

# 50th Anniversary Perspective: Living Polymerization—Emphasizing the Molecule in Macromolecules

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**ABSTRACT:** The ideal of *living polymerization* has defined research in polymer chemistry over the past 50 years. In this Perspective, we present the case that this concept has enabled the treatment of polymers as organic molecules, rather than impure mixtures of species, and allowed the translation of methods developed by synthetic organic chemists into ever more accessible living and/or controlled polymerization methods. The concurrent development of rapid analytical methods for screening new polymerization methods for living characteristics, chiefly size exclusion chromatography, has greatly aided in the expansion of living polymerization methods.



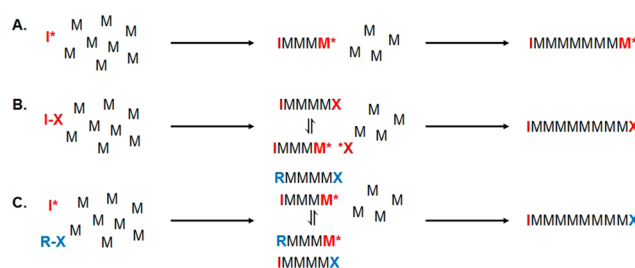
## INTRODUCTION

*Dear Colleague, abandon your idea of large molecules, organic molecules with molecular weights exceeding 5000 do not exist. Purify your products such as rubber, they will crystallize and turn out to be low molecular weight compounds.—Advice from H. Wieland to H. Staudinger, early 1920s<sup>1</sup>*

Historically, polymer chemistry has been a sloppy affair. Even after the eventual acceptance of Staudinger's macromolecular hypothesis and the development of polymer chemistry as a respectable field of study,<sup>2</sup> one could still hear otherwise reasonable organic chemists describing the material left in their still pots as "polymer" or explaining away decomposition of a sensitive product as resulting from "polymerization". The roots of this acceptance lie in the recognition by Wallace Carothers and others in the early 20th century that large molecules could be built up from smaller molecules through the repetition of simple organic reactions, which laid the foundation for the growth of polymer chemistry as a molecular science.<sup>3</sup> In this Perspective, we present the case that it was the subsequent development of the idea of *living polymerization* and, after that, the development of accessible living (or close-to-living) polymerization methods, supplemented by the development of size exclusion chromatography (SEC) as a rapid screening method for "livingness", which have driven the rapid growth of polymer chemistry and its expansion into allied research areas. In particular, *living polymerization* has the promise of enabling macromolecules to be designed and prepared with precision approaching that of natural product synthesis.

The concept of *living polymerization* is central to current synthetic polymer chemistry. There is an appealing simplicity to the idea: monomer and initiator in an environment devoid of impurities that would interfere with polymerization, under conditions where the enthalpic gain of converting double bonds to single bonds (or the relief of ring strain when opening cyclic

monomers) outweighs the entropic penalty of stringing many monomer molecules together into fewer polymer chains, with each chain growing at the same average rate until all monomer has reacted to result in polymers with narrow molecular weight distributions (in most cases) and end groups determined by whichever initiating and terminating species are used (Figure 1A). While the general concept of a living polymerization is simple—all polymer chains in a giving polymerization grow at the same rate with no irreversible transfer or termination



**Figure 1.** Illustration of living and living-like polymerization schemes. (A) *Living polymerization* with no termination or transfer. The propagating active site (\* = anion, cation, radical, catalyst) remains active after monomer is depleted. (B) Reversible deactivation polymerization in which equilibrium between dormant and active chain ends can lead to polymerization with living characteristics. Upon completion of polymerization, the majority of chains are capped with the reversible deactivating moiety (X). (C) Reversible deactivation polymerization in which chain transfer with rapid exchange between chain ends can lead to polymerization with living characteristics. Upon completion of polymerization, the majority of polymer chains are capped with the transfer agent (X).

Received: July 6, 2017

Revised: August 25, 2017

Published: September 17, 2017

reactions—there are subtleties that often necessitate some additional level of explanation for specific cases. In living polymerizations where the rate of initiation ( $k_i$ ) is greater than the rate of propagation ( $k_p$ ) and the addition of monomer to polymer chain ends occurs irreversibly, the breadth of the molecular weight distribution becomes extremely narrow (dispersity,  $\bar{D}$ , approaches 1); however, as Gold recognized in the late 1950s, even relatively high  $k_p/k_i$  ratios can lead to Poisson-type distributions with dispersity values ( $\bar{D} < 1.4$ ) well below those found in conventional polymerizations.<sup>4</sup>

More recently, a number of essentially living polymerization methods—methods in which some degree of termination or transfer occurs despite propagation being the predominant fate of monomer molecules—relying upon either reversible termination of active chain ends (Figure 1B) or rapid degenerate exchange between dormant and active chain ends (Figure 1C) have been developed. Such polymerizations, which retain the important characteristics of living polymerizations, chiefly low  $\bar{D}$  and efficient chain-end functionalization, but are blemished by some occurrence of termination or transfer reactions, such as the reversible deactivation radical polymerization (RDRP) methods, are often described as “living” or controlled (Figure 1B,C).<sup>5,6</sup>

Though Michael Szwarc published the landmark work on living anionic polymerization in *Nature* in 1956,<sup>7</sup> the general description of polymer chains as “alive” or “dead”, in reference to individual chains in radical polymerization as either radical species capable of further growth or chains which have undergone termination reactions, predates this by a number of years. Staudinger described polymerization as a chain reaction in 1935 (“Über die Polymerization als Kettenreaktion”),<sup>8</sup> but while typical descriptions of chain reactions at the time used death-related terms to describe the termination of chain processes (in one notable example, Mark uses *vernichten* “destroy” and *Abbruch* “cancellation” in describing termination events<sup>9</sup>), it did not seem usual to describe a chain reaction as living. As early as 1939, Melville described polymer chains as “alive” and “dead” in a discussion of chain growth kinetics.<sup>10</sup> In 1940, Flory essentially described *living polymerization*, without using the term *living*, in discussing the narrow molecular weight distributions expected to result for polymerizations (in this case, ethylene oxide) in which the rate of initiation is comparable to the rate of propagation and the total number of propagating chains does not change over the course of the polymerization.<sup>11</sup> The realization of living polymerizations took somewhat longer. The anionic polymerization of butadiene was reported by Ziegler in 1936,<sup>12</sup> and the polymerization of ethylene oxide was reported by Perry and Hibbert in 1940.<sup>13</sup> In 1949, Waley and Watson reported the preparation of synthetic polypeptides with “extremely sharp” molecular weight distributions through the careful polymerization of sarcosine *N*-carboxyanhydride.<sup>14</sup> While these early efforts seem likely to have met the criteria for *living polymerizations*, it was still a few more years before Szwarc coined the name that stuck. The general tenets of living polymerization were laid out well before they were realized.<sup>11</sup> Does this render Szwarc’s achievements a case of efficient engineering to prove a long-known hypothesis, rather than a groundbreaking discovery? Perhaps, but it is inarguable that Szwarc’s fundamental insights into the chemistry of electron transfer and awareness of how these and related synthetic processes could be translated into polymerization processes were critical contributions. For his initial discovery and later efforts, Szwarc is rightly regarded as the progenitor of living polymerization.

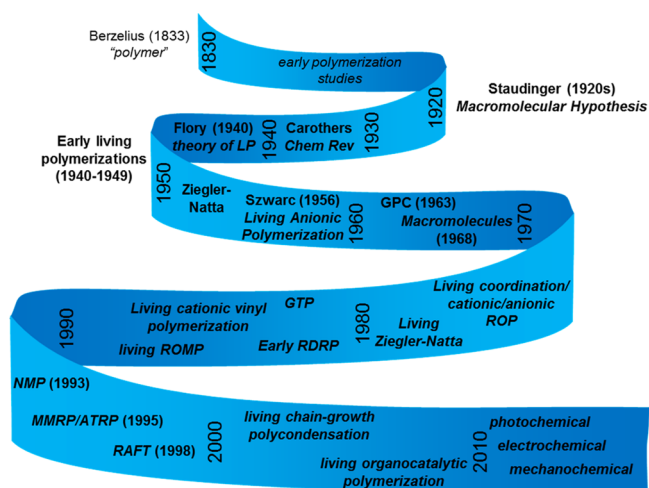
In 1962, in a much less celebrated contribution to the field (though one pointed out by Matyjaszewski and Müller in an editorial introduction to an informative series of reviews on many aspects of *living polymerization* in 2006<sup>15</sup>), Szwarc and co-workers also described an early example of reversible deactivation of living polymer chains in the anionic polymerization of styrene in the presence of anthracene.<sup>16</sup> While in this case, because of the robust nature of the polymerization system, reversible deactivation is not necessary to guarantee living-like behavior, the general concept has since been used in a range of polymerization systems, especially radical polymerizations but also cationic polymerizations,<sup>17</sup> to minimize the occurrence of side reactions resulting from either too-reactive end groups or bimolecular termination reactions between active chain ends.

The choice of *living* as a modifier for a specific class of polymerization has naturally led to some misconceptions about these polymerization processes, but *livingness* has nonetheless become a defining concept in polymer synthesis since Szwarc’s work. The general concept has been extended from its origins in anionic polymerization, with accommodations to specific requirements of given mechanisms, to encompass polymerization methods including coordination/organometallic polymerization, cationic polymerization, and radical polymerization as well as methods that conventionally proceed by step-growth polymerization methods. A number of excellent review articles and books discussing important aspects of living polymerization have appeared over the past 50–60 years.<sup>18–26</sup> It is not the intent of this Perspective to attempt another comprehensive review of living polymerization, but rather to celebrate the concept with three main points: (1) the rise of *living polymerization* as a general method for the preparation of well-defined polymers allowed polymers to be regarded as macromolecules, rather than ill-defined mixtures; (2) the discovery of new living polymerization methods accelerated after the development of size exclusion chromatography (SEC) as a rapid analytical technique to replace tedious fractionation methods; and (3) the development of accessible living methods, particularly ring-opening polymerization of lactones and cycloalkenes with organic, inorganic, or organometallic catalysts and reversible-deactivation radical polymerization (RDRP) methods, which are often not living by the strictest definition, for preparation of classes of polymers previously only accessible through technically demanding living polymerization methods, has revolutionized polymer science.

## ■ A BRIEF AND SELECTIVE HISTORY OF THE DEVELOPMENT OF LIVING POLYMERIZATION

From its roots in anionic polymerization, living (and/or “living”) polymerization strategies have been developed for most other major polymerization methods, including organometallic/coordination polymerization, cationic polymerization, and radical polymerization (Figure 2).

In 1833, Berzelius introduced the term *polymer* for compounds with the same empirical formula but different molecular weights—a much broader definition than is used currently, but it has clearly proven a useful term.<sup>27</sup> From the 1830s through the 1920s, early polymerization studies appear to have either been driven by the desire to produce materials with useful properties without much concern for chemistry or, more commonly, carried out by accident and only later recognized for what they were. Notably, Regnault noted the formation of white powder (“une matière blanche non cristalline”) from exposure of vinylidene chloride to light,<sup>28</sup> and Simon found an oil distilled from *Storax* resin (styrene) thickened into a “durchsichtigen gallertartigen



**Figure 2.** A brief and selective timeline of the development of living polymerization.

Masse” (transparent gelatinous mass) after sitting for several months.<sup>29</sup> Presumably other polymers were made much earlier, but there is little information in the indexed literature.

It was in 1917 that Staudinger first presented his *Macromolecular Hypothesis*, which marked the beginning of the modern era of polymer chemistry (interestingly, Staudinger also published a number of letters and essays arguing that Germany should end World War I<sup>30</sup>) and was supported with further work in the 1920s.<sup>31,32</sup> In the late 1920s, Ziegler began to carry out early studies on the anionic polymerization.<sup>33</sup> At the beginning of the 1930s, Carothers’ comprehensive review with the one-word title, “Polymerization”, appeared in *Chemical Reviews*.<sup>3</sup> By the mid-1930s, Staudinger clearly described certain polymerization processes as occurring through chain reactions, with activation, growth, and termination steps.<sup>8</sup> Ziegler, Medvedev, and others continued to investigate anionic polymerization.<sup>12,34</sup> Kharasch and co-workers began investigating the addition of radicals to

unsaturated hydrocarbons, which laid the foundation for the much later development of ATRP and other RDRP methods.<sup>35</sup>

As described above, Flory postulated in 1940 that polymers with narrow molecular weight distributions should result from polymerizations in which chain growth proceeds at a rate comparable to initiation and no termination or transfer reactions occur.<sup>11</sup> Synthetic support for this idea was offered later that year by Perry and Hibbert.<sup>13</sup> By the end of the decade, Waley and Watson reported the aforementioned polymerizations of NCA monomers that resulted in narrow molecular weight distributions.<sup>14</sup>

The 1950s are highlighted both by Szwarc’s work on living anionic polymerization<sup>7,36–39</sup> and by the development of olefin polymerization catalysts by Ziegler,<sup>40,41</sup> Natta,<sup>42</sup> Hogan, and Banks at Phillips Petroleum,<sup>43</sup> Breslow and Newburg at Hercules,<sup>44</sup> and Fellow and Field at Standard Oil of Indiana.<sup>45</sup> The first patent on what would come to be known as ring-opening metathesis polymerization (ROMP) was issued to DuPont in 1955.<sup>46</sup> A heroic early attempt at carrying out a living-like radical polymerization was reported by Zimm and co-workers in 1957:<sup>47</sup> relying on the Smith–Ewart model of emulsion polymerization in which there should never be more than one growing polymer chain per micelle,<sup>48</sup> controlled periods of exposure of the photoinitiated polymerization to light with long periods in the dark resulted in the preparation of “monodisperse” polystyrene. Shell began to market polyisoprene prepared by anionic polymerization.<sup>49,50</sup>

Momentous developments in polymer chemistry continued through the 1960s. The development of ill-defined ROMP catalyst systems continued in a number of research groups, notably at DuPont<sup>51</sup> and in Natta’s group,<sup>52,53</sup> and Calderon and co-workers at Goodyear carried out fundamental work into understanding the metathesis mechanism and applications.<sup>54,55</sup> Szwarc introduced the concept of reversible deactivation of a living chain end and demonstrated that rapid exchange between active and dormant chain ends could still result in a living polymerization.<sup>16</sup> This general concept would be critical in the later development of living cationic polymerization and RDRP.<sup>15</sup>

# Macromolecules

Published bimonthly by the American Chemical Society

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**Figure 3.** Masthead from the first issue of *Macromolecules*, January 1968. Reproduced with permission from ref 61.

Lenz and co-workers at Dow reported that condensation polymerizations could exhibit chainlike character under certain conditions—a first step in the later development of condensation polymerizations with living character. Dreyfuss and Dreyfuss discovered conditions under which cyclic ethers could be polymerized in a living fashion,<sup>56,57</sup> as did Saegusa's group.<sup>58</sup> Shell began production of polystyrene-*block*-polyisoprene-*block*-polystyrene (Kraton D) and polystyrene-*block*-polybutadiene-*block*-polystyrene block copolymers.<sup>59</sup> Toward the end of the decade, *Macromolecules* was founded (1968; Figure 3), and Fetters and Morton described how careful design of living anionic polymerization chemistry could be used in the preparation of thermoplastic elastomers.<sup>60</sup>

The 1960s also brought about what was arguably the most important enabling invention in the further development of living polymerization methods, in the form of the first commercial size exclusion chromatograph (SEC), which was brought to market by Waters in 1963.<sup>62</sup> As we will discuss later, the ability to rapidly screen new polymerization methods by narrowness of molecular weight distribution as a proxy for *livingness*, which was also facilitated by advances in computational power, made future developments much more rapid than they otherwise would have been.

Living polymerization methods continued to expand beyond anionic polymerization through the 1970s to cationic and Ziegler–Natta polymerization. The living cationic ring-opening polymerization of 2-methyl-2-oxazoline was reported by Saegusa and co-workers in *Macromolecules* in 1972.<sup>63</sup> In the mid-70s, Pepper came to the sad conclusion about living cationic polymerization of alkenes: “it seems to me unlikely that any cationic polymerization will display living characteristics in their full perfection.”<sup>64</sup> However, by the end of the decade, Kennedy reported the preparation of styrene/isobutylene block copolymers<sup>65</sup> and Higashimura and Sawamoto described conditions for the preparation of methoxystyrene/vinyl ether block copolymers<sup>66,67</sup> by cationic polymerization. Great progress was made in understanding the living ring-opening polymerization of lactones by the groups of Teyssie,<sup>68</sup> Penczek,<sup>69</sup> and Boileau.<sup>70</sup> Doi and co-workers found that low-temperature polymerization of propene with a soluble vanadium catalyst system could proceed without termination or transfer events, in contrast with previous Ziegler–Natta catalyst systems.<sup>71,72</sup> While the development of living ROMP would have to wait until the 1980s, the groundwork was laid with the design of discrete metallocarbene initiators.<sup>73,74</sup> Another notable attempt at the development of a living radical polymerization method was carried out by Horie and co-workers, in which oxidized polypropylene was used as a heterogeneous radical initiator for emulsion polymerization before it was removed by filtration to generate long-lived radical species within growing polymer particles that could be grown into block copolymers, though with poor control over molecular weight.<sup>75,76</sup>

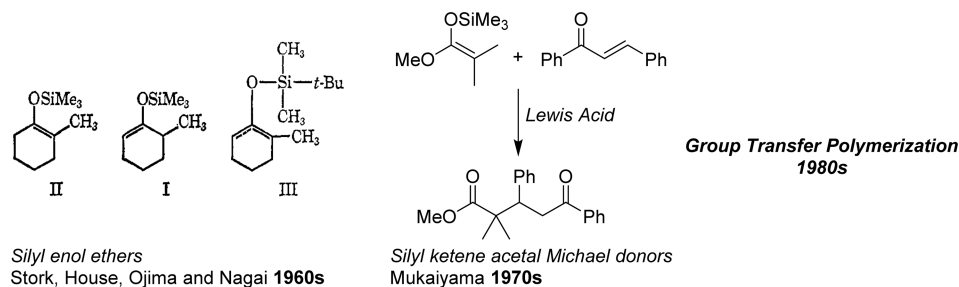
The 1980s saw continued expansion of living cationic polymerization and the establishment of the principles that would lead to the development of controlled radical polymerization in the 1990s. Sawamoto and Higashimura confirmed the living characteristics of the cationic polymerization of vinyl ethers and continued to optimize polymerization conditions,<sup>77–80</sup> as did Kennedy, Faust, and co-workers with isobutylene.<sup>81–83</sup> Owen Webster and co-workers at DuPont developed group transfer polymerization (GTP) as a method for the living polymerization of methacrylates and, in doing so, provided a clear example for how synthetic organic chemistry could

significantly influence the design of new living polymerization methods, as will be discussed below.<sup>84,85</sup> Conditions for carrying out the living ROMP of norbornene with titanacyclobutane initiators were disclosed by Gilliom and Grubbs.<sup>86</sup> Subsequently, Schrock and co-workers reported a similar accomplishment with a tantalum catalyst,<sup>87</sup> as did Schrock, Grubbs, and co-workers with a tungsten catalyst.<sup>88</sup> Where prior efforts at achieving living radical polymerization relied on minimizing termination in emulsion polymerization systems,<sup>47,75,76</sup> efforts in the 1980s used reversible deactivation strategies, akin to the anthracene-mediated anionic polymerization described by Szwarc in 1962.<sup>16</sup> Enikolopyan and co-workers discovered that cobalt–porphyrin complexes were very efficient chain transfer agents, which would later be exploited to control the radical polymerization of methacrylates and eventually supplant GTP as a practical method for the synthesis of methacrylate polymers.<sup>89</sup> Otsu described the use of thiuram disulfide and related disulfides as *iniferters* (initiator–transfer agent–terminator) to control the polymerization of styrene and methacrylates, which would set the stage for the later development of reversible addition–fragmentation chain transfer (RAFT) polymerization.<sup>90,91</sup> Solomon, Rizzardo, Moad, and co-workers at CSIRO carried out fundamental work into mechanisms of initiation for radical polymerization with nitroxides as chain-trapping agents,<sup>92,93</sup> which led directly to the development of nitroxide-mediated radical polymerization.<sup>94</sup> In 1986, Fischer introduced the concept that has become known as the *persistent radical effect*,<sup>95</sup> which informed the development of later RDRP methods.<sup>96,97</sup>

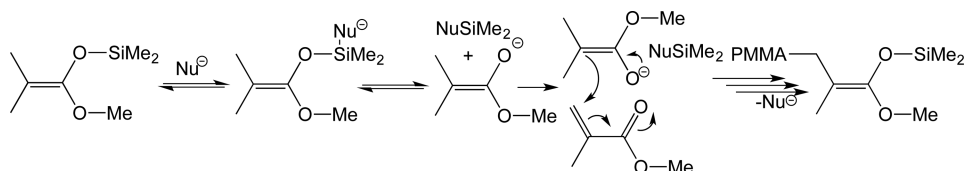
Research into what was variously termed “controlled radical polymerization”, “living radical polymerization”, or just “living radical polymerization” (IUPAC has recommended the term “reversible deactivation radical polymerization” (RDRP))<sup>5</sup> took off in the 1990s. While Druliner's early efforts to use arylazaoxyl radicals as reversible chain terminating agents were capable of producing block copolymers with broad molecular weight distributions,<sup>98</sup> further investigation of TEMPO and related nitroxides as agents to control radical polymerization by groups at Xerox (Georges and co-workers)<sup>99</sup> and IBM (Hawker and co-workers)<sup>100,101</sup> led to the development of nitroxide-mediated radical polymerization (NMP) as the first widely accessible RDRP method for styrene derivatives (and later, acrylate and diene monomers). Wayland and co-workers extended the use of cobalt–porphyrin complexes to enable the living polymerization of acrylates.<sup>102</sup> In 1995, two fundamental papers describing the metal-mediated radical polymerization process that would come to be known widely as atom transfer radical polymerization (ATRP), one by Sawamoto and co-workers<sup>103</sup> and the other from Matyjaszewski's group,<sup>104</sup> appeared. Given the broad applicability of ATRP to acrylate, methacrylate, and styrene derivatives, it was quickly adopted across disciplines.<sup>17,105</sup> Within a short period of time, a number of other research groups added to the range of initiators and catalysts that were effective with ATRP.<sup>106,107</sup> In the waning years of the century, the third of the three major controlled radical polymerization methods, reversible addition–fragmentation chain transfer (RAFT) polymerization, was described by Moad, Rizzardo, Thang, and co-workers.<sup>108</sup> The versatility of RAFT polymerization and relative ease with which it can be conducted overcame early aversions to the use of thiol derivatives as chain transfer agents and have led to its widespread adoption.<sup>109</sup> *Macromolecules* played in a key role in publishing much of the early work in RDRP.

Significant progress toward living coordination polymerization of ethylene and  $\alpha$ -olefins was also achieved in the 1990s.

Scheme 1. Preparation of Silyl Enol Ethers (Structures on Left Reproduced with Permission from Ref 138)



Scheme 2



Brookhart and co-workers reported the living polymerization of ethylene at room temperature with a cobalt catalyst system.<sup>110</sup> McConville,<sup>111</sup> Brookhart,<sup>112</sup> and Schrock<sup>113</sup> all described systems that enabled the living polymerization of propylene and higher olefins.

After the turn of the century, the use of RDRP methods continued to grow. Contributions to living polymerization were made in several key areas. Sita and co-workers described the stereospecific living polymerization of 1-hexene.<sup>114</sup> Earlier efforts to understand how what are traditionally step-growth polymerizations can be induced to proceed by chain growth mechanisms by Lenz,<sup>115</sup> Heitz,<sup>116</sup> Percec,<sup>117</sup> Robello,<sup>118</sup> Yokozawa,<sup>119,120</sup> and others,<sup>121</sup> bore fruit in the development of methods for the preparation of conjugated polymers (which, despite these developments, are still largely prepared via step-growth polymerization through aryl-aryl coupling reactions, particularly Stille,<sup>122</sup> Suzuki-Miyaura,<sup>123</sup> and direct arylation<sup>124</sup> coupling reactions) in a living fashion by Yokozawa<sup>121,125,126</sup> and McCullough.<sup>127,128</sup> The continuing exploration of organocatalyst systems, including thiourea derivatives, amidines, and guanidines, for the living ring-opening polymerization of lactones by Waymouth and Hedrick has provided a range of methods for the preparation of a wide variety of polyester architectures.<sup>129–131</sup>

## ■ POLYMERS AS MACROMOLECULES

The development of living anionic polymerization made it abundantly clear that polymers could be thought of as organic (macro)molecules: functionalized initiators could be used to introduce functional groups to one chain end, functionalized terminating agents could be used to introduce functionalized chain-ends, sequential addition of different monomers could be used to prepare block copolymers, and so forth. Instead of an ill-defined mixture of polymer chains with average molecular weights and average degrees of functionalization, polymers could now be thought of as precisely defined macromolecules with specific functional groups, though still with distributions of molecular weights, albeit much narrower than typically prepared before. Living polymerization and allied methods have led to the design of macromolecular architectures that would be inconceivable with nonliving methods: well-defined star, graft, brush, multiblock, cyclic, and telechelic polymers have all been realized with multiple types of living polymerization methods.<sup>132–134</sup>

While high-vacuum anionic polymerization remains the most precise method for carrying out *living polymerization*, the development of more accessible procedures that produce acceptably narrow molecular weight distributions and allow preparation of block copolymers with high efficiency has led to tremendous advances in polymer science. The ability to accurately control polymer molecular weight, dispersity, composition, and chain-end functional groups has enabled careful studies of polymer physical properties.<sup>26,134,135</sup>

## ■ ORGANIC ROOTS

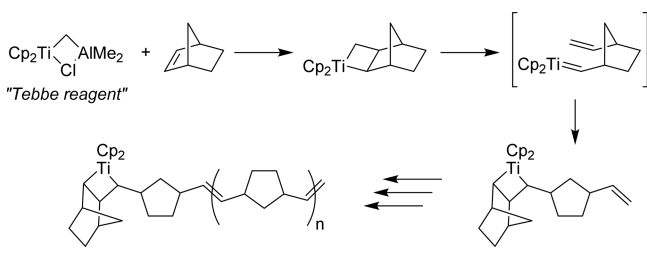
The genesis of many living polymerization methods can be traced directly to methods developed by synthetic organic chemists. While the construction of complex organic molecules requires a broad range of functional group transformations that can proceed efficiently in the presence of a diversity of functional groups, the precise preparation of any given polymer calls for a single highly efficient reaction that can be induced to occur over and over again.

**Group Transfer Polymerization (GTP).** The group at DuPont headed by Owen Webster introduced organic chemists to use of standard organic reactions for the production of well-defined polymers in the early 1980s. Group transfer polymerization (GTP) developed from earlier work by Mukaiyama and others on the use of silyl ketene acetals as donors in the Michael reaction for the synthesis of  $\delta$ -ketoesters,<sup>136,137</sup> which in turn was built upon the development of accessible methods for the preparation of silyl enol ethers by Stork,<sup>138</sup> House,<sup>139</sup> and Ojima and Nagai<sup>140</sup> (Scheme 1). In GTP, silyl enolates are activated by either nucleophiles or Lewis acids to undergo a condensation with methacrylates. Polymerization occurs by sequential transfer of the terminal silyl group of the growing polymer chain to methacrylate monomers as they are added to the chain end to produce poly(methyl methacrylate) chains with low dispersity, which could be coupled with suitable terminating agents into more complex architectures such as star polymers (Scheme 2).<sup>141</sup> It also helped that, at about the same time, SEC had advanced to the stage where it was readily available so that organic chemists, already accustomed to the use of HPLC for analysis of organic products, could easily adopt SEC for analysis of polymers by purchasing new columns and perhaps a new detector. A related process to produce poly(vinyl alcohol) was also developed.<sup>142</sup>

The star polymers produced by the condensation of living PMMA chains with multifunctional methacrylates demonstrated that unusual properties could be derived from such controlled polymerization techniques.<sup>143</sup>

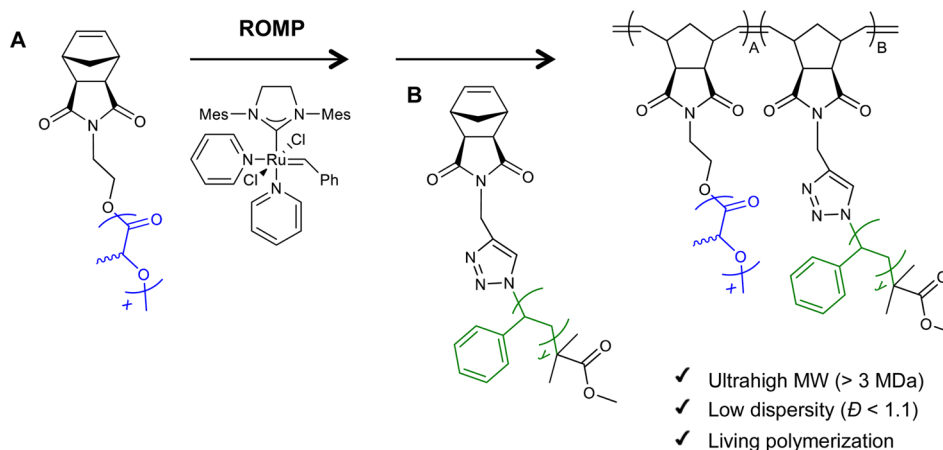
**Ring-Opening Metathesis Polymerization (ROMP).** At a similar time, Fred Tebbe at DuPont was studying titanium methylene complexes that became known as the “Tebbe Reagent” and demonstrated that they would undergo a basic olefin metathesis reaction where the terminal methylenes of olefins could be exchanged.<sup>74</sup> At Caltech, it was demonstrated that the “Tebbe Reagent” would react with norbornene in the presence of a pyridine base to produce a stable metallacycle. When this metallacycle was heated with more norbornene, a living polymerization of norbornene was observed (Scheme 3).<sup>86</sup> By tuning the structure of the initiator to give faster initiation, polymers with narrow dispersity and block copolymers could be prepared.<sup>144</sup>

Scheme 3



Since this time, a number of stable initiators for olefin metathesis have been discovered. All the stable metathesis initiators have been shown to produce living polymers. In many cases, manipulation of the initiation rate is required to produce narrow dispersity polymers.<sup>145</sup> These newer initiators based on molybdenum and ruthenium are being used widely to produce well-defined polymers with low dispersities.<sup>146</sup> Some of the largest polymers made by living polymerization are the brush-block copolymers that are initiated by ruthenium-based initiators (Scheme 4).<sup>147</sup> The ruthenium-based ROMP initiators have become widely used in organic synthesis, making metathesis a notable case in which a discovery in the polymerization field has resulted in the development of new organic reactions, rather than the reverse.

Scheme 4



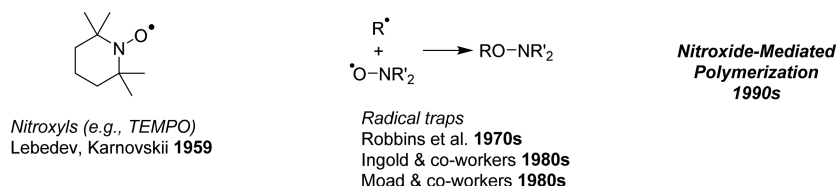
**Nitroxide-Mediated Polymerization (NMP).** Edmond Frémy’s discovery of his eponymous salt,<sup>148</sup> which was later identified as a stable free radical,<sup>149–151</sup> was the root of the later development of diaryl<sup>152</sup> and dialkylaminoxyl radicals<sup>153,154</sup> as organic spin-labels,<sup>155</sup> radical traps,<sup>156</sup> oxidizing agents,<sup>157</sup> polarizing agents for dynamic nuclear polarization NMR,<sup>158</sup> and ultimately, at least from a polymer chemistry perspective, as reversible traps for propagating radical chain ends in RDRP (Scheme 5).<sup>159,160</sup>

**Atom-Transfer Radical Polymerization (ATRP)/Metal-Mediated Radical Polymerization.** Kharasch’s discovery in the 1930s that the presence of a radical initiator could change the regiochemistry of hydrogen halide addition to alkenes<sup>35</sup> laid the foundation for the development of what would become known as atom transfer radical addition (Scheme 6).<sup>161,162</sup> Minisci’s realization that such additions could be catalyzed by metal species ultimately paved the way for the development of metal-mediated RDRP methods (Scheme 6),<sup>163,164</sup> which are discussed in detail elsewhere.<sup>17,105</sup>

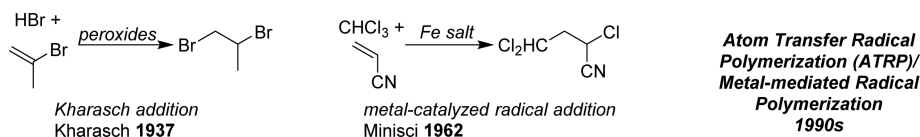
**Reversible Addition–Fragmentation Chain Transfer (RAFT) Polymerization/Macromolecular Design via Interchange of Xanthates (MADIX).** Tetraalkylthiuram disulfides, originally described by Grodzki in the 1880s,<sup>165</sup> had found use in the vulcanization of rubber by the 1920s. In the 1950s, Otsu,<sup>166,167</sup> Kern,<sup>168</sup> Tobolsky,<sup>169</sup> and others explored the use of tetraalkylthiuram disulfides and related sulfides and disulfides as polymerization initiators (Scheme 7). In the 1970s, as the mechanism for the Barton–McCombie deoxygenation reaction and other thiocarbonyl-dependent transformations were explored,<sup>170</sup> the utility of xanthate esters as radical precursors was recognized. Otsu further developed tetraalkylthiuram and related thiocarbonyl compounds as initiation–transfer–termination (“iniferter”) agents in radical polymerization in the 1980s.<sup>90,91,171</sup> These earlier efforts culminated, at least from a polymer-centric perspective, in the development of the xanthate, dithioester, and trithiocarbonate transfer-agent-based RDRP methods termed macromolecular design via interchange of xanthates (MADIX)<sup>172,173</sup> and reversible addition–fragmentation chain transfer (RAFT) polymerization.<sup>174</sup> The details of these developments are left to the recent Perspective by Perrier.<sup>175</sup>

**Organocatalytic Polymerization.** Organocatalysis has a long tradition in organic chemistry, especially as simpler methods to achieve the stereoselectivity of enzymatic transformations

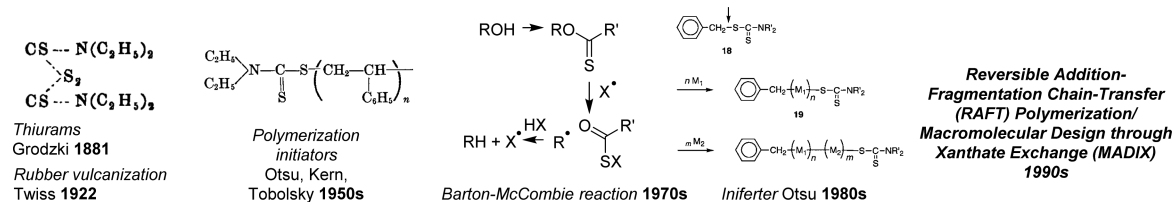
## Scheme 5



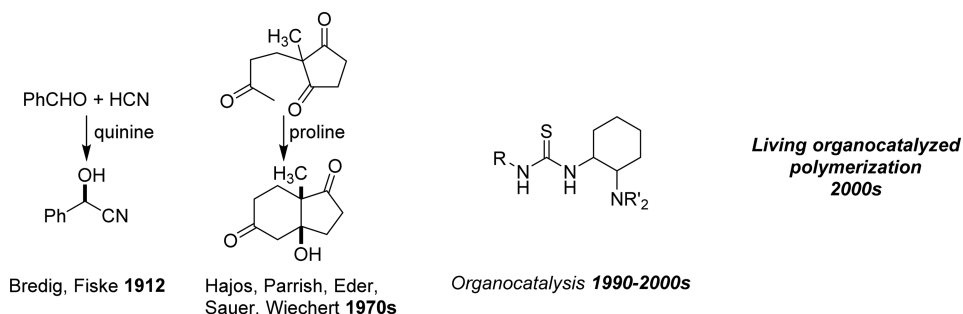
## Scheme 6



**Scheme 7.** Thiuram Structure on Left (Reproduced with Permission from Ref 165. Copyright 1881 Wiley-VCH Verlag GmbH & Co. KGaA); Polymerization Initiators Structure (Reproduced with Permission from Ref 167; Copyright 1957 John Wiley & Sons, Inc.); Barton–McCombie Reaction Scheme (Adapted with Permission from Ref 176. Copyright 1975 Royal Chemical Society); Iniferter Scheme (Reproduced with Permission from Ref 171. Copyright 2000 John Wiley & Sons, Inc.)



## Scheme 8



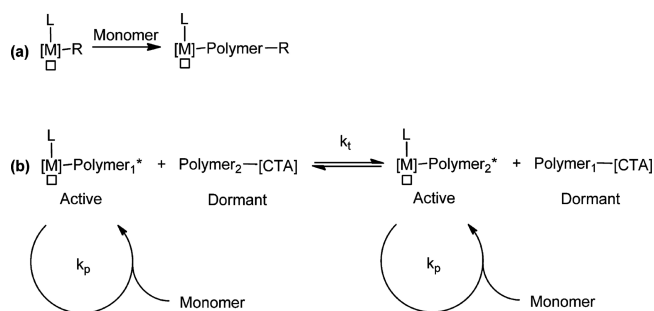
were sought. From the early efforts by Bredig and Fiske to use quinine and quinidine in the asymmetric synthesis of cyanohydrins,<sup>177</sup> to the rational design of organocatalysts in the 1970s and 1980s, the understanding and application of organocatalysis in organic synthesis have blossomed in recent decades (Scheme 8).<sup>178–181</sup> In many respects, it is surprising that it took as long as it did for the full-throttled application of organocatalysis to living polymerization, but through the combined efforts of Waymouth, Hedrick, and others, the catalysts and principles developed for organic synthesis have been successfully adapted, optimized, and used as inspiration for the development of new generations of organocatalysts for the living ring-opening polymerization of a range of cyclic monomers.<sup>129–131,182–184</sup>

## ■ THE METAL CATALYST PROBLEM

When it comes to living polymerizations, polyolefins (and any other polymers made by a polymerization mechanism in which any growing polymer chain must be associated with a catalytic site) are a particularly sticky case. Polyethylene and polypropylene are the most widely used polymers because the

monomers are inexpensive, and highly efficient catalysts for their polymerization have been developed.<sup>185</sup> Living polymerization systems for olefins have been developed, but these all require the association of one metal center with each growing chain end, thus significantly increasing cost as molecular weight of the polymer decreases. Because relatively low molecular weight polymers are often desirable for block copolymers (where higher molecular weights make processing and annealing difficult) and for end-functionalized polymers (where the utility of functional end groups is lessened through dilution at higher molecular weights), the costs associated with increased catalyst loading likely outweigh any benefits afforded by the use of a living polymerization method.

Coordinative chain transfer polymerization (CCTP) methods have been developed that significantly reduce the amount of catalyst required through exploitation of rapid exchange of active chain ends with cheaper chain transfer agents (Figure 4).<sup>186–191</sup> CCTP systems that are specifically designed so that polymer chains are shuttled between different metal centers, each of which favors polymerization of different monomers, enables the preparation of blocklike polyolefins while similarly minimizing



**Figure 4.** (a) Coordination polymerization compared with (b) coordinative chain transfer polymerization (CCTP). Reproduced with permission from ref 190.

catalyst content.<sup>192–194</sup> Because these methods rely explicitly on transfer reactions, they do not meet the formal definition of *living*, but it is difficult to argue with the results: several olefin block copolymer elastomers prepared by CCTP strategies have been rapidly commercialized.<sup>195</sup> Other chain-transfer strategies involving reversible deactivation of polymer chains are being developed for ROMP.<sup>196</sup>

## ■ SIZE EXCLUSION CHROMATOGRAPHY (SEC)

A narrow molecular weight distribution is typically the first characteristic that one looks for in a new polymerization suspected to be living. More careful analyses of kinetics and the relationship between conversion and molecular weight typically follow. It was only after the widespread availability of SEC systems, facilitated by the development of separation media compatible with organic solvents and desktop computers with enough computational power to rapidly process SEC data, that estimating average molecular weights and dispersities of synthetic polymers became a relatively nononerous task.<sup>62,197,198</sup> While SEC is not without significant limitations—accurate estimation of molecular weights requires significant investment in detectors and maintenance as well as careful calibration, interactions of samples with separation media can give inaccurate results, and meaningful results can be difficult to obtain for polymers with complex architectures—the ability to take a polymer sample with minimal workup and estimate  $M_n$  and  $\mathcal{D}$ , typically in under an hour, has tremendously accelerated the screening of new polymerization methods and has arguably

had an incalculable effect in accelerating the development of new living polymerization methods (Figure 5).

Sixty years after Flory's initial prediction,<sup>11</sup> SEC played an important role in the demonstration that careful living anionic polymerization can result in a Poisson distribution of molecular weights.<sup>200</sup> This work also illustrated the usefulness of complementary techniques, chiefly thermal gradient interaction chromatography (TGIC),<sup>201–203</sup> in providing information about molecular weight distributions that is not available from SEC analysis.

The maturation of MALDI-TOF MS as a method for polymer characterization has also helped in enabling more accurate molecular weight calculations, though reliable detection of higher molecular weight samples is not always easy. As a result MALDI-TOF MS has not to date had nearly the effect on the development of living polymerization methods that SEC did and is typically used as a secondary method to validate SEC results. It has, however, proven invaluable as a method for carrying out detailed analyses of polymer structure, including identification of undesirable side reactions and termination reactions that can occur during polymerization, which can enable the development of more *living* polymerizations from less-living methods.<sup>204,205</sup>

The recent demonstration that real-time systems for automating SEC analysis during polymerization (ACOMP: automated continuous online monitoring of polymerization)<sup>206</sup> can be used to control molecular weight and molecular distribution for a given polymerization<sup>207</sup> suggests that there is still great potential for SEC to influence the further development of living polymerization methods.

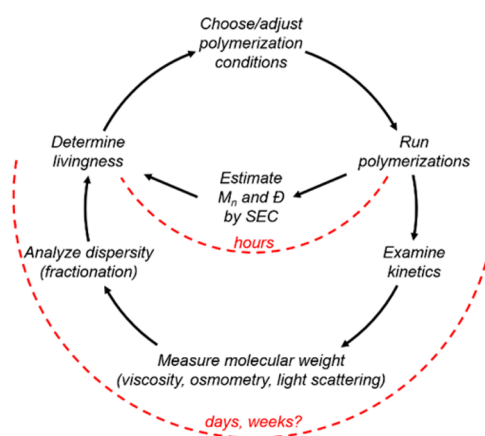
Continuing advances in rapidity and accuracy of NMR diffusivity measurements as a method for the estimation of polymer molecular weight and dispersity could lead to challenges to the primacy of SEC for such analyses, especially given the widespread availability of high-field spectrometers and gradient probes.<sup>208–212</sup>

## ■ DISPERSITY: NOTHING BUT A NUMBER?

While living polymerization is typically thought of as a route to polymers with a narrow distribution, it is increasingly being recognized that various living methods can also be used with specific procedural modifications to prepare polymers with broader but controllable molecular weight distributions. It would

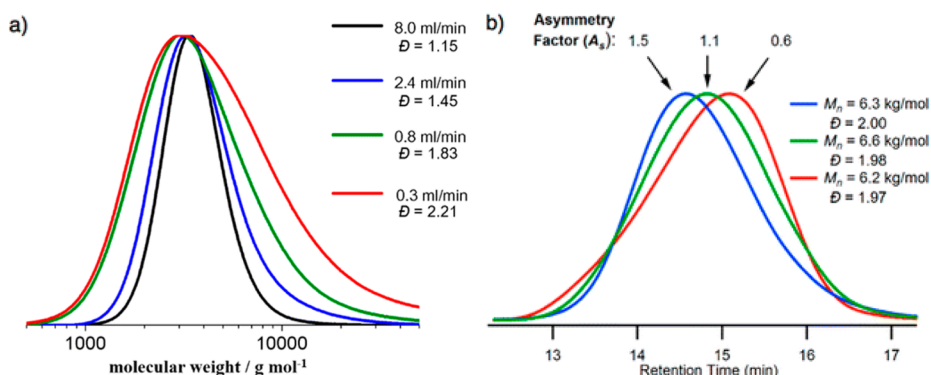


**CHECK.** Dow's John C. Moore checks chromatogram obtained by gel permeation chromatography, which separates a polymer's constituents by molecular weight



**Figure 5.** Left: an early size exclusion chromatography (SEC)/gel permeation chromatography system (original appeared in ref 199). Right: advantages of SEC for rapid assessment in the development of new living polymerization methods.





**Figure 6.** (a) Effect of changing flow rate in a continuous flow reactor on dispersity of polystyrene samples prepared by anionic polymerization ( $M_n = 3400 \text{ g mol}^{-1}$ ). Decreasing the flow rate leads to higher dispersity. Reproduced with permission from ref 232. (b) Changing NMP initiator addition rate profile leads to changes in the symmetry of the molecular weight distribution of polystyrene at constant  $\bar{D}$ . Reproduced with permission from ref 231.

seem peculiar at first glance to expend greater effort to reduce control over a polymerization process, but there are clear reasons to explore these types of polymers. For many materials, a broad molecular weight distribution can aid in processability and results in materials with superior properties to those prepared from polymers with narrow molecular weight distributions. It has also been shown that dispersity can have significant effects on degradation/release<sup>213,214</sup> and electronic properties<sup>215</sup> of polymers.

A growing body of literature suggests that controlling the breadth of the molecular weight distribution in addition to the molecular weight can provide an additional level of control over physical properties.<sup>216–229</sup> This is especially true for block copolymers, where polydisperse block copolymers can show significantly larger domain spacings than monodisperse block copolymers of comparable molecular weights and compositions,<sup>217,222,225,227</sup> though this effect does not appear to occur in the strong segregation limit.<sup>226</sup> Dispersity has also been shown to influence self-assembly of block copolymers in solution, in some cases favoring the formation of nonspherical micelles,<sup>224</sup> though the dispersity of block copolymer stabilizers in emulsion polymerization has been found have little effect upon the resulting polymers.<sup>230</sup> Methods for controlling dispersity through metered addition of anionic<sup>231,232</sup> or RDRP initiators<sup>233</sup> to polymerization have been recently refined (Figure 6).

At the same time that comfort with higher dispersities is growing, the effects of the absence of dispersity<sup>234</sup> on synthetic polymer properties are being explored, largely through heroic synthetic and purification efforts (echoing Wieland's advice to Staudinger quoted at the beginning of this Perspective).<sup>235–238</sup> While most of these examples do not involve *living polymerization*, a notable recent exception described by Hawker, Gutekunst, and co-workers describes the use of ATRP or ROP to prepare oligomer mixtures with narrow molecular weight distributions that can then be separated by automated chromatography into discrete oligomers ( $\bar{D} = 1$ ).<sup>237</sup> As has been shown for high-dispersity polymers, truly monodisperse oligomers show markedly different behavior from polymers with narrow molecular weight distributions. For example, both Palmans, Meijer, and co-workers<sup>236</sup> and Hawker, Bates, and co-workers<sup>239</sup> have demonstrated that block copolymers with one or more monodisperse blocks tend to assemble into structures with narrower domain spacings and lower order-disorder transition temperatures than comparable polymers with higher dispersities. The key message here seems to be that obtaining a polymer with a narrow molecular weight distribution

is not as important as obtaining a polymer with the appropriate molecular weight distribution for its intended application.

## ■ FUTURE DIRECTIONS

At this point in history, it is difficult to argue that the near future of *living polymerization*, both in application and in development, will not continue to be defined by the most accessible polymerization methods: RDRP (particularly ATRP and RAFT), ROMP, and ROP of cyclic esters. There are a number of potential research directions that *living polymerization* could influence and, through which, the scope of *living polymerization* could be expanded.

**Supramolecular Polymerization.** An increasing number of reports on supramolecular/noncovalent polymerization strategies that proceed with some degree of living character have appeared.<sup>240–243</sup> While the range of subunits that can be polymerized by these methods—notably, poly(ferrocenylsilane) block copolymers,<sup>244,245</sup> molecules capable of  $\pi$ - $\pi$  stacking and hydrogen bonding,<sup>246–249</sup> and corannulenes capable of switching from intramolecular hydrogen bonding in the monomer to intermolecular hydrogen bonding in the polymer<sup>250</sup>—continues to expand, the development of more general living supramolecular methods and their combination with more traditional living polymerization methods would be greatly desirable.

**Polymerization-Induced Self-Assembly.** The combination of time-honored emulsion polymerization techniques with RDRP macroinitiator-based stabilizers has been honed into the widely adopted polymerization-induced self-assembly (PISA) method which allows the direct simultaneous preparation of amphiphilic block copolymers and their assemblies in solution.<sup>251</sup> RDRP has enabled the rapid growth of this method to allow the preparation of defined copolymer assemblies at relatively high concentrations in solvents that are incompatible with traditional ionic methods.<sup>251,252</sup> Extension of PISA to additional polymerization methods is inevitable, though the requirement that the solvophobic block(s) be prepared from monomers that are soluble in the polymerization solvent will provide restrictions on the range of accessible copolymer systems.

**Extension of Chain-Shuttling to Other Monomer Systems.** CCTP strategies, while not living by the standard definition, have been successfully used for the preparation of polyolefin block copolymers.<sup>186–190,192–194</sup> Further tuning of shuttling and polymerization rates, as well as the incorporation of catalysts capable of tolerating polar monomers such as methyl methacrylate, would make these techniques even more useful.

**Continued Adoption of Synthetic Organic Chemistry Techniques.** As the interest of organic chemists in photochemical transformations has reached new peaks, presumably due to the development of photocatalysts that function with visible light and the widespread availability of low-cost LED sources as substitutes for earlier mercury-based UV lamps, these techniques have been quickly adopted by polymer chemists and adapted to living polymerization methods.<sup>253–256</sup> Living or close-to-living photopolymerizations have to date been demonstrated for RAFT polymerization,<sup>257</sup> ATRP,<sup>258,259</sup> cationic polymerization,<sup>260</sup> ROMP,<sup>261</sup> organotellurium-mediated radical polymerization,<sup>262</sup> and ROP of *N*-carboxyanhydrides.<sup>263</sup> Photoinduced RAFT polymerization has been successfully used in PISA strategies for the preparation of block copolymer assemblies.<sup>264,265</sup> Similarly, electrochemical<sup>266,267</sup> and mechanochemical<sup>268</sup> methods have begun to be exploited to control polymerizations.

As interest in flow chemistry as a general method for the synthesis of complex organic molecules continues to grow,<sup>269–272</sup> it is likely that these techniques will be adapted for use with living polymerization methods for the synthesis of complex polymer architectures.<sup>273</sup> Kilogram-scale living anionic polymerization of styrene in a continuous reactor has recently been demonstrated.<sup>274</sup> Semibatch conventional radical polymerization with an automatic molecular weight controller has been used to control the molecular weight distribution of polyacrylamide.<sup>275</sup> An iterative exponential growth strategy for the construction of well-defined oligomers through flow chemistry has also been reported.<sup>238</sup> Miyake and co-workers have tied together a number of these threads in their successful execution of photoinduced organocatalyzed ATRP in a continuous flow reactor.<sup>276</sup>

**Higher-Order Sequence Control.** Significant efforts are currently being directed at pushing the structural control made possible by living polymerization methods beyond relatively simple block, random, and alternating structures toward the preparation of polymers with programmable monomer sequences.<sup>277–285</sup> This is an admirable undertaking, and the field is likely to be greatly enriched by the lessons learned along the way. Fabricating synthetic systems that can even begin to approach biological systems in terms of control of sequence and dispersity is daunting. Despite the clear appeal of using *living polymerization* to prepare polymers that show the characteristics of polymers from living systems, there is little in prior literature to suggest that there is any actual connection between the synthetic and biological realms here. The complexity of the molecular machinery that goes into biosynthesis of macromolecules does not suggest an obvious way to simplify the key steps involved into a simpler synthetic model, even if the error-correction capabilities of living systems are ignored. For example, protein biosynthesis involves a sequence-defined mRNA strand (with three sequenced nucleotides for each amino acid residue in the protein), a sequence-defined tRNA (70–100 nucleotides) for each amino acid residue, and a ribosome (in eukaryotes, ~79 proteins, ~4 RNA strands of 120, 160, 1900, and 4700 nucleotides). To expect a simple molecular initiation/propagation system to be capable of organizing structure at this level requires a great deal of optimism.

Another important question raised in the quest for polymerization methods that allow control over monomer sequence is, what sequence should be prepared? Biological systems give clear models for sequences based upon biogenic structures and enforce requirements (e.g., water solubility, biocompatibility,

biodegradability) that provide some boundaries on the range of structures to be explored. For synthetic polymers, a specific application will need to be defined for any system prior to addressing this question. Combinatorial synthesis methods could go a long way toward defining desirable sequences, but successful screening on an adequately short time scale would still be necessary as would the development of strategies for producing useful quantities of functional sequences once they were identified.<sup>286–289</sup>

It might be more fruitful if polymer chemists cast an eye toward other biogenic macromolecules and assemblies that mesh more closely with the strengths of polymer synthesis in their lack of precise structural definition, such as polysaccharides and lipid assemblies. Synthetic carbohydrate chemistry is challenging, but there have long been effective examples of the use of controlled and living polymerization methods in the preparation of saccharide-modified polymers,<sup>290–296</sup> and continuing advances in carbohydrate synthesis through iterative protection/deprotection sequences can be adopted.<sup>297–300</sup> Likewise, there are now many published examples where micelles and vesicles that are analogous to those formed by lipids have been prepared from amphiphilic block copolymers. In polysaccharides and in lipid assemblies (if the latter are treated as supramolecular polymers), structural homogeneity is the exception rather than the rule—oligosaccharides and glycoconjugates often have heterogeneous structures<sup>301</sup>—and cell membranes are a mixture of phospholipids and glycolipids of different chain lengths, sterols, peptides, and other components. Such types of biomimetic targets, as well as structural proteins with relatively simple repeating motifs such as collagen and elastin,<sup>302</sup> are much more accessible through polymerization chemistry than polymers with specific monomer sequences.

**Continued Exploration of Renewable and Degradable Monomers and Polymers.** The identification of low-cost chemical feedstocks derived from renewable sources other than petroleum and coal has long been of importance to synthetic organic chemists, especially in finding renewable replacements for commodity materials as well as chiral feedstocks.<sup>303–305</sup> With the growing recognition of problems with polymer waste streams, there has been tremendous activity in this area with great focus on polymers such as polylactide and other polyesters that can be prepared by living polymerization methods. Many of these efforts are outlined in the recent Perspective by Schneiderman and Hillmyer.<sup>306</sup>

## ■ IS LIVING POLYMERIZATION ALWAYS NECESSARY?

*That is not dead which can eternal lie. And with strange aeons even death may die.*—“The Nameless City,” H. P. Lovecraft (1921)<sup>307</sup>

Many of the desirable qualities of polymers prepared by living polymerization methods can be achieved without the need for the often considerable efforts required to ensure that the conditions for a living polymerization are met. Polymers with blocklike architectures can be readily prepared by step-growth polymerization of suitably functionalized oligomers or polymers (e.g., polyurethanes) or by catalytic chain-shuttling methods. End-functionalized polymers can be prepared either by step-growth polymerization with a slight excess of the monomer unit with the desired functional groups or by conventional radical polymerization with functionalized initiators, terminating agents, and/or chain-transfer agents, though control over molecular weight, dispersity, and any properties that depend upon these

parameters will suffer. Molecular weight and, to some extent, dispersity can be controlled in chain polymerizations by the use of chain-transfer agents. In all of these cases, the level of absolute control over molecular weight and dispersity suffers when compared to living polymerization methods, but for many applications, a narrow molecular weight distribution offers few advantages over a broader one. Developing new living polymerization methods and extending existing living polymerization methods to new monomers are excellent fundamental exercises, but they should not always be taken as entirely necessary goals. Even the *livingest* of living polymerization methods still results in polymers with much broader molecular weight distributions than those that result from biological systems. The quotation-mark-encapsulated “living” has often been used as a descriptor for polymerizations that do not quite meet the strict definition of *living*. Since *living*, as used in the strictest definition by polymer scientists, does not meet even the most generous definition of *living*, as used by the rest of the world, this seems a somewhat arbitrary distinction. Since words sometimes do have two meanings and the weight of history enforces this differentiation in usage, perhaps there is little that can be done to change this, though it is tempting to take the Lovecraftian tack that a polymerization that is not dead might be good enough for most.

## ■ DIVERSITY

*In diversity is life, and where there's life there's hope...—The Word for World is Forest, Ursula K. Le Guin*

Just as diversity in the polymer community has played a large role in the many advances in polymer science,<sup>308</sup> so has the continued development of living and livinglike polymerization methods been crucial to the continued growth of polymer science. Not all monomers can be polymerized by any given method. Not all copolymers can be prepared by any one specific method. Expertise and facility in one general class of polymerization will limit a researcher to a small subset of possible polymers and will likely limit the scope of polymer structures that one can imagine. While there are certain methods that have been widely adopted due to their versatility and ease of use (especially ATRP, RAFT, ROMP, and many of the other ring-opening polymerization methods), it is important for future growth that other methods do not fall by the wayside. There is little in the early history of each of these polymerization methods that suggests that they would necessarily be developed into the powerful techniques they have become. A diverse variety of living polymerization methods—organotellurium, organobismuth, and organolead-mediated radical polymerizations,<sup>309–311</sup> titanocene-catalyzed radical polymerization,<sup>312</sup> polyhomologation<sup>313–315</sup>—that have otherwise been given short shrift in this discussion have been developed that could lead to important advances in the future. Just as the synthesis of complex organic molecules has benefited from the availability of a large toolbox of reactions, the synthesis of complex macromolecular architectures will be facilitated by the maturation of multifarious polymerization methods. For example, interest in photoiniferter-mediated polymerization, originally described by Otsu in the 1980s,<sup>90,91,171</sup> which as a polymerization method has generally been looked over in favor of other RDRP methods, has redeveloped recently. Zhou and Johnson have demonstrated that trithiocarbonates can be used in the synthesis of telechelic poly(*N*-isopropylacrylamide) chains with low dispersity for the subsequent preparation of polymer gels with well-defined structures.<sup>316</sup> Sumerlin and co-workers have recently shown that UV-irradiation of trithiocarbonate and xanthate-based initiators can be effective for the preparation of

exceedingly high molecular weight acrylamides ( $M_n > 8000$  kg/mol) with narrow molecular weight distributions ( $\bar{D} < 1.4$ ).<sup>317</sup>

## ■ CLOSING

The unique beauty of polymers lies in their juxtaposition of the profane—the inevitability (or at least desirability) of their eventual application and co-option by engineers—and the sacred—their identity as organic molecules to which all of the fundamental science of synthesis can be applied.

*Living polymerization* has arguably been the central unifying concept for synthetically inclined polymer scientists and engineers over the past half century, and *Macromolecules* has played an influential role in its development. There is a simple and powerful elegance to the idea of a pool of active polymer chain ends in a pool of monomer with nothing else to do but grow, with a narrow distribution of chain lengths resulting if all of the chains start growing at the same time. These features make *living polymerization* perhaps the easiest general polymerization concept to explain to students new to the area, especially when compared to seemingly outrageous array of kinetic steps possible in conventional radical polymerization and the haphazard growth mechanism of typical step polymerization methods. The overt if incorrect suggestion that the *living* in *living polymerization* ties in somehow to *life* also likely adds to the appeal of the overall concept.

Since the earliest hypotheses about the possibility of producing polymers with controlled structure through chain polymerizations that could be made to proceed without transfer or termination and the subsequent report of living anionic polymerization by Szwarc, a huge amount of fundamental research has been devoted to bending other polymerization methods—cationic, coordination, radical, ring-opening, metathesis, step-growth, and so on—with various degrees of success, to the exacting requirements of living polymerization. The most important results of these efforts have been the development of methods in the past few decades, especially the various flavors of reversible-deactivation radical polymerization (RDRP) and the ever-growing number of methods that allow control over ring-opening polymerizations, that allow almost any sentient creature with access to a fume hood and an inert gas tank to make a vast range of polymers that would only have been imaginable in past decades to expert synthetic chemists with uncanny glass-blowing abilities and an uncommon level of fearlessness.

What shortcomings these methods have when measured against the standard of anionic polymerization are more than overcome by their advantages in being *good enough* for the preparation of such structures as end-functionalized polymers, block copolymers, star copolymers, and graft copolymers. It is also important to not forget that even anionic polymerization has nothing on biology when it comes to monodispersity and sequence control. It would be a foolish endeavor to attempt to predict the future growth of polymer science with any level of precision, but it is surely safe to state that the ideal of *living polymerization* will continue to have a profound influence on the field even if, in practice, the *livingness* of the most widely used methods might sometimes be questionable.

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### Notes

The authors declare no competing financial interest.

### Biographies



Robert B. (Barney) Grubbs is a professor in the Chemistry Department at Stony Brook University. Previously, he has been an associate professor at Dartmouth College (2001–2009), a post-doc at the University of Minnesota with Frank Bates (1998–2001), a graduate student at Cornell University and UC Berkeley with J. M. J. Fréchet (1993–1998), and an undergraduate at Pomona College (1989–1993). His research group is focused on the design and synthesis of polymers and related organic materials.



Robert H. Grubbs is the Victor and Elizabeth Atkins Professor of Chemistry at the California Institute of Technology, where he has been a faculty member since 1978. Bob earned B.S. (1963) and M.S. (1965) degrees in Chemistry working with Merle Battiste at the University of Florida and a Ph.D. (1968) in Chemistry working with Ron Breslow at Columbia University. After working with Jim Collman as an NIH Postdoctoral Fellow at Stanford University (1968–1969), he was a faculty member at Michigan State University from 1969 to 1978. His awards have included the Nobel Prize in Chemistry (2005) and 9 ACS Awards. He has been elected a member of the National Academy of Sciences (1989), a Fellow of the American Academy of Arts and Sciences (1994), an Honorary Fellow of the Royal Society of Chemistry (2006), a member of the National Academy of Engineering (2015), and a Foreign Member of Great Britain's Royal Society (2017). He has 625+ publications and 160+ patents based on his research. The Grubbs group discovers new catalysts and studies their fundamental chemistry and applications. For example, a family of catalysts for the interconversion of olefins and the olefin metathesis reaction have been discovered. These catalysts are used in the synthesis of complex molecules and for the precise synthesis of polymeric materials. Under appropriate conditions these complexes can be used as initiators for the living polymerization of

strained olefins. In addition to their broad usage in academic research, these catalysts are now used commercially.

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