

Investigation of Controlled on Demand Self-Assembly and Disassembly of Polymer Nanostructures

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Abstract

Pristine structure allows proteins to perform complex functions and behaviors; epitomizing the structure/function relationship in polymeric materials.^{1,2} Protein-inspired polymeric materials have the potential to contribute to many technological grand challenges, such as environmental pollution, energy storage and delivery, and human health.³ Single-chain nanoparticles have been studied as structures that mimic the secondary and tertiary structures of proteins.⁴ The capability of protein molecules to assemble on demand into complex hierarchically ordered mesoscale machines that perform complex functions and then disassemble as required has not been met in synthetic polymer systems.

ABA triblock multicompartiment brush polymer particles (MCBP) are used to investigate controlled, on demand self-assembly/disassembly of polymer nanostructures. These polymer systems are simplified synthetic models of quaternary protein structure and as such explore the ability of a synthesized polymer to model protein function and to mimic protein's quaternary structure. The target polymer ABA triblock MCBP contains spatially arranged thermoresponsive units that are expected to permit segmented isolation of domains to afford appropriate architectures for self-assembly/disassembly upon temperature change.

Keywords: Multicompartiment brush polymer particles, thermoresponsive, self-assembly/disassembly

1. Introduction

Protein-inspired polymeric materials epitomize the structure/function relationship seen in proteins.^{1,2} These materials, a subset of bioinspired materials, represent a frontier in polymer chemistry and have the potential to contribute to many technological grand challenges, such as environmental pollution, energy storage and delivery, and human health, by synthesizing degradable polymers from renewable resources and improving methods of drug delivery.³

In nature, protein molecules can assemble on demand into complex hierarchically ordered mesoscale machines that perform complex functions and behaviors before they disassemble as required. Single-chain nanoparticles have been studied as structures that mimic the secondary and tertiary structures of proteins.⁴ The capability of polymers to assemble on demand into complex hierarchically ordered mesoscale machines and then disassemble as required has not yet been met in synthetic polymer systems. By investigating controlled, on demand self-assembly/disassembly of polymer nanostructures, the quaternary structures of proteins can be mimicked in polymer systems. Synthetic polymer systems that mimic quaternary structures can be investigated through a simplified synthetic model of quaternary protein structure (Figure 1).

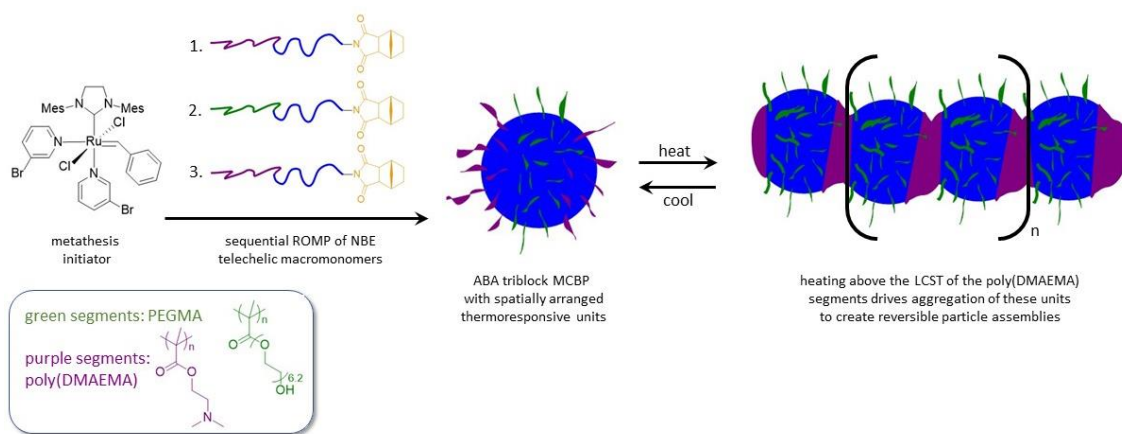


Figure 1: Project overview for synthesis of ABA triblock MCBP and sequential self-assembly/disassembly of MCBP

This project aims to prepare and characterize ABA triblock multicompartiment brush polymer particles (MCBP) through the controlled radical polymerizations of reversible addition-fragmentation chain-transfer (RAFT) polymerization and ring-opening metathesis polymerization (ROMP) and coupling chemistries such as N,N'-Dicyclohexylcarbodiimide (DCC) couplings. MCBP act as simplified synthetic models of quaternary protein structure by affording appropriate architectures for self-assembly/disassembly.

The self-assembly/disassembly of the MCBP is afforded to the poly(ethylene) methacrylate (PEGMA) and poly[2(dimethylamino)ethyl methacrylate] (DMAEMA) segments. When placed at opposite ends of the particle the segments can be used as colloidal monomers that will polymerize and depolymerize in response to thermal stimulus. After heating above the lower critical solution temperature of the DMAEMA segments, the chains will collapse and aggregate to create assemblies that can then be disassembled by lowering the solution temperature.

This article describes the synthesis of two block copolymers to be used in the formation of the MCBP particles. The described assemblies as well as the synthesized polymers are to be characterized by proton nuclear magnetic resonance ($^1\text{H-NMR}$), gel permeation chromatography (GPC), and transmission electron microscopy (TEM).

2. Methodology

2.1. synthesis of norbornene functionalized chain transfer agent (NBI-CTA)

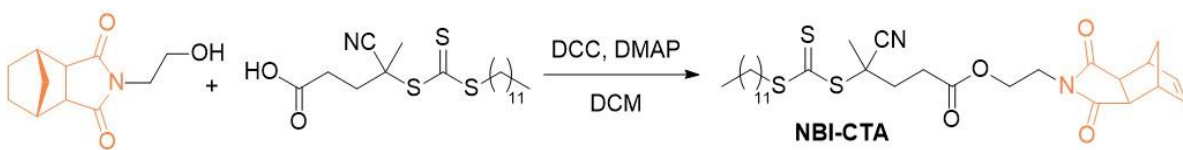
The NBI-CTA was synthesized through DCC coupling (Scheme 1) and purified through column chromatography and characterized by $^1\text{H-NMR}$ and GPC.

2.2. synthesis of polymethyl methacrylate (PMMA) Macro-Chain Transfer Agent (CTA)

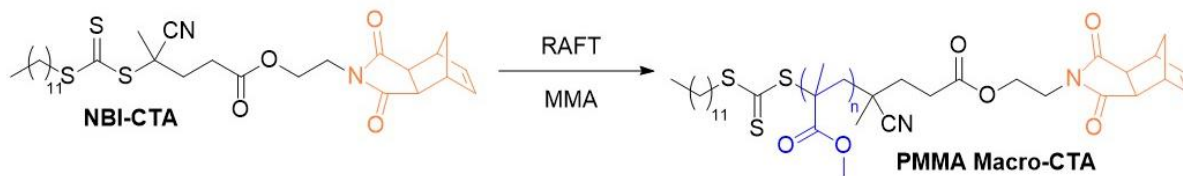
The NBI-CTA was used to produce a macro-CTA through a RAFT polymerization using azobisisobutyronitrile (AIBN) and methyl methacrylate (MMA) (Scheme 1). The macro-CTA was precipitated into cold hexanes, dried at 35°C in a vacuum oven overnight and characterized by $^1\text{H-NMR}$ and GPC.

2.3. synthesis of block copolymers

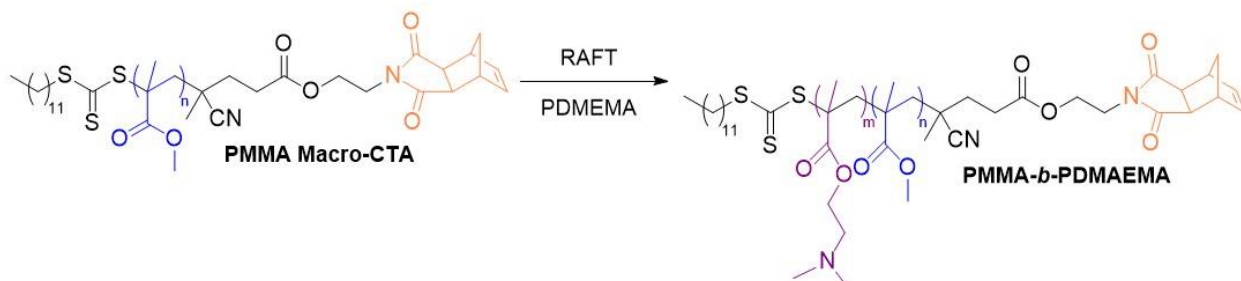
Block copolymers of the macro-CTA with PDMAEMA and PEGMA were synthesized through a RAFT polymerization to form block copolymers PMMA-*b*-PDMAEMA and Synthesis of PMMA-*b*-PEGMA. Schemes 1-4 illustrate the synthetic route to produce the block copolymers. The block copolymers were precipitated into cold hexanes, dried at 35°C in a vacuum oven overnight and characterized by $^1\text{H-NMR}$ and GPC.



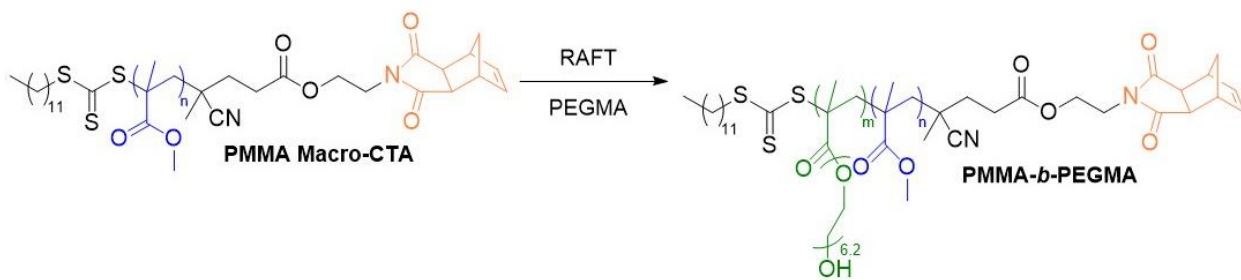
Scheme 1: Synthesis of norbornene functionalized chain-transfer agent



Scheme 2: Synthesis of PMMA Macro-CTA



Scheme 3: Synthesis of PMMA-*b*-PDMAEMA polymer brush



Scheme 4: Synthesis of PMMA-*b*-PEGMA polymer brush

Macro-CTA with target weight of 5000 and 10000 were synthesized with PMMA to PDMAEMA or PEGMA incorporation ratios of 1:1.

3. Results and Discussion

3.1. NMR analysis

Synthesized block copolymers were characterized by NMR and GPC to obtain molecular weight and polydispersity data. NMR spectra for the PMMA Macro-CTA and both the PMMA-*b*-PDMAEMA and PMMA-*b*-PEGMA (Figure 2) showed successful synthesis of the block copolymers with the target 1:1 incorporation.

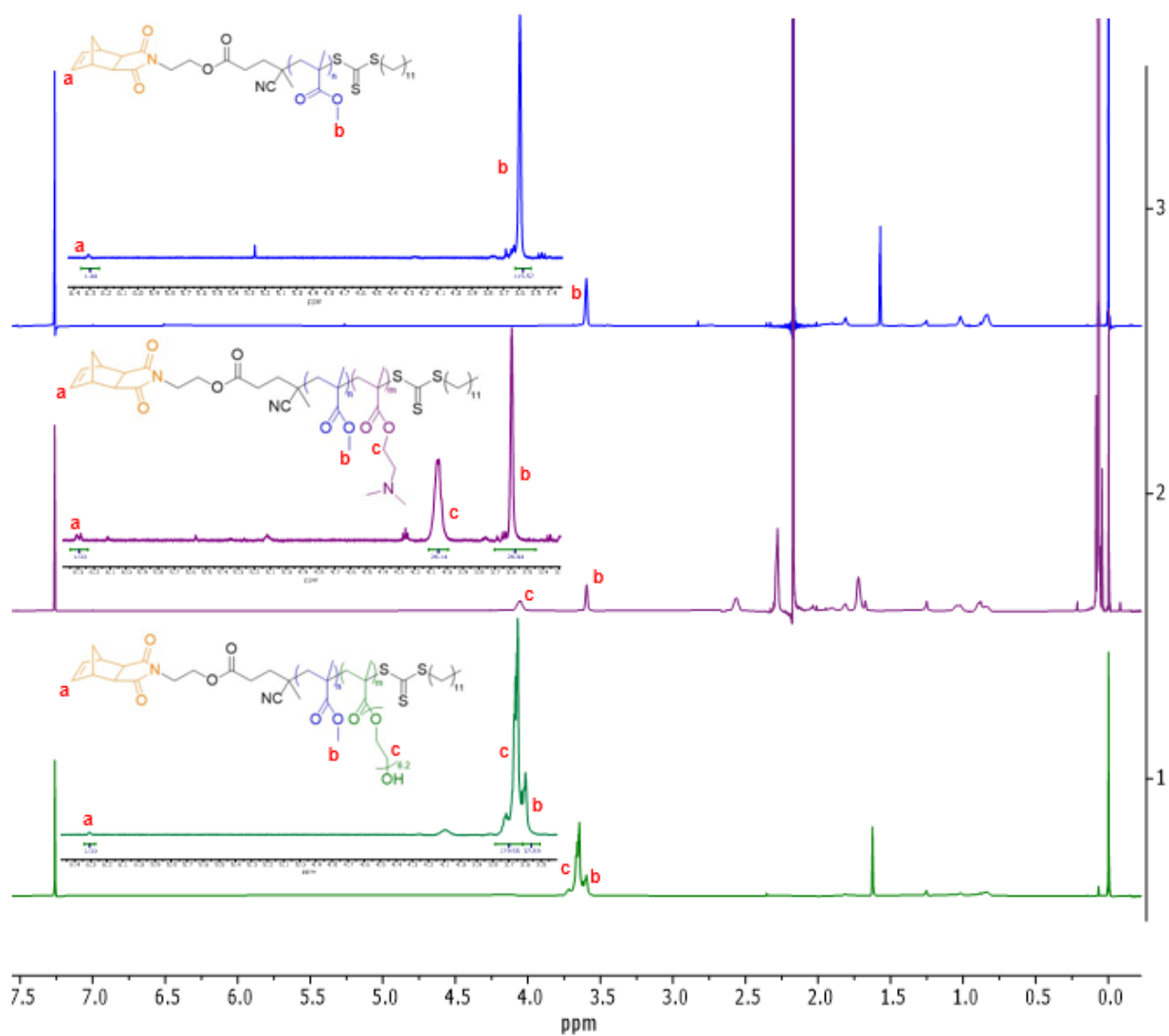


Figure 2: NMR of PMMA Macro-CTA (3), PMMA-*b*-PDMAEMA (2) and PMMA-*b*-PEGMA (1)

Figure 2 shows the full NMR spectra stacked to show the appearance of the PDMAEMA and PEGMA peaks for the spectra labeled 2 and 1, respectively. The NMR spectra are shown on a smaller scale for each synthesis to illustrate the retention of the peak representing the norbornene and the integrations of the peaks. A TMS reference peak is present in all samples at 0 ppm, water in spectra 1 and 3 at 1.56 ppm and acetone and silicone grease in spectrum 2 at 2.17 ppm and 0.07 ppm, respectively.

3.2. GPC analysis

The block copolymers, PMMA-*b*-PDMAEMA and PMMA-*b*-PEGMA (Figure 3), were also characterized by GPC using a MALS detector and RI. The DMAEMA block copolymer showed good polydispersity of 1.109 however, the PEGMA block copolymer calculated polydispersity was 3.304 (Table 1). Previous laboratory work with the PEGMA block copolymer indicated that high polydispersity was expected.

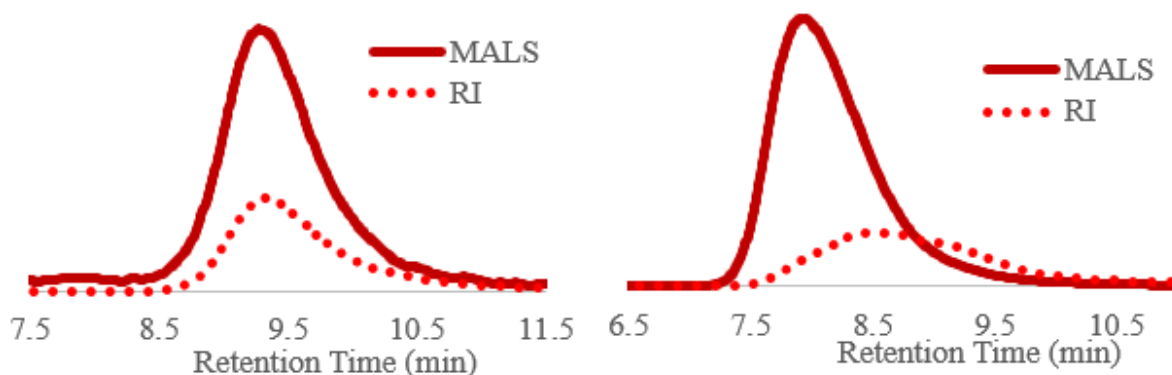


Figure 3: GPC Traces of PMMA-*b*-PDMAEMA (left) and PMMA-*b*-PEGMA (right)

3.3. Calculations

Calculated molecular weight and polydispersity data from the NMR spectra and GPC traces are given in Table 1.

Table 1: GPC and NMR calculated molecular weight data for PMMA Macro-CTA and block copolymers

Species	GPC			NMR	
	Mn (kDa)	Mw (kDa)	Đ	Dp	Mn (kDa)
PMMA	1.833	1.835	1.001	25.74	3.170
				51.22	5.721
PMMA- <i>b</i> -PDMAEMA	13.40	13.66	1.109	26.14	7.279
PMMA- <i>b</i> -PEGMA	38.81	128.2	3.304	14.48	5.312

GPC data was used to calculate the number averages molecular weight, Mn, and the weight averaged molecular weight, MW, to calculate the polydispersity of the synthesized molecules, Đ, which describes the distribution width between the molecular weights. NMR data and peak integration was used to calculate the degree of polymerization, Dp, and Mn. The NMR results were taken to be more accurate than the GPC data due to the clarity of the sample, performance of the RI detector with copolymers,⁵ and the age of the samples when GPC analysis were performed.

4. Conclusion

Block copolymers, PMMA-*b*-DMAEMA and PMMA-*b*-PEGMA, with target 1:1 incorporation have been successfully synthesized from PMMA Macro-CTA of 5000 and 10,000 g/mol target molecular weight. The block copolymers molecular weights were calculated from NMR peak integration and analysis of GPC traces. In addition, the ROMP of PMMA Macro-CTA has been investigated to prepare for the sequential ROMP of the block copolymers to form MCBPs.

5. Future Work

Continued work on this project includes the ROMP of block copolymers to form brush polymers and the sequential ROMP of the brush polymers to form ABA triblock MCBP (Figure 4). Following the successful synthesis of the MCBP, the self-assembly/disassembly of the MCBP will be investigated through temperature change and aggregation analysis. Immediately, additional GPC traces and analysis need to be completed for the full characterization of the synthesized products as well as the continued synthesis of a library of block copolymers including different molecular weights and block incorporations.

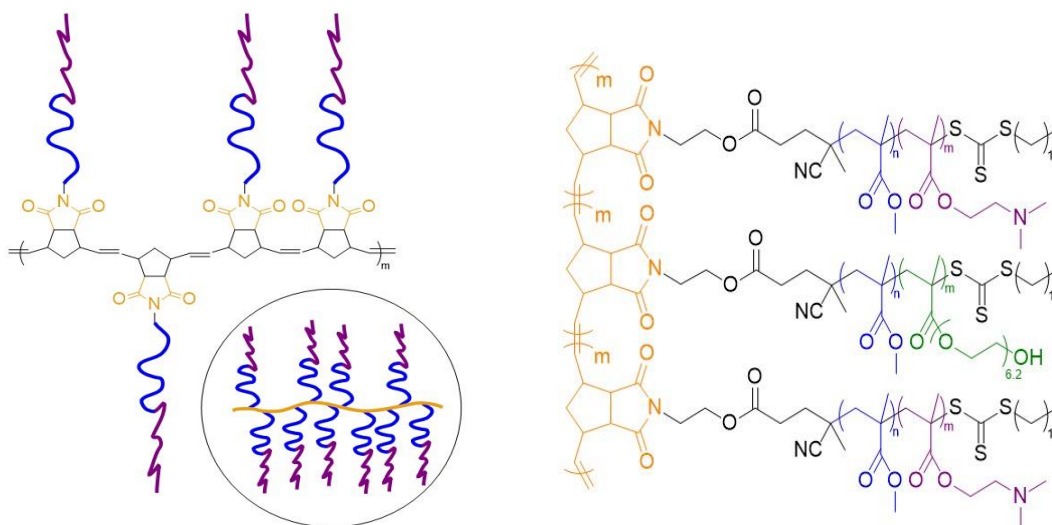


Figure 4: Depiction of ROMP brush polymer PNBI-branch-(PMMA-*b*-PDMAEMA) (left), product of sequential ROMP of brush polymers (right)

6. Acknowledgements

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7. References

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