.23
72	2 h	0.50	0.40	0.11	0.71	0.52

73	2 h	0.50	0.60	0.38	0.70	0.70
74	2 h	0.50	0.70	0.55	0.66	0.78
75	2 h	0.50	0.90	0.85	0.68	0.92
76	2 h	1.00	0.20	0.00	0.92	0.22
77	2 h	1.00	0.40	0.00	0.90	0.45
78	2 h	1.00	0.60	0.19	0.90	0.64
79	2 h	1.00	0.70	0.45	0.77	0.78
80	2 h	1.00	0.90	0.80	0.75	0.93
81	2 h	2.00	0.20	0.00	0.98	0.20
82	2 h	2.00	0.40	0.00	0.96	0.42
83	2 h	2.00	0.60	0.16	0.94	0.63
84	2 h	2.00	0.70	0.15	0.94	0.74
85	2 h	2.00	0.90	0.92	0.92	0.90

Table S 3 Swapping the indexing of monomers in BMA-BA case with BA assigned as M_1 (to be compared with data in Table 1).

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.90	0.91	0.90	0.10	0.87
02	0.05	0.70	0.71	0.74	0.10	0.35
03	0.05	0.50	0.52	0.54	0.16	0.30
04	0.05	0.20	0.22	0.23	0.24	0.10
05	0.25	0.90	0.90	0.99	0.69	0.86
06	0.25	0.70	0.73	0.85	0.59	0.59
07	0.25	0.50	0.51	0.64	0.47	0.34
08	0.25	0.20	0.22	0.28	0.28	0.00
09	0.50	0.90	0.91	1.00	0.91	0.89
10	0.50	0.70	0.71	0.95	0.79	0.64
11	0.50	0.50	0.50	0.71	0.60	0.36
12	0.50	0.20	0.22	0.31	0.60	0.13
13	1.00	0.90	0.90	1.00	0.94	0.89
14	1.00	0.70	0.70	1.00	0.93	0.68
15	1.00	0.50	0.51	0.84	0.83	0.43
16	1.00	0.20	0.20	0.38	0.79	0.15
17	2.00	0.90	0.90	1.00	0.96	0.90
18	2.00	0.70	0.70	1.00	0.96	0.69
19	2.00	0.50	0.51	0.94	0.94	0.47
20	2.00	0.20	0.20	0.58	0.91	0.16

Table S 4. List of experiments designed for the copolymerization of BMA (M_1) and St (M_2) at different BMA molar ratios (f_{10}) and AIBN wt.%. All experiments are performed at 70 °C for 2 h.

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.10	0.11	0.11	0.07	-
02	0.05	0.30	0.29	0.31	0.13	0.28
03	0.05	0.50	0.48	0.50	0.08	0.47
04	0.05	0.80	0.78	0.80	0.19	0.79
05	0.25	0.10	0.10	0.10	0.20	0.09
06	0.25	0.30	0.29	0.30	0.25	0.29
07	0.25	0.50	0.49	0.50	0.26	0.49
08	0.25	0.80	0.81	0.83	0.27	0.72
09	0.50	0.10	0.10	0.10	0.31	0.11
10	0.50	0.30	0.30	0.30	0.33	0.30
11	0.50	0.50	0.50	0.51	0.37	0.49
12	0.50	0.80	0.80	0.83	0.35	0.75
13	1.00	0.10	0.10	0.08	0.49	0.13
14	1.00	0.30	0.30	0.30	0.27	0.31
15	1.00	0.50	0.50	0.51	0.38	0.49
16	1.00	0.80	0.79	0.84	0.46	0.76
17	2.00	0.10	0.10	0.10	0.28	0.11
18	2.00	0.30	0.30	0.29	0.36	0.32
19	2.00	0.50	0.49	0.51	0.55	0.49
20	2.00	0.80	0.80	0.86	0.57	0.76

Table S 5. List of experiments designed for the copolymerization of St (M_1) and BA (M_2) at different St molar ratios (f_{10}) and AIBN wt.%. All experiments are performed at 70 °C for 2 h.

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.10	0.08	0.08	0.30	0.14
02	0.05	0.30	0.26	0.27	0.29	0.34
03	0.05	0.50	0.45	0.46	0.25	0.49
04	0.05	0.80	0.75	0.74	0.28	0.87
05	0.25	0.10	0.08	0.05	0.32	0.22
06	0.25	0.30	0.27	0.23	0.29	0.43
07	0.25	0.50	0.47	0.43	0.34	0.61
08	0.25	0.80	0.76	0.73	0.18	0.92
09	0.50	0.10	0.07	0.03	0.66	0.19
10	0.50	0.30	0.25	0.20	0.39	0.47
11	0.50	0.50	0.46	0.42	0.44	0.60
12	0.50	0.80	0.75	0.74	0.41	0.85
13	1.00	0.10	0.07	0.06	0.64	0.14
14	1.00	0.30	0.26	0.15	0.50	0.41
15	1.00	0.50	0.46	0.40	0.45	0.59
16	1.00	0.80	0.76	0.73	0.36	0.84
17	2.00	0.10	0.05	0.05	0.94	0.11
18	2.00	0.30	0.27	0.09	0.64	0.41
19	2.00	0.50	0.47	0.36	0.51	0.60
20	2.00	0.80	0.76	0.74	0.42	0.88

Table S 6. List of experiments designed for the copolymerization of St (M_1) and MMA (M_2) at different St molar ratios (f_{10}) and AIBN wt.%. All experiments are performed at 70 °C for 2 h.

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.10	0.11	0.09	0.14	0.25
02	0.05	0.30	0.31	0.29	0.13	0.32
03	0.05	0.50	0.51	0.50	0.18	0.58
04	0.05	0.80	0.80	0.80	0.02	0.76
05	0.25	0.10	0.10	0.05	0.29	0.18
06	0.25	0.30	0.30	0.25	0.28	0.40
07	0.25	0.50	0.49	0.47	0.23	0.59
08	0.25	0.80	0.80	0.78	0.16	0.72
09	0.50	0.10	0.11	0.04	0.39	0.22
10	0.50	0.30	0.29	0.23	0.28	0.39
11	0.50	0.50	0.50	0.46	0.27	0.56
12	0.50	0.80	0.80	0.78	0.24	0.76
13	1.00	0.10	0.11	0.00	0.70	0.14
14	1.00	0.30	0.29	0.19	0.50	0.38
15	1.00	0.50	0.50	0.45	0.34	0.56
16	1.00	0.80	0.80	0.78	0.31	0.77
17	2.00	0.10	0.10	0.00	0.94	0.14
18	2.00	0.30	0.30	0.14	0.59	0.36
19	2.00	0.50	0.49	0.41	0.46	0.46
20	2.00	0.80	0.80	0.75	0.36	0.75

Table S 7. List of experiments designed for the copolymerization of GMA (M_1) and BA (M_2) at different GMA molar ratios (f_{10}) and AIBN wt.%. All experiments are performed at 70 °C for 2 h.

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.10	0.10	0.07	0.29	0.25
02	0.05	0.30	0.32	0.29	0.20	0.47
03	0.05	0.50	0.52	0.45	0.31	0.62
04	0.05	0.80	0.82	0.80	0.45	0.82
05	0.25	0.10	0.10	0.02	0.84	0.17
06	0.25	0.30	0.31	0.19	0.63	0.51
07	0.25	0.50	0.53	0.40	0.72	0.66
08	0.25	0.80	0.82	0.74	0.58	0.88
09	0.50	0.10	0.10	0.01	0.81	0.26
10	0.50	0.30	0.31	0.14	0.89	0.47
11	0.50	0.50	0.54	0.36	0.88	0.64
12	0.50	0.80	0.83	0.73	0.89	0.95
13	1.00	0.10	0.11	0.06	0.96	0.11
14	1.00	0.30	0.32	0.07	0.95	0.38
15	1.00	0.50	0.55	0.28	0.97	0.63
16	1.00	0.80	0.81	0.70	0.96	0.86
17	2.00	0.10	0.10	0.00	0.95	0.11
18	2.00	0.30	0.32	0.05	0.97	0.36
19	2.00	0.50	0.53	0.20	0.97	0.59
20	2.00	0.80	0.83	0.62	0.97	0.85

Table S 8. List of experiments designed for the copolymerization of GMA (M_1) and St (M_2) at different GMA molar ratios (f_{10}) and AIBN wt.%. All experiments are performed at 70 °C for 2 h.

Variant	AIBN wt%	$f_{10,\ given}$	$f_{10,\ experimental}$	f_1	X	F_1
01	0.05	0.10	0.13	0.13	0.05	0.26
02	0.05	0.30	0.37	0.34	0.14	0.55
03	0.05	0.50	0.56	0.53	0.17	0.68
04	0.05	0.80	0.84	0.84	0.22	0.87
05	0.25	0.10	0.16	0.14	0.17	0.26
06	0.25	0.30	0.40	0.36	0.20	0.53
07	0.25	0.50	0.58	0.56	0.32	0.63
08	0.25	0.80	0.86	0.91	0.61	0.82
09	0.50	0.10	0.15	0.13	0.20	0.24
10	0.50	0.30	0.37	0.33	0.25	0.48
11	0.50	0.50	0.62	0.57	0.42	0.69
12	0.50	0.80	0.86	0.90	0.56	0.84
13	1.00	0.10	0.14	0.11	0.29	0.21
14	1.00	0.30	0.37	0.32	0.34	0.47
15	1.00	0.50	0.56	0.53	0.44	0.60
16	1.00	0.80	0.85	0.89	0.73	0.83
17	2.00	0.10	0.14	0.10	0.33	0.22
18	2.00	0.30	0.37	0.31	0.44	0.45
19	2.00	0.50	0.59	0.56	0.66	0.60
20	2.00	0.80	0.84	1.00	0.94	0.83

Table S 9. Some of the copolymerization reactivity ratio values reported in literature for monomer pairs studied in the present work. Data is obtained from the online CoPolDB website[2].

Monomer Pair	r_1	r_2	Reaction temperature	Solvent	Reference
M_1 = BMA	2.22	0.37	70	Toluene	This work
M_2 = BA	2.2	0.3	50	Ethyl alcohol	[3]
	0.58	0.73	70	Toluene	This work
	0.31	0.56	60	- (bulk)	[4]
M_1 = BMA	2.52	-0.05	30	- (bulk)	[5]
M_2 = St	0.59	0.74	RT (plasma induced polymerization)	-	[6]
	1.23	0.32	70	Toluene	This work
	0.79	0.25	110	- (bulk)	[7]
	0.79	0.34	150	- (bulk)	[7]
	0.75	0.38	170	- (bulk)	[7]
	1.23	-0.106	25	- (bulk)	[8]
	0.44	0.29	25	- (bulk)	[9]
	1.03	0.34	60	Benzene	[10]
M_1 = St	0.76	0.15	60	- (bulk)	[10]
M_2 = BA	0.8	0.15	60	- (bulk)	[11]
	0.97	0.14	60	Benzene	[11]
	0.63	0.08	60	THF	[11]
	0.698	0.164	50	- (bulk)	[12]
	0.46	0.58	70	Toluene	This work
	0.52	0.46	60	- (bulk)	[13]
	0.59	0.54	130	- (bulk)	[13]
M_1 = St	0.396	0.22	15	- (bulk)	[14]
M_2 = MMA	0.52	0.47	60	Benzene	[15]
	0.48	0.50	60	Chlorobenzene	[15]
	0.38	0.62	60	Benzonitrile	[15]
	0.275	0.314	60	- (bulk)	[16]
M_1 = GMA	1.76	0.24	70	Toluene	This work
M_2 = BA	2.16	0.083	60	- (bulk)	[17]
	0.69	0.32	70	Toluene	This work
M_1 = GMA	0.17	0.60	60	- (bulk)	[18]
M_2 = St	0.63	0.34	65	- (bulk)	[19]
	0.65	0.36	60	- (bulk)	[20]

Table S 10. Composition data for BMA-BA mixtures heated at 75°C. Comparison of feed composition (f10, f1) with experimentally determined monomer conversions (X_{BMA}, X_{BA}, X) across five groups. The data indicates negligible evaporative loss of monomers, as feed and experimental compositions remain equivalent and monomer conversion is negligible within experimental error. Negative conversion results are retained for transparency regardless of their physical nonsensicality and can be attributed to experimental error in NMR.

Group	f_{10}[a]	f_1[b]	X_{BMA}[c]	X_{BA}[c]	X[c]
1	0.10	0.11	-0.04	0.00	0.00
2	0.30	0.30	0.01	0.04	0.03
3	0.50	0.50	0.00	0.02	0.01
4	0.80	0.80	-0.01	0.02	0.00
5	0.90	0.89	0.00	0.01	0.00

[a] *initial molar ratio of BMA as given in the reaction recipe,* [b] *molar ratio of BMA at t_1 calculated from NMR,* [c] *overall monomer conversion calculated from NMR.*

*Table S 11. Statistical comparison of r_1 and r_2 values measured in this work compared to literature based on JCIs. Joint significance estimate: $\chi^2(2) = z\_r_1^2 + z\_r_2^2$ vs. chi-squared distribution (2 d.f.); ns = p > 0.05, * p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001. z values are estimated from JCIs. Measured values: 75 °C, toluene, free-radical solution polymerisation (NLLS fit).*

Monomer System	**r_1 (This Work)**	**95% CI (r_1)**	**r_2 (This Work)**	**95% CI (r_2)**	**Ref.**	**Lit. Conditions**	**r_1 (Lit.) / r_2 (Lit.)**	**Joint Significance**
BMA / BA	2.219	[2.004, 2.516]	0.367	[0.309, 0.441]	[3]	50 °C, EtOH	2.20 / 0.30	ns
BMA / St	0.578	[0.539, 0.617]	0.733	[0.680, 0.786]	[4]	60 °C, bulk	0.31 / 0.56	***
BMA / St					[5]	30 °C, bulk	2.52 / −0.05[a]	***
BMA / St					[6]	RT, plasma	0.59 / 0.74	ns
BMA / St					[7–12]	60–170 °C, various	0.44–1.23 / 0.08–0.38	***[b]
St / MMA	0.462	[0.419, 0.505]	0.582	[0.549, 0.615]	[13–16]	15–130 °C, various	0.275–0.59 / 0.22–0.62	***[c]
GMA / BA	1.765	[1.570, 2.025]	0.239	[0.187, 0.302]	[17]	60 °C, bulk	2.16 / 0.083	***
GMA / St	0.691	[0.624, 0.767]	0.324	[0.273, 0.388]	[18]	60 °C, bulk	0.17 / 0.60	***
GMA / St					[19]	65 °C, bulk	0.63 / 0.34	ns
GMA / St					[20]	60 °C, bulk	0.65 / 0.36	ns

[a] *$r_2 = -0.05$ is physically unreasonable.* [b] *St/BA: 9 literature entries compared; all but one ref. [10] (60 °C, benzene) are statistically significant.* [c] *St/MMA: 7 literature entries compared; all are statistically significant.*

4. Procedure to use Python to remotely control the OT-2 robot and run copolymerisation experiments

File paths used in the codes provided are user-specific and must be updated accordingly before use.

Step 1: Establishing an SSH connection between the computer and the robot.

We followed the instructions below provided by Opentrons to establish an SSH connection and acquired the SSH key pair.

1. https://support.opentrons.com/s/article/Setting-up-SSH-access-to-your-OT-2

2. https://support.opentrons.com/s/article/Connecting-to-your-OT-2-with-SSH

This SSH link was used for a direct connection to the OT-2 robot to transfer files (Secure Copy Protocol-SCP) and execute protocols from Pycharm.

Step 2: Preparing custom labware using the Opentrons Custom Labware Creator tool. We have provided all the custom labware we have used in this work, and the protocol can be adjusted/expanded to cover other labware.

Step 3: Loading custom labware files onto the Opentrons app, then running the "Labware Offset Calculator" protocol on the Opentrons app (protocol file provided) and getting the calibration offset values, which were copy-pasted into the Copolymerisation-Part A and B protocols (both protocols provided).

Step 4: Running the "OT-2-Control-via-SSH" file on Pycharm (Community edition) to load the custom labware onto the robot's directory using the run_subprocess_labware function (need to add this in the block of code that starts with if __name__ == "__main__".)

Then, running the same protocol, now replacing the run_subprocess_labware function with the run_subprocess (to transfer files via SCP) and run_execute (to run the OT-2 protocol) (this is the default layout of the python file provided).

When the OT-2-Control-via-SSH protocol is run, the computer establishes an SSH connection to the robot, uploads the csv file containing reaction volumes (prepared beforehand), and prompts the user to select a python protocol. First, "Copolymerisation-PartA" must be selected in order for the robot to prepare reaction mixtures and t_0 NMR samples. After completion of Part A, the prepared well-plate must be sealed using aluminium foil, then placed in the heater shaker for polymerisation. At this stage the Python protocol in Pycharm will prompt the user to respond to this question: "Continue with the experiments?" When the polymerisation reaction is completed and the well-plate is placed back onto

the robot's deck, the user must type "yes" in the terminal and load "Copolymerisation-PartB" to continue on with the preparation of t_1 samples.

GitHub repository containing all the required files:

https://github.com/PRDMonash/A-Robotic-Approach-to-Polymerization-Kinetics-A-Case-Study-on-Copolymerization-Parameter-Estimation.git

All experimental data are available at the following repository:

https://doi.org/10.26180/32015067)

Comparison of simulated copolymer composition curves from reactivity ratios measured via 96-well plate and 48-well reactor formats

The copolymer composition plots were generated in Python (NumPy/Matplotlib) by evaluating the Mayo-Lewis equation on an evenly spaced feed composition grid $f_1 \in [0,1]$ with 200 points, using the best fit reactivity ratios (r_1, r_2) calculated for each reactor / well-plate parameter set. For each system and condition, a central curve is plotted from the best fit values, and an uncertainty band is obtained by re-evaluating the equation at $(r_1 \pm \Delta r_1, r_2 \pm \Delta r_2)$ using the confidence intervals obtained via Contour. The ideal random copolymerisation line $F_1 = f_1$ is included for reference. To quantify the similarity between the two curves being compared, 8000 Monte Carlo samples of (r_1, r_2) are drawn for each condition from a two-piece normal distribution centred at the best-fit values with the reported lower/upper errors as the left/right standard deviations, the corresponding ensembles of F_1 curves are computed over the same grid, and at each f_1 point the overlap coefficient between the two empirical F_1 distributions is estimated via histograms (60 bins) and then averaged over f_1 to give a single similarity score printed on the plot. Trivial boundary points where all curves converge to 0 or 1 are removed prior to binning to prevent overinflation of similarity scores. All plots are exported as high-resolution PNG files. The relevant Python code is included on the open-source GitHub repository for reference.

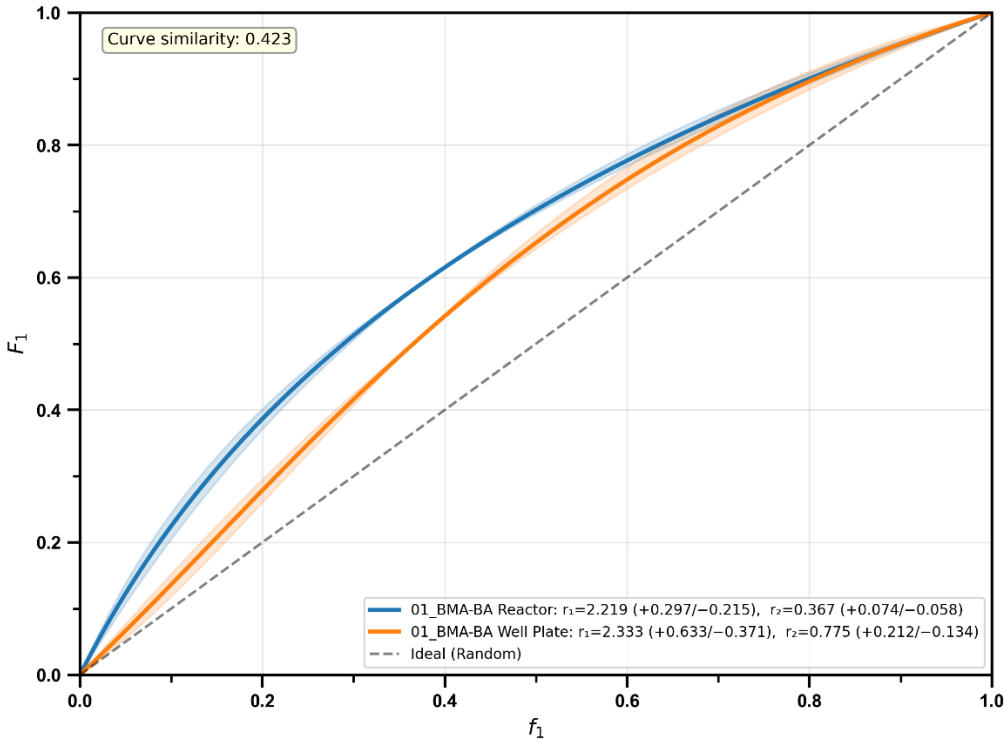


Figure S 10. Comparison of Copolymer Composition Curves for BMA-BA. The Mayo-Lewis copolymer composition curves from BMA-BA reactivity ratios derived using the reactor (blue solid line) and well plate (orange solid line) formats.

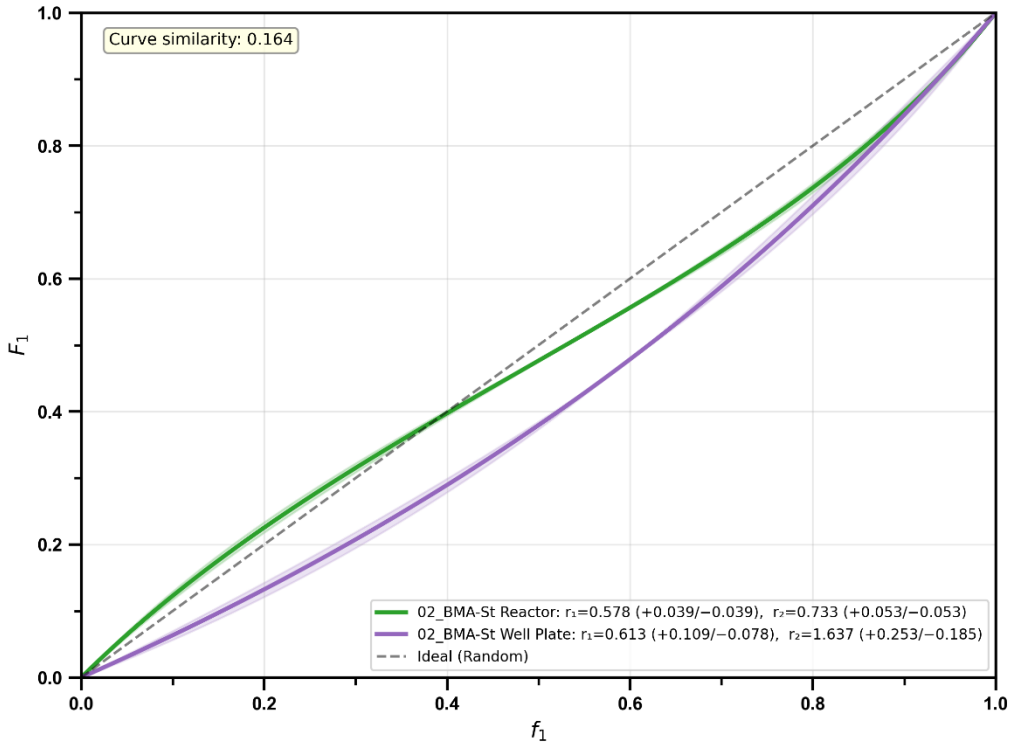


Figure S 11. Comparison of Copolymer Composition Curves for BMA-St. The Mayo-Lewis copolymer composition curves from BMA-St reactivity ratios derived using the reactor (green solid line) and well plate (purple solid line) formats.

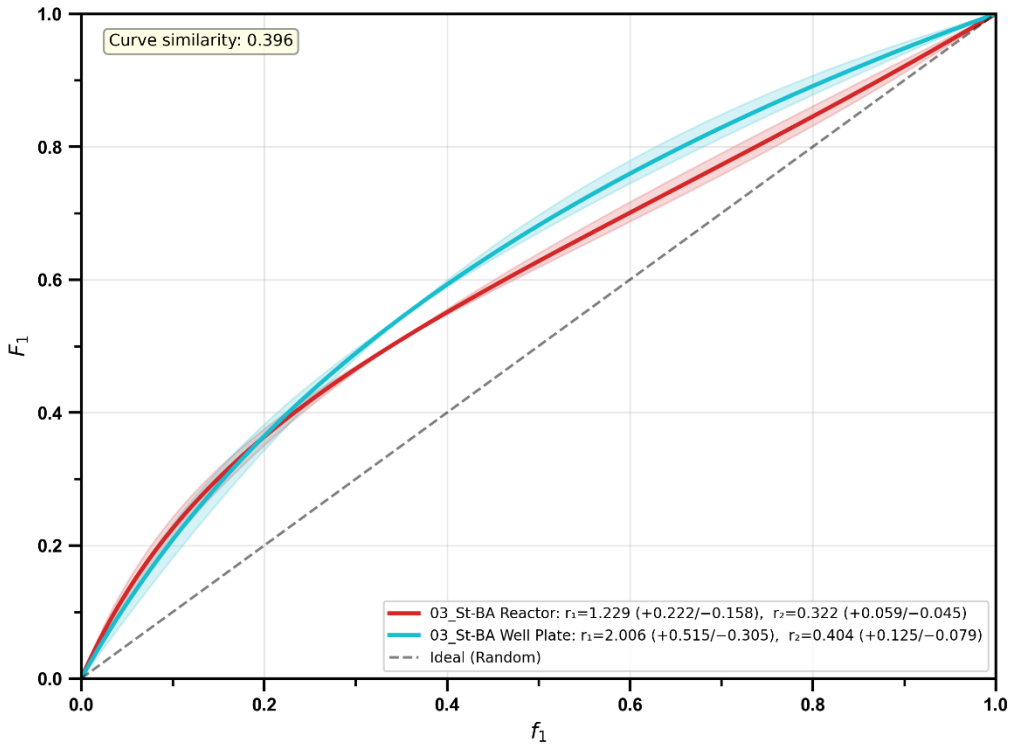


Figure S 12. Comparison of Copolymer Composition Curves for St-BA. The Mayo-Lewis copolymer composition curves from St-BA reactivity ratios derived using the reactor (red solid line) and well plate (teal solid line) formats.

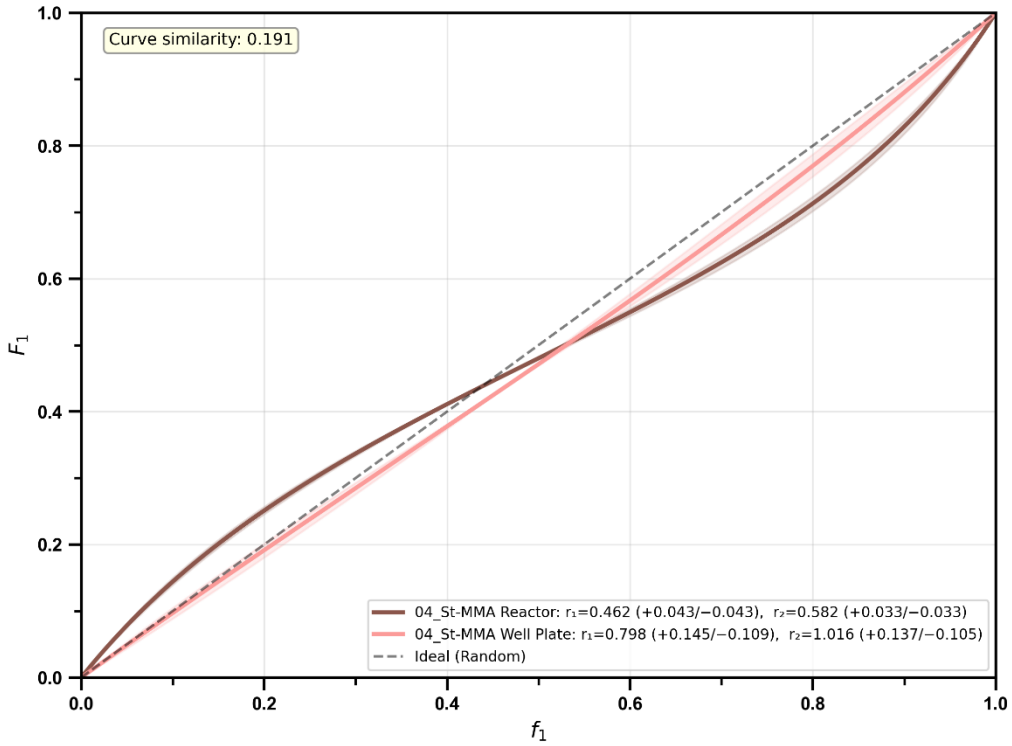


Figure S 13. Comparison of Copolymer Composition Curves for St-MMA. The Mayo-Lewis copolymer composition curves from St-MMA reactivity ratios derived using the reactor (brown solid line) and well plate (pink solid line) formats.

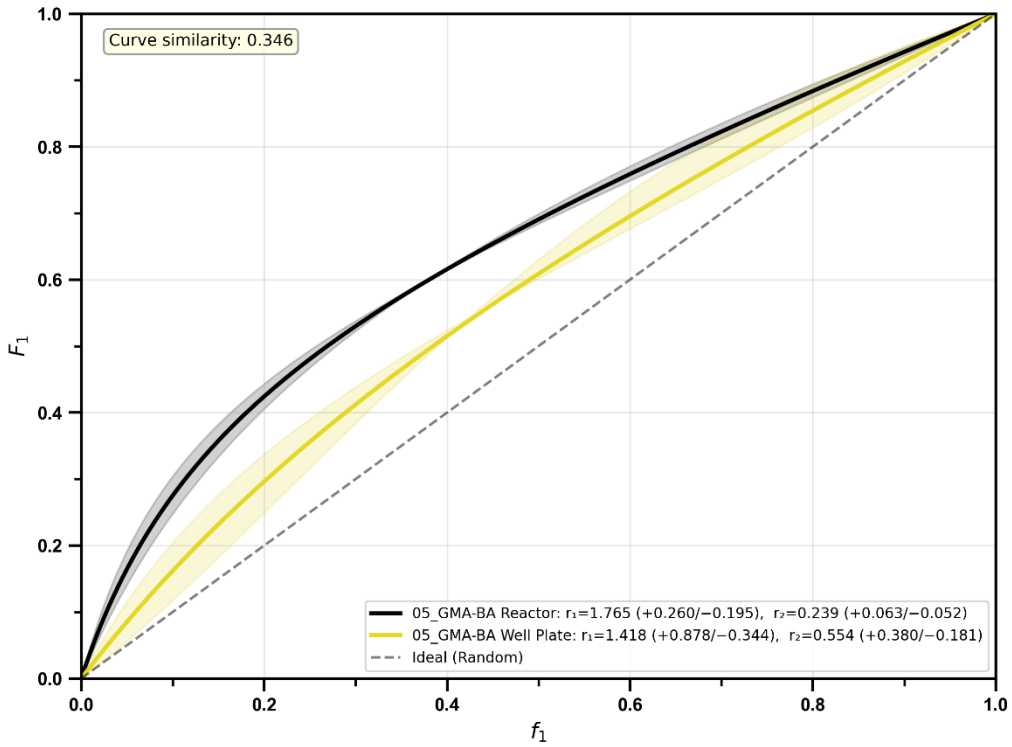


Figure S 14. Comparison of Copolymer Composition Curves for GMA-BA. The Mayo-Lewis copolymer composition curves from GMA-BA reactivity ratios derived using the reactor (black solid line) and well plate (yellow solid line) formats.

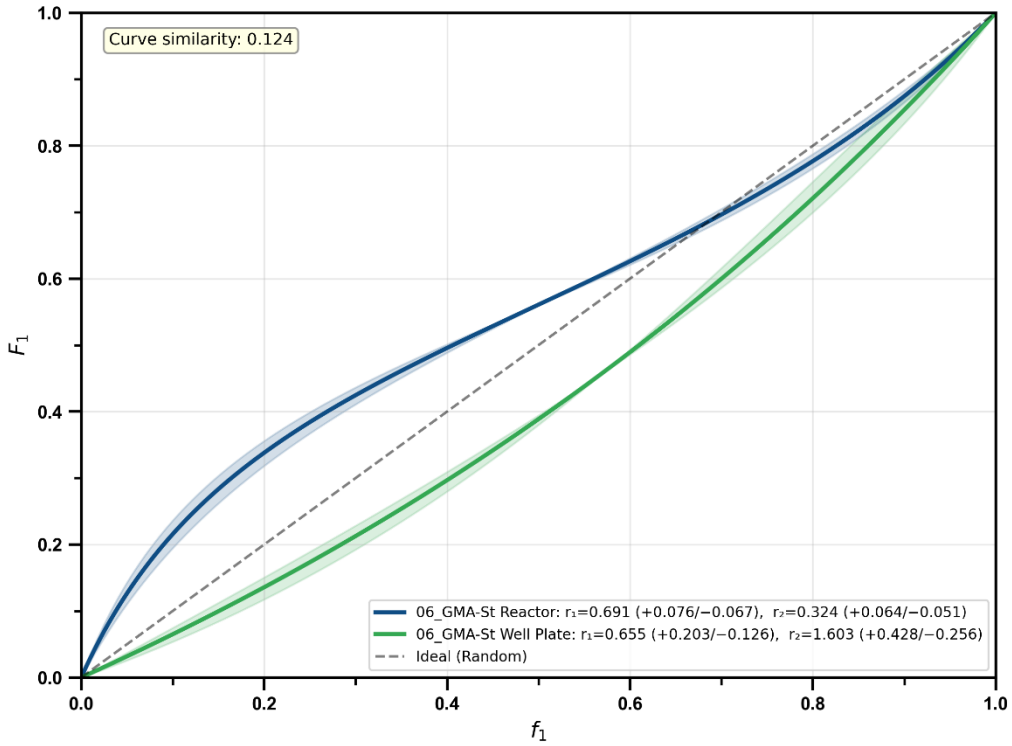


Figure S 15. Comparison of Copolymer Composition Curves for GMA-St. The Mayo-Lewis copolymer composition curves from GMA-St reactivity ratios derived using the reactor (navy solid line) and well plate (green solid line) formats.

5. NMR Spectra for Copolymerisations

The below figures show the stacked NMR spectra of t_0 and t_1 samples for all comonomer pairs. Notably, within the t_0 spectra, the changing monomer fractions can be seen with the increase in intensity of monomer 1 peaks (orange) and decrease in intensity of monomer 2 peaks (yellow) across experiments sharing the same AIBN loading. Within the t_1 spectra, the effect of increased AIBN loading can be seen with the decrease in intensity of both monomer 1 and monomer 2 peaks (e.g., samples 1-4 share 0.05 wt% AIBN loading and are of higher intensity than samples 17-20 which are of 2.00 wt% AIBN loading).

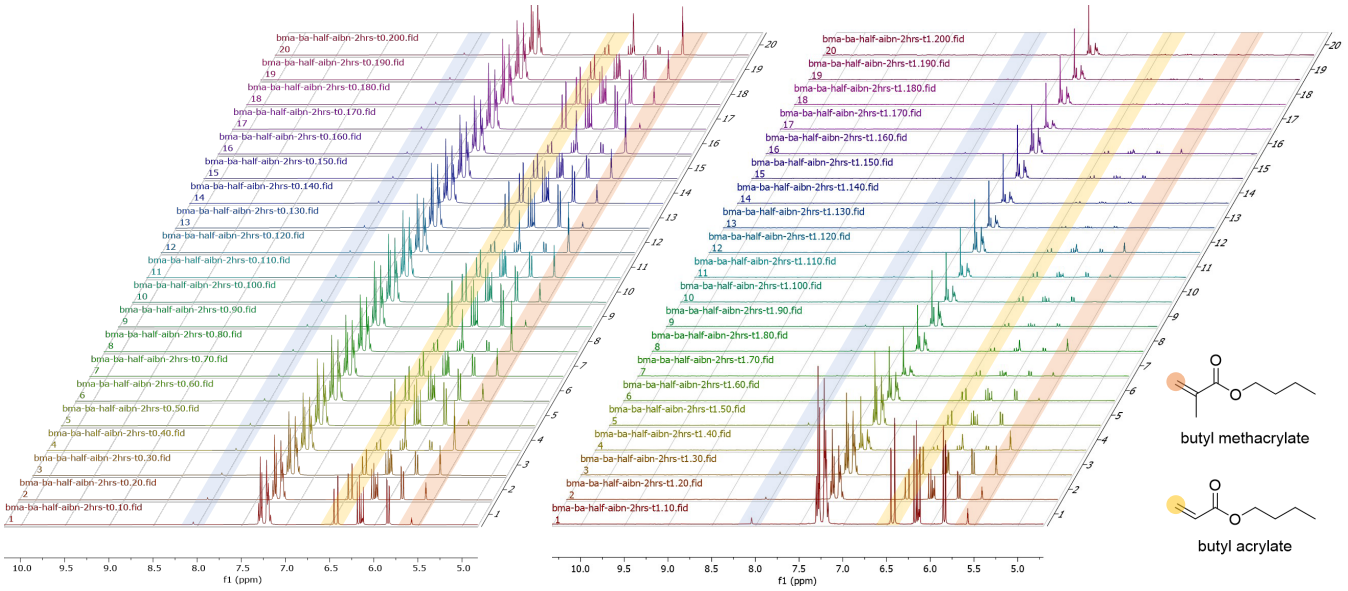


Figure S 16. Stacked ^{1}H NMR spectra of BMA and BA for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for BMA (orange), BA (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

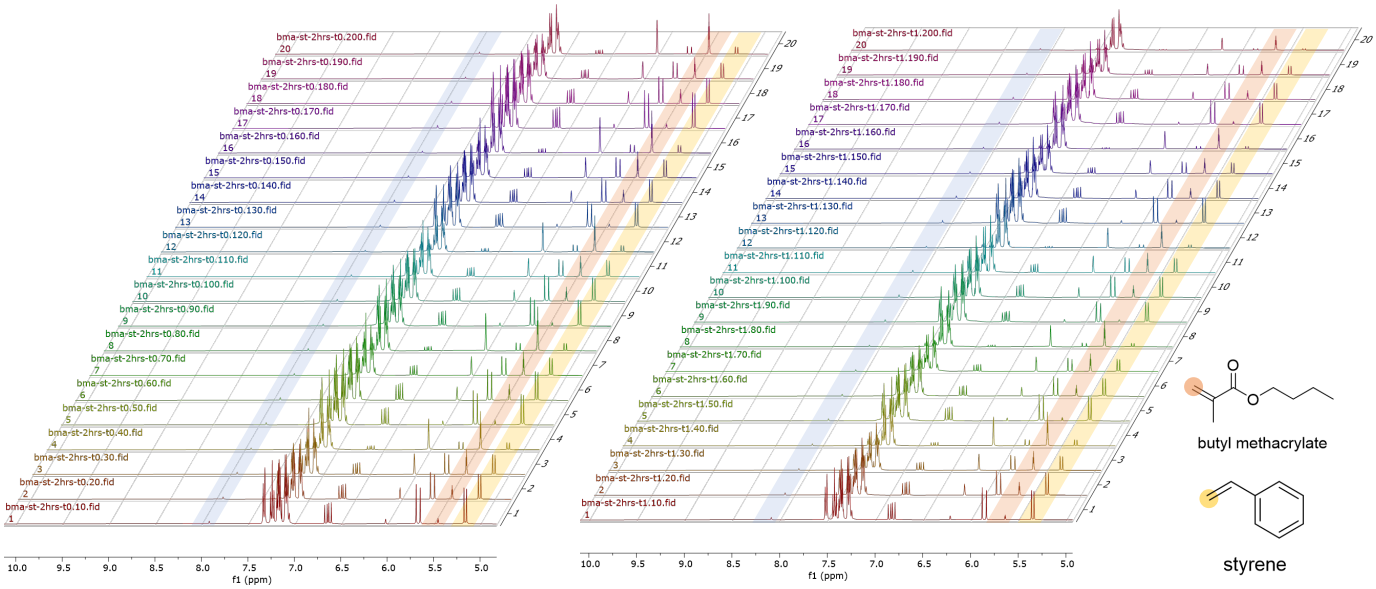


Figure S 17. Stacked ^{1}H NMR spectra of BMA and St for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for BMA (orange), St (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

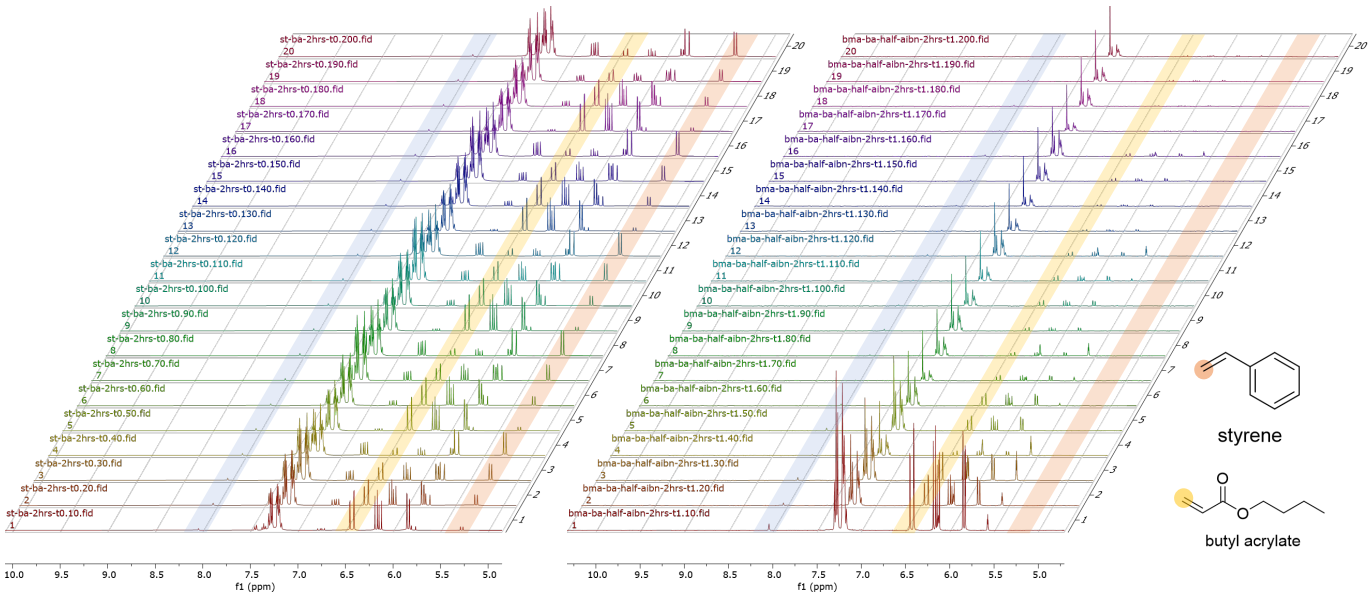


Figure S 18. Stacked ^{1}H NMR spectra of St and BA for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for St (orange), BA (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

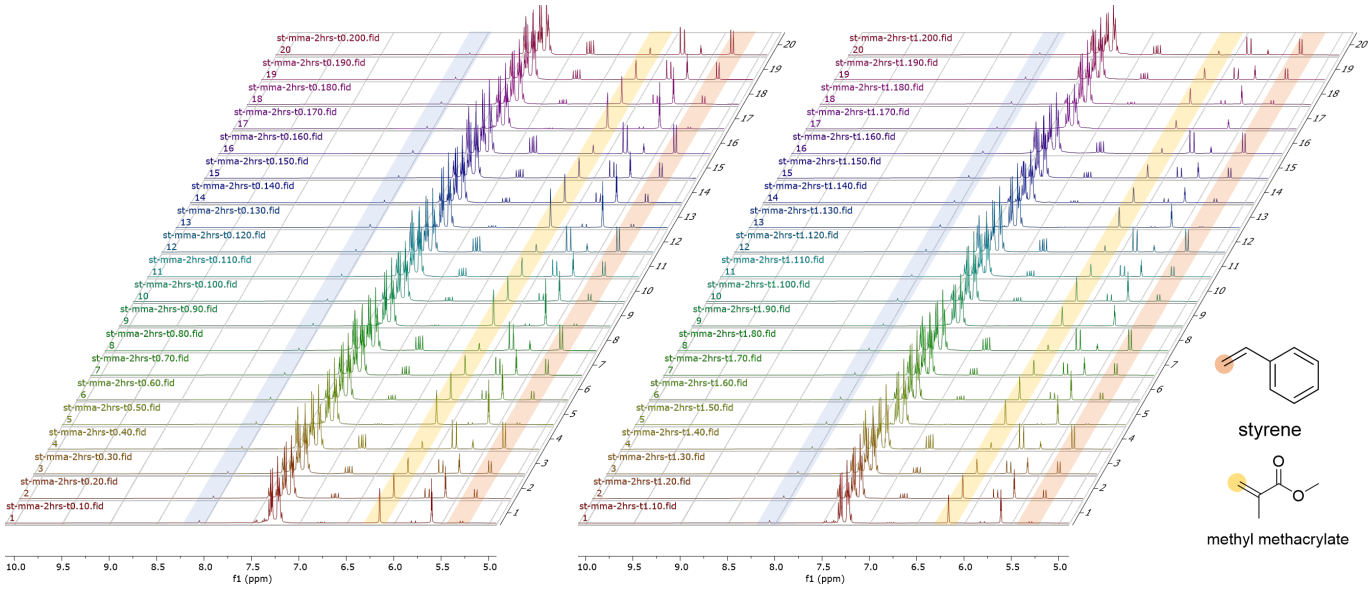


Figure S 19. Stacked ^{1}H NMR spectra of BMA and MMA for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for BMA (orange), MMA (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

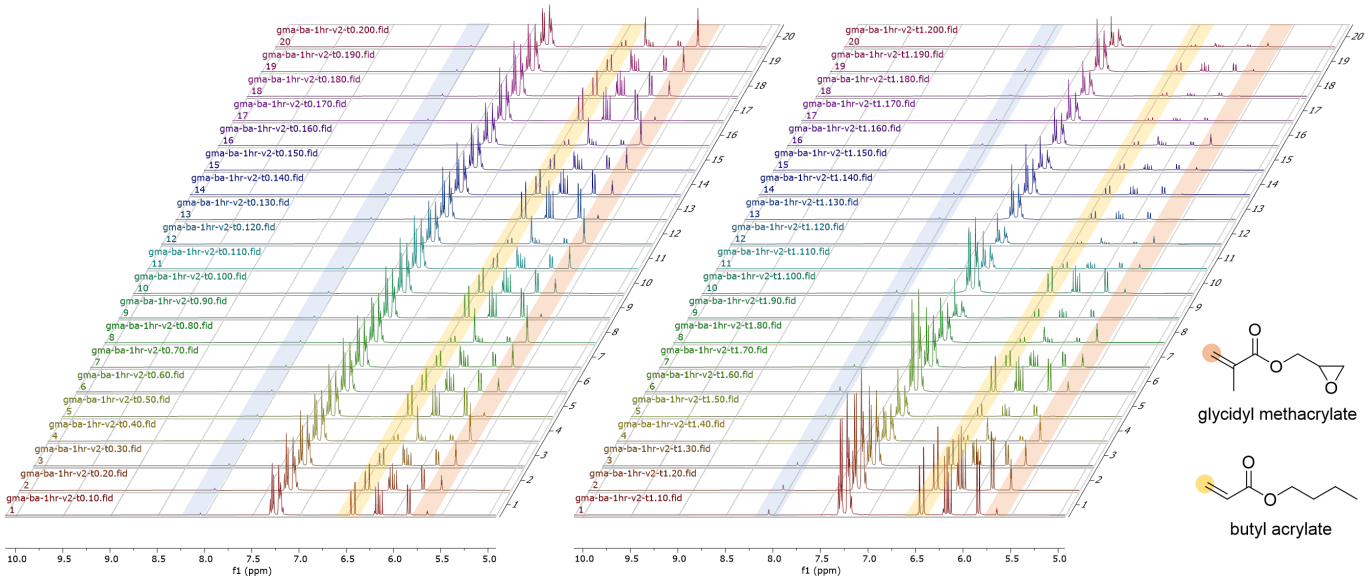


Figure S 20. Stacked ^{1}H NMR spectra of GMA and BA for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for GMA (orange), BA (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

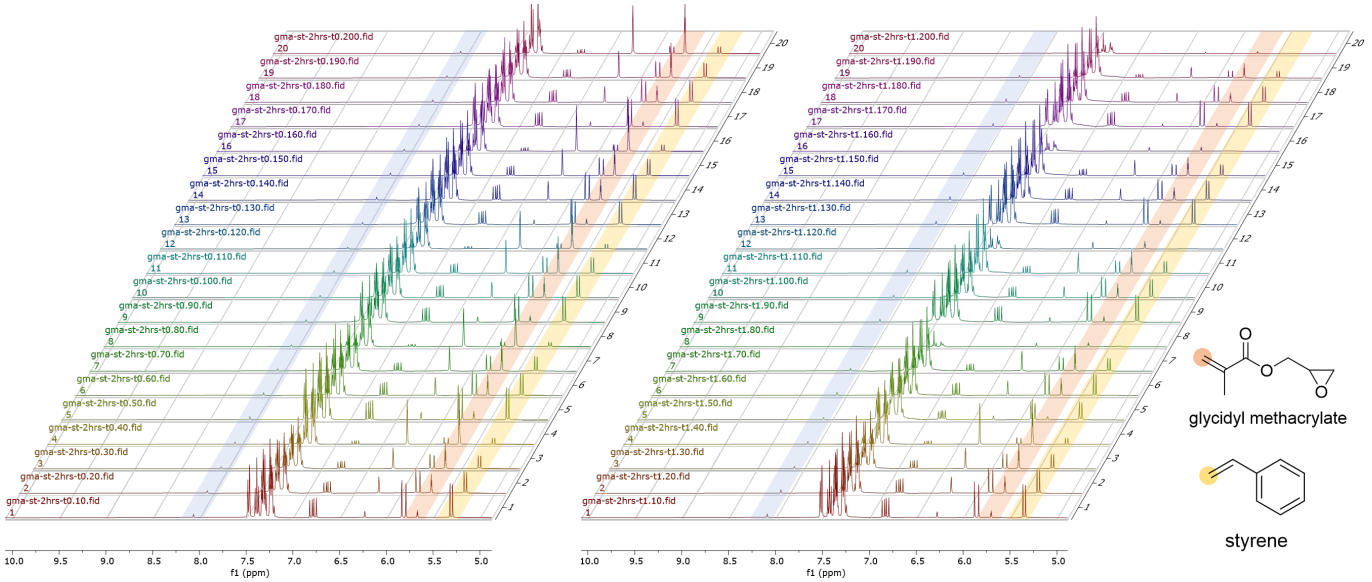


Figure S 21. Stacked ^{1}H NMR spectra of GMA and St for t_0 (left) and t_1 (right) samples shown side-by-side. Highlights contain the peaks that were picked and integrated for GMA (orange), St (yellow), and the DMF internal standard (blue). The specific vinyl protons integrated for each monomer are indicated on the provided structures.

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