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Flow Mediated Metal-Free PET-RAFT Polymerisation for Upscaled and Consistent Polymer Production

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Materials

N,N'-dimethylacrylamide (DMAm, 99%) was purchased from Sigma-Aldrich and *N,N'*-diethylacrylamide (DEAm, 98%) was purchased from TCI chemicals. The monomers were deinhibited by percolation through basic alumina (Ajax Chemical, AR) column before use. Eosin Y (EY), rose Bengal (RB), phloxine B (PB), and erythrosine B (EB) were purchased from Sigma-Aldrich and used as received. Solvents dimethylsulfoxide (DMSO, 99%) and *N,N'*-dimethylacetamide (DMAc, 99 %), were all supplied by Ajax Chemical and used as received. 2-((dodecylthio)carbonylthio)thio)propanoic acid (DTPA, 97%) was obtained from Boron Molecular and used as received. 2-(*n*-butyltrithiocarbonate) butylpropionic acid (BTPA) was synthesised according to the literature.[1]

Instrumentation

Gel Permeation Chromatography (GPC) was used to characterise synthesised polymer with dimethylacetamide (DMAc) as the eluent. The GPC instrument consists of Shimadzu modular system with an auto-injector, a Phenomenex 5.0 µm bead size guard column (50 × 7.5 mm) followed by four Phenomenex 5.0 µm bead size columns (10^5 , 10^4 , 10^3 and 10^2 Å) for the DMAc system. The DMAc GPC system was calibrated based on narrow molecular weight distribution poly(methyl methacrylate) standards with molecular weights of 200 to 10^6 g mol^{-1}. Nuclear Magnetic Resonance (NMR) spectroscopy was carried out with Bruker Avance III with SampleXpress operating at either 300 or 400 MHz for ^1H using $CDCl_3$ as solvent. Tetramethylsilane (TMS) was used as a reference. The data obtained was reported as chemical shift (δ) measured in ppm downfield from TMS. UV−Vis spectroscopy spectra were recorded using a CARY 300 spectrophotometer (Varian) equipped with a temperature controller.

Flow reactor

The photo-flow reactor used during this work was composed of an outer PVC pipe to which LED strips are attached. An inner PMMA pipe is used to attach the fluorinated ethylene propylene (FEP) tubing which the reaction mixture flows through. The flow reactor utilised 5050 SMD LEDs at 60 LEDs per meter drawing a maximum power of 14.4 W/m, at 12-24 V, set to green (525-535 nm, 3.8 W/m^2 max intensity at the tube surface as measured using a Newport 843-R power meter). The total LED coil length inside the tubular reactor was 10 m. A New Era NE-1000 multi-phaser syringe pump was used in conjunction with NormJect syringes to inject solutions into the FEP tubing which purchased from John Morris Scientific. Poly(vinylidene fluoride) (PVDF) luer valve connectors, Y connectors and straight connectors used were also purchased from John Morris Scientific. All reactions were performed at room temperature (measured as 22 ˚C +/- 2 ˚C). The dimensions of the photo-flow reactor are shown in our previous work.[2]

General Procedure for the synthesis of poly(*N*,*N*-dimethylacrylamide) (PDMAm) via PET-RAFT polymerization in batch in the absence and presence of oxygen

Polymerisation of *N*,*N*-dimethylacrylamide (DMAm) was carried out in a 4 mL glass vial with DMSO (700 µL, 9.86 mmol), DMAm (300 µL, 2.80 mmol), 2-((*n*-butylthio)carbonylthio)thio) propanoic acid (BTPA, 3.34 mg, 14.03 µmol), and EB (0.123 mg, 0.14 µmol). If degassing was required, the vial was sealed with a rubber septum and parafilm then wrapped in aluminium foil and degassed under nitrogen for 20 min. For polymerisation in the presence of air this step was skipped. Reaction mixtures were then irradiated under LED light at room temperature (measured to be 22 ˚C). After irradiation, the reaction mixture was removed from the light source in order to be analysed by ^{1}H NMR ($CDCl_3$) and GPC (DMAc) to determine monomer conversions, number-average molecular weights (M_n) and dispersities ($Đ$).

General procedure for the synthesis of poly(*N*,*N*-dimethylacrylamide) (PDMAm) via PET-RAFT polymerization in the flow reactor

1 mL of reaction mixture with the same composition as the batch system was firstly prepared in a 4 mL glass vial, sonicated for ~20 s, then transferred into a new 5 mL NormJect syringe. The syringe was fastened to New Era NE-1000 syringe pump and connected to the reactor tubing via a luer valve connector. Then, the LED lights were turned on and a two-pump system was used to inject reaction mixture into the flow reactor under ambient conditions, i.e., no deoxygenation procedures were performed, and the reaction was performed on the benchtop. The two-pump system is composed of one-pump which was used to inject a homogenised reaction mixture (pump 1), and another pump that injected gas (pump 2) into the photo-flow reactor via syringes (**Figure S1**).

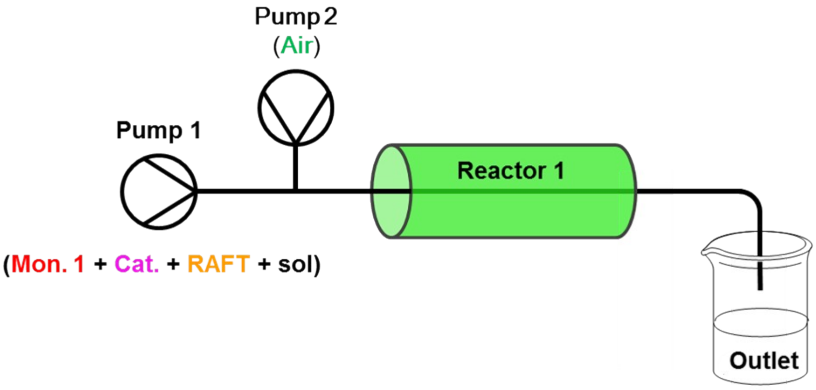

Figure S1. Two-pump reactor system. Pump one injected a reaction mixture containing RAFT agent, solvent, monomer, and catalyst, pump 2 injected air.

While pump 2 was injecting gas, pump 1 was stopped and vice versa, such that the liquid slug could be effectively separated into discrete sections. The flow rate for injection of gas into the reactor was always identical to the flow rate of the reactant slug to ensure correct residence times were maintained for all polymerisation mixtures. To limit human error, the injection of reactants and air was autonomously controlled by pumping programs on the New Era NE-1000 syringe pumps.

For the flow polymerisation presented in **Table 1**, **Figure 4**, and **Figure 5**, pump 1 was started to inject 600 µL of reaction mixture; after the injection finished, pump 1 was immediately stopped and pump 2 was started simultaneously to inject 200 µL of air. Subsequently, a 50 mL NormJect syringe filled with DMSO was used to push the reaction mixture through the reactor tube (28200 µL) at a designated rate (e.g. 117.5 µL/min for 4 h residence time) from pump 1. After polymerization, the reaction mixture was collected into a new 4 mL glass vial covered with aluminium foil and vigorously shaken before ^{1}H NMR and GPC analyses.

General procedure for the synthesis of PDMAm-*b*-PDMAm copolymers in flow

An identical procedure as above was followed for the formation of the first block. Following, a mixture of DMSO (700 µL, 9.86 mmol) and DMAm (300 µL, 2.80 mmol) was prepared in a 4 mL glass vial and sonicated for ~20 s, then withdrawn into a 5 mL NormJect syringe. A two pump system was again used for injection; the first pump injected the polymerisation mixture from the outlet of the first reactor into a 60 mL section of dark tubing (FEP covered in foil, *i.d.* = 3.18 mm), while the second pump simultaneously injected 600 µL of the solvated monomer solution into the same 60 mL section of dark tubing. The flow rate for the second pump (solvated monomer) was set to 1.05 times the flow rate of pump 1 to compensate for the reduction in volume of the polymerisation mixture formed in the first reactor. As such, the polymerisation mixture was mixed with the solvated monomer solution during the injection. The second pump was stopped after injecting 600 µL of the solvated monomer solution while the first pump continued; as a result, the chain extension mixture was separated into a discrete slug by the 200 µL air slug that followed the polymerisation mixture from the synthesis of the first block (vide supra). The first pump was then set to a high flow rate (4500 µL/min) to allow thorough mixing of the solution in the 60 mL section of dark tubing, prior to the chain extension mixture entering a second identical 28200 µL flow reactor. Flow rates for the chain extension were calculated and controlled as before (via a 50 mL NormJect syringe filled with DMSO), and sampling was performed as outlined previously.

General procedure for the upscaled synthesis of poly(*N*,*N*-dimethylacrylamide) (PDMAm) via PET-RAFT polymerization in the flow reactor under fully continuous conditions

The fully continuous upscaled procedure utilised a two pump system. Pump 1 was started and injected 56000 μL of reaction mixture; after the injection finished pump 1 was immediately stopped and pump 2 was started simultaneously to inject 500 μL of air. A small section of DMSO (1 mL) was subsequently injected from a 50 mL NormJect syringe syringe connected to pump 1, in order to collect any polymer that was not eluted with the bulk reaction mixtures. Subsequently, a small section of air (~500 μL) was injected from pump 2, and then 28200 μL of DMSO was injected from the 50 mL NormJect syringe filled with DMSO to push the remaining reaction mixture through the reactor tube at a designated rate (e.g. 117.5 μL/min for 4 h residence time) from pump 1. Product collection was the same as outlined previously, with the cumulative polymer product being kept separate from the instantaneous samples.

General procedure for the upscaled synthesis of poly(*N*,*N*-dimethylacrylamide) (PDMAm) via PET-RAFT polymerization in the flow reactor under slug flow conditions

For the upscaled slug flow polymerisation, pump 1 was started and injected 1000 μL of reaction mixture; after the injection finished, pump 1 was immediately stopped and pump 2 was started simultaneously to inject 200 μL of air. After the injection of air, pump 2 was immediately stopped and pump 1 was started simultaneously to inject another 1000 μL of reaction mixture. This process was repeated until 47 slugs of reaction mixture with 1000 μL volume and 47 slugs of air with 200 μL volume had been injected into the flow reactor in an alternating fashion. A small section of DMSO (1 mL) was subsequently injected from a 50 mL NormJect syringe syringe connected to pump 1, in order to collect any polymer that was not eluted with the bulk reaction mixtures. Subsequently, a small section of air (~500 μL) was injected from pump 2, and then 28200 μL of

DMSO was injected from the 50 mL NormJect syringe filled with DMSO to push the remaining reaction mixture through the reactor tube at a designated rate (e.g. 117.5 µL/min for 4 h residence time) from pump 1. Notably, the alternating injection of reaction mixture and air can be continued indefinitely given that there is sufficient reaction mixtures available for injection. In the present case, the DMSO block was injected to reduce required the quantities of starting materials.

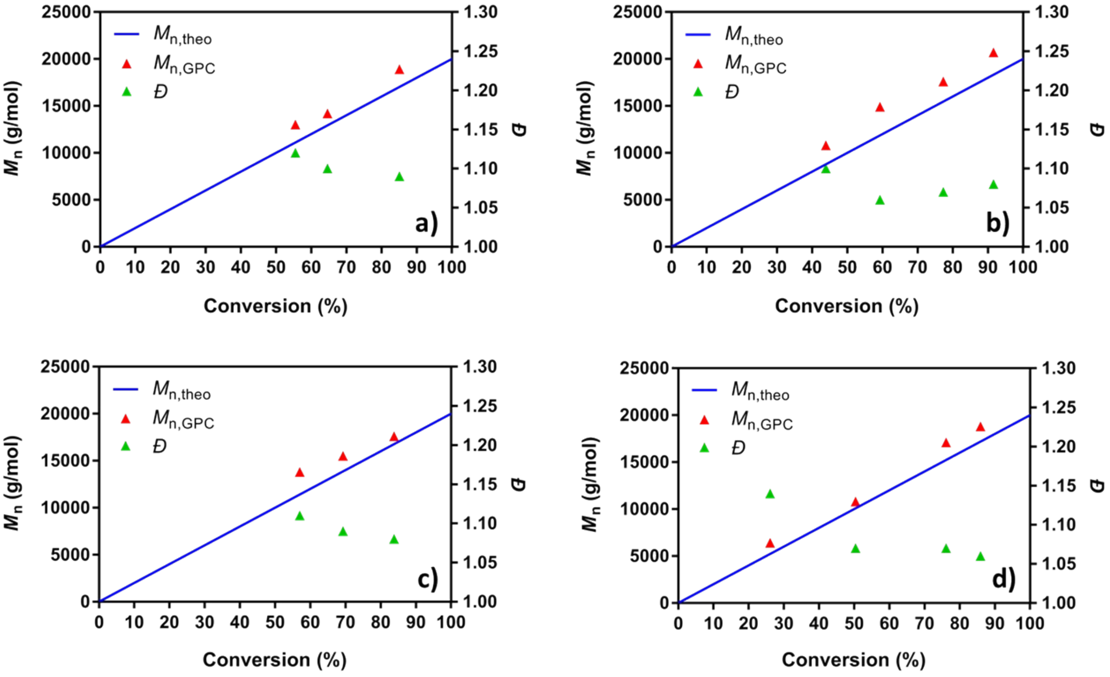

Figure S2 Number-average molecular weight (M_n) and dispersity (*Đ*) *vs* monomer conversion for PET-RAFT polymerization in flow mediated by a) EY, b) EB, c) PB, d) RB.

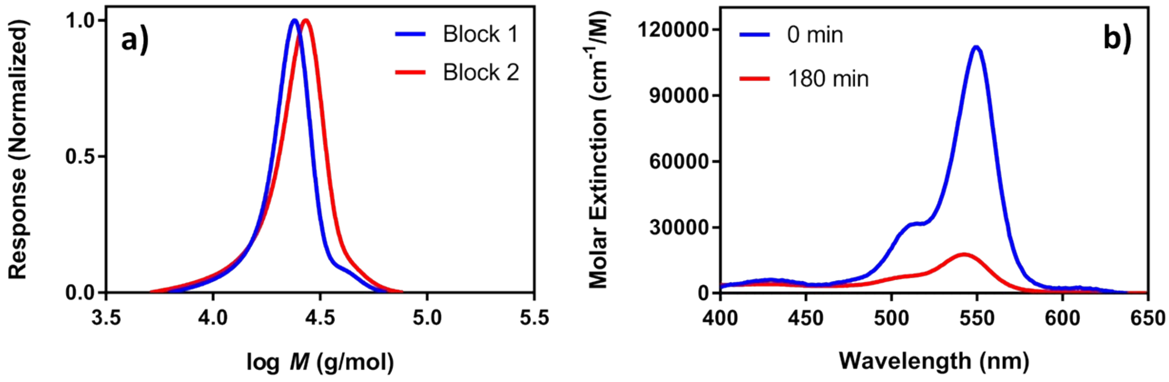

Figure S3 Unseccessful chain extension in one-pass two-reactor flow system. a) GPC curves for PDMAm homopolymer and PDMAm-*b*-PDMAm chain extension; b) UV-Vis spectra of reaction mixture before and after irradiation.

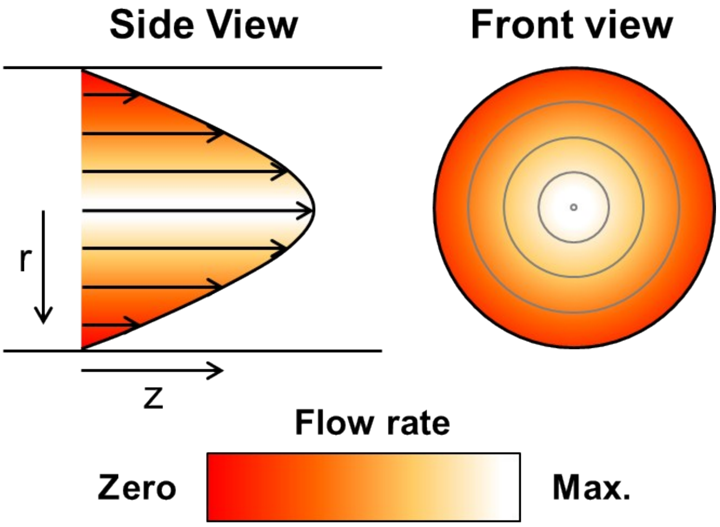

Figure S4 Laminar flow profiles.

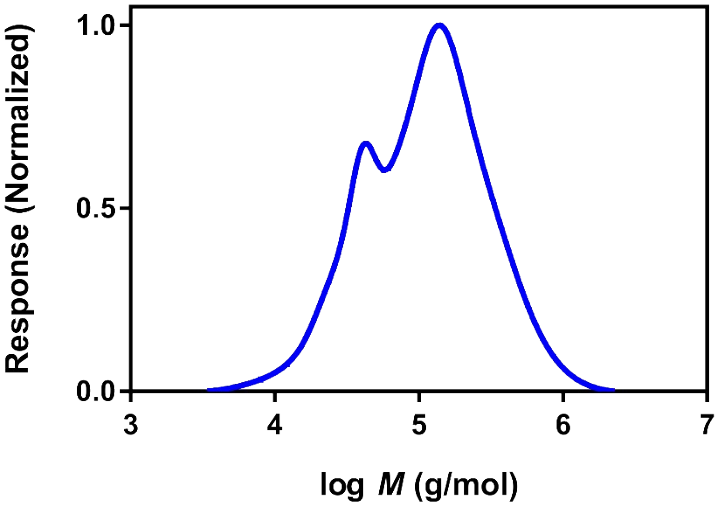

Figure S5 Broadly distributed high molecular weight polymer formed in fully continuous process.

Additional References:

1. C. J. Ferguson, R. J. Hughes, D. Nguyen, B. T. T. Pham, R. G. Gilbert, A. K. Serelis, C. H. Such and B. S. Hawkett, *Macromolecules*, 2005, **38**, 2191-2204.
2. N. Corrigan, D. Rosli, J. W. J. Jones, J. Xu and C. Boyer, *Macromolecules*, 2016, **49**, 6779-6789.