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## Continuous synthesis of block copolymer nanoparticles *via* telescoped RAFT solution and dispersion polymerisation in a miniature CSTR cascade†

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Miniaturised continuous-flow reactors offer a safe, economical, and scalable route to explore the synthesis of high-value chemical products. In the context of polymer synthesis, precisely defined and tuneable products can be prepared *via* reversible de-activation radical polymerisation (RDRP) techniques such as reversible addition-fragmentation chain-transfer (RAFT), for which tubular reactors are commonly reported. Herein, we present a miniature continuous stirred-tank reactor (CSTR) cascade for continuous-flow RAFT polymerisation with active mixing throughout, which is found to perform close to a theoretical CSTR cascade for the polymerisations considered in this study. The performance of the reactor is evaluated for both the aqueous solution RAFT polymerisation of *N,N*-dimethylacrylamide (DMAM) and the RAFT dispersion polymerisation of diacetone acrylamide using a poly(DMAM) macromolecular chain transfer agent (macro-CTA). It was determined that the residence time distribution (RTD) is important for informing the properties of the resulting polymers, with more CSTRs resulting in a narrower molar mass distribution. For particle synthesis by polymerisation-induced self-assembly (PISA), a series of block copolymers were prepared in separate batch and flow experiments for which the particles obtained were found to vary despite comparable molecular weights. Towards the development of a high throughput screening platform, a multi-stage, telescoped tubular-CSTR cascade reactor configuration was applied for inline macro-CTA synthesis and subsequent block extension. Differences in product properties between the processing methods used supports the idea that polymers are so-called ‘products-by-process’; indeed different polymer products can be accessed from the same chemistry through the application of alternative synthesis approaches.

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### 1. Introduction

Reversible addition-fragmentation chain transfer (RAFT) polymerisation is a reversible de-activation radical polymerisation (RDRP) technique that affords access to more complex polymer architectures than free radical polymerisation. RAFT polymerisation in flow-reactors is well established,<sup>1–6</sup> and is typically conducted in tubular systems. CSTRs and CSTR cascades are relatively unexplored in their application to RAFT polymerisation,<sup>7</sup> with only few examples

in the literature applied primarily to miniemulsion polymerisation.<sup>8,9</sup> This is likely as a result of the inherently broad RTD of the CSTR which is known to broaden the molecular weight distribution of polymers prepared by RAFT.<sup>10</sup> Despite this drawback, there are a number of benefits to the use of CSTRs – and especially CSTR cascades – which make their application to continuous-flow RAFT polymerisation worth exploring. Firstly, active mixing provided by an agitator is known to enhance mass transfer, which is particularly important in multiphase systems. Secondly, using multiple CSTRs in series yields a narrower RTD, resulting in a more precisely defined product. In addition, higher conversion can be achieved with a smaller total reactor volume, and in the case of first order kinetics – such as for ideal RAFT polymerisations – the optimum design is conveniently that of equally sized CSTRs.<sup>11</sup> Finally, CSTRs are a favourable choice for larger scale continuous processes, however engineering challenges associated with scale-up can

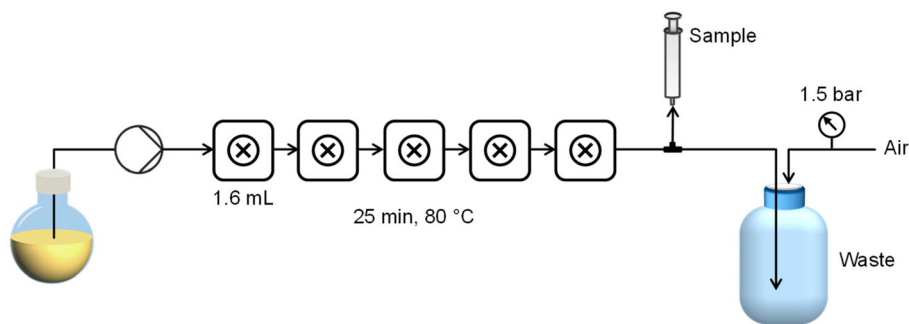
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**Fig. 1** Reactor platform for polymer synthesis in a miniature five-CSTR cascade. All five reactors are heated from the same temperature-controlled heating block, with stirring provided by five pairs of neodymium magnets glued to 5 V DC computer fans located underneath the heating block.

conveniently obtain RTDs for one and five CSTRs at increased viscosities.

#### 2.4. Macro-CTA synthesis by aqueous solution RAFT polymerisation of dimethylacrylamide (DMAm)

A typical procedure for batch synthesis of PDMAm macro-CTA (Scheme 1) with a target degree of polymerisation (DP) of 40 involves adding DMAm (17.16 g, 0.174 mol, 40 eq.), CCTP (1.10 g, 4.4 mmol, 1 eq.), and ACVA (0.12 g, 0.44 mmol, 0.1 eq.) to a round-bottom flask. Water (43.0 g) was added to make a 30% w/w solution. A magnetic stirrer bar was added before the flask was sealed and the reaction solution sparged with nitrogen for at least 30 minutes. The flask was lowered into a temperature-controlled oil bath at 80 °C for 25 minutes before being quenched by cooling and exposing to air. The product was used without purification for subsequent syntheses.

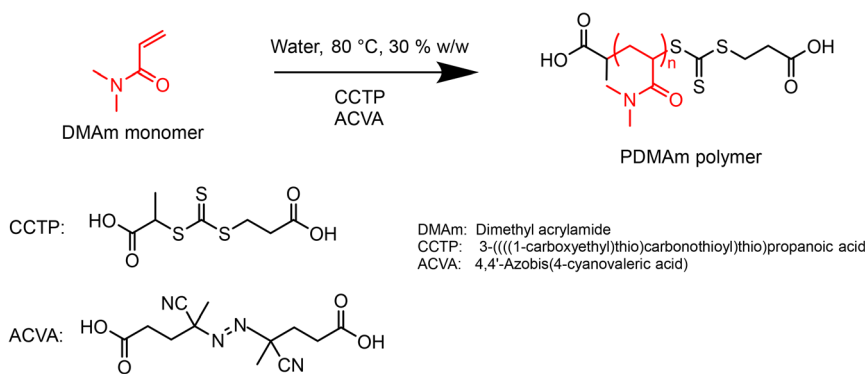
For the equivalent continuous-flow reaction, a reaction mixture of the same composition was prepared in a sealed flask and sparged with nitrogen for at least 30 minutes. The reactor was prepared by filling with purified water and feeding through any trapped air bubbles at an arbitrary high flow rate. The downstream pressure was increased to 1.5 bar by opening the air inlet to the waste container, before the reactor was heated to the required set temperature. To target a residence time of 25 minutes, the flow rate of purified

water was set to  $0.35 \text{ mL min}^{-1}$ , requiring a set temperature of 92 °C to give a mean fluid temperature of 80 °C. The temperature was allowed to stabilise before the pump was switched from water to the reaction solution. After 3.5 residence times (87.5 min) the three-way valve downstream of the reactor was switched to the sample position and a sample manually extracted.

#### 2.5. Aqueous dispersion RAFT polymerisation of diacetone acrylamide (DAAm) using PDMAm macro-CTA

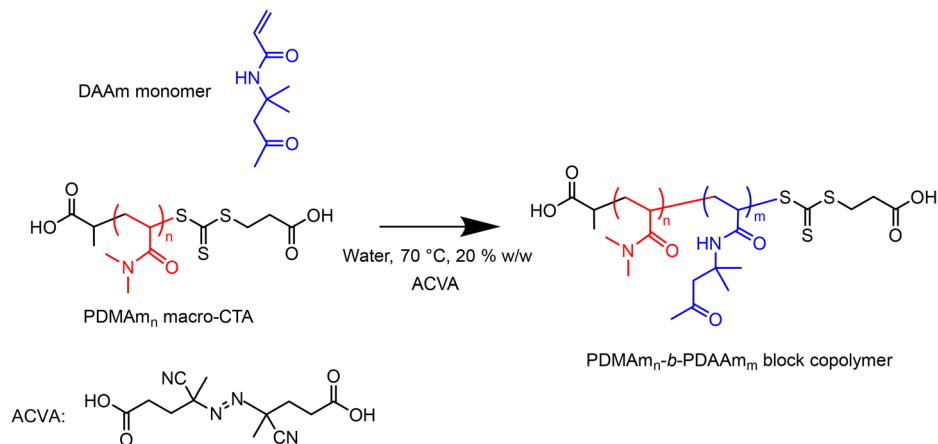
A typical procedure for the batch synthesis of PDMAm<sub>n</sub>-b-PDAAm<sub>m</sub> (Scheme 2) for  $n = 100$ ,  $m = 400$  involves adding DAAm (7.00 g, 41.4 mmol, 400 eq.), the pre-prepared 30% w/w macro-CTA solution (3.50 g total, 1.05 g macro-CTA, 0.10 mmol, 1 eq.), ACVA (2.9 mg, 0.01 mmol, 0.1 eq.) to a round-bottom flask. Water (29.76 g) was added to make a 20% w/w solution. A magnetic stirrer bar was added before the flask was sealed and the reaction solution sparged with nitrogen for at least 30 minutes. The flask was lowered into a temperature-controlled oil bath at 70 °C for 50 minutes before being quenched by cooling and exposing to air.

The equivalent flow reaction was performed by preparing a reaction solution of the same composition which was sealed and sparged with nitrogen for at least 30 minutes. The reactor was prepared by filling with purified water and



**Scheme 1** RAFT aqueous solution polymerisation of dimethylacrylamide (DMAm) at 30% w/w in the presence of a CCTP CTA using ACVA as initiator ([CTA] : [initiator] = 10 : 1) to produce a poly(dimethylacrylamide) (PDMAm)<sub>n</sub> macromolecular chain transfer agent.





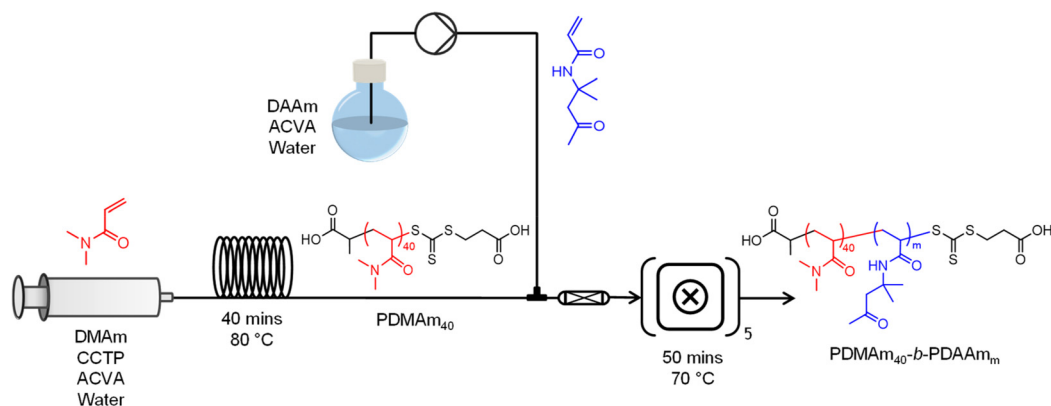
**Scheme 2** Poly(dimethylacrylamide)<sub>n</sub>-*b*-poly(diacetone acrylamide)<sub>m</sub> (PDMAm<sub>n</sub>-*b*-PDAAm<sub>m</sub>) nanoparticle synthesis via RAFT aqueous dispersion polymerisation of DAAm at 30% w/w in the presence of a PDMAm<sub>n</sub> macro-CTA using ACVA as initiator ([mCTA] : [initiator] = 10 : 1).

feeding through any trapped air bubbles at an arbitrary high flow rate. The downstream pressure was increased to 1.5 bar by opening the air inlet to the waste container, before the reactor was heated to the required set temperature. To target a residence time of 50 minutes, the flow rate of purified water was set to 0.17 mL min<sup>-1</sup>, requiring a set temperature of 80.5 °C to give a fluid temperature of 70 °C. The temperature was allowed to stabilise before the pump was switched from water to the reaction solution. After 3.5 residence times (175 min) the three-way valve downstream of the reactor was switched to the sample position and a sample manually extracted.

## 2.6. Synthesis of poly(dimethylacrylamide)<sub>n</sub>-*b*-poly(diacetone acrylamide)<sub>m</sub> (PDMAm<sub>n</sub>-*b*-PDAAm<sub>m</sub>) nanoparticles via telescoped macro-CTA and RAFT dispersion polymerisation

With the aim of optimising a platform for continuous-flow synthesis of copolymer systems which undergo PISA, a

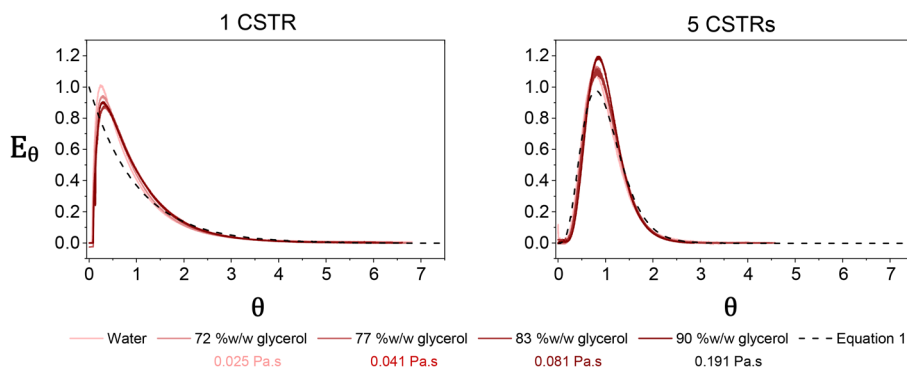
stainless-steel tubular reactor (1 mL total volume, 1/16" OD, ID = 0.762 mm) was installed upstream of the CSTR cascade for inline macro-CTA synthesis and subsequent block extension (Fig. 2). The temperature of the tubular reactor was set by submerging it in a temperature-controlled oil bath, and the outlet fed into the first CSTR of the miniature CSTR cascade *via* a packed bed mixer. A typical procedure for performing the telescoped synthesis of PDMAm<sub>40</sub>-*b*-PDAAm<sub>400</sub> is as follows. DMAm (0.989 g, 10.00 mmol, 40 eq.), CCTP (63 mg, 0.25 mmol, 1 eq.), and ACVA (7 mg, 0.03 mmol, 0.1 eq.) were added to a round-bottom flask (flask A). Water (12.02 g adjusted to pH 2.50) was added to make an 8.1% w/w solution. DAAm (17.60 g, 0.10 mol) and ACVA (7 mg, 0.03 mmol) were added to a second round-bottom flask (flask B). Water (62.40 g) was added to make a 22.0% w/w solution. Both flasks were sealed and sparged with nitrogen for at least 30 minutes. A gas-tight stainless-steel syringe was degassed by filling and emptying with three volumes of nitrogen before being filled with the contents of flask A and



**Fig. 2** Telescoped tubular-CSTR cascade configuration for sequential RAFT solution polymerisation of DMAm and RAFT dispersion polymerisation of DAAm. The inlet to the tubular reactor contains a 30% w/w solution of DMAm, CCTP, and ACVA (40 : 1 : 0.1) and was heated in a temperature-controlled oil bath at 80 °C. Both the outlet of the tubular reactor and a second monomer inlet containing a solution of DAAm and ACVA (see ESI† for composition details) were fed through a packed bed mixer to the first CSTR of the cascade which was temperature-controlled to give a fluid temperature of 70 °C.







**Fig. 3** Residence time distributions measured in one (left) and five (right) miniature CSTRs using mixtures of glycerol and water to represent the rheology of different PDMAm polymers. Traces were obtained by monitoring the UV absorption at the reactor outlet after injecting 10  $\mu\text{L}$  of tracer. Dashed lines represent the theoretical distributions based on eqn (1).

shear rates between 0.1 to 500  $\text{s}^{-1}$  and had viscosities ranging from 0.025 to 0.191 Pa s (Fig. S5†). To conveniently measure the RTD of the miniature CSTRs at viscosities corresponding to these polymers, four glycerol and water mixtures with increasing weight fractions of glycerol were identified which reflected the rheology of the four homopolymers (72% w/w for PDMAm<sub>50</sub>, 77% w/w for PDMAm<sub>100</sub>, 83% w/w for PDMAm<sub>200</sub>, and 90% w/w for PDMAm<sub>400</sub>). RTD measurements for these mixtures revealed that the mixing performance was largely unaffected by the increasing viscosity of the polymerisation, with only slight broadening of the RTD when a 90% w/w mixture of glycerol and water is used *versus* pure water (Fig. 3). Despite this, it is important to note that attempts to evaluate viscosities much higher than those shown here introduced challenges with stirrer bars decoupling from the driving magnets.

### 3.2. Aqueous solution RAFT polymerisation using a miniature CSTR cascade

The four batch polymers were prepared in equivalent continuous-flow reactions using the miniature CSTR cascade, with high conversion and comparable  $M_n$  values achieved (Table 1). During polymer synthesis the temperature increased much more rapidly due to the exotherm inherent to the polymerisation. Indeed, the exotherm could typically be observed at residence times of 5 minutes and above,

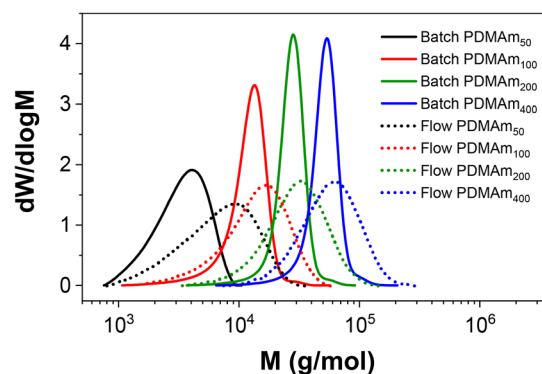
**Table 1** Summary of polymer properties for 30% w/w solution PDMAm prepared in batch and flow using the miniature CSTR cascade for target DPs of 50, 100, 200, and 400. Average reaction/residence time = 25 minutes. [CTA] : [initiator] = 10 : 1

Polymer	Conversion (%)		$M_n$ ( $\text{g mol}^{-1}$ )		$D$	
	Batch	Flow	Batch	Flow	Batch	Flow
PDMAm <sub>50</sub>	98	96	2900	5200	1.25	1.59
PDMAm <sub>100</sub>	99	97	10 500	10 700	1.19	1.44
PDMAm <sub>200</sub>	97	92	25 400	24 700	1.09	1.38
PDMAm <sub>400</sub>	99	92	47 900	48 100	1.10	1.34

which helped to qualitatively identify the reactor in which most of the polymerisation occurred (Fig. S2†).

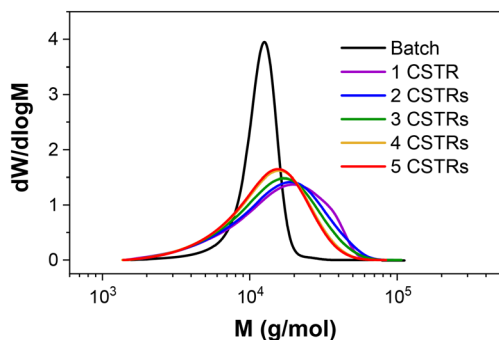
Importantly, the MWDs of the polymers prepared in flow are much broader as a direct result of the RTD within the reactor (Fig. 4), even when using five CSTRs in series. In batch where there is no RTD, the dispersity reduces for larger DP values to a minimum of approximately 1.10. This reduction due to the chemistry is also apparent across the four samples prepared in flow, but the overall molar mass dispersities are higher, ranging from 1.59 for PDMAm<sub>50</sub> to 1.34 for PDMAm<sub>400</sub>. Hence there is a clear influence of the RTD on the dispersity of the products, however this does not overshadow the potential to observe trends associated with the chemistry. This is important, since the RTD is easily measured, meaning the effects on the polymer are predictable and so may be disregarded where the benefits in productivity of flow are more important than the final molar mass distribution. In principle, the method also offers a simplified opportunity to tune the shape of the MWD if desired without having to manipulate the chemistry.<sup>23</sup>

To further investigate the effect of RTD on polymerisation, the aqueous solution polymerisation of DMAm was attempted (target DP = 100) with different numbers of CSTRs



**Fig. 4** Comparison of aqueous solution RAFT PDMAm polymers prepared in batch *versus* continuous-flow in a miniature CSTR cascade. All polymers were prepared at 30% w/w, 80  $^{\circ}\text{C}$ , 25 minutes.





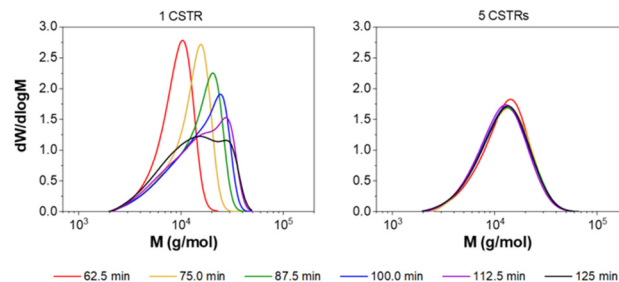
**Fig. 5** MWDs for different CSTR cascade configurations versus the batch MWD for the aqueous solution RAFT polymerisation of 30% w/w PDMAm<sub>100</sub> at 80 °C. Average reaction/residence time = 25 minutes. [CTA] : [initiator] = 10 : 1.

to manipulate the RTD. As expected, a narrowing in MWD is observed as the number of CSTRs is increased (Fig. 5), reaching a minimum of 1.44 (Table 2). Interestingly, when a single CSTR is used, a significant shoulder is observed, suggesting the presence of a second population of higher molecular weight material. This is a direct consequence of the RTD acting on the chemistry, where within one CSTR, the RTD measurements (Fig. S3†) show that some of the material recirculates well beyond the mean residence time. The monomers chosen (acrylamides) tend to terminate by recombination at long reaction times, where the probability of terminative events is much higher. This method of termination thus likely results in the large MW shoulder as a result of two polymer chains combining to give a single chain with double the molecular weight.

A further experiment to investigate this phenomenon was conducted whereby samples were collected from a similar synthetic formulation at different time points after feeding had started at a set flow-rate. Where one CSTR was used, the formation of this second higher MW population is clearly observed (Fig. 6). For three CSTRs (Fig. S6†) the irregular MWDs over the course of the experiment suggest the persistence of the second population, which makes obtaining steady state difficult on a reasonable timescale. The narrower RTD of the five CSTR configuration reduces the significance of such terminative events, and the reactor can quickly achieve steady state (Fig. 6). In addition, reaching a stable steady state in under three residence times (75 min) confirms

**Table 2** Summary of polymer properties for 30% w/w PDMAm prepared via solution RAFT polymerisation using different numbers of reactors in the CSTR cascade versus batch. Average reaction/residence time = 25 minutes. [CTA] : [initiator] = 10 : 1

Sample	Conversion (%)	$M_n$ (g mol <sup>-1</sup> )	$\bar{D}$
Batch	97	10 700	1.11
1 reactor	83	11 700	1.60
2 reactors	96	11 800	1.58
3 reactors	97	11 200	1.53
4 reactors	97	10 700	1.45
5 reactors	97	10 700	1.44



**Fig. 6** MWDs obtained at different time points for the aqueous solution RAFT polymerisation of DMAM at 80 °C in either one (left) or five (right) CSTRs. Average residence time of 25 minutes, [CTA] : [initiator] = 10 : 1.

this as an appropriate equilibration time, and suggests that continuous manufacture is feasible.

### 3.3. Synthesis of PDMAm-*b*-PDAAm via RAFT dispersion polymerisation

Since the molecular weight dispersity obtained in the CSTR cascade is typically broad on account of its RTD, it might be more appropriate to use a traditional tubular reactor for continuous synthesis when minimising dispersity is more important. However, the lack of agitation afforded by tubular reactors can lead to gradual fouling,<sup>4</sup> which makes the CSTR cascade a valuable tool for polymerisations involving multiple phases, where mass transfer and phase stability are important. One such heterogeneous system is the aqueous RAFT dispersion polymerisation of diacetone acrylamide (DAAm) in the presence of a PDMAm macro-CTA which forms nanoparticles as a result of polymerisation-induced self-assembly (PISA).<sup>21</sup> Using a PDMAm<sub>40</sub> macro-CTA prepared in batch, a series of dispersion polymers were synthesised in equivalent batch and flow reactions using the miniature CSTR cascade to compare their performance where different morphologies might be obtained.<sup>21</sup> For each polymer, simultaneous batch and flow reactions were performed from the same reaction solution to target the following block copolymers: PDMAm<sub>40</sub>-*b*-PDAAm<sub>100</sub>, PDMAm<sub>40</sub>-*b*-PDAAm<sub>200</sub>, PDMAm<sub>40</sub>-*b*-PDAAm<sub>300</sub>, and PDMAm<sub>40</sub>-*b*-PDAAm<sub>400</sub>. Table 3 summarises the properties of the resulting products. Molecular weight measurements of each product again revealed a larger molar mass dispersity from the CSTR cascade likely as a consequence of the same RTD effects observed in the homopolymer synthesis, however values of  $M_n$  were broadly comparable for each (Fig. 7). As the target DP increased, the reaction conversion achieved in batch reduced, accounting for the lower value of  $M_n$  for the batch PDMAm<sub>40</sub>-*b*-PDAAm<sub>400</sub> where conversion was only 84% compared to 94% in flow. This may be attributed to the enhanced heat and mass transfer achieved in continuous-flow which becomes more important at lower initiator concentrations.

Although the  $M_n$  values and monomer conversion of the resulting batch and flow polymers are similar, there are large



**Table 3** Characterisation of block copolymers prepared via RAFT dispersion polymerisation using three synthetic approaches. Macro-CTA is prepared either in batch, or inline using a tubular reactor. Block copolymerisation is performed either in batch or using the mini-CSTR cascade. [CTA] : [initiator] = 10 : 1. Particle sizes reported based on number-average values. Multimodal particle size distributions are indicated by the multiple values given

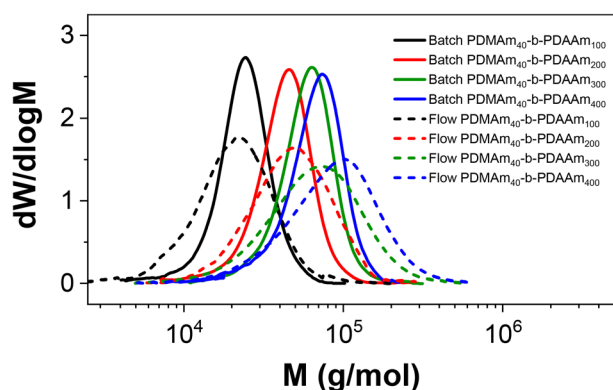
Polymer	Synthesis method		Conversion (%)	$M_n$ ( $\text{g mol}^{-1}$ )	$D$	Particle size (nm)
	Macro-CTA	Copolymerisation				
PDMAM <sub>40</sub> - <i>b</i> -PDAA <sub>100</sub>	Batch	Batch	100	21 400	1.18	47/92/235
	Batch	CSTR cascade	98	17 300	1.36	16/38
	Tube	CSTR cascade	98	18 600	1.39	12/33
PDMAM <sub>40</sub> - <i>b</i> -PDAA <sub>200</sub>	Batch	Batch	98	38 300	1.19	82/307
	Batch	CSTR cascade	97	39 200	1.37	65
	Tube	CSTR cascade	96	33 500	1.66	164/342
PDMAM <sub>40</sub> - <i>b</i> -PDAA <sub>300</sub>	Batch	Batch	93	53 600	1.18	236
	Batch	CSTR cascade	97	51 100	1.57	97
	Tube	CSTR cascade	97	43 100	1.48	104
PDMAM <sub>40</sub> - <i>b</i> -PDAA <sub>400</sub>	Batch	Batch	84	58 000	1.22	280
	Batch	CSTR cascade	94	65 700	1.57	124
	Tube	CSTR cascade	96	63 100	1.63	300/1623

differences in properties of the corresponding particles obtained. According to DLS measurements (Fig. 8), the particles obtained in flow for these systems are smaller than those prepared in a batch process, indicating that the particle self-assembly is influenced by the hydrodynamics of the reactor. Number-average distributions are used to demonstrate the major particle populations obtained, however intensity-average distributions (Fig. S7†) indicated the presence of larger particles (visible in the long ‘tails’ of the size distributions). These minor populations contribute to broadening of the particle size distributions and are likely a further consequence of the reactor RTD. As a result of the inherent RTD, each CSTR will contain material at many different stages of the reaction. Since these particles are known to undergo morphological transitions during growth, it is likely that the CSTRs provide a unique environment in which particles with a broad range of shapes and sizes coexist, particularly in the first few reactors. On this basis, it becomes challenging to suggest a precise explanation for the

observed differences in particle structure in the absence of a detailed mechanistic understanding, which is beyond the scope of this work.

#### 3.4. Telescoped RAFT synthesis of PDMAM macro-CTA and copolymerisation in a tubular-CSTR cascade configuration

Since the self-assembly behaviour of a given polymer system is complex and difficult to predict, we suggest an experimental approach that utilises the benefits of continuous-flow chemistry to enable high-throughput screening of the polymer dispersions obtained from these various systems. Towards this end, the above acrylamide block copolymers were sequentially synthesised in a telescoped reactor system comprising a 1 mL tubular coil followed by the five-stage CSTR cascade to perform both parts of the block copolymerisation in a single experiment. Four products were targeted with varying copolymer block lengths from the same target macro-CTA. In each case, the tubular reactor was used to prepare a PDMAM<sub>40</sub> macro-CTA via solution RAFT polymerisation, to which a solution of DAAM was added in the first stage of the mini-CSTR cascade for chain extension with a second block. For the macro-CTA syntheses at 30% w/w above, a residence time of 25 minutes was sufficient to reach >95% conversion, and so initially the residence time in the tubular reactor was set to 25 minutes. To maintain the same residence time and final concentration for each reaction, the copolymer block length was manipulated by adjusting the concentration (% w/w) of the reaction solutions. For PDMAM<sub>40</sub>-*b*-PDAA<sub>400</sub> the required macro-CTA concentration was therefore 5.1% w/w, whilst for PDMAM<sub>40</sub>-*b*-PDAA<sub>100</sub> the required macro-CTA concentration was 17.2% w/w. The polymer dispersions collected appeared very viscous and gel-like, particularly for the higher molecular weight copolymers. Surprisingly, this did not cause any significant operational challenges within the reactor. This is likely due to the shear thinning behaviour observed in gel-like copolymer dispersions synthesised by traditional<sup>24</sup> or



**Fig. 7** Molecular weight distributions of PDMAM<sub>40</sub>-*b*-PDAA<sub>m</sub> copolymers prepared simultaneously in batch and a miniature CSTR cascade for a reaction time of 50 minutes at 70 °C. The same batch synthesised PDMAM<sub>40</sub> macro-CTA was used in each case. [CTA] : [initiator] = 10 : 1.





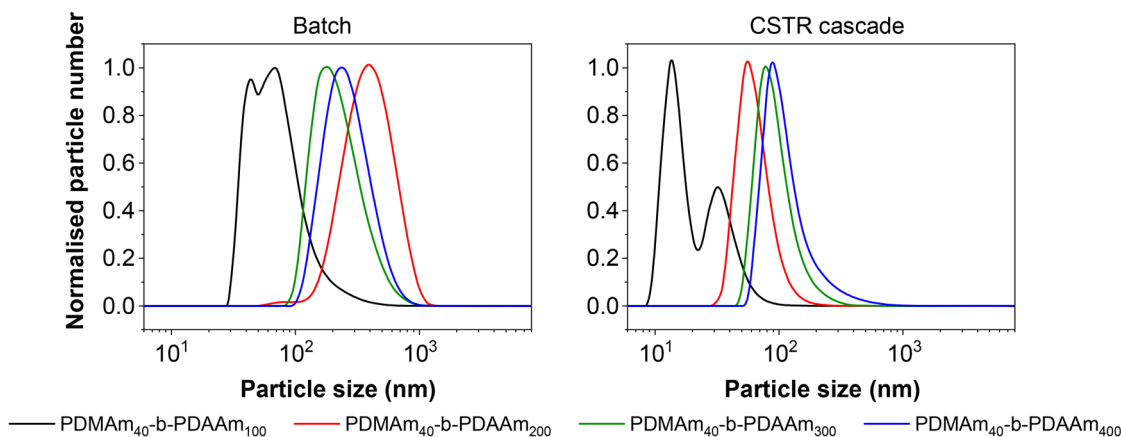


Fig. 8 Particle size distributions of PDMAm<sub>40</sub>-b-PDAAm<sub>m</sub> copolymers prepared simultaneously in batch (left) and a miniature CSTR cascade (right) for a reaction time of 50 minutes at 70 °C. The same batch synthesised PDMAm<sub>40</sub> macro-CTA was used in each case. [CTA] : [initiator] = 10 : 1.

RAFT aqueous dispersion polymerisation.<sup>25</sup> Analysis of the particle characteristics indicated the formation of large nano-scale and even micro-scale structures (Fig. S8†). This often indicates the presence of non-spherical nano-objects during RAFT dispersion polymerisation,<sup>21,26</sup> but may also indicate insufficient conversion in preparing the macro-CTA or insufficient mixing of the second monomer with the macro-CTA solution. Both of these issues may allow uncontrolled free-radical polymerisation to proceed. To ensure differences in product properties were not a consequence of this uncontrolled radical polymerisation a longer 40 minute residence time was used for the PDMAm<sub>40</sub> macro-CTA synthesis to guarantee high DMAM conversion (as determined by <sup>1</sup>H NMR to be >90%) and a pre-mixer was included before the first CSTR to ensure the PDMAm and DAAM solutions were well mixed.

Once the optimised set up was used for these experiments, the resulting polymers were similar to those prepared using a

batch macro-CTA (see Table 3 and Fig. 9). However, there were clear differences in the properties of the self-assembled polymer nano-objects (Fig. 10), and a small population of micro-scale objects persisted for the telescoped synthesis of PDMAm<sub>40</sub>-b-PDAAm<sub>400</sub>.

## 4. Conclusions

Alongside the growing demand for new functional materials comes a growing cost of the materials required to develop them. Continuous-flow chemistry offers an avenue to explore the synthesis of valuable chemical products which is economical, safe, and scalable. We have demonstrated the first instance of a reversible de-activation radical polymerisation performed in CSTRs on a miniature scale for both single phase systems and indeed for more complex multi-phasic polymerisations.

The miniaturised reactor had characteristics which agreed well with the established theory of CSTR cascades, and reliably handled the preparation of block copolymers *via* both RAFT solution and dispersion polymerisation. Clear differences in molar mass dispersity between equivalent products prepared in batch were attributed to the broad residence time distribution of the flow reactor for both solution and dispersion systems. During PDMAm<sub>n</sub>-b-PDAAm<sub>m</sub> particle synthesis, the complex dynamics of particle nucleation and growth within a mixed flow reactor resulted in particle characteristics which were different to those obtained in batch despite relatively similar molar mass values. For a telescoped process, the integration of an inline tubular reactor for macro-CTA synthesis (*via* solution RAFT) produced polymers with very similar molar mass characteristics to those prepared from a stock batch of macro-CTA. Despite the similarity of the polymer properties, the sensitivity of the particle characteristics to the synthetic method was indicated by the differences in the particle size distributions. These results indicate the potential for products with different macroscopic behaviour to be prepared from the same chemical inputs, and implies that new functional materials may be obtained by taking alternative synthetic

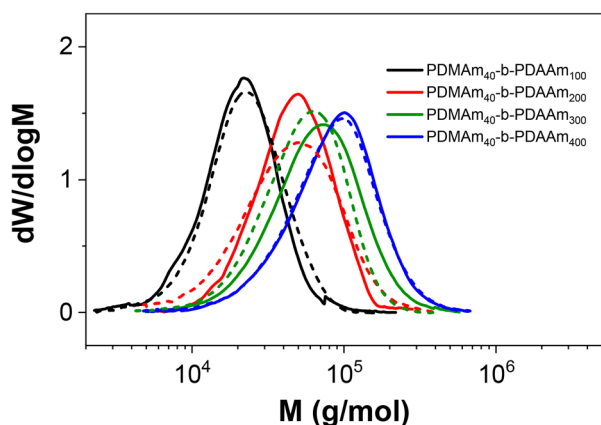
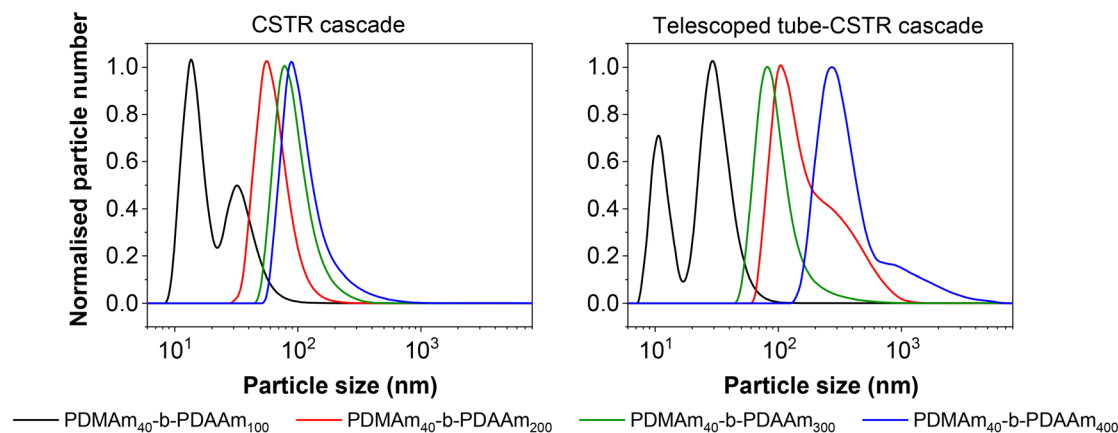


Fig. 9 Molecular weight distributions of PDMAm<sub>40</sub>-b-PDAAm<sub>m</sub> copolymers prepared in a miniature CSTR cascade using a batch macro-CTA (solid lines) *versus* a telescoped configuration with macro-CTA prepared inline using a tubular reactor (dashed lines). PDMAm<sub>40</sub> macro-CTA was prepared at 80 °C for 40 minutes, with copolymerisation at 70 °C for 50 minutes. [CTA] : [initiator] = 10 : 1.





**Fig. 10** Particle size distributions of PDMA<sub>40</sub>-*b*-PDAA<sub>*m*</sub> copolymers prepared via RAFT dispersion polymerisation in a miniature CSTR cascade using a batch macro-CTA (left) versus in a miniature CSTR cascade with a macro-CTA prepared upstream in a telescoped tubular reactor (right). PDMA<sub>40</sub> macro-CTA was prepared at 80 °C for 40 minutes, with copolymerisation at 70 °C for 50 minutes. [CTA]:[initiator] = 10:1.

approaches. The technology developed here offers a unique approach to the high-throughput exploration of multiphasic polymerisations. The prevalence of CSTRs as a manufacturing tool means that the developed system also presents an opportunity to gather early insights for scale-up operations. We anticipate several challenges for this, which we intend to explore in future studies.

## Author contributions

PMP – data curation, investigation, methodology, writing-original draft, writing-review and editing; GG – investigation; STK – investigation, data curation, writing-review and editing; OJC – supervision, writing-review and editing; NK – conceptualisation, supervision, writing – review and editing; NJW – conceptualisation, funding acquisition, supervision, project administration, writing – review and editing.

## Conflicts of interest

There are no conflicts to declare.

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