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Perspective

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Macromolecular Engineering by Atom Transfer Radical Polymerization

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ABSTRACT: This Perspective presents recent advances in macromolecular engineering enabled by ATRP. They include the fundamental mechanistic and synthetic features of ATRP with emphasis on various catalytic/initiation systems that use parts-per-million concentrations of Cu catalysts and can be run in environmentally friendly media, e.g., water. The roles of the major components of ATRP—monomers, initiators, catalysts, and various additives—are explained, and their reactivity and structure are correlated. The effects of media and external stimuli on polymerization rates and control are presented. Some examples of precisely controlled elements of macromolecular architecture, such as chain uniformity, composition, topology, and functionality, are discussed. Syntheses of polymers with complex architecture, various hybrids, and bioconjugates are illustrated. Examples of current and forthcoming applications of ATRP are covered. Future challenges and perspectives for macromolecular engineering by ATRP are discussed.

1. INTRODUCTION

Macromolecular engineering comprises precise design, synthesis, processing, and characterization of well-defined polymers with specific properties suitable for targeted applications.[1] The days when a new polymeric material was an ill-defined substance, often an insoluble residue in the flask, are long past. Currently, polymers can be synthesized with precision matching that of pharmaceutically active organic compounds. For example, preparation of ultrahigh-molecular-weight polyethylene (PE), suitable for body armor and cut-resistant gloves, with number-average molecular weight (MW) of M_n > 10,000,000 requires a chemoselectivity of propagation over chain-breaking reactions of 99.9999%. Synthetic polymers can be prepared with chains displaying unrivaled uniformity, predefined MW, controlled topology, and precisely selected end groups. Individual macromolecules can be prepared in the shapes of stars, combs, bottlebrushes, and rings or as networks with well-defined mesh size. The composition of individual copolymer chains can follow certain statistics, or change periodically, in either a smooth gradient fashion or abruptly, as in block copolymers that can spontaneously phase-separate into various predefined nanostructured morphologies. Useful functionalities can be precisely incorporated into macromolecules, whether it is at the end group, the center, or other specifically selected positions, to provide targeted properties. Thus, macromolecular engineering resembles, in some sense, total synthesis of natural products, where the entire macromolecule is accurately designed to provide the desired properties and a sequence of synthetic steps is used to create a specific polymer architecture with desired placement of functional groups. The very precise control of every detail of the macromolecular structure and chain architecture has enabled the development of numerous advanced polymeric materials that are needed in fields as diverse as coatings and adhesives, electronics, medicine and cosmetics, environment, and countless others.[1a,c]

Until recently, such advanced specialty polymers were made by living ionic or coordination polymerization, where chain-breaking reactions such as transfer or termination could be eliminated, but at the expense of elimination of any impurities, especially moisture, from the polymerization medium. On the other hand, nearly half of all polymers are produced by conventional radical polymerization (RP) under more "relaxed" conditions, often directly in water. These polymers include low-density PE, polystyrene (PS), and poly(vinyl chloride) (PVC) that are predominantly used as commodity materials. However, control over molecular structure in a RP is essentially impossible because radicals are very reactive intermediates and their lifetime, prior to irreversible termination, is less than 1 s.[2] It is impossible to execute control over macromolecular structure during such a short time. A new concept was introduced in order to tame this uncontrolled radical behavior. By inserting periods of ca. 1 min dormancy after each ca. 1 ms of activity, the overall life of propagating chains was extended from ca. 1 s to more than 1 day.[3] Thus, the 1 s of radical activity is expanded, as in an accordion, to several hours with hundreds of intermediate dormancy periods. This would be like extending person's life from 100 years to 3000 years, if after each 1 day of activity a person could be dormant for 1 month. This extension of the lifetime of growing chains from 1 s to over several hours was accomplished by insertion of multiple reversible radical deactivation steps. It has enabled synthesis of well-defined, essentially tailor-made polymers via macromolecular engineering.

Controlled radical polymerization (CRP; IUPAC recommends the term reversible-deactivation radical polymerization, RDRP) is a rapidly developing area of chemistry and polymer science with over 2000 papers published annually, the majority of which are on atom transfer radical polymerization (ATRP). Reversible deactivation is at the core of many modern controlled polymerizations, including carbocationic, ring-opening, or coordination polymerization, where active and dormant species

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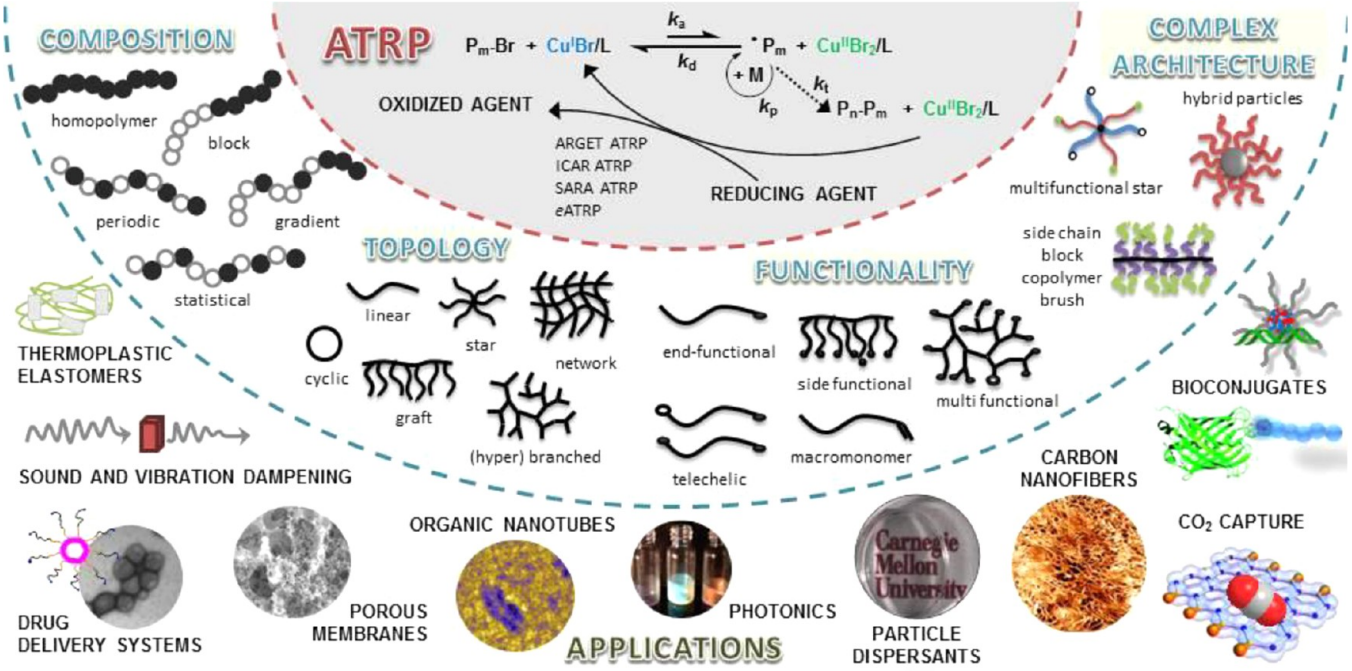
Scheme 1. Overview of New ATRP Techniques with ppm Amounts of Cu Catalysts, Engineering Macromolecular Architecture, and Applications of Resulting Materials[a]



[a]Adapted with permission from the works cited in ref 9.

dynamically exchange or reshuffle. Providing that the exchange reaction is fast compared to propagation, the small population of active species that is continuously replenished from the large pool of dormant species assures concomitant growth of all chains.

In classical RP, a low stationary concentration of growing radicals is established by balancing the rate of termination with a very slow continuous initiation. In order to grow chains with a high degree of polymerization, e.g., DP = 1000, the rate of propagation must be 1000 times faster than that of termination. This also means that rate of initiation must be 1000 times slower than that of propagation. This condition does not allow synthesis of well-defined polymers with complex architecture, as chains are continuously and slowly initiated and terminate after ca. 1 s lifetime. In most CRPs, a stationary steady-state concentration of radicals (generally lower but sometimes even higher than in RP) is established by balancing the rates of activation (conversion of the chains from dormant to active state) and deactivation. Termination still must be 1000 times slower than propagation but initiation can be as fast as, or even faster than propagation, resulting in concurrent growth of all chains and enabling synthesis of block copolymers, stars, bottlebrushes, and various well-defined hybrid materials. There are two key requirements for a successful CRP: (i) selection of appropriate conditions that ensure low proportion of irreversibly terminated chains and (ii) use of initiators/catalysts or chain-transfer reagents that provide concurrent growth of all chains via fast initiation and fast dynamic exchange between dormant and active species. The first condition requires an appropriate match of polymerization rate (i.e., concentration of radicals) with targeted degree of polymerization (concentration of dormant species/initiators). Thus, the concentration of radicals should be sufficiently low, unless low-MW polymers are targeted; otherwise, a high fraction of chains will be terminated. The second condition requires fast activation of initiators and transfer agents, in comparison with reactivation of macromolecular dormant species, as well as selection of mediating agents, including reversible radical traps, catalysts, and transfer agents, that react with growing radicals at rates comparable to the rate of propagation.

The three CRP systems that have been most often used are stable free-radical polymerization (SFRP),[4] catalytic atom transfer radical polymerization (ATRP),[5] and degenerative chain-transfer polymerization (DT).[6] In all these procedures control is achieved through establishing a dynamic equilibrium between the predominating dormant species and a low concentration of propagating radicals.[2b,7] ATRP is an attractive and highly translational technique across laboratories, disciplines, and levels of chemical expertise, due to the simple experimental setup, broad range of monomers and solvents used, and commercial availability of initiators (alkyl halides, which can also be easily attached to surfaces or biological molecules) and catalyst components, while maintaining exquisite control and versatility.

The aim of this Perspective is illustrated in Scheme 1, which presents recent advances in macromolecular engineering enabled by ATRP. We will first briefly discuss the fundamental mechanistic features of ATRP and review various initiation systems, especially those that employ very low concentrations of Cu catalysts. The low catalyst concentration methods are of major interest because their development has minimized the need for product purification, which in turn has made ATRP a "green" method. These techniques allow for the synthesis of high-MW polymers with designed molecular weight distribution (MWD). We will also review the role of the major components of ATRP reactions, including monomers, initiators, catalysts, and various additives. Then, the effect of media and external stimuli on polymerization rates and control will be discussed. Subsequently, we will present examples of elements of macromolecular architecture that can be precisely controlled, including chain length uniformity, shape, composition, and

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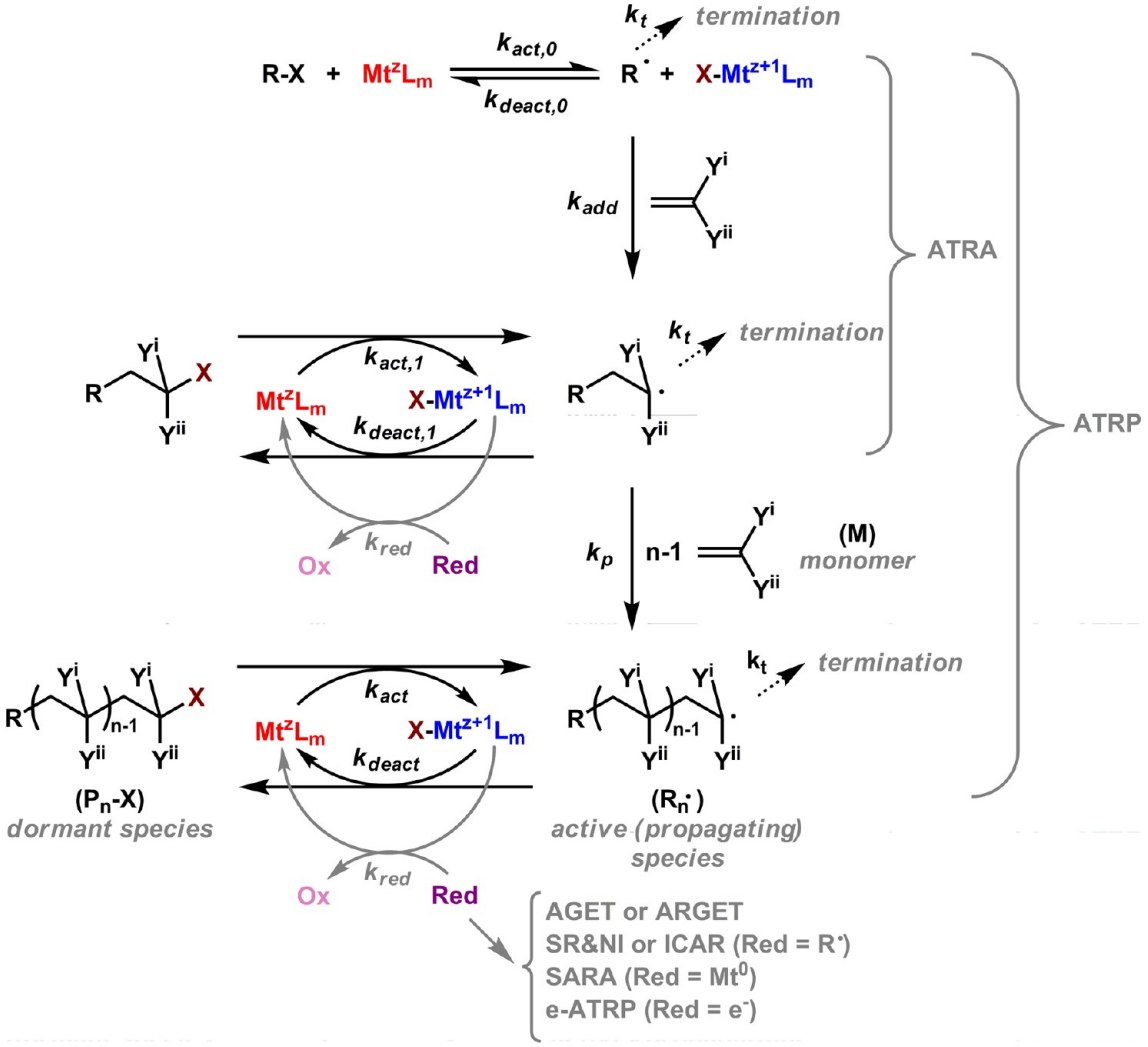
Scheme 2. Mechanism of Transition Metal Complex-Mediated ATRA and ATRP and Low-Catalyst-Concentration ATRA and ATRP Techniques in the Presence of Excess of Reducing Agents



functionality, as well as synthesis of polymers with complex architecture, including various hybrids and bioconjugates. We will also cover some examples of current and forthcoming applications of ATRP. We will conclude with some future directions and an outlook. An interested reader can consult earlier reviews on various aspects of ATRP.[3,5b,d−g,8]

2. KINETICS AND MECHANISM OF ATRP

ATRP relies on establishing an equilibrium between alkyl halide[3] or pseudohalide[10] initiating species, R-X, and radicals that are produced by the cleavage of the C−X bond by a redox-active, low-oxidation-state metal complex, Mt^zL_m (the activator, where Mt^z represents the metal atom or ion in oxidation state z and L is a ligand; throughout this text, for simplicity, the charges of ionic species are not shown). In the activation step (characterized by the rate constant k_{act}), the activator is oxidized to the corresponding high-oxidation-state metal complex with a coordinated (pseudo)halide ligand, $X\text{-}Mt^{z+1}L_m$ (the deactivator), which is able to rapidly transfer the atom or group X back to the radicals (deactivation, k_{deact}), transforming them into dormant alkyl (pseudo)halides. If the initially produced radicals reacted with a monomer, affording polymeric radicals $P_n^\bullet$ (n is the degree of polymerization, DP), the alkyl halide oligo- or polymeric molecules produced via deactivation are designated as P_n-X. From a mechanistic point of view, ATRP is closely related to the radical addition of alkyl halides across an unsaturated C−C bond, known as *atom transfer radical addition* (ATRA) or *atom transfer radical cyclization*.[11] ATRP is in fact ATRA, which involves both reactivation of the alkyl halide adduct of the unsaturated compound (monomer) and reaction of the formed radical with additional monomer molecules (propagation). Activation and deactivation occur throughout the polymerization. The deactivation should be sufficiently fast to ensure that only a small number of monomer units are added to the propagating radicals during each period of activity. ATRA and ATRP are presented in Scheme 2, which also shows ATRP initiating techniques in the presence of reducing agents, as will be discussed below.

The number-average degree of polymerization (DP_n) of the produced polymers is determined by the initial concentration ratio of monomer to initiator, $[M]_0/[R\text{-}X]_0$ (often referred to as targeted DP at complete conversion, $DP_{n,targ}$), and the monomer conversion. With fast initiation, no chain-breaking reactions, and a small number of monomer units added during each activation step, the formed polymers are characterized by a narrow MWD or low dispersity ($Đ = M_w/M_n$, where M_w is the weight-average

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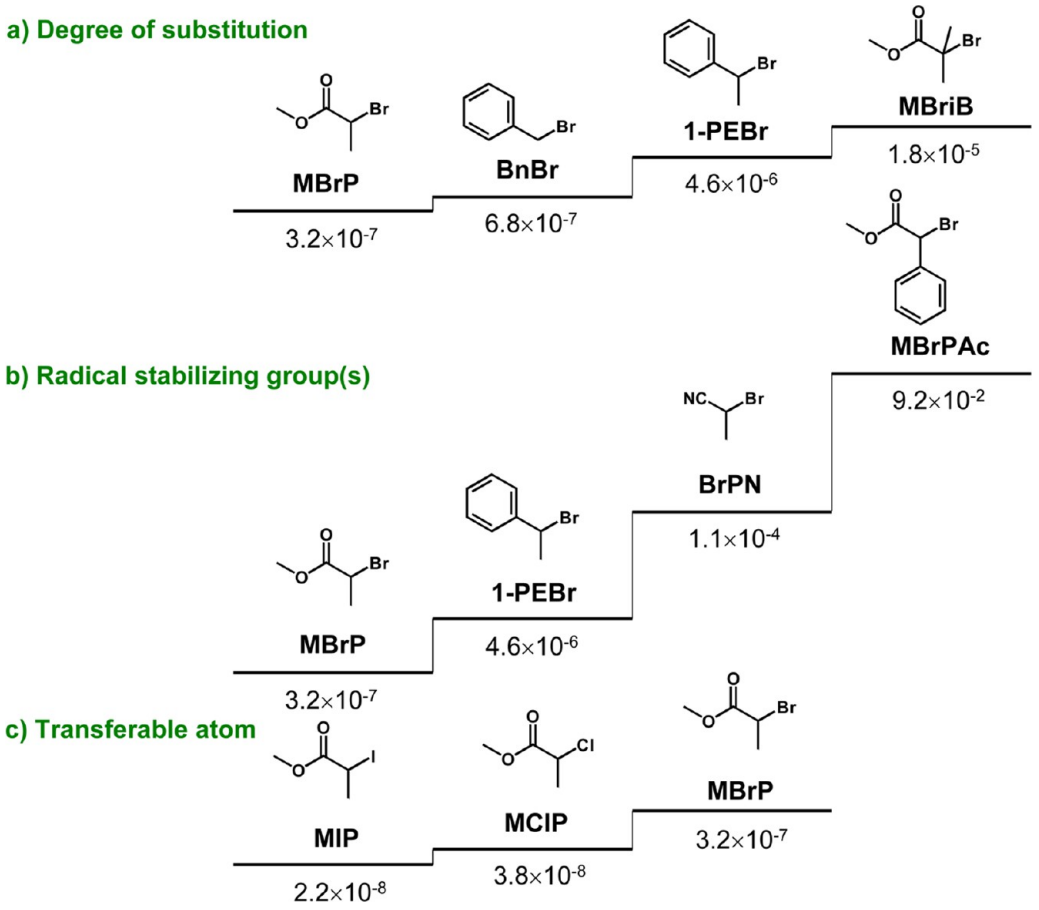

Figure 1. Effects of the degree of substitution (a), type of radical stabilizing groups (b), and nature of the transferable atom (c) on the values of K_{ATRP} for the reaction between various alkyl halides and the Cu^{I} complex of tris(2-pyridylmethyl)amine (TPMA) in acetonitrile at 22 °C. Data from ref 26a.

MW), close to unity. The value of $Đ$ decreases with conversion and with $k_{deact}[X\text{-}Mt^{z+1}L_m]$ according to eq 1.[12]

$$\frac{M_w}{M_n} = 1 + \frac{1}{DP_n} + \left(\frac{[R\text{-}X]_0 k_p}{k_{deact}[X\text{-}Cu^{II}L_m]}\right)\left(\frac{2}{conv.} - 1\right) \quad (1)$$

ATRP was discovered in the mid-1990s,[5a,c,13] and since then, many metal complexes, including those of Ti, Re, Ru, Fe, Rh, Ni, Pd, Co, Os, and predominantly Cu, have been employed as polymerization mediators, leading to excellent control with a range of monomers. Examples of useful metal catalysts are summarized in recent reviews.[5b,e,g,12,14]

Reaction Rates and Functionality. In ATRP, as in any radical process, continuous termination takes place. If a given CRP proceeds with the same rate as a conventional RP, then the concentration of propagating radicals, the rate of termination, and the concentration of terminated chains should be very similar to those of the RP. However, in conventional RP, essentially all chains are "dead", with the exception of very small fraction of growing chains that are continuously generated, and terminate after a very short period of growth (usually <1 s). In contrast, in ATRP, the large majority of chains are "living", mostly in the dormant state. However, the ever-present termination yields dead chains that cannot be reactivated, and it is important to quantify the amount or fraction of dead chains. The fractions of ω-chain end-functionalized (i.e., living, P_n-X) and terminated (T) chains depend upon the reaction conditions, e.g., the temperature, the nature of the monomer (through the reaction coefficients k_p and k_t), $DP_{n,targ}$, and the monomer conversion. In ATRP, the fraction of T (or the dead chain fraction, DCF, equal to the ratio $[T]/[R\text{-}X]_0$) is given by eq 2, in which it is assumed that the termination occurs exclusively via disproportionation (in order to keep the number of chains constant).[15]

$$DCF \equiv \frac{[T]}{[R\text{-}X]_0} = \frac{2DP_{n,targ}k_t[\ln(1 - conv.)]^2}{[M]_0 k_p{}^2 t} = \frac{2k_t[\ln(1 - conv.)]^2}{[R\text{-}X]_0 k_p{}^2 t} \quad (2)$$

According to eq 2, slower polymerization (longer t), particularly at comparatively low monomer conversion, leads to formation of a higher fraction of functionalized chains with preserved ω-ends, i.e., a lower fraction of dead chains. For example, to prepare poly(methyl methacrylate) (PMMA) at 80 °C with $DP_n = 60$ within 5 h, it is better to target a $DP_{n,targ} = 150$ and stop the reaction at 40% monomer conversion (the DCF in this case will be as low as 0.025) than to target a $DP_{n,targ} = 75$ and stop the reaction at 80% conversion (DCF = 0.123). The minimal reaction time required to reach a desired DP_n with preserved chain end functionality depends upon the reactivity of the monomer. It is possible to prepare poly(methyl acrylate) with DCF of only 10% (90% preserved chain ω-ends) for $DP_{n,targ}$ =

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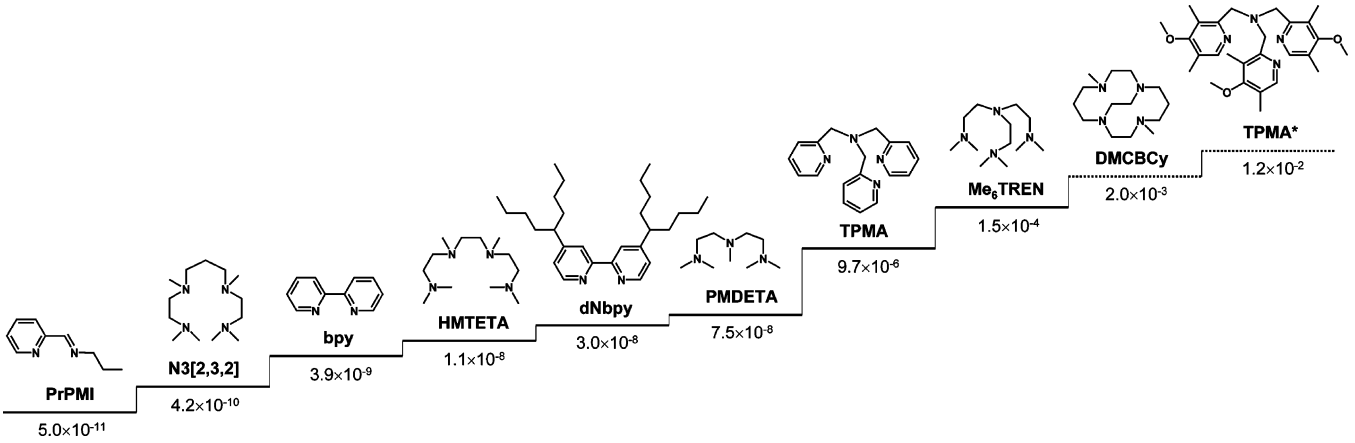

Figure 2. Effect of the ligand on the value of K_{ATRP} for the reaction between ethyl 2-bromoisobutyrate and Cu^I complexes in acetonitrile at 22 °C. The value for the DMCBCy[17] complex was estimated on the basis of the differences in reactivities of the Cu^I complexes of Me_6TREN and DMCBCy toward methyl chloroacetate and those of the Cu^I complex of Me_6TREN toward methyl chloroacetate and ethyl 2-bromoisobutyrate. The value for the TPMA* complex is estimated on the basis of the differences in reactivities of the Cu^I complexes of TPMA and TPMA* toward MBrP and those of the Cu^I complex of TPMA toward MBrP and ethyl 2-bromoisobutyrate. Data from refs 22b and 26a.

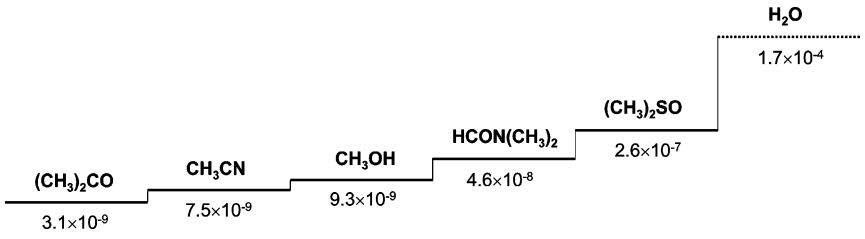

Figure 3. Effect of solvent on the value of K_{ATRP} for the reaction between 2-bromoisobutyrates with the Cu^I complex of HMTETA at 25 °C. The value for water was estimated from the equilibrium constant for the Cu^I complex of TPMA and the ratio of the reactivities of the HMTETA and TPMA complexes toward ethyl 2-bromoisobutyrate in acetonitrile. Data from ref 20.

500 at 60% monomer conversion in only 37 s. The same level of control requires 13 h for PMMA and 2.8 days for PS.[3]

ATRP Equilibrium. The ATRP process is characterized by the ATRP equilibrium constant (Scheme 2), which determines the reaction rate, as shown by eq 3.

$$R_p = k_p[M][R^\bullet] = k_p K_{ATRP}\frac{[M][P\text{-}X][Mt^z L_m]}{[X\text{-}Mt^{z+1}L_m]} \quad (3)$$

The value of K_{ATRP} ($= k_{act}/k_{deact}$) is determined by the strength of both the C−X and the Cu^{II}−X (or Mt^{z+1}−X) bonds. K_{ATRP} increases with the strength of the Cu^{II}−X or the *halogenophilicity* of the Cu^I complex and decreases with the strength or the bond dissociation energy (BDE) of the C−X bonds.

The values of K_{ATRP} for reactions mediated by the same complex increase with the degree of substitution at the carbon bonded to the transferable atom (e.g., compare the values of K_{ATRP} of BnBr and 1-PEBr, or of MBrP and MBriB, in Figure 1a). Also, the values of K_{ATRP} increase with the addition of strong radical-stabilizing groups (aryl, carbonyl, ester, cyano) attached to the carbon forming the C−X bond (Figure 1b). This is related to resonance stabilization as well as polar and steric effects.[16] The C−X BDE decreases in the order C−Cl > C−Br > C−I, but halogenophilicity of Cu^I is the lowest toward I and higher for Br and Cl. As a result of the two opposing trends, the values of K_{ATRP} of alkyl iodides are the lowest (due to very low iodophilicity of Cu^I) and increase as the halogen is changed to Cl and Br, respectively, as shown in Figure 1c.

The effect of the ligand on K_{ATRP} is profound (Figure 2) and is directly related to the Cu^I complex halogenophilicity, which is, unfortunately, not easy to determine experimentally. The halogenophilicity can formally be split into three parameters, which can be determined experimentally: (i) electron affinity of the transferable atom X, (ii) reducing power of the Cu^I complex with L (i.e., the redox potential of the $Cu^{II}L_m/Cu^IL_m$ couple, related to the ratio of the stability constants of the Cu^{II} and the Cu^I complexes),[18] and (iii) affinity of the $Cu^{II}L_m$ complex toward halide ions (*halidophilicity*[19] or stability constant of the X-$Cu^{II}L_m$ complex). For reactions with the same alkyl halide under the same conditions, the values of K_{ATRP} depend only on the reducing power of the Cu^I complex and the halidophilicity of the Cu^{II} complex. Both parameters can be measured simultaneously by determining the redox potential of the X-Cu^{II}L/Cu^IL complex redox couple. Electrochemistry is an important tool in assessing not only the reducing power of the activator but also the halidophilicity of the higher-oxidation-state metal complex.[18b,20] Numerous values of redox potentials of Cu complexes, relevant to ATRP, have been collected.[21] Ligands that form more-reducing complexes and more-halidophilic, higher-oxidation-state complexes yield more-active ATRP catalysts. As the electron-donating power of the substituents increases, the redox potential becomes more negative, increasing the ATRP catalytic activity.[22]

Bidentate ligands form Cu complexes of relatively low activity, although with many of them (e.g., derivatives of 2,2′-bipyridine or pyridineimine) the polymerization control is excellent for more-reactive monomers that form stabilized propagating radicals. For aliphatic amine-type ligands, the nature and size of the linker between the donor atoms influences the activity of the corresponding Cu^I complex. The number of C atoms

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between any two adjacent N donor atoms determines the coordination angle and strain in each chelate ring, and the mutual arrangement of contiguous chelate rings, both related to the stability of the complexes.[23] Ligands with a C_3 bridge between the N atoms form less-active Cu^I catalysts, as compared to ligands with C_2 bridges. Branched ligands form very active catalyst complexes. The most-active Cu-based ATRP activators are derived from tetradentate branched ligands such as cross-bridged cyclam (DMCBCy)[17] and particularly tris[2-(3,5-dimethyl-4-methoxy)pyridylmethyl]amine (TPMA*).[22b]

The values of K_{ATRP} change by several orders of magnitude as the solvent is changed, as shown in Figure 3.[20] The linear solvation energy relationship was employed to correlate catalyst activity in a number of organic solvents.[20] The very high values of K_{ATRP} predicted for aqueous media were experimentally confirmed.[24] A solvent can lead to an increase of one or two of the parameters that determine the magnitude of the halogenophilicity and to a decrease of the other(s). The reducing power of Cu^I complexes and the electron affinity of halogens are typically lower in acetonitrile than in alcohols, but the halidophilicity of the Cu^{II} complexes is markedly higher in acetonitrile. As a result of these opposing effects, the values of K_{ATRP} in acetonitrile and methanol are similar (Figure 3). The very low halidophilicity of Cu^{II} complexes in water (which leads to the poor deactivation efficiency in aqueous solvents) is more than compensated by the very high values of halogen electron affinity and the reducing power of the Cu^I complexes. As a result, the values of K_{ATRP} in water are extremely high (over 20,000-fold higher than in acetone or acetonitrile).[24,25]

Control in ATRP depends not only on K_{ATRP} but also on the rate constants of activation and deactivation. They determine how many monomer units are added during each intermittent activation step and directly affect the dispersity of the obtained polymers. Generally, activation rate coefficients increase and deactivation rate coefficients decrease as K_{ATRP} increases.[26]

Initiation Techniques in ATRP. *Normal, Reverse, Simultaneous Reverse, and Normally Initiated ATRP, and ATRP with Activators Generated by Electron Transfer.* The quest for a simple, robust ATRP, particularly on a large scale, that did not require handling oxidatively unstable reaction mixtures started as early as ATRP was discovered. In the original reports on ATRP, a combination of an alkyl halide and a lower-oxidation-state transition metal complex was used to reversibly generate the initiating radicals. The lower-oxidation-state metal complexes used as ATRP activators are sensitive to air, so removal of air was necessary. An alternative initiation technique was developed, termed *reverse ATRP*,[27] in which the higher-oxidation-state deactivating complex was added to the reaction mixture along with a radical source, such as a conventional radical initiator. After deoxygenation, the reactions started with the thermal decomposition of the radical initiator. The produced radicals reduced *in situ* the deactivator to the activator, and the ATRP equilibrium was established. The method required large catalyst concentrations and an approximately equimolar amount of radical initiators. Although various methods for catalyst removal were described,[28] it was highly desirable to develop low-catalyst-concentration ATRP, in which the need for purifying the final product would be eliminated or minimized. A combined initiation strategy was introduced, termed *simultaneous reverse and normally initiated* (SR&NI) ATRP,[29] in which the reaction mixture contained an alkyl halide, a smaller amount of radical source, and the oxidatively stable deactivator. As the radical source decomposed, the produced radicals initiated some chains and reduced the ATRP deactivator to form the activator, which then activated the alkyl halide and concurrently mediated normal ATRP. Active catalysts could be used at low concentrations, but the use of radical initiators led to formation of a fraction of chains that were not initiated by the alkyl halide. The next important step toward highly functionalized polymers was the development of *activators generated by electron transfer* (AGET) ATRP.[30] The method was a logical extension of work with zero-valent metals[31] and other reducing agents such as monosaccharides[32] or phenols.[33] AGET ATRP uses a combination of an alkyl halide initiator with an active ATRP catalyst in its higher oxidation state in conjunction with a reducing agent, which cannot initiate polymerization but can only reduce the deactivator. Numerous reducing agents have been employed in AGET ATRP, including Sn^{II} compounds,[30a] sulfites,[34] and ascorbic acid.[30b,35] AGET ATRP could also be conducted in the presence of limited amounts of air, provided that a sufficiently large amount of reducing agent was added to the system.[35]

ATRP in the Presence of ppm Amounts of Cu and Excess of Reducing Agents: ARGET and ICAR ATRP. In traditional ATRP, relatively large amounts of catalyst were used, often comparable to the amount of the initiator. Although very active ATRP catalysts were developed, they could not be used at very low concentrations because in ATRP, as in any other radical polymerization, radical termination occurs, leading to irreversible accumulation of the deactivator, $X\text{-}Mt^{z+1}L_m$, at the expense of the activating complex, Mt^zL_m, i.e., due to the persistent radical effect.[36] As a consequence, when all the activator is irreversibly transformed to deactivator, which can happen at low monomer conversion, the reactions stop. However, the rate of ATRP depends only upon the ratio of activator and deactivator concentrations but not upon their absolute concentrations (eq 3). If that ratio could be kept constant throughout the polymerization, the ATRP rate should remain high. To reach this goal, an additional redox cycle was employed that converted the higher-oxidation-state deactivator complex, formed during termination events, to the lower-oxidation-state activator. In the presence of reducing agents, ATRP could be successfully conducted to high monomer conversion at very low (often single-digit ppm) amounts of catalyst.[11d]

Both nonradical (Sn^{II} compounds, amines, hydrazines, etc.) and radical-based reducing agents have been successfully used, and the corresponding processes have been dubbed *activators regenerated by electron transfer* (ARGET)[37] and *initiators for continuous activator regeneration* (ICAR) ATRP (Scheme 2). In ICAR ATRP, similar to SR&NI ATRP or RAFT, some chains (typically 5−15 mol%) are generated that originate from the radical source used as reducing agent; therefore, if pure α,ω-end-functionalized or block copolymers are desired, ICAR ATRP is not the most appropriate synthetic procedure. Scaling-up ICAR ATRP may be challenging due to the large amounts of radical initiator needed, which, if the temperature is not controlled precisely, may quickly decompose and lead to fast and exothermic polymerization. Slow dosing of the initiator improves the process.[38] These problems could be avoided with nonradical-forming reducing agents. This was realized in ARGET ATRP, the protocol of choice for the synthesis of α-end functionalized or block copolymers free of nonfunctionalized homopolymers.[39] Only catalysts with a high value of K_{ATRP} successfully mediated a well-controlled ICAR or ARGET ATRP due to the sufficient fraction of deactivator.[40]

Catalyst may be involved not only in activation/deactivation processes but also in side reactions with propagating radicals

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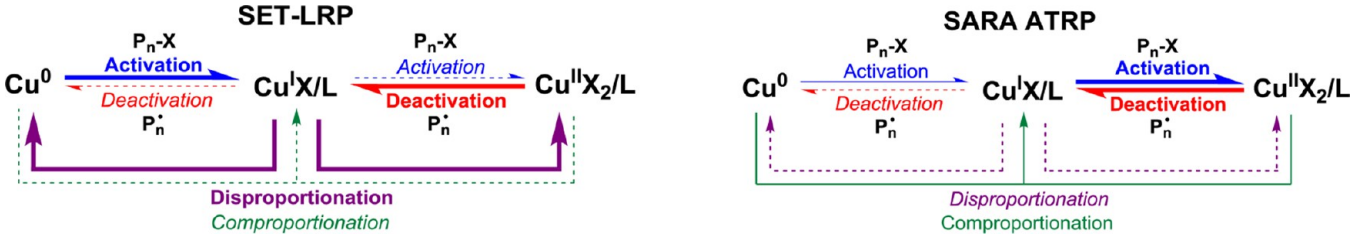
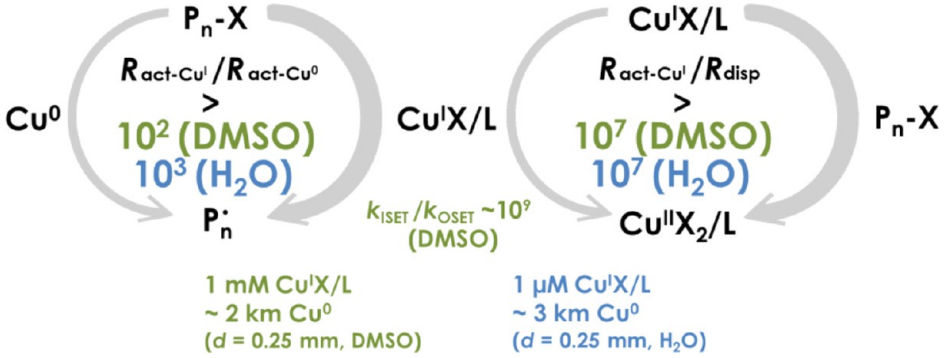
Scheme 3. Proposed Mechanisms of SET ATRP (Left) and SARA ATRP (Right)[a]



[a]The line thickness corresponds to the values of rates of the corresponding reactions; dotted lines indicate the slowest reactions that can be kinetically neglected. For simplicity, $P_n^{\bullet}$ formed in activation, P_n-X formed in deactivation and stoichiometry for disproportionation/comproportionation are neglected. In the originally proposed SET-LRP, no activation by Cu^I or comproportionation took place.[45] In SARA ATRP, absolute values of the rates determined at ca. 70% conversion in MA polymerization in DMSO ($[MA]_0$:$[MBrP]_0$:$[Me_6TREN]_0$ = 200:1:0.1, MA/DMSO = 2/1 (v/v), V = 4.5 mL, S = 1.27 cm^2 (l = 4 cm, d = 1 mm), T = 25 °C) are ca. 3×10^{-3} M/s (propagation, activation by Cu^I and deactivation by Cu^{II}), 10^{-6} M/s (termination and supplemental activation by Cu^0), 10^{-7} M/s (comproportionation), 10^{-9} M/s (deactivation by Cu^I), and 10^{-10} M/s (disproportionation).[48]

Scheme 4. Comparison of Activation Rates of Alkyl Halides (Left, by Cu^0 and Right, by Cu^I) and Role of Cu^I (Left, Disproportionation and Right, Activation) in Polymerization of Acrylates in DMSO and in Water[a]



[a]Bottom part illustrates unrealistic lengths of Cu^0 wire (d = 0.25 mm) needed to match activity of [Cu^I/Me_6TREN] = 1 mM in DMSO and [Cu^I/Me_6TREN] = 1 μM in water.

(oxidation/reduction, formation of organometallic species, or β-H elimination) and irreversible termination, which limit attainable MWs in classic ATRP.[41] Reaching high MWs became possible[42] when the low-catalyst-concentration ATRP techniques were developed, because in such systems the ratio of the rates of propagation to side reaction was higher.[41,43] Importantly, the MWD width could be controlled by adjusting the amount of catalyst, which cannot be achieved by other CRP methodologies.[44]

Zero-Valent Metals as Supplemental Activators and Reducing Agents. The use of zero-valent metals (Cu^0 and Fe^0) in ATRP was first reported in 1997,[31] and the metals were used to regenerate the lower-oxidation-state activators via reduction of the deactivators. They were also used as direct activators in the absence of added Cu^{II} species. In 2006, the polymerization of acrylates initiated by alkyl halides in the presence of Cu^0 and Me_6TREN in polar solvents was reinvestigated.[45] Alkyl halides were proposed to be exclusively activated by Cu^0 via an outer-sphere electron-transfer (OSET) process, yielding radical anions $RX^{\bullet-}$ and subsequently radicals. The Cu^I generated in the activation was claimed to instantaneously disproportionate to reform the activator, Cu^0, and a Cu^{II} halide-based deactivator. The only species playing an active role in the polymerization control were postulated to be Cu^0 and Cu^{II}. The process was given a new name, *single-electron-transfer living radical polymerization* (SET-LRP),[46] although all components (Cu^0, polar solvents, acrylates, and Me_6TREN) were previously used in ATRP.[5b] The proposed mechanism of the SET-LRP process is depicted on the left-hand side of Scheme 3. The right-hand side of Scheme 3 shows an alternative mechanism of the same reaction based on *supplemental activators and reducing agents* (SARA) ATRP.[47] It should be noted that the reactions involved in both mechanisms are the same (with exception that alkyl halides are activated by OSET in SET-LRP and by inner-sphere electron transfer (ISET) in SARA ATRP), but the contributions to the activation of alkyl halides by Cu^0 and/or Cu^I as well as disproportionation/comproportionation equilibrium are dramatically different. Thus, detailed kinetic studies under conditions relevant to polymerization were performed to ascertain which of the proposed mechanisms better describes the polymerization reactions.

Electrochemical,[49] kinetic (including experimental[50] and simulations[48,50b]), and computational[49,51] studies demonstrated that in systems where Cu^0, Cu^I, and Cu^{II} coexist, alkyl halides are predominantly activated by Cu^I, although some supplemental (<1%) activation by Cu^0 also takes place. Furthermore, the activation of alkyl halides by either Cu^0 or Cu^I via ISET is ca. 9 orders of magnitude faster than that by OSET, and the calculated activation rate coefficients assuming the OSET mechanism are vastly lower than the experimentally observed ones.[49,52]

Contrary to the originally claimed[45] rapid and complete disproportionation of Cu^I, the disproportionation/comproportionation process is relatively slow in DMSO. In fact, in typical polymerizations, the disproportionation equilibrium may not be

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reached due to the low values of the rate constants and very low concentrations of Cu^I species, and the polymerization control is dictated by a much faster classical ATRP activation/deactivation equilibrium. In these systems, Cu^0 serves as a SARA to compensate for radicals "lost" in termination reactions.

It is interesting to note that even in aqueous media, where disproportionation is thermodynamically favored, it does not contribute significantly in polymerization because of the exceptionally low [Cu^I], dictated by the extremely high activity of Cu^I in the activation process and high K_{ATRP} values.[53] Thus, proper assessment of the overall mechanism in the presence of solid Cu^0 requires precise determination of all rate coefficients and concentrations of the involved reagents. The surface area of Cu^0 newly formed during polymerization via disproportionation or mechanical scrubbing constitutes only 1% of the originally used wire.[47,54] If the newly formed (due to disproportionation) Cu^0 were extremely active, it would lead to excessive termination processes and a loss of chain end functionality, contrary to experimental observations.

Under typical polymerization conditions in polar media and also in water, alkyl halides are activated over 10^2 times faster by Cu^I than by Cu^0. Activation proceeds by ISET ca. 10^9 faster than by OSET, and disproportionation of Cu^I is 10^7 times slower than activation of alkyl halides and also slower than comproportionation, as shown in Scheme 4. Thus, polymerization in the presence of Cu^0 proceeds via the SARA ATRP mechanism, depicted on the right-hand side of Scheme 3 and not SET-LRP (left-hand side), because none of the postulated mechanistic features of SET-LRP (including instantaneous Cu^I disproportionation, OSET activity in activation, and formation of alkyl halide radical anions) could be experimentally validated.

3. ATRP TOOLBOX: MANIPULATING THE OUTCOME OF THE REACTION

ATRP is a catalytic process, and one has to consider a number of factors that affect the outcome of the polymerization to select the proper reaction conditions needed for a specific well-defined polymer.

Monomers. The range of monomers polymerized by ATRP in a controlled fashion is extremely large. However, some challenges still remain. For instance, the polymerization of acidic ((meth)acrylic acid, 4-vinylbenzoic acid, sulfonic or phosphonic acids) or strongly coordinating monomers, in the presence of which the deactivator halidophilicity is very low, would require the development of new, strongly halidophilic catalysts. The successful ATRP of monomers forming difficult-to-activate alkyl halide chain ends (vinyl esters, *N*-vinylpyrrolidone) will require the development of catalysts more active than those currently available.

Solvents. ATRP has been successfully carried out in a broad range of solvents, including both common organic solvents and the "greener"[5e] ones such as protic solvents (alcohols, water),[39b,55] supercritical CO_2,[56] ionic liquids,[57] and poly(ethylene oxide).[58] In addition, heterogeneous ATRP has been reported, mostly in aqueous media.[59] Solvents affect conventional radical polymerization due to changes in the values of the propagation rate constants k_p,[60] or due to viscosity effects on the termination rates. In ATRP, the solvent can interact with the catalytically active complexes in both oxidation states, which can have dramatic consequences on the reaction rate (owing to effects on the value of K_{ATRP}[12,20,25,43]) and the polymerization control (often due to X-Cu^{II}/L dissociation, particularly important at low catalyst concentrations, and/or competitive complexation[18b,19b]). In some instances, mostly due to solubility of monomers or polymers, the use of slightly acidic or coordinating solvents may be required. To be able to carry out ATRP in such solvents, the development of more-halidophilic catalysts is needed.

Reducing Agents and External Stimuli. To select the proper reducing agent for ICAR and ARGET ATRP, one has to be aware of its reactivity toward all reaction mixture components. ARGET ATRP could be the process of choice when monomers are inert to the reducing agent and the product of its oxidation.[61] Reducing agents that yield relatively strong acids upon oxidation may protonate the ligand of the ATRP catalyst, leading to catalyst "poisoning" and loss of control or even preventing polymerization. Basic or nucleophilic reducing agents (e.g., hydrazine or phenylhydrazine) can coordinate to the metal center of the catalyst or participate in nucleophilic substitution[62] or elimination reactions with the alkyl halide-type chain ends. The nucleophilic substitution is slower for alkyl chlorides than for alkyl bromides.

Photochemical initiation of ATRP has been reported,[63] in which switching the light on and off could start and stop the reaction. ATRP can also be started, stopped, and restarted by the application of electric field. This approach, named electrochemically mediated ATRP or eATRP,[24,64] allows for the use of very low concentrations of catalyst. In eATRP, activator regeneration is accomplished by electrons supplied by the cathode.

Complex-Forming Compounds. The addition of Lewis acids to an ATRP reaction mixture can have a negative impact on the polymerization control, due to competitive complexation to the ligands forming the ATRP catalyst or abstraction of the halide ligand from the deactivator. However, ATRP carried out in the presence of complex-forming compounds can lead to the formation of well-defined polymers with controlled stereosequence. For instance, the addition of Y^{III} or Yb^{III} trifluoromethanesulfonate (triflate) allows for stereocontrol in the ATRP of *N*,*N*-dimethylacrylamide, which is due to preferential complexation of the cations to the ultimate polymer unit. This allowed preparation of the first stereoblock copolymers by ATRP.[65] Similar results have been observed in the ATRP of acrylamide.[66] Grafting of highly isotactic poly(*N*-isopropylacrylamide) arms from polymeric backbones yielded polymer brushes with altered hydrophilicity.[67] Fluorinated alcohols were also used to control the stereospecificity of the polymerization.[68]

Temperature. Temperature can affect the reactivities of all species involved in an ATRP reaction and also the stability of the catalytically active complexes. Complexation is exothermic, and increasing the temperature destabilizes both oxidation states of the catalyst.[19b] The temperature affects the rate constants of activation.[69] The entropies of activation with Cu^I/PMDETA complex were negative (from −156 to −131 kJ mol^{-1} depending on the alkyl halide), which implied the formation of ordered transition-state structures.

Pressure. The preparation of high-MW polymers can be achieved not only via low-catalyst-concentration ATRP but also at high pressures which increase the ratio k_p/k_t.[70] Propagation has a negative, whereas termination has a positive volume of activation, and increasing the pressure increases the ratio k_p/k_t. ATRP under high pressure yielded polymers with significantly higher MW than the reactions carried at ambient pressure.[70] While pressure increases the values of K_{ATRP} in Cu-mediated ATRP,[71] it decreases K_{ATRP} in some Fe-mediated ATRP.[72]

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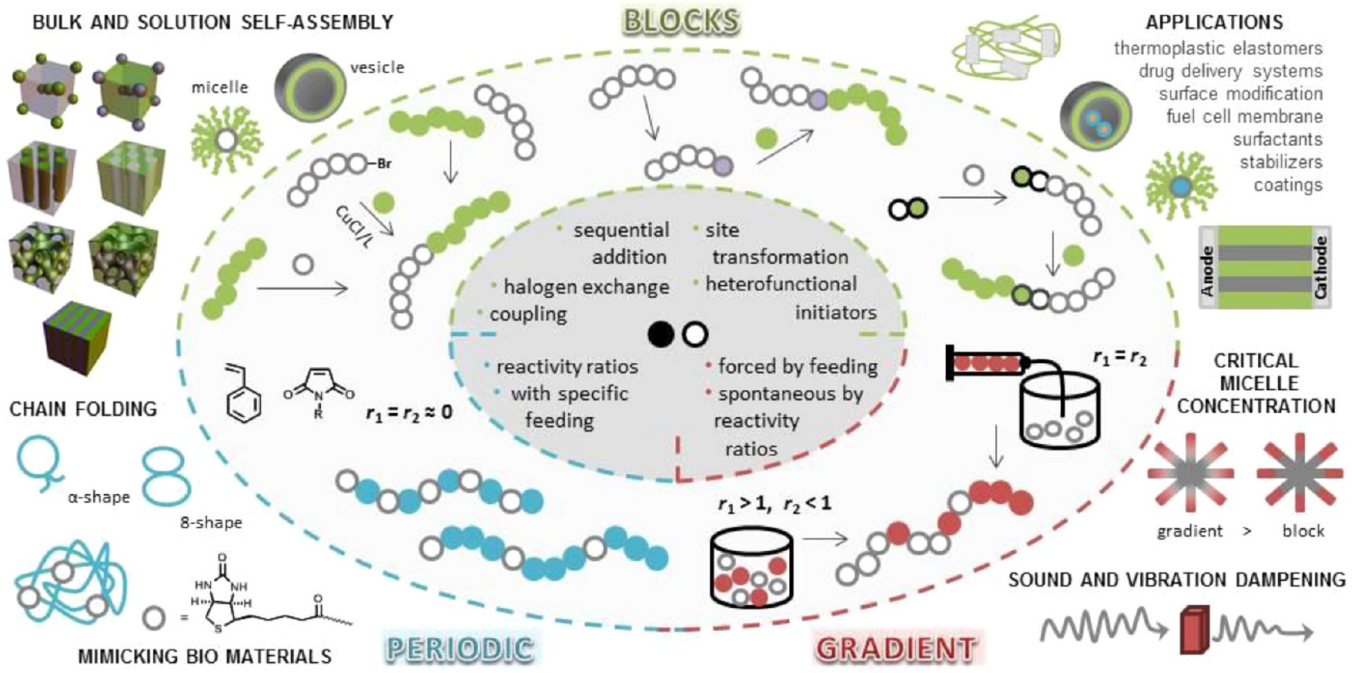
Scheme 5. Synthetic Routes for the Preparation of Block, Gradient, and Periodic Copolymers and Their Applications



Further studies on the effect of pressure in ATRP will be of both fundamental and practical importance.

4. ELEMENTS OF CONTROL AND NANOSTRUCTURED MATERIALS BY ATRP

ATRP and other CRP processes offer a dramatic expansion of various elements of macromolecular engineering for production of functional polymeric materials, in comparison with conventional RP, which provides only ill-defined homopolymers and statistical copolymers. These elements include (cf. Scheme 1) (i) control of MW and MWD; (ii) chain composition in the form of periodic, gradient, and segmented copolymers (blocks and grafts); (iii) shape or topology of polymer chains, exemplified by linear, cyclic, branched (including regular combs or stars), molecular brushes, and networks; (iv) site-specific chain functionality, such as end-functional telechelics with various functional side- or mid-chain groups, multifunctional stars prepared from functional monomers, initiators, or capping agents, and functional polymers formed via various postpolymerization techniques; and (v) hybrid materials, including hybrids with polymers prepared by other polymerization methods, with inorganics or natural products (bioconjugates).

RP shows an excellent tolerance to many functional groups; however, it has two fundamental limitations: unavoidable radical termination and poor stereocontrol, due to the sp^2 hybridization of propagating radicals.[2a] In ATRP, the appropriate selection of reaction conditions and monomers strongly suppresses the fraction of terminated chains,[15] allowing for preparation of polymers with low dispersities, high MWs, and precisely controlled architectures. In addition, polymerization in the presence of specific additives can enhance stereocontrol, especially in the polymerization of acrylamides.[65]

Current synthetic efforts in polymer chemistry are focused on the preparation of materials with well-defined structures and low dispersities. Many of the resulting (co)polymers, particularly those with segmented structures, self-organize during processing but often require a very narrow fabrication window in order to exhibit all attainable unique properties.[73] During the past several years, synthesis of such (co)polymers was the main focus in many synthetic laboratories and resulted in the successful development of a plethora of materials, many of which were previously inaccessible. However, instead of a constant race focused on preparing polymers with lower dispersities, an exploration of materials with controlled heterogeneities may be equally attractive.[74] Polymers with controlled heterogeneities may lead to a paradigm shift in selection of materials for high-value applications. As discussed in previous sections, the diminished level of catalyst in ATRP concurrently reduces the environmental impact of transition-metal catalyst and provides the ability to control/design MWD, according to eq 1. Dispersity depends on the corresponding rate coefficients and targeted degree of polymerization ($[R\text{-}X]_0$), on conversion, and reciprocally on $[X\text{-}Cu^{II}L]$. Thus, by simple alteration of the total amount of copper catalyst in the system, one can affect $Đ$; this also is possible by adjusting the K_{ATRP} value (by selecting the ligand).

MWD becomes an important tool for controlling polymer morphology. It may provide access to stable, bicontinuous microstructures, which are especially interesting for membranes, biomedical applications, and conducting polymers.[75] This approach opens access to materials with new, stable morphologies and also relaxes the processing regime and widens the processing window.

Chain Composition. Chain composition is an important parameter that affects macroscopic properties of materials.[76] Although the reactivity ratios of comonomers used in conventional RP and ATRP are essentially the same, the living character of ATRP provides an easy access to block, periodic, and gradient copolymers not accessible by conventional RP. Small differences in polymers made by ATRP and RP can be assigned to competitive activation/deactivation equilibria.[76b] Scheme 5 presents some examples of copolymers with controlled chain composition.

The upper part of Scheme 5 shows examples of block copolymers that can self-assemble in bulk or in solution. Their

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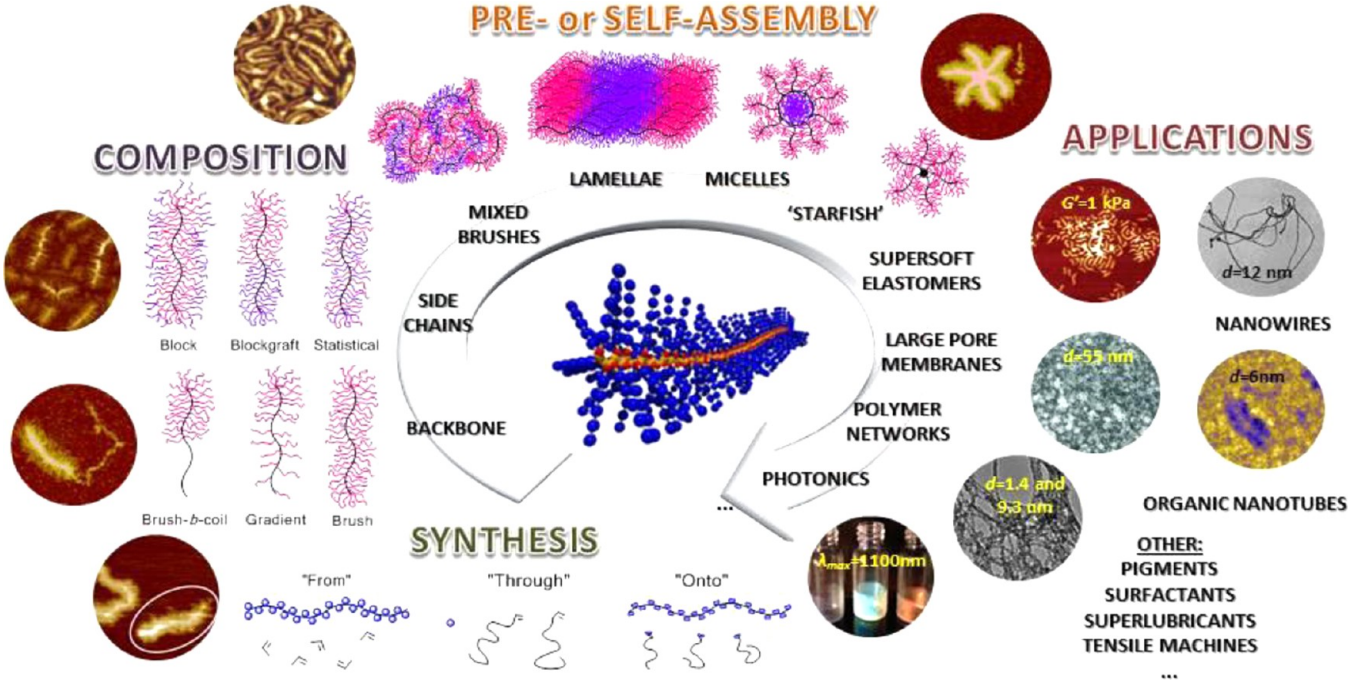
Scheme 6. Molecular Bottlebrushes with Various Composition and Architecture, Their Properties, and Potential Applications[a]



[a]Adapted with permission from refs 9c, e, and 92.

applications range from thermoplastic elastomers to drug delivery systems, coatings, sealants, templates, or membranes.[77] There are two important requirements for synthesis of well-defined block copolymers: efficient initiation/cross-propagation and preservation of chain end functionality, i.e., "livingness". Thus, in the synthesis of segmented copolymers, it is important to follow a block order based on the reactivities of the chain ends derived from each monomer, or more precisely on the ATRP equilibrium constants. In ATRP, this order is acrylonitrile > methacrylates > styrene ~ acrylates > acrylamides and is dictated by a combination of polar and steric effects.[16] However, ATRP offers an additional tool, halogen exchange, that provides a unique ability to efficiently chain-extend, for example, a polyacrylate macroinitiator with a methacrylate.[78] It is possible to prepare multiblock copolymers with several or even 10 consecutive blocks by using the same class of comonomers (acrylates) with ca. 90% (by weight), and 54% (by number) efficiency.[79] Stereoblock copolymers were prepared in a one-pot process by ATRP of dimethylacrylamide with $Y(OTf)_3$ complexing agent.[65a]

Block copolymers have also been prepared by combination of ATRP with polymer segments prepared by other mechanisms. For instance, several macroinitiators with halogen end-functionality were prepared by step-growth polymerization, coordination, anionic or cationic vinyl polymerization, ring-opening polymerization (cationic, anionic, metathesis), or even conventional radical polymerization or two different CRP techniques.[80] It is possible to carry out ATRP concurrently with segments prepared by some other polymerization mechanism, for example, ring-opening metathesis polymerization (ROMP) or anionic ring-opening polymerization (AROP), as they do not interfere with one another and can be independently controlled by different catalysts.[81] For example, Sn^{II} octoate catalyzes AROP of lactones but also acts as a reducing agent in AGET or ARGET ATRP.[82] In fact, this type of concurrent AROP/ATRP process led to discovery of AGET ATRP.[30a]

ATRP is an efficient tool for preparation of gradient copolymers[83] by spontaneous copolymerization, based on different reactivity ratios of comonomers, or through continuous controlled feeding of one monomer. An important property of gradient copolymers is the quality of the gradient, i.e., a deviation of composition along the copolymer chain from the ideal gradient behavior. This quality can be correlated with the dynamics of intermittent activation/deactivation and, consequently, with the dispersity of MW and was recently visualized by AFM.[84] The term "gradient" may refer to not only copolymer composition but also stereoregularity.[65b] Gradient copolymers can also be formed in ATRP when one comonomer is converted *in situ*, during polymerization, into another one.[85] Gradient copolymers show very broad glass transition temperatures and can be used as sound or vibration dampening materials; they have high critical micelle concentrations and can be used as efficient surfactants for dispersed media and also for polymer blends.

Periodic copolymers employ copolymerization of a strong electron-accepting monomer and an electron-donating comonomer.[86] It is possible to feed one comonomer periodically and generate either regular or irregular periodic systems. It is also possible to preorganize comonomers in a specific sequence and subsequently copolymerize them by either a cyclopolymerization or a step-growth radical polymerization.[87] Neither process currently offers access to high-MW polymers, and the step-growth process is typically characterized by a broad MWD. Another approach to periodic copolymers employs coupling the active chain end of functional block copolymers. For example, "click" coupling of propargyl ether with diazido-terminated pentablock copolymer PS-b-P*n*BA-PMMA-b-P*n*BA-PS (P*n*BA = poly(*n*-butyl acrylate) resulted in formation of periodic block copolymers.[88] The multisegmented block copolymers prepared by step-growth coupling had higher glass transition temperatures

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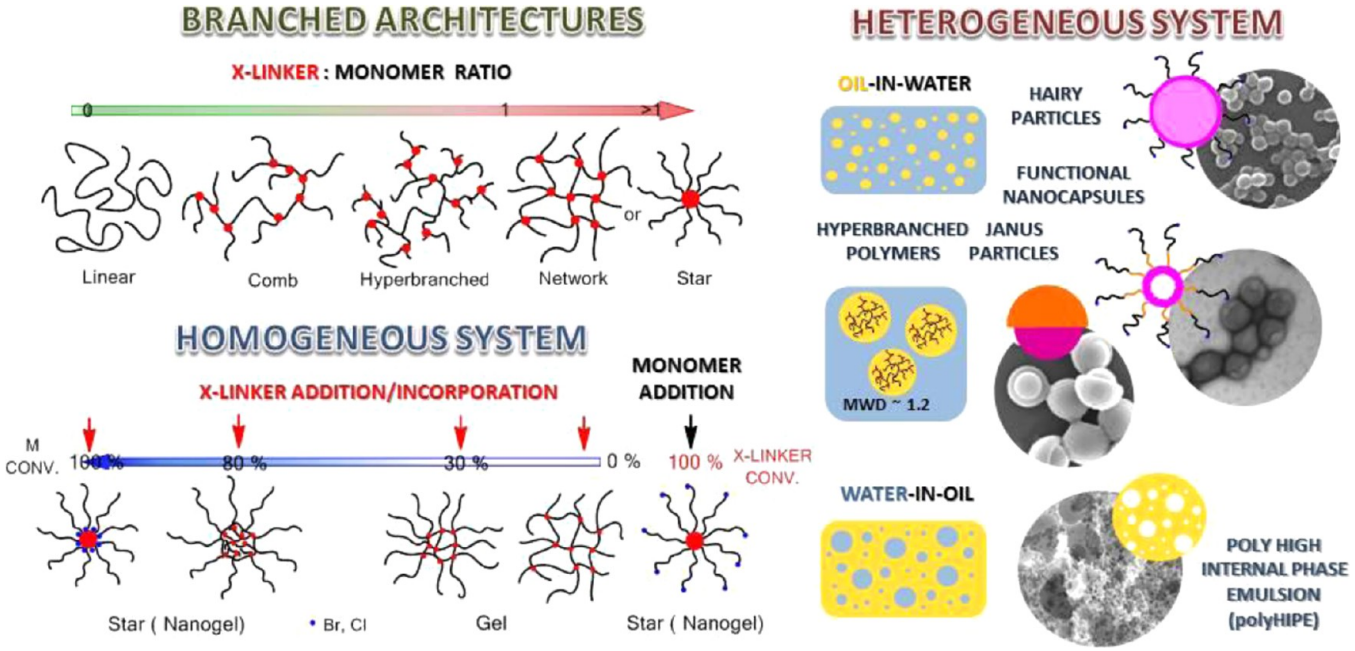
Scheme 7. Polymers with Branched Architectures via Copolymerization of Monomer and Cross-linker[a]



[a]Structures depend on the cross-linker:monomer ratio and the moment of cross-linker incorporation. Adapted with permission from refs 9b and 102.

and higher modulus than the lower-MW precursors. A more-detailed perspective on chain composition is presented in section 6.

Chain Topology. In ATRP, the use of either a monofunctional or difunctional initiator leads to formation of linear polymers, growing in one or two directions, respectively. The resulting mono- and difunctional macroinitiators can be used as precursors for AB diblock and ABA triblock copolymers, respectively. With difunctional initiators, chains can grow concurrently in two directions, and it is easier to reach higher MW. Also, if termination proceeds by coupling, although dispersity would increase, chains can continue to grow, due to the preserved functionalities, at both ends.[89]

Multifunctional initiators attached to a central core can yield star or graft polymers by the core-first approach.[90] Growth from polymer chains with several initiating sites leads to graft copolymers, with density of grafts defined by the distance separating the initiating sites. Molecular brushes shown in Scheme 6 are the ultimate example of graft copolymers with very high graft density, with side chains emanating from essentially every repeating unit. They can be formed by grafting-from the backbone but also by grafting-through (using macromonomers) and by grafting-onto (by attaching end functional polymers to a backbone with multiple reactive sites). The majority of molecular brushes are prepared by the grafting-from procedure. The individual molecules can reach $M_n > 10^7$ and length exceeding 1 μm and can be easily imaged by AFM.[8c] Some examples of brushes with various architectures are shown in Scheme 6. In addition to "simple" homopolymer brushes with uniform density, gradient brushes or brush−coil architectures, core−shell, block−graft, statistical brushes, and star-shaped polymers with three, four, and six brush-based arms have been prepared.[91] Other topologies include mikto-arm brushes, cyclics, and brushes peripherally decorated with various functional groups such as dyes or pH-, light-, or temperature-sensitive moieties.[8b]

Brushes may self-assemble into lamellar structures with periodicity in the range of hundreds of nanometers and display photonic properties.[93] They can serve as templates and form ordered intercalated structures, or self-assemble to materials with large or smaller pores, organic nanotubes, and nanowires.[93b] They are excellent models for probing chemical bond strengths as molecular tensile machines. They can be slightly cross-linked and form stable supersoft elastomers with moduli of ca. 1 kPa.[94] Thus, they resemble hydrogels, but they can never dry, as the network is "diluted" by covalently attached side chains that are short enough to prevent entanglement instead of solvent. Brush polymers also have excellent lubricating properties.[94c]

(Hyper)branched Polymers, Stars, and Networks. Most homopolymers prepared by ATRP are linear due to a small extent of transfer to polymer. Branching can be intentionally enhanced by addition of branching reagents. One approach is based on inimers, i.e., compounds that act as initiators and monomers. Various combinations of (meth)acrylic monomers with haloester initiators were used to generate hyperbranched homopolymers by ATRP.[95] The degree of branching can reach 50%, depending on the reaction conditions and structure of monomers. As in other AB* inimer systems, including AB_2 monomers in step-growth reactions, there should be no gelation.[96] Branching density can be "diluted" by copolymerization with other vinyl monomers. Incorporation of a (bio)-degradable linker between the ATRP initiating site and vinyl group yields degradable branched polymers.[97]

Branched polymers can also be formed by copolymerization with a divinyl monomer, as shown in Scheme 7.[98] In contrast to conventional radical polymerization, where cross-linking and gelation occur at very low monomer conversion, leading to nonuniform networks, in ATRP the gel point and network structure can be precisely controlled.[99] The gel point depends not only on the initial stoichiometry but also on the moment of addition of the cross-linker to the reaction mixture and its reactivity or functionality. For example, if the divinyl compound is added at the end of polymerization, stars are efficiently formed. If the divinyl compound is homopolymerized by ATRP under high dilution first, it can form a soluble multifunctional core that

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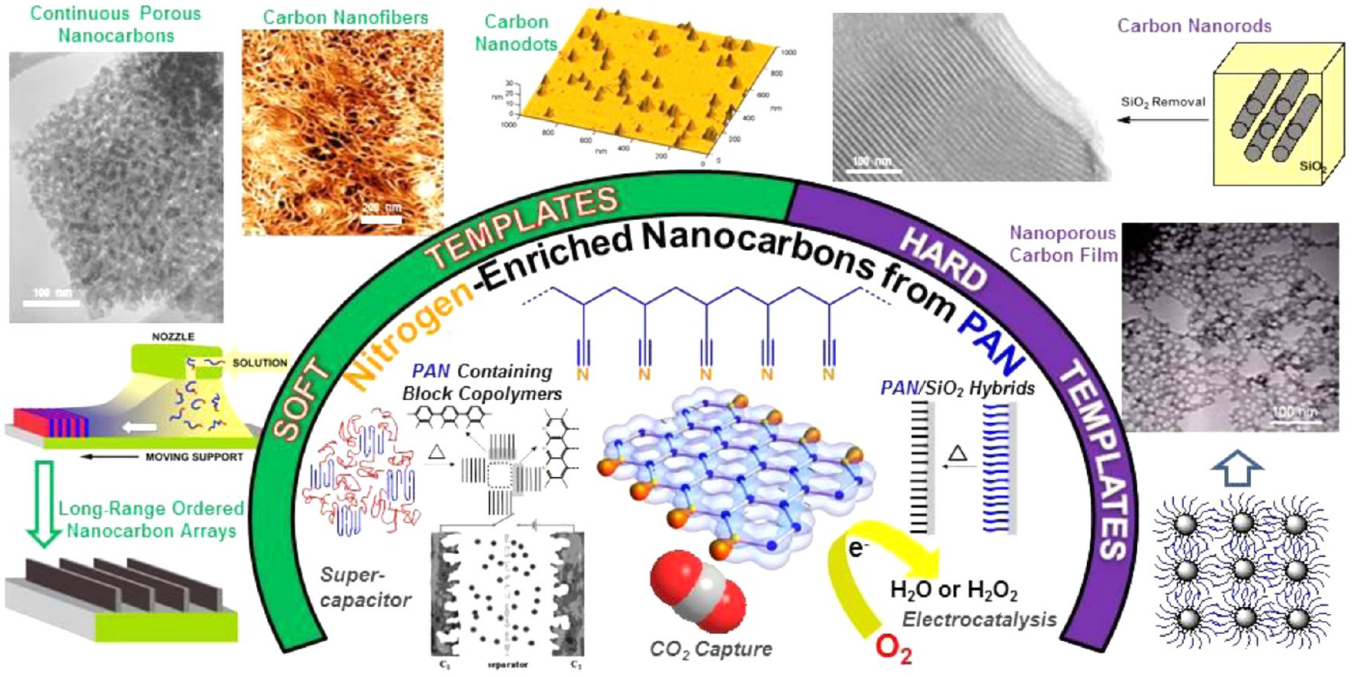
Scheme 8. Preparation of Multifunctional N-Enriched Nanostructured Carbon Materials from Polyacrylonitrile-Based Precursors Engineered via ATRP[a]



[a]In the center is shown polyacrylonitrile (PAN), a semi-crystalline polymer, as a precursor for partially graphitic carbon materials. The carbonization involves stabilization under air at >200 °C and fusing ladder structures under Ar or N_2 above 500 °C. Above the arc, to the left is shown soft templating based on the self-assembly of PAN block copolymers: carbon nanodots from pre-assembled poly(acrylic acid)-*b*-PAN micelles, with PAA outer-shells; carbon nanofibers from phase-separated P*n*BA-*b*-PAN copolymer with a cylindrical morphology, with PBA as a sacrificial block; PBA-*b*-PAN with a bicontinuous morphology for continuous porous nanocarbons; and zone-casting to form long-range ordered lamellar carbon arrays. To the right is shown hard templating with etchable SiO_2: PAN grafted from the concave surface of mesoporous silica, yielding carbon nanorods (d = 10 nm); and nanoporous carbon films synthesized from PAN grafted from silica nanoparticles, with mesopores (d = 15 nm) after etching silica. Below the arc, it is shown that the partially graphitic nanocarbons contain pyridinic N-atoms at the graphene edges with potential applications: electrode materials for supercapacitors mediating reversible proton-coupled ET, sorbents for selective CO_2 capture, and electrocatalysts for oxygen reduction reaction via a four-electron-transfer process with the same overpotential as a Pt catalyst. Adapted with permission from refs 9d and 105.

can be used to grow arms of stars by a one-pot core-first approach. Under high dilution, it is possible to obtain soluble cross-linked polymers, sometimes even single molecules.[100] Using templated polymerization of cross-linkers under ATRP conditions allows for the preparation of ladder-shaped macromolecules.[101]

An interesting opportunity is offered by cross-linking in dispersed media, not only oil in water but also water in oil, i.e., inverse miniemulsion. Instead of macroscopic gels, one can prepare "living" alkyl halide-functionalized nanogels. They can be loaded with drugs and other cargo or complexed with nucleic acids, and, for cross-linkers with (bio)degradable groups, the nanogels are still able to degrade to short primary chains, facilitating efficient release of their content. Such gels contain accessible dormant/living chains that can be extended with other monomers, forming "hairy" particles.[103]

Polymerization in a confined environment provides an additional advantage of initiating polymerization not only inside the droplets but also from the interface.[102a] This can be accomplished by using amphiphilic block copolymers with ATRP-reactive functionality as surfactants. Such block copolymers can contain latent functionalities (e.g., azides, which do not interfere with ATRP) and act as dual-reactive surfactants.[104] This approach provides a facile route to cross-linked droplets with peripheral functionality and functional nanocapsules. The peripheral functionality can be used to grow other chains or click on certain dyes or targeting moieties. For degradable cross-linkers with acetal, ester, or disulfide units, nanocapsules can be efficiently degraded and release their content.

An interesting example is thermal self-cross-linking of polyacrylonitrile (PAN). It is commercially used, with the subsequent graphitization step, for production of micrometer-sized carbon fibers. Similar cross-linking and carbonization can be used to generate N-doped nanostructured carbons via either soft templating with block copolymer or hard templating with mesoporous silica and silica nanoparticles (cf. section 5), as shown in Scheme 8. A more-detailed perspective on chain topology is presented in section 6.

Functionalities. In linear polymers, functional groups can be placed (i) at the α-end (tail), (ii) in the backbone (repeat units), or (iii) at the ω-end (growing head). For the α-end group, initiators with desired functionality or its precursor is used, as presented in the left part of Scheme 9.[8e] (Macro)initiators with azide, alkene (e.g., allyl),[106] or alkyne[107] functionality are attractive for click-coupling and other functionalization reactions. Dihalide or multihalide macroinitiators containing (bio)-degradable functional groups[108] (e.g., disulfide[109]) can incorporate functionality in the center of the chain; they are relevant in the biomedical field. ATRP initiators with *N*-succinimidyl or disulfide groups can react with exposed thiol groups from proteins.[110] A biotin-containing ATRP initiator was used to prepare a polymer that selectively reacted with avidin.[111]

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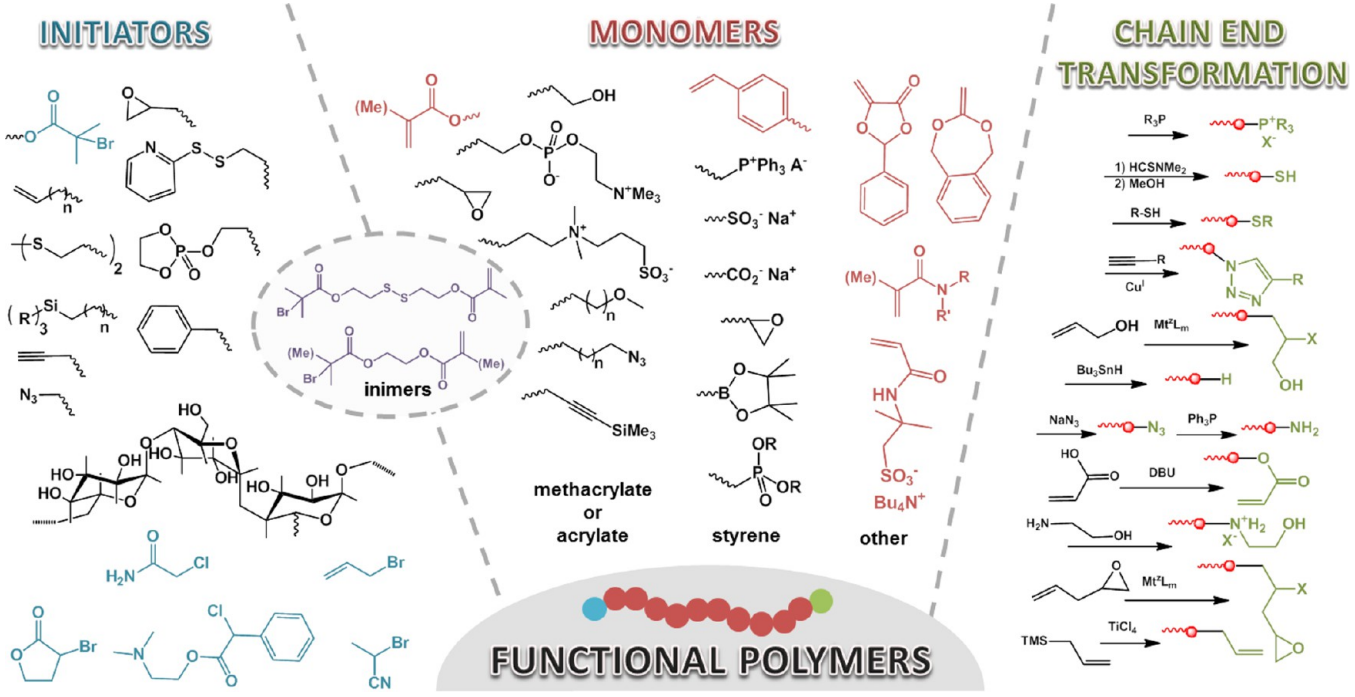
Scheme 9. Examples of Molecules Used To Form Functional Polymers by ATRP, from Functional Initiators (Blue), Monomers (Red), and Inimers, and by Chain End Transformation (Green)



Multiple functional groups can be incorporated into the backbones of polymers prepared by ATRP using either direct polymerization of functional monomers or polymerization of monomers in their protected form. Their density and distribution can be regulated by statistical copolymerization and/or monomer feeding. ATRP is tolerant to many polar functional groups, with the exception of those that are incompatible with any radical process or those that destroy the catalyst or alkyl halide chain ends. A number of water-soluble, hydrophilic, or polar monomers—neutral,[19a,55,112] ionic (cationic[19a,113] and anionic[114]), and zwitterionic[115]—have been polymerized in a controlled fashion by ATRP. The polymerizations could be carried out in protic, alcohol, or water-based media.[5e,12,116] Naturally derived and bio-based (renewable) monomers[117] have been successfully polymerized by ATRP.[118] Monomers with epoxide (glycidyl) groups[61,119] serve as precursors to many functional polymers. With the development of the very efficient azide−alkyne[88] and thiolene and thiolyne[120] click chemistry,[121] a vast number of functional polymers[122] have become accessible. Many of these click-type approaches can be and have been successfully combined with ATRP.

Polymers prepared by ATRP are actually macromolecular alkyl halides, and chemical transformation via nucleophilic substitution or radical or electrophilic addition leads to ω-end-functional polymers. The nucleophilic substitution of halides with azide ions yields azide-capped polymers.[123] They can participate in click reactions or be reduced to amine-capped polymers.[88] Other radical or electrophilic additions and nucleophilic substitutions of the alkyl halide chain ends of ATRP polymers have been employed.[8e] The generation of macroradicals from polymers prepared by ATRP via reaction with an ATRP catalyst, followed by monoaddition to nonpolymerizable alkenes with a functional group, is an efficient yet somewhat under-explored approach to ω-functional polymers.

In addition to functional initiators and monomers, Scheme 9 also shows functional compounds (containing ester or disulfide[97] groups) that are both monomers and initiators, i.e., inimers, the polymerization of which yields functional hyperbranched polymers, as mentioned above.

Organic/Inorganic Hybrids. Synthesis of organic/inorganic hybrid materials is among the most rapidly developing fields of materials science, and the development has largely been facilitated by ATRP.[9a] Some fundamental principles of surface-initiated (SI) ATRP, including elements of control and examples of hybrid materials, are presented in Scheme 10. Generally, grafting-from SI ATRP is much more often used than grafting-through or grafting-onto procedures for preparation of hybrid materials.[124] The process starts with the attachment of ATRP initiator onto a surface that can be concave, convex, or flat. For the modification of silica or oxidized silicon surfaces, chlorosilanes and alkoxysilanes with covalently attached ATRP initiators are used. Thiol- and disulfide-containing ATRP initiators are used to attach the initiating groups to gold, and the corresponding carboxylates or phosphonates are used for iron oxides. Use of phosphine oxides, catechols, and other functionalities is also successful. Grafting density can reach up to 1 chain/nm^2 but can be easily decreased by using a mixture of tetherable compounds some of which contain active ATRP functionalities and the other(s) − "dummy" functionalities.[125] Densely grafted chains are strongly elongated, cannot entangle, and form surfaces with extremely low friction.[126] Less-dense brushes start to entangle and can eventually form mushroom-like structures.[127] Chain growth from surfaces proceeds with kinetics similar to that determined for solution ATRP.[126a,128] However, efficient exchange reactions, especially from flat surfaces, require either addition of sacrificial initiator or an additional deactivator, since the latter cannot be formed in a sufficient amount via a spontaneous persistent radical effect.[124] Radical termination between chains grown from the surfaces of different nano-

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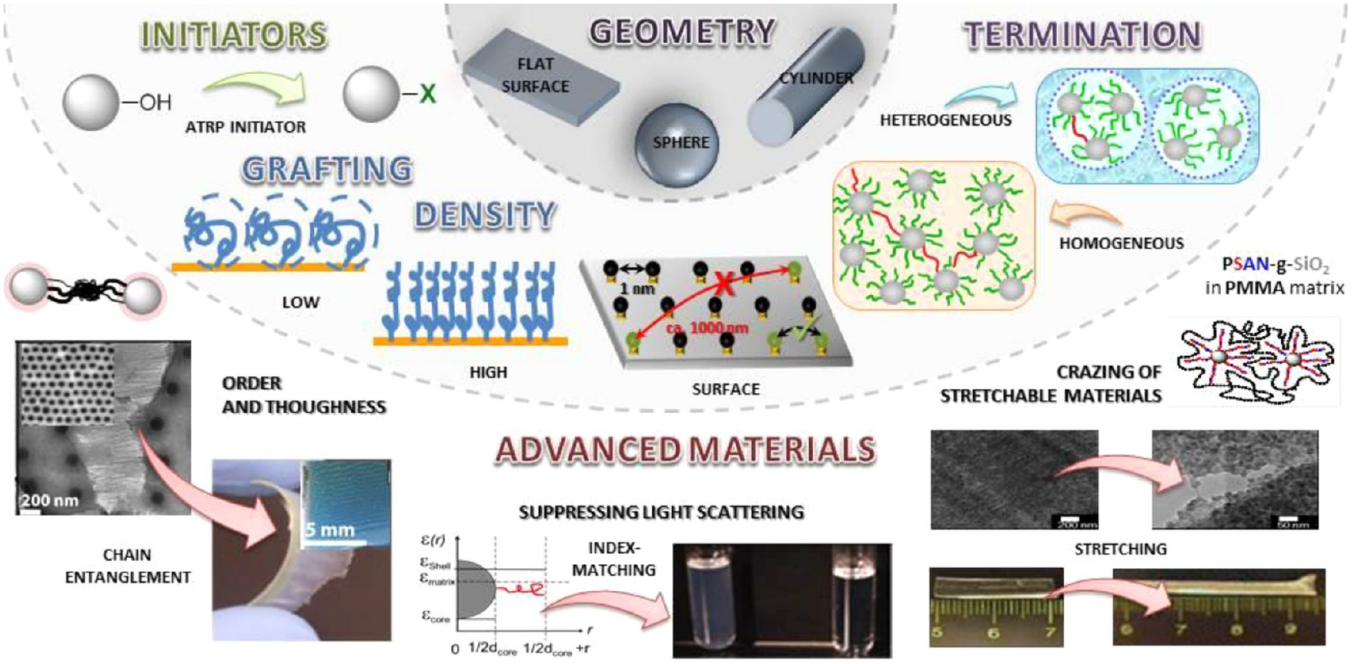
Scheme 10. Synthesis of Well-Defined Polymer/Inorganic Hybrids via SI ATRP and Some Examples of Hybrid Materials[a]



[a]Shown are surface modification of inorganic supports with various geometries and composition with tetherable ATRP initiators; control of grafting density by tetherable initiators with either ATRP active or inactive sites; principle of termination on flat surfaces via "migration effect" and suppression of macroscopic gelation in miniemulsion; self-assembly of tough hybrids (via chain entanglement) into ordered photonic materials with strong iridescence; null scattering by matching the overall refractive index of hybrids with that of a solvent or polymeric matrix; and stretchable and optically clear materials with 70 wt% silica based on blends of hybrids with short poly(styrene-*co*-acrylonitrile) (PSAN)-grafted brushes (DP = 20), dispersed in PMMA matrix. Adapted with permission from refs 9a, 125, and 131.

particles can lead to formation of a gel. It is possible to prevent macroscopic gelation by conducting the reaction in a miniemulsion or under high pressure.[129] Intra-arm termination on flat surfaces can happen only if the chains are sufficiently close. Since only a ppm fraction of the polymeric species is in the form of radicals, the latter are separated on average by ca. 1000 nm. However, the radical centers can "migrate" via activation and deactivation and eventually can terminate.[130]

It is possible to control MW, MWD, and density of the tethered brushes on the surface in addition to their composition and topology. In addition, brushes with bimodal distribution of the grafts, binary/mikto-arm brushes, Janus particles, and nanoparticles with variable and controlled cross-linking were prepared.[126a,128b,132]

Properties of hybrid materials can synergistically combine the best of inorganic and organic constituents. SI ATRP is an efficient methodology to modify various membranes[133] and to prepare biofunctional hybrid materials.[134] Brushes from flat surfaces have excellent self-lubricating and tribological properties.[126b,c] They have very good antifouling and antimicrobial properties. They can be switched from superhydrophobic to superhydrophilic, providing self-cleaning surfaces. Brushes grown from nanoparticles can improve their dispersibility and stabilize them, or enhance mechanical properties, while retaining other properties (magnetic, optical, luminescent, etc.). A careful selection of brush length is needed to reach a chain entanglement regime, which depends upon graft density, curvature of the surface, and nature of polymers, to increase the toughness of bulk hybrid particles.[135] The resulting nonbrittle one-component hybrid materials can be highly ordered, forming flexible, iridescent structures that could be used as photonic paints.[136] Optical properties of hybrids can be fine-tuned by matching the refractive index (RI) of the organic and inorganic parts (by manipulating size, MW, and graft density) to the RI of the solvent or matrix and making them "invisible", with essentially null scattering.[125,136] It is possible to uniformly disperse nanoparticles with low-MW polymeric brushes within a high-MW matrix if the enthalpy of mixing is favorable, as is the case for poly(styrene-*co*-acrylonitrile) and PMMA,[131] as shown in Scheme 10.

Bioconjugates. Another very rapidly expanding area for materials prepared by ATRP includes various bioconjugates with proteins, nucleic acids, carbohydrates, and other biomolecules (Scheme 11).[137] The bioconjugates can be formed by several general procedures: (i) synthesis of polymer with a functionality capable of bonding to a natural product, followed by a coupling reaction;[138] (ii) modification of a natural product with an ATRP initiating site, followed by ATRP of selected monomers;[139] (iii) modification of an ATRP end group to grow a natural product via classical protection/deprotection pathways;[140] and (iv) radical copolymerization of conventional monomers with those containing biomolecules, such as sugars, lipids, and fragments of nucleic acids or peptides, often in the protected form.[137a,b,141] Each of these procedures has some advantages and limitations.[141] Scheme 11 presents some examples of bioconjugates.

Synthesis of protein polymer hybrids by coupling procedures is most often accomplished via clicking the *N*-maleimide-terminated polymer chains with a SH-cysteine moiety in proteins or the activated ester-terminated chains with an NH_2 moiety (e.g., from lysine).[137,142] The process generally provides a random or statistical distribution of polymer chains attached to the protein. Another approach is to incorporate an anchoring group in a specific position in the protein using genetic engineering. The most common ligation procedure is via azide or alkyne using Cu-catalyzed azide/alkyne cycloaddition (AAC)

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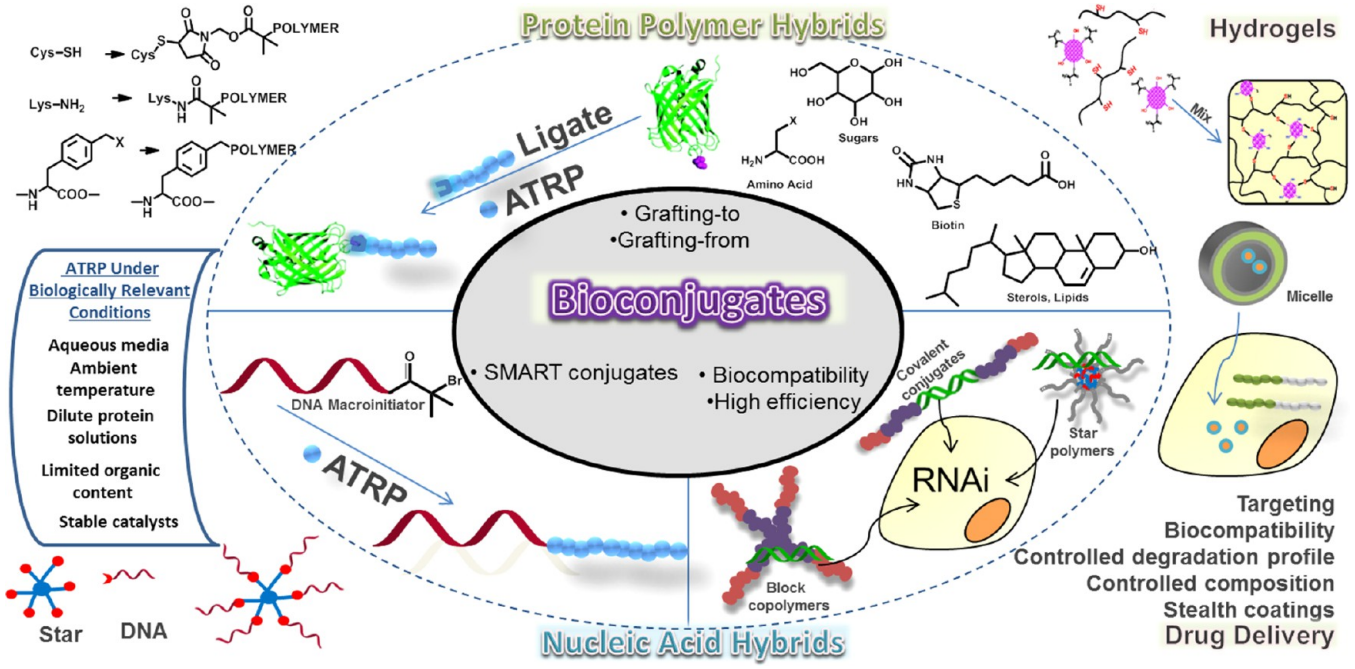
Scheme 11. Bioconjugates Prepared by ATRP



with a complementary group in a polymer chain. Instead of utilizing an azide/alkyne group, it is possible to directly incorporate ATRP initiator and grow polymer chains directly from the protein.[143] ATRP should be carried out under biorelevant conditions, at ambient temperature in water or even buffer and high dilution, using ppm amounts of stable, very active Cu/TPMA complexes.[39b,139] Ascorbic acid was used as the reducing agent; it was slowly and continuously fed to the reaction mixture to compensate for activators lost in radical termination.

ATRP has been also successfully combined with nucleic acids.[138,144] Both clicking via AAC and growing a block copolymer from DNA with a terminal ATRP initiating moiety were successful. Moreover, conjugates of proteins with ATRP-prepared polymers were complexed with DNA to form stars or even reversible networks.[138] Nucleic acids such as siRNA were complexed with stars and nanogels with cationic charges, e.g., protonated polymers derived from (2-(*N*,*N*-dimethylamino)-ethyl methacrylate (DMAEMA) or polymers derived from quaternized DMAEMA) prepared by ATRP and then released inside cells to "silence" enzymes. Similarly, plasmid DNA was released to increase enzyme expression.[145] Another interesting approach relied on covalent attachment of polymeric escorts to the passenger strand of siRNA (PEPsi RNA), which was then conjugated with a guide strand to form a precisely controlled molecular complex.[146] Other structures with controlled release and degradation profiles prepared by ATRP useful for gene or drug delivery include micelles formed from amphiphilic copolymers, nanogels, or injectable hydrogels prepared from thiolated hyaluronic acid, and degradable nanogels with peripheral acrylate functionality.[147] A more-detailed perspective on hybrids and bioconjugates is presented in section 6.

5. APPLICATIONS

The prerequisite for a successful commercial application of any synthetic methodology is an appropriate balance between cost and product performance. The recently developed ATRP methods, using ppm amounts of Cu in the presence of reducing agents,[148] are less expensive and environmentally more benign than the original ATRP processes.[149] ATRP can be carried out in bulk, in organic solvents, and in water under homogeneous and heterogeneous conditions. High conversions can be also attained in relatively short times under specific conditions, noted above. The range of monomers polymerizable by ATRP is constantly expanding, including monomers from renewable resources, such as various lactones, e.g., Tulipalin A,[118] rosin acid derivatives, itaconates, and other vinyl monomers.[117]

Polymers prepared by ATRP have been commercially produced in the United States, Japan, and Europe since 2002.[150] These polymers can be used as sealants,[151] lubricants,[152] oil additives with improved thickening behavior and shear stability, and viscosity modifiers.[153] End-functional and telechelic copolymers,[154] gradient copolymers,[155] block copolymers,[156] and star and comb polymers can be used as wetting agents, blend compatibilizers,[157] pigment dispersants,[158] surfactants,[159] or cosmetic additives.[160] The pigment stabilizers were used for coating compounds, prints, images, inks, or lacquers and other disperse systems.[156] Segmented copolymers containing polyolefin segments and polar blocks/grafts enhance blend miscibility, surface hydrophilicity, conductivity, and antibacterial properties.[161]

Polar thermoplastic elastomers were prepared by a continuous bulk ATRP process or by sequential addition of monomers to an ongoing emulsion ATRP.[162] They are oil resistant and recyclable. They can also be synthesized in a one-pot process using ARGET ATRP or by ICAR with initiator feeding.[38] Multifunctional initiators were used to prepare star-blocks, grafts, or brushes with block side chains. For example, a polar P*n*BA-*b*-PAN three-arm star-block copolymer shows thermoplastic properties over a broad temperature range, from −50 to +270 °C.[163] Bottlebrush macromolecules with a long backbone and densely grafted soft P*n*BA side chains behave as supersoft elastomers with a very low modulus plateau in the soft gel range around 1 kPa,[94a] making the material extremely soft. Bottlebrush macromolecules can also be designed to function as excellent ionic conductors.[164]

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ATRP was successfully used for "grafting-from" flat, convex, and concave surfaces, with the thickness of the polymer brushes precisely controlled by systematic variation of grafting density and DP_n of the tethered polymers.[124,165] Modification of surfaces with thin polymer films can be done to tailor surface properties such as hydrophilicity/hydrophobicity, (bio)compatibility, adhesion, adsorption, corrosion resistance, and friction. The surface properties can also be tuned by tethering block copolymers, with the composition and size of each polymer segment affecting the morphology and behavior of the polymer brushes.[166] Polymers with quaternary ammonium ions effectively kill cells and spores by disrupting cell membranes. Monomers such as DMAEMA or 4-vinylpyridine that can be quaternized and provide biocidal activity were polymerized by ATRP and generated antibacterial materials.[167] Antimicrobial surfaces were prepared by grafting-from[168] or grafting-onto surfaces[168b] or by depositing onto the surfaces of other polymers.[169] A similar approach was applied for grafting-from various nanoparticles, providing a simple approach to transportable, reusable water purification composite materials.[170] ATRP-functionalized solid particles were utilized as the stationary phase for analytical metal affinity chromatography columns for separation of proteins and synthetic prion peptides.[171]

Functional copolymers prepared by ATRP were used for drug delivery.[8d] Triblock acrylate-based block copolymers were prepared by ATRP as matrices for paclitaxel delivery from coronary stents.[172] Stable, biodegradable poly(oligo(ethylene oxide) monomethyl ether methacrylate) nanogels, cross-linked with cleavable disulfide linkages, prepared by ATRP in inverse miniemulsion, could be used for targeted drug delivery scaffolds that degraded into lower-MW polymers to release the encapsulated (bio)molecules.[8f,173] Nanostructured hybrid hydrogels, with sizes of ca. 100 nm, were incorporated into larger three-dimensional matrices, generating drug delivery scaffolds suitable for tissue engineering applications.[147a] Poly(ethylene glycol) (PEG) star polymers containing GRGDS peptide sequences on the star periphery were synthesized by ATRP of oligo(ethylene glycol) methyl ether methacrylate via an "arm-first" method. Those star polymers were biocompatible, and their rapid cellular uptake was observed by flow cytometry.[174] Stars and nanogels with degradable cationic cores were successfully used for gene delivery.[145] Various natural products were successfully covalently conjugated with polymers prepared by ATRP via grafting-from and grafting-onto procedures.[137a,b,142,143,175]

6. FUTURE PERSPECTIVES

Mechanism and Process Optimization. The profound mechanistic understanding of ATRP provides a more efficient way to prepare better-defined polymers by increasing the selectivity of the polymerization, reducing the amount of catalyst, and expanding the range of polymerizable monomers. Future research directions should include procedures for incorporation of new initiators with (pseudo)halogens that can be directly used in subsequent reactions (e.g., in step-growth reactions as polyurethane precursors) and new monomers, such as those from renewable resources and those with lower ATRP reactivity (e.g., vinyl esters) and unprotected acidic functionality. The continued development of new catalysts is perhaps even more important, as it will enable expansion of the range of monomers and reduction of the amount of transition metals used in the procedures. The new ligands should strongly stabilize both Cu^I and Cu^{II} species to "survive" dissociation at ppm concentrations and avoid displacement under acidic conditions and by anions or other nucleophiles that can competitively coordinate with Cu species. They should form complexes with very high values of K_{ATRP} (governed by redox potential and halidophilicity) but should also provide a very fast deactivation, essentially diffusion controlled. High halidophilicity is especially important in aqueous media, where the $X-Cu^{II}$ bond is easily cleaved heterolytically. This can be compensated by addition of salts with halide anions or by pseudohalide anions with much stronger affinity to Cu^{II}. The design of new ligands should include electronic effects (charge- and electron-donating substituents).[176] The very active Cu^I species may not only react with alkyl halides but also form a direct bond with alkyl radicals, generating organometallic species[22b] that can either dissociate back or participate in catalytic chain transfer or catalytic radical termination.[41] To overcome these problems, ligands with some auxiliary functionality should be designed to prevent formation of organometallic species and β-H elimination. New ATRP catalysts could be bio-inspired, based on some known redox-active enzymes such as laccase or hemin.[177] The ATRP catalysts could potentially be metal-free, as successfully used for ATRP with alkyl iodides.[178]

It is also important to develop new reducing agents and understand the reduction process (mechanism, factors affecting the rates) in ARGET and SARA as well as potential side reactions that may occur in some systems. Nonchemical reducing agents such as electrical current or light have been already successfully used. Reducing agents could be fed continuously and could be regenerated to the original state and release halogens that could be used again for the synthesis of initiators. Although some applications may not require catalyst removal at the ppm of Cu level, some others may need extensive purification of the materials down to ppb of residual metal. Thus, efficient and economical ways to remove and reclaim residual Cu are needed; they may include special absorbents, smart systems responding to external stimuli such as temperature or magnetic forces, electrodeposition,[64b] and other not yet explored techniques.

New additives should be developed that could complex reversibly with monomers and plausibly affect chemoselectivity (alter reactivity ratios and diminish extent of termination) or stereoselectivity (tacticity). They can simultaneously act as reducing agents. It will be very interesting to design catalysts and additives that can be temporarily activated by external stimuli and provide control of rates of even relative comonomer reactivities.

Conversion of ATRP batch systems to continuous processes is very attractive.[179] This will require exploration of various feeding processes and knowledge of complex stabilities, heat dissipation, or various transport phenomena.[180] The use of organic solvents should be reduced. They can be replaced by water in either homogeneous or heterogeneous systems. The reactions could be run in bulk, ideally to high conversion, or to a limited conversion with recovery of unreacted monomer. The effect of temperature and pressure should be fully explored to optimize reaction conditions, speed up the ATRP process, avoid vitrification, and at the same time diminish contributions of side reactions.

To summarize, new ATRP and other CRP systems should allow fast, clean, selective, and environmentally benign synthesis of various well-defined polymers in inexpensive and robust processes with an expanding range of monomers.

Polymer Architecture. ATRP offers exceptional control over macromolecular architecture using many commercially available reagents under undemanding reaction conditions. Various aspects of chain topology, composition, and function-

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ality (even tacticity) can be well controlled by ATRP. Development of new, low-catalyst-concentration ATRP systems (ICAR, ARGET, SARA, photo-ATRP, and eATRP) provides not only more environmentally benign and industrially scalable processes but also new tools for designed dispersity, defined by the catalyst content. This can be considered as a new concept of controlled heterogeneity.[74a] This heterogeneity will include designed MWDs, stabilizing novel nanostructured morphologies,[44a] gradient copolymers,[83] and materials with variable branching.[8a]

Thus, two orthogonal directions can be anticipated in the area of polymer architecture. One direction will be the synthesis of polymers with even more-complex and precisely controlled architecture, with various combined elements of chain composition, topology, and functionality. Such macromolecules or macromolecular objects can specifically self-assemble, optionally under external stimuli, and generate smart, self-repairing, or interactive materials.[181] Alternatively, materials with controlled imperfections and controlled heterogeneity will become progressively more interesting, as they will offer more-tolerant processing windows and should reduce the cost and improve the cost−performance relationship of fabricated articles. Many of these materials will be invaluable for fundamental research and studies of structure−property−application correlations.

Hybrid Materials. Hybrid materials prepared by ATRP are among the most dynamically developing areas of polymer and (bio)materials science. Covalent attachment of uniform polymers to inorganic surfaces and natural products creates new classes of grafts/brushes and bioconjugates. Compositionally controlled organic/inorganic hybrids allow efficient dispersion of nanoparticles in various matrices. The resulting materials can be made optically transparent by refractive index matching or can be organized in the form of plastic photonic crystals with enhanced mechanical, thermal, or electronic properties.[135] They can form self-repairing, shape-memory materials that can respond to external stimuli.[182] Surfaces with densely grafted brushes can provide extraordinary lubricity, switchable superhydrophobic or superhydrophilic self-cleaning materials, and antifouling or antimicrobial properties.

Equally interesting are bioconjugates of synthetic polymers with carbohydrates, nucleic acids, and proteins or other biomolecules. Polymers can be attached to, or grown by ATRP from viruses, bacteria, or even surfaces of living cells. After development of ATRP under biorelevant conditions[139] and demonstration of successful bioconjugation, systems could be designed for a specific function, such as drug or gene delivery or tissue engineering. Bioconjugation with stimuli-responsive polymers, with targeting moieties, and with either complexed or covalently attached (via degradable linkers) drugs and/or nucleic acids will be developed. More-complex nanoobjects such as stars and nanogels or even macroscopic hydrogels can be precisely built and can be degraded to well-defined short primary chains that can be cleared from the body. It will also be interesting to combine both classes of hybrids (inorganic and natural) together in areas related to biomineralization, bone engineering, or targeted delivery using magnetic forces.

This brief Perspective demonstrates that, in less than 2 decades, ATRP has emerged as an extremely powerful synthetic technique that has enabled the preparation of a plethora of new materials with numerous applications. The success of the method can be attributed to detailed mechanistic studies that paved the way for creating rules for the rational selection of reaction conditions to achieve the synthesis of the desired well-defined functional macromolecules.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Matyjaszewski, K.; Gnanou, Y.; Leibler, L., Eds. *Macromolecular Engineering. Precise Synthesis, Materials Properties, Applications*; Wiley-VCH: Weinheim, 2007. (b) Kennedy, J. P.; Ivan, B. *Carbocationic Macromolecular Engineering*; Hanser: Munich, 1991. (c) Matyjaszewski, K., Moeller, M., Eds. *Polymer Science: A Comprehensive Reference*; Elsevier BV: Amsterdam, 2012.

(2) (a) Matyjaszewski, K.; Davis, T. P., Eds. *Handbook of Radical Polymerization*; Wiley-Interscience: Hoboken, NJ, 2002. (b) Goto, A.; Fukuda, T. *Prog. Polym. Sci.* **2004**, *29*, 329−385.

(3) Matyjaszewski, K. *Macromolecules* **2012**, *45*, 4015−4039.

(4) (a) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661−3688. (b) Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux, B. *Prog. Polym. Sci.* **2013**, *38*, 63−235. (c) Poli, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 5058−5070. (d) Allan, L. E. N.; Perry, M. R.; Shaver, M. P. *Prog. Polym. Sci.* **2012**, *37*, 127−156.

(5) (a) Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614−5615. (b) Matyjaszewski, K.; Xia, J. H. *Chem. Rev.* **2001**, *101*, 2921−2990. (c) Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721−1723. (d) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689−3745. (e) Tsarevsky, N. V.; Matyjaszewski, K. *Chem. Rev.* **2007**, *107*, 2270−2299. (f) Matyjaszewski, K.; Tsarevsky, N. V. *Nat. Chem.* **2009**, *1*, 276−288. (g) di Lena, F.; Matyjaszewski, K. *Prog. Polym. Sci.* **2010**, *35*, 959−1021.

(6) (a) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559−5562. (b) Matyjaszewski, K.; Gaynor, S.; Wang, J. S. *Macromolecules* **1995**, *28*, 2093−2095. (c) Gregory, A.; Stenzel, M. H. *Prog. Polym. Sci.* **2012**, *37*, 38−105.

(7) (a) Greszta, D.; Mardare, D.; Matyjaszewski, K. *Macromolecules* **1994**, *27*, 638−644. (b) Matyjaszewski, K.; Gaynor, S.; Greszta, D.; Mardare, D.; Shigemoto, T. *J. Phys. Org. Chem.* **1995**, *8*, 306−315. (c) Tsarevsky, N. V., Sumerlin, B. S., Eds. *Fundamentals of Controlled/Living Radical Polymerization*; RSC: Cambridge, 2013.

(8) (a) Gao, H.; Matyjaszewski, K. *Prog. Polym. Sci.* **2009**, *34*, 317−350. (b) Lee, H.-i.; Pietrasik, J.; Sheiko, S. S.; Matyjaszewski, K. *Prog. Polym. Sci.* **2010**, *35*, 24−44. (c) Sheiko, S. S.; Sumerlin, B. S.; Matyjaszewski, K. *Prog. Polym. Sci.* **2008**, *33*, 759−785. (d) Siegwart, D. J.; Oh, J. K.; Matyjaszewski, K. *Prog. Polym. Sci.* **2012**, *37*, 18−37. (e) Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26*, 337−377. (f) Oh, J. K.; Drumright, R.; Siegwart, D. J.; Matyjaszewski, K. *Prog. Polym. Sci.* **2008**, *33*, 448−477.

(9) (a) Hui, C. M.; Pietrasik, J.; Schmitt, M.; Mahoney, C.; Choi, J.; Bockstaller, M. R.; Matyjaszewski, K. *Chem. Mater.* **2014**, *26*, 745−762. (b) Li, W.; Yoon, J. A.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2010**, *132*, 7823−7825. (c) Miyake, G. M.; Weitekamp, R. A.; Piunova, V. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2012**, *134*, 14249−14254. (d) Zhong, M.; Natesakhawat, S.; Baltrus, J. P.; Luebke, D.; Nulwala, H.; Matyjaszewski, K.; Kowalewski, T. *Chem. Commun.* **2012**, *48*, 11516−11518. (e) Huang, K.; Rzayev, J. *J. Am. Chem. Soc.* **2011**, *133*, 16726−16729.

(10) Nicolay, R.; Kwak, Y. *Isr. J. Chem.* **2012**, *52*, 288−305.
(11) (a) Minisci, F. *Acc. Chem. Res.* **1975**, *8*, 165. (b) Bellus, D. *Pure Appl. Chem.* **1985**, *57*, 1827−1838. (c) Clark, A. J. *Chem. Soc. Rev.* **2002**, *31*, 1−11. (d) Pintauer, T.; Matyjaszewski, K. *Chem. Soc. Rev.* **2008**, *37*, 1087−1097.
(12) Tsarevsky, N. V.; Matyjaszewski, K. In *Fundamentals of Controlled/Living Radical Polymerization*; Sumerlin, B. S., Ed.; RSC: Cambridge, 2013; pp 287−357.
(13) Wang, J. S.; Matyjaszewski, K. *Macromolecules* **1995**, *28*, 7901−7910.
(14) Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109*, 4963−5050.
(15) Zhong, M.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 2668−2677.
(16) Lin, C.-Y.; Marque, S. R. A.; Matyjaszewski, K.; Coote, M. L. *Macromolecules* **2011**, *44*, 7568−7583.
(17) Tsarevsky, N. V.; Braunecker, W. A.; Tang, W.; Brooks, S. J.; Matyjaszewski, K.; Weisman, G. R.; Wong, E. H. *J. Mol. Catal. A: Chem.* **2006**, *257*, 132−140.
(18) (a) Zanello, P. *Inorganic Electrochemistry: Theory, Practice and Application*; RSC: Cambridge, 2003. (b) Bortolamei, N.; Isse, A. A.; Di Marco, V. B.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2010**, *43*, 9257−9267. (c) Lingane, J. J. *Chem. Rev.* **1941**, *29*, 1. (d) Rossotti, F. J. C.; Rossotti, H. *The Determination of Stability Constants*; McGraw Hill: New York, 1961.
(19) (a) Tsarevsky, N. V.; Pintauer, T.; Matyjaszewski, K. *Macromolecules* **2004**, *37*, 9768−9778. (b) Tsarevsky, N. V.; Braunecker, W. A.; Vacca, A.; Gans, P.; Matyaszewski, K. *Macromol. Symp.* **2007**, *248*, 60−70.
(20) Braunecker, W. A.; Tsarevsky, N. V.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 6348−6360.
(21) Zanello, P. In *Stereochemical Control, Bonding and Steric Rearrangements*; Bernal, I., Ed.; Elsevier: Amsterdam, 1990; Vol. *4*, pp 181−366.
(22) (a) Magenau, A. J. D.; Kwak, Y.; Schroeder, K.; Matyjaszewski, K. *ACS Macro Lett.* **2012**, *1*, 508−512. (b) Schroder, K.; Konkolewicz, D.; Poli, R.; Matyjaszewski, K. *Organometallics* **2012**, *31*, 7994−7999. (c) Wang, Y.; Kwak, Y.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 5911−5915.
(23) Martell, A. E.; Hancock, R. D. *Metal Complexes in Aqueous Solutions*; Plenum Press: New York, 1995.
(24) Bortolamei, N.; Isse, A. A.; Magenau, A. J. D.; Gennaro, A.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 11391−11394.
(25) Wang, Y.; Kwak, Y.; Buback, J.; Buback, M.; Matyaszewski, K. *ACS Macro Lett.* **2012**, *1*, 1367−1370.
(26) (a) Tang, W.; Kwak, Y.; Braunecker, W.; Tsarevsky, N. V.; Coote, M. L.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 10702−10713. (b) Pintauer, T.; Matyjaszewski, K. *Coord. Chem. Rev.* **2005**, *249*, 1155−1184.
(27) (a) Xia, J. H.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 7692−7696. (b) Xia, J.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 5199. (c) Wang, J.-S.; Matyjaszewski, K. *Macromolecules* **1995**, *28*, 7572−7573.
(28) (a) Faucher, S.; Zhu, S. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 553−565. (b) Shen, Y.; Tang, H.; Ding, S. *Prog. Polym. Sci.* **2004**, *29*, 1053.
(29) Gromada, J.; Matyjaszewski, K. *Macromolecules* **2001**, *34*, 7664−7671.
(30) (a) Jakubowski, W.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 4139−4146. (b) Min, K.; Gao, H.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2005**, *127*, 3825. (c) Bai, L.; Zhang, L.; Cheng, Z.; Zhu, X. *Polym. Chem.* **2012**, *3*, 2685−2697.
(31) Matyjaszewski, K.; Coca, S.; Gaynor, S. G.; Wei, M.; Woodworth, B. E. *Macromolecules* **1997**, *30*, 7348.
(32) de Vries, A.; Klumperman, B.; de Wet-Roos, D.; Sanderson, R. D. *Macromol. Chem. Phys.* **2001**, *202*, 1645.
(33) Gnanou, Y.; Hizal, G. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 351.
(34) Cordeiro, R. A.; Rocha, N.; Mendes, J. P.; Matyjaszewski, K.; Guliashvili, T.; Serra, A. C.; Coelho, J. F. J. *Polym. Chem.* **2013**, *4*, 3088−3097.
(35) Min, K.; Jakubowski, W.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2006**, *27*, 594.
(36) Fischer, H. *Chem. Rev.* **2001**, *101*, 3581−3610.
(37) Jakubowski, W.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 4482−4486.
(38) Jakubowski, W. *ACS Symp. Ser.* **2012**, *1100*, 203−216.
(39) (a) Mueller, L.; Jakubowski, W.; Tang, W.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 6464−6472. (b) Simakova, A.; Averick, S. E.; Konkolewicz, D.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 6371−6379.
(40) Matyjaszewski, K.; Jakubowski, W.; Min, K.; Tang, W.; Huang, J. Y.; Braunecker, W. A.; Tsarevsky, N. V. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 15309−15314.
(41) Wang, Y.; Soerensen, N.; Zhong, M.; Schroeder, H.; Buback, M.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 683−691.
(42) Jakubowski, W.; Kirci-Denizli, B.; Gil, R. R.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2008**, *209*, 32−39.
(43) Tsarevsky, N. V. *Isr. J. Chem.* **2012**, *52*, 276−287.
(44) (a) Listak, J.; Jakubowski, W.; Mueller, L.; Plichta, A.; Matyjaszewski, K.; Bockstaller, M. R. *Macromolecules* **2008**, *41*, 5919−5927. (b) Jakubowski, W.; Tsarevsky, N. V.; McCarthy, P. *ACS Symp. Ser.* **2009**, *1023*, 343−355.
(45) Percec, V.; Guliashvili, T.; Ladislaw, J. S.; Wistrand, A.; Stjerndahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S. *J. Am. Chem. Soc.* **2006**, *128*, 14156−14165.
(46) Rosen, B. M.; Percec, V. *Chem. Rev.* **2009**, *109*, 5069−5119.
(47) Konkolewicz, D.; Wang, Y.; Zhong, M.; Krys, P.; Isse, A. A.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 8749−8772.
(48) Zhong, M.; Wang, Y.; Krys, P.; Konkolewicz, D.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 3816−3827.
(49) Lin, C. Y.; Coote, M. L.; Gennaro, A.; Matyaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 12762−12774.
(50) (a) Guliashvili, T.; Mendonca, P. V.; Serra, A. C.; Popov, A. V.; Coelho, J. F. J. *Chem.—Eur. J.* **2012**, *18*, 4607−4612. (b) Harrisson, S.; Couvreur, P.; Nicolas, J. *Macromolecules* **2012**, *45*, 7388−7396. (c) Wang, Y.; Zhong, M.; Zhu, W.; Peng, C.-H.; Zhang, Y.; Konkolewicz, D.; Bartolomei, N.; Isse, A. A.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 3793−3802. (d) Peng, C.-H.; Zhong, M.; Wang, Y.; Kwak, Y.; Zhang, Y.; Zhu, W.; Tonge, M.; Buback, J.; Park, S.; Krys, P.; Konkolewicz, D.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 3803−3815.
(51) Isse, A. A.; Gennaro, A.; Lin, C. Y.; Hodgson, J. L.; Coote, M. L.; Guliashvili, T. *J. Am. Chem. Soc.* **2011**, *133*, 6254−6264.
(52) (a) Isse, A. A.; Lin, C. Y.; Coote, M. L.; Gennaro, A. *J. Phys. Chem. B* **2011**, *115*, 678−684. (b) Isse, A. A.; Bortolamei, N.; De Paoli, P.; Gennaro, A. *Electrochim. Acta* **2013**, *110*, 655−662.
(53) (a) Konkolewicz, D.; Krys, P.; Gois, J. R.; Mendonca, P. V.; Zhong, M.; Wang, Y.; Gennaro, A.; Isse, A. A.; Fantin, M.; Matyjaszewski, K. *Macromolecules* **2014**, *47*, 560−570. (b) Konkolewicz, D.; Wang, Y.; Krys, P.; Zhong, M.; Isse, A. A.; Gennaro, A.; Matyjaszewski, K. *Polym. Chem.* **2014**, DOI: 10.1039/c4py00149d.
(54) Levere, M. E.; Nguyen, N. H.; Sun, H.-J.; Percec, V. *Polym. Chem.* **2013**, *4*, 686−694.
(55) Coca, S.; Jasieczek, C. B.; Beers, K. L.; Matyjaszewski, K. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 1417.
(56) (a) Xia, J.; Johnson, T.; Gaynor, S. G.; Matyjaszewski, K.; DeSimone, J. *Macromolecules* **1999**, *32*, 4802. (b) Duxbury, C. J.; Wang, W.; de Geus, M.; Heise, A.; Howdle, S. M. *J. Am. Chem. Soc.* **2005**, *127*, 2384.
(57) (a) Biedron, T.; Kubisa, P. *Polym. Int.* **2003**, *52*, 1584. (b) Sarbu, T.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2001**, *202*, 3379. (c) Xie, M.; Han, H.; Ding, L.; Shi, J. *J, Macromol. Sci., Part C: Polym. Rev.* **2009**, *49*, 315−338.
(58) Perrier, S.; Gemici, H.; Li, S. *Chem. Commun.* **2004**, 604.
(59) (a) Qiu, J.; Charleux, B.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26*, 2083. (b) Cunningham, M. F. *Prog. Polym. Sci.* **2002**, *27*, 1039−1067.

(c) Zetterlund, P. B.; Kagawa, Y.; Okubo, M. *Chem. Rev.* **2008**, *108*, 3747−3794. (d) Elsen, A. M.; Burdynska, J.; Park, S.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 7356−7363.
(60) (a) Beuermann, S.; Buback, M. *Prog. Polym. Sci.* **2002**, *27*, 191−254. (b) Beuermann, S. *Macromol. Rapid Commun.* **2009**, *30*, 1066−1088.
(61) Tsarevsky, N. V.; Jakubowski, W. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 918−925.
(62) Woodruff, S. R.; Davis, B. J.; Tsarevsky, N. V. *ACS Symp. Ser.* **2012**, *1100*, 99−113.
(63) (a) Kwak, Y.; Matyjaszewski, K. *Macromolecules* **2010**, *43*, 5180−5183. (b) Mosnacek, J.; Ilcikova, M. *Macromolecules* **2012**, *45*, 5859−5865. (c) Konkolewicz, D.; Schroder, K.; Buback, J.; Bernhard, S.; Matyjaszewski, K. *ACS Macro Lett.* **2012**, *1*, 1219−1223. (d) Dadashi-Silab, S.; Tasdelen, M. A.; Asiri, A. M.; Khan, S. B.; Yagci, Y. *Macromol. Rapid Commun.* **2014**, *35*, 454−459. (e) Fors, B. P.; Hawker, C. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 8850−8853.
(64) (a) Magenau, A. J. D.; Strandwitz, N. C.; Gennaro, A.; Matyjaszewski, K. *Science* **2011**, *332*, 81−84. (b) Magenau, A. J. D.; Bortolamei, N.; Frick, E.; Park, S.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 4346−4353.
(65) (a) Lutz, J.-F.; Neugebauer, D.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2003**, *125*, 6986−6993. (b) Kamigaito, M.; Satoh, K. *Macromolecules* **2008**, *41*, 269−276.
(66) Jiang, J.; Lu, X.; Lu, Y. *Polymer* **2008**, *49*, 1770−1776.
(67) Idota, N.; Nagase, K.; Tanaka, K.; Okano, T.; Annaka, M. *Langmuir* **2010**, *26*, 17781−17784.
(68) Miura, Y.; Satoh, T.; Narumi, A.; Nishizawa, O.; Okamoto, Y.; Kakuchi, T. *Macromolecules* **2005**, *38*, 1041−1043.
(69) (a) Tang, W.; Nanda, A. K.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2005**, *206*, 1171. (b) Seeliger, F.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 6050−6055.
(70) (a) Kwiatkowski, P.; Jurczak, J.; Pietrasik, J.; Jakubowski, W.; Mueller, L.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 1067−1069. (b) Arita, T.; Kayama, Y.; Ohno, K.; Tsujii, Y.; Fukuda, T. *Polymer* **2008**, *49*, 2426−2429.
(71) Morick, J.; Buback, M.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2011**, *212*, 2423−2428.
(72) Schroeder, H.; Yalalov, D.; Buback, M.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2012**, *213*, 2019−2026.
(73) Ruzette, A.-V.; Tence-Girault, S.; Leibler, L.; Chauvin, F.; Bertin, D.; Guerret, O.; Gerard, P. *Macromolecules* **2006**, *39*, 5804−5814.
(74) (a) Matyjaszewski, K. *Science* **2011**, *333*, 1104−1105. (b) Hustad, P. D. *Science* **2009**, *325*, 704−707.
(75) (a) Lynd, N. A.; Meuler, A. J.; Hillmyer, M. A. *Prog. Polym. Sci.* **2008**, *33*, 875−893. (b) McCullough, L. A.; Matyjaszewski, K. *Mol. Cryst. Liq. Cryst.* **2010**, *521*, 1−55.
(76) (a) Badi, N.; Chan-Seng, D.; Lutz, J. F. *Macromol. Chem. Phys.* **2013**, *214*, 135−142. (b) Matyjaszewski, K. *Macromolecules* **1998**, *31*, 4710−4717.
(77) Bates, F. S.; Fredrickson, G. H. *Phys. Today* **1999**, *52*, 32.
(78) (a) Matyjaszewski, K.; Shipp, D. A.; Wang, J.-L.; Grimaud, T.; Patten, T. E. *Macromolecules* **1998**, *31*, 6836−6840. (b) Peng, C.-H.; Kong, J.; Seeliger, F.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 7546−7557.
(79) Boyer, C.; Soeriyadi, A. H.; Zetterlund, P. B.; Whittaker, M. R. *Macromolecules* **2011**, *44*, 8028−8033.
(80) (a) Kwak, Y.; Nicolay, R.; Matyjaszewski, K. *Aust. J. Chem.* **2009**, *62*, 1384−1401. (b) Coca, S.; Paik, H.-j.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 6513−6516. (c) Coca, S.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 2808−2810. (d) Matyjaszewski, K.; Beers, K. L.; Kern, A.; Gaynor, S. G. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 823−830. (e) Shinoda, H.; Matyjaszewski, K. *Macromolecules* **2001**, *34*, 6243−6248. (f) Shinoda, H.; Miller, P. J.; Matyjaszewski, K. *Macromolecules* **2001**, *34*, 3186−3194. (g) Roos, S. G.; Mueller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 8331−8335. (h) Pyun, J.; Matyjaszewski, K.; Kowalewski, T.; Savin, D.; Patterson, G.; Kickelbick, G.; Huesing, N. *J. Am. Chem. Soc.* **2001**, *123*, 9445−9446.
(81) (a) Mecerreyes, D.; Moineau, G.; Dubois, P.; Jérôme, R.; Hedrick, J. L.; Hawker, C. J.; Malmström, E. E.; Trollsas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1274−1276. (b) Bielawski, C. W.; Louie, J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 12872−12873.
(82) Jakubowski, W.; Lutz, J.-F.; Slomkowski, S.; Matyjaszewski, K. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 1498−1510.
(83) Matyjaszewski, K.; Ziegler, M. J.; Arehart, S. V.; Greszta, D.; Pakula, T. *J. Phys. Org. Chem.* **2000**, *13*, 775−786.
(84) Elsen, A. M.; Li, Y.; Li, Q.; Sheiko, S. S.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2014**, *35*, 133−140.
(85) Nakatani, K.; Ogura, Y.; Koda, Y.; Terashima, T.; Sawamoto, M. *J. Am. Chem. Soc.* **2012**, *134*, 4373−4383.
(86) (a) Zamfir, M.; Lutz, J. F. *Nat. Commun.* **2012**, *3*, No. 1138. (b) Srichan, S.; Chan-Seng, D.; Lutz, J. F. *ACS Macro Lett.* **2012**, *1*, 589−592.
(87) Satoh, K.; Ozawa, S.; Mizutani, M.; Nagai, K.; Kamigaito, M. *Nat. Comm.* **2010**, *1*, No. 6.
(88) Golas, P. L.; Matyjaszewski, K. *Chem. Soc. Rev.* **2010**, *39*, 1338−1354.
(89) Sarbu, T.; Lin, K.-Y.; Spanswick, J.; Gil, R. R.; Siegwart, D. J.; Matyjaszewski, K. *Macromolecules* **2004**, *37*, 9694−9700.
(90) (a) Gao, H.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 1118−1125. (b) Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Mays, J. *Prog. Polym. Sci.* **2006**, *31*, 1068−1132.
(91) (a) Boerner, H. G.; Beers, K.; Matyjaszewski, K.; Sheiko, S. S.; Moeller, M. *Macromolecules* **2001**, *34*, 4375−4383. (b) Lee, H.-I.; Matyjaszewski, K.; Yu, S.; Sheiko, S. S. *Macromolecules* **2005**, *38*, 8264−8271. (c) Stals, P. J. M.; Li, Y.; Burdynska, J.; Nicolay, R.; Nese, A.; Palmans, A. R. A.; Meijer, E. W.; Matyjaszewski, K.; Sheiko, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 11421−11424.
(92) (a) Lee, H.; Jakubowski, W.; Matyjaszewski, K.; Yu, S.; Sheiko, S. S. *Macromolecules* **2006**, *39*, 4983−4989. (b) Wu, D.; Nese, A.; Pietrasik, J.; Liang, Y.; He, H.; Kruk, M.; Huang, L.; Kowalewski, T.; Matyjaszewski, K. *ACS Nano* **2012**, *6*, 6208−6214. (c) Min, K.; Yu, S.; Lee, H.-i.; Mueller, L.; Sheiko, S. S.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 6557−6563. (d) Djalali, R.; Li, S.-Y.; Schmidt, M. *Macromolecules* **2002**, *35*, 4282−4288.
(93) (a) Lee, H.-i.; Matyjaszewski, K.; Yu-Su, S.; Sheiko, S. S. *Macromolecules* **2008**, *41*, 6073−6080. (b) Rzayev, J. *ACS Macro Lett.* **2012**, *1*, 1146−1149. (c) Xia, Y.; Olsen, B. D.; Kornfield, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 18525−18532.
(94) (a) Neugebauer, D.; Zhang, Y.; Pakula, T.; Sheiko, S. S.; Matyjaszewski, K. *Macromolecules* **2003**, *36*, 6746−6755. (b) Pakula, T.; Zhang, Y.; Matyjaszewski, K.; Lee, H.-i.; Boerner, H.; Qin, S.; Berry, G. C. *Polymer* **2006**, *47*, 7198−7206. (c) Banquy, X.; Burdyńska, J.; Lee, D. W.; Matyjaszewski, K.; Israelachvili, J. *J. Am. Chem. Soc.* **2014**, DOI: 10.1021/ja501770y.
(95) Matyjaszewski, K.; Gaynor, S. G. *Macromolecules* **1997**, *30*, 7042−7049.
(96) (a) Fréchet, J. M. J.; Henmi, M.; Gitsov, I.; Aoshima, S.; Leduc, M. R.; Grubbs, R. B. *Science* **1995**, *269*, 1080−1083. (b) Kim, Y. H.; Webster, O. W. *Macromolecules* **1992**, *25*, 5561−5572.
(97) Tsarevsky, N. V.; Huang, J.; Matyjaszewski, K. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 6839−6851.
(98) Li, Y.; Armes, S. P. *Macromolecules* **2005**, *38*, 8155−8162.
(99) Gao, H.; Li, W.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 2335−2340.
(100) Li, W.; Yoon, J. A.; Zhong, M.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 3270−3275.
(101) Saito, R. *Polymer* **2008**, *49*, 2625−2631.
(102) (a) Tanaka, T.; Okayama, M.; Kitayama, Y.; Kagawa, Y.; Okubo, M. *Langmuir* **2010**, *26*, 7843−7847. (b) Chabrol, V.; Léonard, D.; Zorn, M.; Reck, B.; D'Agosto, F.; Charleux, B. *Macromolecules* **2012**, *45*, 2972−2980.
(103) Min, K.; Gao, H.; Yoon, J. A.; Wu, W.; Kowalewski, T.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 1597−1603.
(104) Li, W.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 5578−5585.
(105) (a) Frackowiak, E. *Phys. Chem. Chem. Phys.* **2007**, *9*, 1774−1785. (b) Zhong, M.; Kim, E. K.; McGann, J. P.; Chun, S.-E.; Whitacre, J. F.;

Jaroniec, M.; Matyjaszewski, K.; Kowalewski, T. *J. Am. Chem. Soc.* **2012**, *134*, 14846−14857. (c) Zhong, M.; Tang, C.; Kim, E. K.; Kruk, M.; Celer, E. B.; Jaroniec, M.; Matyjaszewski, K.; Kowalewski, T. *Mater. Horizons* **2014**, *1*, 121−124. (d) Tang, C.; Qi, K.; Wooley, K. L.; Matyjaszewski, K.; Kowalewski, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 2783−2787. (e) Tang, C.; Bombalski, L.; Kruk, M.; Jaroniec, M.; Matyjaszewski, K.; Kowalewski, T. *Adv. Mater.* **2008**, *20*, 1516−1522. (f) McGann, J. P.; Zhong, M.; Kim, E. K.; Natesakhawat, S.; Jaroniec, M.; Whitacre, J. F.; Matyjaszewski, K.; Kowalewski, T. *Macromol. Chem. Phys.* **2012**, *213*, 1078−1090. (g) Kruk, M.; Dufour, B.; Celer, E. B.; Kowalewski, T.; Jaroniec, M.; Matyjaszewski, K. *Chem. Mater.* **2006**, *18*, 1417−1424. (h) Tang, C.; Tracz, A.; Kruk, M.; Zhang, R.; Smilgies, D.-M.; Matyjaszewski, K.; Kowalewski, T. *J. Am. Chem. Soc.* **2005**, *127*, 6918−6919.

(106) Jakubowski, W.; Tsarevsky, N. V.; Higashihara, T.; Faust, R.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 2318−2323.

(107) Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3558−3561.

(108) Tsarevsky, N. V. In *Green Polymerization Methods: Renewable Starting Materials, Catalysis and Waste Reduction*; Meier, M. A. R., Ed.; Wiley-VCH: Weinheim, 2011; pp 235−261.

(109) (a) Tsarevsky, N. V.; Matyjaszewski, K. *Macromolecules* **2002**, *35*, 9009−9014. (b) Tsarevsky, N. V.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3087−3092.

(110) Bontempo, D.; Heredia, K. L.; Fish, B. A.; Maynard, H. D. *J. Am. Chem. Soc.* **2004**, *126*, 15372−15373.

(111) Qi, K.; Ma, Q.; Remsen, E. E.; Clark, C. G.; Wooley, K. L. *J. Am. Chem. Soc.* **2004**, *126*, 6599.

(112) (a) Wang, X. S.; Lascelles, S. F.; Jackson, R. A.; Armes, S. P. *Chem. Commun.* **1999**, 1817−1818. (b) Wang, X. S.; Armes, S. P. *Macromolecules* **2000**, *33*, 6640. (c) Robinson, K. L.; Khan, M. A.; de Paz Banez, M. V.; Wang, X. S.; Armes, S. P. *Macromolecules* **2001**, *34*, 3155. (d) Perrier, S.; Haddleton, D. M. *Macromol. Symp.* **2002**, *182*, 261−272. (e) Tsarevsky, N. V.; Braunecker, W. A.; Brooks, S. J.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 6817−6824.

(113) (a) Li, Y.; Armes, S. P.; Jin, X.; Zhu, S. *Macromolecules* **2003**, *36*, 8268. (b) Borguet, Y.; Tsarevsky, N. V. *Polym. Chem.* **2012**, *3*, 2487−2494.

(114) Wang, X. S.; Jackson, R. A.; Armes, S. P. *Macromolecules* **2000**, *33*, 255−257.

(115) (a) Lobb, E. J.; Ma, I.; Billingham, N. C.; Armes, S. P.; Lewis, A. L. *J. Am. Chem. Soc.* **2001**, *123*, 7913−7914. (b) Ma, I. Y.; Lobb, E. J.; Billingham, N. C.; Armes, S. P.; Lewis, A. L.; Lloyd, A. W.; Salvage, J. *Macromolecules* **2002**, *35*, 9306.

(116) Tsarevsky, N. V.; Matyjaszewski, K. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5098−5112.

(117) Yao, K.; Tang, C. *Macromolecules* **2013**, *46*, 1689−1712.

(118) Mosnacek, J.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 5509−5511.

(119) (a) Tsarevsky, N. V.; Bencherif, S. A.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 4439−4445. (b) Matyjaszewski, K.; Coca, S.; Jasieczek, C. B. *Macromol. Chem. Phys.* **1997**, *198*, 4011.

(120) (a) Hoyle, C. E.; Lee, T. Y.; Roper, T. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 5301−5338. (b) Kade, M. J.; Burke, D. J.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 743−750. (c) Lowe, A. B. *Polym. Chem.* **2010**, *1*, 17−36.

(121) (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021. (b) Iha, R. K.; Wooley, K. L.; Nyström, A. M.; Burked, D. J.; Kade, M. J.; Hawker, C. J. *Chem. Rev.* **2009**, *109*, 5620−5686. (c) Sumerlin, B. S.; Vogt, A. P. *Macromolecules* **2010**, *43*, 1−13.

(122) (a) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15−54. (b) Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. J. *Chem. Rev.* **2009**, *109*, 5620−5686. (c) Lutz, J.-F.; Schlaad, H. *Polymer* **2008**, *49*, 817−824.

(123) Matyjaszewski, K.; Nakagawa, Y.; Gaynor, S. G. *Macromol. Rapid Commun.* **1997**, *18*, 1057.

(124) Matyjaszewski, K.; Miller, P. J.; Shukla, N.; Immaraporn, B.; Gelman, A.; Luokala, B. B.; Siclovan, T. M.; Kickelbick, G.; Vallant, T.; Hoffmann, H.; Pakula, T. *Macromolecules* **1999**, *32*, 8716−8724.

(125) Bombalski, L.; Dong, H.; Listak, J.; Matyjaszewski, K.; Bockstaller, M. R. *Adv. Mater.* **2007**, *19*, 4486−4490.

(126) (a) Tsujii, Y.; Ohno, K.; Yamamoto, S.; Goto, A.; Fukuda, T. *Adv. Polym. Sci.* **2006**, *197*, 1−45. (b) Chen, M.; Briscoe, W. H.; Armes, S. P.; Klein, J. *Science* **2009**, *323*, 1698−1701. (c) Kobayashi, M.; Terayama, Y.; Hosaka, N.; Kaido, M.; Suzuki, A.; Yamada, N.; Torikai, N.; Ishihara, K.; Takahara, A. *Soft Matter* **2007**, *3*, 740−746.

(127) Boyes, S. G., Granville, A. M., Baum, M., Akgun, B., Mirous, B. K., Brittain, W. J., Eds. *Polymer Brushes: Synthesis, Characterization, Applications*; Wiley: Weinheim, 2004.

(128) (a) Kruk, M.; Dufour, B.; Celer, E. B.; Kowalewski, T.; Jaroniec, M.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 8584−8591. (b) Barbey, R.; Lavanant, L.; Paripovic, D.; Schüwer, N.; Sugnaux, C.; Tugulu, S.; Klok, H. A. *Chem. Rev.* **2009**, *109*, 5437−5527.

(129) (a) Pietrasik, J.; Hui, C. M.; Chaladaj, W.; Dong, H.; Choi, J.; Jurczak, J.; Bockstaller, M. R.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2011**, *32*, 295−301. (b) Bombalski, L.; Min, K.; Dong, H.; Tang, C.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 7429−7432.

(130) Gao, X.; Feng, W.; Zhu, S.; Sheardown, H.; Brash, J. L. *Macromol. React. Eng.* **2010**, *4*, 235−250.

(131) Ojha, S.; Dang, A.; Hui, C. M.; Mahoney, C.; Matyjaszewski, K.; Bockstaller, M. R. *Langmuir* **2013**, *29*, 8989−8996.

(132) Ye, P.; Dong, H.; Zhong, M.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 2253−2260.

(133) Ran, J.; Wu, L.; Xu, T. *Prog. Polym. Sci.* **2014**, *39*, 124−144.

(134) (a) Fristrup, C. J.; Jankova, K.; Hvilsted, S. *Soft Matter* **2009**, *5*, 4623−4634. (b) Xu, F. J.; Neoh, K. G.; Kang, E. T. *Prog. Polym. Sci.* **2009**, *34*, 719−761. (c) Lavanant, L.; Klok, H.-A. *Chimia* **2008**, *62*, 793−798.

(135) Choi, J.; Hui, C. M.; Pietrasik, J.; Dong, H.; Matyjaszewski, K.; Bockstaller, M. R. *Soft Matter* **2012**, *8*, 4072−4082.

(136) Choi, J.; Hui, C. M.; Schmitt, M.; Pietrasik, J.; Margel, S.; Matyjaszewski, K.; Bockstaller, M. R. *Langmuir* **2013**, *29*, 6452−6459.

(137) (a) Lutz, J.-F.; Boerner, H. G. *Prog. Polym. Sci.* **2008**, *33*, 1−39. (b) Nicolas, J.; Mantovani, G.; Haddleton, D. M. *Macromol. Rapid Commun.* **2007**, *28*, 1083−1111. (c) Wallat, J. D.; Rose, K. A.; Pokorski, J. K. *Polym. Chem.* **2014**, *5*, 1545−1558.

(138) Averick, S.; Paredes, E.; Li, W.; Matyjaszewski, K.; Das Subha, R. *Bioconjugate Chem.* **2011**, *22*, 2030−2037.

(139) Averick, S.; Simakova, A.; Park, S.; Konkolewicz, D.; Magenau, A. J. D.; Mehl, R. A.; Matyjaszewski, K. *ACS Macro Lett.* **2012**, *1*, 6−10.

(140) Meszynska, A.; Badi, N.; Boerner, H. G.; Lutz, J.-F. *Chem. Commun.* **2012**, *48*, 3887−3889.

(141) Baradel, N.; Fort, S.; Halila, S.; Badi, N.; Lutz, J.-F. *Angew. Chem., Int. Ed.* **2013**, *52*, 2335−2339.

(142) Heredia, K. L.; Bontempo, D.; Ly, T.; Byers, J. T.; Halstenberg, S.; Maynard, H. D. *J. Am. Chem. Soc.* **2005**, *127*, 16955−16960.

(143) Peeler, J. C.; Woodman, B. F.; Averick, S.; Miyake-Stoner, S. J.; Stokes, A. L.; Hess, K. R.; Matyjaszewski, K.; Mehl, R. A. *J. Am. Chem. Soc.* **2010**, *132*, 13575−13577.

(144) (a) Schnitzler, T.; Herrmann, A. *Acc. Chem. Res.* **2012**, *45*, 1419−1430. (b) Averick, S. E.; Paredes, E.; Grahacharya, D.; Woodman, B. F.; Miyake-Stoner, S. J.; Mehl, R. A.; Matyjaszewski, K.; Das, S. R. *Langmuir* **2012**, *28*, 1954−1958.

(145) (a) Averick, S. E.; Paredes, E.; Irastorza, A.; Shrivats, A. R.; Srinivasan, A.; Siegwart, D. J.; Magenau, A. J.; Cho, H. Y.; Hsu, E.; Averick, A. A.; Kim, J.; Liu, S.; Hollinger, J. O.; Das, S. R.; Matyjaszewski, K. *Biomacromolecules* **2012**, *13*, 3445−3449. (b) Cho, H. Y.; Averick, S. E.; Paredes, E.; Wegner, K.; Averick, A.; Jurga, S.; Das, S. R.; Matyjaszewski, K. *Biomacromolecules* **2013**, *14*, 1262−1267.

(146) (a) Averick, S. E.; Paredes, E.; Dey, S. K.; Snyder, K. M.; Tapinos, N.; Matyjaszewski, K.; Das, S. R. *J. Am. Chem. Soc.* **2013**, *135*, 12508−12511. (b) Averick, S. E.; Dey, S. K.; Grahacharya, D.; Matyjaszewski, K.; Das, S. R. *Angew. Chem., Int. Ed.* **2014**, *53*, 2739−2744.

(147) (a) Bencherif, S. A.; Washburn, N. R.; Matyjaszewski, K. *Biomacromolecules* **2009**, *10*, 2499−2507. (b) Loczenski Rose, V.; Winkler, G. S.; Allen, S.; Puri, S.; Mantovani, G. *Eur. Polym. J.* **2013**, *49*, 2861−2883.

(148) Matyjaszewski, K.; Jakubowski, W.; Spanswick, J. Int. Patent WO025310A1, 2007.
(149) Matyjaszewski, K.; Wang, J.-S. Int. PatentWO30421A1, 1996.
(150) Matyjaszewski, K.; Spanswick, J. *Mater. Today* **2005**, *8*, 26−33.
(151) (a) Hasegawa, N.; Shimizu, Y.; Nakagawa, Y. U.S. Patent US6784240, 2004. (b) Balk, S.; Loehden, G.; Kautz, H.; Troemer, C.; Maerz, M.; Zander, L.; Lueckert, J.; Klein, J.; Moeller, T. Int. Patent WO144082, 2009; Eur. Patent EP054364, 2009.
(152) Camenzind, H.; Dubs, P.; Hanggi, P.; Martin, R.; Muhlebach, A.; Rime, F. U.S. Patent US7615522, 2009.
(153) Roos, S.; Eisenberg, B.; Mueller, M. Int. Patent WO0140317, 2001.
(154) Fujita, N.; Shimizu, Y.; Hasegawa, N.; Nakagawa, Y. Int. Patent WO0190224, 2001.
(155) Knischka, R.; Eckstein, E.; Auschra, C.; Matsumoto, A. Int. Patent WO074969, 2006.
(156) Auschra, C.; Eckstein, E.; Zink, M.-O.; Muehlebach, A. Int. Patent WO0346029, 2003.
(157) Koulouri, E. G.; Kallitsis, J. K.; Hadziioannou, G. *Macromolecules* **1999**, *32*, 6242−6248.
(158) Woodworth, B. E.; Coca, S.; O'Dwyer, J. B. Int. Patent WO0144376, 2001.
(159) (a) Muehlebach, A.; Rime, F.; Auschra, C.; Eckstein, E. Int. Patent WO0151534, 2001. (b) White, D.; Coca, S.; O'Dwyer, J. B. U.S. Patent US6642301, 2003. (c) Ohata, T.; Endou, N.; Okada, H.; Kawaguchi, A.; Tanooka, H.; Ijima, Y.; Sako, N. Int. Patent WO156148, 2008.
(160) Jakubowski, W.; McCarthy, P.; Mueller, L. Int. Patent WO163635A1, 2011.
(161) Matsugi, T.; Saito, J.; Kawahara, N.; Matsuo, S.; Kaneko, H.; Kashiwa, N.; Kobayashi, M.; Takahara, A. *Polym. J.* **2009**, *41*, 547−554.
(162) Min, K.; Gao, H.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 10521−10526.
(163) Dufour, B.; Koynov, K.; Pakula, T.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2008**, *209*, 1686−1693.
(164) Zhang, Y.; Costantini, N.; Mierzwa, M.; Pakula, T.; Neugebauer, D.; Matyjaszewski, K. *Polymer* **2004**, *45*, 6333−6339.
(165) (a) Matyjaszewski, K.; Dong, H.; Jakubowski, W.; Pietrasik, J.; Kusumo, A. *Langmuir* **2007**, *23*, 4528−4531. (b) Ejaz, M.; Yamamoto, S.; Ohno, K.; Tsujii, Y.; Fukuda, T. *Macromolecules* **1998**, *31*, 5934−5936.
(166) Yamamoto, S.; Ejaz, M.; Tsujii, Y.; Fukuda, T. *Macromolecules* **2000**, *33*, 5608−5612.
(167) (a) Jaeger, W.; Bohrisch, J.; Laschewsky, A. *Prog. Polym. Sci.* **2010**, *35*, 511−577. (b) Ladd, J.; Zhang, Z.; Chen, S.; Hower, J. C.; Jiang, S. *Biomacromolecules* **2008**, *9*, 1357−1361. (c) Jiang, S.; Cao, Z. *Adv. Mater.* **2010**, *22*, 920−932.
(168) (a) Lee, S. B.; Koepsel, R. R.; Morley, S. W.; Matyjaszewski, K.; Sun, Y.; Russell, A. J. *Biomacromolecules* **2004**, *5*, 877−882. (b) Huang, J.; Murata, H.; Koepsel, R. R.; Russell, A. J.; Matyjaszewski, K. *Biomacromolecules* **2007**, *8*, 1396−1399.
(169) (a) Lenoir, S.; Pagnoulle, C.; Galleni, M.; Compere, P.; Jerome, R.; Detrembleur, C. *Biomacromolecules* **2006**, *7*, 2291−2296. (b) Ravikumar, T.; Murata, H.; Koepsel, R. R.; Russell, A. J. *Biomacromolecules* **2006**, *7*, 2762−2769.
(170) Dong, H.; Huang, J.; Koepsel, R. R.; Ye, P.; Russell, A. J.; Matyjaszewski, K. *Biomacromolecules* **2011**, *12*, 1305−1311.
(171) McCarthy, P.; Chattopadhyay, M.; Millhauser, G. L.; Tsarevsky, N. V.; Bombalski, L.; Matyjaszewski, K.; Shimmin, D.; Avdalovic, N.; Pohl, C. *Anal. Biochem.* **2007**, *366*, 1−8.
(172) Richard, R. E.; Schwarz, M.; Ranade, S.; Chan, A. K.; Matyjaszewski, K.; Sumerlin, B. *Biomacromolecules* **2005**, *6*, 3410−3418.
(173) Oh, J. K.; Siegwart, D. J.; Lee, H.-i.; Sherwood, G.; Peteanu, L.; Hollinger, J. O.; Kataoka, K.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2007**, *129*, 5939−5945.
(174) Cho, H. Y.; Gao, H.; Srinivasan, A.; Hong, J.; Bencherif, S. A.; Siegwart, D. J.; Paik, H.-j.; Hollinger, J. O.; Matyjaszewski, K. *Biomacromolecules* **2010**, *11*, 2199−2203.
(175) (a) Lele, B. S.; Murata, H.; Matyjaszewski, K.; Russell, A. J. *Biomacromolecules* **2005**, *6*, 3380−3387. (b) Cummings, C.; Murata, H.; Koepsel, R.; Russell, A. J. *Biomacromolecules* **2014**, *15*, 763−771.
(176) Schröder, K.; Mathers, R. T.; Buback, J.; Konkolewicz, D.; Magenau, A. J. D.; Matyjaszewski, K. *ACS Macro Lett.* **2012**, *1*, 1037−1040.
(177) (a) Sigg, S. J.; Seidi, F.; Renggli, K.; Silva, T. B.; Kali, G.; Bruns, N. *Macromol. Rapid Commun.* **2011**, *32*, 1710−1715. (b) Ng, Y.-H.; di Lena, F.; Chai, C. L. L. *Polym. Chem.* **2011**, *2*, 589−589. (c) Ng, Y.-H.; di Lena, F.; Chai, C. L. L. *Chem. Commun.* **2011**, *47*, 6464−6466. (d) Silva, T. B.; Spulber, M.; Kocik, M. K.; Seidi, F.; Charan, H.; Rother, M.; Sigg, S. J.; Renggli, K.; Kali, G.; Bruns, N. *Biomacromolecules* **2013**, *14*, 2703−2712. (e) Simakova, A.; Mackenzie, M.; Averick, S. E.; Park, S.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 12148−12151.
(178) (a) Goto, A.; Wakada, T.; Fukuda, T.; Tsujii, Y. *Macromol. Chem. Phys.* **2010**, *211*, 594−600. (b) Goto, A.; Suzuki, T.; Ohfuji, H.; Tanishima, M.; Fukuda, T.; Tsujii, Y.; Kaji, H. *Macromolecules* **2011**, *44*, 8709−8715. (c) Goto, A.; Ohtsuki, A.; Ohfuji, H.; Tanishima, M.; Kaji, H. *J. Am. Chem. Soc.* **2013**, *135*, 11131−11139.
(179) Shen, Y.; Zhu, S. *AIChE J.* **2002**, *48*, 2609−2619.
(180) Chan, N.; Cunningham, M. F.; Hutchinson, R. A. *J. Polym. Sci., Part A Polym. Chem.* **2013**, *51*, 3081−3096.
(181) (a) Nicolay, R.; Kamada, J.; Van Wassen, A.; Matyjaszewski, K. *Macromolecules* **2010**, *43*, 4355−4361. (b) Kamada, J.; Koynov, K.; Corten, C.; Juhari, A.; Yoon, J. A.; Urban, M. W.; Balazs, A. C.; Matyjaszewski, K. *Macromolecules* **2010**, *43*, 4133−4139. (c) Amamoto, Y.; Kamada, J.; Otsuka, H.; Takahara, A.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 1660−1663. (d) Yoon, J. A.; Kamada, J.; Koynov, K.; Mohin, J.; Nicolay, R.; Zhang, Y.; Balazs, A. C.; Kowalewski, T.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 142−149. (e) Chen, Y.; Kushner, A. M.; Williams, G. A.; Guan, Z. *Nat. Chem.* **2012**, *4*, 467−472. (f) Kushner, A. M.; Guan, Z. *Angew. Chem., Int. Ed.* **2011**, *50*, 9026−9057. (g) Yong, X.; Kuksenok, O.; Matyjaszewski, K.; Balazs, A. C. *Nano Lett.* **2013**, *13*, 6269−6274.
(182) (a) Chen, Y.; Kushner, A. M.; Williams, G. A.; Guan, Z. *Nat. Chem.* **2012**, *4*, 467−472. (b) Hentschel, J.; Kushner, A. M.; Ziller, J.; Guan, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 10561−10565. (c) Chen, Y.; Guan, Z. *Polym. Chem.* **2013**, *4*, 4885−4889.