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Atom transfer radical polymerization in aqueous dispersed media

Invited review

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Abstract: During the last decade, atom transfer radical polymerization (ATRP) received significant attention due to its exceptional capability of synthesizing polymers with pre-determined molecular weight, well-defined molecular architectures and various functionalities. It is economically and environmentally attractive to adopt ATRP to aqueous dispersed media, although the process is challenging. This review summarizes recent developments of conducting ATRP in aqueous dispersed media. The issues related to retaining "controlled/living" character as well as colloidal stability during the polymerization have to be considered. Better understanding the ATRP mechanism and development of new initiation techniques, such as activators generated by electron transfer (AGET) significantly facilitated ATRP in aqueous systems. This review covers the most important progress of ATRP in dispersed media from 1998 to 2009, including miniemulsion, microemulsion, emulsion, suspension and dispersed polymerization.

Keywords: *ATRP • Controlled radical polymerization • Dispersed media • Emulsion*

1. Introduction and scope of the review

It has been a long-standing goal in polymer chemistry to develop a process that combines the robustness of radical polymerization with precise control over all aspects of polymer structure, a feature typical for living anionic polymerization. This is the reason why controlled/living radical polymerization (CRP) procedures immediately received a large attention since their debut [1-5]. In the past two decades, various CRP techniques, especially nitroxide mediated polymerization (NMP) [6,7], atom transfer radical polymerization (ATRP) [8-11] and degenerative transfer systems [12] such as reversible addition-fragmentation chain transfer (RAFT) polymerization [13,14], have been introduced, defined and refined.

As a consequence of the improved understanding of homogeneous CRP systems, increasing attention was paid towards development of CRP in heterogeneous media, preferably with water as the continuous phase. Aqueous dispersed media are commonly recognized as a diverse and benign means for conducting industrial scale polymerization. The use of water as the dispersion medium is environmentally friendly, as compared to using volatile organic solvents. The presence of water also allows excellent heat dissipation during the course of polymerization. The low viscosity of the dispersed medium allows access to high weight fractions of polymer not readily accessible in solution or bulk polymerizations. Additionally, ease of mixing of raw materials and handling of the final products (latex) lead to simple scale-up production of aqueous dispersion polymerization [15]. During the polymerization, radicals are compartmentalized within the dispersed phase and hence they cannot terminate with radicals located in different loci. This compartmentalization effect results in a higher polymerization rate and a higher molecular weight in free radical emulsion polymerization than those achieved in solution/bulk [16,17]. It has been more than

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half a century since free radical polymerizations were first applied to aqueous dispersed media. Commercialization of CRP will likely benefit from the use of aqueous dispersed media.

Many challenges were encountered when chemists initially attempted to conduct a CRP in aqueous dispersed media. Because of the multi-component nature of the procedures required for CRP, as well as the complex nature of aqueous dispersed media, simply adding a reagent that can adopt CRP from a bulk or solution polymerization to an aqueous dispersed polymerization procedure, resulted in a loss of many of the desirable features of both processes. Observed problems included decreased colloidal stability, a wide particle size distribution, loss of control over polymerization, and low initiation efficiency. In addition, each CRP method has its own set of unique features. A strategy that had proven successful in one type of CRP processes has not been necessarily efficient for another CRP method. In short, implementing CRP in dispersed media requires careful consideration of every aspect of the mechanism of each process.

Despite all these challenges, remarkable progress has been achieved in understanding the specific requirements and hence application of CRP to aqueous dispersed media in the recent five years. Several exciting and innovative developments have been reported that successfully allow application of CRPs in aqueous dispersions. The progress in this field has been covered in several recently published reviews [15,18-25]. Advances in NMP and RAFT systems have primarily progressed with respect to a better understanding of how the particular "mediating" chemistry behaves in a multi-phase environment. In contrast, ATRP has undergone a series of significant improvements in its basic chemistry, particularly with regards to how the polymerization is initiated, that have facilitated and, in some instances, been driven by its adaptation to aqueous dispersions.

This mini-review will discuss the recent progress on the application of ATRP to aqueous dispersed media and summarize the exploration of the fundamental mechanism of ATRP that has played a significant role in advancing this field and greatly benefited the on-going research.

2. Background on ATRP and aqueous dispersed media

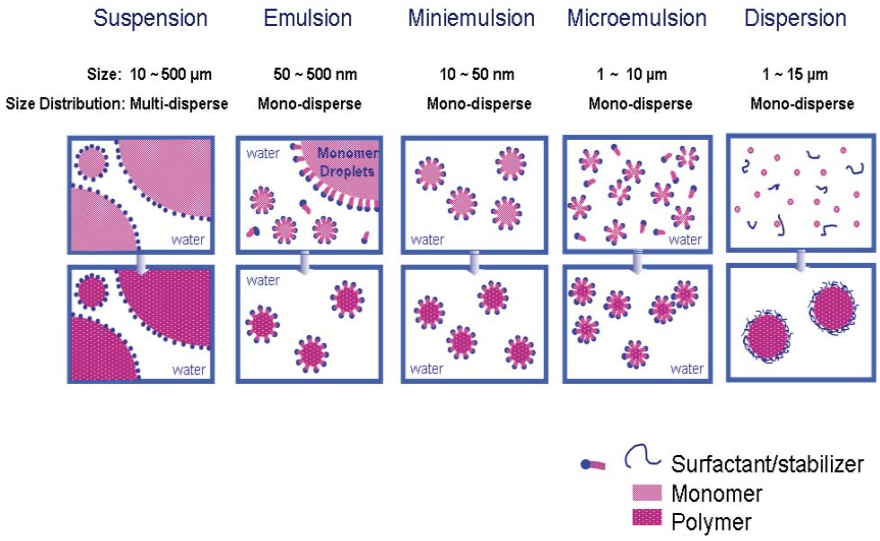
2.1. ATRP

ATRP was first reported in 1995 and has emerged as one of the most powerful synthetic techniques for preparation of well-defined polymeric materials [4,8]. Mechanistically, ATRP originates from a widely used organic reaction known as atom transfer radical addition (ATRA) [26,27]. In this synthetic organic chemistry technique, a halogen atom is transferred homolytically from a dormant halide species to a transition metal complex, forming a free radical which reacts with an unsaturated molecule and is quickly and irreversibly deactivated by a back-transfer of the halogen atom from the transition metal complex to the organic radical species. Compared to ATRA, ATRP requires a system in which the formed deactivated species can be reactivated to allow further monomer addition and hence controlled chain growth. Selection of a suitable catalyst enables the system to establish a dynamic equilibrium between propagating chains and dormant chains, as well as to assure fast initiation, reduction of the contribution of the inevitable radical-radical termination reactions which ultimately results in the controlled/"living" character of the polymerization [28]. In an ATRP, the catalyst is usually a transition metal complex, in which the ligand plays a critical role in determining the reactivity of the catalyst complex [10,29-34]. In addition, the ligand also strongly influences the solubility of the complex, and consequently the concentration of activators and deactivators in the reaction medium [18,35-40].

Compared with other controlled living radical polymerization methods, such as NMP and RAFT polymerization, ATRP provides a simple pathway to polymers with well defined chain-end functionality [41]. It is also the most efficient methods for synthesis of polymers with complex architectures, such as block copolymers, star polymers and graft copolymers [42,43]. ATRP is also well-known for its capability of synthesizing low molecular weight polymers. In addition surface modification is relatively simple using ATRP since it is only necessary to pre-modify the surface with an alkyl halide based ATRP initiators which can be easily introduced to the surfaces of most substrates [44-46]. Furthermore, a significant advantage of ATRP is that all necessary components are commercially available [4,47].

2.2. Polymerizations in aqueous dispersed media

Polymerizations in aqueous dispersed media are the most widely used methods for preparation of colloidal particles with a variety of sizes. This process usually occurs in a bi-phasic system, with water as the continuous phase and monomer/polymer in the form of a fine dispersion in water. The terminology of various aqueous dispersed polymerization systems adopted here is employed by most polymer chemists,



Scheme 1. Polymerizations in various aqueous dispersed media.

and the terms "suspension", „emulsion", "miniemulsion", "microemulsion", "dispersion" and "precipitation" are clearly distinguished on the basis of the following four criteria: 1) initial state of the polymerization mixture; 2) kinetics of polymerization; 3) mechanism of particle formation; and 4) size of the final polymer particles [48]. It is noteworthy that the complexity of aqueous dispersed polymerizations has resulted in ambiguities, regarding some terminologies. For instance, the term "dispersion polymerization" was sometimes used to represent all heterogeneous polymerizations [49] but in other situations it stands for a particular polymerization method [48]. To reduce the possibility of confusion, the definitions used for various aqueous dispersed media are described below in detail. The general feature of each polymerization technique is illustrated in Scheme 1.

Suspension polymerization has the longest history among all aqueous dispersed polymerizations [50]. In suspension polymerization the initiator is soluble in the monomer phase, which is dispersed into the dispersion medium (usually water) to form droplets. Suspension polymerization proceeds in the droplet phase, and in most cases, occurs by a radical mechanism. Suspension polymerization is suitable for the production of polymer beads within the size range of 10 μm – 0.5 mm [50].

Emulsion polymerization is similar to suspension polymerization in that it is applicable to monomers that are insoluble (or scarcely soluble) in water, but in this case the suspension is emulsified by the addition of a surfactant whose concentration exceeds the critical micelle concentration (CMC) [16,17,51]. The initiator is generally soluble in water, although hydrophobic initiators are sometimes used. Initially, most of the monomer is present in the form of 1-10 μm or larger droplets. A small percentage of the monomer also exists in the form of surfactant-solubilized micelles, with size *ca.* 5-10 nm, and molecularly dissolved in water, depending on the nature and concentration of the monomer and emulsifier. During the polymerization, particles are formed in the aqueous phase *via* micellization and/or homogeneous nucleation. The primary consumption of monomer in the polymerizing particles drives the diffusion of monomer from droplets to particles. Emulsion polymerization normally yields colloidal particles with diameter 50-500 nm and relatively narrow size distribution.

Mass transfer of very hydrophobic monomers, *e.g.*, lauryl and stearyl methacrylate, through the aqueous phase to active micelle/particles is very difficult. Miniemulsion was developed to address this problem, since the system avoids transport issues. The process of forming a miniemulsion requires mixing of all the required components followed by a pre-shearing step (such as ultrasonic homogenization) during which the droplet size is mechanically reduced to retard Ostwald ripening (transfer of monomer from small droplets to large droplets so as to reduce the total surface energy of the system) and relatively small droplets with narrow size distribution are formed [52]. Usually a co-stabilizer is necessary for preparation of a stable miniemulsion. After the homogenization process, the system relaxes to a stabilized state that particle aggregation is reduced. Polymerization is then initiated in the stable system and forms colloidal particles.

Miniemulsion shares many similarities with emulsion polymerization, such as monomer range and surfactant

choice. However, there are also distinct differences in terms of particle nucleation and mass transportation phenomena. Miniemulsion polymerization begins with relatively stable submicron monomer droplets, prepared by applying high shearing forces in an emulsification/homogenization process. No micelles are present in the miniemulsion, since all surfactant molecules have been adsorbed onto the large droplet-water interfacial area. Particle nucleation occurs primarily *via* entry of free radicals into the pre-formed monomer droplets, which represent the main polymerization loci. Mass transport, except for the radicals, is not involved in the ideal case. Hence, each monomer droplet should have equal probability to be nucleated and can be considered as a "mini-bulk" reactor. Ideally, these isolated reactors are absent of any collision and aggregation, each of them turning into a polymeric particle after polymerization. Due to these features, the miniemulsion system is considered the most suitable system for direct application of CRP techniques to the aqueous dispersed media.

In contrast to the opaque and milky appearance of emulsion and miniemulsion latexes, a microemulsion is an isotropic, optically transparent or translucent system with thermodynamic stability [53,54]. The microemulsion is formed spontaneously by mixing oil (monomer) and water in the presence of appropriate amounts of surfactant and co-surfactant, without the requirement of vigorous agitation or homogenization. Polymerization is initiated by the entry of radicals into the monomer-swollen micelles, or by homogeneous nucleation. These nucleated particles grow by transport of monomer through the outer phase or by particle collision. Microemulsion polymerization allows the synthesis of ultra-fine polymer latex particles in the size range of 10-50 nm. The very large surface area of such particles is easily modified by simple copolymerization or post-polymerization reactions. Additionally, a high molecular weight is regularly observed for polymers prepared by microemulsion polymerization.

Compared to the above aqueous dispersed media, dispersion/precipitation polymerization is more frequently applied to systems using a dispersant phase other than water [55]. Precipitation polymerization starts as a homogeneous system but is quickly converted to heterogeneous polymerization. This occurs during the polymerization of a monomer where the polymer formed is insoluble in the reaction medium. The polymerization proceeds in the polymer particles formed *via* precipitation of the polymers and absorption of free monomer and initiator (and/or initiating radicals). Dispersion polymerization can be defined as a type of precipitation polymerization that employs a suitable polymeric stabilizer soluble in the reaction medium [48,55]. The nucleation process starts when the radicals react with soluble monomer molecules to form oligomeric radicals which, at a critical chain length, precipitate as small nuclei. These nuclei may then grow to the final size by a variety of mechanisms, *e.g.,* by aggregation of small nuclei, by polymerization of monomer in the swollen nuclei, and/or through seeded polymerization of monomer on the surface of the nuclei. The stabilizer in a dispersion polymerization is adsorbed (sometimes grafted [56]) onto the particle surface and thereby stabilizes the particles by a process which is only qualitatively understood. Dispersion polymerization is an attractive method for production of micron-size monodisperse polymer particles (1-15 μm) in a single batch process.

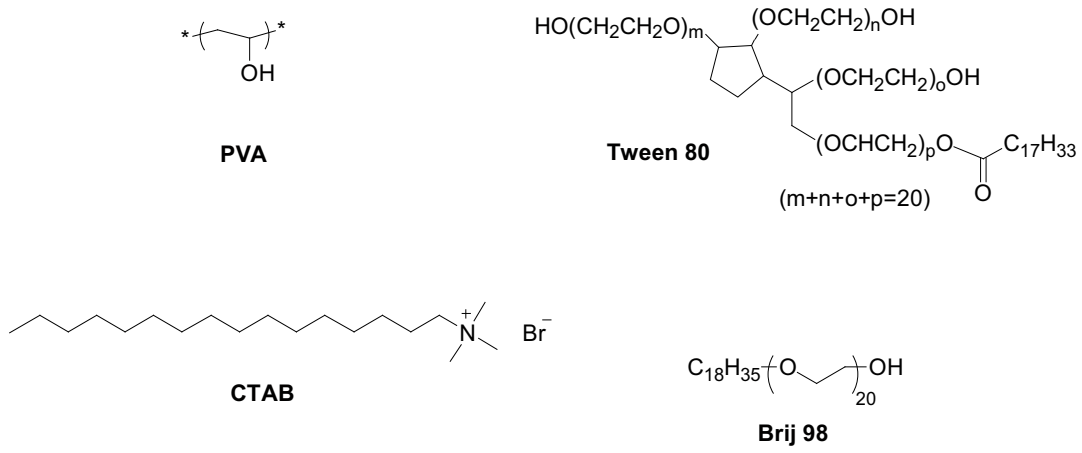
2.3. Critical factors for ATRP in aqueous dispersed media

Aside from the efforts of extending the monomer range and increasing the architecture control in ATRP, adapting ATRP to aqueous dispersed media has been successfully progressing. However, the transformation of ATRP from homogeneous media to aqueous dispersed media is not straightforward.

Initial attempts at conducting an ATRP in aqueous dispersed media, in particular, emulsion medium were reported in early 1998 [57]. CuBr/2,2'-bipyridine (bpy) was used as catalyst and sodium dodecyl sulfate (SDS) was used as surfactant for ATRP of methyl methacrylate (MMA) at 60-80°C. In spite of the relatively high polymer yield, the molecular weight distribution (MWD) was broad, indicating a poorly controlled polymerization. Coincidently, the first attempts to conduct other CRP techniques in aqueous dispersed media used emulsion as the model system [58,59], simply because emulsion polymerization has been the most popular dispersed aqueous system in industry. These initial attempts generally failed, due to the problems associated with mass transport of monomer and catalyst during the polymerization. In the case of ATRP, the failure motivated further research on determining the feasibility and/or criteria for a well controlled ATRP to be carried out in aqueous dispersed media. In fact, according to the studies disclosed in detail below, the selection of catalyst, surfactant and the type of aqueous dispersed media all display significant influence on colloidal stability and level of control over the polymerization [18].

2.3.1. Surfactant choice

The choice of emulsifier, or surfactant, is a crucial factor affecting the success of ATRP in aqueous dispersed media. The surfactant plays an important role in retaining the catalyst complex in the oil phase. The major function



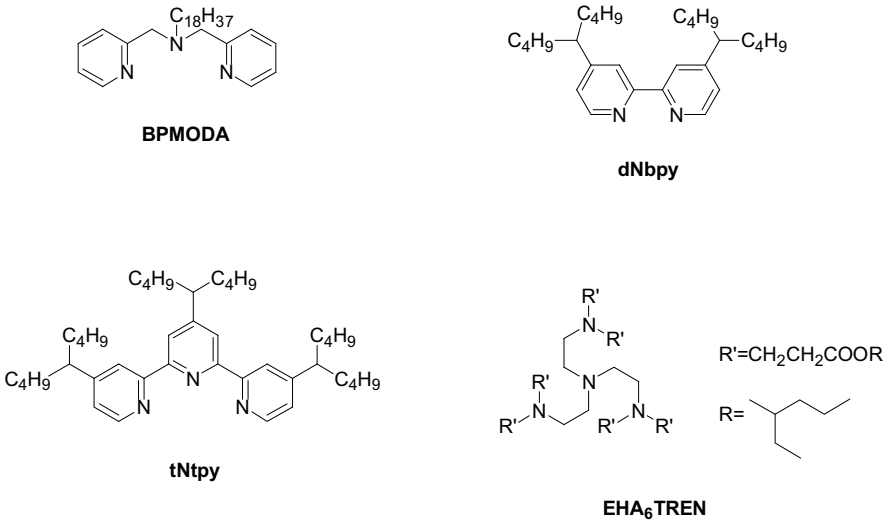
Scheme 2. Structures of common surfactants used for ATRP in aqueous dispersed media.

of surfactant is to assure colloidal stability of the latex particles. However, this is not the only criterion for a surfactant. In ATRP systems, interactions between the surfactant and the radical mediator may lead to a loss of polymerization control. A good surfactant for a controlled ATRP in aqueous dispersed media should at least meet the following two criteria: (i) provide a stable dispersed system throughout the polymerization and (ii) do not interfere with the equilibrium between the radicals and the dormant species. There have been no reports published using an anionic surfactant in emulsion based ATRP since most anionic species would interact with ATRP catalysts, especially the Cu(II) complexes. Selection of an appropriate anionic surfactant remains a challenge for ATRP systems.

To date, non-ionic surfactant with hydrophilic lipophilic balance (HLB) [60] values close to 14, such as commercially available polyoxyethylene(20) oleyl ether (Brij 98) were successfully applied to a controlled ATRP in aqueous dispersed media. Okubo *et al.* also reported the use of Tween 80 [61,62] and poly(vinyl alcohol) (PVA) [63] as non-ionic surfactant for ATRP. Cationic surfactants, such as cetyltrimethylammonium bromide (CTAB), have also been used successfully for a controlled ATRP as well as preparation of stable latex particles [64]. The chemical structures of these surfactants are illustrated in Scheme 2.

Reactive surfactants represent a special group of surfactants. They are generally amphiphilic molecules containing a reactive double bond and/or an initiating site [65]. They can efficiently bind surfactant with the latex particles, and avoid the possible surfactant migration from the latex upon film formation. Recently, an amphiphilic block copolymer was used as a surfactant as well as a macroinitiator for ATRP in miniemulsion [66]. A well-defined poly(ethylene oxide)-*b*-polystyrene diblock copolymer (PEO-*b*-PSt-Br) was synthesized using ATRP for chain extension from a halogen-functionalized PEO macroinitiator. This block copolymer was utilized as a stabilizer and a macroinitiator in the miniemulsion ATRP of *n*-butyl methacrylate (*n*BMA), styrene (St), and *n*-butyl acrylate (*n*BA). The results indicated that a higher concentration of macroinitiator increased the rate of polymerization, but decreased the molecular weight of the obtained triblock copolymer at a given conversion. In parallel, the average particle diameter also decreased with increasing macroinitiator concentration. Follow-up research included the examination of a combination of small molecule initiator ethyl 2-bromoisobutyrate (EBiB) and the PEO-b-PSt-Br macroinitiator. The addition of a co-initiator allowed the use of less reactive surfactant, while targeting polymers with low molar mass [67]. This novel approach reduced the number of reagents and led to the preparation of surfactant-free functional polymer latexes with submicron-size particles and solids contents as high as 25 wt%.

Charleux *et al.* explored cationic reactive surfactant and successfully applied the recently developed activators regenerated by electron transfer (ARGET) ATRP (Section 3.1) technique to miniemulsion media, significantly reducing the amount of copper in the final latex [68]. The surfactant, 11'-(*N,N,N*-trimethylammonium bromide) undecyl-2-bromo-2-methyl propionate, mimicked the structure of CTAB but with an initiating site at the hydrophobic end. Indeed, the final amount of copper in the latex was reduced by a factor of ten in the ARGET experiment, 0.76 mmol L^{-1}, compared to AGET experiments with a preserved acceptable control. It is possible that the existence of bromide anion in aqueous phase limited the diffusion of Cu(II) out of the active latexes and led to a successful ARGET ATRP.



Scheme 3. Structures of common ligands used for ATRP in aqueous dispersed media.

2.3.2. Cu(II) distribution and ligand choice

As discussed above, the identification of the proper catalyst, especially the ligand, is crucial in ATRP because it greatly influences the equilibrium between the active and dormant species. The multiphase nature of aqueous dispersed media adds new challenges to identify an appropriate catalytic system. For instance, Cu(II) species are more soluble in the aqueous phase and the dissociation of the deactivator in the aqueous phase leads to formation of inactive Cu(II) complexes that are unable to deactivate propagating radicals [11]. Only Cu(II) complexes in the form of $[Br\text{-}Cu(II)L_m]^+$ (L: ligand; m: number of ligands per complex) can function as deactivators for ATRP [69]. With the loss of deactivator in the polymerization loci, the ATRP equilibrium is shifted toward the active state, and consequently, an increase is observed in polymerization rate and partial loss of control/livingness due to the enhanced termination.

Not every ligand that works in bulk or solution ATRP can form efficient complexes for ATRP in aqueous dispersed systems. In addition to having sufficient binding affinity towards the metal (in order to compete with water as a potential ligand), the ligand should form a complex, soluble in the organic phase, where the polymerization takes place. Many hydrophobic ligands have been screened and many have proven successful in providing a well controlled ATRP. The structures of some representative ligands are listed in Scheme 3. Picolyl amines, such as bis(2-pyridylmethyl) octadecylamine (BPMODA), bipyridines, such as 4,4'-dinonyl-2,2'-bipyridine (dNbpy) and terpyridines, such as 4',4''-tris(5-nonyl)-2,2':6',2''-terpyridine (tNtpy), have been selected frequently for ATRP in aqueous dispersed media. Cunningham *et al.* have reported successful application of substituted TREN-based ligands, tris{2-bis [3-(2-ethylhexoxy)-3-oxopropyl]aminoethyl}amine (EHA_6TREN) for ATRP in miniemulsion [64,70], although this ligand is less efficient in homogeneous organic media [71].

Even if a hydrophobic ligand is selected, problems associated with partition of catalyst species in the aqueous phase, especially deactivators, could still exist. Early studies on partitioning of catalysts between the two phases were carried when ATRP was first attempted in aqueous dispersed media. The partitioning of Cu(I) and Cu(II) species and dNbpy between *n*BMA and water was studied. While there was a negligible partitioning of the ligand itself to the aqueous phase, there was as much as 20-30% of Cu(I) and 80-99% of Cu(II) species located in the aqueous phase at 90°C (partitioning experiments with 15 wt% *n*BMA, 85 wt% water) [72]. The partitioning of both Cu(I) and Cu(II) complexes in the aqueous phase increased with increasing temperature. The role of partitioning and other effects was recently investigated, using simulation and experiments for St/CuBr/dNbpy systems. The results suggest that Cu(II) partitioning led to higher polymerization rates only in the pre-stationary state. If a stationary state was achieved, the effect of Cu(II) partitioning was reduced [63].

2.3.3. Compartmentalization

Compartmentalization is an intrinsic feature of polymerization in dispersed systems [16], and it affects the polymerization in two ways: a segregation effect and a confined space effect [73]. The former effect refers to a fact that two radicals located in separate particles cannot

react together, *i.e.,* a termination rate is decreased. The result of the latter effect is an increased reaction rate (both termination and deactivation) since their local concentration is much higher. In terms of standard free radical emulsion polymerizations, the consequence of the compartmentalization effect was an increase of polymerization rate due to a decreased termination rate. A smaller droplet/particle size leads to a more significant compartmentalization effect. However, the situation is more complex and difficult to predict when CRP is carried out in discrete particles/droplets, because both radicals and deactivators are compartmentalized.

Recent modeling results show that significant compartmentalization effect requires a small particle size [73]. However, experimental evidence of compartmentalization effect on CRPs in aqueous dispersed media is still not clear [74]. The experimental results showed that ATRP carried out in miniemulsion generally exhibited a higher polymerization rate than that in bulk, likely due to the inevitable diffusion of deactivators, Cu(II) complexes, out of the miniemulsion particles. Simulation results showed that the compartmentalization effect could be significant when ATRP is conducted in microemulsion systems, where the particle size is sufficiently small [75]. However, effects of compartmentalization, such as a reduced polymerization rate, was not observed [76], possibly due to the large interfacial area of microemulsion particles, inducing a higher diffusion rate of ATRP deactivators.

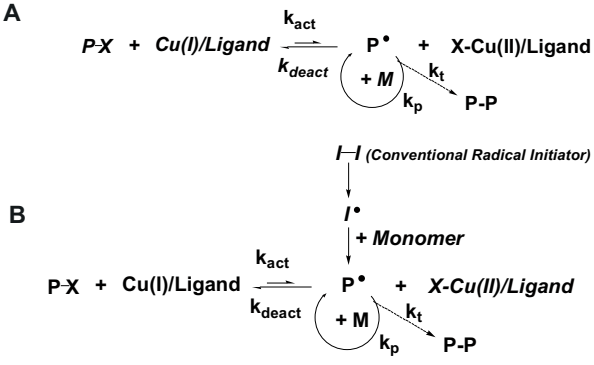
3. Development of ATRP in miniemulsion (including suspension)

Miniemulsion is the most straightforward aqueous dispersed ATRP system, due to the fact that no ingredients need to be transported through the aqueous medium during the polymerization. Given an appropriate selection of catalysts and surfactants, the miniemulsion behaves very similar to a "mini-bulk" system and an ATRP is expected to be easily carried out. However, proper initiation procedures for ATRP should be applied, in order to provide easy handling of catalysts under ultrasonic homogenization, and efficiently prepare well-defined polymers with pre-determined composition and topology.

3.1 Initiation techniques

A normal ATRP initiating system (Scheme 4A) [8] consists of an alkyl halide initiator and transition metal catalyst in the lower oxidation state. It works well for systems that are relatively insensitive to air. However, as more active catalysts have been developed in order to polymerize less reactive monomers and also to diminish a total amount of catalyst, the systems inherently become oxidatively less stable. Traces of air in the reagents or equipment could lead to irreversible oxidation and loss of the ATRP activator. An additional concern is that aqueous media are difficult to be deoxygenated in industrial scale vessels. A development of a robust scalable initiation process could help large scale synthesis.

Higher oxidation state catalysts, such as Cu(II) complexes are oxidatively stable. In a reverse ATRP, the catalyst precursor is added to the reaction system in the form of the Cu(II) species (Scheme 4B) [77]. After deoxygenation, the polymerization is initiated by the reaction of Cu(II) with radicals, generated by thermal decomposition of conventional thermal initiators. This circumvents the problem associated with oxidation of catalysts.

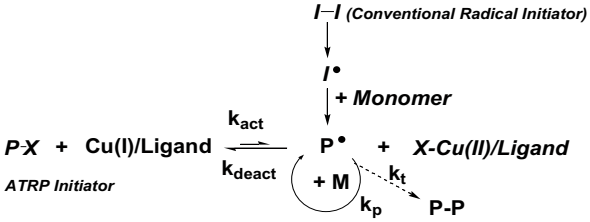


Scheme 4. Proposed mechanisms for (A) normal ATRP and (B) reverse ATRP. The activation and deactivation steps proceed with the rate constants k_{act} and k_{deact}. Generated free radicals propagate and terminate with rate constants k_p and k_t. All ingredients present in the initial system are highlighted in italics.

In a standard bulk ATRP, a highly active catalyst system is needed to maintain control over the polymerization at the reduced catalyst concentration. For instance, a controlled polymerization of methyl acrylate (MA) was attained using only 0.1 equivalents of CuBr/tris [2-(*N,N*-dimethylamino)ethyl]amine (Me_6TREN), relative to the initiator. The reaction reached 41% conversion in one hour at 22°C under bulk polymerization conditions [78]. However, there is a stoichiometric limitation that does not allow one to reduce the level of catalyst in a reverse ATRP process. The amount of catalyst cannot be independently reduced for a given targeted degree of polymerization (DP). It must be comparable to the concentration of the radical initiator, since the Cu(II) complex provides the only source of the transferable halogen atoms. Furthermore, block copolymers

cannot be synthesized using a reverse ATRP, unless a macromolecular radical initiator is used.

These problems were solved, to a significant degree, for bulk ATRP by the development of a Simultaneous Reverse and Normal Initiation (SR&NI) process [79]. In a SR&NI initiation procedure, ATRP initiators, *i.e.,* alkyl halides or halogen-terminated macroinitiator, are added to the reaction together with a conventional thermal initiator (Scheme 5). Both reagents contribute to the ATRP equilibrium, so that the relative amount of catalysts can be dramatically decreased, and the synthesis of block copolymers can be achieved.



Scheme 5. Proposed mechanism for SR&NI process in ATRP. All ingredients present in the initial system are highlighted in italics.

SR&NI ATRP provided a way to reduce the catalyst concentration without sacrificing the level of control over polymerization. This was demonstrated in bulk systems by the use of 0.1 equivalents of a highly active catalyst system in its higher oxidation state (*e.g.,* $CuBr_2$/Me_6TREN) and a dual initiator system consisting of 0.062 equivalents of 2,2'-azobisisobutyronitrile (AIBN) and 1 equivalent of alkyl halide [79]. The amount of Cu(II) used was less than 1/10 of the catalyst level used in a typical reverse ATRP. A small amount of activating catalyst complex (*e.g.,* CuBr/Me_6TREN) was generated by the slow decomposition of AIBN. Since the initial concentration of alkyl halide was much higher than that of AIBN, the majority of the polymer chains were initiated by the alkyl halide *via* a normal ATRP process and the DP was predominantly controlled by the concentration of alkyl halide, as expressed by the equation below:

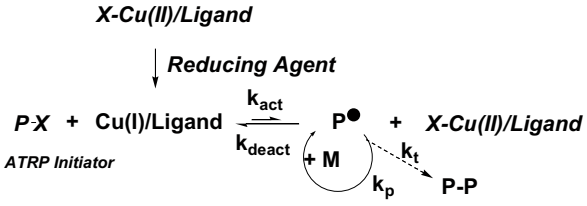
$$DP = \frac{\Delta[M]}{[RX]_0 + (2 \times f \times [AIBN]_0)}$$

where f is the initiation efficiency of AIBN, $[RX]_0$ is the initial concentration of alkyl initiator, Δ[M] is the difference of monomer concentration between time 0 and time t.

Well-defined P*n*BA and PSt were successfully synthesized *via* SR&NI ATRP in bulk system [79].

While SR&NI is a significant improvement over reverse ATRP, the SR&NI process has an intrinsic deficiency when it is used to synthesize block copolymers. This results from a thermal initiator used to reduce the catalyst complex. It introduces new initiating radicals into the system, in addition to radicals originating from ATRP initiator. Those radicals produce new homopolymer chains from the second monomer, and compete with the block copolymers originating from the macroinitiator. Therefore, the final product contains a small fraction of homopolymer, in addition to the desired block copolymer. Pure block copolymers are essentially impossible to synthesize using SR&NI ATRP.

In order to overcome this limitation, and prepare a pure block copolymer without contamination by homopolymers, an initiation procedure named Activators Generated by Electron Transfer (AGET) was developed for ATRP [80,81]. Instead of a conventional radical initiator, a reducing agent was used to react with the Cu(II) complex and to generate the activator without involvement of organic radicals or formation of reaction products which could initiate new chains (Scheme 6).



Scheme 6. Proposed mechanism for AGET ATRP initiation. All ingredients present in the initial system are highlighted in italics.

In AGET ATRP, no initiating radicals are introduced during the polymerization, and therefore no homopolymer is formed when a block copolymer is targeted. Another important feature of this initiation technique is that the polymerization rate can be directly controlled by the amount of added reducing agent, since it influences the ratio of Cu(I) and Cu(II) species. The key requirement for this technique is selection of a reducing agent that can rapidly react with Cu(II) complexes without introducing new radicals to the reaction system. Tin(II) 2-ethylhexanoate ($Sn(EH)_2$), Cu(0), hydrazine, tertiary amine, ascorbic acid, *etc.* were used as reducing agents [81-91].

In fact, based on the development of SR&NI and AGET techniques discussed above, new initiation methods, such as Initiation for Continuous Activators Regeneration (ICAR) and ARGET, were recently developed [83,84,92]. In both systems, a large excess of reducing agents (either free radicals from thermal initiator or external reducing agent) were used for a continuous regeneration of very low levels of catalyst activators. By using ICAR or ARGET initiation techniques, the amount of Cu catalyst necessary for an ATRP was lowered from several thousand ppm under normal conditions to <50 ppm while still maintaining excellent control over molecular weight and MWD.

It is worth noting that under certain conditions, the SR&NI technique might be still favored. For instance, for surface modification of particles by "grafting-from", the un-tethered polymer chains initiated by the free radical initiators can participate in termination reactions. Therefore the contribution of particle-particle termination is decreased, resulting in a delayed macroscopic gel formation. In addition, the un-tethered polymer can be used as an "indicator" since it is easy to obtain the information on molecular weight and chemical composition from the "free" polymers [44].

3.2. Application of various ATRP techniques in miniemulsion

3.2.1. Normal and reverse ATRP

Both normal and reverse ATRP were applied to miniemulsion in 2000 [93]. The use of a non-ionic surfactant Brij 98, a hexadecane costabilizer that facilitates formation of a stable latex, and a hydrophobic ligand dNbpy, provided controlled miniemulsion polymerizations, as indicated by a linear increase of the molecular weight with the monomer conversion and a narrow MWD. In the normal ATRP system, it was observed that a fraction of the Cu(I) complexes were oxidized by the presence of adventitious air. This issue is more pronounced in miniemulsion than in bulk, because it is very difficult to prevent oxygen diffusing into the samples during the ultrasonication procedure, necessary for preparing submicron monomer droplets prior to polymerization. Since the handling of catalysts for reverse ATRP is much easier because of the use of air-insensitive Cu(II) species, reverse ATRP has proven to be the better pathway to initiate ATRP in miniemulsion.

Simms and Cunningham reported successful reverse ATRP of *n*BMA using the cationic emulsifier CTAB at 90°C with EHA_6TREN as ligand and VA-044 as thermal initiator [64], although some phase separation was observed at conversion >75%. The high temperature was discounted as the primary reason of the destabilization. A loading of CTAB as low as 1 wt%, relative to monomer, provided sufficient colloidal stability, *i.e.,* considerably lower than that when non-ionic surfactant Brij 98 was used as surfactant.

Recently, Simms and Cunningham continued their research of reverse ATRP in miniemulsion and reported the synthesis of P*n*BMA and PMMA with unusually high molecular weight (M_n = 0.3-1.0 ×10^6 g mol^{-1}) [70]. A hydrogen peroxide/ascorbic acid redox initiation system was used, and has been ascribed as the key for the synthesis of polymers with such high molecular weights. However, in this system, the initiation efficiency was possibly rather low, *i.e.* the experimental molecular weight was much higher than the calculated valued based on monomer conversions. This was likely due to termination reactions occurring at the early stage of the polymerization. It is likely that the presence of ascorbic acid reducing agent resulted in a regeneration of the activators and further drove the polymerization. Nevertheless, this indicated preservation of very high chain-end functionality in miniemulsion droplets.

3.2.2. SR&NI ATRP

SR&NI ATRP was successfully applied in miniemulsion for the preparation of well-defined linear and star-shaped block copolymers. Matyjaszewski *et al.* obtained controlled polymer compositions and high colloidal stability (average hydrodynamic diameter D_h~250 nm) in SR&NI miniemulsion ATRP of *n*BMA at 80°C using the ligands EHA_6TREN, BPMODA or tNtpy [94,95]. These ligands are hydrophobic and form highly active catalyst complexes. Compared to a reverse ATRP process, the amount of $CuBr_2$/ligand was reduced by a factor of 5-8 in the SR&NI miniemulsion ATRP. Well-defined polymers with low polydispersities (P*n*BMA, P*n*BA and PSt) were obtained by SR&NI ATRP in miniemulsion when BPMODA and tNtpy were used as ligand. However, with EHA_6TREN as a ligand, the polymers displayed a broader MWD.

Well controlled diblock, triblock, and 3-arm star block copolymers (polydispersity index M_w/M_n ~ 1.18-1.37) were prepared in miniemulsion by using this technique with tNtpy or BPMODA as ligands at 60°C by employing mono-, di-, and trifunctional macroinitiators. Additionally, a series of spontaneous gradient copolymers of *n*BMA and *n*BA (r_{nBMA}=2.2, r_{nBA}=0.3) was synthesized by using SR&NI ATRP in miniemulsion [96]. Besides the synthesis of linear and branched polymers, cross-linked latex particles containing degradable disulfide cross-link were also prepared in miniemulsion by using SR&NI ATRP [97]. The efficient degradation of the latex particles into homopolymers, upon the addition of tri(*n*-butyl) phosphine reducing agent, was monitored by dynamic light scattering measurements.

3.2.3. AGET ATRP

Although SR&NI ATRP was a creative combination of normal and reverse ATRP, it was not broadly applied because meanwhile a new AGET technique was developed. It quickly became a preferred initiation system for ATRP in miniemulsion. Instead of employing a conventional radical initiator, a reducing agent is used to react with Cu(II) complex and generate the activator without any involvement of organic radicals, preventing initiation of new chains. On one hand, AGET retains the main advantage of a SR&NI process: an air insensitive

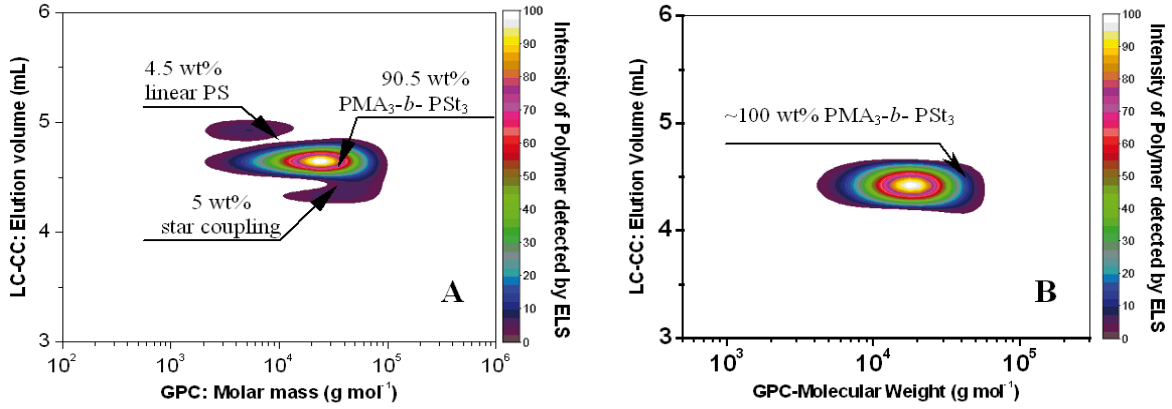


Figure 1. 2-Dimensional contour plots of the resulting 3-arm block copolymer synthesized using 3-arm trifunctional PMA macroinitiator *via* SR&NI ATRP (A) and AGET ATRP (B) in an aqueous styrene miniemulsion. In the 1st dimension, values were obtained with liquid adsorption chromatography at the critical condition (LC-CC) of PSt, and in the 2nd dimension, with gel permission chromatography (GPC). Signal was collected by evaporative light scattering (ELS) detector [80]. Reproduced with permission from the American Chemical Society.

Cu(II) complex is initially added to the reaction as the precursor of the active catalyst, allowing an easy manipulation of the process. On the other hand, this procedure inherits the advantage of normal ATRP. All radicals are generated exclusively from the alkyl halide, or macroinitiator if a block or grafted copolymer is targeted. The final products only consist of the desired segmented copolymer with no homopolymer impurity. Thus, AGET has proved to be the best technique to synthesize pure block copolymers by ATRP in miniemulsion.

Matyjaszewski *et al.* carried out AGET ATRP of *n*BA and St in miniemulsion by using ascorbic acid as a reducing agent with BPMODA as a ligand and Brij 98 as a surfactant [98]. Ascorbic acid, a water-soluble compound, reduced the Cu(II) complexes located in the aqueous phase and/or at the monomer droplet surface, generating the less water-soluble Cu(I) complex, which partitions mostly to the monomer droplets or active polymeric particles. The amount of ascorbic acid added to a polymerization is a crucial parameter. Too much ascorbic acid results in compromising the degree of control/livingness, whereas an insufficient amount reduces the polymerization rate. However, an extra amount of ascorbic acid can be used to remove oxygen from the system and allow an ATRP to be successfully carried out without deoxygenation [99].

AGET ATRP was successfully used for the synthesis of pure block copolymers and star copolymers of MA and St [80,100]. The product was analyzed by 2-dimensional liquid chromatography, which separates polymers not only by their molecular weights but also by their chemical compositions. As seen in Fig. 1, by using AGET ATRP, no homopolymer was detected. Star-star coupling reactions were suppressed by stopping the reaction at a lower conversion.

The AGET technique is also superior to SR&NI for preparation of a forced gradient copolymer in miniemulsion [101]. The SR&NI technique failed in this synthesis, because the radicals generated by the thermo-initiators initiated free radical polymerization in aqueous phase. The formed polymer deteriorated the colloidal stability of the miniemulsion system. In contrast, AGET allows all initiators to be "locked" in the miniemulsion droplets while the newly fed monomer can only diffuse into the polymerizing particles to participate in polymerization. Various monomer pairs were examined in this study, including *n*BA/*tert*-butyl acrylate (*t*BA) (assuming similar reactivities), *n*BMA/MMA (reactivity ratio: r_{BMA} = 1.26 and r_{MMA} = 0.98), and *n*BA/St (reactivity ratio: r_{St} = 0.698, r_{nBA} = 0.164). The shape of the gradient along the backbone of the copolymers was influenced by the molar ratio of the monomers, the reactivity ratio of the comonomers as well as the feeding rate of the second monomer and the relative hydrophobicity of the comonomers.

In addition to synthesis of linear polymers with controlled chemical composition and chain sequence distribution, AGET miniemulsion ATRP has been extensively used for synthesis of polymers with complex structures, including molecular brushes [102] and hybrid nanoparticles [103,104]. It is noteworthy that the miniemulsion led to the preparation of polymer brushes and hybrid particles in higher yields with less radical-radical coupling, when compared to bulk or solution methods. The confinement of polymerization in miniemulsion droplets avoids the possibility of macroscopic gelation in the presence of multifunctional initiators.

In addition to preparation of polymers with complex architectures and compositions, AGET ATRP

in miniemulsion also provides a platform to directly compare bulk/solution and aqueous dispersed media polymerizations. As discussed, implementation of a normal ATRP in miniemulsion is complicated by the fact that some oxidation of CuBr during ultrasonication is inevitable. Comparison between miniemulsion and solution polymerizations is an integral part of the present work, and this would be rendered difficult by unknown levels of oxidation of CuBr in setting up the miniemulsion system. AGET ATRP is sufficiently similar to a normal ATRP and is accompanied by less side reactions. Kagawa *et al.* used AGET ATRP in miniemulsion to successfully compare their simulations with experiments of normal solution ATRP for the partitioning effect of Cu(II) in aqueous dispersed media [63].

3.2.4. ARGET ATRP in miniemulsion

In section 2.3.1, the requirements for choice of surfactant was discussed, including the example by Charleux *et al.* who reported the first successful ARGET ATRP carried out in miniemulsion [68]. In this experiment, synthesis of a cationically charged surface-active ATRP initiator for miniemulsion allowed a significant reduction of the amount of copper in the final latex, which could benefit the commercial ATRP processes.

3.3. Combination of ATRP and other polymerization techniques in miniemulsion

Recently, Héroguez *et al.* reported a simultaneous ring opening metathesis polymerization (ROMP) of norbornene and ATRP of MMA in miniemulsion [105]. A single amphiphilic ruthenium macroinitiator, *i.e.,* PEO modified "first generation" Grubbs catalyst, was used to initiate ROMP. This species was also capable of regulating a controlled ATRP in miniemulsion. A stable miniemulsion was obtained and the resulting latex showed clear phase separation as analyzed by transmission electron microscope. Chain ends of polymers prepared by other mechanisms can be converted to ATRP initiating moieties and extended to form block copolymers [106].

3.4. ATRP in inverse miniemulsion

Parallel to the research on ATRP in miniemulsion, there is an increasing demand for water-soluble (or hydrophilic) polymers produced in inverse miniemulsion polymerization in which the continuous phase is oil. Inverse miniemulsion ATRP shares many process advantages with aqueous miniemulsion ATRP, *e.g.,* occurrence of reaction in monomer droplets and no need for the transportation of monomers and catalysts during polymerization. Since the polymerization is performed in the aqueous phase, a hydrophilic, but highly coordinating ligand, tris [(2-pyridyl)methyl]amine (TPMA), was selected, to ensure control over polymerization. Hydrophilic polymers such as poly(oligo(ethylene oxide) monomethyl ether methacrylate) (POEOMA), and double-hydrophilic PEO-*b*-poly(2-hydroxyethyl methacrylate) (PEO-*b*-PHEMA) block copolymer were prepared by AGET ATRP in inverse miniemulsion with good control [107].

The successful exploration of AGET ATRP in inverse miniemulsion opened the possibility of preparing hydrophilic polymeric microgels with more homogeneous structure and preserved chain-end functionality [107,108]. The particles had size D_h ~250 nm and the swelling ratio of such particles in tetrahydrofuran (THF) was significantly higher than microgels prepared by conventional radical polymerization. The particles were suitable loading vehicles for guest molecules, modeled by fluorescent molecules.

3.5. ATRP in suspension

Haddleton *et al.* demonstrated a suspension ATRP for synthesis of particles containing P*n*BMA with diameter 1–3 μm [109]. In this research the choice of surfactants included non-ionic polymer PEO-*b*-PMMA and cationic polymer PMMA-*b*-P(2-dimethylaminoethyl methacrylate) polymer, with the quaternized second block. Both of the surfactants were synthesized by ATRP. A variety of ligands were compared in this study and it was reported that ligands with higher hydrophobicity led to polymerization with a better control.

Stover *et al.* reported the synthesis of larger diameter particles (200–800 μm) using suspension ATRP of MMA with poly(ethylene glycol) monomethacrylate (PEGMA) using poly(*N*-vinyl pyrrolidone) (PVP) as a stabilizer and dNbpy as ligand [110]. The system was unusual because these two monomers have different hydrophilicity but a sufficient control was achieved (M_w/M_n =1.20-1.35) although a higher ratio of PEGMA resulted in a broader MWD. This research suggests that polar copolymers can be prepared by the incorporation of water soluble monomer in suspension ATRP despite extensive partitioning of the water-soluble monomer into the water phase. However, this understanding may not be easily applied to ATRP in other aqueous dispersed media. Colloidal stability is a more delicate issue for miniemulsions and emulsions; a slight variation by using hydrophilic monomers may induce a loss of control over the polymerization.

4. Development of ATRP in microemulsion

ATRP of MMA and St was performed in microemulsion media by using normal ATRP (EBiB as initiator), reverse

ATRP (V-50 as initiator), as well as AGET ATRP (EBiB as initiator and ascorbic acid as reducing agent) employing Brij 98 as surfactant and BPMODA as ligand, at 65°C [76]. The polymers obtained in the normal ATRP microemulsion displayed a bimodal distribution, mainly attributed to the loss of Cu(II) complexes from monomer-swollen micelles. Due to the small size, the number of total Cu complexes per monomer-swollen micelle is pretty low, ~15. Therefore, most micelles contained only one propagating radical and even the loss of one Cu(II) deactivator by diffusion into water phase could result in an uncontrolled redox initiated polymerization. However, in parallel in the micelles with sufficient Cu(II) controlled polymerization occurred, resulting in bimodal MWD (see Fig. 2). Reverse ATRP led to polymers with monomodal distribution, but with broad MWD (M_w/M_n = 1.61) due to slow initiator decomposition. The slow initiation also resulted in the larger particle size (D_h ~ 70 nm), as compared to the 10-nm monomer-swollen micelles present before polymerization was initiated. The best results were obtained using AGET ATRP, which resulted in a good control of the polymers (M_w/M_n = 1.28) and a narrow particle size distribution with D_h ~ 43 nm. The selection of ascorbic acid as reducing agent ensured rapid reduction of Cu(II) in the aqueous phase or at the interface, to Cu(I) activator, which catalyzed polymerization by reaction with EB*i*B after entry into monomer-swollen micelles. The same AGET ATRP microemulsion procedure has also been successfully applied for polymerization of *n*BA.

In another report, Okubo *et al.* described a normal ATRP of *iso*-butyl methacrylate (*i*BMA) in microemulsion by employing dNbpy as ligand and the cationic emulsifier tetradecyltrimethylammonium bromide (TTAB) at 40°C [111]. The polymerization resulted in a monomodal and relatively narrow MWD (M_w/M_n = 1.32) and a transparent emulsion with D_n ~ 13 nm. Compared to the results from Min and Matyjaszewski [76], this success is likely due to the manner of adding the EBiB initiator. Matyjaszewski added EBiB after the system was emulsified and heated to reaction temperature. Thus the possibility of lack of deactivator in some micelles cannot be ignored. However, Okubo *et al.* added EBiB together with the activators before the polymerization was emulsified. Therefore each micelle contained similar mole ratio of EBiB initiator and activator. The simultaneous loading of initiator and activators improved the control over normal ATRP in microemulsion, although the risk of pre-reaction initiation should not be excluded.

5. Development of ATRP in emulsion

While the miniemulsion is a robust process delivering a satisfactory control over the polymers and latexes, it requires the use of a high shearing force, such as sonication or emulsification, which is challenging for large scale reactions. The development of effective ways to conduct ATRP in emulsion systems is certainly desirable from an industrial perspective, because the method is directly applicable to current industrial facilities, without requiring significant modification. However, conducting ATRP in emulsion is more complicated than in miniemulsion systems.

The initial attempt to extend ATRP to an emulsion system in 1998 using normal ATRP initiation techniques [57] was followed by many additional efforts [112-115]. Generally, good control over molecular weight and MWD was achieved. However, colloidal stability was a constant problem. In an emulsion system, radicals generated by the decomposition of thermal initiator should first react with monomer in aqueous phase until the propagating oligo-radicals are absorbed in monomer-swollen micelles, leading to nucleation. This nucleation process cannot be approached when a normal ATRP is carried out in emulsion. The hydrophobic initiators and catalysts are distributed in both monomer-swollen micelles and monomer droplets, depending on their volume fraction. Thus, the initiation would predominantly occur in the monomer droplets since their volume is thousands times larger than that of the micelles. Monomer droplets nucleation is believed to be detrimental to emulsion latex stability. Therefore, most of the attempts to apply normal ATRP in emulsion resulted in a relatively large particle size and broad particle size distribution of the final product. In fact, the product behaved more like a “minisuspension” rather than an emulsion system. Matyjaszewski *et al.* also explored the use of hydrophilic initiator (2-hydroxyethyl 2-bromoisobutyrate) for normal ATRP in emulsion, expecting an increase in the probability of nucleation in micelles rather than the monomer droplets. However, the colloidal stability was still poor and severe coagulation was observed [116].

A true emulsion ATRP was approached when a reverse ATRP was employed to ensure that nucleation did not occur in the monomer droplets [117,118]. The colloidal stability problems were successfully resolved because the initiation and nucleation process were very similar to those of a standard free radical emulsion polymerization. Matyjaszewski *et al.* reported successful reverse ATRP of *n*BMA and MMA in emulsion using water-soluble initiators, V-50 and VA-044 [117]. Both systems resulted in small particles with a relatively narrow particle size distribution and polymers with low

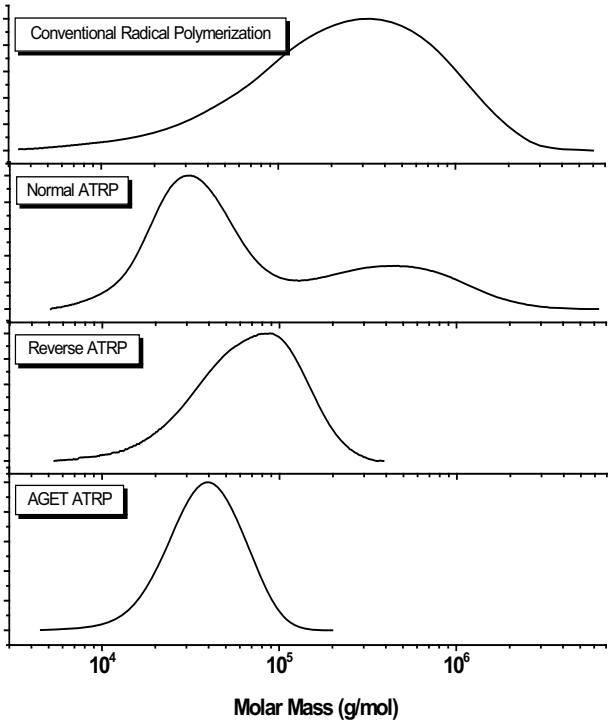


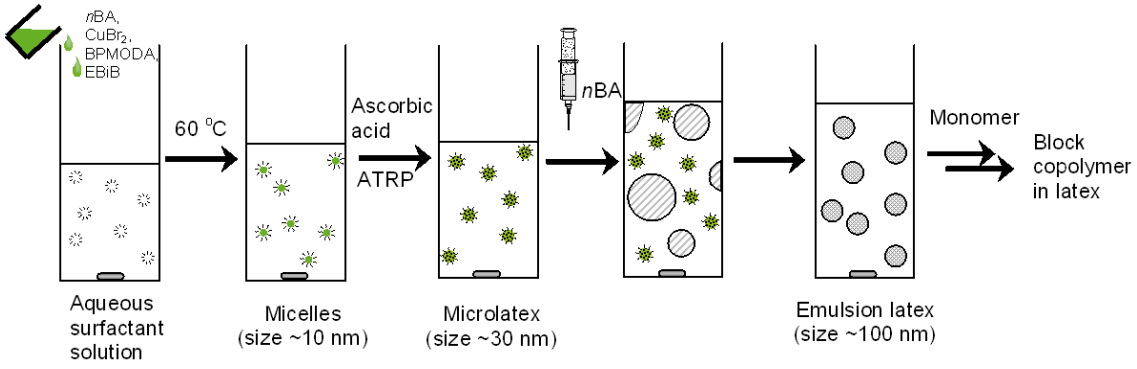
Figure 2. Typical GPC traces of the polymers from conventional radical polymerization, normal ATRP, reverse ATRP, AGET ATRP of MMA in microemulsion [76]. Reproduced with permission from the American Chemical Society.

polydispersity. However, most of the oil-soluble catalysts were still initially distributed in the large monomer droplets and did not diffuse across the aqueous phase to the micelles. Consequently, the insufficient concentration of catalyst at the polymerization loci resulted in low initiation efficiency, *i.e.,* preparation of polymers with higher molecular weights than the theoretical values.

The primary explanation for unsuccessful ATRP in an emulsion process is the inefficient transport of Cu-based catalysts from monomer droplets to the active micelles and polymerizing particles. Therefore, based on the successful results from ATRP carried out in microemulsion, Matyjaszewski *et al.* developed a two-step emulsion ATRP procedure to overcome this problem, as seen in Scheme 7 [119]. In this method, an emulsion was formed by adding pure monomer to an ongoing microemulsion ATRP. This ensures that all ATRP initiators, catalysts and a small amount of monomer were encapsulated into microemulsion micelles. This was accomplished in the absence of any high shear environment. After activating the catalyst and initiating the reaction, the rest of the monomer was fed to the polymerization system. During the polymerization, pure monomer diffused from monomer droplets to the polymerizing particles containing the catalyst, thereby mimicking a normal emulsion system. This procedure avoids the need to transport catalysts through the aqueous media during the polymerization and therefore facilitates a controlled ATRP in the active latexes. The surfactant concentration was efficiently decreased to ~2 wt% (~10 wt% *vs.* monomer) by decreasing catalyst concentration and changing the ratio of the monomer added to the microemulsion stage and the monomer added afterwards to form the emulsion. A controlled emulsion ATRP was obtained, leading to the synthesis of polymers with narrow MWD (M_w/M_n = 1.2-1.4). This two-stage emulsion technique requires no sonication and is quite similar to how many industrial emulsion polymerization processes are conducted, with in situ formation of a dilute seed followed by monomer swelling and further polymerization [15].

The high chain-end functionality of the polymer obtained in this novel emulsion procedure was illustrated by conducting an in-situ chain extension to form a block copolymer P*n*BA-*b*-PSt [119].

Conducting copolymerization of a monomer and a divinyl cross-linker in the microemulsion ATRP stage of this procedure led to the direct synthesis of hairy nanoparticles in one-pot [120]. The first stage was a microemulsion atom transfer radical copolymerization of monomer MMA and cross-linker ethylene glycol dimethacrylate (EGDMA), leading to the preparation of uniform nanogels (D_h ~ 30 nm). The nanogels could be



Scheme 7. Schematic illustration of ATRP in an emulsion by using the two-step procedure.

chain extended by polymerizing the additionally added monomer *n*BA, forming hairy particles with tethered linear polymer chains. The hairy particles showed size D_h = 40-100 nm when swollen in THF and absolute weight-average molecular weight of $M_{w,MALLS}$ = 7-25×10^6 g mol^{-1}, determined by GPC with a multi-angle laser light scattering (MALLS) detector. The differential scanning calorimetry measurement showed two distinct T_g peaks, 20°C and -50°C, due to the plasticized P(MMA/EGMDA) cores with P*n*BA that grew inside, and the pure PBA hairs, respectively.

ATRP was also successfully applied to a combination of miniemulsion and seeded emulsion methods [62]. The seed particles containing well controlled P*i*BMA were first prepared using the normal ATRP process under miniemulsion conditions at 40°C for 48 h. The particles had a diameter of 200 nm and consisted of P*i*BMA with M_n =23,100 g mol^{-1} and M_w/M_n =1.2. In the presence of the seed particles, the second stage emulsion ATRP of St was conducted at 70°C, resulting in well controlled P*i*BMA-*b*-PSt block copolymers with M_n = 31,100 g mol^{-1} and M_w/M_n =1.1. Interestingly, the resulting particles had an onion-like multilayered morphology with *ca.* 19 nm thickness of each layer.

6. Development of ATRP in dispersion (including precipitation) polymerization

Dispersion polymerization is a useful method for synthesis of micron- and submicron-sized polymer particles with narrow size distribution. The commonly used solvents include hydrocarbons, *e.g.,* alkanes, and more polar media, such as alcohol/water mixture [55]. Recently, supercritical carbon dioxide ($scCO_2$) has received attention as a more environmentally benign alternative to the traditional organic solvents used in dispersion polymerization [121].

The combination of dispersion polymerization with CRP offers several benefits in addition to the preparation of uniform micron-sized particles. First of all, particles prepared by CRPs contain polymers with preserved chain-end functionality. They are suitable for post-polymerization modification, forming materials that satisfy the requirements of a spectrum of applications. The particles obtained from CRP can be designed to contain functional polymers with targeted molecular weight. They can be swollen by addition of solvents or a second monomer and are used as macroinitiators for preparation of block copolymers or tethering other materials to the particle surface [122].

Initial attempt to apply ATRP to dispersion polymerization encountered challenges [123]. The key issue was a prolonged nucleation stage. Compared to free radical polymerization, ATRP needs a longer time for polymers to reach the critical chain length and to precipitate from the media because of the simultaneous, slow growth of all chains. This prolonged nucleation stage yielded particle seeds with diverse sizes, resulting in production of particles with broad size distribution. In order to shorten the nucleation stage, and provide monodisperse polymeric particles, a "two-stage" technique was borrowed from the RAFT dispersion polymerization process [124] and applied to the ATRP system [125]. The first stage of the polymerization only involved a conventional radical polymerization of St in ethanol, forming a low fraction of high molecular weight polymer. The fast polymerization of St under conventional RP conditions resulted in a short and clean nucleation stage, and improved uniformity in the size of the particles. In the second stage, *i.e.,* after *ca.* 3% conversion of monomer, an ATRP deactivator, $CuBr_2$/TPMA, was added into the reaction, converting the system into a reverse ATRP. Since the system was transformed into a reverse ATRP at very low St conversion most of the polymers produced in the reaction exhibited the characteristics of materials formed in a

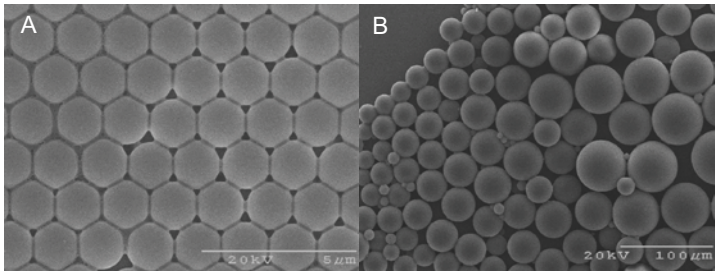


Figure 3. Scanning electron microscopic images of polystyrene particles prepared by (A) one-batch reverse ATRP and (B) two-stage reverse ATRP, respectively [123]. Reproduced with permission from the American Chemical Society.

controlled polymerization process. Dispersion ATRP of St was performed in ethanol at 70°C with PVP (average M_w ~ 55,000 g mol^{-1}) and octylphenol ethoxylate (Triton X-305, 70% in water) as stabilizer, producing particles with a narrow size distribution (shown in Fig. 3). The GPC traces of the polymers indicated the livingness of the system. This two-stage technique was also applied to preparation of a cross-linked system by adding both DVB cross-linker and $CuBr_2$/TPMA deactivator after the initial nucleation.

Wan and Pan carried out dispersion ATRP of 4-vinylpyridine (4VP) in ethanol/water at 60°C, using PEO-monomethylether 2-bromoisobutyrate as both initiator and stabilizer and N,N,N',N",N"-pentamethyldiethylenetriamine (PMDETA) as ligand [126]. The system showed a good control, yielding particles with $d \approx 30$ nm and relatively narrow size distribution. The use of the PEO-based initiator improved the control over polymerization and provided uniform particle size, because it led to a slightly different nucleation than the normal dispersion polymerization. Nucleation was proposed to proceed *via* formation of micelles, involving the *in situ* formed diblock copolymer. The fast initiation in ATRP avoided the secondary nucleation in the system, which guaranteed the preparation of uniform particles. The conversion was limited, <60%, possibly related to unfavorable monomer partitioning between the particles and the continuous phase. Cross-linked particles were also prepared with the cross-linker *N*,*N*'-methylene bis(acrylamide). Au/polymeric composite nanoparticles were prepared by complexing $HAuCl_4$ salt into P4VP nanoparticles, followed by in-situ reduction with $NaBH_4$.

Matyjaszewski and DeSimone carried out both precipitation and dispersion ATRP of MMA in $scCO_2$ at 85°C using methyl 2-bromopropionate/CuCl/Cu(0). 4,4'-Di(tridecafluoro-1,1,2,2,3,3-hexahydrononyl)-2,2'-bipyridine ($dR_{f6}bpy$), was specifically chosen as the ligand for its high solubility in $scCO_2$ [127]. The difference between precipitation and dispersion polymerization was the addition of poly(1,1-dihydroperfluorooctyl acrylate) as stabilizer. High conversion was obtained in the dispersion polymerization, and the polymer was collected as a free flowing powder after venting the CO_2. Reasonable control of the polymers was obtained with GPC molecular weight similar to the theoretical values and $M_w/M_n = 1.41$.

7. Summary and Outlook

Significant progress has been accomplished over the past decade in procedures to conduct ATRP in aqueous dispersed media, which could benefit the commercial ATRP processes. The success can be attributed to the development of new initiation techniques and the realization that all aspects of the mechanism of the process are crucial to design synthetic procedures resulting in colloidally stable latexes, while retaining the control over polymerization in aqueous dispersed media.

It is noteworthy that aqueous dispersed media provide unparallel advantages compared to bulk or solution media. Polymerization in compartmentalized loci can lead to improved control/livingness under appropriate conditions and the preparation of polymers with very high molecular weight. Another example is the significantly improved yield of molecular brushes and hybrid nanoparticles in miniemulsion ATRP, when compared to bulk/solution systems.

Future challenges include: 1) Expansion of the choice of surfactants; the concentration of ionic surfactants in the latex can be especially reduced. 2) Expansion of the choice of ligand; concentration of highly active hydrophobic ligands for ATRP could be diminished. 3) Extension of ATRP to new range of monomers, especially functional monomers. 4) Development of new procedures to remove copper catalyst from latex colloids, this could be simpler than in organic media, since submicron latexes have very high surface area and Cu(II) prefers the aqueous phase; 5) Development of the reaction engineering aspects for heterogeneous ATRP, and other CRPs; this will be essential for a future commercialization of CRPs.

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