

Electronic Supplementary Information (ESI)

Extrapolation performance improvement by quantum chemical calculations for machine-learning-based predictions of flow-synthesized binary copolymers

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Flow synthesis reactor:

Table S1. List of flow reactor components.

Part name	Product number	Manufacturer
Screw cap bottle 4 port cap set	017270-3A	SIBATA SCIENTIFIC TECHNOLOGY
Medium bottle	FB-800-500	Fisher Scientific
Stainless steel cooling bath	HPS-100	AS ONE Corporation
Magnetic stirrer	HS-30DN	AS ONE Corporation
PFA Tubing ϕ 3.17 (1/8) \times ϕ 1.59 (1/16)	NSP66-3.17X1.59-1	GUNZE LIMITED
Plunger pump	FC-F-PP-410S	Device for FlowChemistry
Feral	YMC-P-0012	YMC
Connector	YMC-P-0002	YMC
Mixer housing	YMC-P-0030-02	YMC
Micro mixer	KC-M-Y-GL	YMC
Inline temperature sensor	FC-TCK-SW1.6	Device for FlowChemistry
PFA Tubing 2 \times 3 ϕ	TOMBO No.9003-PFA	NICHIAS Corporation
Oil bath	NWB-250	NISSIN
Powerful magnetic stirrer	F-205D	Tokyo Garasu Kikai



Figure S1. Photographs of flow reactor setup.

Reagents

Methyl methacrylate (MMA), glycidyl methacrylate (GMA), styrene (St), tetrahydrofurfuryl methacrylate (THFMA), and 2,2'-azobis(2,4-dimethylvaleronitrile) were purchased from FUJIFILM Wako (Osaka, Japan). Cyclohexyl methacrylate (CHMA) and *p*-acetoxystyrene (PACS) were supplied by Tokyo Chemical Industry (Tokyo, Japan) and Tosoh Finechem (Yamaguchi, Japan), respectively. 1-Methoxy-2-propanol was received from Sigma-Aldrich (Burlington, Massachusetts, United States).

Polymer synthesis and characterization

Synthesis conditions:

The selection was exhaustive for each condition. We selected points around the central condition where each monomer does not have extremely high/low conversion rates so that the transition of monomer conversion can be checked, and so that the number of points does not increase excessively. In particular, when the conversion rate for each monomer is extremely high, clogging of the tubes occurs.

- Monomer A/B composition ratio: A/B = 70/30, 50/50, and 30/70.
- SM: 2, 4, and 10.
- Amount of initiator: 1 and 5 mol%.
- Reaction temperature: 60 and 80°C.
- Reaction time: 5, 10, 20, and 30 min.

HPLC conditions:

High-performance liquid chromatography (HPLC, Shimadzu, (DGU-20A3, LC-20AB, SIL-20A, SPD-M20A, CTO-20A)), using a separation column (GL Science, ODS-3 5 μ m 4.6 \times 250 mm), was employed for the analyses of the copolymerization composition.

- Flow rate: 1.0 mL/min
- Elution solvent volume ratio: Acetonitrile/Ultrapure water = 55/45
- Sample concentration: 0.2 mass%
- Sample injection volume: 1 μ L
- Column temperature: 40°C
- Detector: UV-visible spectrophotometer at 210 nm

Each monomer concentration is calculated from a calibration curve.

Table S2-1. List of synthesized copolymers.

Sample No.	M1	M1 composition ratio [mol%]	M2 composition ratio [mol%]	Initiator composition ratio [mol%]	SM	Flow velocity [ml./min.]	Temperature [°C]	Reaction time [min]	M1 conversion [%]	M2 conversion [%]	M1 ICR [mol%]
F-52-1	CHMA	50	50	5	4	6.28	60	5	18.52	18	50.71
F-52-2	CHMA	50	50	5	4	3.14	60	10	27.35	25.29	51.96
F-52-3	CHMA	50	50	5	4	1.57	60	20	42.3	36.79	53.48
F-52-4	CHMA	50	50	5	4	1.05	60	29.9	52.62	46.56	53.06
F-53-1	CHMA	30	70	5	4	6.28	60	5	16.54	15.07	31.98
F-53-2	CHMA	30	70	5	4	3.14	60	10	25.23	22.74	32.23
F-53-3	CHMA	30	70	5	4	1.57	60	20	39.18	34.93	32.46
F-53-4	CHMA	30	70	5	4	1.05	60	29.9	50.65	44.3	32.89
F-54-1	CHMA	70	30	5	4	6.28	60	5	19.22	15.91	73.81
F-54-2	CHMA	70	30	5	4	3.14	60	10	27.58	22.78	73.86
F-54-3	CHMA	70	30	5	4	1.57	60	20	42.21	34.81	73.89
F-54-4	CHMA	70	30	5	4	1.05	60	29.9	53.17	44.39	73.65
F-55-1	CHMA	50	50	5	4	6.28	80	5	36.94	32.52	53.19
F-55-2	CHMA	50	50	5	4	3.14	80	10	54.41	47.24	53.53
F-55-3	CHMA	50	50	5	4	1.57	80	20	66.91	57.85	53.63
F-55-4	CHMA	50	50	5	4	1.05	80	29.9	73.36	64.46	53.23
F-56-1	CHMA	50	50	1	4	6.28	60	5	11.9	11.46	50.94
F-56-2	CHMA	50	50	1	4	3.14	60	10	16.47	15.07	52.23
F-56-3	CHMA	50	50	1	4	1.57	60	20	25.86	22.56	53.42
F-56-4	CHMA	50	50	1	4	1.05	60	29.9	34.53	29.8	53.68
F-57-1	CHMA	50	50	5	10	6.28	60	5	12.2	10.47	53.81
F-57-2	CHMA	50	50	5	10	3.14	60	10	14.65	10.97	57.17
F-57-3	CHMA	50	50	5	10	1.57	60	20	27.66	22.01	55.69
F-57-4	CHMA	50	50	5	10	1.05	60	29.9	35.84	29.08	55.21
F-58-1	CHMA	50	50	5	2	6.28	60	5	22.65	20.07	53.02
F-58-2	CHMA	50	50	5	2	3.14	60	10	33.58	29.57	53.18
F-58-3	CHMA	50	50	5	2	1.57	60	20	53.31	45.36	54.03
F-58-4	CHMA	50	50	5	2	1.05	60	29.9	63.28	56.24	52.94
F-1r1_1	GMA	50	50	5	4	6.28	60	5	25.46	17.71	58.97
F-1r1_2	GMA	50	50	5	4	3.14	60	10	32.65	24.76	56.86
F-1r1_3	GMA	50	50	5	4	1.57	60	20	45.11	35.68	55.83
F-1r1_4	GMA	50	50	5	4	1.05	60	29.9	55.29	45.77	54.7
F-1r2_1	GMA	50	50	5	4	6.28	60	5	24.86	16.94	59.46
F-1r2_2	GMA	50	50	5	4	3.14	60	10	32.49	24.1	57.41
F-1r2_3	GMA	50	50	5	4	1.57	60	20	44.04	34.76	55.88
F-1r2_4	GMA	50	50	5	4	1.05	60	29.9	56.29	46.97	54.51
F-1r3_1	GMA	50	50	5	4	6.28	60	5	25.31	17.96	58.49
F-1r3_2	GMA	50	50	5	4	3.14	60	10	32.48	24.71	56.78
F-1r3_3	GMA	50	50	5	4	1.57	60	20	44.41	36.04	55.2
F-1r3_4	GMA	50	50	5	4	1.05	60	29.9	53.75	44.83	54.52
F-1r4_1	GMA	50	50	5	4	6.28	60	5	24.11	16.78	58.95
F-1r4_2	GMA	50	50	5	4	3.14	60	10	31.72	23.64	57.28
F-1r4_3	GMA	50	50	5	4	1.57	60	20	43.88	30.89	58.68
F-1r4_4	GMA	50	50	5	4	1.05	60	29.9	53.59	44.6	54.57
F-1r5_1	GMA	50	50	5	4	6.28	60	5	24.38	16.06	60.28
F-1r5_2	GMA	50	50	5	4	3.14	60	10	32.38	23.17	58.28
F-1r5_3	GMA	50	50	5	4	1.57	60	20	44.67	35.01	56.05
F-1r5_4	GMA	50	50	5	4	1.05	60	29.9	54.97	44.72	55.14
F-2_1	GMA	50	50	5	4	6.28	80	5	40.41	31.6	56.11
F-2_2	GMA	50	50	5	4	3.14	80	10	54.63	45.22	54.7
F-2_3	GMA	50	50	5	4	1.57	80	20	71.87	63.33	53.15
F-2_4	GMA	50	50	5	4	1.05	80	29.9	77.15	69.18	52.71
F-4_1	GMA	50	50	5	10	6.28	60	5	17.81	10.16	63.67
F-4_2	GMA	50	50	5	10	3.14	60	10	22.73	14.72	60.69
F-4_3	GMA	50	50	5	10	1.57	60	20	30.44	21.48	58.62
F-4_4	GMA	50	50	5	10	1.05	60	29.9	38.44	29.12	56.89
F-5_1	GMA	50	50	1	4	6.28	60	5	18	10.16	63.91
F-5_2	GMA	50	50	1	4	3.14	60	10	21.52	12.86	62.59
F-5_3	GMA	50	50	1	4	1.57	60	20	27.88	18.18	60.53
F-5_4	GMA	50	50	1	4	1.05	60	29.9	34.54	24.25	58.75
F-6_1	GMA	50	50	5	10	6.28	80	5	28.29	19.66	59
F-6_2	GMA	50	50	5	10	3.14	80	10	39.82	29.88	57.12

Table S2-2. List of synthesized copolymers.

Sample No.	M1	M1 composition ratio [mol%]	M2 composition ratio [mol%]	Initiator composition ratio [mol%]	SM	Flow velocity [mL/min.]	Temperature [°C]	Reaction time [min]	M1 conversion [%]	M2 conversion [%]	M1 ICR [mol%]
F-6_3	GMA	50	50	5	10	1.57	80	20	52.96	42.93	55.22
F-6_4	GMA	50	50	5	10	1.05	80	29.9	59.82	49.92	54.5
F-7_1	GMA	50	50	1	4	6.28	80	5	30.56	21.47	58.74
F-7_2	GMA	50	50	1	4	3.14	80	10	39.74	29.32	57.55
F-7_3	GMA	50	50	1	4	1.57	80	20	54.05	43.44	55.45
F-7_4	GMA	50	50	1	4	1.05	80	29.9	63.75	53.84	54.21
F-8_1	GMA	70	30	5	4	6.28	60	5	23.5	14.21	79.42
F-8_2	GMA	70	30	5	4	3.14	60	10	30.74	20.6	77.69
F-8_3	GMA	70	30	5	4	1.57	60	20	43.45	31.74	76.16
F-8_4	GMA	70	30	5	4	1.05	60	29.9	54.7	42.93	74.83
F-9_1	GMA	30	70	5	4	6.28	60	5	22.78	14.64	40.01
F-9_2	GMA	30	70	5	4	3.14	60	10	29.06	21.34	36.86
F-9_3	GMA	30	70	5	4	1.57	60	20	42.93	35.15	34.36
F-9_4	GMA	30	70	5	4	1.05	60	29.9	51.43	43.74	33.51
F-17-1	GMA	30	70	1	4	6.28	80	5	29.64	22.05	36.56
F-17-2	GMA	30	70	1	4	3.14	80	10	42.01	34.28	34.44
F-17-3	GMA	30	70	1	4	1.57	80	20	57.71	50.32	32.96
F-17-4	GMA	30	70	1	4	1.05	80	29.9	67.08	59.6	32.55
F-18-1	GMA	30	70	1	4	6.28	60	5	16.91	10.21	41.52
F-18-2	GMA	30	70	1	4	3.14	60	10	20.19	12.18	41.54
F-18-3	GMA	30	70	1	4	1.57	60	20	27.69	19.86	37.4
F-18-4	GMA	30	70	1	4	1.05	60	29.9	34.8	27.97	34.77
F-21-1	GMA	30	70	5	4	6.28	80	5	39.7	32.05	34.68
F-21-2	GMA	30	70	5	4	3.14	80	10	54.87	47.45	33.14
F-21-3	GMA	30	70	5	4	1.57	80	20	72.3	64.92	32.31
F-21-4	GMA	30	70	5	4	1.05	80	29.9	79.58	73.07	31.82
F-33-1	GMA	60	40	5	4	6.28	60	5	24.51	16.64	68.84
F-33-2	GMA	60	40	5	4	3.14	60	10	31.74	23.26	67.18
F-33-3	GMA	60	40	5	4	1.57	60	20	43.96	33.59	66.25
F-33-4	GMA	60	40	5	4	1.05	60	29.9	53.87	43.75	64.87
F-35-1	GMA	20	80	5	4	6.28	60	5	20.22	13.37	27.43
F-35-2	GMA	20	80	5	4	3.14	60	10	27.32	20.06	25.4
F-35-3	GMA	20	80	5	4	1.57	60	20	40.57	34.08	22.93
F-35-4	GMA	20	80	5	4	1.05	60	29.9	50.61	43.53	22.51
F-37-1	GMA	40	60	1	4	6.28	60	5	16.17	9.63	52.81
F-37-2	GMA	40	60	1	4	3.14	60	10	20.28	12.43	52.08
F-37-3	GMA	40	60	1	4	1.57	60	20	27.45	20.76	46.85
F-37-4	GMA	40	60	1	4	1.05	60	29.9	35.47	28.67	45.19
F-38-1	PACS	50	50	5	4	6.28	60	5	8.77	11.83	42.56
F-38-2	PACS	50	50	5	4	3.14	60	10	10.67	12.47	46.11
F-38-3	PACS	50	50	5	4	1.57	60	20	16	16.87	48.68
F-38-4	PACS	50	50	5	4	1.05	60	29.9	20.46	20.44	50.02
F-39-1	PACS	30	70	5	4	6.28	60	5	13.24	11.47	33.1
F-39-2	PACS	30	70	5	4	3.14	60	10	16.14	13.31	34.2
F-39-3	PACS	30	70	5	4	1.57	60	20	23.28	18.69	34.81
F-39-4	PACS	30	70	5	4	1.05	60	29.9	31.98	26.12	34.42
F-40-1	PACS	70	30	5	4	6.28	60	5	9.39	11.26	66.05
F-40-2	PACS	70	30	5	4	3.14	60	10	11.2	12.84	67.06
F-40-3	PACS	70	30	5	4	1.57	60	20	14.83	16.58	67.6
F-40-4	PACS	70	30	5	4	1.05	60	29.9	19.02	21.93	66.93
F-41-1	PACS	50	50	5	4	6.28	80	5	20.77	21.11	49.59
F-41-2	PACS	50	50	5	4	3.14	80	10	29.43	28.72	50.62
F-41-3	PACS	50	50	5	4	1.57	80	20	41.25	37.69	52.25
F-42-1	PACS	50	50	1	4	6.28	60	5	5.04	8.58	37.03
F-42-2	PACS	50	50	1	4	3.14	60	10	7.06	9.28	43.19
F-42-3	PACS	50	50	1	4	1.57	60	20	9.94	11.76	45.81
F-42-4	PACS	50	50	1	4	1.05	60	29.9	13.11	14.64	47.24
F-43-2	PACS	50	50	5	10	3.14	60	10	11.33	9.61	54.12
F-43-3	PACS	50	50	5	10	1.57	60	20	14.3	12.28	53.8
F-43-4	PACS	50	50	5	10	1.05	60	29.9	17.01	14.28	54.36
F-44-1	PACS	50	50	5	2	6.28	60	5	11.09	12.93	46.17
F-44-2	PACS	50	50	5	2	3.14	60	10	14.94	17	46.78

Table S2-3. List of synthesized copolymers.

Sample No.	M1	M1 composition ratio [mol%]	M2 composition ratio [mol%]	Initiator composition ratio [mol%]	SM	Flow velocity [mL/min.]	Temperature [°C]	Reaction time [min]	M1 conversion [%]	M2 conversion [%]	M1 ICR [mol%]
F-44-3	PACS	50	50	5	2	1.57	60	20	21.68	22.59	48.98
F-44-4	PACS	50	50	5	2	1.05	60	29.9	27.65	27.82	49.85
F-75-1	PACS	30	70	5	4	6.28	80	5	26.79	20.9	35.46
F-75-2	PACS	30	70	5	4	3.14	80	10	39.47	29.74	36.26
F-75-3	PACS	30	70	5	4	1.57	80	20	57.04	42.37	36.58
F-3_1	ST	50	50	5	4	6.28	60	5	6.26	9.5	39.73
F-3_2	ST	50	50	5	4	3.14	60	10	8.25	11.35	42.1
F-3_3	ST	50	50	5	4	1.57	60	20	13.39	15.6	46.2
F-3_4	ST	50	50	5	4	1.05	60	29.9	16.66	18.39	47.54
F-10_1	ST	70	30	5	4	6.28	60	5	4.19	9.64	50.36
F-10_2	ST	70	30	5	4	3.14	60	10	6.36	11.6	56.11
F-10_3	ST	70	30	5	4	1.57	60	20	9.2	14.63	59.47
F-10_4	ST	70	30	5	4	1.05	60	29.9	12.51	18.19	61.6
F-11_1	ST	50	50	5	4	6.28	80	5	15.17	17.35	46.65
F-11_2	ST	50	50	5	4	3.14	80	10	22.98	23.32	49.62
F-11_3	ST	50	50	5	4	1.57	80	20	32.25	31.06	50.93
F-11_4	ST	50	50	5	4	1.05	80	29.9	37.99	35.86	51.43
F-12_1	ST	70	30	5	4	6.28	80	5	11.61	16.21	62.56
F-12_2	ST	70	30	5	4	3.14	80	10	18.93	22.97	65.79
F-12_3	ST	70	30	5	4	1.57	80	20	24.58	28.78	66.59
F-12_4	ST	70	30	5	4	1.05	80	29.9	27.41	31.27	67.16
F-13_1	ST	30	70	5	4	6.28	80	5	22.29	17.85	34.86
F-13_2	ST	30	70	5	4	3.14	80	10	33.41	25.7	35.78
F-13_3	ST	30	70	5	4	1.57	80	20	45.46	34.51	36.08
F-13_4	ST	30	70	5	4	1.05	80	29.9	51.56	39.21	36.04
F-14-1	ST	50	50	5	10	6.28	80	5	15.16	13.75	52.46
F-14-2	ST	50	50	5	10	3.14	80	10	19.23	17.32	52.63
F-14-3	ST	50	50	5	10	1.57	80	20	28.13	24.04	53.94
F-14-4	ST	50	50	5	10	1.05	80	29.9	33.98	29.08	53.89
F-15-1	ST	50	50	1	4	6.28	80	5	9.38	12.14	43.58
F-15-2	ST	50	50	1	4	3.14	80	10	14.62	16.97	46.27
F-15-3	ST	50	50	1	4	1.57	80	20	20.42	22.05	48.07
F-15-4	ST	50	50	1	4	1.05	80	29.9	26.82	27.91	49
F-22-1	ST	50	50	5	10	6.28	60	5	7.78	8.02	49.27
F-22-2	ST	50	50	5	10	3.14	60	10	8.73	9.04	49.15
F-22-3	ST	50	50	5	10	1.57	60	20	10.63	10.58	50.14
F-22-4	ST	50	50	5	10	1.05	60	29.9	13.28	12.54	51.44
F-24-1	ST	30	70	5	4	6.28	60	5	11.38	11.15	30.43
F-24-2	ST	30	70	5	4	3.14	60	10	13.8	12.76	31.67
F-24-3	ST	30	70	5	4	1.57	60	20	19.19	16.46	33.33
F-24-4	ST	30	70	5	4	1.05	60	29.9	24.31	20.42	33.78
F-25-1	ST	50	50	5	2	6.28	60	5	10.24	10.51	49.35
F-25-2	ST	50	50	5	2	3.14	60	10	11.26	11.48	49.52
F-25-3	ST	50	50	5	2	1.57	60	20	16.22	16.58	49.45
F-25-4	ST	50	50	5	2	1.05	60	29.9	19.97	20.66	49.14
F-28r1-1	ST	80	20	5	4	6.28	60	5	5	8.24	70.81
F-28r1-2	ST	80	20	5	4	3.14	60	10	7.61	11.54	72.51
F-28r1-3	ST	80	20	5	4	1.57	60	20	10.19	14.28	74.06
F-28r1-4	ST	80	20	5	4	1.05	60	29.9	12.52	17.51	74.1
F-29r1-1	ST	60	40	5	4	6.28	60	5	7.19	11.33	48.76
F-29r1-2	ST	60	40	5	4	3.14	60	10	8.62	12.91	50.03
F-29r1-3	ST	60	40	5	4	1.57	60	20	10.86	14.32	53.24
F-29r1-4	ST	60	40	5	4	1.05	60	29.9	14.68	18.64	54.16
F-30r1-1	ST	40	60	5	4	6.28	60	5	10.03	12.09	35.61
F-30r1-2	ST	40	60	5	4	3.14	60	10	10.91	12.49	36.79
F-30r1-3	ST	40	60	5	4	1.57	60	20	16.11	16.3	39.72
F-30r1-4	ST	40	60	5	4	1.05	60	29.9	20.29	20.03	40.31
F-31r1-1	ST	20	80	5	4	6.28	60	5	12.4	9.43	24.74
F-31r1-2	ST	20	80	5	4	3.14	60	10	15.87	11.39	25.83
F-31r1-3	ST	20	80	5	4	1.57	60	20	23.8	16.92	26.01
F-31r1-4	ST	20	80	5	4	1.05	60	29.9	29.62	20.3	26.73
F-36-1	ST	60	40	1	4	6.28	60	5	14.02	19.31	52.13

Table S2-4. List of synthesized copolymers.

Sample No.	M1	M1 composition ratio [mol%]	M2 composition ratio [mol%]	Initiator composition ratio [mol%]	SM	Flow velocity [mL/min.]	Temperature [°C]	Reaction time [min]	M1 conversion [%]	M2 conversion [%]	M1 ICR [mol%]
F-36-2	ST	60	40	1	4	3.14	60	10	14.24	19.53	52.24
F-36-3	ST	60	40	1	4	1.57	60	20	15.56	20.96	52.7
F-36-4	ST	60	40	1	4	1.05	60	29.9	17.27	22.35	53.69
F-45-1	THFMA	50	50	5	4	6.28	60	5	16.73	17.47	48.92
F-45-2	THFMA	50	50	5	4	3.14	60	10	26.04	25.25	50.77
F-45-3	THFMA	50	50	5	4	1.57	60	20	39.15	37.75	50.91
F-45-4	THFMA	50	50	5	4	1.05	60	29.9	50.24	46.68	51.84
F-46-1	THFMA	30	70	5	4	6.28	60	5	17.28	18.15	28.98
F-46-2	THFMA	30	70	5	4	3.14	60	10	24.83	24.47	30.31
F-46-3	THFMA	30	70	5	4	1.57	60	20	39.37	37.75	30.88
F-46-4	THFMA	30	70	5	4	1.05	60	29.9	48.66	46.3	31.06
F-47-1	THFMA	70	30	5	4	6.28	60	5	18.18	16.65	71.81
F-47-2	THFMA	70	30	5	4	3.14	60	10	27.29	23.96	72.66
F-47-3	THFMA	70	30	5	4	1.57	60	20	41.21	36.67	72.39
F-47-4	THFMA	70	30	5	4	1.05	60	29.9	51.81	46.58	72.19
F-48-1	THFMA	50	50	5	4	6.28	80	5	37.54	35.29	51.54
F-48-2	THFMA	50	50	5	4	3.14	80	10	53.5	50.14	51.62
F-48-3	THFMA	50	50	5	4	1.57	80	20	66.22	61.93	51.67
F-48-4	THFMA	50	50	5	4	1.05	80	29.9	70.39	65.58	51.77
F-49-1	THFMA	50	50	1	4	6.28	60	5	9.45	9.97	48.69
F-49-2	THFMA	50	50	1	4	3.14	60	10	14.96	15.69	48.81
F-49-3	THFMA	50	50	1	4	1.57	60	20	24.15	22.81	51.42
F-49-4	THFMA	50	50	1	4	1.05	60	29.9	31.94	29.82	51.72
F-50-1	THFMA	50	50	5	10	6.28	60	5	13.06	11.88	52.37
F-50-2	THFMA	50	50	5	10	3.14	60	10	17.15	15.77	52.08
F-50-3	THFMA	50	50	5	10	1.57	60	20	25.99	23.41	52.61
F-50-4	THFMA	50	50	5	10	1.05	60	29.9	33.8	30.1	52.9
F-51-1	THFMA	50	50	5	2	6.28	60	5	21.76	21.36	50.46
F-51-2	THFMA	50	50	5	2	3.14	60	10	32.7	31.29	51.1
F-51-3	THFMA	50	50	5	2	1.57	60	20	50.14	47.25	51.48
F-51-4	THFMA	50	50	5	2	1.05	60	29.9	61.82	58.1	51.55
F-59-1	THFMA	30	70	5	4	6.28	80	5	34.93	33.07	31.16
F-59-2	THFMA	30	70	5	4	3.14	80	10	51.32	48.3	31.29
F-59-3	THFMA	30	70	5	4	1.57	80	20	62.94	58.76	31.46
F-60-1	THFMA	70	30	5	4	6.28	80	5	37.89	33.48	72.53
F-60-2	THFMA	70	30	5	4	3.14	80	10	54.49	49.48	71.99
F-60-3	THFMA	70	30	5	4	1.57	80	20	71.93	66.47	71.63
F-61-1	THFMA	30	70	1	4	6.28	60	5	10.23	10.53	29.41
F-61-2	THFMA	30	70	1	4	3.14	60	10	14.67	14.8	29.82
F-61-3	THFMA	30	70	1	4	1.57	60	20	24.32	23.54	30.69
F-61-4	THFMA	30	70	1	4	1.05	60	29.9	31.09	29.54	31.09
F-62-1	THFMA	70	30	1	4	6.28	60	5	11.19	10.24	71.84
F-62-2	THFMA	70	30	1	4	3.14	60	10	14.49	12.83	72.49
F-62-3	THFMA	70	30	1	4	1.57	60	20	25.11	21.96	72.74
F-62-4	THFMA	70	30	1	4	1.05	60	29.9	33.18	29.19	72.62
F-63-1	THFMA	30	70	5	10	6.28	60	5	11.47	11.64	29.71
F-63-2	THFMA	30	70	5	10	3.14	60	10	17.53	16.87	30.8
F-63-3	THFMA	30	70	5	10	1.57	60	20	26.34	24.95	31.15
F-63-4	THFMA	30	70	5	10	1.05	60	29.9	33.6	31.21	31.57
F-64-1	THFMA	70	30	5	10	6.28	60	5	12.99	8.67	77.76
F-64-2	THFMA	70	30	5	10	3.14	60	10	18.71	13.89	75.86
F-64-3	THFMA	70	30	5	10	1.57	60	20	28.09	22.58	74.38
F-64-4	THFMA	70	30	5	10	1.05	60	29.9	36.19	30.65	73.37
F-65-1	THFMA	30	70	5	2	6.28	60	5	21.14	17.46	34.16
F-65-2	THFMA	30	70	5	2	3.14	60	10	31.56	28.03	32.55
F-65-3	THFMA	30	70	5	2	1.57	60	20	48.01	44.76	31.49
F-65-4	THFMA	30	70	5	2	1.05	60	29.9	59.84	56.32	31.29
F-66-1	THFMA	70	30	5	2	6.28	60	5	21.45	21.22	70.23
F-66-2	THFMA	70	30	5	2	3.14	60	10	33.99	31.74	71.42
F-66-3	THFMA	70	30	5	2	1.57	60	20	51.49	47.44	71.69
F-66-4	THFMA	70	30	5	2	1.05	60	29.9	63.74	59	71.59

Representative HPLC traces (St-MMA copolymer)

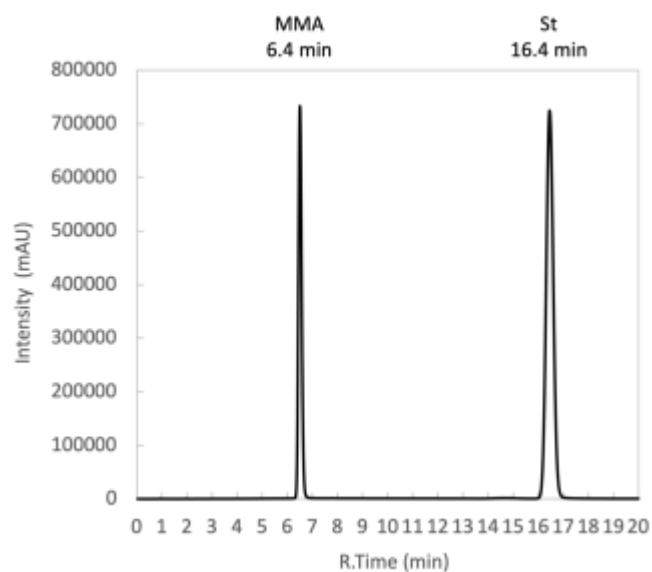


Figure S2. HPLC trace for St-MMA copolymer (F-3_1).

Among the 50 (meth)acrylic and styrene monomers listed in Ref S1, the reactivity of GMA, CHMA, THFMA, ST, and PACS with MMA was considered. Herein, Figure S3 shows that CHMA is more extrapolative.

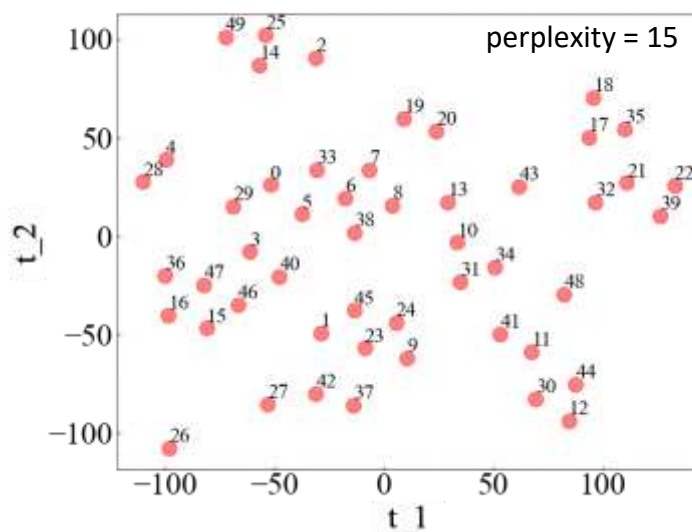


Figure S3. Using t-SNE to visualize 50 molecular structural features (RDKit: 208 features).

Table S3. List of 50 (meth)acrylic and styrene monomers in Ref S1.

No.	Monomer name	CAS No.
0	Methyl Methacrylate	80-62-6
1	Glycidyl Methacrylate	106-91-2
2	Styrene	100-42-5
3	Methyl (Z)-3-methoxyacrylate	5739-81-1
4	Methacrylic Acid	79-41-4
5	Ethyl Methacrylate	97-63-2
6	Butyl Methacrylate	97-88-1
7	Isobutyl Methacrylate	97-86-9
8	tert-Butyl Methacrylate Monomer	585-07-9
9	(3-Ethyloxtan-3-yl)methyl Methacrylate	37674-57-0
10	2-Ethylhexyl Methacrylate	688-84-6
11	Dodecyl Methacrylate	142-90-5
12	Stearyl Methacrylate	32360-05-7
13	Cyclohexyl Methacrylate	101-43-9
14	Benzyl Methacrylate	2495-37-6
15	2-Hydroxyethyl Methacrylate	868-77-9
16	2-Hydroxypropyl methacrylate	923-26-2
17	3-Hydroxy-1-methacryloyloxyadamantane	115372-36-6
18	3,5-Dihydroxy-1-adamantyl methacrylate	115522-15-1
19	2-(Dimethylamino)ethyl Methacrylate	2867-47-2
20	2-(Diethylamino)ethyl Methacrylate	105-16-8
21	Dicyclopentanyl Methacrylate	34759-34-7
22	Dicyclopentenylmethoxyethyl methacrylate	68586-19-6
23	Tetrahydrofurfuryl Methacrylate	2455-24-5
24	2-Propenoic acid, (3-ethyl-3-oxetanyl)methyl ester	41988-14-1
25	4-Vinylphenyl Acetate	2628-16-2
26	Acrylamide Monomer	79-06-01
27	2-Acrylamido-2-methylpropanesulfonic Acid	15214-89-8
28	Acrylic Acid	79-10-7
29	Methyl Acrylate	96-33-3
30	Isooctadecyl acrylate	93841-48-6
31	Isononyl Acrylate	51952-49-9
32	Isobornyl Acrylate	5888-33-5
33	Isobutyl Acrylate	106-63-8
34	n-Octyl Acrylate	2499-59-4
35	1-Acryloyloxy-3-hydroxyadamantane	216581-76-9
36	4-Hydroxybutyl Acrylate	2478-10-6
37	2-[2-(Vinylloxy)ethoxy]ethyl acrylate	86273-46-3
38	tert-Butyl acrylate	1663-39-4
39	Dicyclopentenylmethoxyethyl acrylate	65983-31-5
40	2-Methoxyethyl acrylate	3121-61-7
41	Dodecyl acrylate	2156-97-0
42	Ethyl 3,3-diethoxyacrylate	32002-24-7
43	1,4-Cyclohexanedimethanol monoacrylate	23117-36-4
44	Stearyl acrylate	4813-57-4
45	Tetrahydrofurfuryl acrylate	2399-48-6
46	2-Hydroxyethyl acrylate	818-61-1
47	2-hydroxypropyl acrylate	999-61-1
48	4-Hydroxybutyl acrylate glycidyl ether	119692-59-0
49	2-Phenoxyethyl acrylate	48145-04-6

Examination 1 (Search for interpolated regions using double cross validation)

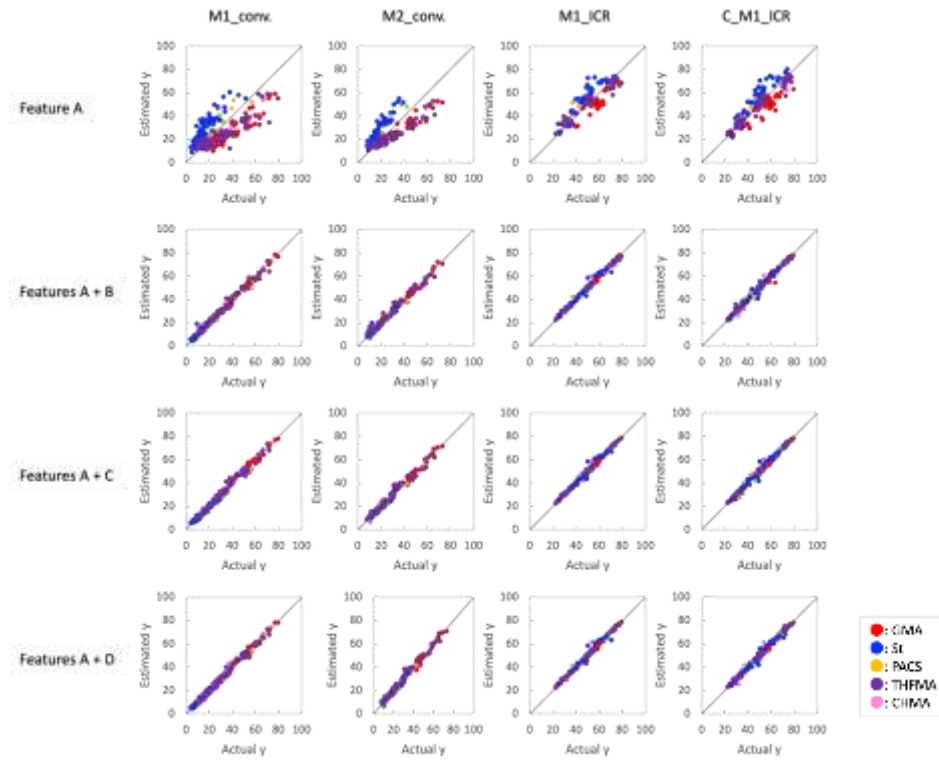


Figure S4. Plots of actual y vs. estimated y for each objective variable in v -SVR in interpolated region.

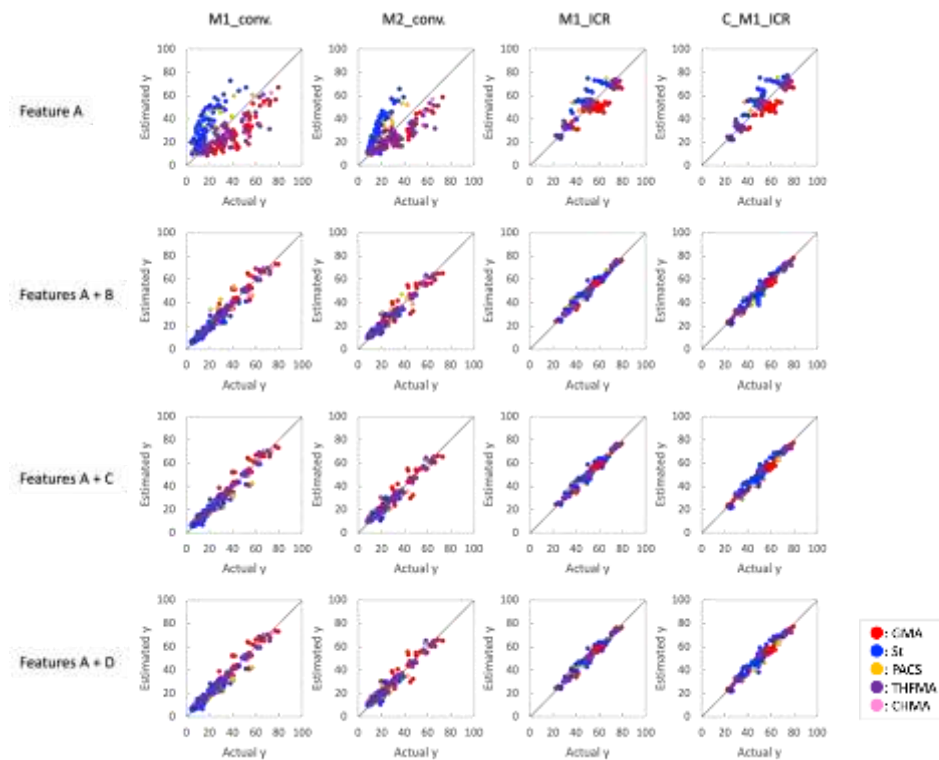


Figure S5. Plots of actual y vs. estimated y for each objective variable in RF in interpolated region.

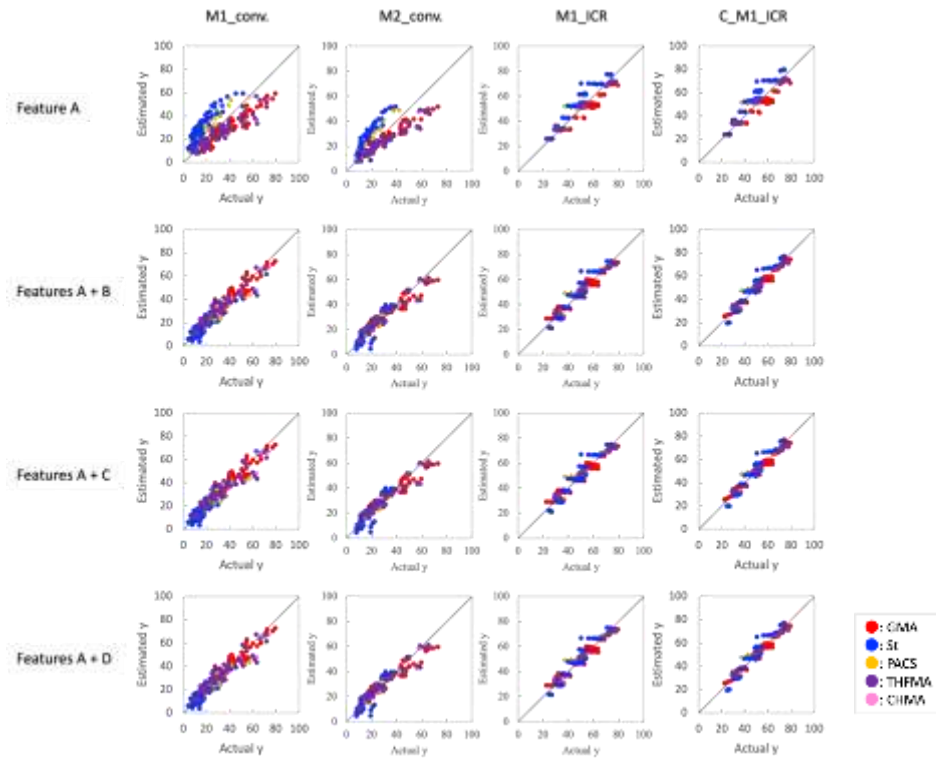


Figure S6. Plots of actual y vs. estimated y for each objective variable in PLS in interpolated region.

Table S4. Calculated R^2 and MAE values for each model in interpolated region.

Model	Feature sets	M1_conv.		M2_conv.		M1_ICR		C_M1_ICR	
		R^2	MAE	R^2	MAE	R^2	MAE	R^2	MAE
v-SVR	-	0.42	11.15	0.57	8.05	0.82	4.25	0.80	4.49
	A	0.99	1.43	0.98	1.42	0.99	0.85	0.98	1.04
	B	0.99	1.48	0.98	1.53	0.99	0.76	0.99	1.00
	D	0.99	1.42	0.98	1.40	0.99	0.82	0.99	1.05
RF	-	0.12	13.46	0.32	9.80	0.79	4.55	0.78	4.78
	A	0.95	2.57	0.94	2.40	0.98	1.39	0.96	1.91
	B	0.96	2.48	0.95	2.27	0.98	1.40	0.96	1.90
	D	0.96	2.49	0.95	2.27	0.98	1.39	0.96	1.92
PLS	-	0.49	10.48	0.57	7.75	0.87	3.66	0.87	3.73
	A	0.91	4.05	0.90	3.41	0.94	2.64	0.95	2.28
	B	0.91	4.05	0.90	3.40	0.94	2.65	0.95	2.30
	D	0.91	4.06	0.90	3.41	0.94	2.65	0.95	2.28

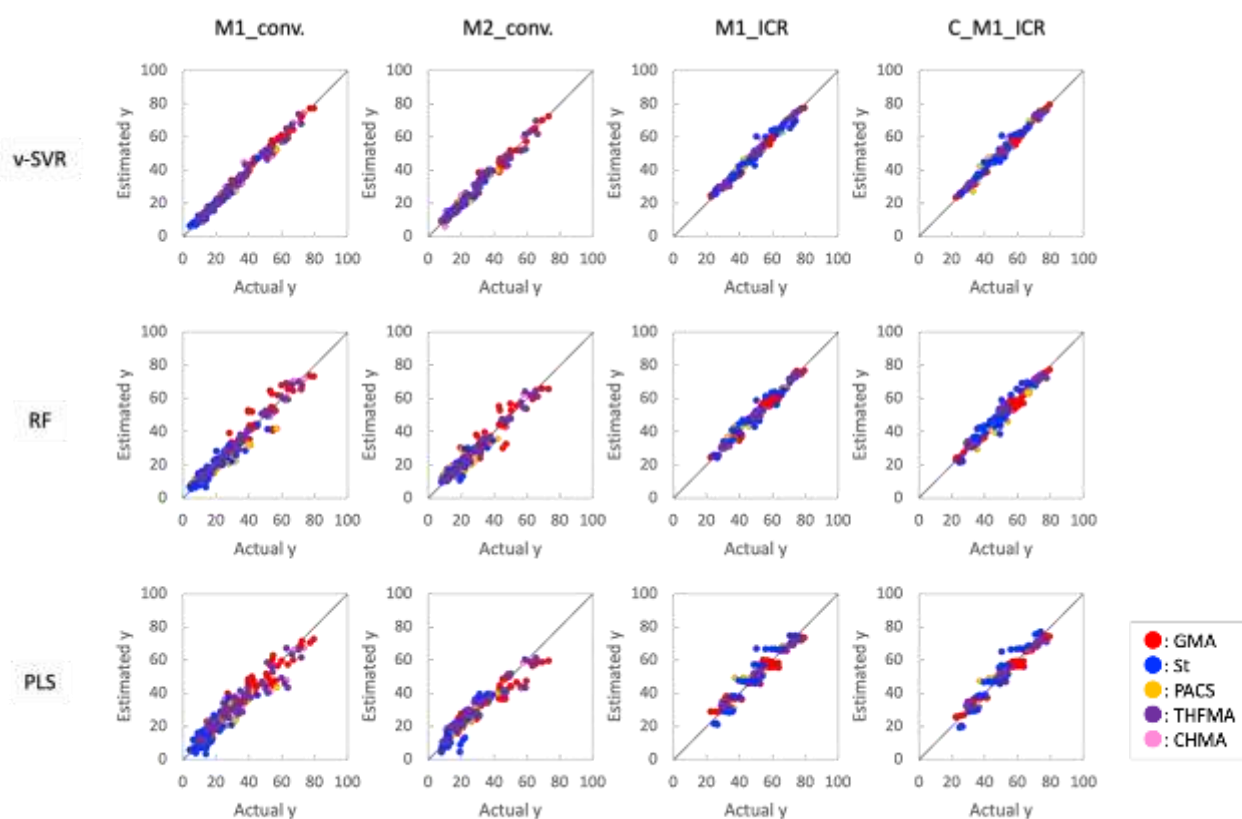


Figure S7. Plots of actual y vs. estimated y for each model using all objective variables (A + B + C + D) in interpolated region.

Table S5. Calculated R^2 and MAE values for each model using all objective variables (A + B + C + D) in interpolated region.

Model	Feature sets	M1_conv.		M2_conv.		M1_ICR		C_M1_ICR	
		R^2	MAE	R^2	MAE	R^2	MAE	R^2	MAE
v-SVR		0.99	1.51	0.98	1.63	0.99	0.96	0.99	1.03
RF	A + B + C + D	0.95	2.49	0.95	2.27	0.98	1.40	0.93	1.90
PLS		0.91	4.05	0.90	3.40	0.94	2.64	0.95	2.29

Examination 2 (Search for extrapolated regions using molecular extrapolation validation)

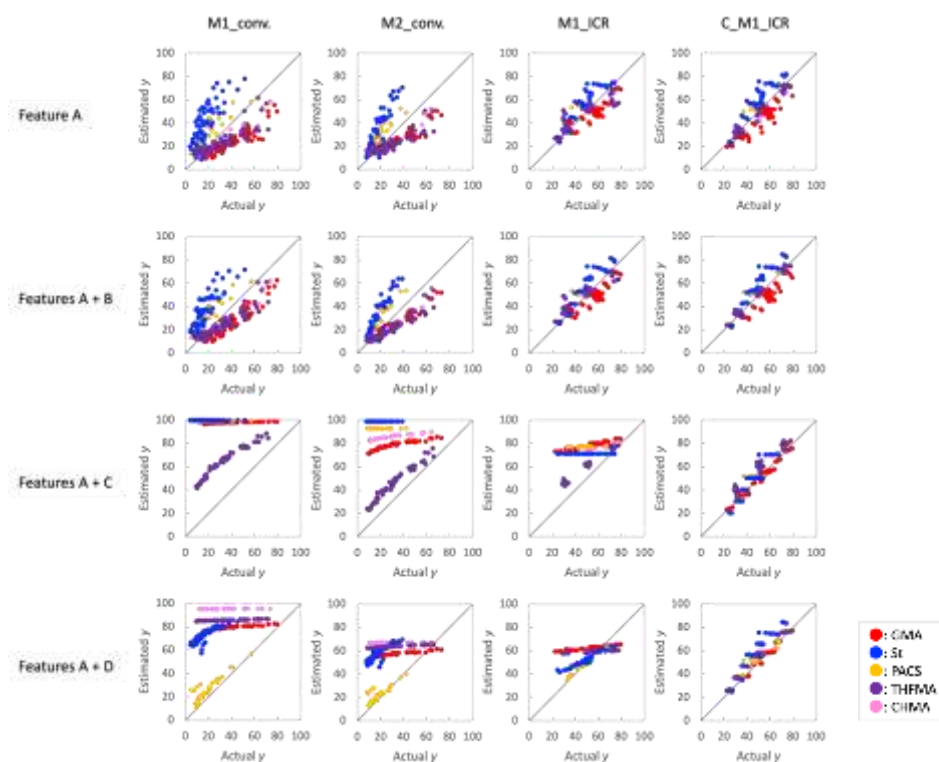


Figure S8. Plots of actual y vs. estimated y for each objective variable in v-SVR in extrapolated region.

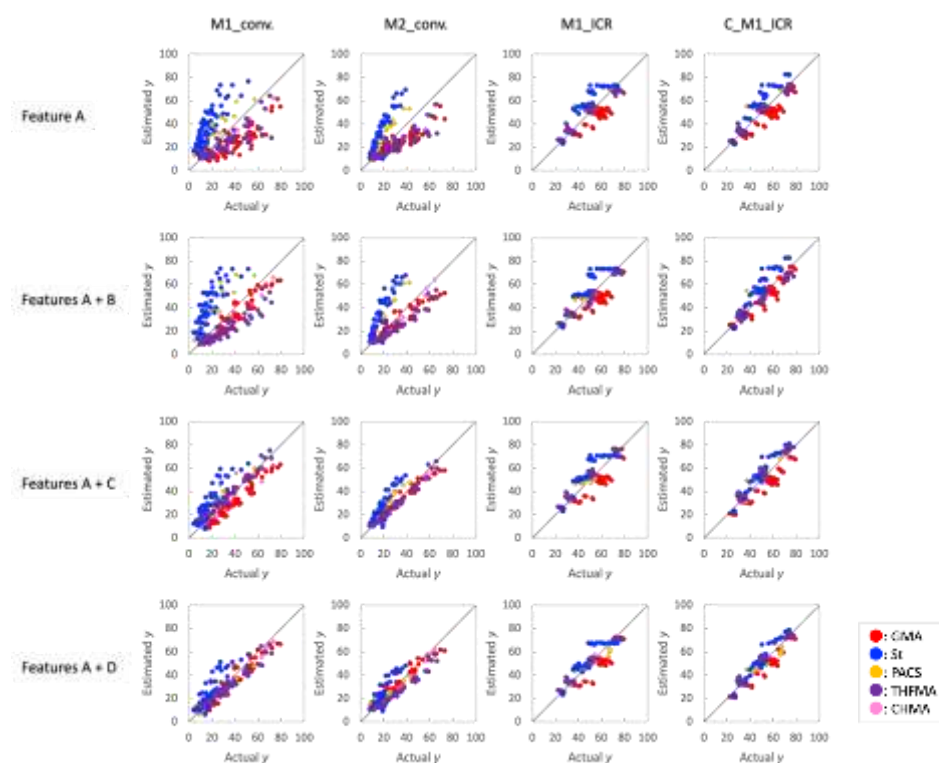


Figure S9. Plots of actual y vs. estimated y for each objective variable in RF in extrapolated region.

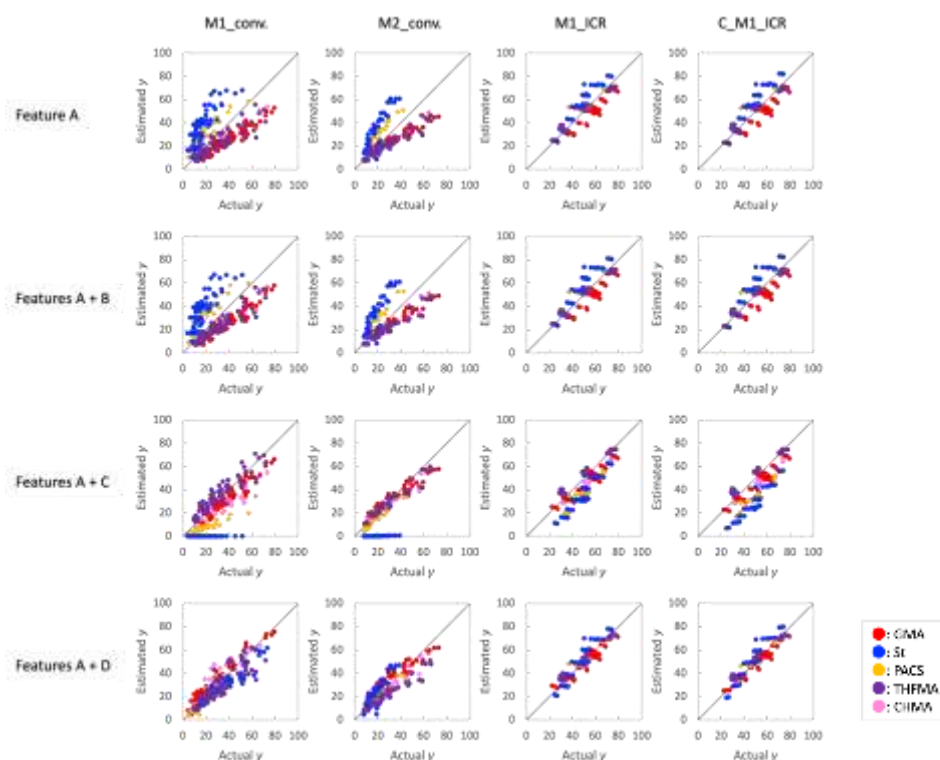


Figure S10. Plots of actual y vs. estimated y for each objective variable in PLS in extrapolated region.

Table S6. Calculated R^2 and MAE values for each model in extrapolated region.

Model	Feature sets	M1_conv.		M2_conv.		M1_ICR		C_M1_ICR	
		R^2	MAE	R^2	MAE	R^2	MAE	R^2	MAE
v-SVR	-	-0.11	15.15	0.17	10.61	0.65	6.07	0.71	5.42
	A	0.17	13.43	0.34	9.75	0.74	5.16	0.77	4.80
	B	-13.3	60.69	-14.9	51.54	-2.33	21.60	0.85	3.96
	D	-7.18	44.82	-4.13	29.28	0.01	10.17	0.79	4.91
RF	-	-0.03	14.63	0.21	10.46	0.73	5.26	0.74	5.20
	A	0.04	13.72	0.23	10.08	0.73	5.31	0.81	4.53
	B	0.66	8.17	0.82	4.71	0.76	5.01	0.79	5.05
	D	0.84	5.46	0.84	4.26	0.81	3.97	0.88	3.46
PLS	-	0.10	13.81	0.29	9.89	0.79	4.78	0.79	4.80
	A	0.17	13.41	0.33	9.69	0.80	4.62	0.79	4.66
	B	0.42	10.34	0.49	7.26	0.42	8.53	0.06	10.42
	D	0.81	5.64	0.76	5.53	0.89	3.53	0.90	3.20

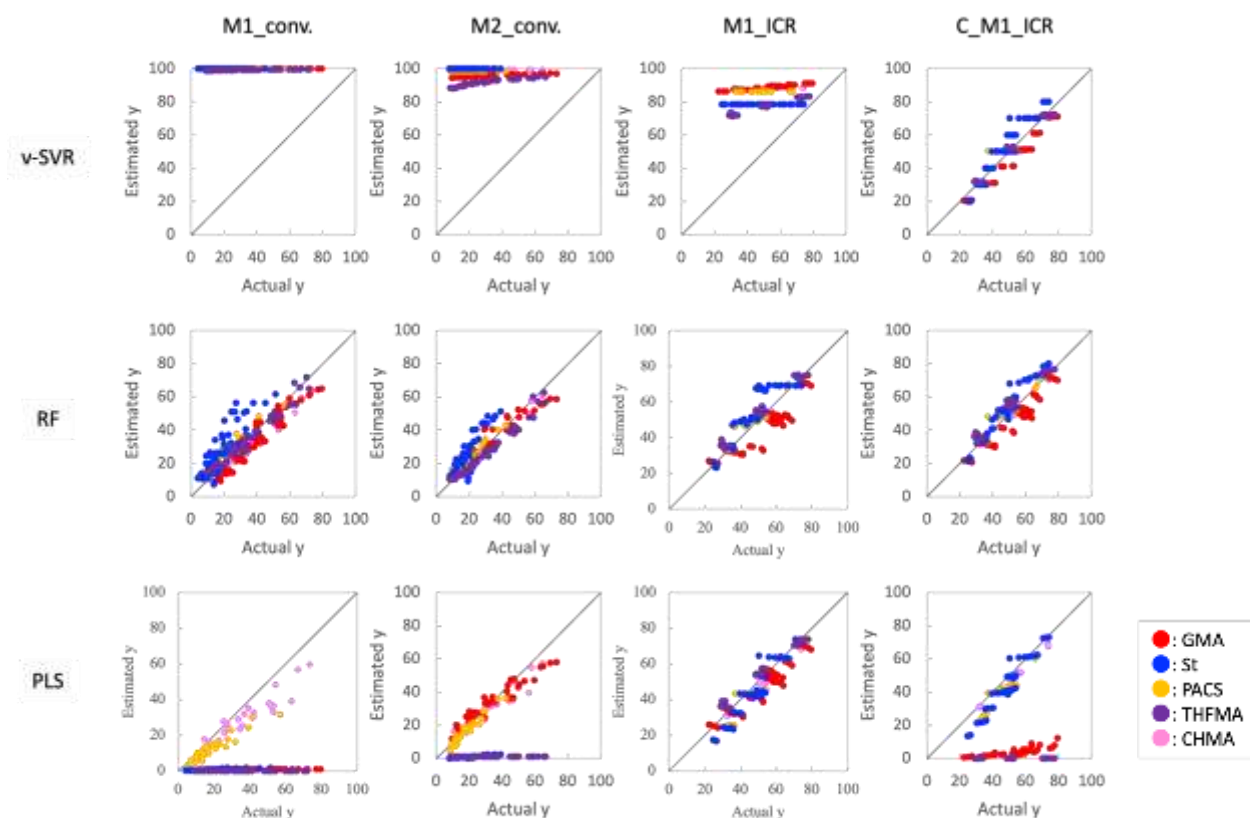


Figure S11. Plots of actual y vs. estimated y for each model using all objective variables (A + B + C + D) in extrapolated region.

Table S7. Calculated R^2 and MAE values for each model using all objective variables (A + B + C + D) in extrapolated region.

Model	Feature sets	M1_conv.		M2_conv.		M1_ICR		C_M1_ICR	
		R^2	MAE	R^2	MAE	R^2	MAE	R^2	MAE
v-SVR		-16.55	69.80	-23.38	70.09	-5.71	32.54	0.86	3.94
RF	A + B + C + D	0.77	6.58	0.85	4.48	0.79	4.48	0.85	4.16
PLS		-2.21	24.86	-0.75	13.18	0.81	4.92	-6.92	29.21

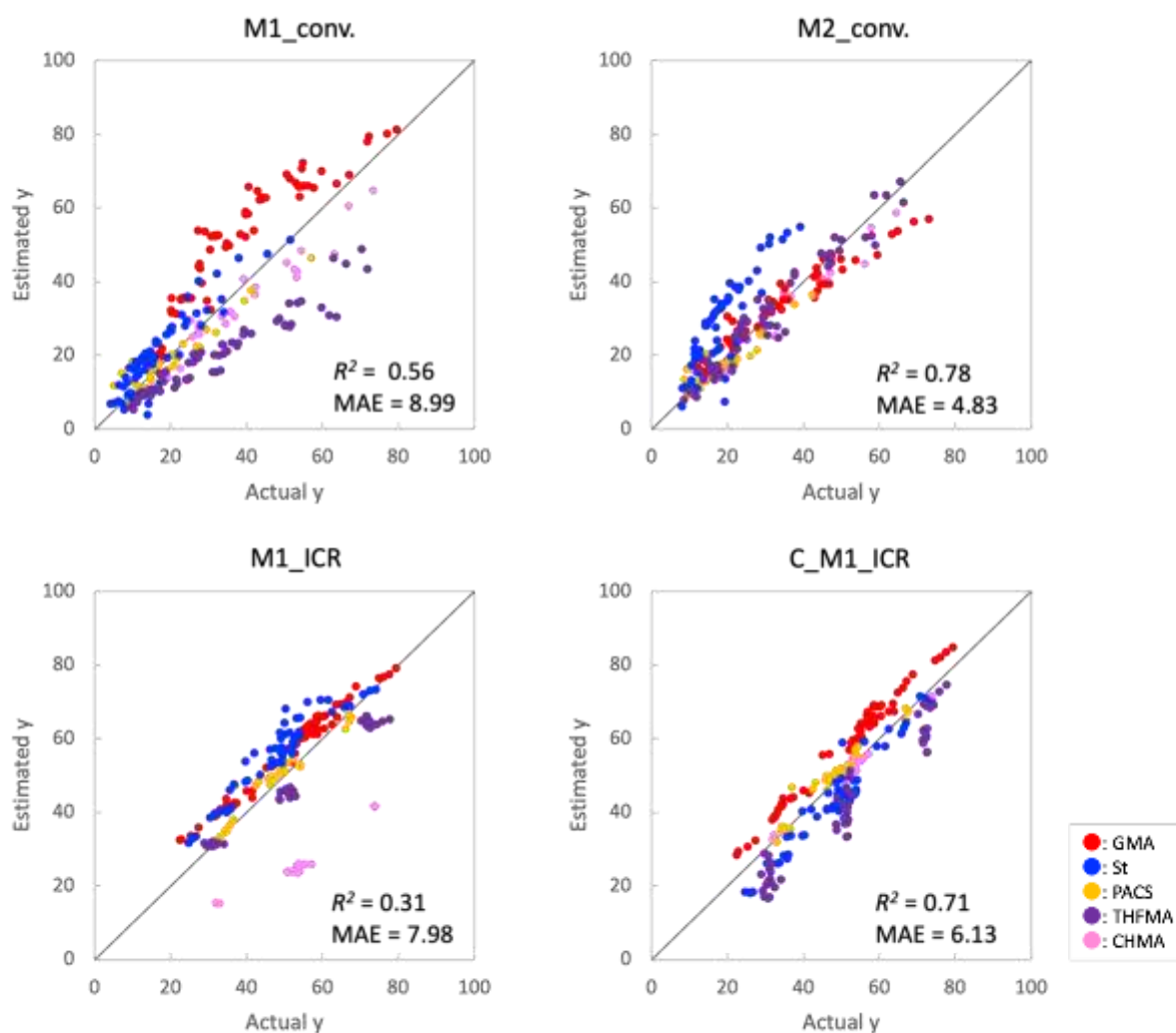


Figure S12. Plots of actual y vs. estimated y for the neural network using feature A + D in extrapolated region.

Model Architecture: contains 256 neurons in the first hidden layer, 64 neurons in the second hidden layer, and 16 neurons in the third hidden layer with 200 iterations (max).

Recursive feature elimination (RFE)

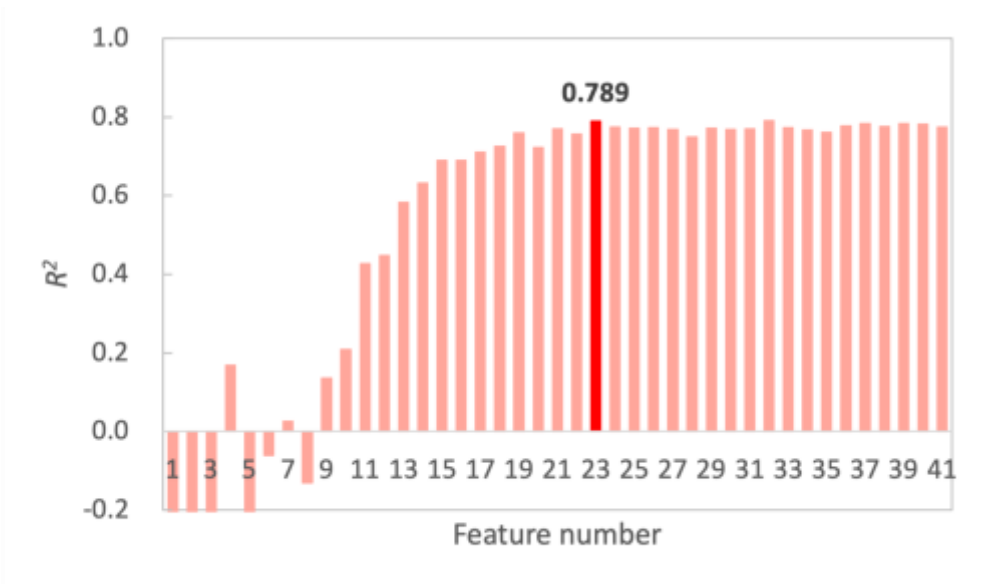


Figure S13. Calculated R^2 for each feature.

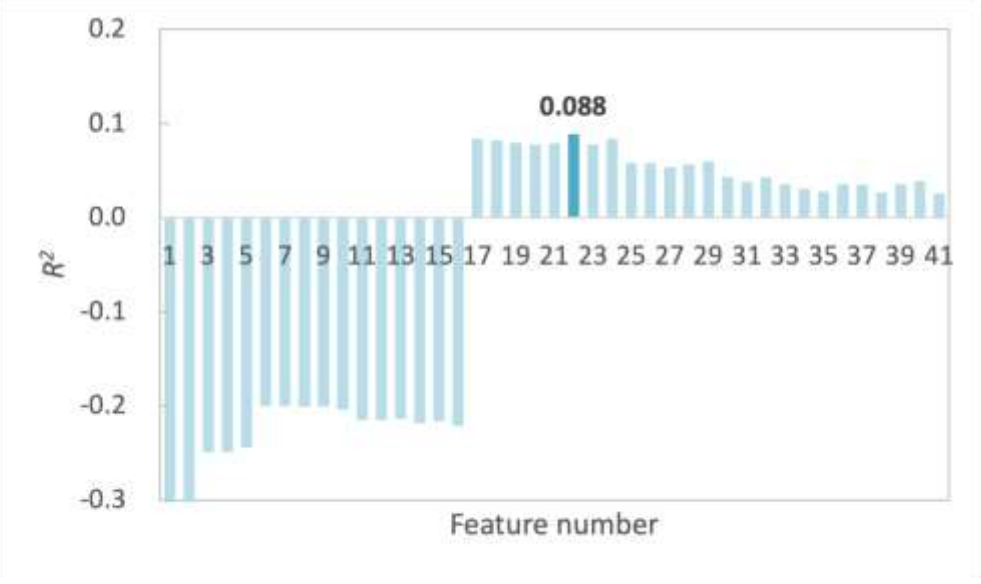


Figure S14. Calculated R^2 for each feature.

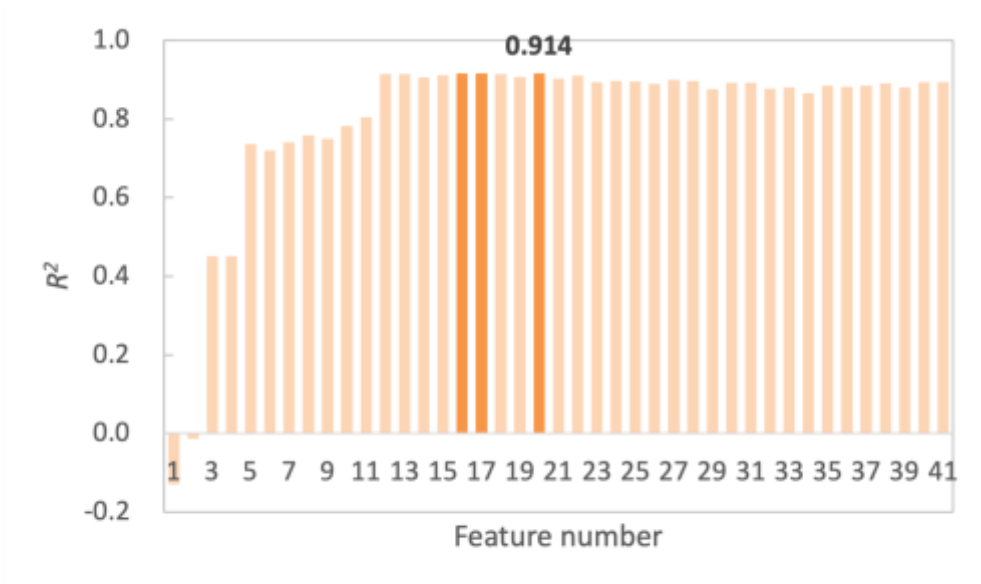


Figure S15. Calculated R^2 for each feature

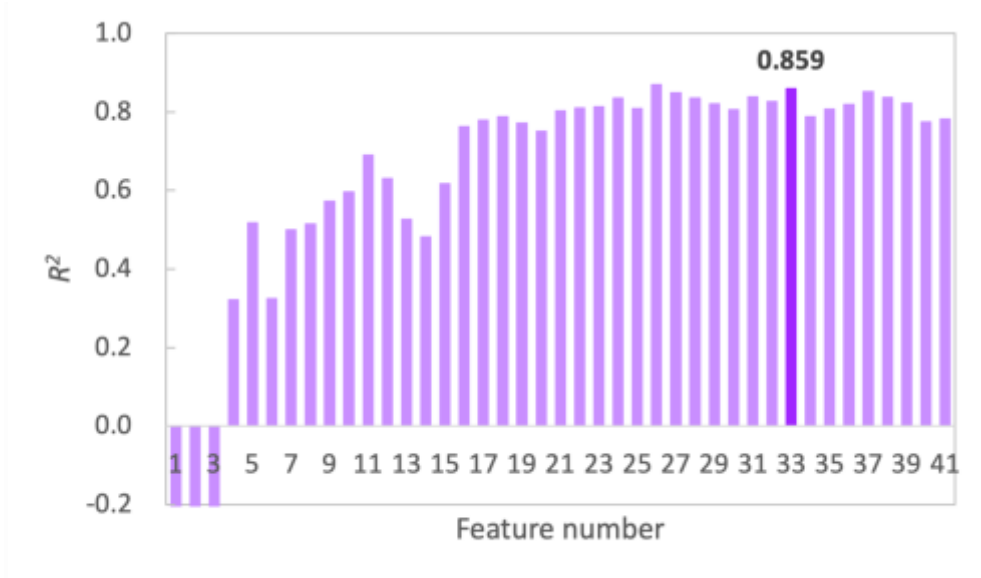


Figure S16. Calculated R^2 for each feature.

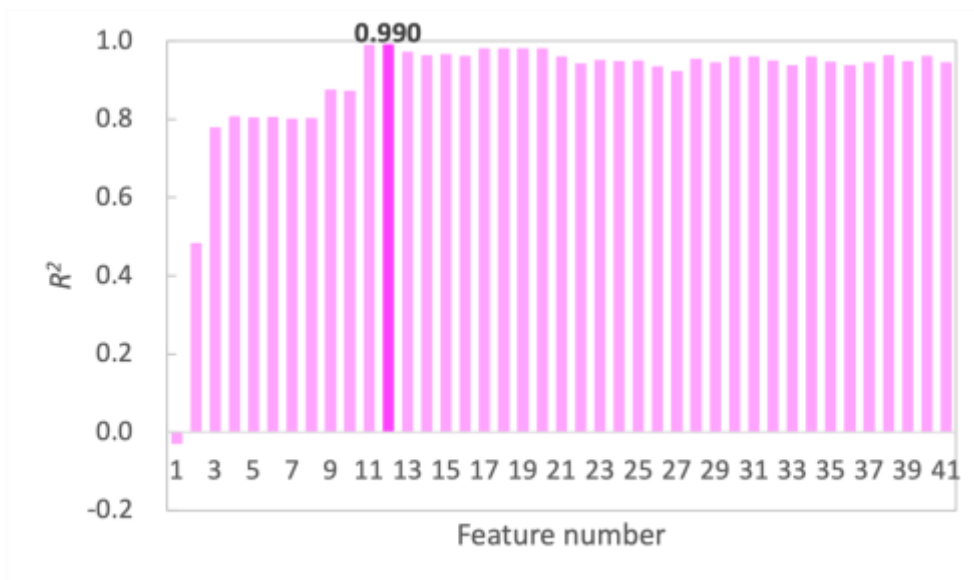


Figure S17. Calculated R^2 for each feature.

Explanatory variables

Table S8. List of parameters calculated by DFT method.

Monomer	GMA	St	CHMA	THFMA	PACS
DE_M00_TS_theta60	-0.003015671	0.000453725	-0.009129773	-0.005293026	0.000555753
Real_theta_M00_theta60	70.23564207	56.15353136	72.17562408	51.25233077	54.50603002
DE_M00_TS_theta180	-0.005512013	-0.002199144	-0.005819303	-0.005126284	-0.002725805
Real_theta_M00_theta180	173.2057863	178.3675235	189.8003006	204.3511202	177.7359104
DE_M00_TS_theta300	-0.004917453	-0.000958591	-0.007041858	-0.004227422	-0.000846792
Real_theta_M00_theta300	305.4991493	308.446018	324.7409414	308.213834	308.1126372
DE_00M_TS_theta60	-0.004686666	-0.002790514	-0.005954314	-0.003727761	-0.002996113
Real_theta_00M_theta60	74.6871307	60.12718366	41.13362743	51.46198515	59.7782855
DE_00M_TS_theta180	-0.007332908	-0.004174637	-0.005377352	-0.005700981	-0.004324217
Real_theta_00M_theta180	156.2884273	208.3674353	182.8188912	171.7563309	208.3641054
DE_00M_TS_theta300	-0.006948181	-0.002935987	-0.009390278	-0.006105677	-0.003096496
Real_theta_00M_theta300	308.3303933	291.6177967	289.5383495	311.6937046	290.1038477
DE_MM_TS_theta60	-0.004612167	0.001509026	-0.007397412	-0.006006008	0.001635736
Real_theta_MM_theta60	79.76837866	57.2356454	80.5529613	39.68781394	62.05845262
DE_MM_TS_theta180	-0.008853995	-0.000525124	-0.011625977	-0.007061631	-0.008330683
Real_theta_MM_theta180	164.6841998	176.5712775	174.9017246	180.1318468	173.2780436
DE_MM_TS_theta300	-0.01027043	0.001540489	-0.006675079	-0.004991215	0.001424407
Real_theta_MM_theta300	258.2276633	291.4854858	271.0157861	284.4189013	292.6451545
E_M_Rad_SOMO	-0.22108451	-0.178146229	-0.21339748	-0.216737169	-0.175182529
E_M_Rad_LUMO	0.035405137	-0.009196424	0.040121638	0.038501022	-0.0150155
E_M_Mon_HOMO	-0.275241871	-0.230830579	-0.271586573	-0.253740925	-0.225539183
E_M_Mon_LUMO	-0.052799579	-0.042225132	-0.044570869	-0.048291459	-0.045912177
DE_M_decomposition_head	0.062134228	0.063061185	0.061804369	0.061256585	0.063245575
DE_M_decomposition_tail	0.038719349	0.038749391	0.039385516	0.037937566	0.038492683
E_00_Rad_SOMO	-0.214231645	-0.214231645	-0.214231645	-0.214231645	-0.214231645
E_00_Rad_LUMO	0.044572116	0.044572116	0.044572116	0.044572116	0.044572116
E_00_Mon_HOMO	-0.273330301	-0.273330301	-0.273330301	-0.273330301	-0.273330301
E_00_Mon_LUMO	-0.045363064	-0.045363064	-0.045363064	-0.045363064	-0.045363064
DE_00_decomposition_head	0.061518379	0.061518379	0.061518379	0.061518379	0.061518379
DE_00_decomposition_tail	0.0385338	0.0385338	0.0385338	0.0385338	0.0385338
DE_M00_SHgap	0.052245791	0.095184072	0.059932821	0.056593132	0.098147772
DE_M00_SLgap	0.175721446	0.132783165	0.168034416	0.171374105	0.129819465
DE_00M_SHgap	0.061010226	0.016598934	0.057354928	0.03950928	0.011307538
DE_00M_SLgap	0.161432066	0.172006513	0.169660776	0.165940187	0.168319468
DE_MM_SHgap	0.054157361	0.05268435	0.058189093	0.037003756	0.050356654
DE_MM_SLgap	0.168284931	0.135921097	0.168826611	0.168445711	0.129270352

References

S1) Chemical Daily Co. Ltd., Chemical products handbook-17019. Chemical Daily Co. Ltd., Tokyo, 2019 (in Japanese).