What happens in the dark? Assessing the temporal control of photo-mediated controlled radical polymerizations

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ABSTRACT: A signature of photo-mediated controlled polymerizations is the ability to modulate the rate of polymerization by turning the light source 'on' and 'off.' However, in many reported systems, growth can be reproducibly observed during dark periods. In this study, emerging photo-mediated controlled radical polymerizations are evaluated with *in situ* ^{1}H NMR monitoring to assess their behavior in the dark. Interestingly, it is observed that Cu-mediated ATRP systems undergo long-lived, linear growth during dark periods in organic media.

KEYWORDS: photopolymerization, controlled radical polymerization, *in-situ* monitoring

The utility and sweeping impact of controlled radical polymerization (CRP) has fundamentally changed the direction of polymer synthesis. By enabling the accurate control of molecular weight, architecture, and dispersity (*Đ*) for a wide variety of functional monomers, the synthesis of complex polymeric materials such as extended multiblocks[1], surface-modified nanoparticles[2,3], and bioconjugates[4–6] is now possible. Recently, the use of external stimuli, such as light[7,8], reducing agents[9], applied voltage[10], and mechanical forces[11] to mediate CRP processes has further increased the usefulness and impact of CRP. Of these stimuli, light is particularly attractive, as it is environmentally benign and highly tunable.[12–14] Numerous examples of photo-mediated controlled radical polymerization (photo-CRP) have recently been developed, including Cu-mediated atom transfer radical polymerization (Cu-ATRP)[15–17], Cu-free ATRP[8,18–21], and photo induced electron transfer-reversible addition-fragmentation chain transfer (PET-RAFT).[22,23] These systems operate over a wide variety of wavelengths, catalysts, and monomer classes[24–26] with the broad scope of these systems leading to the development of well-defined, functional materials. Notable examples include patterned polymer brushes[27,28], organic light-emitting diodes[29], soft gels[30,31], and complex polymer architectures[32,33].

In photo-CRP, temporal control is typically demonstrated through sequential 'on' - 'off' cycles. This cycling is performed by irradiating the reaction mixture, polymerization then initiates/propagates, followed by a 'dark' period where, in an ideal scenario, no additional conversion takes place. However, for many reported photo-CRP systems, a small yet reproducible amount of polymer growth can be

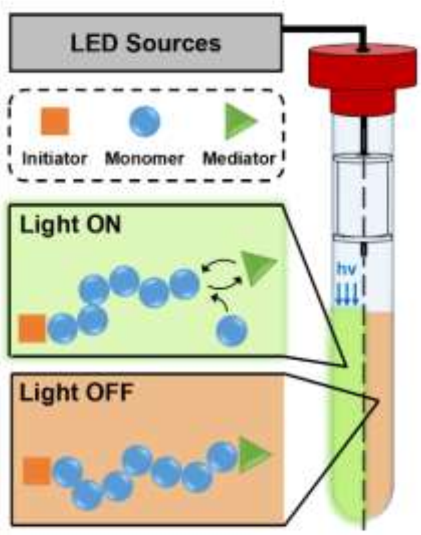

Figure 1: Schematic of the *in situ* fiber-coupled NMR system showing idealized schemes for photo-CRP in active ('on') and dormant ('off') states.

observed during the 'off' cycles.[16,21,34–37] This apparent growth has been attributed to several factors, from experimental error to residual active catalyst. While the kinetics of growth and the presence of side reactions has been extensively studied for 'on' periods[5,38,39], no systematic examination of the polymerization reaction during the 'off' or 'dark' periods has been conducted.

To address this challenge and provide insight into photo-CRP processes, a recently developed *in situ* NMR spectroscopy method is utilized to evaluate temporal control for a selection of widely shows a representative schematic).[40] Compared to conventional sampling methods, this approach is uniquely suited for studying temporal control of photo-CRPs, allowing accurate modulation of irradiation intensity and wavelength through the combination of LEDs and fiber optics. In addition, *in situ* coupling with NMR spectroscopy permits rapid and repeated measurements to be taken without invasive sampling of the polymerization reaction. As a result, accurate polymerization kinetics can be obtained in both the 'on' and 'off' states.

In this study, PET-RAFT, Cu-free ATRP, and Cu-mediated ATRP and RDRP systems were selected as representative examples of photo-CRP methods. To facilitate an unbiased comparison across techniques, irradiation conditions were held constant (equivalent photon flux) and polymerization conditions, such as monomer concentration and targeted degree of polymerization, were fixed at 33 wt% and DP=150. Temporal control experiments were also carried out with equal 'on' and 'off' times targeting conversions of ~40% with an initial 'off' period conducted to establish a baseline before exposure to light. To show the general trends of a given technique, a representative catalyst/ligand combination will be discussed, however full data for all catalysts studied is available in the Supporting Information.

As they both utilize the photocatalyst as an electron transfer agent, the initial systems chosen for study were PET-RAFT and Cu-free ATRP.[41] Under traditional PET-RAFT conditions, the polymerization of methyl acrylate (MA) in DMSO was examined, (**Figure 2a**) and after an inhibition period attributed to residual oxygen being consumed,[23,42,43] the polymerization demonstrated linear kinetics with termination being observed only at high conversions (**Figure 2b**). As expected, the polymerization of methyl methacrylate (MMA) under Cu-free ATRP conditions (**Figure 3a**) was slower than the polymerization of MA by PET-RAFT due to the increased k_p values. However, in both the PET-RAFT and Cu-free ATRP experiments, linear kinetics with little to no deviation were observed up to conversions of 30–40%. To simplify comparison, this conversion range was thereby targeted in the temporal control studies (**Figure 2c, 3c**). Significantly, for all PET-RAFT and Cu-free ATRP systems studied, high fidelity is observed with no observable conversion being measured during the 'dark' period.

Unlike PET-RAFT and Cu-free ATRP, which directly drive polymerization through excitation events, Cu-mediated ATRP generates Cu in a secondary fashion, potentially leaving residual

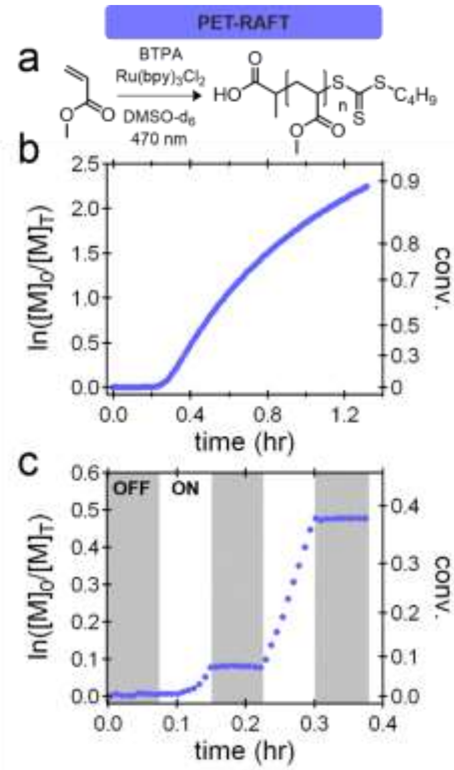

Figure 2: a) PET-RAFT conditions for the polymerization of methyl acrylate (MA) using λ = 470 nm light and tris(2,2′-bipyridyl)dichlororuthenium(II) hexahydrate. b) Kinetic plots of the polymerizations at a fixed photon flux. c) Temporal control experiments for the PET-RAFT demonstrate ideal temporal control.

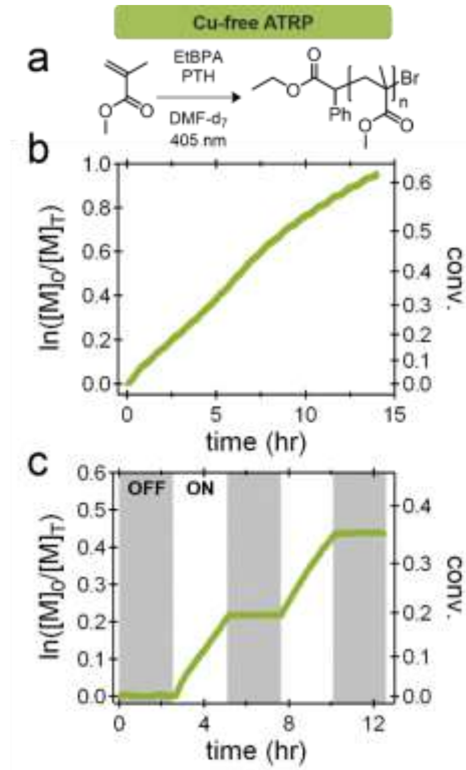

Figure 3: a) Cu-free ATRP conditions for the polymerization of methyl methacrylate (MMA) using λ = 405 nm light and 10-phenylphenothiazine. b) Kinetic plots of the polymerizations at a fixed photon flux. c) Temporal control experiments for the Cu-free ATRP reactions demonstrate ideal temporal control.

catalytic Cu(I) in solution after irradiation has stopped. To examine this behavior and compare Cu-ATRP to both PET-RAFT and Cu-free ATRP, Me_6TREN and $CuBr_2$ was employed in the polymerization of both MA and MMA (**Figure 4a**). Although there are differences in the overall behavior of the polymerization of MA and MMA compared to the PET-RAFT and Cu-free ATRP examples, namely a lack of inhibition for MA and evidence of severe termination for MMA, both systems show linear kinetics up to conversions of ~30–40% (**Figure 4b**).

For both MA and MMA, significant differences were observed during ‘off’ periods (**Figure 4c**). While the initial ‘dark’ periods did not result in any monomer conversion, the Cu-ATRP systems exhibited substantial polymer growth during the subsequent ‘dark’ periods (~5–10% of the ‘on’ rate in both the MA and MMA systems). Interestingly, upon extending the dark window from ~10 minutes to ~5 hours, linear polymerization kinetics in the ‘off’ state is still observed. Even at high conversions, the Cu catalyst was active with linear kinetics being observed (86 to 91%) despite being in an ‘off’ or ‘dark’ period for 3.5 hours (**Figure S23**). These results suggest that during the ‘off’ periods a significant amount of Cu(I) (initially produced by reduction of Cu(II)) remains in solution and is responsible for polymer growth through a conventional ATRP mechanism, rather than a photo-mediated ATRP process. To further investigate the temporal control of Cu-mediated ATRP systems, the dark periods were extended for different Cu/ligand pairs (Me_6TREN and TPMA). The equilibrium constants for Me_6TREN and TPMA are reported in the literature, and

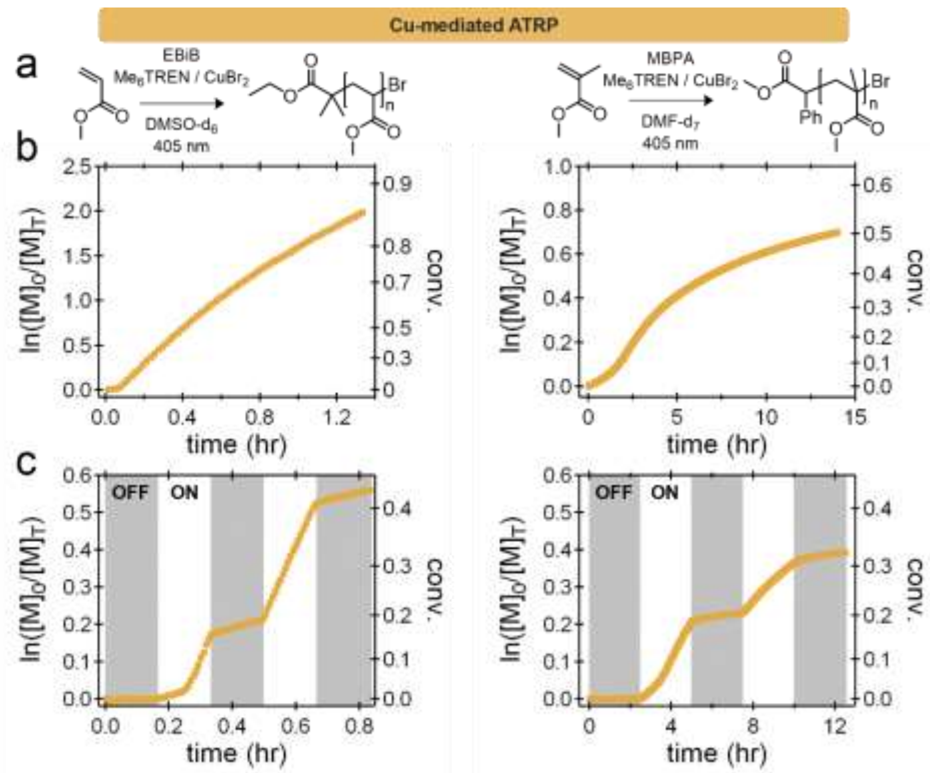

Figure 4: a) Cu-mediated conditions for the polymerization of MA and MMA using $CuBr_2$ and tris[2-(dimethylamino)ethyl]amine (Me_6TREN). b) Kinetic plots of the polymerizations at a fixed photon flux. c) Temporal control experiments wherein distinct linear growth during dark periods after initial irradiation are observed for both polymerizations (~10–15% of the 'on' rate).

it has been shown that TPMA has a K_{ATRP} value approximately an order of magnitude lower than Me_6TREN.[44] After initial irradiation to similar conversions, both systems did show growth during the 'dark' period. However, Me_6TREN displays a considerably higher rate of conversion (approximately an order of magnitude) when compared to the corresponding TPMA system (**Figure 5**). This result illustrates that Cu-ATRP in organic media does not exhibit ideal temporal control for any of the conditions/ligands studied due to the unwanted presence and extended lifetime of CuBr during 'dark' periods.

To improve the temporal control of Cu-ATRP, we envisage that a system must exhibit rapid consumption of residual Cu(I) catalyst during the 'off' cycles. Aqueous systems are subject to high equilibrium constants, and the concentration of Cu(I) should therefore decrease rapidly during 'dark' periods, translating to increased temporal control relative to the corresponding organic systems. As a control, Cu-mediated polymerization of poly(ethylene glycol) methyl ether acrylate (PEGA, M_n 480) using $Me_6TREN/CuBr_2$ was conducted in organic and aqueous media (**Figure 6**). In analogy with Cu-mediated polymerization of MA in DMSO, a linear increase in conversion for PEGA occurs during an extended 'dark' period of ~5 hours after initial irradiation (**Figure 6b**). To achieve a comparable controlled polymerization of PEGA in water, the copper loading was increased 5x relative to that used in DMSO.[45] Interestingly, after irradiation at λ = 365 nm, rapid polymerization continued for 2 hours in the dark (though in a non-linear fashion) before decreasing to undetectable levels. Importantly, the polymerization continued upon further irradiation, highlighting that the end groups were still active and implying that the active Cu(I) was consumed during the 'off' period, presumably by conversion to Cu(II). While this aqueous system demonstrated the potential for improved temporal control compared to a similar polymerization in organic media, significant monomer conversion does occur in the 'dark' after turning off the light source. In an attempt to increase fidelity further, it was hypothesized that a lower amount of initial $CuBr_2$ would generate less residual catalyst, which could then be deactivated more rapidly in the absence of light. In order to maintain control with a reduced amount of $CuBr_2$, NaBr was therefore added to the polymerization mixture.[45] Indeed, under these conditions, nearly immediate cessation of the polymerization was observed upon switching the light 'off,' leading to a high degree of temporal control. These results highlight the importance of mechanistic understanding in the development of strategies for temporal control of Cu-ATRP processes.

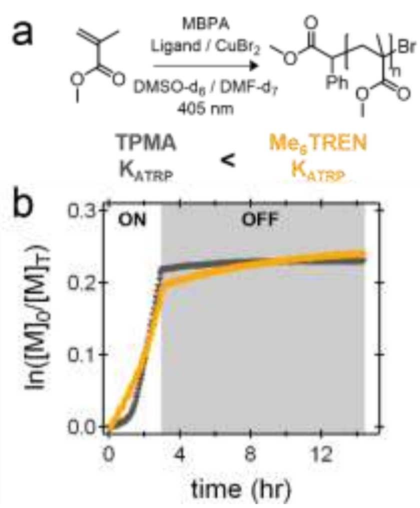

Figure 5: Kinetics of MMA polymerizations using $Me_6TREN/CuBr_2$ ($DMF-d_7$) and $TPMA/CuBr_2$ ($DMSO-d_6$) photosystems at equal loadings. Me_6TREN undergoes more growth in the dark period due to its higher activity (K_{ATRP}).

In summary, a modular *in situ* NMR technique was utilized to investigate monomer conversion during the 'on' and 'off' cycles for a selection of photo-CRP procedures. Temporal control during metal-free ATRP and PET-RAFT was shown to occur with high fidelity and little to no conversion is observed during 'dark' periods. In direct contrast, Cu mediated polymerization conducted in DMSO showed significant growth during 'off' cycles, which is attributed to the increased lifetime of residual Cu(I) catalyst after initial photoactivation. The findings of non-ideal temporal behaviour herein also illustrate the necessity for employing long 'off' periods when studying temporal control to ensure measurement fidelity and accuracy.

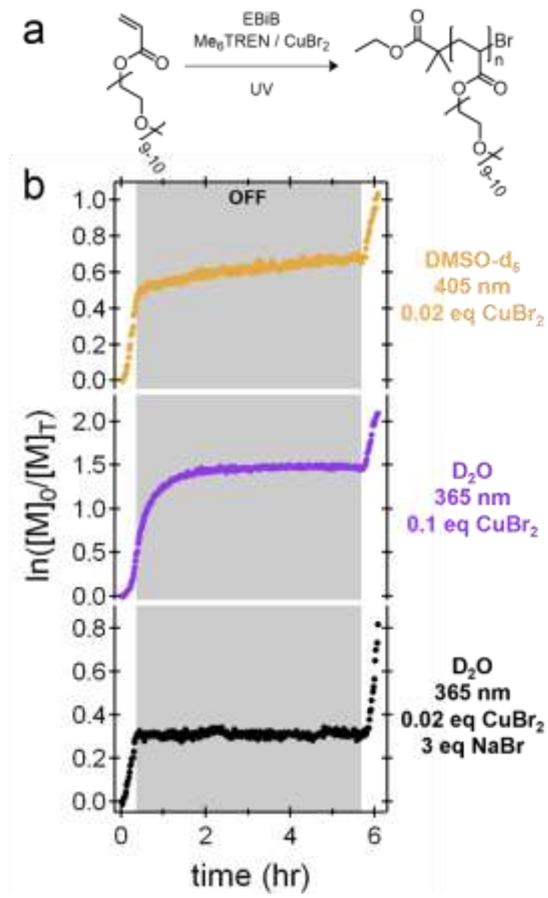

Figure 6: a) General reaction scheme for polymerization of poly(ethylene glycol) methyl ether acrylate (PEGA) macromonomers. b) Temporal experiments for PEGA polymerized in DMSO (top), water at an elevated Cu concentration (middle), and water with a reduced Cu content and NaBr (bottom). Only the reduced Cu aqueous polymerization shows ideal temporal behavior.

The use of aqueous conditions (low Cu(II) concentration and added NaBr) quickly consumes the residual catalytic species and alleviates this problem. This allows well-controlled polymers with no observable 'dark' growth to be obtained. It should be noted that these conditions cannot currently be broadly generalized with understanding and improving the temporal control in Cu-ATRP in organic media being an area of future focus.

EXPERIMENTAL

See Supporting Information for full experimental details.

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GRAPHICAL ABSTRACT

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