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Effect of Molecular Structure of Side Chain Polymers on "Click" Synthesis of Thermosensitive Molecular Brushes

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Effect of Molecular Structure of Side Chain Polymers on "Click" Synthesis of Thermosensitive Molecular Brushes

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Abstract

Molecular bottlebrushes are graft copolymers with side chain polymers densely attached to the main backbone chains. Understanding how the side chain composition affects the overall brush structure is important in designing polymer brushes for different purposes. To gain insight into ways to control the brush architecture, we synthesized 3 molecular bottlebrushes using the same azide functionalized backbone chain but different side chains, namely poly(methoxydi(ethylene glycol) acrylate) (PDEGMA), poly(methoxydi(ethylene glycol methacrylate) (PDEGMMA) and poly(methoxytri(ethylene glycol) acrylate) (PTEGMA). All side chains have similar repeat units (Degree of Polymerization (DP)= ca. 45) but vary in terms of the presence of either an extra methyl or ethylene glycol group. The effect of the side chain composition on the grafting density of the resulting molecular brushes will be investigated.

The PDEGMA, PDEGMMA and PTEGMA side chains and the backbone polymers are synthesized using atomic transfer radical Polymerization (ATRP) and grafted onto the backbone chain by copper-catalyzed azide-alkyne cycloaddition reaction, or "click" reaction. The synthesis reactions will be monitored using ^{1}H-Nuclear Magnetic Resonance (^{1}H-NMR) and Size Exclusion Chromatography (SEC). The grafting densities of all 3 brushes will then be determined using data from the SEC.

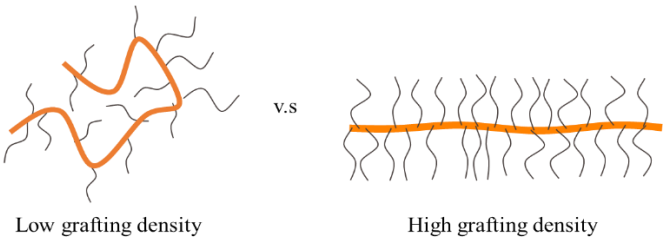
Introduction

Bottlebrush polymers consist of polymer side chains attached to a linear polymer backbone. The steric interaction between the side chains cause the backbone chains to be partially or fully extended to a wormlike conformation, giving it unique characteristics that cannot be found in their linear counterparts. Unlike linear polymers, bottlebrush polymers do not

entangle. The composition of the side chains determines how the brushes respond to different stimuli such as temperature, pH and light, and can be modified to address a wide range of applications including stimuli responsive coatings, drug delivery and lithographic patterning (Verduzco et al.).

Knowing how to control the molecular architecture of the bottlebrush polymers is crucial in understanding their structure-property relationships so that they can be targeted for different purposes. One way to do so is through modifying the grafting density of the brushes. Brushes with higher grafting density will have more side chains attached to the main backbone chain, leading to molecules with more extended backbone chains. Grafting density plays a vital role in shaping the physical properties, self-assembly and stimuli responsiveness of the brush polymers (Lin et al.).

Figure 1: Illustration of the effect of grafting density on the molecular brush structure

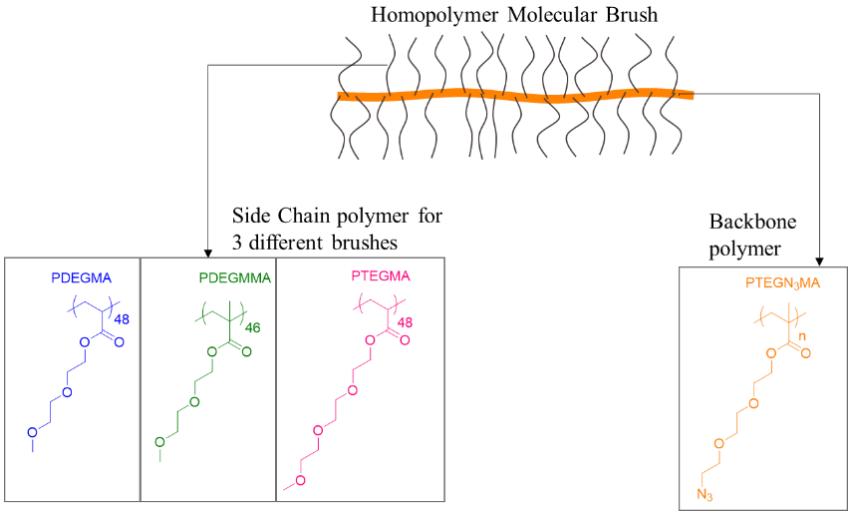


ATRP is a commonly used procedure for synthesizing linear polymers with a specific degree of polymerization (DP) and narrow molecular weight distribution (low dispersity (Đ)). The linear chains can then be coupled to form molecular brushes. Molecular brushes are synthesized either by “grafting from”, “grafting through” or “grafting to” methods. The “grafting to” method requires side chains to be synthesized separately from the backbone. The side chain polymers then undergo “click” reaction, with the backbone polymers. “Click” reaction is

commonly used for the "grafting to" approach because of its high efficiency and moderate reaction temperatures (25-70°C) (Binder and Sachsenhofer). One common problem of the "grafting to" approach is that the grafting density of the resulting brushes are usually very low due to steric congestion between the side chains and the reactive sites of the backbone chains. While reacting the backbone polymers with excessive side chains can potentially solve this problem, purifying the resulting brush polymers by multiple fractionation to remove the remaining unreacted linear chains is very difficult (Gao and Matyjaszewski). Other potential methods to increase grafting efficiency include choosing side chain repeat units with less steric hindrance.

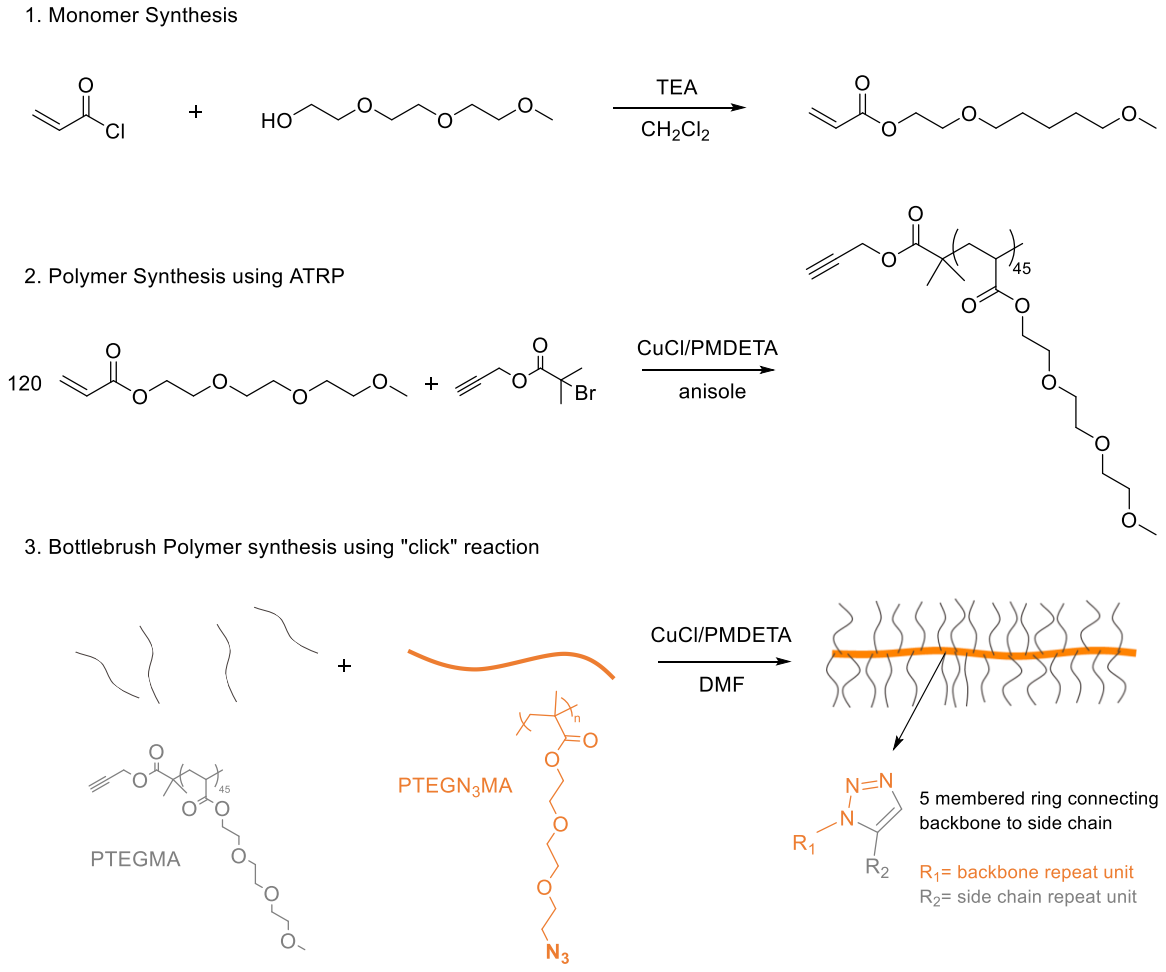
Herein, we investigate ways in which the chemical composition of the side chains affect the grafting density of the resulting homopolymer molecular brushes. ATRP is used to synthesize the side chain and backbone polymers, which are then coupled using the "click" reaction. All brushes have the same azide functionalized backbone ($PTEGN_3MA$) with the same number of repeat units. However, they have different alkyne-containing side chains: poly(methoxydi(ethylene glycol) acrylate) (PDEGMA), poly(methoxydi(ethylene glycol methacrylate) (PDEGMMA) and poly(methoxytri(ethylene glycol) acrylate) (PTEGMA). PDEGMMA differs from PDEGMA in that it has an additional methyl group whereas PTEGMA differs from both PDEGMMA and PDEGMA in that it has an additional ethylene glycol group. All side chains will have similar repeat units (DP = ca. 45). The final grafting density are determined by comparing the theoretical and actual mass of side chains used for brush synthesis.

Figure 2: Representative drawing of a densely grafted homopolymer molecular brush.



Results and Discussion

Scheme 1: General overview of the brush synthesis process, with PTEGMA brushes used as an example. Monomers undergo ATRP to form the polymer side chains and backbone chains before being grafted to the azide group of the backbone chain through the "click" reaction.



Backbone polymer synthesis. $PTEGN_3MA$ (DP=707, Đ= 1.18) was synthesized by ATRP of tri(ethylene glycol)mono(tert-butyldimethylsilyl) ether methacrylate (TEGSiMA) and a series of post-polymerization reactions to remove the tert-butyldimethylsilyl ether protecting group and add an azide functionalized end group, which will be involved in the "click" reaction.

Based on past ^{1}H NMR analysis, azide functionalization for the backbone chain is 99% (Henn et al).

Side chain polymer synthesis. PDEGMA,PDEGMMA and PTEGMA side chains were also synthesized by ATRP using propargyl 2-bromoisobutryrate (PgBiB) as the initator, Copper(I) Chloride (CuCl) as the catalyst, N,N,N',N",N"'-pentameethyldiethylenetriamine (PMDETA) as the ligand and anisole as the solvent. The reactions were first degassed 3 times by freeze-pump-thaw cycles. Polymerization of PDEGMA and PTEGMA were then carried out at 35°C and polymerization of PDEGMMA was carried out at 80°C. The monomer to initiator molar ratio for all 3 reactions were kept the same at 120:1. A high monomer to initiator ratio is used to reduce the chance of polymer chains coupling during ATRP. This happens when the alkyne end groups of 2 chains react and the resulting polymer chain is unable to graft onto the backbone chain, which leads to a lower grafting efficiency. To purify the polymers, repeated fractionation is carried out using a combination of methanol and cyclohexane.

Figure 3: ^{1}H-NMR graphs focusing on the 2 main peaks used for ^{1}H-NMR analysis. 'b' represents 2 H atoms on the monomer peak while 'a' represents 2 H atoms on the polymer peak.

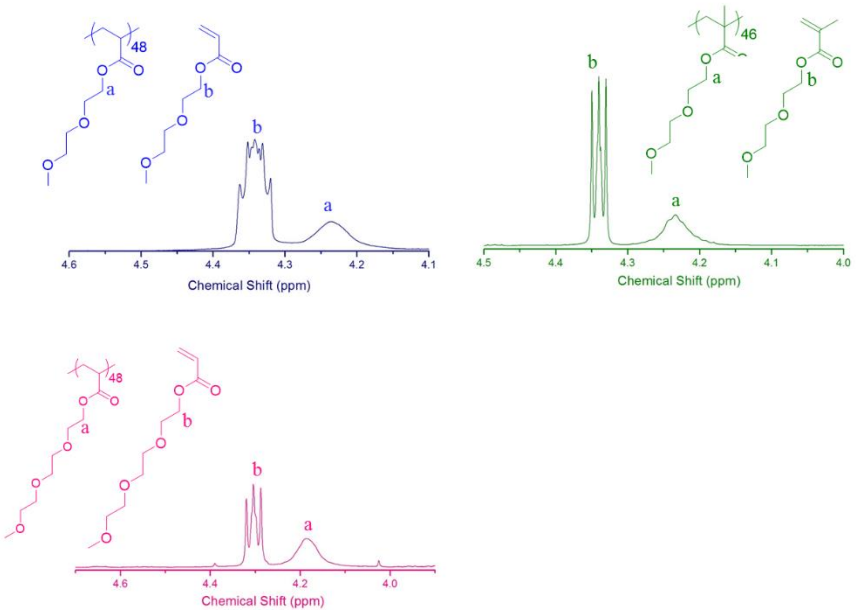


Figure 3 shows the ^{1}H NMR spectrography graphs for all 3 side chains. By analyzing the NMR graph, the % conversion ($\%Conversion = \frac{area\ of\ peak\ a}{area\ of\ peaks\ a+b}$) and degree of polymerization (DP) of the resulting polymer chain $\left(DP = \frac{number\ of\ monomers}{number\ of\ initiators} * \%\ Conversion\right)$ can be calculated. The DP values are further confirmed using Size Exclusion Chromatography (SEC). The SEC is also used to determine the number average molecular weight (M_n) and the dispersity index (Đ) of the side chain and backbone polymers, as shown in Table 1.

Table 1: Characterization of side chain and backbone polymers. The $M_{n,\ SEC}$ and Đ for side chain polymers were determined by SEC relative to polystyrene standards using PL-GPC 20 with THF as the solvent. $M_{n,\ SEC}$ and Đ for backbone polymers were determined using PL-GPC 50 Plus

system with DMF containing 50mM LiBr as the mobile phase. The DP was first calculated based on the ^{1}H NMR graph and confirmed with SEC.

Side Chain / Backbone	DP	$M_{n,\ SEC}$ (kDa)	Đ
PDEGMA	48	8.5	1.18
PDEGMMA	46	9.2	1.06
PTEGMA	48	10.6	1.35
$PTEGN_3MA$	707	121.8k	1.18

For PDEGMA to have a DP of 48, the ATRP reaction ran for 48h, which is significantly higher than the reaction time for PDEGMMA of 2h 10min to reach a similar DP of 46 and for PTEGMA of 19h 40min to reach the same DP of 48. One possible reason is that the catalyst deactivates the growing PDEGMA chains faster than PDEGMMA and PTEGMA, causing the chains to stay in the dormant state longer and for longer periods of time.

Đ of PTEGMA is also much higher than that of PDEGMA and PDEGMMA, meaning the polymer chains have a greater disparity in molecular weight distribution; some of the PTEGMA polymer chains might have coupled during the polymerization, leading to some chains with much higher polymer weights and therefore increasing the dispersity among molecular weights. This is evident in the SEC graph of PTEGMA as shown on the left, where there is a slight shoulder on the left representing the coupled chains. To achieve a more desirable dispersity index for PTEGMA, either more ligands can be used or Cu(II) Cl can be added to have a better control over the polymerization.

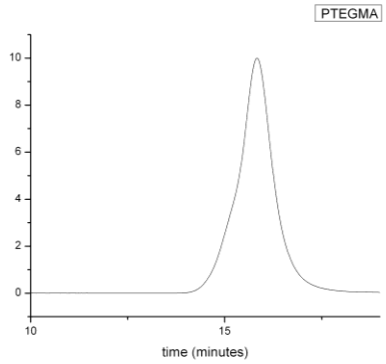
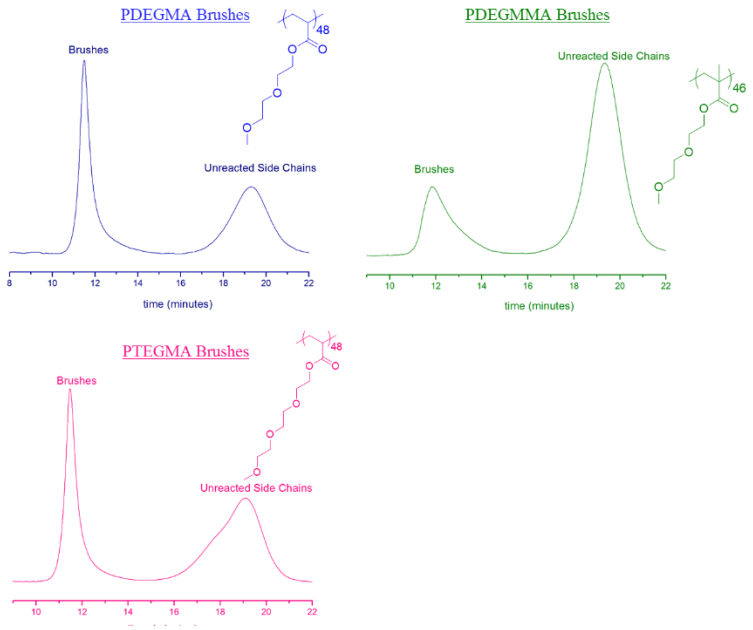


Figure 4: PTEGMA SEC

Molecular Brush polymer synthesis. Once the linear backbone and side chain polymers were synthesized, they undergo copper-catalyzed azide-alkyne cycloaddition reaction, or "click" reaction. The side chain to backbone polymer ratio is 2.2 for PDEGMA, 1.98 for PDEGMMA and 2.0 for PTEGMA. CuCl, PMDETA and DMF are used as the catalyst, ligand and solvent respectively. The reaction was carried out at room temperature for at least 22h. aliquots of each sample were then taken for SEC, as shown in figure 5.

Figure 5: SEC data for all 3 different brushes. The first peak corresponds to the brush peak which elutes at around 10-12 minutes while the remaining unreacted side chain peak elutes at around 18-22minutes.



SEC data in figure 5 shows that the methacrylates (i.e. PDEGMA and PTEGMA) result in brushes with a narrower molecular weight distribution and more side chains were grafted onto the backbone chain compared to the methyl methacrylate (PDEGMMA). The actual grafting efficiency can be found in Table 2 below.

Table 2: Characterization of molecular brushes using PL-GPC 50 Plus system with DMF containing 50mM LiBr as the mobile phase. The M_n and Đ values were obtained from the SEC and the grafting efficiency was calculated based on SEC data.

Brush	Đ	$M_{n,\,SEC}$ (kDa)	Grafting Efficiency
PDEGMA	1.09	750	95.26%
PDEGMMA	1.14	555	40.1%
PTEGMA	1.05	817	87.6%

Calculating Grafting Density of Molecular Bottlebrushes. The following is the method used to calculate the grafting density for PTEGMA. The feed for PTEGMA click reaction contained 3.46mg backbone polymer (m_{b0}) and 304mg side chain polymer (m_{sc0},) giving a total of 307.48mg starting polymer. At 100% grafting efficiency, stoichiometric calculations based on molecular weights of the backbone monomer ($MW_{b,monomer}$)and side chain polymer (MW_{sc}) show that only 150.8mg of side chain polymer can react with the backbone. SEC data shows that the reaction mixture contained 43.0% brushes by mass based on the peak areas of the brushes and side chains. Using the above information, the following formula is used to calculate grafting efficiency (Henn et al.) :

$$Grafting\ Efficiency = \frac{actual\ number\ of\ side\ chains\ reacted}{number\ of\ side\ chains\ that\ can\ react\ at\ 100\%\ grafting\ efficiency}$$

$$= \frac{\left(actual\ \%\ brushes * (m_{b0} + m_{sc0})\right) - m_{b0}}{m_{b0} * \frac{MW_{sc}}{MW_{b,monomer}}}$$

$$= \frac{0.43 * 307.48 - 3.46}{3.46 * \frac{10600}{243.27}} = \mathbf{87.6\%}$$

Previous work from the same group has confirmed that the peak areas in the SEC are proportional to the masses of the polymers (Henn et al.). The grafting density of PDEGMA and PDEGMMA are calculated using the same method. The calculated grafting densities for all brushes are given in table 2.

The grafting efficiency for PDEGMMA of 40.1% is significantly lower than that of PDEGMA and PDEGMMA. This is because the extra methyl group on PDEGMMA creates a great steric hindrance, making it harder for more of the side chains to couple with the backbone chain. The extra ethylene glycol group on PTEGMA also leads to PTEGMA having a slightly lower grafting density of 87.6% compared to that of PDEGMA of 95.26%. There are also more PTEGMA side chains that coupled with each other during ATRP; these chains lack the alkyne group necessary for the "click" reaction to take place, therefore lowering the grafting efficiency of PTEGMA.

Conclusions

This work shows how the chemical composition of methacrylate and methyl methacrylate side chains can alter the grafting density of the resulting bottlebrush polymers. The polymers were synthesized with ATRP and the side chains were grafted onto the backbone chain using "click" reaction. The steric hindrance, which in this project is the extra methyl group on PDEGMMA, significantly affects the grafting density of the molecular brushes (22.4% for PDEGMMA compared to 49% for PDEGMA). Having a longer repeating side chain unit slightly decreases the grafting density of the brushes, but its effect is not as significant as that of the steric hindrance (43.4% for PTEGMA compared to 49% for PDEGMA).

Future work will include synthesizing PTEGMMA molecular brushes and comparing it to the rest of the brushes. Doing so will allow us to understand how the presence of both an extra methyl group and ethyl glycol group will affect the grafting density. All the molecular brushes synthesized in this project are also temperature responsive. At specific lower critical solution temperatures (LCST), the brushes can self-assemble from a wormlike structure to a compact globular structure. The effect of grafting efficiency on LCST will be determined in the future.

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