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Kinetics of Segment Formation in Nitroxide-Mediated Controlled Radical Polymerization: Comparison with Classic Theory

Lin Wang and Linda J. Broadbelt*

Department of Chemical and Biological Engineering, Northwestern University, Evanston, Illinois 60208

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ABSTRACT: The kinetic details of segment formation in living radical polymerization (LRP) were investigated by studying styrene (S)/methyl methacrylate (MMA) copolymerization via nitroxide-mediated controlled radical polymerization (NM-CRP) using kinetic Monte Carlo (KMC) simulations. It was demonstrated that the classic theory describing the distribution of instantaneous segment lengths developed for conventional free radical polymerization (FRP) does not always hold in LRP. Segment formation can be controlled by deactivation through coupling of growing radicals and nitroxide radicals instead of selective preference during propagation due to different reactivity ratios and composition of competing monomers if the transient lifetime is too short. Mathematical equations were proposed for determining in a facile way whether the segment growth is controlled by deactivation under given reaction conditions. The uniformity of segment growth was analyzed as well. It takes a surprisingly long time to allow the majority of the chains to be reactivated at least once in an S-rich reaction system, which leads to high polydispersity in monomer sequences formed on different chains. It was also demonstrated that there inevitably exists a distribution of segment lengths at a given monomer composition no matter how "ideal" the livingness is. This distribution is determined by the "intrinsic" kinetics of copolymerization and is not manipulated by the features of LRP.

Introduction

Living radical polymerization (LRP) has attracted significant attention recently because it can provide low-polydispersity polymers using relatively simple synthesis methods.[1] LRP is distinguished from conventional free radical polymerization (FRP) by a unique reversible activation/deactivation procedure, which renders the majority of radicals dormant during the reaction and thus suppresses the occurrence of termination to a great extent. Another benefit of this reversible activation/deactivation procedure is a significant extension of the lifetime of a free radical in LRP compared to that in FRP. Since the lifetime of a free radical can be maintained almost as long as the reaction time in LRP, it is possible to vary the monomer composition of the reactant mixture in a predetermined manner during the growth of a chain and thus incorporate segments of various sequence lengths into the same copolymer chain.[2] Therefore, one of the most important applications of LRP is to prepare copolymers with well-defined microscopic monomer sequences.[3−6]

It has been reported that LRP is able to produce block copolymers as well as gradient copolymers.[7] The latter type of copolymer is relatively new and is composed of segments that vary in length according to a certain pattern from one end to the other,[3] as depicted in Scheme 1. Gradient copolymers have attracted much attention recently.[2] It was demonstrated by both experimental and theoretical studies that the material properties of the copolymer, such as interfacial behavior, can be affected significantly by its monomer sequence. With a well-defined monomer sequence along the chain, gradient copolymers are good candidates for unraveling the explicit relationships between monomer sequence and material properties as well as exploring the potential applications related to these relationships.[2,8−12]

Although the kinetics of LRP have been studied intensely in the past decade, the majority of research efforts have been focused on improving the uniformity of overall chain growth in LRP, i.e., to achieve a low molecular weight polydispersity.[7,13−15] Few efforts have been devoted to study the kinetics affecting the formation of segments and the uniformity of monomer sequences in different chains prepared by LRP. This is mostly because of the difficulties in measuring monomer sequence directly by current experimental techniques and the limited capacity of conventional simulation techniques, such as continuum models, to track the complete monomer sequences along the chain.[2,16,17] Recently, we have reported a simulation framework based on kinetic Monte Carlo, which can predict the explicit sequence formed along each chain by tracking the growth of each individual chain instead of concentration.[18,19] By using KMC simulations, the kinetic details related to sequence formation, which cannot be predicted by other conventional simulation techniques, can be studied in a facile way. Our previous work reveals that current synthesis methods for preparing gradient copolymers may not be able to produce well-defined monomer sequences along the chain such as the one depicted in Scheme 1.[18,20] Since copolymers with well-defined monomer sequences are attracting much attention at present and are being involved in a growing body of research, it is of utter importance to understand the underlying kinetic basis of segment formation and the uniformity of monomer sequences prepared by LRP.

In this work, we discuss the kinetic factors governing segment formation and the uniformity of monomer sequences formed on different chains in an S/MMA copolymerization system via NM-CRP with BlocBuilder as the unimolecular initiator. This system serves as an appropriate platform for understanding the kinetics of LRP because S/MMA copolymerization by NM-CRP has been widely studied and detailed kinetic parameters are available in the literature.[14,21−34] With the presence of S, copolymerization involving MMA can be better controlled as living in NM-CRP. The formation of segments at a given instant in NM-CRP was studied and compared to that predicted by the classic theory of instantaneous segment length distribution, which has been

*To whom correspondence should be addressed.

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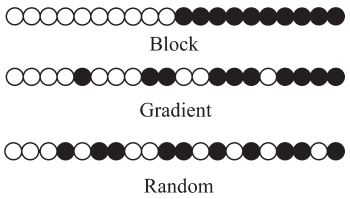
Scheme 1. Schematic Representation of the Composition in Block, Gradient, and Random Copolymers, in Which the Open Circles Denote Monomer A and the Closed Circles Denote Monomer B



considered universal in many copolymerization systems.[16] The underlying kinetics governing the uniformity of monomer sequences formed on different chains are discussed as well. Since all living radical polymerization processes involve a reversible activation/deactivation step in some form, the observations based on these common features of LRP can also be generalized for other types of living radical polymerization other than NM-CRP.

KMC Simulations

KMC is a stochastic simulation method. The reaction channel that occurs is determined by eq 1:

$$\sum_{v=1}^{\mu-1} P_v < r_1 < \sum_{v=1}^{\mu} P_v \tag{1}$$

where μ is the index of the selected reaction channel, P_v is the probability of the vth reaction channel, and r_1 is a random number uniformly distributed between 0 and 1. The time interval between any two reactions is determined by eq 2:

$$\tau = \frac{1}{\sum_{v=1}^{M} R_v} \ln\left(\frac{1}{r_2}\right) \tag{2}$$

where R_v is the stochastic rate of the vth reaction and r_2 is a second random number uniformly distributed between 0 and 1.

The model was developed based on elementary reactions including initiation, propagation, termination, and combination/dissociation with nitroxyl radicals (SG1, in our system). The kinetic parameters associated with these reactions are listed in the Supporting Information. More details about this simulation setup can be found in our earlier work.[18] The KMC model has been validated by the experimental data measured in our own lab as well as those reported in the literature. It was demonstrated that the KMC simulations were able to capture all these experimental data very well.

In this KMC framework, the explicit sequence of each chain is tracked by recording the length of each individual segment, which is the number of repeating units comprising the segment, in sequence from the initiation of the chain to the end of reaction or the termination of the chain. A new segment is generated when a cross-propagation reaction occurs, and the length of a segment is increased by one when a homopropagation reaction occurs.

In all the simulations reported in this work, no fewer than 10^6 chains were generated in the reaction system in each simulation run. $10^{10}-10^{11}$ monomers were initially put into the reactor in the beginning of the reaction depending on the initial concentration of initiator which was either 0.001 or 0.0001 mol/L in all the results reported. Because the concentration of nitroxyl radical is closely related to the time scale of activation/deactivation cycles, the concentration of SG1 was maintained as a constant in all the simulation runs by adding extra SG1 into the system during the reaction. The concentration of SG1 is specified for each simulation run. In this work, the reaction temperature was fixed at 95 °C for all the simulation runs. The sample size has been verified to be sufficiently large based on the fact that the simulation results were in very close agreement with those from simulations generating 10^7 chains initially.

Results and Discussion

I. Segment Length Distribution in Living Radical Polymerization. The instantaneous segment length distribution of a binary copolymerization system is determined by the selective preference of one type of monomer over the other in addition reactions in many types of polymerization, such as free radical polymerization and anionic polymerization. For terminal model kinetics, in which propagation with a certain type of monomer depends only on the type of the ultimate unit of the radical, the probability of forming segments of monomer i with exactly k units long at a given instant, $S_{i,k}^{\text{inst}}$, is a function of P_{ii}, i.e., the probability of a monomer i adding to a radical chain with the same type of monomer as the ultimate unit as shown in eq 3.[16]

$$S_{i,k}^{\text{inst}} = (1 - P_{ii}) P_{ii}^{k-1} \tag{3}$$

For penultimate model kinetics, in which not only the ultimate unit but also the penultimate unit of a radical can affect the propagation rate with a certain type of monomer, the probability of finding a segment of monomer i with exactly k units long at a given instant in a free radical polymerization is[16]

$$S_{i,1}^{\text{inst}} = 1 - P_{jii} \tag{4}$$

$$S_{i,k}^{\text{inst}} = P_{jii}(P_{iii})^{k-2}(1 - P_{iii}) \qquad k \geq 2 \tag{5}$$

where P_{iii} is the probability of the addition of a monomer i to a propagating chain with monomer i as the ultimate unit and penultimate unit, and P_{jii} is the probability of the addition of a monomer i to a propagating chain with monomer i as the ultimate unit and j as the penultimate unit. The probabilities P_{iii} and P_{jii} can be expressed as follows:[16]

$$P_{iii} = \frac{r_{ii} f_i / f_j}{1 + r_{ii} f_i / f_j} \tag{6}$$

$$P_{jii} = \frac{r_{ji} f_i / f_j}{1 + r_{ji} f_i / f_j} \tag{7}$$

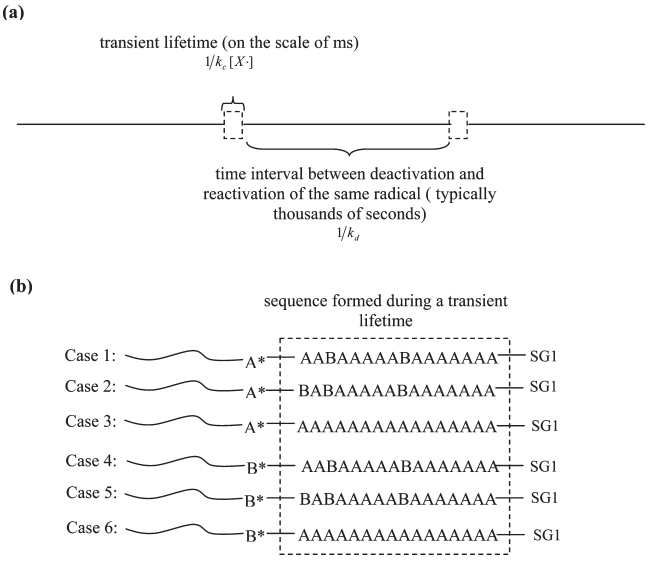
Based on the classic theory of instantaneous segment length distribution, the instantaneous number-average segment lengths for kinetics adhering to the penultimate model can be expressed as follows:[16]

$$N_{\text{inst},i}^{\text{classic}} = 1 + \frac{P_{jii}}{1 - P_{iii}} \tag{8}$$

It has been demonstrated that the S/MMA comonomer pair has strong penultimate effects.[27] Thus, in S/MMA copolymerization, the instantaneous segment length based on classic theory can be calculated by eq 8.

Although small deviations of reactivity ratios in living radical polymerization have been observed,[35] it is still quite common to treat living radical copolymerization as completely analogous to its conventional free radical counterpart.[13] Thus, it seems natural to assume that the kinetics governing

Scheme 2. Schematic Representation of (a) the Activation/Deactivation Cycles during the Lifetime of a Free Radical[a] and (b) Six Possible Scenarios for Formation of New and Continuation of Existing Segments of A during a Transient Lifetime



[a] X· denotes a nitroxide radical, k_c is the rate coefficient for coupling, and k_d is the rate coefficient for uncoupling.

the formation of segments at any instant in LRP resemble those in FRP. In order to validate this assumption, we simulated the instantaneous segment length of monomer i, $N_{\text{inst},i}^{\text{KMC}}$, in S/MMA copolymerization via NM-CRP using KMC simulations which were validated by experimental data in our earlier work.[18] In KMC simulations, the number-average segment length formed at an instant can be predicted as follows:

$$N_{\text{inst},i}^{\text{KMC}} = \frac{\mathrm{d}M_i}{\mathrm{d}n_i} \tag{9}$$

where $\mathrm{d}M_i$ is the amount of monomer i incorporated into copolymer chains at any instant and $\mathrm{d}n_i$ is the number of segments to which $\mathrm{d}M_i$ was added at that instant. In free radical polymerization, $\mathrm{d}n_i$ can be approximated as the number of *new* segments of monomer i created at a given instant because propagation is very fast and formation of segments can be considered to be completed instantly. For LRP, however, this is not always an appropriate assumption. Because radicals stay dormant during the majority of the reaction, as shown in Scheme 2a, the propagation can be slowed down to a great extent in LRP. Thus, the details of the segment formation during a transient lifetime need to be taken into account in simulating $\mathrm{d}n_i$ in living radical polymerization.

As shown in Scheme 2b, there are six possible scenarios of how monomer A can be incorporated into radical chains during an activation/deactivation cycle. The number of segments to which monomer A is added during a transient lifetime, $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$, will be discussed in detail for each case. In case one, an existing segment of A is resumed in the very beginning of the transient lifetime, and additional segments of A are incorporated to the active chain later. Because monomer A is incorporated to an existing segment, $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$ equals the increase in the number of segments of A plus one, to take into account the segment that already existed. In case two, a new segment of monomer B was created right after the chain is reactivated. In this case, $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$ equals the increase in the number of segments of A. In case three, the growth of an existing segment of A is resumed and is not completed by the end of this activation cycle. Since monomer A was added to only one existing segment, $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$ is only one under this circumstance. For cases four to six, the ultimate unit of the reactivated radical is monomer B, and thus $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$ is simply equal to the increase in the number of segments of A. The number of segments to which monomer A was added at an instant, $\mathrm{d}n_{\mathrm{A}}$, can then be calculated by summing up $\mathrm{d}n_{\mathrm{A},\Delta t_{\text{activation}}}$ of each activation/deactivation cycle that occurred over a short period of reaction which is used to define instantaneous properties.

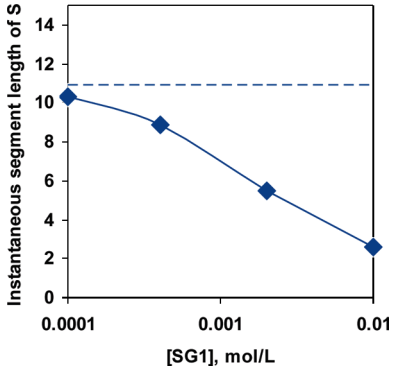


Figure 1. Under a fixed monomer composition of $f_S = 0.95$, comparison of the instantaneous number-average segment length of S predicted by KMC simulations, $N_{\text{inst},i}^{\text{KMC}}$ (diamonds with solid line drawn to guide the eye), and that predicted by eq 8 according to classic theory, $N_{\text{inst},i}^{\text{classic}}$ (dashed line), as a function of [SG1].

The instantaneous segment lengths of S synthesized under an S-rich environment with monomer composition fixed at f_S equal to 0.95 were investigated under different concentrations of nitroxyl radicals ([SG1] varies between 0.0001 and 0.01 mol/L). Under a given concentration of SG1, $N_{\text{inst,S}}^{\text{KMC}}$ was determined by the average value of instantaneous segment length predicted by KMC simulations between 400 and 3600 s of reaction time, which captures when the transient initiation phase is completed and pseudo steady state is achieved. Figure 1 compares $N_{\text{inst,S}}^{\text{KMC}}$ and $N_{\text{inst,S}}^{\text{classic}}$, which is calculated based on the classic theory of instantaneous segment length distribution. According to eq 8, $N_{\text{inst,S}}^{\text{classic}}$ is a constant since the probabilities P_{iii} and P_{jii} are the same for all three cases. However, as shown in Figure 1, $N_{\text{inst,S}}^{\text{KMC}}$ is clearly smaller than $N_{\text{inst,S}}^{\text{classic}}$ when the concentration of nitroxyl radical is high. For example, $N_{\text{inst,S}}^{\text{KMC}}$ is only about two units long when [SG1] is 0.01 mol/L, while $N_{\text{inst,S}}^{\text{classic}}$ is around 11 units long. $N_{\text{inst,S}}^{\text{KMC}}$ is close to $N_{\text{inst,S}}^{\text{classic}}$ only when [SG1] is very low.

As discussed above, the free radicals stay dormant during the majority of the reaction and can only propagate during the transient lifetime. Because the transient lifetime is inversely proportional to the concentration of capping agent in NM-CRP, the transient lifetime is shortened when the concentration of nitroxyl radical is increased in the system. When one type of monomer is highly preferred in propagation, long segments of the same type are likely to be formed. However, if the transient lifetime is shorter than the time needed for developing the segments to their full lengths, the growth of a segment can be arrested by deactivation before it is fully completed by a cross-propagation reaction or termination. In other words, even if a long segment of monomer i is likely to be formed because the same type of monomer is highly preferred in propagation, it cannot be completed over a short period of reaction because of the interruption of chain growth by deactivation.

In order to obtain a quantitative sense of how often segment growth can be interrupted during a given transient

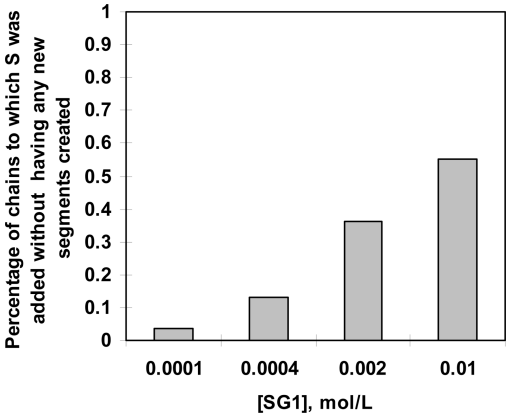


Figure 2. Percentage of chains to which S was added without having any new segments created in all the chains that have propagated at an instant with different concentrations of SG1 at a fixed monomer composition of $f_S = 0.95$ and $f_{MMA} = 0.05$.

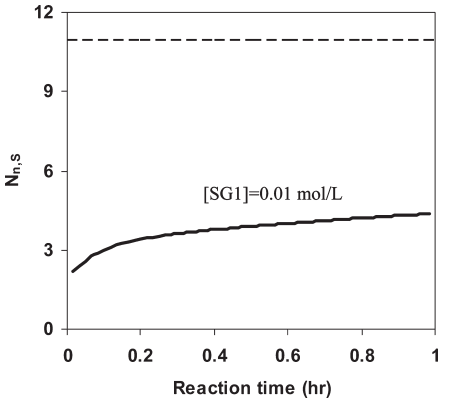


Figure 3. Evolution of number-average segment length of S, $N_{n,S}$, as a function of reaction time at a fixed monomer composition of $f_S = 0.95$ with [SG1] equal to 0.01 mol/L (solid line) and $N_{inst,S}^{classic}$ calculated by eq 8, which is the average segment length determined merely by selective preference according to classic theory (dashed line). The conversion values of S and MMA after 1 h are 10% and 4%, respectively.

lifetime, we tracked the percentage of chains which propagated with S monomer but did not add any new segments out of the chains that were reactivated at least once at an instant under different [SG1] at a fixed monomer composition ($f_S = 0.95$). As described in the third case in Scheme 2b, the growth of segments in these chains is significantly interrupted by deactivation, in which an existing segment was resumed but was not completed by the end of an activation/deactivation cycle. As shown in Figure 2, the percentage of these chains increases with increasing concentration of nitroxyl radicals. When [SG1] is as high as 0.01 mol/L, about 60% of all the chains that have been reactivated were apparently interrupted by deactivation before a segment can be completed.

The underdeveloped segments are still "alive" and can thus be resumed in later activation cycles. We simulated the average segment length of S in the whole copolymer population, $N_{n,S}$, synthesized with [SG1] as 0.01 mol/L at a fixed monomer composition of $f_S = 0.95$. As shown in Figure 3, $N_{n,S}$ increases with increasing reaction time, indicating that the underdeveloped segments can continue to grow at later stages of reaction. Theoretically, if the reaction time is long enough to allow all segments to be fully developed, $N_{n,S}$ can reach the value of $N_{inst,S}^{classic}$, which is the same as the number-average segment length determined merely by the selective preference based on propagation. However, the growth of

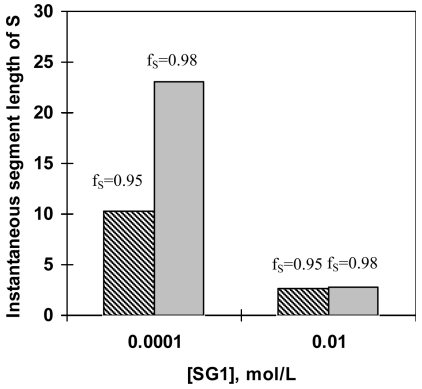


Figure 4. Instantaneous segment length of S predicted by KMC, $N_{inst,S}^{KMC}$, at different monomer compositions with f_S equal to 0.95 (■) and 0.98 (□) with different concentrations of SG1. Based on eq 8 according to classic theory, $N_{inst,S}^{classic}$ is around 11 when f_S is equal to 0.95 and $N_{inst,S}^{classic}$ is around 26 when f_S is 0.98.

the segments is actually very slow when it is strongly restricted by the length of the transient lifetime, which makes it difficult to produce long segments within a reasonably short reaction time in practice. As shown in Figure 3, $N_{n,S}$ increases extremely slowly with increasing reaction time. After 1 h, the average segment length of S is only 4.5, which is far below $N_{inst,S}^{classic}$ calculated for the specified monomer composition. This is mainly because the time interval between deactivation and reactivation is thousands of seconds in this reaction system, and thus it takes a long cumulative reaction time to allow for full development of a long segment which needs more than one activation cycle to grow.

The formation of segments has been traditionally considered to be controlled only by selective preference; i.e., the length of a segment is determined by the preference of one type of monomer over the other one in propagation. However, our results suggest that the formation of segments in LRP can be controlled by the frequency of deactivation instead. Under this circumstance, the instantaneous segment length of monomer i is mainly determined by the length of the transient lifetime instead of the preference of monomer i in propagation. Thus, the classic theory of segment formation does not always hold in LRP.

To illustrate this point more clearly, we show that if a reaction is deactivation controlled, the instantaneous segment length of monomer i cannot be further increased by increasing f_i. Figure 4 shows the instantaneous segment length predicted by KMC simulations, $N_{inst,S}^{KMC}$, for copolymers synthesized at two different monomer compositions, f_S equal to 0.95 and 0.98, and using different concentrations of nitroxyl radical. According to the classic theory, the instantaneous average segment length of S should be increased dramatically from around 11 units long to around 20 six units long when f_S is increased from 0.95 to 0.98. However, when the reaction is deactivation controlled with [SG1] equal to 0.01 mol/L, the instantaneous segment length of S is much shorter than the prediction according to classic theory and almost independent of the increase in f_S. Thus, only when segment growth is not restricted by the time scale of activation cycles can the instantaneous average segment length be elongated by adjusting the monomer composition. For example, $N_{inst,S}$ is increased dramatically from around 10 units long to over 20 units long when f_S is changed from 0.95 to 0.98 when [SG1] is lowered to 0.0001 mol/L.

It should be noted that all the scenarios discussed above are styrene-rich environments, in which β-hydrogen transfer to the nitroxide SG1 is rare.[36] In the cases where the

monomer composition strongly favors MMA, β-hydrogen transfer may also interrupt the segment growth of MMA and generate segments whose lengths are shorter than the prediction based on classic copolymerization theory.

II. Average Propagation Steps during a Transient Lifetime. One of the most important applications of LRP is to prepare copolymers with predesigned monomer sequences along the chain. Since the monomer sequence formed under deactivation-controlled conditions can be dramatically different from that formed under selective preference-controlled conditions, it is of great importance to develop a precise but convenient method to tell whether a reaction is deactivation controlled for syntheses in practice. A simple method would be particularly helpful for experimentalists who do not have access to complex modeling capabilities such as KMC. For this purpose, we derived equations to calculate the average number of steps that can occur over a transient lifetime in which only homopropagation of monomer i can take place, $N_{\mathrm{prop},i}$. If $N_{\mathrm{prop},i}$ is much larger than the instantaneous average segment length based on classic theory, $N_{\mathrm{inst},i}^{\mathrm{classic}}$, segment formation is mainly controlled by selective preference during propagation (i.e., selective preference-controlled); otherwise, segment formation is mainly controlled by the frequency of deactivation (i.e., deactivation-controlled).

When the conditions of pseudo steady state are satisfied in the reaction system, monomers can be considered to be only consumed by propagation reactions. The rate that monomer i is consumed is

$$\frac{\mathrm{d}[\mathrm{M}_i]}{\mathrm{d}t} = k_{\mathrm{p}}[\mathrm{M}_i][\mathrm{P}^{\bullet}] \tag{10}$$

where $[\mathrm{M}_i]$ and $[\mathrm{P}^{\bullet}]$ are the concentrations of monomer i and active free radicals, respectively, and k_{p} is the rate coefficient for propagation. The average transient lifetime is defined as $k_{\mathrm{deact}}{}^{-1}$ where k_{deact} for a mechanism involving decoupling/coupling is[7]

$$k_{\mathrm{deact}} = k_{\mathrm{c}}[\mathrm{X}^{\bullet}] \tag{11}$$

where $[\mathrm{X}^{\bullet}]$ is the concentration of capping radicals and k_{c} is the rate coefficient for coupling. Thus, the average number of propagation steps that a chain can take during a transient lifetime, $N_{\mathrm{prop},i}$, can be estimated as follows:

$$N_{\mathrm{prop},\,i} = \frac{\dfrac{1}{k_{\mathrm{c}}[\mathrm{X}^{\bullet}]}\dfrac{\mathrm{d}[\mathrm{M}_i]}{\mathrm{d}t}}{[\mathrm{P}^{\bullet}]} \tag{12}$$

After simplification, $N_{\mathrm{prop},i}$ for a given $[\mathrm{X}^{\bullet}]$ can be calculated by eq 13:

$$N_{\mathrm{prop},\,i} = \frac{k_{\mathrm{p}}[\mathrm{M}_i]}{k_{\mathrm{c}}[\mathrm{X}^{\bullet}]} \tag{13}$$

In order to validate eq 13, we monitored $N_{\mathrm{prop,S}}$ using our KMC framework explicitly and compared it to the results of eq 13. As shown in Figure 5, $N_{\mathrm{prop,S}}$ as a function of [SG1] calculated by eq 13 matches very well with that predicted by KMC simulations. Another striking feature revealed by Figure 5 is that $N_{\mathrm{prop,S}}$ can be rather small at a moderate concentration of SG1. For example, a chain can only incorporate at most four more repeat units of S during an activation/deactivation cycle even when [SG1] is as low as 0.004 mol/L. These underdeveloped segments cannot be fully developed under typical synthesis conditions because the monomer composition typically varies

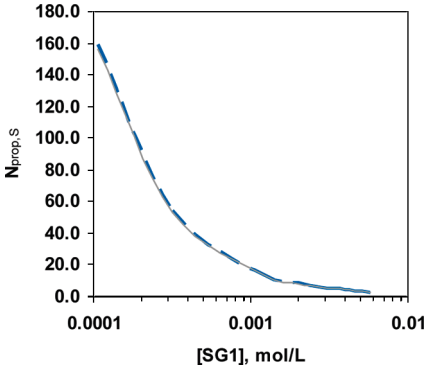


Figure 5. $N_{\mathrm{prop,S}}$ as a function of [SG1] predicted by KMC simulations (continuous line) and that predicted by eq 13 (dashed line).

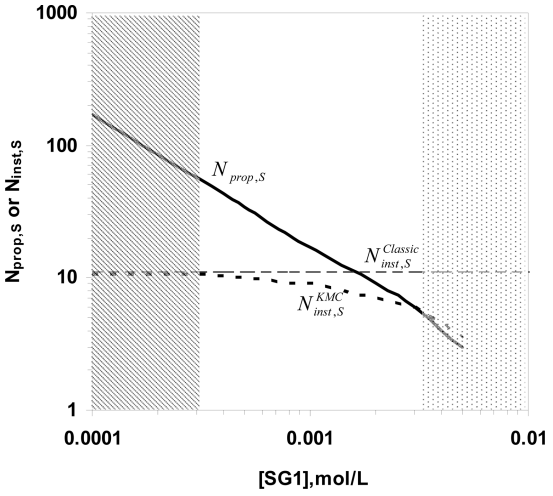


Figure 6. Comparison of $N_{\mathrm{prop,S}}$ and the instantaneous average segment length of S predicted by KMC simulations, $N_{\mathrm{inst,S}}^{\mathrm{KMC}}$, under different concentrations of SG1 at a fixed monomer composition of f_{S} equal to 0.95. The average segment length of S at this monomer composition based on classic theory, $N_{\mathrm{inst,S}}^{\mathrm{classic}}$, is plotted as well for comparison purposes. The region in which the segment formation is mainly controlled by selective preference in propagation is marked as a shadow with lines, and the region in which the segment formation is mainly controlled by deactivation is marked as a dotted region.

quickly during the reaction, and the growth of segments is very slow.

It can be estimated in a facile way whether the segment growth is restricted by the time scale of activation/deactivation cycles by comparing $N_{\mathrm{prop},i}$ and the average segment length determined by classic theory, $N_{\mathrm{inst},i}^{\mathrm{classic}}$, under a given reaction condition. Figure 6 shows the variation of $N_{\mathrm{prop,S}}$ and that of instantaneous segment length predicted by KMC simulations, $N_{\mathrm{inst,S}}^{\mathrm{KMC}}$, as a function of [SG1] under a fixed monomer composition with f_{S} equal to 0.95. $N_{\mathrm{prop,S}}$ decreases monotonically with increasing concentration of SG1, while $N_{\mathrm{inst,S}}^{\mathrm{KMC}}$ remains on a plateau when [SG1] is low and then decreases with increasing concentration of SG1 and almost overlaps with $N_{\mathrm{prop,S}}$ at very high [SG1]. When [SG1] is less than 0.0004 mol/L, $N_{\mathrm{inst,S}}^{\mathrm{KMC}}$ is close to the average segment length determined at this monomer composition by the classic theory, $N_{\mathrm{inst,S}}^{\mathrm{classic}}$, showing that the segment growth is mainly controlled by selective preference. Under this circumstance, $N_{\mathrm{prop,S}}$ is much higher than $N_{\mathrm{inst,S}}^{\mathrm{classic}}$, which indicates that the average activation/deactivation cycle is much longer than the time needed to develop segments. When [SG1] is greater than 0.003 mol/L, $N_{\mathrm{inst,S}}^{\mathrm{KMC}}$ is much less than $N_{\mathrm{inst,S}}^{\mathrm{classic}}$ but very close to $N_{\mathrm{prop,S}}$. This is because the

average activation/deactivation cycle is much shorter than the time needed to fully develop segments and the instantaneous segment length is mainly determined by the time scale of activation/deactivation cycles; i.e., the segment growth is mainly controlled by deactivation in this case. Although segment growth is less interrupted by deactivation with a lower SG1 concentration, it should be noted that the livingness of the reaction can suffer because the transient lifetime is too long to suppress termination efficiently. Therefore, a careful balance is needed between the instantaneous segment length and the control of livingness when designing synthesis recipes.

III. Uniformity of Segment Growth. Another interesting problem in preparing copolymers with well-defined sequences is how uniformly the segments can be incorporated into different chains. Living radical polymerization is well-known for providing low-polydispersity polymers. However, compared to the uniformity of the overall chain length, it is much harder to achieve similar monomer sequences on different chains, which requires a highly uniform development of chain length of all radicals in the system as well as a narrow distribution of segment lengths added onto different radicals of similar length throughout the reaction. The uniformity of chain propagation over a short period of reaction can affect the uniformity of monomer sequence dramatically because the reaction conditions, such as monomer composition, typically change continuously during synthesis and the length of segments can change significantly under different monomer compositions. Furthermore, the distribution of segments incorporated to different chains under a certain reaction condition can also affect the uniformity of monomer sequences of different chains. The first aspect is mostly determined by the features of activation/deactivation cycles in LRP, while the second one is most relevant to the intrinsic kinetics of copolymerization. These two aspects will be discussed in the following sections.

a. Frequency of Reactivation of Chains. In some cases, the length of segments can change dramatically when monomer composition has only minor changes. Under this circumstance, the majority of chains should be reactivated at least once over a reasonably short period of time when the reaction conditions remain similar. Otherwise, if only a small fraction of chains can be activated under a certain reaction condition, the length of segments incorporated in radicals of similar lengths can be dramatically different, which leads to quite different monomer sequences from chain to chain even when the overall molecular weight PDI is low.

How fast can all the chains in a system be reactivated at least once? Since the KMC framework can trace the growth of each chain throughout the reaction, this question can be answered through simulation in a facile way. Here, we simulated the percentage of chains that have been reactivated at least once during a certain time interval, Δt, in an S-rich environment with [SG1] equal to 0.001 mol/L. As shown in curve a of Figure 7, it takes a relatively long time to allow the majority of chains to be reactivated at least once. Only 3% of the total chains are reactivated, and their propagation is resumed in a time period of 60 s. It takes more than 1 h to allow over 80% of the total chains to be reactivated at least once. In current syntheses, the monomer composition typically changes fast. Therefore, even if the molecular weight polydispersity is reasonably low, the lengths of segments incorporated to radicals of similar length can be quite different because the chains were reactivated at different monomer compositions.

As shown in Scheme 2a, dormant chains can be reactivated every $1/k_d$ seconds, where k_d is the rate coefficient for decoupling of capped chains, and deactivated back to a dormant status after $1/k_c[X^\bullet]$ seconds on average, where $[X^\bullet]$ is the concentration of nitroxyl radicals in NM-CRP and k_c is the rate coefficient for coupling between free radicals and capping agent.[7] Since the time interval between deactivation/reactivation is very long for the typical LRP conditions studied here, it was found that the frequency of reactivation of chains is mainly determined by the time scale of deactivation cycles, i.e., the value of k_d for a given reaction system. In order to enable more chains to be reactivated over a given period of reaction time, the time interval between deactivation and reactivation of the same radical needs to be decreased. To explore this, we increased both the coupling parameter, k_c, and the decoupling parameters, k_d, between SG1 and the different radicals by a factor of 10 in order to shorten the deactivation cycles without changing the equilibrium constant K (k_d/k_c). As shown in curve b in Figure 7, the percentage of chains reactivated during Δt increases dramatically with increasing k_d.

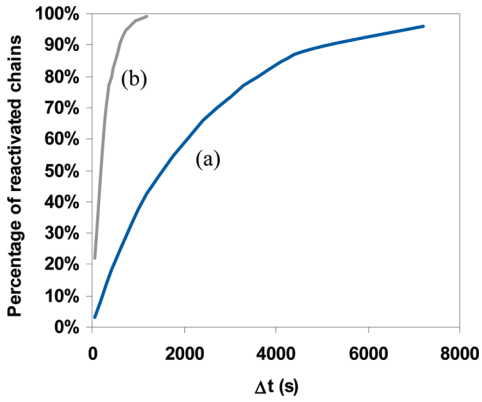


Figure 7. Percentage of chains that have been reactivated in the whole population of chains during Δt with [SG1] = 0.001 mol/L and f_S = 0.95 (a) with the original coupling and decoupling parameters, k_c and k_d, listed in Table S1 (b) with k_c and k_d that are both 10 times larger than the original ones.

In general, a higher frequency in chain reactivation, which corresponds to a higher k_d, is beneficial for the uniformity of monomer sequences on different chains because more chains can grow at a given reaction condition. However, it should be noted that the ratio between transient lifetime and the time interval between deactivation and reactivation needs to be maintained within a certain range to keep the reaction as living. Therefore, if k_d is increased, k_c or the concentration of capping agents needs to be adjusted accordingly as well.

b. Segment PDI under a Certain Monomer Composition. Although the distribution of overall molecular weight can be narrowed to a great extent by the reversible deactivation/reactivation procedure characteristic of LRP, we found that the distribution of segment lengths formed under a certain monomer composition cannot be efficiently controlled in LRP. The number-average segment length, $N_{n,S}$, and the polydispersity of segment lengths of S, $N_{w,S}/N_{n,S}$, of the whole population were investigated for two different scenarios which had different concentrations of nitroxyl radicals but were under the same fixed monomer composition with f_S equal to 0.95.

As shown in Figure 8c, the molecular weight PDI of both systems decreases with increasing reaction time. The molecular weight PDI of the system with higher [SG1] is lower than that of the other system. However, as shown in Figure 8b, $N_{w,S}/N_{n,S}$ of both systems actually increases with increasing reaction time, indicating that while the distribution of overall chain lengths is being narrowed, the distribution of segment lengths in the system is getting broader instead.

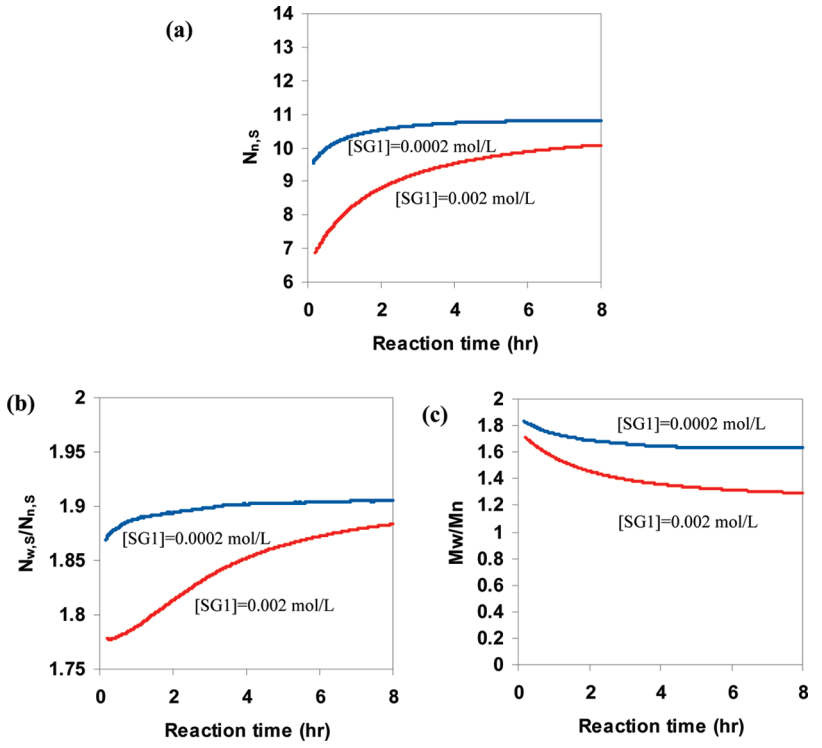


Figure 8. Evolution of (a) average segment length, $N_{n,S}$, (b) segment PDI, $N_{w,S}/N_{n,S}$, and (c) molecular weight PDI, M_w/M_n, as a function of reaction time for different [SG1] of 0.0002 and 0.002 mol/L but the same fixed monomer composition ($f_S = 0.95$).

For the system with [SG1] equal to 0.0002 mol/L, $N_{n,S}$ increases as a function of reaction time and approaches a value of 11 units long which is consistent with the number-average segment length synthesized at this monomer composition in FRP predicted by eq 8, as shown in Figure 8 a. However, $N_{w,S}/N_{n,S}$ of this reaction system increases with increasing $N_{n,S}$ and approaches the value of segment length PDI predicted in FRP when $N_{n,S}$ reaches the plateau.[16] Thus, while the segments are getting longer, their distribution is also getting more broad, which is counter to what is desired. For the system with higher [SG1] equal to 0.002 mol/L, similar trends were observed: $N_{w,S}/N_{n,S}$ increases with number-average segment length and will eventually reach a plateau when the segment length distribution formed at this particular monomer composition is close to fully developed. Therefore, the polydispersity of segment lengths added to chains at an instant is related to the number-average segment length formed at the moment. These results reveal that there inevitably exists a distribution of segment length no matter how "ideal" the livingness is. This distribution is determined by the "intrinsic" kinetics of copolymerization and cannot be effectively changed in LRP. Thus, it is relatively hard to make very long segments with an extremely narrow distribution by LRP.

Conclusions

The kinetics of segment formation in LRP were investigated by studying S/MMA copolymerization via NM-CRP. A KMC framework was used to study the kinetic details of segment formation and the factors affecting the uniformity of monomer sequences in different chains. Our results reveal that the classic theory describing the distribution of instantaneous segment lengths in FRP does not always hold in LRP. Segment formation can be controlled by deactivation instead of selective preference during propagation when the transient lifetime is too short. When the reaction is controlled by deactivation, segment lengths cannot be further improved by increasing the monomer composition of the same type of monomer. Since the monomer sequences formed under deactivation-controlled conditions can be dramatically different from those formed under selective preference-controlled conditions, it is of great importance to develop a precise but convenient method to determine whether a reaction is deactivation-controlled under practical synthesis conditions. To this end, we derived equations to calculate the average number of steps that can occur during a transient lifetime in which only homopropagation of monomer i can take place, $N_{prop,i}$. If $N_{prop,i}$ is much shorter than $N_{inst,i}^{classic}$, segment formation is mainly controlled by deactivation.

The uniformity of segment growth was analyzed as well. Compared to the uniformity of the overall chain length distribution, it is much harder to achieve similar monomer sequences on different chains, which requires highly uniform development of chain lengths of all radicals in the system as well as a narrow distribution of segment lengths added onto different radicals of similar length throughout the reaction. Our results reveal that it takes a surprisingly long time to allow the majority of chains to be reactivated at least once in an S-rich reaction system, which can lead to high polydispersity in monomer sequences formed on different chains. It was also demonstrated that there inevitably exists a distribution of segment lengths given a particular monomer composition no matter how "ideal" the livingness is. This distribution is determined by the "intrinsic" kinetics of copolymerization and cannot be effectively changed in LRP.

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Supporting Information Available: All kinetic parameters, including reactivity ratios, used in the model are tabulated. This material is available free of charge via the Internet at http://pubs.acs.org.

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