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Progresses in Reactor Engineering of Controlled Radical Polymerization: A Comprehensive Review

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Abstract

Controlled radical polymerization (CRP) represents an important advancement in polymer chemistry. It allows synthesis of polymers with well-controlled chain microstructures. Reactor engineering is essential in bringing lab-scale chemistry to industrial realization. This paper reviews the research progress in reactor engineering of CRP, namely, atom transfer radical polymerization (ATRP), reversible addition-fragmentation chain transfer radical polymerization (RAFT), and nitroxide-mediated stable free radical polymerization (NMP or SFRP). Research activities in semi-batch reactor, tubular reactor, and continuous stirred-tank reactor (CSTR) of both homogeneous (bulk and solution) and heterogeneous (emulsion, mini-emulsion, heterogeneous catalyst, etc.) CRP systems are summarized. Typical examples are selected and discussed in detail. Perspectives on the current status and future development are also provided.

Keywords: controlled radical polymerization, CRP, reactor engineering, tubular reactor, continuous stirred tank reactor, CSTR, semi-batch reactor

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Abbreviations

ATRP	Atom transfer radical polymerization
AGET ATRP	Activator generated by electron transfer ATRP
ARGET ATRP	Activator regenerated by electron transfer ATRP
ICAR ATRP	Initiator for continuous activator regeneration ATRP
SARA ATRP	Supplemental activator and reducing agent ATRP
SET-LRP	Single-electron transfer living radical polymerization
CCD	Copolymer composition distribution
CF	Constant feeding
ICF	Increasing constant feeding
CRP	Controlled radical polymerization
CRcoP	Controlled radical copolymerization
CSTR	Continuous-stirred tank reactor
FRP	Conventional free radical polymerization
MMFP	Model-based monomer feeding policy
NMP	Nitroxide-mediated polymerization
PF	Programmed feeding
PFTR	Plug flow tubular reactor
RAFT	Reversible addition-fragmentation chain transfer
RT	Residence time
RTD	Residence time distribution
MWD	Molecular weight distribution
MW	Molecular weight
U	Uniform
LG	Linear gradient
SG	“S” shape gradient
DB-1	Di-block
DB-2	Di-block with a gradient block

TB-1	Tri-block
TB-2	Tri-block with one middle gradient block
TB-3	Tri-block with two terminal gradient blocks
PDI	Polydispersity index (also referred to as dispersity, Đ)

Chemical abbreviations

2-MPA	2-Methoxypropyl acetate
AA	Acrylic acid
AcGalEA	2-(2',3',4',6'-Tetra-o-acetyl- d-galactosyloxy)ethyl acrylate
AM	Acrylamide
AN	Acrylonitrile
AS	4-Acetoxystyrene
BA	n-Butyl acrylate
BIEM	2-(2-Bromoisobutyryloxy) -ethyl methacrylate
BisAM	N,N'-Methylenebis(acrylamide)
BMA	n-Butyl methacrylate
Bu	Butadiene
BzMA	Benzyl methacrylate
DFMA	Dodecafluoroheptyl methacrylate
DMA	N,N-Dimethylacrylamide
DMAEMA	2-(Dimethylamino)ethyl methacrylate
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
EHA	2-Ethylhexyl acrylate
EO	Ethylene oxide
EtOAc	Ethyl acetate
HEMA	2-Hydroxyethyl methacrylate
HEMA-TMS	2-(Trimethylsilyl)ethyl methacrylate
HFBMA	2,2,3,3,4,4,4-Heptafluorobutyl methacrylate

HPMA	2-Hydroxypropylmethacrylate
IBA	Isobornyl acrylate
LMA	Lauryl methacrylate
MA	Methyl acrylate
MMA	Methyl methacrylate
MS	4-Methylstyrene
NIPAM	N-Isopropyl acrylamide
NM2P	N-Methyl-2-pyrrolidone
ODA	Octadecyl acrylate
St	Styrene
tBA	tert-Butyl acrylate
tBMA	tert-Butyl methacrylate
TFEMA	2,2,2-Trifluoroethyl methacrylate
VAc	Vinyl acetate

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1. Introduction

Free radical polymerization is one of the most commonly employed processes for large-scale production of polymers, owing to its versatility in polymerizing a wide range of monomer types under facile conditions. However, in the conventional free radical polymerization (FRP) system, a polymer chain grows to completion in a matter of seconds. The almost-instantaneous growth makes it difficult to impose control over the polymer architectures. In addition, each polymer chain experiences different growing environment, depending on the time it is initiated during the polymerization period. This different experience coupled with the presence of various side reactions, such as termination and transfer, result in polymers possessing a broad molecular weight distribution (MWD).[1,2] Meanwhile, there is a growing market demand for polymers with well-controlled architectures and narrow MWD to obtain highly tailored properties required in specific applications.

Living polymerization was discovered by Szwarc in 1956.[3] The advent of living polymerization, including anionic[4-7] and cationic,[8-10] has made it possible to synthesize polymer materials with well-controlled and complex architectures. In an ideal living polymerization system, all polymer chains are initiated at the beginning of polymerization and continue to propagate throughout the whole polymerization period, providing same experience for all chains. The side reactions, such as chain transfer and termination, are absent in this system when conducted under an appropriate condition. As a result, the polymers synthesized by living polymerization possess narrow MWD. However, there are two main disadvantages of living polymerization: (1) only a limited variety of monomers can be polymerized through this mechanism (due to incompatibility between the active center of propagating chains with functionalized monomers); (2) the required experimental conditions are stringent to avoid undesirable side reactions (water, oxygen, and other impurities must not be present). These two disadvantages severely limit the use of living polymerization in the industry.

Researchers have been trying to combine the advantages of FRP and living polymerization.[11-14] As a result, controlled radical polymerization (CRP) was discovered in the 1980's. CRP, also referred to as reversible deactivation radical polymerization (RDRP),[15] provides middle ground between these two extremes of chain-growth polymerization mechanisms. In CRP, polymerization proceeds in a controlled manner, with active chains growing throughout the polymerization, along with suppression of side reactions. The improved livingness and control in CRP, when compared to FRP, produces narrowly distributed polymer chains, which is expected to have MWD between those produced by living polymerization and FRP.[16,17] This method also allows polymer chains to be extended to form block copolymers more efficiently. Furthermore, because the lifetime of propagating radical chains is extended from a matter of seconds to hours, this allows design and control of detailed chain microstructural properties from end to end along backbone, by various engineering means. It also provides sufficient time for polymer chains to come into contact with each other, which is especially useful for branching and cross-linking polymerization. Therefore, CRP has opened a path to control the polymer architectures. Polymer materials with controlled MW and narrow MWD, along with well-defined architectures, have been extensively synthesized by CRP in homogeneous and heterogeneous systems.[2,18-21]

What's surprising when conducting literature review in CRP is the big gap between the limited industrial applications and the extensive research works in the lab.[22] Majority of the research work on CRP are conducted in small-scale batch reactors, usually in round-bottom flasks. Reactor engineering of CRP can help overcome this gap and bridge the lab-scale research to industrial applications.[23] The use of various reactor configurations must be evaluated for the different CRPs and targeted products to ensure that appropriate choices are made. There have been some major works done in utilizing reactor engineering concepts to further the development of CRP. The pioneering work on investigating the use of semi-batch reactors for CRP was reported by Matyjaszewski's group in 1997 under constant comonomer feeding rate operation.[24-26] Their work demonstrated that semi-batch reactor allows better control over copolymer composition distribution (CCD) than batch reactor. However, constant feeding rate operation still lacks in versatility to control CCD and to tailor the synthesis of copolymers with more sophisticated CCD. Zhu's group first introduced programmed feeding rate operation for CRP in semi-batch reactor, whereby the comonomer feeding rate was controlled according to mathematical model.[27-33] By using model-based design to vary the feeding rate, the CCD could be designed at will and tailored as required to a higher degree of precision. The development of CRP into continuous processes was pioneered by Zhu's group.[34-36] This first work for continuous CRP utilized packed column reactors in order to overcome the drawback of batch reactor and to eliminate the need for costly catalyst separation.

In this section, the basic reaction mechanisms of various types of CRP will be briefly discussed, followed by introduction of the reactor types commonly employed in the polymer industry. The last part of this section provides an outline of this review.

1.1. Controlled radical polymerization (CRP)

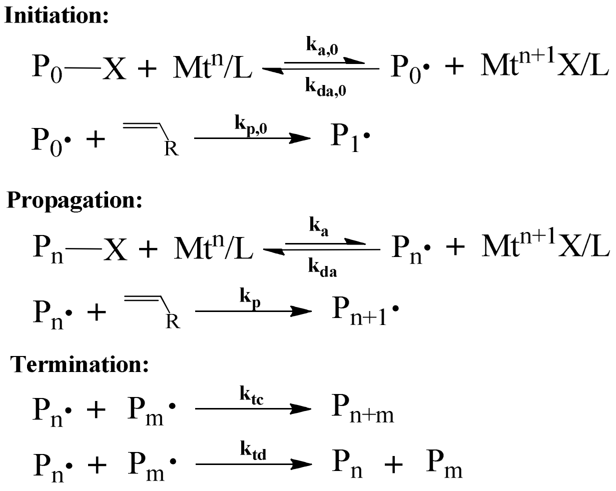
CRP can be divided into three main types based on the reaction mechanism[22,37,38]: (1) reversible deactivation by atom transfer[37,39-41]; (2) reversible deactivation by degenerative transfer[42-45]; (3) reversible deactivation by coupling[46-48]. The three most studied types of CRP following each of these mechanisms are atom transfer radical polymerization (ATRP),[37,39-41] reversible addition-fragmentation chain transfer (RAFT) polymerization,[42,49-51] and nitroxide-mediated polymerization (NMP).[46,52,53] For brevity sake, this review only covers these three types of CRP.

1.1.1. ATRP

ATRP, first reported in 1995[39] has the generally accepted mechanism shown in Scheme 1.[37,54,55] There are two steps involved in the initiation process of ATRP. The first is the generation of radical

($P_0^\bullet$) by the homolytic cleavage of the alkyl halogen bond of the ATRP initiator, *i.e.*, the alkyl halide (P_0-X), through oxidation of the transition metal complex (Mt^n/L) with an initial activation rate constant $k_{a,0}$.[55] The second step involves propagation of the initial radical with a vinyl monomer (propagation reaction rate constant $k_{p,0}$) to form a propagating radical chain with one monomer unit ($P_1^\bullet$). Propagating chains ($P_n^\bullet$) can undergo further propagation (k_p) and grow longer as polymer chains. Alternatively, these chains can also undergo reversible deactivation with a deactivation rate constant k_{da}, to form a halide-capped dormant chain (P_nX).[54,55]

During the activation-deactivation of dormant-radical pairs, the metal complex, Mt^n/L, forms a higher oxidation state complex (Mt^{n+1}X/L). The metal complexes, Mt^n/L and Mt^{n+1}X/L, consist of transition metal (Mt) and ligand (L), which is commonly nitrogen-based. Transition metal that is commonly used in ATRP is copper (Cu), however other metals (*e.g.*, Fe, Ru, Pd) have also been used.[55,56] These metal complexes act as a catalyst and a deactivator in ATRP system.



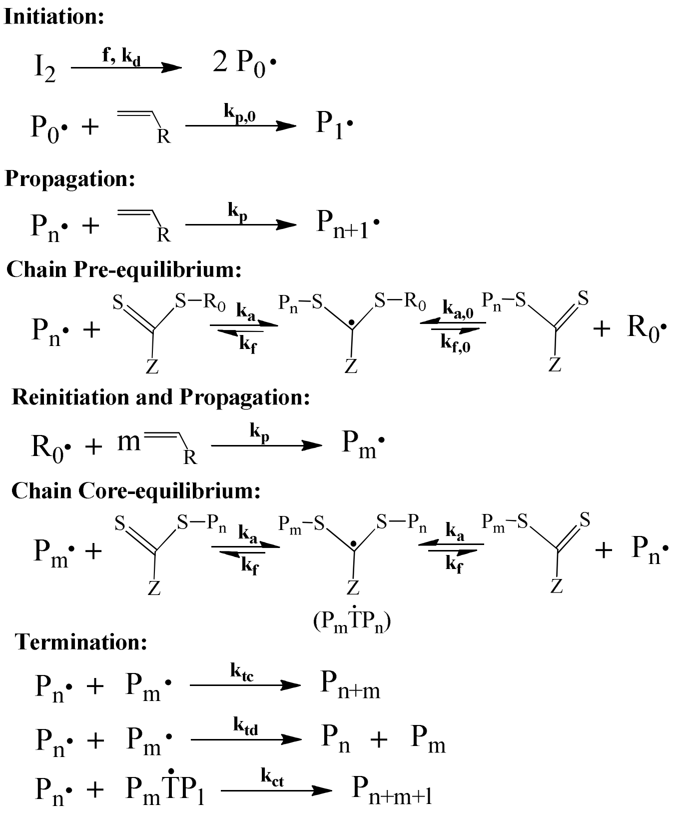
Scheme 1. A general mechanism of ATRP[37,54,55]

As a result of the activation-deactivation reactions, a dynamic equilibrium between $P_n^\bullet$ and P_nX is established. In this equilibrium, the deactivation reaction is much more favored than the activation reaction ($k_{da} >> k_a$), resulting in a much higher concentration of dormant chains than that of the propagating radical chains. In addition to these reactions, the propagating radical chains can also be terminated by either combination (k_{tc}) or disproportionation (k_{td}) to form dead chains.

ATRP has played a very important role in the development of polymer chemistry to produce highly tailored polymer architectures. However, the high catalyst loading and residual transition metal present in the final polymer products limit the commercial exploitation of ATRP, due to the high post-polymerization separation cost needed. Therefore, one of the main questions in ATRP commercialization is on how to reduce the amount of copper, while maintaining a moderate polymerization rate and an acceptable level of control. In recent years, researchers have developed a series of modified ATRPs requiring less catalyst to overcome this problem. The new ATRP are: (1) simultaneous reverse and normal initiation (SR&NI)[57]; (2) activator generated by electron transfer (AGET)[58,59]; (3) initiators for continuous activator regeneration (ICAR)[60-62]; (4) activators regenerated by electron transfer (ARGET)[63-66]; (5) single-electron transfer-living radical polymerization (SET-LRP)[67-71]; (6) electrochemically mediated ATRP (eATRP)[72] and photochemically mediated ATRP (photoATRP)[73]. Albeit being referred to as SET-LRP in some works, Matyjaszewski's group used both experimental and simulation approaches to show that the polymerization occurs based on the mechanism of supplemental activator and reducing agent (SARA) ATRP, not SET-LRP mechanism.[74] However, the term SET-LRP will be used in this review to maintain consistency with the original articles. Among these new variants of ATRP, normal ATRP, ARGET ATRP, and SET-LRP are the most commonly used in semi-batch and continuous reactors. Several universities and companies have participated in the commercialization effort of ATRP.[22,75]

1.1.2. RAFT

RAFT polymerization was discovered by CSIRO group in Australia in the late 1990's.[42,76,77] During the same period, a technology called Macromolecular Design by Interchange of Xanthate (MADIX) was developed in France.[78] The MADIX mechanism is a special case of RAFT process with the use of xanthate as chain transfer agent. Scheme 2 gives the general mechanism of RAFT.[42,79] The initiation stage of RAFT involves the generation of initial radicals by conventional initiators, which is followed by propagation with monomers to form propagating radical chains ($P_n^\bullet$). Aside from adding monomers, the initial radical can also react with a RAFT agent to form a primary intermediate radical chain with initial addition rate constant $k_{a,0}$.[42] This primary intermediate radical chain can reversibly fragment to release the initial radical ($P_0^\bullet$) from the RAFT agent (with rate constant $k_{f,0}$), which can also initiate polymerization.[42] There is a dynamic equilibrium between propagating radical chains, intermediate radical chains, and dormant chains through reversible addition and fragmentation reactions.



Scheme 2. A general mechanism of RAFT[42,79]

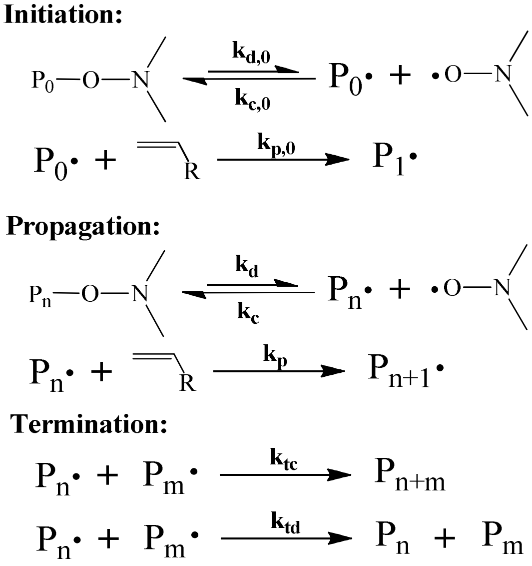
There are two theories in choosing the value of reaction rate constants in RAFT polymerization, namely slow fragmentation and intermediate termination theories.[80-83] As the name suggests, slow fragmentation theory proposes that the fragmentation reaction of intermediate radical occurs at a slow rate. Moreover, this theory assumes intermediate radical does not undergo any other reaction but fragmentation. This results in a long lifetime of the intermediate radicals (*i.e.*, $k_{ct} = 0$ and low

k_f).[80] On the other hand, the intermediate termination theory proposes that the intermediate radical chains cannot propagate with monomers, but undergo fast fragmentation and can also cross terminate with propagating radical chains (*i.e.*, $k_{ct} \neq 0$ and high k_f).[81,83] Therefore, dead chains are generated by self-termination of propagating radical chains (k_t) and cross-termination between propagating radical chains and intermediate radical chains (k_{ct}).[79]

Compared to ATRP system, conducting polymerization by RAFT is simpler. A controlled polymerization can usually be obtained by a simple addition of RAFT agents into conventional free radical polymerization system. Furthermore, some RAFT agents have already been made commercially available.[22] Similar to ATRP, industrial development of RAFT technologies has also been reported.[84-86]

1.1.3. NMP

NMP was developed by Dupont[87] and Xerox[46] by using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the control agent. Scheme 3 shows a general mechanism of NMP.[88] Initial free radical ($P_0^\bullet$) and stable nitroxide radical are generated by homolytic dissociation of alkoxyamine-based initiator with an initial dissociation rate constant of $k_{d,0}$. This initial radical can then propagate with monomers (with rate constant $k_{p,0}$) to form propagating radical chains ($P_n^\bullet$), or it can reversibly recombine with stable nitroxide radical ($k_{c,0}$).[88] The stable nitroxide radical acts as a control agent that cannot react with monomers or participate in any other reaction other than the reversible combination reaction with active radicals ($P_0^\bullet$ and $P_n^\bullet$).[88] Other than reacting with monomer (k_p) and reversibly combining with stable nitroxide radical (k_c), the propagating radical chains $P_n^\bullet$ can also irreversibly terminate (k_t) to form dead chain.[89] Progresses on the industrial development of NMP technologies have been reported in the literature.[22,90]

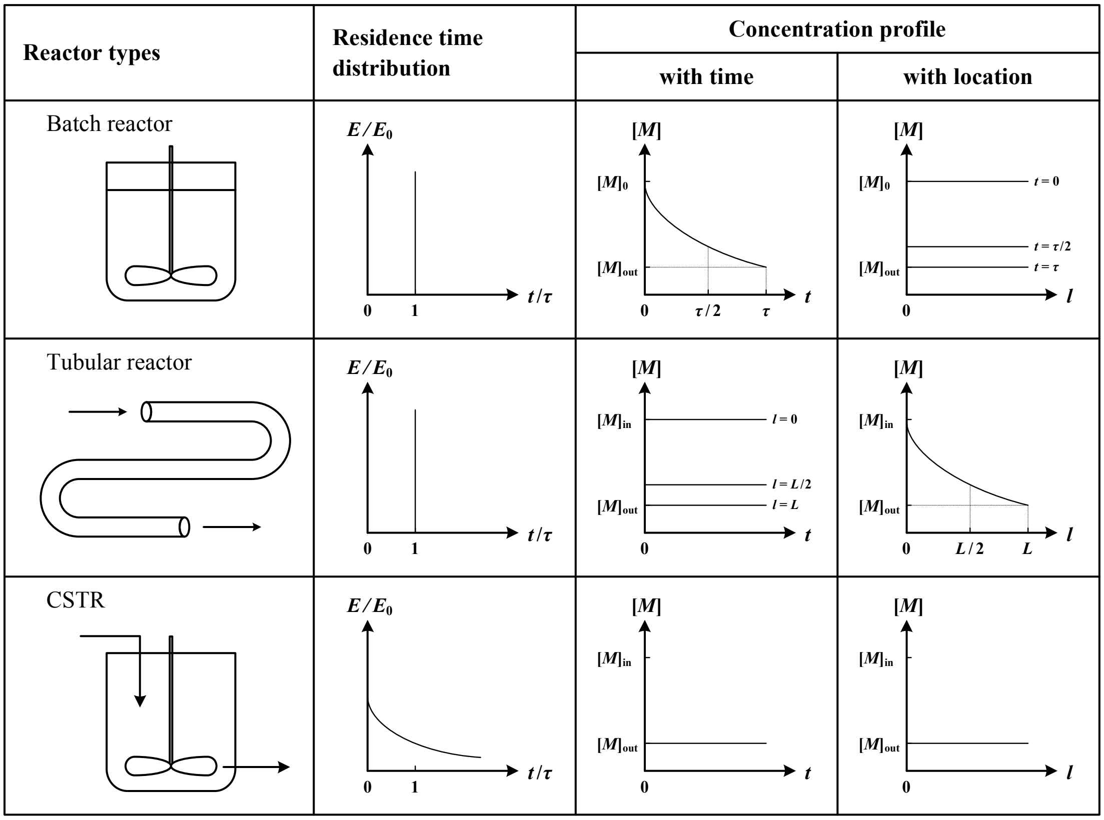


Scheme 3. A general mechanism of NMP[88]

By comparing the mechanisms of ATRP, RAFT and NMP, it is clear that the core of CRP lies in the equilibrium or reversible transfer between dormant and propagating radical chains. Owing to this reversible transfer, propagating chains have longer lifetime, *i.e.*, continuous growth throughout the course of polymerization. Moreover, termination is suppressed and all the polymer chains grow at the same time, thus are exposed to the same growing environment. This results in a linear growth of molecular weight (MW) with respect to conversion and a narrow molecular weight distribution (MWD).

1.2. Reactor type

The type of reactors used (continuous, semi-batch, and batch reactors) has a significant impact on the polymerization behavior and the resulting polymer properties, such as MWD and copolymer composition distribution (CCD). This is because different reactors have different residence time distribution and concentration profiles, as shown in Scheme 4. Therefore, one must carefully consider the reactor type (or the use of multiple reactors in various configurations) in order to efficiently and precisely synthesize various polymers. For example, semi-batch reactor is widely used in the production of copolymers to avoid composition drifting. Semi-batch reactor is not included in Scheme 4 because of the endless possible curves that can be obtained by varying the flow rate.



Scheme 4. Residence time distribution (RTD) and concentration profiles of ideal reactors. The symbols t, τ, l, and L represent the reaction time, residence time, location inside the reactor, and total length of tubular reactor, respectively. E/E_0 and [M] represent fraction of reaction mixture having residence time between t and ($t + dt$) and the concentration of a reactant, respectively

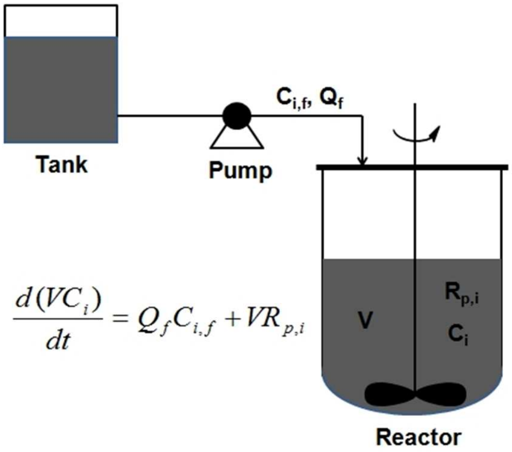
Ideal continuous reactors that are usually considered in the polymerization industry are the tubular reactor (also referred to as plug-flow tubular reactor, PFTR) and the continuous stirred tank reactor (CSTR). Residence time distribution (RTD) is an important parameter for continuous reactors, because it greatly influences the resulting MWD. The effect of RTD depends on the residence time (RT) of polymer chain relative to the time needed to form a complete chain, *i.e.*, it depends on the polymerization mechanism. For FRP, an individual chain completes in seconds, which means the

RT of polymer chain is much longer than the time needed for that chain to fully grow. Therefore, the MW of an individual chain is not affected by its RT. The MWD of the instantaneous chain population generated at a small time interval is not affected much by the RTD. However, for CRP, the RT of polymer chain is smaller than the formation time of the chain, since polymer chains continue to grow as long as they are in the reactor. Therefore, the RTD has a strong impact on the resulting MWD for CRP.

The type of reactors not only affects the MWD of polymers, but also affects the resulting CCD. It is well known that CCD is mainly dependent on the mole ratio of two monomers and their reactivities, therefore varies with reactor types due to different concentration profiles (See Scheme 4). In a batch reactor or in a tubular reactor, for a given feeding ratio of two monomers, "drifting" in CCD is usually observed due to different monomer reactivity. However, in CSTR, CCD is uniform along polymer chain due to the constant mole ratio of two monomers at any given instance.

1.2.1. Semi-batch reactor

In a semi-batch reactor, some reactants are fed into the reactor continuously, as shown in Scheme 5, or some by-products are removed from the reactor during the polymerization process. Control of the reaction rate is easily accomplished in a semi-batch reactor by feeding monomers and/or initiator, which is also beneficial for controlling the heat removal and product properties.



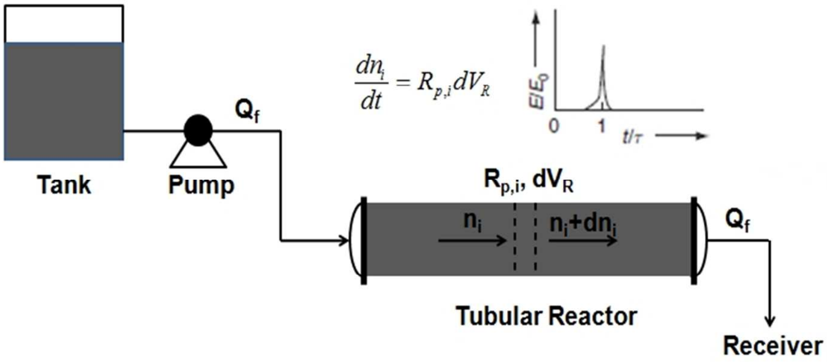
Scheme 5. Schematic of a semi-batch reactor

One of the main advantages of using a semi-batch reactor is the ability to control the copolymer composition distribution (CCD). In a batch reactor, CCD drifts due to different reactivities of monomers. On the other hand, in a semi-batch reactor, the problem of CCD drifting can be readily solved by feeding comonomers into the reactor to maintain a fixed concentration ratio of monomers in the reactor. Furthermore, similar to linear copolymerization, monomer feeding is also effective to control topologies in nonlinear copolymerization.

Another advantage of using a semi-batch reactor is the control over branching or cross-linking density distribution. This is achieved by feeding monomers to maintain a certain concentration ratio of monovinyl monomer and divinyl monomer. Moreover, gelation can be avoided by feeding divinyl monomers to maintain a low concentration of divinyl monomers in the reactor. Control of CCD and topologies in semi-batch reactors has been well investigated.[91-94] Polymer products with low molecular weight can also be produced by feeding monomer and initiator with a defined ratio.

1.2.2. Tubular reactor

Tubular reactor is a type of continuous reactors illustrated in Scheme 6. In a tubular reactor, reactants are fed continuously into the reactor, while the products and unreacted reactants are removed continuously from the reactor. When the operation is at a steady state, unique properties of products (such as uniform MWD and CCD) can be obtained. The RTD of an ideal tubular reactor is a Dirac delta function, similar to that of a batch reactor (See Scheme 4). Thus, the reaction kinetics and the polymer properties synthesized using CRP in a tubular reactor are expected to be similar to those produced in a batch reactor.

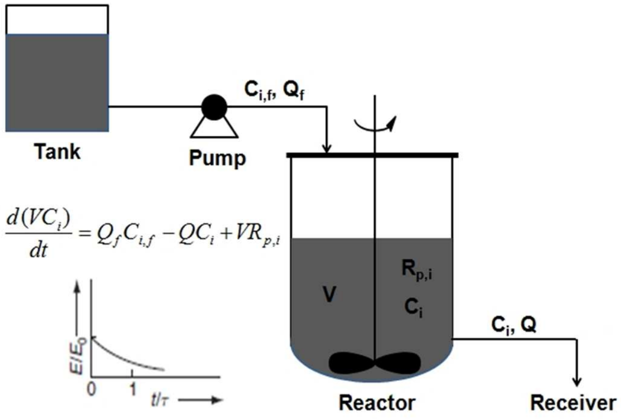


Scheme 6. Schematic of a tubular reactor

One of the biggest selling points of using a tubular reactor is the excellent heat removal due to its large surface-to-volume ratio. Therefore, in terms of safety, tubular reactor is more advantageous than batch reactor and continuous stirred-tank reactor (CSTR). However, tubular reactor usually faces mixing problem, which may broaden the RTD away from the Dirac delta function, as shown in Scheme 6. This affects the properties of polymers produced in a tubular reactor to deviate from those produced in a batch reactor. Solutions available for the mixing problem include the design of modified tubular reactors, including loop reactors, wicker-tube reactors and pulsed-flow reactors.

1.2.3. Continuous stirred tank reactor (CSTR)

CSTR (shown in Scheme 7) is another type of continuous reactors that has the advantages of uniform product property, low operating cost, and easy operation. Similar to tubular reactor, there are continuous inlet and outlet flow into and from the reactor in the CSTR system. Usually, polymerization processes are conducted in a single CSTR or in a CSTR train (multiple CSTRs configured in series). The main purpose of using CSTR train is to increase the monomer conversion. CSTR is advantageous for large volume polymerization systems.



Scheme 7. Schematic of a continuous stirred tank reactor (CSTR)

The RTD of a CSTR is an exponential decay function. Due to the broader RTD in CSTR than those in batch and tubular reactors, the polymers synthesized in CSTR experienced different reaction time from one another. Therefore, these polymer chains are expected to possess a broader MWD. The RTD of a large number of CSTRs in series approaches that of a tubular reactor. Also, the RTD of a tubular reactor with large volume reflux or recycling approaches that of a CSTR.

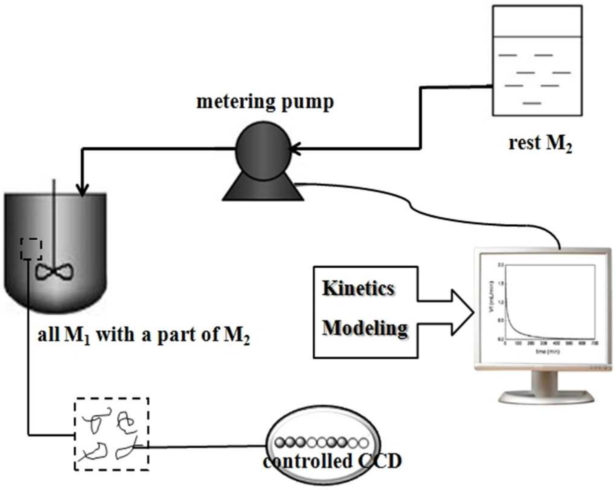
1.3. Review scope

To date, there are only a few reviews discussed polymerization in various types of reactors. Steinbacher and McQuade reviewed flow microreactor technologies that produce various polymer materials including bead, microcapsules and fibers.[95] Schork and Guo summarized miniemulsion polymerization works in semi-batch and continuous reactors.[96] Microreactors for polymer synthesis by ionic and radical polymerization methods were respectively reviewed by Frey et al[97,98] and Nagaki et al.[99] Recently, copper-mediated CRPs in continuous flow reactors were reviewed by Cunningham et al.[100]

This work provides a comprehensive review for the progresses in the reactor engineering of CRP systems including ATRP, RAFT, and NMP. Homogeneous and heterogeneous CRP processes in semi-batch reactors, tubular reactors, and CSTRs are summarized and discussed in detail. The differences of semi-batch reactors and continuous reactors compared to batch reactors are highlighted based on the published experimental data. Perspectives on the future of reactor engineering of CRP are also offered.

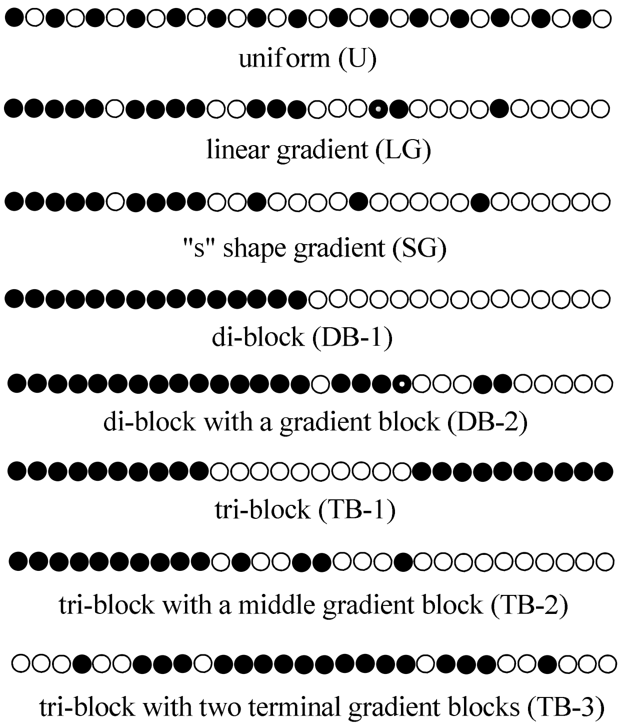
2. Semi-batch reactor

The feasibility of controlling copolymer composition distributions (CCDs) by semi-batch reactors has been well demonstrated. Coupling the advantage of semi-batch reactor with the slow chain growth of CRP has provided the opportunity to control the copolymer composition to have various CCDs. Most copolymerization experiments in semi-batch reactors used constant feeding of monomers (CF) to control the CCD. As the name implies, this process involves feeding monomers to the reactor at a constant feeding rate. However, the degree of control of CCDs synthesized by using CF is not very precise. In the recent years, a model-based monomer feeding policy (MMFP) was developed to produce polymers with pre-designed CCDs, shown by Scheme 8.[27-33] In MMFP, a kinetic model for controlled radical copolymerization (CRcoP) process is first developed and then correlated to the batch experimental data for parameter estimation. The model is then combined with semi-batch reactor model for targeting the pre-designed CCD using the comonomer feeding rate as an operating variable. The obtained comonomer feeding rate is actually controlled by a computer-programmed pump, thus this process is also referred to as programmed feeding (PF) in this review. Using programmed feeding, polymer products with the pre-designed CCD can be produced with a high degree of precision in semi-batch CRcoP. This precise control over the polymer structures for targeted properties represents an emerging trend in polymer reaction engineering.



Scheme 8. Model-based monomer feeding policy[27]

To date, many different variations of CCDs have been obtained by utilizing semi-batch CRcoP. These CCDs can be divided into eight groups as shown in Scheme 9: (1) uniform (U); (2) linear gradient (LG); (3) S-shape gradient (SG) including hyperbolic, parabolic and sigmoidal; (4) di-block (DB-1); (5) di-block with a gradient block (DB-2); (6) tri-block (TB-1); (7) tri-block with one middle gradient block (TB-2); (8) tri-block with two terminal gradient blocks (TB-3).



Scheme 9. Different CCDs by semi-batch CRcoP

2.1. ATRP

2.1.1. Solution polymerization

Matyjaszewski's group first conducted CRcoP in semi-batch reactor to control the resulting CCDs.[24-26] The advantages of semi-batch reactors over batch reactors in synthesizing copolymers with pre-designed CCDs were well demonstrated in their studies. In a batch reactor, only copolymers with a random composition or a spontaneous gradient were produced. LG and SG St/BA and styrene/acrylonitrile (St/AN) copolymers were successfully produced by constant feeding via semi-batch homogeneous ATRP.[24-26] In a semi-batch reactor, the instantaneous gradient composition could be designed to vary from 0 to 1.0, depending on the choice of reactants to be fed and the feed rate. In St/AN system, a linear gradient (LG) profile was obtained by constant feeding of AN at 0.01 ml/min. Meanwhile, copolymers with S-shape gradients (SG) were obtained by constantly feeding AN at a slightly faster rate of 0.02 and at 0.08 ml/min.[26]

Similar syntheses were reported by the same group for 2-(dimethylamino)ethyl methacrylate/n-butyl methacrylate (DMAEMA/BMA) and BA/isobornyl acrylate (BA/IBA) copolymers. The copolymers with LG profile were synthesized by constant feeding in semi-batch reactors, while the random and block copolymer counterparts were synthesized in batch reactors (reactions **S-ATRP-1** and **S-ATRP-2** in Table 1).[101,102] Luo et al has also used constant feeding in semi-batch solution ATRP to synthesize LG tert-butyl acrylate/2,2,3,3,4,4,4-heptafluorobutyl methacrylate (tBA/HFBMA) copolymers by using HFBMA as the feeding monomer in the solution ATRP of tBA (reaction **S-ATRP-3**).[103]

Albeit useful to produce LG copolymers, constant feeding cannot control the CCD at will and to a high precision. Programmed feeding (PF) was developed by Zhu's group to produce copolymers with more sophisticated CCDs and better precision.[27-33] Zhao et al. used PF to produce a series of tert-butyl methacrylate/MMA (tBMA/MMA) copolymers with uniform (U), LG, S-shape gradient (SG), tri-block with a middle gradient block (TB-2) and di-block (DB-1) composition profiles in semi-batch solution ATRP (reactions **S-ATRP-4** to **S-ATRP-8**).[32,33] Good agreements between the experimental CCDs and the theoretically targeted CCDs were obtained, clearly showing the power of PF for the precise copolymer production. Similar successes were reported by Gallow et al. They synthesized a series of 2-hydroxyethyl methacrylate/DMAEMA (HEMA/DMAEMA) copolymers with LG and SG composition profiles by PF via semi-batch solution ATRP (reactions **S-ATRP-9** and **S-ATRP-10**).[104,105]

Copolymers with different composition profiles can be further used as the backbone for synthesis of molecular brushes. The properties of these brushes depend on the profile of the copolymer backbones. Novel molecular brushes with LG backbone composition profile were synthesized by Matyjaszewski's group[106] and Luo's group.[107] The methyl methacrylate/HEMA-TMS (MMA/HEMA-TMS) copolymer backbone with LG profile was synthesized by constant feeding of HEMA-TMS during the solution ATRP of MMA (reactions **S-ATRP-11** and **S-ATRP-12**).[106,108] Inverse CCD was obtained when MMA was chosen as the feeding monomer during ATRP of HEMA-TMS (**S-ATRP-13**).[108] The MMA/HEMA-TMS copolymer backbone with random and block profiles were also synthesized in batch and sequential batch reactors by Luo et al. The same group also compared the solution properties of molecular brushes with LG, random, and block backbone profiles.[107]

Other than controlling CCDs, semi-batch reactors also have been employed to synthesize polymers with low MW, which are used as coating resins. Fu et al. first used a semi-batch reactor to produce low-MW polystyrenes (PSt) with M_n = 6.0-11.5 kg/mol.[109] Both polymerization rate and initiator efficiency in the semi-batch reactor were found to be lower than those in a counterpart batch reactor. For example, in the semi-batch reactor, a conversion of about 90% was obtained after 600 min of reaction with an initiator efficiency of 0.30. As comparison, the same conversion was achieved after only 360 min with an initiator efficiency of 0.75 (reaction **S-ATRP-14** in Table 1) in the batch reactor.[109] They attributed the decrease to the higher initiator concentration at the beginning of polymerization in the semi-batch reactor. The initiator efficiency can be improved by initially charging a small amount St to the reactor or by decreasing the final monomer content, at the cost of slowing down the polymerization.[109] The same group also synthesized low-MW poly(butyl acrylate) (PBA) in a similar system (reaction **S-ATRP-15**).[110] For controlling CCDs in semi-batch reactors, Fu et al. also synthesized a series of low-MW St/BA copolymers with U, LG, and DB-2 composition profiles.[110]

Numerous investigations have been conducted on establishing the relationships between the properties of copolymers with their composition profiles. Comparison of the thermal properties of LG copolymers with those of random and block copolymers was conducted by Matyjaszewski et al for DMAEMA/BMA and BA/IBA copolymers systems.[101,102] Luo et al also studied the effect of CCD on the glass transition temperature (T_g) of MMA/HEMA-TMS copolymers.[108] Both groups found that the LG copolymers exhibit broad T_g, while the random and block copolymers possess narrow T_g and two distinct T_g's, respectively. The effect of copolymer composition profiles on the pH responsivity and micelle formation of MAA/MMA copolymers (formed by hydrolyzing tBMA/MMA under acidic condition) was reported and found to be significant.[32] Moreover, the cloud points of HEMA/DMAEMA copolymers in solution were shown to greatly depend on their composition profiles.[104,105]

The works summarized above clearly demonstrate the high potential in exploiting novel properties of polymer products by designing and controlling CCDs via constant feeding and programmed feeding in semi-batch reactors. Moreover, these works allow investigation of the structure-property relationships. With the relationships, it is possible to further design the CCD to produce polymer products with tailor-made properties.

Table 1. Selected examples of homogeneous ATRP in semi-batch reactors

Reaction No.	Monomers M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	Solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-ATRP-1	DMAEMA/BMA	Solution	200:1:1:2	0.74 [0.80]	LG [random]	Water/2-propanol	25	N/A [210]	N/A [87.2]	20.96 [30.87]	1.30 [1.27]	CF Batch	101 101
S-ATRP-2	BA/IBA	Solution	533:1:4.38:3.6	0.59	LG	Anisole/ diphenyl ether	50	378	82.3	74.80	1.13	CF	102
S-ATRP-3	tBA/HFBMA	Solution	100:1:1:2	0.50	LG	Toluene	80	480	72.0	10.66	1.45	CF	103
S-ATRP-4	tBMA/MMA	Solution	200:1:1:2	0.50	LG [random]	p-Xylene	100	590 [570]	94.0 [96.0]	26.00 [25.00]	1.12 [1.14]	PF Batch	31
S-ATRP-5	tBMA/MMA	Solution	200:1:1:2	0.50	SG	p-Xylene	100	670	94.0	24.00	1.14	PF	31
S-ATRP-6	MMA/tBMA	Solution	200:1:1:2	0.50	U	p-Xylene	100	N/A	93.9	21.70	1.17	PF	32
S-ATRP-7	tBMA/MMA	Solution	200:1:1:2	0.50	DB-1	p-Xylene	100	N/A	93.0	21.00	1.24	PF	32
S-ATRP-8	tBMA/MMA	Solution	200:1:1:2	0.50	TB-2	p-Xylene	100	N/A	99.0	25.00	1.18	PF	32
S-ATRP-9	HEMA/DMAEMA	Solution	300:1:1.4:1.4	0.40-0.67	LG	DMSO	50	600	N/A	38.0-48.0	1.04-1.07	PF	104
S-ATRP-10	HEMA/DMAEMA	Solution	300:1:1.4:1.4	0.31-0.68 [0.64]	SG [random]	DMSO	50	600	N/A	36.0-101.0 [34.00]	1.06-1.08 [1.05]	PF Batch	104
S-ATRP-11	MMA/HEMA-TMS	Solution	525:1:1.65:3.31	0.48	LG	Xylene /anisole	90	420	47.7	56.70	1.22	CF	106
S-ATRP-12	MMA/HEMA-TMS	Solution	450:1:1.37:2.62	0.56	LG	Toluene	90	420	47.1	43.00	1.12	CF	108
S-ATRP-13	HEMA-TMS/MMA	Solution	450:1:1.37:2.62	0.44	LG	Toluene	90	420	53.6	50.00	1.05	CF	108
S-ATRP-14	St	Solution	50:1:1-0.1:1 [50:1:1:1]	1.00	Homo	Toluene	110	720-900 [360]	80.0-96.0 [93.0]	6.00-11.5 [6.70]	1.05-1.16 [1.07]	CF Batch	109 109
S-ATRP-15	BA	Solution	40:1:1:1	1.00	Homo	Toluene	90 [90]	420 [240]	97.0 [99.0]	7.60 [4.80]	1.62 [1.18]	CF Batch	110 110

Reaction condition = total mole ratios of M: RX:C:L; M = monomer; RX = ATRP initiator; C = catalyst; L = ligand; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; DMSO = dimethyl sulfoxide

2.1.2. Miniemulsion polymerization and heterogeneous catalyst

The semi-batch reactor approaches were also employed in heterogeneous ATRP and its variants for controlling CCDs.[111,112] Min et al. from Matyjaszewski's group synthesized a series of SG copolymers via semi-batch miniemulsion AGET ATRP (reactions **S-ATRP-16** to **S-ATRP-18**).[111] The initial mole ratio of comonomers, their reactivities, feeding rates, and hydrophobicities all played important roles in the resulting composition profiles. The miniemulsion particles were stable in the whole polymerization process. The number-average MW increased linearly with the total monomer conversion and it was very close to the theoretical MW, suggesting a high initiation efficiency in this miniemulsion system.[111]

The recently developed SET-LRP, having the advantages of low catalyst loading, fast polymerization rate, and low polymerization temperature, has attracted some attention.[67-70] Zhou and Luo synthesized a series of LG MMA/tBA copolymer by constant feeding via semi-batch SET-LRP with Cu(0) and conventional ATRP ligands as the catalyst system at 25°C (**S-ATRP-19**).[112] Programmed feeding for precise production in heterogeneous ATRP systems has not been reported to date.

Table 2. Selected examples of heterogeneous ATRP in semi-batch reactors

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-ATRP-16	BA/tBA	Miniemulsion	200:1:0.2:0.2	0.50	SG	-	80	N/A	50.0	12.0	1.22	CF	111
					[random]				[55.0]	[12.5]	[1.18]	Batch	111
S-ATRP-17	BMA/MMA	Miniemulsion	300:1:0.2:0.2	0.67	SG	-	75	N/A	85.0	N/A	1.20-1.26	CF	111
S-ATRP-18	BA/St	Miniemulsion	200:1:0.2:0.2	0.50	SG	-	80	N/A	100	22.00	1.22	CF	111
S-ATRP-19	tBA/MMA	Heterogeneous catalyst	200:1:0.1:0.1, 200:1:0.25:0.25, 200:1:0.5:0.5	0.50	LG	DMF	25	330	56.8-68.9	13.77-16.02	1.38-1.45	CF	112

Reaction condition = total mole ratios of M: RX:C:L; M = monomer; RX = ATRP initiator; C = catalyst; L = ligand; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; Homo = homopolymer; DMF = N,N-dimethylformamide.

2.2. RAFT

2.2.1. Solution polymerization

Several research works about the control of CCDs by constant feeding in homogeneous (solution and bulk) RAFT systems have been reported.[113,114] The effects of synthesis routes on the copolymer composition profiles were investigated in-depth by Billon et al.[113] Copolymers of St/2-(2',3',4',6'-tetra-o-acetyl-d-galactosyloxy)ethyl acrylate (St/AcGalEA) with DB-2 composition profile were synthesized by running styrene polymerization for a period of time, followed by constant feeding of AcGalEA to the reaction media (reaction **S-RAFT-1** in Table 3).[113] Chen et al. synthesized LG acrylic acid/2,2,2-trifluoroethyl methacrylate (AA/TFEMA) copolymers by constant feeding of TFEMA via semi-batch solution RAFT polymerization (reaction **S-RAFT-2**).[114]

Programmed feeding for precise production in homogeneous RAFT systems was first developed by Sun et al.[29,30] A series of St/BA copolymers with various pre-designed CCDs were successfully produced using PF in semi-batch RAFT (reactions **S-RAFT-3 to S-RAFT-6**).[29,30] The effects of composition profiles on the thermal properties of these products were also carefully investigated by DSC analysis.[30] Their results clearly indicated that programmed feeding was feasible for design and precise control over CCDs to produce polymer products with tailor-made properties.

Semi-batch reactor technologies are most employed in linear CRP systems. In CRP, individual chains grow slowly, providing ample time for chains to come into contact with each other, which could also facilitate inter-chain reactions for nonlinear polymers. Wang et al first employed semi-batch technologies in vinyl/divinyl CRP to control gelation and to synthesize hyperbranched polymer products.[115-117] A large amount of RAFT agents (mole ratio of RAFT to divinyl monomers greater than 0.5) is usually required in batch RAFT, to synthesize branched polymers without gelation.[118-121] In Wang's work, a series of hyperbranched polyacrylamides (PAMs) were synthesized, free of gels, by constantly feeding divinyl monomer N,N'-methylenebis(acrylamide) (BisAM) in a semi-batch solution RAFT copolymerization (reactions **S-RAFT-7** and **S-RAFT-**

8).[115-117] Using this strategy, hyperbranched polymers were successfully produced with low mole ratio of RAFT agents to divinyl monomers (no more than 0.1).[115-117] Furthermore, a more uniform branching density distribution was obtained in the semi-batch reactor than in a counterpart batch reactor.[116]

Table 3. Selected examples of homogeneous RAFT polymerization in semi-batch reactors

Reaction No.	Monomer M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-RAFT-1	St/AcGalEA	Solution	232:1:0.12	0.81	DB-2	DMAc	90	450	49.8	10.27	1.18	CF	113
			[217:1:0.13]	[0.80]	[random]			[1440]	[55.0]	[13.3]	[1.26]	Batch	113
S-RAFT-2	AA/TFEMA	Solution	200:1:0.25	0.50	N/A	1,4-dioxane	60-80	480	54.2-78.7	N/A	N/A	CF	114
S-RAFT-3	BA/St	Solution	200:1:0.40	0.25	U	Toluene	70	2160	80.0	15.00	1.35	PF	29
S-RAFT-4	BA/St	Solution	200:1:0.25	0.25	LG	Toluene	70	2160	70.0	15.75	1.24	PF	29
S-RAFT-5	BA/St	Solution	333:1:0.22	0.50	SG	Toluene	88	N/A	N/A	29.00	1.30	PF	30
S-RAFT-6	BA/St	Solution	333:1:0.22	0.50	TB-2	Toluene	88	N/A	N/A	31.25	1.30	PF	30
S-RAFT-7	AM/BisAM	Solution	630:1:0.50	0.95	Branched	*	60	120-300	95.5-99.5	180.0-245.0	6.85-8.15	CF	116
								[110]	[68.0]	[145.0]	[4.50]	Batch	116
S-RAFT-8	AM/BisAM	Solution	610-630:1:0.50	0.95-0.98	Branched	*	60	210	95.0-98.0	80.00-180.0	2.00-8.00	CF	116

Reaction condition = total mole ratios of M: RAFT:I; M = monomer; RAFT = RAFT agent; I = conventional initiator; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature; t = polymerization time; X = total monomer conversion; M_n = number-average molecular weight; PDI = polydispersity index; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; * sodium acetate/acid acetate buffer solution with pH = 5.

2.2.2. Emulsion and miniemulsion polymerization

Charmot et al. were the first to use semi-batch reactors for heterogeneous RAFT systems.[43] Homopolymers were synthesized by constant feeding of monomers in RAFT emulsion systems (reactions **S-RAFT-9 and S-RAFT-10** in Table 4).[43] According to their work, higher initiation efficiencies of RAFT agents were achieved in semi-batch reactors than in batch reactors. Moreover, polymers with better defined MW could be produced in the semi-batch reactors.[43]

Several research works have investigated the control of CCDs in RAFT (mini)emulsion systems. Luo and Liu synthesized a series of DB-2 MMA/St copolymers by constant feeding of St at 8 ml/h after complete copolymerization of MMA and St (reaction **S-RAFT-11**).[122] Similar to Luo and Liu's work, Wang et al. synthesized DB-2 St/butadiene (St/Bu) copolymers by constant feeding of Bu at 80 ml/h after 1 hour of RAFT miniemulsion polymerization of St (reaction **S-RAFT-12**).[123] Zhang et al. synthesized DB-1 butyl methacrylate/dodecafluoroheptyl methacrylate (BMA/DFMA) copolymers by constant feeding of DFMA at 2 ml/h after complete RAFT polymerization of BMA (reaction **S-RAFT-13**).[124] In the work of Zhu et al, a series of TB-1 St/BA copolymers with various MW were synthesized by first feeding BA at a constant rate of 20 g/h until completion of St, followed by constant feeding of St at the same rate until completion of BA (reaction **S-RAFT-14**).[125] Their data also showed that thermoplastic elastomer products can be produced by semi-batch RAFT emulsion block polymerization.[125] Recently, Chen et al. synthesized SG acrylic acid/2,2,2-trifluoroethyl methacrylate (AA/TFEMA) copolymers by constant feeding of TFEMA in an emulsifier-free RAFT emulsion polymerization (reaction **S-RAFT-15**).[126]

The use of PF for precise production has well been demonstrated in homogeneous CRP systems.[29-32] However, high product separation costs and poor heat transfer limit their commercial exploitation. These problems could be countered by employing heterogeneous systems (such as emulsion and miniemulsion). Li et al was the first to develop programmed feeding in heterogeneous RAFT systems. A series of U and LG St/BA copolymers products were successfully produced by programmed feeding in semi-batch RAFT miniemulsion polymerization (reactions **S-RAFT-16** and

S-RAFT-17).[33] Also, Li et al extended this PF strategy for the control of topology in heterogeneous systems. A series of hyperbranched polystyrenes having uniform branching density distributions were produced via semi-batch RAFT miniemulsion polymerization (reaction **S-RAFT-18**).[127]

Table 4. Selected examples of heterogeneous RAFT polymerization in semi-batch reactors

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-RAFT-9	St	Emulsion	N/A	1.00	Homo	-	85	N/A	N/A	16.60-90.60	2.10-3.30	CF	43
S-RAFT-10	BA	Emulsion	N/A	1.00	Homo	-	85	N/A	70.0-100	20.6-81.00	1.40-2.30	CF	43
S-RAFT-11	MMA/St	Miniemulsion	260-300:1:0.30	0.25-0.90	DB-2	-	60	N/A	95.0-100	22.67-24.32	1.27-1.44	CF	[122]
S-RAFT-12	St/Bu	Miniemulsion	N/A	0.25	DB-2	-	70	660	92.0	40.70	1.41	CF	[123]
S-RAFT-13	BMA/DFMA	Miniemulsion	81:1:0.3	0.78	DB-1	-	75	720	90.9	10.25	1.22	CF	[124]
S-RAFT-14	BA/St*	Emulsion	N/A	N/A	TB-1	-	70	190-240	90.0-97.0	76.80-338.1	1.41-3.19	CF	[125]
S-RAFT-15	AA/TFEMA	Emulsion	233:1:0.5	0.57	SG	5% acetone aqueous	70	300	93.5	200.0	1.71	CF	[126]
S-RAFT-16	BA/St	Miniemulsion	333:1:0.33	0.50, 0.75	U	-	70	420, 540	82.0, 88.0	36.00, 40.00	1.04, 1.13	PF	33
				[0.50]	[Random]			[300]	[80.0]	[37.00]	[1.15]	Batch	33
S-RAFT-17	St/BA	Miniemulsion	333:1:0.33	0.50, 0.75	LG	-	70	420, 540	73.3, 85.8	30.88, 40.00	1.07, 1.08	PF	33
S-RAFT-18	TEGDMA/St	Miniemulsion	100:1:0.1	0.005	-	-	70	600	75.0	13.24	2.87	PF	[127]

Reaction condition = total mole ratios of M: RAFT:I; M = monomer; RAFT = RAFT agent; I = conventional initiator; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature; t = polymerization time; X = total monomer conversion; M_n = number-average molecular weight; PDI = polydispersity index; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; Homo = homopolymer; * BA and St are both feeding monomers

2.3. NMP

2.3.1. Bulk and solution polymerization

Cunningham et al first developed semi-batch technologies to produce low MW products for coating.[128,129] PSt products with M_n = 7000 g/mol and PDI = 1.5 were produced by constant feeding in a semi-batch NMP of St (reaction **S-NMP-1** in Table 5).[129] Control of CCDs by constant feeding in homogeneous NMP systems was extensively investigated by Billon et al and Torkelson et al. Karaky et al. synthesized LG and SG N,N-dimethylacrylamide/BA (DMA/BA) copolymers by constant feeding of DMA at various feeding rates (reaction **S-NMP-2**).[130,131] LG DMA/BA copolymers were synthesized by slow feeding (feeding rates were 1.4 and 0.8 ml/h), while SG DMA/BA copolymers were synthesized by fast feeding (feeding rates was 2.8 ml/h).[130,131] By using the same feeding policy, LG and SG St/BA, octadecyl acrylate/methyl acrylate (ODA/MA), and BA/MMA copolymers were also synthesized by Billon et al (reactions **S-NMP-3** to **S-NMP-5**).[132-134] Borisova et al reported the synthesis of DB-2 AA/St copolymers by constant feeding of St to solution NMP of AA after it ran for 4 hours (reaction **S-NMP-6**).[135] Similar to this feeding policy, TB-3 AA/St copolymers were also synthesized by feeding St at constant rate 14 ml/h after 4 hours of AA NMP with difunctional initiators (reaction **S-NMP-7**).[136] The pH-controlled self-assembly behaviors of these DB-2 and TB-3 copolymers were also thoroughly investigated.[135,136]

Torkelson et al contributed significantly to the control of CCDs in homogeneous NMP systems. A series of LG St/4-methylstyrene (St/MS) (reaction **S-NMP-8**),[137] St/MMA (reaction **S-NMP-9**),[138] St/tBA (reaction **S-NMP-10**),[139-141] St/4-acetoxystyrene (St/AS) (reaction **S-NMP-11**),[140,142-147] St/BA (reaction **S-NMP-12**),[140,148] St/BMA (reaction **S-NMP-13**),[140] and St/4-vinylpyridine (St/4VP)[140,147] copolymers were synthesized by constant feeding methods.[137-148] A series of DB-2 St/AS copolymers were also synthesized by constant feeding of AS at the beginning of bulk NMP of St with PSt used as macroinitiator or by constant feeding of AS after 2 hours of bulk NMP of St (reaction **S-NMP-14**).[142,149,150]

In semi-batch reactors, constant feeding is often used to produce LG copolymer products. Torkelson's group first developed a new feeding policy, referred to as increasing constant feeding (ICF) in this review, to produce SG (such as sigmoidal gradient) copolymer products. For example, SG St/MMA copolymers can be produced by constant feeding of MMA at 10 ml/h for the first 3 hours, 15 ml/h for the next 3 hours, and 20 ml/h for the final 3 hours during NMP of St (reaction **S-NMP-15**).[151,152] By using similar feeding policy, a series of St/BA (reaction **S-NMP-16**)[140,144,145,147,148,153] copolymers were also synthesized by Torkelson et al. The synthesis of St/AS copolymers with DB-2 composition profile by ICF of AS at 0.03 ml/min for the first 2 hours and 0.08 ml/min for the final 4 hours with PSt macroinitiators was also reported (reaction **S-NMP-17**).[154] The properties of these copolymer products with different composition profiles were also thoroughly investigated. The use of programmed feeding for precise control over CCD has not been reported for the homogeneous NMP systems.

Table 5. Selected examples of homogeneous NMP in semi-batch reactors

Reaction No.	Monomer M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-NMP-1	St	Solution	N/A	1.00	Homo	Xylene	138	400-1300	40.0-98.0	2.000-10.50	1.20-1.50	CF	129
S-NMP-2	BA/DMA	Solution	500:1	0.51	LG, SG	Toluene	112	240-800	55.1-83.7	24.00-35.00	1.24-1.48	CF	130
S-NMP-3	BA/St	Bulk	480:1	0.42	LG,	-	120	430,	77.8,	51.80	1.21	CF	132
					SG			240	73.7	40.70	1.16		
S-NMP-4	ODA/MA	Solution	500:1	0.27	SG	Toluene	112	215	44.5	21.35	1.21	CF	133
S-NMP-5	BA/MMA	Bulk	500:1	0.50	SG	-	115	720	91.0	61.90	1.32	CF	134
					[random]			[390]	[70.0]	[48.60]	[1.24]	Batch	134
S-NMP-6	AA/St	Solution	230:1	N/A	DB-2	1,4-dioxane	120	N/A	N/A	14.00-15.30	N/A	CF	135
S-NMP-7	AA/St	Solution	230:1	N/A	TB-3	1,4-dioxane	120	N/A	63.0	12.55	1.25	CF	136
			400:1						70.0	17.00	1.33		
S-NMP-8	St/MS	Solution	N/A	0.42	LG	cyclohexane	90	840	100	84.60	1.33	CF	137
S-NMP-9	St/MMA	Bulk	N/A	0.51	LG	-	93	480	100	55.20	1.44	CF	138
S-NMP-10	St/tBA	Bulk	N/A	0.55-0.72	LG	-	115	480	95.0-100	38.60-91.80	1.32-1.48	CF	141
S-NMP-11	St/AS	Bulk	N/A	0.56	LG	-	115	300	100	93.80	1.40	CF	143
S-NMP-12	St/BA	Bulk	N/A	0.60	LG	-	100	480	N/A	72.00	N/A	CF	148
S-NMP-13	St/BMA	Bulk	N/A	0.49-0.71	LG		115	130-180	N/A	57.80-83.00	1.37-1.39	CF	140
S-NMP-14	St/AS	Bulk	N/A	0.25-0.76	DB-2	-	90	N/A	N/A	48.00-67.00	N/A	CF	142
S-NMP-15	St/MMA	Bulk	N/A	0.55	SG	-	93	540	N/A	102.0	1.58	ICF	151,152
S-NMP-16	St/BA	Bulk	N/A	0.60	SG	-	100	540	100	95.00	1.37	ICF	153
S-NMP-17	St/AS	Bulk	N/A	0.58	DB-2	-	90	360	100	53.80	1.11	ICF	154

Reaction condition = total mole ratios of M: PT; M = monomer; PT = NMP initiator; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature; t = polymerization time; X = total monomer conversion; M_n = number-average molecular weight; PDI = polydispersity index; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; Homo = homopolymer.

2.3.2. Emulsion and microemulsion polymerization

Reports on NMP heterogeneous systems in semi-batch reactors are scarce. In the work of Charleux et al, stable NMP emulsion system was achieved by a simple two-stage process in batch reactors.[155,156] Compared to batch reactors, conducting emulsion polymerization in semi-batch reactors allows easier control over the latex properties by feeding of monomers, initiators and/or surfactants.[157] Nicolas et al. first developed semi-batch technologies for NMP emulsion systems.[158] Stable PBA latexes with average particle diameters ranging from 285 to 555 nm were prepared by constant feeding of BA after a short time of NMP emulsion polymerization (reaction **S-NMP-18** in Table 6).[158] Thomson et al reported the synthesis of stable PBA latexes with high solid content (45 wt%) by two-stage NMP emulsion polymerization, the monomer BA was fed during the second stage after the formation of PBA latexes in the first stage (**S-NMP-19**).[159] Using the same method, Li et al synthesized stable PBA latexes with particle sizes ranged from 20-100 nm by NMP microemulsion polymerization of BA (**S-NMP-20**).[160]

From an industrial point of view, surfactant-free NMP emulsion systems are attractive. However, the problems of multi-step polymerization, broad particle size distribution (PSD) and/or bimodal PSD have limited their commercial potential.[161,162] Recently, Thomson et al reported a one-step surfactant-free NMP emulsion copolymerization of BMA with a small amount of St. By constant feeding of BMA and St mixture, stable surfactant-free emulsion systems with monomodal PSDs were successfully prepared (reactions **S-NMP-21** and **S-NMP-22**).[163]

Table 6. Selected examples of heterogeneous NMP in semi-batch reactors

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	T	t	X	M_n	PDI	Feeding policy	Ref
S-NMP-18	BA	Emulsion	270:1	1.00	Homo	-	112	390-600	70.0-97.0	27.00-42.50	1.20-1.55	CF	[158]
S-NMP-19	BA	Emulsion	N/A	1.00	Homo	-	120	450	94.0-100	43.28-81.85	2.06-4.46	CF	[159]
S-NMP-20	BA	Microemulsion	155-618:1	1.00	Homo	-	120	360	78.0-100	16.60-53.30	1.38-3.26	CF	[160]
S-NMP-21	BMA/St*	Emulsion	147:1	0.86	N/A	-	90	1320	30.0	11.00	1.55	CF	[163]
S-NMP-22	BMA/St/MA**	Emulsion	266-279:1	0.87-0.89	N/A	-	90	1320-1386	36.4-67.5	16.18-38.40	1.48-1.92	CF	[163]

Reaction condition = total mole ratios of M:PT; M = monomer; PT = NMP initiator; F_{1t} = targeted mole fraction of M_1 (M_2 is feeding monomer); T = polymerization temperature; t = polymerization time; X = total monomer conversion; M_n = number-average molecular weight; PDI = polydispersity index; N/A = not available in literature; Homo = homopolymer; * both BMA and St are feeeding monomers; ** both BMA and St are feeding monomers, and MA are added to improve initiator efficiency.[163]

2.4. Summary

Semi-batch reactors have been most frequently employed to control CCDs by feeding comonomers. Table 7 summarized different kinds of polymer products with different CCDs, which were made by semi-batch CRP. It is well known that copolymers produced by one-step polymerization in batch reactors only possess random profiles. The synthesis of di-block copolymers usually requires two-step polymerization in batch reactors with macroinitiators synthesized in the first step. However, the purification of the macroinitiator from the first step is both time consuming and costly. Synthesis of di-block copolymers in semi-batch reactors does not require any purification for the macroinitiators. In semi-batch reactors, di-block copolymers (poly[M_1-b-M_2], DB-1) can be produced by feeding M_2 upon completion of M_1. Tri-block copolymers (poly[M_1-b-M_2-b-M_3], TB-1) can also be produced by the same feeding policy in semi-batch reactors. Therefore, semi-batch reactors are preferred to batch reactors in synthesizing copolymers with pre-specified composition profiles.

The methods for producing copolymers with the other types of CCDs in semi-batch reactors are summarized according the literatures as follow: uniform copolymers (poly[M_1-u-M_2], U) are produced by feeding both M_1 and M_2, or by feeding the fast comonomers. Di-block copolymers with a gradient block (poly[M_1-b-(M_1-grad-M_2)], DB-2) are produced by feeding M_2 after M_1 is polymerized for some time. Linear gradient copolymers (poly[M_1-lg-M_2], LG) and 's' shape gradient copolymers (poly[M_1-sg-M_2], SG) are both produced by feeding M_2 from the beginning of M_1 polymerization. Tri-block copolymers with a gradient middle block (poly[M_1-b-(M_1-grad-M_2)-b-M_2], TB-2) are produced by feeding M_2 after polymerizing M_1 for some time, while tri-block copolymers with two gradient terminal blocks (poly[(M_1-grad-M_2)-b-M_1-(M_1-grad-M_2)], TB-3) are produced by feeding M_2 after M_1 is homopolymerized for some time using difunctional initiators. As shown in Table 7, semi-batch reactors are most employed to produce LG and SG copolymers, while reports on tri-block copolymers are very rare.

Feeding policies for control of CCDs can be divided into three kinds: constant feeding (CF), increasing constant feeding (ICF), and programmed feeding (PF). CF is the most commonly used feeding policy to control CCDs. ICF was developed to produce SG (such as sigmoidal gradient) copolymers. However, CF and ICF cannot control CCDs at will to a high degree of precision. Zhu's group first developed PF to produce polymer products with pre-designed CCDs, allowing precise control of CCDs. The influence of CCD on copolymer properties is significant and it has been demonstrated with various monomers combinations. It is clear that control over CCD is invaluable in producing polymers having tailored properties. Therefore, further research should focus on targeting product properties, *i.e.*, to produce polymer products with tailor-made properties, based on structure-property relationships.

Table 7. Summary of different compositions made by CRP in semi-batch reactors

System	Homo	U	DB-1	DB-2	LG	SG	TB-1	TB-2	TB-3
Homogeneous ATRP	S-ATRP-14 S-ATRP-15	S-ATRP-6	S-ATRP-7		S-ATRP-1 S-ATRP-2 S-ATRP-3 S-ATRP-4 S-ATRP-9 S-ATRP-11 S-ATRP-12 S-ATRP-13	S-ATRP-5 S-ATRP-10		S-ATRP-8	
Heterogeneous ATRP					S-ATRP-19	S-ATRP-16 S-ATRP-17 S-ATRP-18			
Homogeneous RAFT		S-RAFT-3		S-RAFT-1	S-RAFT-4	S-RAFT-5		S-RAFT-6	
Heterogeneous RAFT	S-RAFT-9 S-RAFT-10	S-RAFT-16	S-RAFT-13	S-RAFT-11 S-RAFT-12	S-RAFT-17	S-RAFT-15	S-RAFT-14		
Homogeneous NMP	S-NMP-1			S-NMP-6 S-NMP-14 S-NMP-17	S-NMP-2 S-NMP-3 S-NMP-8 S-NMP-9 S-NMP-10 S-NMP-11 S-NMP-12 S-NMP-13	S-NMP-2 S-NMP-3 S-NMP-4 S-NMP-5 S-NMP-15 S-NMP-16			S-NMP-7
Heterogeneous NMP	S-NMP-18 S-NMP-19 S-NMP-20								

Homo = homopolymer; U = uniform; DB-1 = di-block; DB-2 = di-block with a gradient block; LG = linear gradient; SG = 's' shape gradient; TB-1 = tri-block; TB-2 = tri-block with a middle gradient block; TB-3 = tri-block with two terminal gradient blocks.

3. Tubular Reactor

Owing to the narrow residence time distribution (RTD), the polymerization kinetics in a tubular reactor is similar to that in a batch reactor. Tubular reactors are popular in industry due to their excellent capacity of heat removal. In this chapter, the progresses of ATRP, RAFT, and NMP in tubular reactors are reviewed. Moreover, comparisons of polymers produced from tubular reactors with those from batch reactors are also discussed wherever applicable.

3.1. ATRP

3.1.1. Solution polymerization

The feasibility of solution ATRP in tubular reactor was well demonstrated by Haddleton's[164] and Cunningham's[165] groups. Noda et al. investigated the feeding rate, targeted chain length, and polymerization temperature on the kinetics of ATRP of MMA in tubular reactor (reactions **T-ATRP-1** to **T-ATRP-3** in Table 8).[164] The number-average molecular weight (M_n) grew linearly with monomer conversion, which was controlled by the feed flowrate. The PDI remained around 1.10. A living and well-controlled polymerization was achieved in the tubular reactor. Under the same experimental conditions, the polymerization rates in batch and tubular reactors were similar, but the PDI obtained in tubular reactor was found to be lower.[166] Increasing polymerization temperature led to an increase in the polymerization rate, but it had a negative effect on the targeted chain length (reactions **T-ATRP-2** and **T-ATRP-3**).[164]

The living characteristics of ATRP of St and BA in tubular reactors were also investigated by Cunningham et al (reactions **T-ATRP-4** and **T-ATRP-5**).[165] The initial polymerization rates in tubular reactors were higher than in batch reactors due to the operation mode, while M_n and PDI were similar. Moreover, they showed that the tubular reactor gave a narrow RTD, indicating a nearly ideal plug flow condition. PDI after 71% conversion was 1.09 for BA system, while PDI at 50% conversion was 1.14 for St system.[165] The same group employed modified ATRP technology

(ARGET ATRP) in tubular reactor with tin(II) 2-ethylhexanoate ($Sn(EH)_2$) as the reducing agent.[167,168] Low amount Cu catalysts (ppm level), stoichiometric ratio of ligand to Cu, and unpurified monomers and solvents were used in their experiments.[167] A much slower polymerization rate was observed in a tubular reactor than in a batch reactor when reducing agent used was 10% of the initiator (83% vs. 19% conversion in batch and tubular reactors, respectively). However, increasing the ratio to 40% resulted in comparable polymerization rates, with 97% vs. 96% conversion in batch and tubular reactors, respectively (reaction **T-ATRP-6**).[167] This work demonstrated industrial feasibility of ARGET ATRP.

Wu et al reported controlled ATRP of 2-hydroxypropylmethacrylate (HPMA) in a continuous microfluidic reactor (reaction **T-ATRP-7**).[169] Chastek et al. reported solution ATRP of MMA in a continuous microfluidic reactor and in a batch reactor for comparison (reaction **T-ATRP-8**).[170] Other studies by the same group extended this concept to synthesize di-block[171] and brush[172,173] polymers. Additionally, Wenn et al performed UV-induced SET-LRP of methyl acrylate (MA) in a tubular UV-reactor, the polymerization gave good control over polymer molecular weight (reaction **T-ATRP-9**).[174]

In tubular reactors, DB-1 copolymers are usually produced by employing macroinitiators or by using two tubular reactors. Wu et al synthesized a series of ethylene oxide/2-hydroxypropyl methacrylate (EO/HPMA) DB-1 copolymers with PEO as macroinitiators in a microchannel reactor (reaction **T-ATRP-10**).[171] Compared to batch reactor, the polymerization rate was somewhat lower at the beginning in the microchannel reactor, but it became slightly higher as the polymerization progressed. The PDI's observed from both reactors were very similar.[171] The same method was used by Chastek et al. to synthesize DB-1 MMA/lauryl methacrylate (MMA/LMA) copolymers by using PMMA macroinitiators in a microfluidic reactor (reaction **T-ATRP-11**).[170] On the other hand, Haddleton et al reported the use of two tubular reactors in series to synthesize DB-2 MMA/BMA and MMA/benzyl methacrylate (MMA/BzMA) (reactions **T-ATRP-12** and **T-ATRP-13**).[164]

Many studies have been conducted on non-linear polymerization in tubular reactors. Bally et al first reported branching polymerization by CRP in tubular reactor. A series of branched polymers was synthesized by self-condensing vinyl copolymerization (SCVCP) through solution ATRP of MMA and BIEM in a tubular microreactor.[175] The polymerization rate and branching efficiency were both higher in the tubular microreactor than those in batch reactor under the same experimental conditions.[175] For example, after 120 minutes of polymerization, the conversion and branching efficiency of MMA was 64% and 44% in tubular microreactor but only 58% and 28% in batch reactor, respectively (reaction **T-ATRP-14**).[175] Their study demonstrated that tubular microreactors can be used for better control of the branching process in CRP systems than batch reactors. Moreover, tubular microreactors offer excellent heat transfer and fast mixing, resulting in improved polymer products.[176-178] Furthermore, Parida et al also used coil flow inverter microreactor to synthesize branched poly(2-(dimethylamino)ethyl methacrylate)) (PDMAEMA) by ATRP, and it was found that the branching efficiency was in the order of coil flow inverter microreactor > normal coiled tube microreactor > batch reactor (reaction **T-ATRP-15**).[179]

Table 8. Selected examples of homogeneous ATRP in tubular reactors

Reaction No.	Monomer M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
T-ATRP-1	MMA	Solution	100:1:1:2.2	1.00	Homo	Toluene	N/A	90	27-300	13.7-89.9	5.85-13.80	1.05-1.17	164
							Batch		[240]	[80.5]	[9.820]	[1.24]	166
T-ATRP-2	MMA	Solution	50-200:1:1:2.2	1.00	Homo	Toluene	N/A	90	27-300	13.7-89.9	4.26-13.80	1.05-1.36	164
T-ATRP-3	MMA	Solution	100:1:1:2.2	1.00	Homo	Toluene	N/A	60-100	120-165	16.1-83.7	3.27-12.60	1.04-1.27	164
T-ATRP-4	BA	Solution	39.6:1:0.15:0.49	1.00	Homo	Acetonitrile	170.7	80	320	71.0	4.160	1.09	165
							Batch		[360]	[82.0]	[4.797]	[1.09]	165
T-ATRP-5	St	Solution	50.2:1:0.50:1.0	1.00	Homo	Toluene	170.7	110	240	50.0	2.807	1.14	165
									[380]	[75.0]	[4.426]	[1.13]	
T-ATRP-6	BMA	Solution	100:1:0.005:0.005	1.00	Homo	Anisole	300	90	540-600	19.0-96.0	2.80-13.80	1.28-1.34	167
							Batch		[360]	[97.0]	[13.90]	[1.31]	167
T-ATRP-7	HPMA	Solution	N/A	1.00	Homo	Water/methanol	N/A	N/A	12-120	17.0-92.0	2.77-6.24	1.19-1.32	169
T-ATRP-8	MMA	Solution	300:1:0.5:1	1.00	Homo	Anisole	280	50	N/A	44.0	14.0	1.28	170
							Batch		[300]	[65.0]	[21.80]	[1.38]	170
T-ATRP-9	MA	Solution	47:1:0.02:0.12	1.00	Homo	DMSO	20	15	N/A	80.0	2.500	1.16	174
T-ATRP-10	EO/HPMA	Solution	100:1:1:2	N/A	DB-1	Water/methanol	N/A	N/A	16-188	27.0-69.0	5.60-10.20	1.17-1.24	171
							Batch		[210]	[63.0]	[8.80]	[1.25]	171
T-ATRP-11	MMA/LMA	Solution	255:1:0.5:1	N/A	DB-1	Anisole	90	50	N/A	33.0	42.90	1.46	170
T-ATRP-12	MMA/BMA	Solution	N/A	N/A	DB-2	Toluene	N/A	90	305-365	N/A	15.50-16.30	1.09-1.14	164
T-ATRP-13	MMA/BzMA	Solution	N/A	N/A	DB-2	Toluene	N/A	90	305-365	N/A	15.30-15.70	1.22-1.32	164
T-ATRP-14	MMA/BIEM	Solution	300:1:3.0:1.1	0.95	Branched	DMF	60	60	120	64.0	5.30	2.15	175
							Batch			[58.0]	[3.10]	[2.01]	175
T-ATRP-15	DMAEMA/BIEM	Solution	N/A	0.90	Branched	DMF	120	75	120	77.0	2.218	2.50	179
				0.95						74.5	3.618	2.20	

Reaction condition = total mole ratios of M: RX:C:L; M = monomer; RX = ATRP initiator; C = catalyst; L = ligand; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index; Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; DMSO = dimethyl sulfoxide; DMF = dimethylformamide.

3.1.2. Heterogeneous catalyst systems

As previously mentioned, one of the major challenges in ATRP commercialization is the large amount of residual catalysts in the final products.[180] In batch reactors, catalysts are usually removed from the final products by passing reaction mixture through silica-gel or aluminum oxide column for post-polymerization purification. Research work on catalyst separation in ATRP systems has been thoroughly reviewed by Shen et al.[181] The separation of catalyst from the polymer product is both time-consuming and costly. In general, there are two approaches that can be used to solve this problem. One is to use modified ATRP to reduce the catalyst content.[57-70] The other is to use supported catalyst system to improve the catalyst efficiency.[182-186] Especially, the use of silica-gel-supported catalysts during ATRP process is an effective way to improve catalytic efficiency in batch reactors.[187-194] Zhu and co-workers have demonstrated that silica-gel-supported copper bromide-hexamethyltriethylenetetramine (CuBr-HMTETA) catalyst could provide good control over solution ATRP of MMA in a batch reactor.[188] Furthermore, the recycled catalysts showed an even better control over ATRP of MMA. In order to overcome the drawback of batch reactor, Shen et al first used ATRP in a packed column reactor with silica-gel-supported CuBr-HMTETA catalysts.[34-36] Their work pioneered the development of CRP in continuous processes. They were the first who employed tubular reactors for continuous ATRP and demonstrated an easy control of polymer molecular weight by regulating flow rate of the tubular reactors. They also connected two tubular reactors in series for facile synthesis of block copolymers.

Well-controlled MMA polymerization by catalyst-supported ATRP in a column reactor was demonstrated by Zhu's group (reaction **T-ATRP-16** in Table 9).[34] A linear relationship between M_n and monomer conversion at different RT was observed, indicating a well-controlled polymerization. The PDI was about 1.8 at 90% conversion, which was slightly higher than the value observed in batch reactor.[188] The higher PDI in tubular reactor may be due to back-mixing in this column reactor or due to some trapped polymers inside the silica-gel pores, thus broadening the RTD.[34] A high stability of column packed with silica gel and a high retention of catalyst reactivity were also reported in this work. Steady-state operation was maintained at monomer conversion of 80% for more than 120 h with feeding rate of 1.2 ml/h. In addition, the effects of polymerization temperature and targeted chain length were both investigated in the column reactor (reactions **T-ATRP-17** and **T-ATRP-18**).[36] The polymerization was faster when conducted at a higher polymerization temperature or when conducted with lower targeted chain length. The same conclusions were also reported by Haddleton et al.[164]

The synthesis of DB-2 MMA/BMA copolymers using two column reactors in series was demonstrated by Zhu et al. DB-2 MMA/BMA copolymers with M_n = 11 kg/mol and PDI = 1.70 were produced by feeding BMA at 1.2 ml/h. When the feeding rate of BMA was increased to 1.8 ml/h, the concentration of BMA in the second column reactor increased, resulting in faster polymerization. Moreover, the DB-2 MMA/BMA copolymers produced in system with faster feeding rate possess M_n = 18 kg/mol and PDI = 1.84 (reaction **T-ATRP-19**).[36]

There are numerous studies in the literature on SET-LRP conducted in batch reactors at an ambient temperature. Chan et al first employed SET-LRP in continuous reactor.[195] SET-LRP of MA was carried out in a copper tubular reactor, with the copper tubing acted as a catalyst source. A high surface area of the copper tubular reactor resulted in a high catalytic efficiency. A monomer conversion of up to 67% was obtained with only 16 min residence time (RT) (reaction **T-ATRP-20**).[195] When the ligand concentration was decreased by five times, the conversion was only reduced from 67 to 47% at the same 16 min RT (reaction **T-ATRP-21**).[195] This is important for cost reduction in commercial applications. The chain extension experiments showed that the polymers prepared via SET-LRP in the copper tubular reactor possessed higher livingness than in a batch reactor.[195] However, using copper tubular reactor as a catalyst source is associated with possible damage to the reactor, with copper continuously dissolved from the reactor wall into the reaction mixture. To overcome this problem, Chan et al combined a short copper tubular reactor with a long stainless steel tubular reactor.[196] The short copper tubular reactor was used to initiate the polymerization by providing soluble copper species. Majority of the polymerization occurred in the long stainless steel tubular reactor. In systems with copper tubular reactor alone, the conversion could go as high as 53% with RT of only 16 min.[195] On the other hand, in the combined reactor, a conversion of 55% could only be achieved when the RT was increased to 62 min.[196] In order to enhance the polymerization rate, ascorbic acid (AA) was added to the stainless steel tubular reactor (reactions **T-ATRP-22** and **T-ATRP-23**).[196] Similar to the work of Cunningham's, Chen et al. used SET-LRP of acrylonitrile (AN) in an iron tubular reactor by using iron tube as the catalyst source without the use of ligand (reaction **T-ATRP-24**).[197] Additionally, Burns et al performed SET-LRP of MA in a PTFE tubular reactor with a copper wire threaded through the tubing (reaction **T-ATRP-25**).[198]

Table 9. Selected examples of heterogeneous ATRP in tubular reactors

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
T-ATRP-16	MMA	Heterogeneous catalyst	*	1.00	Homo	Toluene	38-300	90	N/A	20.0-90.0	3.500-11.00	1.50-1.80	34
T-ATRP-17	MMA	Heterogeneous catalyst	[M]:[RX] = 100:1	1.00	Homo	Toluene	60-560	70,80	N/A	8.00-80.0	3.050-12.00	1.30-1.75	36
T-ATRP-18	MMA	Heterogeneous catalyst	[M]:[RX] = 100:1, 200:1	1.00	Homo	Toluene	120-460	80	N/A	8.00-80.0	3.800-19.40	1.38-1.63	36
T-ATRP-19	MMA/BMA	Heterogeneous catalyst	N/A	N/A	DB-2	Toluene	N/A	80	27000-34500	N/A	11.00-18.00	1.70-1.84	36
T-ATRP-20	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.05	1.00	Homo	DMSO	4-16	23-25	50-176	43.0-67.0	4.930-6.660	1.22-1.44	195
T-ATRP-21	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.05, 100:1:0.01	1.00	Homo	DMSO	16	23-25	136, 144	67.0, 47.0	6.660, 4.390	1.44, 1.30	195
T-ATRP-22	MA	Heterogeneous catalyst	[M]:[RX]:[L]:[AA] =200:1:0.01:0.02	1.00	Homo	DMSO	8-62 Batch	23-25 [30]	210-350 [60]	27.0-78.0 [96.0]	4.670-13.84 [16.59]	1.27-1.47 [1.21]	196 196
T-ATRP-23	MA	Heterogeneous catalyst	[M]:[RX]:[L]:[AA] = 200:1:0.01:0.01-0.04	1.00	Homo	DMSO	35	23-25	227	65.0-67.0	11.80-12.23	1.42-1.47	196
T-ATRP-24	AN	Heterogeneous catalyst	[M]:[RX]:[L] =200:1:0	1.00	Homo	NM2P	N/A	25	80	41.2	6.430	1.28	197
T-ATRP-25	MA	Heterogeneous catalyst	[M]:[RX] = 50:1	1.00	Homo	DMSO	13-80	25	N/A	69.0-90.0	3.200-4.200	1.14-1.17	198

Reaction condition = total mole ratios of M: RX:C:L; M = monomer; RX = ATRP initiator; C = catalyst; L = ligand; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index； Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; * [M]:[RX] = 100:1 and [C]:[L] = 1:1; DMSO = dimethyl sulfoxide; NM2P = N-methyl-2-pyrrolidone, AA = ascorbic acid.

3.2. RAFT

3.2.1. Solution polymerization

A large variety of monomers have been successfully polymerized through RAFT polymerization. Diehl et al. first used tubular microreactor system to conduct homogeneous RAFT polymerization of N-isopropylacrylamide (NIPAM).[199] Monomer conversion of 62% was obtained in 4 min without losing control over polymer molecular weight. Faster polymerization rate was obtained in the tubular reactor than in a batch reactor due to a higher homogeneity, which was a result of the better mixing and heat transfer in the tubular reactor. For example, after 60 min of reactions, polymerization in the tubular reactor reached 88% conversion, in contrast to the 40% conversion obtained in the batch reactor (reaction **T-RAFT-1** in Table 10).[199] The effect of temperature on RAFT polymerization of NIPAM in a continuous tubular microreactor was studied by Hornung et al. (reaction **T-RAFT-2**).[200] Additionally, the kinetics of RAFT polymerization in some other monomer systems (N,N-dimethylacrylamide (DMA), BA, and vinyl acetate (VAc)) were also investigated (reactions **T-RAFT-3** to **T-RAFT-5**).[200] Comparable kinetics were observed between these polymerization systems with those conducted in a batch reactor.[200] Hornung et al. also synthesized poly(acrylamide) by RAFT polymerization at 70-80°C, yielding low PDI (1.14-1.23) even at high conversion in tubular reactor.[201]

RAFT agents are often added to conventional free radical polymerization to provide a better control at the cost of polymerization rate. However, increasing reaction temperature and pressure represents a possible solution to counter this problem, *i.e.*, increasing the polymerization rate without losing control over polymer molecular weight.[202,203] Koch and Busch first developed RAFT polymerization into tubular reactors at elevated temperature and pressure.[204] A series of RAFT polymerization runs of St at 120°C and 50 bar with different residence time were carried out (reaction **T-RAFT-6**).[204] PDIs of PSt were found to be between 1.20 to 1.24 at the elevated temperature and pressure, showing well-controlled polymerization.

RAFT block copolymerization of homogeneous systems was also reported using tubular reactors.[204-206] Koch and Busch synthesized DB-1 St/MA and St/MMA copolymers by RAFT polymerization using PSt as macro-RAFT agents at elevated temperature and pressure in tubular reactors.[204] Hornung et al. synthesized various DB-1 copolymers by combining two tubular reactors in series.[205] Most work reporting block copolymerization using CRP limited the synthesis of block copolymers with no more than three blocks, regardless if it was conducted in batch, semi-batch, or continuous reactors. This is because of an accumulation of dead chains in each block addition, which broadens the MWD. The synthesis of block copolymers with more than three blocks yet possessing narrow MWD is still challenging. Vandenbergh et al first reported the synthesis of multiblock copolymers by RAFT polymerization in continuous tubular microreactor.[206] The polymerization for each block was all kept at 100°C within 5 to 20 min. The first step was RAFT polymerization of BA to produce PBA as macroRAFT agent (reaction **T-RAFT-7**).[206] This macroRAFT agent was used in sequential block polymerization (reactions **T-RAFT-8** to **T-RAFT-11**),[206] with the final polymer products having five blocks (poly[BA-b-tBA-b-EHA-b-BA-tBA]) with cumulative M_n = 31.20 kg/mol and PDI = 1.46 (reaction **T-RAFT-11**).[206] Similar polymerization steps were conducted in batch reactor under the same reaction condition as in the continuous microreactor. However, only tri-block copolymers (poly[BA-b-tBA-b-EHA]) with M_n = 9.30 kg/mol and PDI = 1.93 could be produced. Their work clearly demonstrated how continuous tubular microreactor could benefit consecutive polymerization while maintaining good control and high livingness.

In ATRP systems, polymers are produced with deep color due to a large residual amount of copper catalyst. Similar to ATRP systems, RAFT-derived polymers also display deep color because of thiocarbonylthio end groups. Removal and modification of the end groups are often required.[207] Hornung et al. reported a radical-induced RAFT end group removal at 100°C in tubular reactor.[208] RAFT polymerizations of AM, MA and St were first conducted in batch reactor to produce RAFT-derived polymers at 70-100°C. RAFT end group removal was then conducted in a continuous tubular reactor in either organic solvents or water at 100°C. Recently, Hornung et al. also reported the RAFT polymerization and end-group removal both in flow tubular reactor by sequential two-step process.[209] Vandenbergh and Junkers reported end group modification of RAFT-derived polymers in a continuous microreactor.[210] RAFT-derived PBA polymers were modified by aminolysis/thiol-ene reactions and it took only 20 min. Moreover, the reactor could be easily scaled up from the production of hundred grams to kilograms per day. Furthermore, Vandenbergh et al reported the modification of ATRP-derived and RAFT-derived polymers and produced DB-1 copolymers via click chemistry in tubular microreactors.[211]

Table 10. Selected examples of homogeneous RAFT polymerization in tubular reactors.

Reaction No.	Monomer M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
T-RAFT-1	NIPAM	Solution	200:1:0.1	1.00	Homo	1,4-dioxane	60	90	60	88.0	21.50	1.15	199
							Batch			[40.0]	[N/A]	[N/A]	199
T-RAFT-2	NIPAM	Solution	200:1:0.6	1.00	Homo	EtOAc	60	70-100	120	79.0-94.0	20.50-23.60	1.17-1.32	200
							Batch			[83.0-99.0]	[19.50-22.20]	[1.13-1.24]	200
T-RAFT-3	DMA	Solution	200:1:0.6	1.00	Homo	dioxane	60	80	120	98.0	15.90	1.16	200
							Batch			[99.0]	[16.60]	[1.12]	200
T-RAFT-4	BA	Solution	200:1:0.6	1.00	Homo	EtOAc	60	80	120	85.0	24.80	1.27	200
							Batch			[87.0]	[24.90]	[1.25]	200
T-RAFT-5	VAc	Solution	62.5:1:0.25	1.00	Homo	EtOAc	60	100	120	81.0	4.570	1.28	200
							Batch			[87.0]	[4.620]	[1.26]	200
T-RAFT-6	St	Solution	[RAFT]:[I] = 4:3	1.00	Homo	Toluene	10-40	120	N/A	N/A	12.00-15.00	1.20-1.24	204
T-RAFT-7	BA	Solution	10:1:0.05	1.00	Homo	Butyl acetate	N/A	100	5	54.0	1.100	1.20	206
							Batch		[10]	[N/A]	[1.400]	[1.14]	206
T-RAFT-8	BA/tBA	Solution	80:1:0.05	N/A	DB-1	Butyl acetate	N/A	100	5	N/A	8.300	1.14	206
							Batch		[100]		[8.100]	[1.36]	206
T-RAFT-9	BA/tBA/EHA	Solution	80:1:0.05	N/A	Multiblock (= 3)	Butyl acetate	N/A	100	5	N/A	10.70	1.28	206
							Batch		[10]		[9.300]	[1.93]	206
T-RAFT-10	BA/tBA /EHA/BA	Solution	120:1:0.05	N/A	Multiblock (= 4)	Butyl acetate	N/A	100	10	N/A	16.50	1.32	206
T-RAFT-11	BA/tBA /EHA/BA/tBA	Solution	130:1:0.05	N/A	Multiblock (= 5)	Butyl acetate	N/A	100	10	N/A	31.20	1.46	206

Reaction condition = total mole ratios of M: RAFT:I; M = monomer; RAFT = RAFT agent; I = conventional initiator; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index； Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; EtOAc = ethyl acetate; EHA = 2-ethylhexyl acrylate.

3.2.2. Emulsion and miniemulsion polymerization

Only several studies investigated heterogeneous RAFT polymerization in continuous processes, which were first reported by Russum et al.[212-214] RAFT miniemulsion polymerization of St was conducted in a multi-tubular reactor[212] with the initial emulsion mixture continuously fed into a sonication vessel from a feed tank. After miniemulsion was formed, it was fed to the tubular reactor. Their system consisted of five tubes connected together to form a multi-tube reactor system, with RT ranged from 79-424 min. Similar polymerization kinetics were found in tubular reactor compared to batch reactor with the same experimental recipe (reaction **T-RAFT-12** in Table 11).[212] Polymerization conducted in the tubular reactor was slightly faster and gave slightly higher PDI than that conducted in the batch reactor. The higher PDI may be due to back mixing or axial dispersion. The polymers produced in the tubular reactor possessed high living characteristics.

A detailed kinetic comparison was reported for a similar reactor system (reaction **T-RAFT-13**).[213] In the work, a chain extension experiment was conducted to demonstrate the livingness of polymers produced from tubular reactor. Subsequent polymerization in a batch reactor was conducted to produce DB-1 copolymers without additional initiators. Russum et al extended the work on miniemulsion RAFT polymerization of St to a single tubular reactor.[214] The kinetics and flow characteristics of the RAFT miniemulsion polymerization were thoroughly investigated in the tubular reactor (reaction **T-RAFT-14**).[214] Their experimental results indicated that the flow regime and RTD play important roles in resulting PDI. Polymerization conducted in a near-ideal flow regime produced polymers having similar PDI as the ones from a batch reactor.

However, in miniemulsion, ultrasonication is usually used to prepare monomer droplets, and large amount of surfactants is added to stabilize the droplets, which limits commercial application of the system in continuous process. Recently, Li et al. reported a surfactant-free RAFT emulsion polymerization of MMA with 4-cyano-4-(thiobenzoylthio)pentanoic acid (CTBCOOH) playing dual roles as RAFT agent and as emulsion stabilizer in a tubular reactor.[215] The effects of residence time, feeding rate and targeted molecular weight were all investigated, and the chain extension experiment was also carried out, which showed a controlled and living polymerization (reactions **T-RAFT-15** to **T-RAFT-17**).[215]

Table 11. Selected examples of heterogeneous RAFT polymerization in tubular reactors.

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
T-RAFT-12	St	Miniemulsion	300:1:0.1	1.00	Homo	-	79-424	70	420	65.0	23.00	1.50	212
							Batch		[480]	[62.0]	[17.50]	[1.40]	212
T-RAFT-13	St	Miniemulsion	300:1:0.1	1.00	Homo	-	55-226	70	240	52.0	18.00	1.60	213
							Batch		[420]	[68.0]	[N/A]	[1.20]	213
T-RAFT-14	St	Miniemulsion	500:1:1	1.00	Homo	-	70-140	70	N/A	22.0-92.0	11.85-46.40	1.26-1.66	214
							Batch			[24.0-93.0]	[10.39-48.44]	[1.21-1.65]	214
T-RAFT-15	MMA	Emulsion	200:1:0.5	1.00	Homo	Water/DMF	28.9-50.5	90	N/A	7.90-89.8	8.500-23.50	1.05-1.07	215
T-RAFT-16	MMA	Emulsion	200:1:0.5	1.00	Homo	Water/DMF	43.3	90	N/A	39.1-75.3	23.20-27.50	1.05-1.31	215
T-RAFT-17	MMA	Emulsion	300-600:1:0.5	1.00	Homo	Water/DMF	48.1	90	N/A	63.4-79.5	32.50-61.00	1.14-1.31	215

Reaction condition = total mole ratios of M: RAFT:I; M = monomer; RAFT = RAFT agent; I = conventional initiator; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index； Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; DMF = dimethylformamide.

3.3. NMP

3.3.1. Solution polymerization

Most NMP reactions are generally conducted at high temperature (> 100°C). However, batch reactors often have poor heat transfer ability, particularly for highly exothermic polymerization systems. On the other hand, tubular microreactors can handle heat transfer relatively better due to their higher surface to volume ratios. The heat transfer ability of tubular microreactors has been well investigated by Rosenfeld et al.[216] Solution NMP of St and BA were both conducted in tubular microreactor and batch reactor at 140°C, respectively. The exothermicity of BA was much higher than that of St, *i.e.*, more heat was released during BA polymerization. Similar kinetics of NMP of St were found in tubular microreactor and batch reactor (reaction **T-NMP-1** in Table 12).[216] However, NMP of BA in the batch reactor could reach near completion (almost 100% conversion) with high resulting PDI (close to 3), clearly showing loss of control. In the tubular microreactor system, the NMP of BA gave lower conversion but showed much better control, as indicated by the lower PDIs ranged from 1.2 to 1.3 (reaction **T-NMP-2**).[216] The addition of a small amount of acetic anhydride (ACA) to the tubular reactor could increase the conversion by at least 20% without loss of the control.[216]

Fukuyama et al. also reported NMP of St (reactions **T-NMP-3** and **T-NMP-4**),[217] BA (reaction **T-NMP-5**),[217] and MMA (reactions **T-NMP-6**)[217] in tubular microreactors. They reported better control in the tubular microreactor than in a batch reactor. For example, with the residence time of 300 min, PSt with M_n = 8.8 kg/mol and PDI = 1.09 was prepared at 48% conversion in the tubular microreactor. Meanwhile, the batch reactor resulted in a conversion of only 39% after 300 minutes of reaction, with M_n = 7.5 kg/mol and PDI = 1.16 under the same experiment conditions (reaction **T-NMP-3**).[217] Enright et al also investigated the polymerization kinetics of bulk NMP of St in a tubular reactor and in a batch reactor (reaction **T-NMP-7**).[218]

There are several reports on the synthesis of DB-1 copolymers by homogeneous NMP in tubular reactors.[217,219,220] Fukuyama et al. synthesized DB-2 BA/St copolymers via solution NMP by combining two tubular reactors in series (reaction **T-NMP-8**).[217] Rosenfeld et al studied the effects of micromixer type (reaction **T-NMP-9**)[219] and geometry (reactions **T-NMP-10** to **T-NMP-12**)[220] on the properties of DB-1 copolymers, synthesized in two tubular reactors in series. Multilamination and bilamination micromixers were the two types compared in the study. A higher polymerization rate of the comonomer (St in Rosenfeld's work) and a lower PDI were found with the multilamination micromixer. Moreover, combining the two micromixer types in the tubular reactors resulted in better control than a batch reactor.[219] The work also showed that the micromixer geometry, varied by the number of microchannels and characteristic lengths, played an important role in the resulting properties of DB-1 copolymers, which could be optimized to obtain a more efficient mixing.[220]

Table 12. Selected examples of homogeneous NMP in tubular reactors.

Reaction No.	Monomer M_1/M_2	Homogeneous system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	t	T	X	M_n	PDI	Ref
T-NMP-1	St	Solution	288:1:0.05	1.00	Homo	Toluene	100-380	100-380	140	45.0-72.0	15.00-23.00	1.20-1.38	216
							Batch			[52.0-72.0]	[15.00-22.00]	[1.18-1.38]	216
T-NMP-2	BA	Solution	288:1:0.05	1.00	Homo	Toluene	65-380	65-380	140	7.00-28.0	2.500-8.800	1.20-1.30	216
							Batch			[12.0-98.0]	[5.000-30.00]	[1.25-2.80]	216
T-NMP-3	St	Solution	200:1:0	1.00	Homo	2-MPA	30-300	30-300	105	7.00-48.0	2.000-8.800	1.09-1.37	217
							Batch	[300]		[39.0]	[7.500]	[1.16]	217
T-NMP-4	St	Solution	100:1:0	1.00	Homo	2-MPA	30-300	30-300	140	26.0-87.0	6.200-18.50	1.12-1.19	217
							Batch	[300]		[78.0]	[16.70]	[1.26]	217
T-NMP-5	BA	Solution	100:1:0	1.00	Homo	2-MPA	60, 120	N/A	120	77.0, 89.0	10.10 11.30	1.41, 1.35	217
T-NMP-6	MMA	Solution	100:1:0	1.00	Homo	2-MPA	30-300	30-300	90	38.0-62.0	6.100-11.60	1.53-1.94	217
T-NMP-7	St	Solution	N/A	1.00	Homo	-	75	75-345	135	7.00-9.00	1.490-2.285	1.17-1.18	218
							Batch	[75]		[17.0-17.8]	[3.126-3.186]	[1.14-1.17]	218
T-NMP-8	BA/St	Solution	200:1:0	0.50	DB-2	2-MPA	240	N/A	120-140	76.0	16.30	1.26	217
T-NMP-9	BA/St	Solution	N/A	N/A	DB-1	Toluene	380	N/A	125	96.0-99.0*	26.60-36.60	1.40-1.73	219
							Batch			[99*]	[33.60]	[1.74]	219
T-NMP-10	BA/St	Solution	N/A	N/A	DB-1	Toluene	380	N/A	125-140	92.0-98.0*	28.40-36.60	1.28-1.52	220
T-NMP-11	BA/St	Solution	N/A	N/A	DB-1	Toluene	340	N/A	125-140	97.0-98.0*	39.70-45.70	1.40-1.47	220
T-NMP-12	BA/St	Solution	N/A	N/A	DB-1	Toluene	290	N/A	125-140	98.0-99.0*	44.50-49.60	1.42-1.46	220

Reaction condition = total mole ratios of M: PT: NR; M = monomer; PT = NMP initiator; NR = nitroxide radical; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index; Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a tubular reactor at similar experimental conditions; 2-MPA = 2-methoxypropyl acetate; * BA conversion.

3.3.2. Miniemulsion polymerization

The heterogeneous NMP in tubular reactor was investigated by Cunningham et al.[221] Enright et al reported NMP miniemulsion polymerization of St in a tubular reactor at 135°C (reaction **T-NMP-13** in Table 13).[221] The polymerization was under good control, as evident from the linear growth of M_n with monomer conversion and from the low PDI (less than 1.5). Furthermore, chain extension experiments showed that a majority of the chains were still living. Both tubular and batch reactors exhibited stable particle latexes and similar kinetics. Conversions at the later stage of polymerization were slightly lower in tubular reactor than in batch reactor, which might be due to axial mixing in the tubular reactor. The volume-average diameters of final particles were 170 nm and 164 nm in tubular and batch reactors, respectively. In addition, they synthesized PSt oligomers from a low conversion (20%) bulk NMP using a batch reactor and used the oligomers as co-stabilizer in the miniemulsion polymerization. The polymerization was then conducted in a tubular reactor. Particles were actually formed before the miniemulsion polymerization, because the monomer/polymer mixtures were used as the organic phase, thus eliminating complex nucleation in the tubular reactor. This work was not a fully continuous process, since the bulk NMP of St was first conducted in a batch reactor prior to the miniemulsion in the continuous tubular reactor. In a subsequent work, the same group developed the whole tubular reactor process.[218] The kinetics of NMP miniemulsion polymerization in the tubular reactor were shown in reaction **T-NMP-14**.[218] The volume-average diameter of final particles ranged from 148 to 188 nm. The PDI obtained ranged from 1.19 to 1.34, demonstrating feasibility of producing narrow MWDs of PSt by NMP miniemulsion polymerization in tubular reactors.

The synthesis of DB-1 and TB-1 St/BA copolymers was also reported in a complete continuous tubular reactor by using macroinitiators.[218] DB-1 St/BA copolymers having M_n = 20.5-39.3 kg/mol and PDI = 1.25-2.02 were produced with PSt as macroinitiator (reaction **T-NMP-15**).[218] The volume-average diameter of the final particles ranged from 160 to 200 nm. TB-1 St/BA/St copolymers having M_n = 58.60 kg/mol and PDI = 2.95 were produced with DB-1 St/BA copolymer as macroinitiator (reaction **T-NMP-16**)[218] and the volume-average diameter of the final particles was 213 nm. Both PDI and particle size increased with increasing number of blocks.

Table 13. Selected examples of heterogeneous NMP in tubular reactors.

Reaction No.	Monomer M_1/M_2	Heterogeneous system	Reaction condition	F_{1t}	Copolymer profile	Solvent	RT	T	t	X	M_n	PDI	Ref
T-NMP-13	St	Miniemulsion	N/A	1.00	Homo	-	N/A	135	200	87.0	24.00	1.30	[221]
							Batch		[210]	[94.0]	[27.00]	[1.32]	[221]
T-NMP-14	St	Miniemulsion	N/A	1.00	Homo	-	180	135	N/A	82.6-99.1	15.50-25.23	1.19-1.34	[218]
T-NMP-15	St/BA	Miniemulsion	N/A	N/A	DB-1	-	180	135	N/A	85.6-99.9*	20.50-39.30	1.25-2.02	[218]
T-NMP-16	St/BA	Miniemulsion	N/A	N/A	TB-1	-	120	135	N/A	91.5*	58.60	2.95	[218]

Reaction condition = total mole ratios of M: PT: NR; M = monomer; PT = NMP initiator; NR = nitroxide radical; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index； Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a tubular reactor at similar experimental conditions; * St conversion.

3.4. Summary

Numerous literature reported the investigation of homogeneous and heterogeneous CRP systems using tubular reactors, with pioneering work done by Zhu’s group for ATRP systems. The kinetics observed in tubular reactors were in general similar to those in batch reactors. Moreover, the characteristics of living polymerization in batch reactors were present in tubular reactors. These studies also showed that the mean residence time (RT) and residence time distribution (RTD) play an important role in the polymerization kinetics.

Tubular reactors are efficient for conducting continuous CRP. For example, the column reactor packed with silica-gel supported catalysts and the copper tubular reactor used as catalyst source both improved the catalyst efficiency significantly in the ATRP systems. The removal or modification of RAFT end group takes only minutes to complete in tubular reactors. The large surface-to-volume ratio of tubular reactors offers excellent heat transfer ability, allowing better control over highly exothermic reactions than in a batch reactor.

Table 14 summarizes the polymers having various composition profiles produced from CRP using tubular reactors, with a majority of the studies conducted for homopolymers, followed by di-block copolymers, and then multi-block copolymers having three or more blocks.

Tubular reactors are advantageous for production of block copolymers. For example, in batch reactors, the synthesis of di-block copolymers usually involves two steps. However, di-block copolymers can be prepared by using two tubular reactors in series. Moreover, the di-block copolymer properties can be improved by optimizing the geometry of micromixer. Conducting CRP in tubular reactors also allows production of block copolymers having five blocks with PDI less than 1.5. In comparison, the block copolymers having only three blocks from batch reactors give PDI of 1.9. It should be noted that Table 14 only summarizes linear polymerization in tubular reactors. There was also one paper from Serra et al that reported branching polymerization by ATRP. The polymerization rate and branching efficiency were improved in tubular reactors in comparison to those in batch reactors.

It is evident from Table 14 that tubular reactors are employed mostly in ATRP, much less in NMP. This may be due to the high temperature used in NMP. It is also clear that homogeneous systems are mostly studied in tubular reactors, because they are less complicated than heterogeneous systems. Among the heterogeneous systems, miniemulsion polymerization was mostly studied, with little reported work on emulsion polymerization to date.

Table 14. Summary of different polymers made by CRP in tubular reactors

System	Homopolymer	di-block	Multi-block (> =3)
ATRP (Homogeneous)	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-4 T-ATRP-5 T-ATRP-6 T-ATRP-7 T-ATRP-8 T-ATRP-9	T-ATRP-10 T-ATRP-11 T-ATRP-12 T-ATRP-13	
ATRP (Heterogeneous)	T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-23 T-ATRP-24 T-ATRP-25	T-ATRP-19	
RAFT (Homogeneous)	T-RAFT-1 T-RAFT-2 T-RAFT-3 T-RAFT-4 T-RAFT-5 T-RAFT-6 T-RAFT-7	T-RAFT-8	T-RAFT-9 T-RAFT-10 T-RAFT-11

RAFT (Heterogeneous)	T-RAFT-12 T-RAFT-13 T-RAFT-14 T-RAFT-15 T-RAFT-16 T-RAFT-17		
NMP (Homogeneous)	T-NMP-1 T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-5 T-NMP-6 T-NMP-7	T-NMP-8 T-NMP-9 T-NMP-10 T-NMP-11 T-NMP-12	
NMP (Heterogeneous)	T-NMP-13 T-NMP-14	T-NMP-15	T-NMP-16

4. CSTR

Reports on CRP systems using CSTRs were scattered, with only a few examples with ATRP and RAFT polymerization. Selective CSTR works on ATRP and RAFT are summarized in Table 15 and Table 16, respectively.

4.1. ATRP

Chan et al employed a CSTR system for copper-mediated CRP.[222] In the work, SET-LRP of MA with copper wire was conducted in CSTR at 30°C. The effects of residence time (RT), copper surface area, and ligand concentration on the kinetics of SET-LRP of MA were thoroughly investigated. The increase of RT led to the increase of conversion and M_n, while it had a minor effect on PDI at the steady state. For example, when the RT was increased from 30 to 90 min, the conversion increased from 40.9 to 65.8% and M_n increased from 4.67 to 6.73 kg/mol, while PDI remained unchanged at about 1.78 to 1.79 (reaction **C-ATRP-1**).[222]

A higher copper surface area resulted in a higher rate of polymerization. When the copper surface area was increased from 5.88 to 23.52 cm^2, the steady-state conversion increased from 52.3 to 61.7% with M_n ranged from 6.19 to 6.67 kg/mol and PDI remained around 1.72 to 1.81 (reaction **C-ATRP-2**).[222] Reducing the ligand concentration led to a slight drop in the polymerization rate, but only had a little effect on the control of molecular weight. For example, a reduction of the ligand concentration by five-fold with RT = 60 min and copper surface area of 5.88 cm^2 resulted in a decrease of the steady-state conversion from 56.2 to 52.3%, while M_n and PDI were in the range of

5.87 to 6.33 kg/mol and 1.72 to 1.78, respectively (reaction **C-ATRP-3**).[222]

Furthermore, SET-LRP of MA was also conducted in a train of two CSTRs in series. From the first CSTR to the second CSTR, the conversion increased from 50.0-55.0% to 69.0-73.0%, M_n increased from 6.090 to 7.434 kg/mol, with PDI decreased from 1.70 to 1.55 (reaction **C-ATRP-4**).[222] Chain extension experiments in a batch reactor revealed that polymer chains in the final product were still living.

Recently, Chan et al conducted ARGET ATRP in CSTR.[223] Solution ARGET ATRP of BA and MMA were both conducted in CSTRs with RT = 60, 90, and 120 min at 90°C. Steady states were reached within four mean residence times. When RT increased from 60 to 120 min, BA conversion increased from 38.7 to 56.1%, while M_n increased from 5.85 to 8.50 kg/mol and PDI increased from 1.82 to 1.92. The same increase in RT led to an increase of MMA conversion from 33.7 to 53.5% and M_n from 10.09 to 12.12 kg/mol, but a decrease of PDI from 1.96 to 1.89 (reactions **C-ATRP-5 and C-ATRP-6**).[223] Compared with the batch reactor counterparts, faster rates of polymerization were observed in CSTRs. This is due to a higher steady-state concentration of reducing agent in CSTR, in contrast to a gradual depletion of the reducing agent in batch reactor. Chain extension experiments indicated good livingness despite the broad MWD from CSTR systems.

Table 15. Selected examples of ATRP in CSTRs

Reaction No.	Monomer M_1/M_2	Polymerization system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
C-ATRP-1	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.05	1.00	Homo	DMSO	30-90	30	210-630	40.9-65.2	4.67-6.73	1.78-1.79	222
C-ATRP-2	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.01	1.00	Homo	DMSO	60	30	420	52.3-61.7	6.33-6.67	1.72-1.81	222
C-ATRP-3	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.01, 100:1:0.05	1.00	Homo	DMSO	60	30	420	52.3, 56.2	6.33, 5.87	1.72, 1.78	222
C-ATRP-4*	MA	Heterogeneous catalyst	[M]:[RX]:[L] = 100:1:0.05	1.00	Homo	DMSO	60	30	840	50.0-55.0	6.090	1.70	222
										69.0-73.0	7.343	1.55	222
C-ATRP-5	BA	Solution	100:1:0.005:0.005	1.00	Homo	DMF	60-120	90	420-840	38.7-56.1	5.85-8.50	1.82-1.92	223
							Batch		[360]	[95.0]	[11.46]	[1.36]	223
C-ATRP-6	MMA	Solution	100:1:0.005:0.005	1.00	Homo	Anisole/DMF	60-120	90	420-840	33.7-53.5	10.09-12.12	1.89-1.96	223
							Batch		[360]	[91.0]	[12.30]	[1.46]	223

Reaction condition = total mole ratios of M: RX: C: L; M = monomer; RX = ATRP initiator; C = catalyst; L = ligand; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index; Homo = homopolymer; DMSO = dimethyl sulfoxide; DMF = dimethylformamide; * two CSTRs in series.

4.2. RAFT

Koch and Busch reported the homogeneous RAFT of St in CSTR at elevated temperature and pressure.[204] The effect of RT on polymerization kinetics was investigated. At 120°C and 120 bar, when RT was increased from 10 to 40 min, PSt yield increased about 13 to 20%, M_n increased from 10 to 18.5 kg/mol, while PDI decreased from 1.92 to 1.70 (reaction **C-RAFT-1**).[204]

The only study reported in literature on the heterogeneous RAFT using CSTR was by Schork's group.[224-226] Smulders et al investigated the kinetics of RAFT miniemulsion polymerization of styrene in a train of three CSTRs at 70°C (reaction **C-RAFT-2**).[224] Increasing the number of CSTRs increased the conversion and M_n, and decreased the PDI. However, steady state could not be achieved in this study, as evidenced from the increase of conversion over time. They attributed the unsteady state to the possible continuous formation of oligomeric RAFT agents, which promoted polymerization rate. Compared to batch reactor, particle nucleation efficiencies were lower in CSTRs, because there existed a larger difference in the polymer contents among particles, that could promote coalescences of monomer droplets and particles.

In a subsequent study, Qi et al further investigated the unsteady state observed in continuous RAFT miniemulsion in CSTRs. They considered two different factors that might cause the unsteady state, namely the reaction mechanism itself and the equipment design. By modifying the equipment design and conducting RAFT under similar experimental condition as in the previous work, a steady-state behavior was achieved (reaction **C-RAFT-3**).[225] Therefore, the previously unsteady state was found to be caused by equipment design and operation, not the reaction mechanism itself.

Furthermore, Smulders et al also reported the synthesis of block copolymers by CRP in CSTR. A series of St/BA block copolymers were successfully produced by RAFT miniemulsion polymerization in a train of four CSTRs (reaction **C-RAFT-4**).[226] Their results not only demonstrated the feasibility of block copolymer production using a CSTR train, but also showed that copolymer composition and block chain length could be easily regulated by the monomer feeding rate, the injection point of comonomer, and/or the polymerization temperature.[226]

Table 16. Selected examples of RAFT polymerization in CSTRs.

Reaction No.	Monomer M_1/M_2	Polymerization system	Reaction condition	F_{1t}	Copolymer profile	solvent	RT	T	t	X	M_n	PDI	Ref
C-RAFT-1	St	Solution	[RAFT]:[I] = 4:3	1.00	Homo	Toluene	10-40	120	N/A	N/A	10.00-18.50	1.70-1.92	204
C-RAFT-2*	St	Miniemulsion	300:1:1	1.00	Homo	-	106	70	2620	25.0	10.00	2.60	224
							106	70	2620	45.0	22.00	1.88	
							106	70	2620	60.0	30.00	1.63	
C-RAFT-3*	St	Miniemulsion	300:1:1	1.00	Homo	-	120	70	2340	17.0	4.500	1.77	225
							120	70	2340	30.0	7.400	1.75	
							120	70	2340	41.0	9.700	1.65	
C-RAFT-4**	St/BA	Miniemulsion	480:1:1	0.635	Block	-	133	74	3600	25.0	25.00	2.60	226
							133	74	3600	42.0	31.00	2.13	
							133	71	3600	71.0	46.00	2.70	
							133	71	3600	86.0	53.00	2.65	

Reaction condition = total mole ratios of M: RAFT:I; M = monomer; RAFT = RAFT agent; I = conventional initiator; F_{1t} = targeted mole fraction of M_1; RT = residence time (min); T = polymerization temperature (°C); t = polymerization time (min); X = total monomer conversion (%); M_n = number-average molecular weight (kg/mol); PDI = polydispersity index； Homo = homopolymer; N/A = not available in literature; [] = results in a batch reactor, compared with results in a semi-batch reactor at similar experimental conditions; * three CSTRs in series; ** four CSTRs in series.

4.3. Summary

There are only a few reported studies on CRP conducted in CSTRs. However, the kinetic characteristics of CRP in CSTR can be drawn from these studies. Similar to tubular reactors, both RTD and RT play important roles in the polymerization processes. The steady state can usually be achieved after several RTs. Living characteristics can be retained when CRP is conducted in CSTRs. However, broader MWDs should be expected compared to the polymers produced in batch and tubular reactors, due to the broader RTD in CSTR systems. Both polymerization rate and molecular weight increased with the increasing number of CSTRs in a CSTR train, while an opposite trend was observed for PDI. Block copolymers can also be produced by using CSTRs in series. Furthermore, copolymer composition and block chain length can be controlled by monomer feeding rate and injection point of the comonomer.

Homogenous and heterogeneous ATRP in CSTRs have only been reported by Cunningham’s group. The literature of RAFT miniemulsion polymerization in CSTRs is mainly contributed from Schork's group. To date, little work on NMP in CSTR has been reported. It is not easy to develop CRP from batch reactors to CSTRs. Despite the limited references, the feasibility of conducting CRP in CSTRs is clearly demonstrated.

5. Progress in reaction engineering of CRP

Since CRP was first developed into semi-batch reactors in 1997 by Matyjaszewski's group, and the development into continuous reactors first reported in 2000 by Zhu's group, there have been significant progress made in the reactor engineering of CRP. Numerous fundamental research works on CRP with various reactor configurations have been reported. Semi-batch reactors are mainly used to control copolymer composition distribution (CCD), as summarized in Table 7. More importantly, programmed feeding policies have been developed to precisely synthesize copolymers with pre-defined CCDs at will. Many researchers have also investigated the effects of CCDs on copolymer properties. The development of the relationships between polymer chain structures and polymer material properties becomes essential and has been making good progress. On the other hand, low molecular weight polymers (such as coatings) have also been produced by CRP using semi-batch reactors. The kinetics of CRP in tubular reactors and CSTRs under different operation conditions have also been thoroughly investigated, which provides fundamental insight and practical guidance to optimize polymerization processes and/or to improve polymer properties in continuous reactors. The feasibility of CRP in continuous reactors has been well demonstrated.

Table 17 summarizes the reported residence time (RT) of continuous reactors (tubular reactor and CSTR). Four RT intervals are defined, (1) RT < = 40 min, (2) 40 < RT < = 100 min, (3) 100 < RT < = 200 min and (4) RT > 200 min. The number of literatures on tubular reactors conducted in each RT range is comparable. However, for CSTRs, most studies are conducted in the ranges of 40-100 min and 100-200 min. Moreover, CRP with RT longer than 200 min in CSTR is rare.

The data of conversion, number-average molecular weight and polydispersity index discussed in Table 1-6, Table 8-13, Table 15, and Table 16 are summarized in Table 18, Table 19, and Table 20, respectively. Generally speaking, the conversions obtained in semi-batch reactors are higher than those obtained in continuous reactors, as shown in Table 18. In semi-batch reactors, most CRP can reach high conversions, ranged from 80 to 100%, with only a few reported conversions lower than 40%. In tubular reactors and CSTRs, the conversions are mostly in the range of 40-60% and 60-80%.

The number-average molecular weight of polymers produced by CRP using various reactors mostly fall in the range of 10-50 kg/mol. Semi-batch reactors can produce higher molecular weight ($M_n >$ 100 kg/mol). Such high molecular weight products have not been reported in tubular reactors and CSTRs. However, the number of studies reporting on synthesis of low molecular weight polymers ($M_n < =$ 10 kg/mol) using tubular reactors and CSTRs, is higher than that of semi-batch reactors. A majority of the CRP systems conducted in various reactor types discussed in this review showed good control in the polymerization with the reported PDI from 1.1 to 1.5. However, polymers produced in CSTRs generally possessed higher PDI (PDI > 1.5) than those from semi-batch and tubular reactors.

Table 17. Summary of residence time (RT) of continuous reactors

Reactor type	Residence time (minutes)			
	< = 40	40 – 100	100 - 200	> 200
tubular	T-ATRP-9 T-ATRP-16 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-23 T-ATRP-25	T-ATRP-11 T-ATRP-14 T-ATRP-16 T-ATRP-17 T-ATRP-22 T-ATRP-25	T-ATRP-4 T-ATRP-5 T-ATRP-15 T-ATRP-16 T-ATRP-17 T-ATRP-18	T-ATRP-6 T-ATRP-8 T-ATRP-16 T-ATRP-17 T-ATRP-18
	T-RAFT-6 T-RAFT-15	T-RAFT-1 T-RAFT-2 T-RAFT-3 T-RAFT-4 T-RAFT-5 T-RAFT-12 T-RAFT-13 T-RAFT-14 T-RAFT-15 T-RAFT-16 T-RAFT-17	T-RAFT-12 T-RAFT-13 T-RAFT-14	T-RAFT-12 T-RAFT-13
	T-NMP-3 T-NMP-4 T-NMP-6	T-NMP-1 T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-5 T-NMP-6 T-NMP-7	T-NMP-1 T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-5 T-NMP-6 T-NMP-14 T-NMP-15 T-NMP-16	T-NMP-1 T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-6 T-NMP-8 T-NMP-9 T-NMP-10 T-NMP-11 T-NMP-12
CSTR	C-ATRP-1	C-ATRP-1 C-ATRP-2 C-ATRP-3 C-ATRP-4 C-ATRP-5 C-ATRP-6	C-ATRP-5 C-ATRP-6	
	C-RAFT-1		C-RAFT-2 C-RAFT-3 C-RAFT-4	

Table 18. Summary of conversions made by CRP in reactors

Reactor type	Conversion (%)			
	< = 40	40 – 60	60 - 80	80 - 100
Semi-batch		S-ATRP-11 S-ATRP-12 S-ATRP-13 S-ATRP-16 S-ATRP-19	S-ATRP-3 S-ATRP-14 S-ATRP-19	S-ATRP-2 S-ATRP-4 S-ATRP-5 S-ATRP-6 S-ATRP-7 S-ATRP-8 S-ATRP-14 S-ATRP-15 S-ATRP-17 S-ATRP-18
		S-RAFT-1 S-RAFT-2	S-RAFT-2 S-RAFT-3 S-RAFT-4 S-RAFT-10 S-RAFT-17 S-RAFT-18	S-RAFT-7 S-RAFT-8 S-RAFT-10 S-RAFT-11 S-RAFT-12 S-RAFT-13 S-RAFT-14 S-RAFT-15 S-RAFT-16 S-RAFT-17
	S-NMP-1 S-NMP-21 S-NMP-22	S-NMP-1 S-NMP-2 S-NMP-4 S-NMP-22	S-NMP-1 S-NMP-2 S-NMP-3 S-NMP-7 S-NMP-18 S-NMP-20 S-NMP-22	S-NMP-1 S-NMP-2 S-NMP-5 S-NMP-8 S-NMP-9 S-NMP-10 S-NMP-11 S-NMP-16 S-NMP-17 S-NMP-18 S-NMP-19 S-NMP-20
tubular	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-6 T-ATRP-7 T-ATRP-8 T-ATRP-9 T-ATRP-10 T-ATRP-11 T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-22	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-5 T-ATRP-6 T-ATRP-7 T-ATRP-8 T-ATRP-10 T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-24	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-4 T-ATRP-6 T-ATRP-7 T-ATRP-9 T-ATRP-10 T-ATRP-14 T-ATRP-15 T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-23 T-ATRP-25	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-6 T-ATRP-7 T-ATRP-16 T-ATRP-25
	T-RAFT-14 T-RAFT-15 T-RAFT-16	T-RAFT-7 T-RAFT-13 T-RAFT-14 T-RAFT-15 T-RAFT-16	T-RAFT-2 T-RAFT-12 T-RAFT-14 T-RAFT-15 T-RAFT-16 T-RAFT-17	T-RAFT-1 T-RAFT-2 T-RAFT-3 T-RAFT-4 T-RAFT-5 T-RAFT-14 T-RAFT-15
	T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-6 T-NMP-7	T-NMP-1 T-NMP-3 T-NMP-4 T-NMP-6	T-NMP-1 T-NMP-4 T-NMP-5 T-NMP-6 T-NMP-8	T-NMP-4 T-NMP-5 T-NMP-9 T-NMP-10 T-NMP-11 T-NMP-12 T-NMP-13 T-NMP-14 T-NMP-15 T-NMP-16
CSTR	C-ATRP-5 C-ATRP-6	C-ATRP-1 C-ATRP-2 C-ATRP-3 C-ATRP-4 C-ATRP-5 C-ATRP-6	C-ATRP-1 C-ATRP-2 C-ATRP-4	
	C-RAFT-2 C-RAFT-3 C-RAFT-4	C-RAFT-2 C-RAFT-3 C-RAFT-4	C-RAFT-4	C-RAFT-4

Table 19. Summary of number-average molecular weight (M_n) made by CRP in reactors

Reactor type	M_n (kg/mol)			
	< = 10	10 – 50	50 - 100	> 100
Semi-batch	S-ATRP-14 S-ATRP-15	S-ATRP-1 S-ATRP-3 S-ATRP-4 S-ATRP-5 S-ATRP-6 S-ATRP-7 S-ATRP-8 S-ATRP-9 S-ATRP-10 S-ATRP-12 S-ATRP-13 S-ATRP-14 S-ATRP-16 S-ATRP-18 S-ATRP-19	S-ATRP-2 S-ATRP-10 S-ATRP-11	S-ATRP-10
		S-RAFT-1 S-RAFT-3 S-RAFT-4 S-RAFT-5 S-RAFT-6 S-RAFT-9 S-RAFT-10 S-RAFT-11 S-RAFT-12 S-RAFT-13 S-RAFT-16 S-RAFT-17 S-RAFT-18	S-RAFT-8 S-RAFT-9 S-RAFT-10 S-RAFT-14	S-RAFT-7 S-RAFT-8 S-RAFT-14 S-RAFT-15
	S-NMP-1	S-NMP-1 S-NMP-2 S-NMP-3 S-NMP-4 S-NMP-6 S-NMP-7 S-NMP-10 S-NMP-14 S-NMP-18 S-NMP-19 S-NMP-20 S-NMP-21 S-NMP-22	S-NMP-3 S-NMP-5 S-NMP-8 S-NMP-9 S-NMP-10 S-NMP-11 S-NMP-12 S-NMP-13 S-NMP-14 S-NMP-16 S-NMP-17 S-NMP-19 S-NMP-20	S-NMP-15 S-NMP-16
tubular	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-4 T-ATRP-5 T-ATRP-6 T-ATRP-7 T-ATRP-9 T-ATRP-10 T-ATRP-14 T-ATRP-15 T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-24 T-ATRP-25	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-6 T-ATRP-8 T-ATRP-10 T-ATRP-11 T-ATRP-12 T-ATRP-13 T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-19 T-ATRP-22 T-ATRP-23		
	T-RAFT-5 T-RAFT-7 T-RAFT-8 T-RAFT-15	T-RAFT-1 T-RAFT-2 T-RAFT-3 T-RAFT-4 T-RAFT-6 T-RAFT-9 T-RAFT-10 T-RAFT-11 T-RAFT-12 T-RAFT-13 T-RAFT-14 T-RAFT-15 T-RAFT-16 T-RAFT-17	T-RAFT-17	

	T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-6 T-NMP-7	T-NMP-1 T-NMP-4 T-NMP-5 T-NMP-6 T-NMP-8 T-NMP-9 T-NMP-10 T-NMP-11 T-NMP-12 T-NMP-13 T-NMP-14 T-NMP-15	T-NMP-16	
CSTR	C-ATRP-1 C-ATRP-2 C-ATRP-3 C-ATRP-4 C-ATRP-5	C-ATRP-6		
	C-RAFT-3	C-RAFT-1 C-RAFT-2 C-RAFT-4	C-RAFT-4	

Table 20. Summary of PDI made by CRP in reactors

Reactor type	PDI			
	< = 1.1	1.1 - 1.5	1.5 – 2.0	> 2.0
Semi-batch	S-ATRP-9 S-ATRP-10 S-ATRP-13 S-ATRP-14	S-ATRP-1 S-ATRP-2 S-ATRP-3 S-ATRP-4 S-ATRP-5 S-ATRP-6 S-ATRP-7 S-ATRP-8 S-ATRP-11 S-ATRP-12 S-ATRP-14 S-ATRP-16 S-ATRP-17 S-ATRP-18 S-ATRP-19	S-ATRP-15	
	S-RAFT-16 S-RAFT-17	S-RAFT-1 S-RAFT-3 S-RAFT-4 S-RAFT-5 S-RAFT-6 S-RAFT-10 S-RAFT-11 S-RAFT-12 S-RAFT-13 S-RAFT-14 S-RAFT-16	S-RAFT-8 S-RAFT-10 S-RAFT-14 S-RAFT-15	S-RAFT-7 S-RAFT-8 S-RAFT-9 S-RAFT-10 S-RAFT-14 S-RAFT-18
		S-NMP-1 S-NMP-2 S-NMP-3 S-NMP-4 S-NMP-5 S-NMP-7 S-NMP-8 S-NMP-9 S-NMP-10 S-NMP-11 S-NMP-13 S-NMP-16 S-NMP-17 S-NMP-18 S-NMP-20 S-NMP-22	S-NMP-15 S-NMP-16 S-NMP-18 S-NMP-20 S-NMP-21 S-NMP-22	S-NMP-19 S-NMP-20

tubular	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-4 T-ATRP-12	T-ATRP-1 T-ATRP-2 T-ATRP-3 T-ATRP-5 T-ATRP-6 T-ATRP-7 T-ATRP-8 T-ATRP-9 T-ATRP-10 T-ATRP-11 T-ATRP-12 T-ATRP-13 T-ATRP-17 T-ATRP-18 T-ATRP-20 T-ATRP-21 T-ATRP-22 T-ATRP-23 T-ATRP-24 T-ATRP-25	T-ATRP-16 T-ATRP-17 T-ATRP-18 T-ATRP-19	T-ATRP-14 T-ATRP-15
	T-RAFT-15 T-RAFT-16	T-RAFT-1 T-RAFT-2 T-RAFT-3 T-RAFT-4 T-RAFT-5 T-RAFT-6 T-RAFT-7 T-RAFT-8 T-RAFT-9 T-RAFT-10 T-RAFT-11 T-RAFT-12 T-RAFT-14 T-RAFT-16 T-RAFT-17	T-RAFT-13 T-RAFT-14	
	T-NMP-3	T-NMP-1 T-NMP-2 T-NMP-3 T-NMP-4 T-NMP-5 T-NMP-7 T-NMP-8 T-NMP-9 T-NMP-10 T-NMP-11 T-NMP-12 T-NMP-13 T-NMP-14 T-NMP-15	T-NMP-6 T-NMP-9 T-NMP-10 T-NMP-15	T-NMP-15 T-NMP-16
CSTR			C-ATRP-1 C-ATRP-2 C-ATRP-3 C-ATRP-4 C-ATRP-5 C-ATRP-6	
			C-RAFT-1 C-RAFT-2 C-RAFT-3	C-RAFT-2 C-RAFT-4

6. Outlook and recommendations

It becomes evident that ATRP is one of the most studied CRP types in each reactor category. Approximately half of the reports on CRP are based on ATRP. It is interesting to note that ATRP was also the first CRP system conducted in semi-batch and continuous reactors. The chemicals involved in ATRP are readily available from commercial sources. Moreover, metal complexes used to mediate the ATRP process can now be reduced to a ppm level. The number of reports on RAFT is much lower than ATRP but is comparable to NMP. However, little work has been done in NMP using CSTRs to date.

There are more studies on CRP using semi-batch reactors than tubular or CSTR reactors. In terms of the ease of operation, semi-batch reactor is easier than continuous reactor. Furthermore, it is more feasible to control CCDs using semi-batch reactors by varying the monomer feeding. A narrow MWD of polymer products is a key point for CRP systems, but continuous reactors can result in broader MWD than semi-batch reactors due to the broader RTD in continuous reactors. However, polymer products with more consistent chain properties can be produced from continuous reactors than from semi-batch reactors.

Continuous reactors are preferred in industrial settings for a large-scale production. Continuous CRP processes using various types of reactors must be further developed, particularly for CSTR. The challenges related to the continuous systems need to be tackled. For example, how do we control CCD in continuous reactors? It is well known that polymer products with uniform CCD (U) and block (DB-1) copolymers can be produced in continuous reactors, but how to produce polymer products with novel CCDs (such as LG and SG)? It would represent a significant progress if copolymers with pre-defined CCDs can be precisely synthesized through continuous processes. Fortunately, kinetic modeling works on different kinds of CRPs in continuous reactors have provided a great foundation for precise control of CCDs in continuous processes.[227-231]

More than half of the reported CRP works involve homogeneous systems. However, the heterogeneous systems, such as emulsion polymerization, are favored in industrial applications, because of low energy consumption, low cost of product separation, and green environment with water usually used as solvent. It should be pointed out that heterogeneous CRP systems using different reactors are mainly conducted as miniemulsion. Compared to emulsion, miniemulsion requires extra energy in ultrasonication. Therefore, the emphasis in further research on the heterogeneous CRP with different reactors should be on continuous emulsion polymerization.

Precise control over CCD through programmed feeding policies has been well developed. The goal for the programmed feeding policy has been on targeted CCDs. In applications, tailored made material properties of polymer products, not chain structures, are most desirable. Further development in this area should target on the desired material properties directly, through design and control of chain structures based on the relationships between chain structure and polymer property. On the other hand, there are only a few reports on the control of chain topologies. Reports on nonlinear CRP (such as branching and cross-linking) using different types of reactors are rare. Nonlinear CRP in continuous reactors represents an important research area, yet to be explored.

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