SUPRAMOLECULAR STRUCTURE OF INCLUSION COMPLEXES OF
β-CYCLODEXTRIN WITH POLY(ETHYLENE OXIDE)-BLOCK-
POLY(PROPYLENE OXIDE)-BLOCK-POLY(ETHYLENE OXIDE) COPOLYMERS

A Dissertation

Presented to

The Graduate Faculty of The University of Akron

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

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May, 2011
ABSTRACT

Molecular self-assembly, based on non-covalent interactions and molecular recognition, is a fascinating process that can be exploited to build complex supramolecular structures. The principle of molecular recognition can be exemplified in the formation of complexes of the ‘host-guest’ type. Cyclodextrin (CD), one of the promising hosts for macromolecular recognition, has been studied for constructing supramolecular structures. It has been found that hierarchical self-assembly via inclusion complexation depends on the complexation behavior of CDs with guest polymer.

In this research, a series of inclusion complexes of β-cyclodextrin (β-CD) with poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-b-PPO-b-PEO) copolymers served as a model to examine the formation of supramolecular structure via self-organization of inclusion complexes. The results exhibited that β-CD can form a site-selective complex onto the PPO blocks, but do not complex with the PEO blocks, due to steric fitting and hydrophobic (and/or van der Waals) interaction. Additionally, the mobility of PPO block dramatically decreases, revealing that PPO chain is tightly included inside cavities of β-CDs. Through self-assembly of the PPO blocks with threaded β-CDs, the 3-D well-ordered supramolecular structure was observed and determined to be a monoclinic crystal structure. With the assistance of computer simulation, the packing of inclusion complexes in the supramolecular crystal structure
was visualized. By varying the molecular weight of tethered PEO blocks, the crystallization behavior and crystal orientation of PEO blocks on supramolecular structure were investigated. Three different $c$-axis orientations of PEO crystals were observed with respect to supramolecular structure depending upon crystallization temperature ($T_c$).
ACKNOWLEDGEMENTS

First and foremost, I would like to express my sincerest gratitude to my advisor, Dr. Stephen Z. D. Cheng, who has supported and guided me throughout my research with his patience and knowledge while allowing me the room to work in my own way. During my study in the Department of Polymer Science at University of Akron, Dr. Cheng has been my inspiration as I overcome all obstacles in the completion this research work.

My special thank go to Dr. Rong-Ming Ho, an advisor during my Master Degree in National Chung-Hsing University, Taiwan. Attributing to his encouragement and effort, I was having such a great opportunity to further study knowledge of polymer science in Dr. Cheng’s research group. I greatly appreciate the collaboration with Dr. Minming Guo, a manager of NMR center in department of Polymer Science at University of Akron. With his expertise in NMR technique, not only did he make critical contributions in my research project, but also I learned tremendous amount knowledge of NMR characterization from him. I would also like to thank the chair of my committee: Dr. Darrell H. Reneker and the committee members: Dr. Ali Dhinojwala, Dr. Gustavo A. Carri, and Dr. Alamgir Karim for their patience and helpful instructions.

In addition, I am grateful to Dr. Bernard Lotz for discussion regarding my research. With fruitful knowledge of polymer crystal structures and hands-on experiences, he has offered much advice and insight throughout my research work. I also
would like to thank the following people: Dr. Bojie Wang for his help in TEM technique; Dr. Siwei Leng, Dr. Kwang-Un Jeong, and Dr. Ming-Siao Hsiao for sharing their experiences in polymer physical characterization; Dr. Ryan M. Van Horn, Dr. Wen-Bin Zhang and Dr. Matthew Graham for their tremendous help in manuscript preparations; Dr. Chien-Lung Wang, Ms. I-Fan Hsieh, and Mr. Hao-Jun Sun for discussions about chemistry and physics of polymeric materials, and other group members for their kind help in all aspects.

Finally, I thank my parents for endless contributions throughout all my studies at University. With their influence and encourage, I have had enough confidence to complete my doctorate degree.
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CHAPTER I
INTRODUCTION

The field of supramolecular chemistry has evolved and developed significantly in the past two decades. Research has focused on the systems capable of self-organizing, namely, spontaneous self-assembly of constituent parts, into supramolecular structures. The assembly of such structures relies on molecular recognition and results from the cooperation of various non-covalent interactions.\(^1\) The principle of molecular recognition can be exemplified in the formation of complexes of the ‘host-guest’ type. Cyclodextrin (CD), one of the promising hosts for macromolecular recognition, has been focused on constructing supramolecular structures due to its good water-solubility and ability to include a wide range of guest molecules.\(^2-4\) Recent studies have demonstrated that in inclusion complexes of CDs with block copolymers, CDs can perform “site-selective complexation” on a specific segment of the block copolymer due to intrinsic characteristics of CDs and polymer, which can generate or enhance amphiphilicity of the block copolymers and further self-organize into supramolecular aggregates.\(^5-16\)

Such hierarchical self-assembly via inclusion complexation provides an alternative route to prepare nanostructure. To gain insight into supramolecular structure formation, it is crucial to understand the complexation interaction of CDs with guest polymer.
In this work, we focus on the complexation behavior between poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-b-PPO-b-PEO) and β-CD. Amphiphilic PEO-b-PPO-b-PEO, also known by the trade name, Pluronics, consists of hydrophilic PEO blocks and hydrophobic PPO blocks. Due to complex aggregation behavior and widespread utility, PEO-b-PPO-b-PEO has attracted great interest and has been extensively studied\textsuperscript{17,18}, which provides a good framework for our study. So far, there are a few papers on the complexation behavior of β-CD and PEO-b-PPO-b-PEO, and they suggested that β-CD can site-selective complex onto the PPO blocks to form inclusion complexes in aqueous system, but did not complex with the PEO blocks\textsuperscript{19-25}. However, the question remains whether all the β-CDs exclusively interact with the PPO blocks, or only part of them stay with the PPO blocks and the rest with the PEO blocks. The existing studies only concentrated on the formation of inclusion complexes between β-CDs and PEO-b-PPO-b-PEO copolymer in solution. The interaction between β-CDs and the PPO blocks can be detected using the nuclear overhauser effect technique in solution. However, if part of the β-CDs stayed with the PEO blocks, the interaction between β-CDs and the PEO blocks in solution is too weak to be detected due to longer intermolecular distances. In addition, the dynamics and molecular motion of the PPO block inside the cavity of β-CDs as well as the β-CDs themselves, in the inclusion complexes has not been examined. The motivation of the study is to clarify the dynamics of the inclusion complexation behavior between β-CDs and PEO-b-PPO-b-PEO copolymers. The results indicated that the β-CDs do possess selectivity on PEO-b-PPO-b-PEO complexation, and only thread onto PPO blocks, but not PEO blocks\textsuperscript{26}. Via building blocks of inclusion complex, the self-assembled
supramolecular structure has been observed and exhibited a three-dimensional well-defined monoclinic crystal structure.\textsuperscript{27} This hierarchical self-assembly of a well-ordered crystal structure provides one of the practical strategies to the development of “bottom-up” nanotechnology. Furthermore, with the higher molecular weight of tethered PEO blocks, it provides an opportunity to study crystallization behavior and crystal orientation of PEO onto supramolecular structure with respect to crystallization temperature.

Chapter II in this dissertation provides the information of properties and structure for cyclodextrins and PEO-\textit{b}-PPO-\textit{b}-PEO copolymers, respectively. Recent researches regarding the complexation behavior of cyclodextrins interacting with various kinds of polymers also review. Meanwhile, the different supramolecular structures constructed via self-assembly due to cooperation of interactions between cyclodextrins and polymers are introduced in the following. The crystal structure and crystal orientation of PEO will be briefly introduced in this chapter as well.

Chapter III gives the experimental methods involved in this study, including solid-state and solution nuclear magnetic resonance (NMR), transmission electron microscopy (TEM), one- and two-dimensional wide-angle x-ray diffraction (WAXD), small-angle x-ray scattering (SAXS), and differential scanning calorimetry (DSC), etc. The sample information and preparation are also described.

Chapter IV elucidates the dynamics and inclusion complexation behavior between \(\beta\)-CDs and PEO-\textit{b}-PPO-\textit{b}-PEO utilizing high resolution solid-state \(^{13}\text{C}\) NMR to measure the rates of magnetization exchange between \(\beta\)-CDs and copolymers, and, additionally, employing the proton T\textsubscript{1} relaxation to observe the length scale of inclusion complexes. \(^1\text{H-to-}^{13}\text{C}\) cross-polarization and two-dimensional (2D) wide-line separation NMR
experiments have also been used to investigate the dynamics and molecular motion of the PPO blocks and β-CDs in the inclusion complexes. These results have been compared with those in the un-complexed states.

Chapter V reports the preparation and determination of the supramolecular aggregate formed via hierarchical self-assembly of inclusion complexes. On the basis of fiber diffraction patterns from WAXD experiments, electron diffraction method from TEM technique and computer simulation, the molecular packing in the supramolecular crystal structure can be built. The supramolecular structure exhibits a lozenge-shaped crystal morphology with \{110\} faces. Unlike less-ordered (or disordered) self-assembled aggregates such as micelles and vesicles, the supramolecular structure is constructed from a three-dimensionally well-defined crystal structure in aqueous solution.

Chapter VI focuses on the crystallization behavior and crystal orientation of PEO onto supramolecular structure. The crystallization behavior of PEO blocks among inclusion complex systems shows significant difference through DSC experiments. Using 2D WAXD experiments, the observations of PEO crystal orientation changes with respect to surface of supramolecular structure have been found to be dependent upon crystallization temperature \( (T_c) \).

Finally, a summary of the research highlights is presented in Chapter VII.
CHAPTER II

BACKGROUND

2.1 Cyclodextrins (CDs)

Cyclodextrins are a family of three well known, industrially produced, major cyclic oligosaccharides. The three major cyclodextrins are of a torus-like macro ring structure, built up from glucose units. The historical backgrounds and details of structural features will be discussed in the following sections.

2.1.1 Molecular Recognition Chemistry

The concept and definition of “supramolecular chemistry” was introduced by Dr. Lehn as “chemistry beyond the molecule”. A supramolecule, as a large engineered “molecule”, has many subunits, each designed to perform a specific task. While a supramolecule is still a single molecular entity, it is engineered to function as a whole like a large complex compound, as demonstrated in Figure 2.1. These molecules are held reversibly by intermolecular forces, but not by covalent bonds.
The origin of supramolecular chemistry lies in molecular recognition, which studies how molecules interact and recognize each other. This was described by Dr. Emil Fischer in 1894 as the “key and lock” principle based on the mechanism of the structural fit between the host and guest molecules. It was almost 70 years later that Dr. Pedersen discovered that crown ether showed molecular recognition and opened the door to the research on artificial host molecules. Dr. Cram applied the concept of artificial hosts to various kinds of molecules, and the research of host-guest chemistry has since thrived. In molecular recognition, a guest molecule selectively recognizes its host through complementary molecular interactions, including electrostatic effect, hydrogen bonding, π-π interactions, hydrophobic interactions, and van der Waals forces. Electrostatic interactions occur between charged molecules, in which an attractive force is observed between oppositely charged molecules and a repulsive force between molecules of the same charge. The strength of this interaction is inversely proportional to the dielectric constant of the surrounding medium. Hydrogen bonding is one type of dipole-dipole interaction, where positively polarized hydrogen atoms in donors such as hydroxyl...
groups interact with acceptors with electron rich atoms, such as O in C=O, and N in -NH-. The \( \pi - \pi \) interactions occur between \( \pi \)-conjugated aromatic rings. When the aromatic rings face each other, the overlap of \( \pi \)-electron orbits results in an energetic gain. The hydrophobic interaction plays an important role when in an aqueous medium. The hydrophobic molecules aggregate to minimize the number of water molecules involved in hydrated structure. The van der Waals interaction is weaker and less specific than other interactions, but it is significantly important because of its ubiquitous existence. It is driven by the interactions between dipoles created by instantaneous unbalanced electric distributions. Therefore, a selective and effective molecular recognition, by means of the above-mentioned intermolecular, plays an important role in constructing supramolecular structures in order to achieve their specific functions. In addition, the complexity and the cooperative enhancement in molecular recognition can be perceived when the recognition involves more than a single kind of interaction. The principle of molecular recognitions, exemplified in the formation of ‘host-guest’ complexes, has been focused on the study of low molecular weight compounds over the past few decades.

The role of host, in general, is played by cyclic molecules such as crown ethers, cryptands, and cyclophanes.\textsuperscript{28,31,33} However, the guests recognized by these hosts have been limited to small molecules and simple ions. Consequently, it has been intriguing to develop host molecules that can recognize and respond sensitivity to larger and more complex compounds including polymers.\textsuperscript{16,34,35} Cyclodextrin is one of promising hosts for macromolecular recognition. Recent findings found that cyclodextrin not only can form inclusion complexes with small molecules and homopolymers, but also with copolymers due to cooperative intermolecular interactions.
2.1.2 Chemical Structures and Physical Properties of Cyclodextrins

Cyclodextrins (CDs) are a series of cyclic oligosaccharides formed by the action of certain enzymes on starch, most commonly containing 6, 7, or 8 glucose units connected through $\alpha$-1,4-glycosidic linkages (Figure 2.2a, b, and c). They are abbreviated as $\alpha$-, $\beta$-, and $\gamma$-CD, respectively. The CDs with fewer than six glucose units are too strained to exist, whereas those with more than eight units are highly soluble, and thus, difficult to isolate. The shape of cyclodextrins have been approximated based on molecular dynamics simulation, and the resultant structure is similar to a shallow, truncated cone possessing a hydrophilic outer surface and a hydrophobic cavity. At the primary (narrower-diameter end) and the secondary (wider-diameter end) rims of the molecule, there are hydroxyl groups. The central cavity consists of alkyl groups and glycosidic oxygen atoms and is hydrophobic (Figure 2.2d).

The structures of cyclodextrins are fairly rigid due to intramolecular hydrogen bonds between the secondary O2-H hydroxyl group and O3-H hydroxyl group of adjacent glucose units. Although the structure is stabilized by intramolecular hydrogen bonds, it is still flexible enough to allow deviation from the regular conical shape. In primary hydroxyl groups, they have rotational flexibility around the C5-C6 bond, but the conformations are limited to two types, (+) gauche and (-) gauche, because of torsion angle and steric hindrance. The two gauche conformers are not equal, the (-) gauche form with O6-H pointing “away” from the center of the cavity which is mainly preferred. The (+) gauche orientation with O6-H “toward” the cavity can only be found in crystal
structures when certain packing requirements are met or when a hydrogen bond is formed with a guest molecule. Because of steric hindrance, it is impossible for a complete rotation of the glucose unit around the C1-O-C4’. Hence, protons H3 and H5 are always located within the cavity, whereas protons H1, H2 and H3 always point outwards.

Since hydroxyl groups on the exterior of CDs are fairly polar, cyclodextrins are moderately soluble in water, but easily soluble in strongly polar aprotic solvents such as dimethyl sulfoxide (DMSO), dimethylformamide (DMF), N,N-dimethylacetamide, and pyridine. It is also noted that β-CD show the lowest solubility in aqueous solution among CDs (Table 2.1). The reason is that in β-CD, all of the intramolecular hydrogen bonds are formed on secondary hydroxyl groups, leading to a rigid conformation of β-CD. On the other hand, not all of the hydrogen bonds are formed in α-CD since one of the glucose units is in a distorted position. Therefore, only four of the six possible hydrogen bonds can be formed. The γ-CD is non-coplanar and more flexible. As a result, it is also the most soluble one among the three CDs.
Figure 2.2 Chemical structures of $\alpha$-CD (a), $\beta$-CD (b), $\gamma$-CD (c), and schematic representation of the shape of the CDs (d).
Table 2.1 Characteristics of Cyclodextrins

<table>
<thead>
<tr>
<th></th>
<th>α-CD</th>
<th>β-CD</th>
<th>γ-CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of glucose units</td>
<td>6</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>C_{36}H_{60}O_{30}</td>
<td>C_{42}H_{70}O_{45}</td>
<td>C_{48}H_{80}O_{60}</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>972</td>
<td>1134</td>
<td>1296</td>
</tr>
<tr>
<td>Solubility in water (g/100ml, 25°C)</td>
<td>14.5</td>
<td>1.85</td>
<td>23.2</td>
</tr>
<tr>
<td>Inner cavity diameter (Å)</td>
<td>4.7-5.3</td>
<td>6.0-6.5</td>
<td>7.5-8.3</td>
</tr>
<tr>
<td>External diameter (Å)</td>
<td>14.6 ± 0.4</td>
<td>15.4 ± 0.4</td>
<td>17.5 ± 0.4</td>
</tr>
<tr>
<td>Height (Å)</td>
<td>7.9 ± 0.1</td>
<td>7.9 ± 0.1</td>
<td>7.9 ± 0.1</td>
</tr>
<tr>
<td>Minimum cross section of cavity (Å²)</td>
<td>15</td>
<td>26</td>
<td>43</td>
</tr>
<tr>
<td>Approx. volume of cavity (Å³)</td>
<td>174</td>
<td>262</td>
<td>427</td>
</tr>
</tbody>
</table>

2.1.3 Inclusion Complex of Cyclodextrins

The formation and supramolecular structures of the “host-guest” complexes based on the principle of molecular recognition have attracted great interests in the past four decades. The typical host molecules, such as crown ethers, cryptands, and cyclophanes, have been frequently studied. However, the guest molecules that can be recognized by these hosts are limited to small molecules and simple ions. On the other hand, the cyclodextrins, due to their hydrophilic exterior and hydrophobic cavity, can recognize a wide range of guest molecules, including very complex compounds such as polymers. The CDs possess several features that make their complexation versatile and important in many aspects of application from drug delivery systems technology to food and separation industries: (1) unique structural properties; (2) well-defined chemical structures that has many potential sites for chemical modification and conjugation; (3) a
variety of different cavity sizes; (4) low toxicity and low pharmacological activity; and (5) protection of the included molecules from degradation. Therefore, they can be used to improve the solubility, stability, absorption, and bioavailability of the guest molecules. The formation of inclusion complex of CDs and guest molecules are dependent on their cavity sizes. For example, the \( \alpha \)-CD cavity is too narrow to include a naphthalene ring that can be comfortably accommodated in the \( \beta \)-CD cavity. Therefore, matching the geometrical characteristics of the cyclodextrin cavity with those of the guest molecule is an important prerequisite for the formation and stability of the inclusion complexes. The better the guest molecule fills the CD cavity, the stronger the binding forces will be. Nevertheless, the binding forces become low if the CD is too wide for the guest molecules, as van der Waals significantly decrease with increasing intermolecular distances.

Extensive discussions have attempted to elucidate the driving forces involving complexation behavior of CDs with guest molecules, but until now it’s still unclear and controversial. In general, there are several important driving forces thought to be responsible for the formation of inclusion complexes: (1) enthalpy-entropy compensation (2) van der Waals interactions (3) hydrophobic interaction or (4) hydrogen bonding. From the thermodynamic point of view, the term of entropy doesn’t play the dominant factor, though it favors the dissociation process of inclusion complexation. Hence, the complexation largely depends on enthalpic factors. Therefore, the solvent medium plays an important role in the formation of inclusion complexation. When the complexation is with hydrophobic (or less polar) guest molecules, water as a medium (or other polar mediums) is considered to be a necessity for formation and maintenance of the integrity.
of the inclusion complexes.\textsuperscript{46} The most important contributions are believed to come from (a) the release of the water molecules originally included in the cavity of CDs (b) penetration of the hydrophobic (or less polar) guest molecules into the cavity of CD and (c) dehydration of the guest molecules, which largely compensates for the entropy loss due to inclusion. Van der Waals interaction depends not only on the size but also the shape of guest molecules. When the guest molecules can be completely accommodated within the cavity of cyclodextrin, the distance between guest molecules and is a crucial key to the formation of a stable inclusion complex since these interactions dramatically decrease with increasing intermolecular distance. The role of hydrogen bonding in certain condition show significant contribution to the stability of the inclusion complex. In some cases, considering the complexation with longer guest molecules such as polymers, the hydroxyl groups of CD can form intermolecular hydrogen bonding with adjacent CDs either in a head-to-head or head-to-tail arrangement where the guest molecules are included inside the CDs. These intermolecular hydrogen bonds formed between adjacent CDs can stabilize inclusion complexes (Figure 2.3a and 2.4). However, the interactions responsible for inclusion complexation are not limited to any individual one, but rather, a simultaneous cooperation of several interactions.

2.1.4 Crystal Packing of Inclusion Complex

The crystal packing of inclusion complexes is greatly dependent on relationship between CDs and the included guest molecules. In general, it can be classified into three categories: channel-type, cage-type, and layer-type (Figure 2.3).\textsuperscript{34,44,45}
The channel-type structure is formed with a variety of guest molecules. Since CD molecules are stacked on top of each other to form “endless” columns (Figure 2.3a), in which guest molecules are included. The arrangement of channel-type packing can be either in the form of “head-to-head” or “head-to-tail” (Figure 2.4). In the channel-type packing belonging to head-to-head (or tail-to-tail) arrangement, the O2-H and O3-H secondary hydroxyl groups of CD form intermolecular hydrogen bonds with O2-H and O3-H of an adjacent CD while the O6-H primary hydroxyl groups are also hydrogen bonded to the neighboring O6-H. On the other hand, the hydrogen bonds formed between O2-H and/or O3-H secondary hydroxyl groups and O6-H primary hydroxyl groups lead to the formation of head-to-tail channel-type.
When the guest molecules is small enough to be fully included in the cavity, the CDs crystallize crosswise in herringbone pattern, in which both sides of CD cavity are blocked by neighboring CDs. Hence, the guest molecule is enclosed within an isolated CD cavity and cannot contact with each other (Figure 2.5). It is noteworthy that α-, β-, and γ-CD can also crystallize from water, in which water molecules are the guest molecules, and crystal packing is found to be the cage-type structure.50-52

For layer-type crystal packing, CD molecules are arranged in brick-wall fashion to form “layer” structure. As in such type of packing, the adjacent layers are laterally shifted, and thus both sides of the cavity are blocked by neighboring layers formed by CDs. However, both ends of the cavity aren’t tightly occluded by adjacent CD molecules, but rather loosely attached due to the expanded intermolecular space of the adjacent
layer. As a result, even the guest molecules is too large to be fully included in a single cavity, but still fits in this expanded space (Figure 2.6).

Figure 2.5 The structure of inclusion complexes of $\alpha$-CD with iodine (a),$^{53}$ and the structure of $\beta$-CD complexed with nicotinamide (b).$^{54}$ The CD molecules are arranged in herringbone pattern to form the cage-type packing structure.

Figure 2.6 The structure of inclusion complexes of $\alpha$-CD with p-nitrophenol (a),$^{55}$ and the structure of $\beta$-CD complexed with sulfathiazole (b).$^{56}$ The CD molecules are arranged in brick-wall pattern which forms the layer-type structure.
As a whole, the structure of cyclodextrin complexes are largely regulated by two factors (1) the intrinsic characteristics of CDs, and (2) the packing operation of inclusion complexation. In principle, the geometry and physical properties of the cavity are the most important for the selectivity of guest molecules in CDs. To form inclusion complexes, guest molecules should have proper size and shape to be, at least partially, accommodated in the cavity of CD. The operation of inclusion complexation, then, shows significant influence in crystal packing of complexes. For instance, a phenyl group inserts linearly into cavity of α-CD, leading to channel-type packing, while β-CD with a leaned benzene ring, resulted in cage-type structure. Through examination of crystal packing of complexes, the behavior of inclusion complexation with guest molecules can be perceived.

2.1.5 Inclusion Complexation between CDs and Polymers

In early 1980 the Harada group started to study the inclusion complexation of CDs with various polymers, and, later, they reported the first inclusion complex prepared by α-CD threading onto PEO. Throughout their studies, they found that polymers are highly selective to form inclusion complexes with certain CDs. It was suggested a good accommodation between the cross-sectional area of the polymer chain and the minimum diameter size of the cyclodextrin cavity is the prominent key to the formation of a stable inclusion complex (Table 2.1 and Table 2.2). In addition, the principal driving forces stated in section 2.1.3 are also attributed to formation of a stable inclusion complex with polymers as well. Afterwards, numerous studies have been focused on the formation
of inclusion complexes with different kinds of polymers such as polyethers, polyamines, polyesters, conjugated polymers, polyolefins, and inorganic polymers.\textsuperscript{16,61,62}

A pseudopolyrotaxane (or molecular tube) structure is usually formed when CDs are threaded onto a polymer chain in the channel-type arrangement (Figure 2.7). This kind of pseudopolyrotaxane structure has been recognized as a new building block in constructing nanostructures as well as in novel functionality.

Table 2.2 Characterization of Inclusion Complex between CDs and Polymers.\textsuperscript{16}

<table>
<thead>
<tr>
<th>Polymer</th>
<th>$A_{pol}$ (Å$^2$)</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligoethylene</td>
<td>18.3</td>
<td>$\alpha$</td>
</tr>
<tr>
<td>Poly(ethylene oxide)</td>
<td>21.5</td>
<td>$\alpha$</td>
</tr>
<tr>
<td>Poly(ethylene oxide)</td>
<td>$2 \times 21.5$</td>
<td>$\gamma$</td>
</tr>
<tr>
<td>Poly(tetramethylene oxide)</td>
<td>17.6</td>
<td>$\alpha$</td>
</tr>
<tr>
<td>Poly(propylene oxide)</td>
<td>24.5</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Polysobutene</td>
<td>41.2</td>
<td>$\gamma$</td>
</tr>
<tr>
<td>Polymethylvinyl ether</td>
<td>41.3</td>
<td>$\gamma$</td>
</tr>
</tbody>
</table>

$A_{pol}$ = cross-sectional area of polymer

Figure 2.7 The schematic pseudopolyrotaxane structure formed by inclusion complex between $\alpha$-CDs and PEO (a), scanning tunneling microscopy (STM) image (b).\textsuperscript{63}
The molecular tube formed by CDs can function as insulated molecular wire for conjugated polymers. Conjugated polymers have raised a great interest because of their charge mobility along polymer chain. However, they are sensitive to moisture, light, and oxygen, and limits their applicability. The insulated molecular wires constructed based on CDs can shield the included conjugated polymers from the environmental threats. Furthermore, the nanomolecular devices face a challenge in insulating conjugated polymers and wiring molecules between electrodes which restricts the development of nanoscale electronics. These insulated wires, in which the conjugated polymers stay inside the cavity of CDs, are expected to prevent cross-talking and short-circuits. The preparation of such insulated molecular wires by CDs have been demonstrated in several conjugated polymers including polythiophene (PT), polyaniline (PANI), and poly(azomethine) (PAM), etc (Figure 2.8).\textsuperscript{16,64-67}

![Atomic force microscopy (AFM) topographic image of insulated wire formed by $\alpha$-CDs, in which polyaniline is inside cavity of CDs (a). \textsuperscript{66} STM image of single pseudopolyrotaxane formed by $\beta$-CDs complexed with polyazomethine (b). \textsuperscript{64}](image)

Figure 2.8 Atomic force microscopy (AFM) topographic image of insulated wire formed by $\alpha$-CDs, in which polyaniline is inside cavity of CDs (a).\textsuperscript{66} STM image of single pseudopolyrotaxane formed by $\beta$-CDs complexed with polyazomethine (b).\textsuperscript{64}
The stoichiometry of the inclusion complex between CD and the polymer is highly dependent upon the height of the CD and the length of the polymer repeating unit. Theoretically, one can calculate the number of CDs threaded onto a polymer chain based on the ratio of the height of a CD to the length of the repeating unit of the polymer. Taking the inclusion complex of β-CD with poly(propylene oxide) (PPO) for example, the length of a PO repeat unit is about 3.6 Å when assuming the polymer chain is in the extended conformation. The height of a β-CD ranges from 7.0 Å to 7.9 Å, depending on the conformation of primary hydroxyl group in the crystal packing of the inclusion complex. Therefore, it can be deduced that one β-CD includes two monomer unit of PPO, which is also evidenced by experimental data, and the maximum number of β-CD threading onto a polymer chain can be calculated. However, at certain molecular weight, the quantity of threading CDs doesn’t increase with further increase in molecular weight of the guest polymer. This observation is due to the fact that when the number of CDs threading onto polymer chain the inclusion complexes reaches certain amount, they tend to aggregate and thus precipitate out from solution. The precipitation occurs before the CD molecules can completely cover the polymer chain.

The possibility of selective geometrical accommodation opens an interesting prospect when considering the complexation behavior of CDs with block copolymers. Recent investigations have demonstrated that in inclusion complexes of CDs with block copolymers, CDs can perform “site-selective complexation” on a specific segment of the block copolymer due to steric fitting, hydrophobic (or van der Waals) interaction and/or other interactions between the cavity of CDs and the polymer, which can generate and/or enhance amphiphilicity of the block copolymers and allow further self-organization into
supramolecular aggregates in solution. This provides a new approach to the self-assembly behavior of block copolymers and can be mediated though host-guest interaction based on CD host molecules. Owing to site-selective complexation of CDs, physical supramolecular hydrogels have been prepared in di-block,\textsuperscript{70} tri-block,\textsuperscript{8,71,72} and grafted block copolymers.\textsuperscript{5,6,73-75} Biodegradable poly(ethylene oxide)-poly[(R)-3-hydroxybutyrate]-poly(ethylene oxide) (PEO-\textit{b}-PHB-\textit{b}-PEO) triblock copolymer was found to form supramolecular hydrogels with $\alpha$-CD, in which $\alpha$-CD molecules preferentially thread onto the PEO segment.\textsuperscript{76} The strong macromolecular network is due to cooperative interactions between self-assembly of inclusion complexes formed by $\alpha$-CDs threading onto PEO blocks as well as hydrophobic interactions between PHB blocks (Figure 2.9). This new supramolecular hydrogel has shown relatively long-term sustained controlled release of macromolecular drugs in an injectable formulation. This type of physical hydrogel is temperature-sensitive and undergoes a sol-gel transition at certain temperatures due to dethreading of the CDs from the polymer chain at elevated temperatures. Beside hydrogel supramolecular structure, the micelle and vesicle nanostructures have also been observed through self-assembly process of inclusion complexes at a certain temperature or pH value.\textsuperscript{10,77}
Figure 2.9 The optical photographs of PEO-\textit{b}-PHB-\textit{b}-PEO triblock copolymer in aqueous solution (a), and supramolecular hydrogel formed based on inclusion complexation between PEO-\textit{b}-PHB-\textit{b}-PEO and \textit{\alpha}-CDs (b). The schematic of inclusion complexes formed between \textit{\alpha}-CDs and PEO blocks of PEO-\textit{b}-PHB-\textit{b}-PEO (c), and supramolecular hydrogel formed based on inclusion complexes (d).
However, such self-assembled supramolecular structures are not just limited to less-ordered and/or disordered aggregates such as vesicle and micelle. A well-defined crystal structure is also found in the case of self-assembly of inclusion complexes of $\alpha$-CDs with some block copolymers.\textsuperscript{11,12,14} The supramolecular structure of poly(ethylene oxide-b-$N$-isopropylacrylamide) (PEO-$b$-PNIPAM) diblock copolymer with $\alpha$-CDs showed hexagonal crystal packing as revealed by prominent peaks at 7.6° (100), 12.8° (110), 20.0° (210), and 22.6° (300) (the characteristic ratio $1:3^{1/2}:7^{1/2}:3$) from a one dimensional wide angle x-ray reflection pattern (Figure 2.10).\textsuperscript{12}

![Figure 2.10 1D WAXD powder patterns for PEO-Br, PEO-$b$-PNIPAM, $\alpha$-CD/PEO-$b$-PNIPAM inclusion complexes, and $\alpha$-CD (a). Schematic of self-assembly of $\alpha$-CD/PEO-$b$-PNIPAM inclusion complexes (b).\textsuperscript{12}](image)
The same crystal structure is also observed in poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ethylene glycol)]-b-poly(2-(dimethylamino)ethyl methacrylate) (PDMA-b-PEG-b-PDMA) triblock copolymer.\textsuperscript{11} Due to steric hindrance of PDMA, α-CDs can’t thread through PDMA blocks and onto the PEG segment. Therefore, the inclusion complexes of α-CDs with PEG block are constructed first and PDMA is then chemically tethered on both ends of the inclusion complex. Depending on the pH value in solution, the micelle structure is observed in deionized aqueous solution, while hexagonal ordered structures are formed under the condition of acidic solution. In deionized aqueous solution, the PDMA blocks form hydrogen bonds with hydroxyl groups of α-CD and hinder ordered packing of inclusion complex, leading to the formation of micelle aggregates. On the other hand, the hydrogen interactions could be destroyed in acidic solution and result in ordered crystal structure (Figure 2.11). This kind of hierarchical self-assembly via inclusion complexation based on CD molecules depends on complexation behavior of CDs with guest polymer and properties of tethered polymer blocks as well as medium conditions such as temperature\textsuperscript{6,8}, solvent type\textsuperscript{14}, and pH value.\textsuperscript{10,11} By controlling those parameters, tunable supramolecular structures can be obtained through aggregation of inclusion complexes, which opens a great potential for applications in biomedical technologies and nanoscience.
In this study, we focus on the complexation behavior between a series of block copolymers of poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-b-PPO-b-PEO) and β-CD. Due to complex aggregation behavior and widespread utility, PEO-b-PPO-b-PEO has attracted great interest and has been extensively studied, which provides a good framework for our study of the complexation behavior between PEO-b-PPO-b-PEO and β-CD. So far, there are few papers on this topic\textsuperscript{19,20,25} because this kind of inclusion complex is reversibly soluble and insoluble in response to temperature in aqueous solution (Figure 2.12), and as a result, it demonstrates a model of stimuli-responsive supramolecules for nanoscale devices.\textsuperscript{19,20} From two dimensional Nuclear Overhauser SpectroscopY (2D NOESY) results, it was found that signals of H-3 and H-5 protons of β-CD are correlated with the resonance of methyl
protons of the PPO segment (Figure 2.13). Therefore, it is suggested that β-CD can form a site-selective complex onto the PPO blocks to form inclusion complexes in aqueous system but do not complex with the PEO blocks. However, the question remains whether all the β-CDs exclusively interact with the PPO blocks or only part of them stay with the PPO blocks and the rest with the PEO blocks. The previous studies only concentrated on the formation of inclusion complexes between β-CDs and PEO-b-PPO-b-PEO copolymer in solution. The interaction between β-CDs and the PPO blocks can be detected using the nuclear overhauser effect technique in solution. However, if part of the β-CDs stayed with the PEO blocks, the interaction between β-CDs and the PEO blocks in solution is too weak to be detected due to longer intermolecular distances. Besides, the hierarchical self-assembled supramolecular structure based on this type of inclusion complex has not been prepared and investigated so far.

Figure 2.12 Change in the transmittance of the inclusion complexes with temperature (a). Schematic of thermoresponsive characteristic of inclusion complexes.19
Figure 2.13 2D NOESY NMR spectrum of inclusion complexes in D$_2$O.$^{20}$
2.2 Poly(ethylene oxide)-block-Poly(propylene oxide)-block-Poly(ethylene oxide)

(PEO-b-PPO-b-PEO) Block Copolymers

PEO-b-PPO-b-PEO block copolymers, the amphiphilic characteristics are critically dependent on the molecular architecture, such as total molecular weight, relative block size and block sequence as well as thermodynamic parameters, such as temperature and pressure. In the following sections, the detailed physical properties of this block copolymer will be discussed.

2.2.1 Crystalline-Amorphous Block Copolymers

Block copolymers consist of covalently connected blocks formed by two or more different monomers. The different types of blocks within the copolymer are usually incompatible with one another and, as a consequence, block copolymers self-assemble at different length scales in melts and in solutions. The self-assembly of block copolymers can lead to one-, two-, and three-dimensional periodic structures with the scale of a few tens of nm.\textsuperscript{79,80} Among block copolymers, crystalline-amorphous block copolymers have been extensively studied since the crystallization process of one or more blocks provides additional pathway to manipulate nanostructured morphology. In bulk crystalline-amorphous block copolymer systems, it has been recognized there are three factors that determine the final phase and crystalline morphology of block copolymers, namely, the self-organization of block copolymer (the order-disorder transition temperature, $T_{ODT}$), the crystallization of the crystallizable blocks (the crystallization temperature, $T_c$), and the
vitrification of the amorphous blocks (the glass transition temperature, \( T_{g}^{a} \)). Therefore, competitions among these three processes can be understood by comparing these three temperature parameters for crystalline-amorphous block copolymers. When \( T_{ODT} > T_{g}^{a} > T_{c} \), the crystallization of semicrystalline blocks can be efficiently confined within nanoenvironments when the amorphous blocks vitrify prior to the crystallization. As a result, the existing phase morphology is preserved after crystallization.\(^{81-88}\)

PEO-\( b \)-PPO-\( b \)-PEO block copolymer with crystallizable blocks of PEO and amorphous PPO block in bulk state, on the other hand, is in the case where \( T_{c} > T_{ODT} > T_{g}^{a} \).\(^{89-93}\) The crystallization of semicrystalline block occurs before the phase-separation of block copolymer, since the unconfined crystallization possesses much stronger molecular interactions compared to that in microphase separation. Therefore, the crystallization process drives the final phase morphology and forms an alternating structure consisting of crystalline lamellae and amorphous layers. The crystallization behavior of the PEO in the semicrystalline block copolymers depends on the length of the PEO chain, the length of the amorphous PPO block.\(^{90,91}\) The melting points of PEO in PEO-\( b \)-PPO-\( b \)-PEO block copolymers were found to be lower than that of PEO homopolymer due to increased interfacial free energy. Because of dominant crystallization process and weak phase segregation, the phase-separation in the bulk state of PEO-\( b \)-PPO-\( b \)-PEO block copolymer lacks structural diversity.

2.2.2 Solution Properties of PEO-\( b \)-PPO-\( b \)-PEO copolymers

When block copolymers are mixed in a selective solvent that dissolves only one
of the blocks, the molecules self-associate into specific micellar structures in order to avoid direct contact between the solvent molecules and the insoluble blocks. This self-association gives rise to a wide range of phase behavior, including formation of micelles of various form and size, and complex microstructures. Amphiphilic block copolymers of PEO-\(b\)-PPO-\(b\)-PEO, also known by the trade name as Pluronics, consist of hydrophilic PEO blocks that maintain the copolymer’s solubility in water, and hydrophobic PPO blocks that provide the association behavior in water. Aqueous solutions of PPO exhibit dramatic temperature dependence. Below \(\sim 15^\circ\text{C}\) at ambient pressure, water is a good solvent for PPO, but it starts to segregate at elevated temperature. PEO, on the other hand, is predominantly hydrophilic within the temperature range from 0 to 80\(^\circ\text{C}\). Concentration and temperature-dependent micellization and gel formation are the most characteristic properties of aqueous PEO-\(b\)-PPO-\(b\)-PEO block copolymer solutions. Owing to the marked change in water solubility of the center PPO block with temperature, the block copolymers can form various aggregates, depending on the molecular architecture. Varying the block compositions (PEO/PPO ratios) and the molecular weights allows us to tailor the final properties of these systems to meet the specific application needs in different areas. As a result, PEO-\(b\)-PPO-\(b\)-PEO block copolymers, an important class of surfactants, have widespread industrial applications in detergency, dispersions stabilization lubrication, etc.\textsuperscript{94,95} as well as more specialized applications in pharmaceutics (drug solubilization and controlled release),\textsuperscript{96-98} bioprocessing (protecting microorganisms against mechanical damage),\textsuperscript{99} and separations (solubilization of organics in aqueous solutions).\textsuperscript{100}

The phase and aggregation behavior is highly dependent on temperature,
concentration, and composition of the block copolymers. The phase diagram of $\text{PEO}_{27}-b-\text{PPO}_{39}-b-\text{PEO}_{27}$ copolymer, trade name as Pluronic P85, serves as one example which is shown in Figure 2.14. Figure 2.14 shows complicated aggregation behavior including unimers, micelles and complex gel phases. At low temperature ($T \leq 15^\circ \text{C}$) both PPO and PEO blocks are hydrophilic. The block copolymer, therefore, appears as independent polymer chains, called unimers. When temperature is above critical micelle temperature (CMT), or at concentration of block copolymers above critical micelle concentration (CMC), the hydrophobic nature of PPO caused aggregation of copolymers into micelles with core dominated by PPO and a corona formed by hydrated PEO blocks, a process called “micellization”. The concentration of micelles increased with temperature and/or polymer concentration until either saturation is reached or the volume density of micelles is so high that they “locked” into mesophase structures (gel structures). In this region, PEO-$b$-PPO-$b$-PEO block copolymers of high polymer concentration exhibit a dramatic change in viscosity at temperature close to ambient, demonstrating a “thermoreversible gelation”. The gel formation temperature decreased with increasing polymer concentration. Due to their complex properties of association and gelation, it has found widespread industrial applications, in particular, in the pharmaceutical industry for the encapsulation and delivery of a variety of drugs.
2.2.3 Crystal Structure of Poly(ethylene oxide)

Block copolymer of PEO-\(b\)-PPO-\(b\)-PEO is one noncrystallizable block covalently bonded by two crystallizable blocks. The PEO block can be crystalline (semicrystalline) at ambient temperature when the molecular weight of PEO is larger than 2000 g/mol. The PPO block is amorphous due to a lack of stereoregularity in its configuration.\(^{102}\) There are two crystalline forms for PEO crystal structures. One is a helical chain with a monoclinic crystal structure,\(^ {103,104}\) and the other is a planar-zigzag form with a triclinic crystal structure.\(^ {105}\) The monoclinic PEO forms readily under normal crystallization.
conditions and thus, is the most commonly observed crystal form. On the other hand, the planar-zigzag can only form under strong deformation.

The unit cell of a PEO crystal is shown in Figure 2.15, with parameters, \( a = 0.805 \text{nm}, \ b = 1.304 \text{ nm}, \ c = 1.948 \text{ nm}, \) and \( \beta = 125.4^\circ. \) The space group of \( P2_1/a-C_{2h} \) is determined based on systematic absences of \((h01)\) diffractions at \( h = \text{odd} \) and \((0k0)\) diffractions at \( k = \text{odd} \). There are four helical molecules in one unit cell with the \( c\)-axis nearly perpendicular to the \((104)\) plane. The helix has a \( 3*7/2 \) conformation (Figure 2.15a) and is distorted (Figure 2.15b) due to the flexibility of the PEO molecular chain and the intermolecular interactions in the crystal.

![Figure 2.15 Unit cell of monoclinic PEO in the \( c\)-axis projection, and R and L stand for right- and left-hand helices (a). Molecular model of PEO with helical symmetry \( D_7 \) (left model), and molecular structure of PEO (right model). The figure shows the internal rotation angles (b).](image-url)
PEO single crystals are often square shaped, laterally bounded by (120) faces (Figure 2.16a).\textsuperscript{108} Based on the corresponding electron diffraction pattern of a single lamellar single crystal of PEO (Figure 2.16a), it showed that c-axis of the PEO chain is parallel to the crystal normal, indicating the basal plane of the lamellar crystal is (104) or close to it (Figure 2.16b).\textsuperscript{105}

Figure 2.16 A PEO lamellar single crystal morphology observed via TEM, and corresponding electron diffraction pattern (insert image) (a).\textsuperscript{108} Schematic of a vertical single lamellar crystal (b).\textsuperscript{105}

A two dimensional wide angle x-ray diffraction (WAXD) fiber pattern of PEO crystals uniaxially oriented along the c-axis is as shown in Figure 2.17a.\textsuperscript{109} This fiber diffraction pattern can be constructed by rotating the reciprocal lattice along the c-axis. The uniaxial pattern of a c-axis or [00l], with parameters of $a^* = 1/(a \sin \beta) = 1.524 \text{ nm}^{-1}$,
$b^* = 1/b = 0.767 \text{ nm}^{-1}$, $c^* = 1/(c \sin \beta) = 0.630 \text{ nm}^{-1}$, and $\beta^* = 180-\beta = 54.6^\circ$ (Figure 2.17b). The (120) diffractions (the strongest diffractions) with d-spacing of 0.463 nm are on the equator. Different sets of diffractions almost superimpose in the fiber pattern. A list of d-spacings for each set of diffractions and the angles between diffractions and the c-axis are listed in Table 2.3.

Figure 2.17 The c-axis or [00l] uniaxial fiber pattern of PEO crystals obtained from 2D WAXD (a). The simulated c-axis uniaxial fiber pattern of PEO crystals constructed by rotating the reciprocal lattice along c-axis (b).
Table 2.3 The $d$-spacings and the angles between diffractions and $c$-axis in fiber pattern of PEO crystals.

<table>
<thead>
<tr>
<th>Reflections</th>
<th>$d$-spacing (nm)</th>
<th>Angles with the $c$-axis ($^\circ$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>0.463</td>
<td>90.0</td>
</tr>
<tr>
<td>032</td>
<td>0.381</td>
<td>67.0</td>
</tr>
<tr>
<td>132</td>
<td>0.379</td>
<td>67.1</td>
</tr>
<tr>
<td>112</td>
<td>0.386</td>
<td>66.7</td>
</tr>
<tr>
<td>212</td>
<td>0.378</td>
<td>67.2</td>
</tr>
<tr>
<td>204</td>
<td>0.385</td>
<td>37.7</td>
</tr>
<tr>
<td>004</td>
<td>0.397</td>
<td>35.4</td>
</tr>
<tr>
<td>124</td>
<td>0.390</td>
<td>36.8</td>
</tr>
<tr>
<td>224</td>
<td>0.339</td>
<td>47.1</td>
</tr>
<tr>
<td>024</td>
<td>0.332</td>
<td>45.9</td>
</tr>
<tr>
<td>124</td>
<td>0.254</td>
<td>58.5</td>
</tr>
<tr>
<td>324</td>
<td>0.248</td>
<td>59.4</td>
</tr>
<tr>
<td>044</td>
<td>0.252</td>
<td>58.8</td>
</tr>
<tr>
<td>244</td>
<td>0.249</td>
<td>59.3</td>
</tr>
<tr>
<td>108</td>
<td>0.231</td>
<td>18.8</td>
</tr>
<tr>
<td>308</td>
<td>0.226</td>
<td>21.9</td>
</tr>
<tr>
<td>328</td>
<td>0.213</td>
<td>28.8</td>
</tr>
<tr>
<td>128</td>
<td>0.217</td>
<td>26.8</td>
</tr>
</tbody>
</table>

2.2.4 Crystal Orientation of Poly(ethylene oxide)

The crystallization behavior and crystal orientation of PEO-containing block copolymers has been widely studied during the past few decades. Among these studies,
the most intriguing phenomenon is the finding of PEO chain orientation with respect to substrate surface. Early in the 1960s, poly(ethylene oxide)-block-polystyrene (PEO-b-PS) lamellar single crystal were prepared from dilute solution (Figure 2.18). One PEO single layer forms in between two PS layers to form PS-sandwiched lamellar single crystal (Figure 2.18a). From the electron diffraction (ED) pattern of the single crystal (shown in Figure 2.18b), the chain direction of the PEO crystals (or c-axis of the PEO crystals) was found to be parallel to the normal (n) of the PS substrate surface, known as the homeotropic crystal orientation. Later, the homeotropic crystal orientation was observed in solution cast film of poly(ethylene oxide)-block-polyisoprene-block-poly(ethylene oxide) block copolymer using simultaneous small-angle X-ray scattering (SAXS) and wide-angle X-ray diffraction (WAXD) techniques (shown in Figure 2.19). Figure 2.19a shows the diffraction peaks on the meridian in 2D SAXS pattern, indicating a lamellar microphase-separated structure with the lamellar normal direction along the vertical direction. However, the (120) diffractions of the PEO crystals are on the equator in a 2D WAXD pattern. As the result, it is found that the c-axis of the PEO crystals is parallel to the normal direction of the lamellar microphase-separated structure. In addition, this kind of chain orientation was also found in the system of poly(ethylene oxide)-block-poly(butylene oxide)(PEO-b-PBO). The homeotropic crystal orientation has been used frequently to formulate theoretical approaches and explain experimental results. It is assumed to possess a thermodynamically more stable orientation.
Figure 2.18 Solution-grown PS-sandwiched lamellar single crystals (a) and electron diffraction (b) of PEO-\(b\)-PS block copolymer.\textsuperscript{110}

Figure 2.19 Two-dimensional SAXS (a) and WAXD (b) patterns for solution-cast film of PEO-\(b\)-PI-\(b\)-PEO block copolymer.\textsuperscript{114}
However, homeotropic crystal orientation of PEO crystals was the only observation in PEO-containing block copolymer systems before Dr. Cheng’s group began their studies. Using a series of PEO-\(b\)-PS block copolymers, the PEO crystal orientation changes in a confined microphase-separated lamellar structure obtained after large amplitude oscillatory mechanical shear were systematically studied. The different crystal orientations were first observed in single PEO-\(b\)-PS block copolymer by changing crystallization temperature under confined lamellar microphase-separated structure using combined 2D SAXS and WAXD experiments. Crystal orientation (the \(c\)-axis of PEO crystal) with respect to the confined lamellar geometry was characterized through detailed X-ray diffraction analyses. As shown in Figure 2.20, four different crystal orientations have been observed in four different crystallization temperature (\(T_c\)) regions. (1) When the sample is quickly quenched from melt into liquid nitrogen, the \(c\)-axis of the PEO crystals is randomly oriented. (2) The \(c\)-axis of PEO crystals is oriented perpendicular to normal direction (\(\hat{n}\)) of the lamellar microphase-separated structure, called homogenous crystal orientation when quenched between \(-50^\circ\text{C} \leq T_c \leq -10^\circ\text{C}\). (3) The \(c\)-axis of PEO crystals is inclined to \(\hat{n}\) between \(-5^\circ\text{C} \leq T_c \leq 30^\circ\text{C}\). The tilt angle of the \(c\)-axis with respect to lamellar surface increased with \(T_c\). (4) Finally, the \(c\)-axis of the PEO crystals was parallel to \(\hat{n}\) when \(T_c \geq 35^\circ\text{C}\) (homeotropic crystal orientation).
Figure 2.20 Schematic representation of the different crystal orientations of PEO block in PEO-b-PS in different crystallization temperature regions: quickly quenched into liquid nitrogen (a), $-50 \, ^\circ C \leq T_c \leq -10 \, ^\circ C$ (b), $-5 \, ^\circ C \leq T_c \leq 30 \, ^\circ C$ (c), $T_c \geq 35 \, ^\circ C$ (d).\textsuperscript{116}
Subsequent study revealed the effect of confinement dimensions on the crystal orientation dependence on crystallization temperature, using different molecular weights of lamellar PEO-\(b\)-PS block copolymers as templates.\textsuperscript{117} With increasing confinement sizes, the \(T_c\) region where the \(c\)-axis of PEO crystal is inclined decreased (Figure 2.21). Furthermore, it was found that the PEO crystals formed in the nanoconfined lamellae undergo a change from a one-dimensional to a two-dimensional growth with increasing \(T_c\) (Figure 2.22).\textsuperscript{118,119} Hence, the change of crystal orientation from homogenous to homeotropic with increasing \(T_c\) is explained to be largely governed by the primary nucleation density and crystal growth of PEO blocks to reach the maximum crystallinity.

Figure 2.21 Relationships between tilting angles with respect to \(T_c\) for different molecular weight of PEO-\(b\)-PS block copolymers. EOS1 represents PEO8.7k-\(b\)-PS9.2k (\(d_{\text{PEO}} = 8.8\text{nm}\)), EOS2 refers to PEO23K-\(b\)-PS26k (\(d_{\text{PEO}} = 14.4\text{nm}\)), and EOS3 is PEO57k-\(b\)-PS61k (\(d_{\text{PEO}} = 23.3\text{nm}\)).\textsuperscript{120}
Figure 2.22 Correlation length (apparent crystallite size) analyses for the (120) reflections in the 2D WAXD patterns along the z direction at different $T_c$. I, II, and III represent three temperature regions, respectively: I: $-50 \, ^\circ\text{C} \leq T_c \leq -10 \, ^\circ\text{C}$; II: $-5 \, ^\circ\text{C} \leq T_c \leq 30 \, ^\circ\text{C}$; III: $T_c \geq 35 \, ^\circ\text{C}$.\textsuperscript{121}

Recently, a new approach for the study of PEO crystallization in 1 D lamellar confined environment was achieved using PEO-$b$-PS single crystals grown from dilute solution as a template.\textsuperscript{122,123} In this case, PEO-$b$-PS single crystals have a “sandwich-like” lamellar structure composed of a PEO single crystal and two PS layers covering
both of the PEO single crystal basal surfaces (Figure 2.23). The crystallization and orientation changes of PEO crystals were investigated utilizing simultaneous 2D SAXS and WAXD experiments after the PEO single crystals were melted and recrystallized at different $T_c$ under a 1D confined environment. The $T_c$ dependent crystal orientation change has also been observed and it was found to be affected not only by confined size ($d_{PEO}$) but also reduced tethering density of PEO blocks ($\bar{\sigma}_{PEO}$). The onset temperature of orientation change ($T_{onset}$), at which homogeneous to homeotropic crystal orientation takes place, decreases with increasing $d_{PEO}$ and $\bar{\sigma}_{PEO}$ values (Figure 2.24).

![Figure 2.23 Phase contrast optical microscopy image of PEO-b-PS block copolymer single crystals and the schematic of the sandwiched lamellar structure.](image)
From all of the investigations reported concerning PEO crystal orientation under confined environments, it can be concluded that different crystal orientations may be associated with molecular weight, chemical structure of block copolymers, confined size, reduced tethering density, and nucleation density.
CHAPTER III

EXPERIMENTAL

3.1 Sample Information

Three samples of PEO-b-PPO-b-PEO copolymers with different molecular weights were purchased from Aldrich and were supplied as commercially available samples from BASF. β-cyclodextrin (β-CD) was purchased from Acros. All samples were used as received, and the molecular characteristics of PEO-b-PPO-b-PEO copolymers and β-CD determined using gel permeation chromatography (GPC) and $^1$H NMR are listed in Table 3.1. The chemical structures are shown in Figure 3.1.

Table 3.1. Molecular Characteristics of PEO-b-PPO-b-PEO Copolymers and β-CD.

<table>
<thead>
<tr>
<th>sample</th>
<th>composition$^a$</th>
<th>$M_n$ (g/mol)</th>
<th>$M_w/M_n$</th>
<th>PPO content$^a$ (wt%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPE46</td>
<td>EO$<em>{27}$PO$</em>{39}$EO$_{27}$</td>
<td>4600</td>
<td>~1.6</td>
<td>48</td>
</tr>
<tr>
<td>EPE77</td>
<td>EO$<em>{64}$PO$</em>{37}$EO$_{64}$</td>
<td>7700</td>
<td>~1.2</td>
<td>27</td>
</tr>
<tr>
<td>EPE146</td>
<td>EO$<em>{137}$PO$</em>{44}$EO$_{137}$</td>
<td>14600</td>
<td>~1.2</td>
<td>17</td>
</tr>
<tr>
<td>β-CD</td>
<td>C$<em>{42}$H$</em>{70}$O$_{35}$</td>
<td>1134</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Determined by $^1$H NMR. $^b$ Determined by GPC
Figure 3.1 Chemical structures of triblock copolymer EPE46 (a), EPE77 (b), EPE146 (c), and β-CD (d).

3.2 Preparation of Supramolecular Structures of Inclusion Complexes

An aqueous solution of β-CDs was mixed with an aqueous solution of copolymers in a molar ratio of β-CD/PO = 1:1 at room temperature (Table 3.2). The temperature and concentration of the triblock copolymer solutions were below the CMC (critical micellization concentration). After mixing with the β-CD solution, the copolymer
solution gradually became turbid and finally, produced white precipitates, apparently indicating the formation of a supramolecular structure of inclusion complexes, shown in Figure 3.2. The samples were vacuum-filtered with 0.4 μm filter paper and washed with a limited amount of distilled water. The filtered samples were dried in a vacuum oven at room temperature for three days.

Table 3.2 Solution concentrations prepared for different inclusion complex systems.

<table>
<thead>
<tr>
<th></th>
<th>β-CD/water (% w/v)</th>
<th>Copolymer/water (% w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-CD/EPE46</td>
<td>1.80</td>
<td>0.19</td>
</tr>
<tr>
<td>β-CD/EPE77</td>
<td>1.34</td>
<td>0.26</td>
</tr>
<tr>
<td>β-CD/EPE146</td>
<td>1.80</td>
<td>0.53</td>
</tr>
</tbody>
</table>
β-CD Solution + Polymer Solution

Solution initially clear

The solutions are stirred at room temperature

After 1 day
β-CD/EPE46

After 10 days
β-CD/EPE77

After 14 days
β-CD/EPE146

Figure 3.2 Preparation of inclusion complexes of PEO-β-PPO-β-PEO with β-CD.
3.3 Solid-state $^{13}$C Nuclear Magnetic Resonance (NMR)

High resolution 1D and 2D solid-state $^{13}$C Nuclear Magnetic Resonance (NMR) spectra were obtained on a Varian VNMR 500 MHz ($^1$H frequency) spectrometer. Samples were spun in a Varian 4 mm HXY triple resonance magic angle spinning (MAS) probe at a spinning speed of 10 kHz. $^{13}$C chemical shifts were referenced to hexamethylbenzene ($\delta_{\text{CH}_3} = 17.3$ ppm). Samples were packed into 4 mm silicon nitride rotors with kel-f end caps. Solid-state $^{13}$C CP/MAS NMR spectra were acquired using a ramped cross polarization pulse sequence with a 4 sec relaxation delay, a 3.5 $\mu$s 90° pulse width, and a 71.4 kHz decoupling field.

The proton spin-lattice relaxation ($^{1H}T_1$) experiment was studied that the rate of the spin diffusion among the $^1$H spins of $\beta$-CD, inclusion complexes, and triblock copolymers is monitored. Spin diffusion describes the flow of polarization, initially in a non-equilibrium state, towards internal spin equilibrium, through local polarization-exchange events. The $^{1H}T_1$ values for protons near carbons with different chemical shifts can be determined separately. Therefore, if the chains are intimately and homogenously mixed, the $^1$H spin diffusion occurs quickly among the chemically different components, which equilibrates the magnetization, and a single value of $^{1H}T_1$ is determined. Proton relaxations were measured via CP/MAS model using inversion recovery pulse in the proton channel before contact with carbon. The carbon signals were observed with high power proton decoupling. The data of proton $T_1$ were processed using Varian VNMRJ software.
The cross-polarization dynamics was investigated where differences in relaxation times ($T_{CH}$) are dependent on the strength of the static $^1$H-$^{13}$C dipolar interaction. The dipolar interaction is influenced by the number and proximity of protons surroundings a carbon atom and by any averaging of the interaction resulting from molecular motion. Therefore, the cross polarization process tends to emphasize those $^{13}$C spins in the more rigid regions and discriminates heavily against highly mobile regions because of the intensity dependence upon the static dipolar decoupling between carbon atoms and protons. A relatively low value for $T_{CH}$ (relaxation time) is characteristic of a rigid system.

The $^{13}$C CP/MAS NMR spectra were obtained with contact times ranging from 0.02 to 5 ms which were acquired using a ramped cross polarization pulse sequence with an MAS speed of 10 kHz, a 4 sec relaxation delay, a 3.5 μs 90° pulse width, and a 71.4 kHz decoupling field. The contact time data were processed through Varian VNMRJ software.

$^{13}$C Bloch decay MAS NMR spectra were acquired using a 5 sec relaxation delay, a 3.5 μs 90° pulse width, a 71.4 kHz decoupling field and 1000 transients. With longer delay between pulses, Bloch decay experiment can detect those carbons that are remote from protons or the $^{13}$C spins in relatively mobile regions.

The 2D wide-line separation (WISE) spectra were measured using a 1000 kHz spectral width in the proton dimension and a 50 kHz spectral width in the carbon dimension. Rapid signal decay was observed in the proton dimension, and the maximum evolution time was 128 μs. A 2D wide-line separation experiment correlates carbon chemical shifts recorded with proton lines. During evolution (t1) the different proton line shapes come out, and these proton line shapes related to $^1$H-$^1$H dipolar coupling will be affected by the neighboring carbon group (Figure 3.3). Accordingly, the carbon groups in
mobile domains, the $^1$H-$^1$H coupling are relatively weak which leads to relatively narrow $^1$H lines, while broad proton lines are observed for the rigid domains.

![Diagram](image)

Figure 3.3 The pulse sequence and principle for 2D WISE experiment. The solid line is in the mobile domain, while dash line corresponds to the rigid domain.

3.4 Solution $^1$H Nuclear Magnetic Resonance (NMR)

One-dimensional (1D) and two-dimensional (2D) solution $^1$H NMR spectra were recorded on a Varian VNMRS 500 MHz instrument at room temperature. The 1D $^1$H NMR measurements were carried out with an acquisition time of 2.049 s, a pulse repetition time of 1 s, a 45° pulse width, 8012.8 Hz spectral width, and 32,000 data points. Chemical shifts were referred to a solvent peak ($\delta = 2.50$ ppm for DMSO-d$_6$). $^1$H NMR (500 MHz, DMSO-d$_6$, ppm): $\delta$ 5.71 (7H×12, O-2 H of $\beta$-CD), $\delta$ 4.81 (7H×12, C-2 H of $\beta$-CD), $\delta$ 4.45 (7H×12, O-6 H of $\beta$-CD), $\delta$ 3.27-3.63 (42H×12, C-3 H, C-6 H, C-5 H, C-
2 H, C-4 H of β-CD, 7H ×165, -CH₂CH₂O- of PEO and –CH₂-CHO- of PPO), δ 1.03 (3H 
×37, CH₃ of PPO).

The 2D ¹H-¹H rotating-frame overhauser enhancement spectroscopy (2D ROESY) spectrum was performed with a 2 s relaxation delay, a 6.1 kHz spectral window, 
a 0.4 s mixing time, and a 0.168 s acquisition time; 8 transients were averaged for each of
the 2 × 200 increments using the States method of phase sensitive detection in the f1
dimension. Processing was done with sinebell and shifted sinebell weighting functions
and zero-filling to a 2048 × 1024 data matrix before Fourier transformation.

3.5 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis of these compounds was carried out using a TA TGA
2950. The temperature scale was calibrated using the magnetic null method. The weight
was calibrated with standard materials, and the error was less than 0.001 mg. All samples
were heated from 30 °C to 400 °C at a heating rate of 10 °C/min under both air and
nitrogen atmospheres.

3.6 Differential Scanning Calorimetry (DSC)

The thermal properties of phase transitions were characterized utilizing a Perkin-
Elmer PYRIS Diamond DSC with an Intracooler 2P apparatus. The weights of pans used
in this research were constant to a precision of ± 0.001 mg. The temperature and heat
flow scales were calibrated at different heating and cooling rates (1 - 40 °C/min) using
standard materials. A baseline scan using two empty pans was carried out before the sample run. The baseline was subtracted from each run. The cooling and heating rates were identical. The weight percent crystallinity was calculated using an equilibrium heat of fusion for PEO crystals (7.89 kJ/mol)\textsuperscript{127} and was normalized to the PEO weight fraction in the pure triblock copolymer and inclusion complex samples. The samples recorded in DSC trace for PEO blocks crystallized from aqueous solution are prepared as mentioned in experimental section 3.2. On the other hand, the samples used for PEO blocks crystallized from the melt in DSC experiments are first heated to 80 °C for 10 mins in order to eliminate the thermal history of the PEO crystal and then annealed at -20 °C. All experiments performed in DSC are recorded at rate of 10 °C/min.

3.7 Transmission Electron Microscopy (TEM)

Bright-field (BF) and electron diffraction (ED) images were performed using a Philips Tecnai 12 TEM instrument equipped with tilting stage. The accelerating voltage was 120 kV. Selected area electron diffraction (SAED) patterns were obtained utilizing a TEM tilting stage to determine the crystal structure parameters. The $d$-spacings were calibrated using a thallous chloride (TlCl) standard. Samples for TEM experiments were prepared by pipetting a drop of inclusion complex solution onto a 400-mesh copper grid with a carbon-coated supporting film and washed with water twice. The samples were dried in a vacuum oven for three days at room temperature.
3.8 Wide-Angle X-ray Diffraction (WAXD)

1D WAXD patterns were obtained with a Rigaku Multi-flex 2 kW automated diffractometer using Cu $K_\alpha$ radiation (0.1542 nm). The beam size was controlled by a divergence slit of 1°, a scattering slit of 1°, and a receiving slit of 0.3 mm and the X-ray glancing angle was 6°. A hot stage was equipped to the diffractometer to investigate phase structure transitions at different temperatures. The hot stage was calibrated with a deviation less than ±1°C. The samples were scanned ranging from 2$\theta$ angle of 2° to 35° at a 1 degree/min scanning rate. The samples prepared for 1D WAXD were vacuum-filtered with 0.4 μm filter paper and washed with a limited amount of distilled water. After drying in vacuum at room temperature for three days, the bulk samples were gently ground into powder. For thin layer samples, the WAXD was recorded with the x-ray beam incident to the plane of the thin layer samples; therefore, the samples were lying down on the sample holder.

2D WAXD patterns were recorded on a Rigaku 18 kW rotating anode X-ray generator attached to an R-AXIS-IV image plate system. The radiation wavelength was 0.1542 nm. The exposure time to obtain high-quality WAXD patterns was 45 min. To obtain an oriented supramolecular crystal for 2D WAXD experiments, the samples were prepared from the precipitated inclusion complex by slow sedimentation during filtration on the filter paper which then formed thin layer bulk samples after drying, as illustrated in Figure 3.4. Again the samples were dried in a vacuum oven at room temperature for three days. The thin layer bulk sample is divided into two directions; the sedimentation and edge directions, respectively (Figure 3.4). The fiber diffraction patterns from 2D
WAXD experiments are recorded when the X-ray beam is along the edge direction of the samples. Isothermal crystallization experiments were conducted using an Instec LN2-P2 hot stage equipped with liquid nitrogen cooling system. The isothermal $T_c$ was controlled to within $±0.1°C$. The thin layer samples were preheated to 80°C for 3 minutes and then quickly quenched (switched) to the hot stage at a preset $T_c$ for crystallization. Azimuthal profiles for 2D WAXD patterns were obtained via scans that started on the vertical direction of the patterns. In both 1D and 2D WAXD patterns, the diffraction spots or peaks were calibrated using silicon powder, having a $d$-spacing of 3.315 Å (111), for the high angle region ($>15°$) and silver behenate with a $d$-spacing of 58.38 Å (001) for the low angle region ($<15°$). The crystal unit cells were determined by constructing reciprocal lattices. Computer refinement was conducted to find the solutions with the least error between the calculated values and the experimental results.

Figure 3.4 Preparation of orientated thin layer samples though slow sedimentation process.
3.9 Small-Angle X-ray Scattering (SAXS)

SAXS experiments were conducted at the National Synchrotron Radiation Research Center (NSRRC) in Taiwan. The X-ray beam, monochromated to 1.2 Å in wavelength, was collimated into a beam size of 0.5 mm in height and 0.5 mm in width. A two-dimensional multi-wired area detector was used to record the scattering intensity. The synchrotron X-ray results have been corrected for background, detector sensitivity, and incident beam intensity. The sample preparation for SAXS experiments is the same as the above-mentioned procedure for 2D WAXD experiments. The scattering patterns from 2D SAXS experiments are recorded when the X-ray beam is along the edge direction of the samples.

3.10 Computer Simulations

Computer molecular modeling and analysis of the diffraction patterns were performed using the Cerius² package of Accelrys (Version 4.6). The lowest energy conformation of a pair of β-CDs included with two repeating units of propylene oxide was chosen as the starting conformation. Basic unit cell parameters determined by crystallographic experimental data from 2D WAXD and SAED experiments were used to build the crystal unit cell. The positions of molecules in this unit cell were judged by comparing their calculated diffraction patterns with those of experiments.
CHAPTER IV

FORMATION OF SITE-SELECTIVE INCLUSION COMPLEXATION BETWEEN $\beta$-CYCLODEXTRIN AND POLY(ETHYLENE OXIDE)-BLOCK-POLY(PROPYLENE OXIDE)-BLOCK-POLY(ETHYLENE OXIDE) COPOLYMERS

4.1 Observation of the Threading Process of $\beta$-CD onto PEO-b-PPO-b-PEO in Solution

The inclusion complexes of $\beta$-CDs with PEO-b-PPO-b-PEO copolymers were prepared via aqueous media. Precipitates of the inclusion complexes always formed when the $\beta$-CDs were saturated onto the PPO blocks. As a result, it was difficult to observe the formation of inclusion complexes in the aqueous state. By decreasing the amount of $\beta$-CD to a ratio of $\beta$-CD:PO = 1:5, only a few $\beta$-CDs threaded onto the PPO blocks, which minimized the intermolecular hydrogen bonding between $\beta$-CDs, and the inclusion complexes maintained their solubility in aqueous solution. Figure 4.1 shows 2D ROESY NMR spectra for the inclusion complexes of $\beta$-CD/EPE46, $\beta$-CD/EPE77, and $\beta$-CD/EPE146. The dashed red circles in the ROESY spectrum show the anti-phase real intermolecular ROE cross-peaks between the inner cavity H$_5$ and H$_3$ protons of $\beta$-CD and the methyl protons of the PPO blocks (see Figure 4.1d schematic). This observation reveals that $\beta$-CDs are threaded onto the PPO blocks in solution. However, the cross-
peaks between PEO blocks and β-CDs are difficult to observe or distinguish in the 2D ROESY experiment. Since the interaction between PEO blocks and β-CDs probably are too weak to detect due to longer intermolecular distance, upper limits for observed distances between protons separated by about 4 Å. Besides, the cross-peaks between methylene protons of the PEO blocks and β-CDs as well as CH₂ of the PPO blocks and β-CDs are overlapped and indistinguishable. Therefore, the 2D ROESY results cannot be stand-alone substantial evidence to support the selective complexation behavior of β-CDs. However, the cross peaks between β-CD and the methyl protons of the PPO blocks in 2D ROESY NMR showed that β-CDs can thread onto PEO-b-PPO-b-PEO copolymers and form inclusion complexes.
Figure 4.1 2D ROESY NMR spectra of β-CD/EPE46 inclusion complex (a), β-CD/EPE77 inclusion complex (b), and β-CD/EPE146 inclusion complex (c) in D$_2$O. The schematic β-CD/EPE inclusion complex (d).
4.2 Identification of Inclusion Complex Formation in the Solid State

Figure 4.2 shows the solid-state $^{13}$C CP/MAS NMR spectra of $\beta$-CD (Figure 4.2a), the copolymer EPE146 (Figure 4.2e) and the $\beta$-CD/EPE inclusion complexes (Figure 4.2b, 4.2c, and 4.2d). $\beta$-CD assumes a less symmetrical conformation in the herringbone-type crystal packing with water molecules as a guest. In this case, the spectrum shows resolved carbon resonances from each of the carbon atoms in the glucose residues. The fine structure with several narrow lines appeared as indicated in Figure 4.2a. On the other hand, in the spectra of the $\beta$-CD/EPE inclusion complexes in Figure 4.2b, 4.2c, and 4.2d each carbon of glucose is merged into a single broad peak. These results indicate that $\beta$-CD adopts a more symmetrical conformation, and each glucose unit of the $\beta$-CD is in a similar environment. This is an indication that the PEO-$b$-PPO-$b$-PEO copolymer is included inside the cavity of the $\beta$-CD. Although the main chain resonance of both the PEO and PPO blocks are overlapped with the resonance of C$_{2,3,5}$ of $\beta$-CD (see Figure 4.2), the resonance of the methyl carbon atom at 21.7 ppm provides evidence of the formation of the inclusion complex (Figure 4.2b, 4.2c and 4.2d). In the CP/MAS NMR spectra, the carbon resonance for the methyl group was narrow, and the line-width at half-height was 49.18 Hz, as indicated in Figure 4.2e. However, after forming complexes with $\beta$-CD, the carbon resonance became broader (see Figure 4.2d). The line-width at half-height changed to 194.42 Hz, which is about 4 times broader than the line-width of methyl carbon resonance before complexation. Similar phenomena were observed for the inclusion complexes of $\beta$-CD/EPE46 and $\beta$-CD/EPE77. These solid-state NMR results revealed that the methyl groups of the PPO blocks have a more
restricted mobility compared to the pure sample. This restricted mobility can only occur when the PPO is included inside the cavity of the β-CDs and thus forms the complexed state.

Figure 4.2 The solid-state $^{13}$C CP/MAS NMR spectra of β-CD (a), β-CD/ EPE46 (b), β-CD/ EPE77 (c), β-CD/ EPE146 (d) inclusion complexes, and EPE146 (e) copolymer.
Figure 4.3 shows solid-state $^{13}$C CP/MAS NMR spectra of uncomplexed EPE77 (Figure 4.3a) and β-CD (Figure 4.3d) as well as the β-CD/EPE77 inclusion complexes (Figure 4.3c). In this figure, solid-state Bloch decay $^{13}$C MAS NMR spectrum of β-CD/EPE77 inclusion complexes is also included (Figure 4.3b). As reported in the literature, the cross polarization process discriminates against the mobile species. The intensity of the mobile carbon resonance is thus drastically decreased due to the inefficient proton-carbon cross polarization process. On the other hand, the Bloch decay $^{13}$C MAS NMR spectra are more sensitive towards the mobile species. Combining both of these solid state NMR methods on the same sample is a useful method to identify the different species based on the mobility and the order difference in this type of heterogeneous inclusion complex system. Figure 4.3b shows the solid-state Bloch decay $^{13}$C MAS NMR spectra of β-CD/EPE77 inclusion complexes, in which stronger signals of relatively mobile carbons from the sample were found. This spectrum can be compared with that of $^{13}$C CP/MAS NMR as shown in Figure 4.3c. The relative intensities of the peaks of the methyl carbon of the PPO blocks to those of β-CD in Figure 4.3b are much stronger than those in Figure 4.3c. These results are consistent with the view that β-CD molecules are in a channel configuration, forming a tube-shaped frame of the complexes. Figure 4.3b also exhibits a new resonance at 74.4 ppm that is missing in Figure 4.3c. This resonance is assigned to the mobile species of the PEO block of the triblock copolymer. The line-width at half-height of the resonance is 60.44 Hz which is close to the line-width at half-height of the PEO resonance from the uncomplexed PEO-$b$-PPO-$b$-PEO copolymer (Figure 4.3a). The solid-state CP/MAS and Bloch decay NMR results on the β-CD/EPE77 inclusion complex demonstrates that while the PPO blocks of
the triblock copolymer were included into the cavity of the $\beta$-CDs due to reduce mobility, the PEO blocks did not interact with $\beta$-CDs. This supports the fact that the PEO blocks were not included within the $\beta$-CD. The line-width of the un-included PEO blocks is narrower than the included PPO blocks, revealing that the mobility of the included PPO blocks was more restricted than the PEO blocks due to the formation of inclusion complexes. Therefore, the $\beta$-CDs do possess selectivity in their location of complexation.

Figure 4.3 The solid-state $^{13}$C CP/MAS NMR spectrum of EPE77 (a), Bloch decay MAS NMR spectrum of $\beta$-CD/EPE77 inclusion complex (b), solid-state $^{13}$C CP/MAS NMR spectra of $\beta$-CD/EPE77 inclusion complex (c), and $\beta$-CD (d).
Measurements of proton spin-lattice relaxation times were conducted using an inversion recovery pulse sequence. The carbon signal intensity decay was fitted into a standard first order kinetic expression curve to determine the proton spin-lattice relaxation times for the block copolymers and the inclusion complexes by monitoring the changes in carbon signal intensity as a function of proton delay times. For this particular fit, the C_1 peak at approximately 107.7 ppm is chosen for the β-CD because it is highly resolved in the spectra. However, the same conclusions were obtained for all of the other peaks since they all decay following the same proton spin-lattice relaxation times with the same rate constant due to the effective proton spin diffusion process. We measured the proton relaxation behavior of different carbon atom resonances for the β-CD, EPE copolymers and β-CD/EPE inclusion complexes. First, the relaxation times were independent of the peak chosen for the calculation. For the copolymers, the CHO carbon atom peak at 79.3 ppm was chosen because the methyl group is too mobile. For the inclusion complexes, the methyl group resonance at 21.7 ppm was chosen because it becomes rigid after the complexation. Furthermore, it was highly resolved in all the spectra. The proton T_1 values of the β-CD, copolymer EPE77 and β-CD/EPE77 inclusion complex are listed in Table 4.1. A single component decay behavior of the proton T_1 for the complexes was observed. The proton T_1 value of the inclusion complexes was between the relaxation time values of β-CD and the pure copolymers. This indicated that the spin diffusion occurred quickly among the chemically different constituents, which equilibrated the magnetization; therefore, the chains must be intimately and homogeneously mixed.
Table 4.1 Values of $^{1}T_{1}$ (ms) determined from curve fitting of the spectra acquired with inversion recovery pulse sequence.

<table>
<thead>
<tr>
<th>Sample</th>
<th>PEO-\textit{b}-PPO-\textit{b}-PEO</th>
<th>$\beta$-CD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>c (79.3 ppm) \hspace{1cm} b (21.7 ppm)</td>
<td>$C_1$ (107.7 ppm)</td>
</tr>
<tr>
<td>EPE77</td>
<td>1.32</td>
<td>0.97</td>
</tr>
<tr>
<td>$\beta$-CD/EPE77</td>
<td>0.97</td>
<td>1.05</td>
</tr>
<tr>
<td>$\beta$-CD</td>
<td>0.68</td>
<td></td>
</tr>
</tbody>
</table>

Information about the molecular dynamics of polymers can also be obtained based on the NMR proton line shapes which are broadened by the combination of chemical shift anisotropy and homo- and hetero-nuclear dipolar couplings.\textsuperscript{129,136} Broad lines are commonly observed in the proton spectra, mostly because of the strong proton-proton dipolar couplings (60 kHz). The proton chemical shift range is about 10 ppm (5 kHz using 500 NMR spectrometer), so the individual lines are not resolved. They can, however, be observed indirectly in 2D NMR experiments using wide-line separation (WISE) NMR.\textsuperscript{137} A major advantage of the solid state 2D WISE experiments over the direct measurement of the proton line-shapes is that the proton line-widths are correlated with the carbon chemical shifts. It is thus possible to measure the proton line shapes for each resolved carbon resonance in the spectrum. Figure 4.4 shows the contour plot of the 2D WISE spectra for EPE46, EPE77, and EPE146 copolymers. The proton line shapes obtained from cross sections through the 2D WISE spectra are similar for the different carbon sites and different samples. The line-width at half-height was in the range from 2.3 to 2.7 kHz.
Figure 4.4 The contour plot of the 2D WISE spectra for EPE46 (a), EPE77, and EPE146 (c) copolymers.

Figure 4.5a shows the contour plot and projections of the 2D WISE spectrum of the hydrated $\beta$-CD, a herringbone packing structure when it is complexed with water molecules. Notice here that the spectral widths were 80 kHz for the proton dimension, which is 10 times wider than in the case of the copolymers in Figure 4.4. Figure 4.5b shows the cross sections of the 2D WISE spectrum of the hydrated $\beta$-CD for 107.7 ppm.
(C₁), 85.1 ppm (C₄), 76.8 ppm (C₂,₃,₅), and 64.4 ppm (C₆). The results of Figure 4.5 reveal that a narrow line with its full-width at half-height of about 1.6 to 1.7 kHz was on top of the wide line with its full-width at half-height of about 36 to 38 kHz for both the proton projection and the cross sections of the 2D WISE spectrum in the proton dimension. The narrow line resulted from the complexed water molecules, and the wide lines were from the rigid β-CD. After deconvolution of the proton 1D spectrum, the water content was about 15% of the total sample weight, which matches the thermogravimetric analysis result (about 15% weight is lost at 100 °C as shown in Figure 4.6). Furthermore, the proton full-width at half-height is about 36 to 38 kHz for β-CDs, which is more than 10 times broader than the line-width value of the PEO-b-PPO-b-PEO copolymers.

Figure 4.5 2D WISE spectrum of the hydrated β-CD, the contour plot and projections (a), cross sections at the frequency of the 107.7 ppm of C₁, 85.1 ppm of C₄, 76.8 ppm of C₂,₃,₅, and 64.4 ppm of C₆ (b).
Figure 4.6 TGA of the hydrated $\beta$-CD.

Figure 4.7a shows the contour plot and projections of the 2D WISE spectrum of the inclusion complex of $\beta$-CD/EPE77. Note that the spectral widths were 80 kHz for the proton dimension, which is 10 times broader than the PEO-$b$-PPO-$b$-PEO copolymer in Figure 4.4. Figure 4.7b shows the $^1$H cross sections of the 2D WISE spectrum of the inclusion complex. These 2D spectra indicate that the resolution of the $^{13}$C projection of the 2D WISE spectrum is higher than the 1D $^{13}$C CP/MAS spectrum as shown in Figure 4.3c. The carbon resonance from the PEO block at 74.4 ppm can be unambiguously observed in the $^{13}$C projection of the 2D WISE spectrum. This higher resolution of the 2D spectra allows us to observe the proton line width of the PEO block separately. Moreover, unlike the cross sections of the 2D WISE spectrum of the hydrated $\beta$-CD that showed
both the narrow and broad lines, the cross sections of the 2D WISE spectrum of the \( \beta \)-CD in the complex shows only one broad line. In other words, after the complexation, the guest water molecule is replaced by the copolymer chain. The resonance at 76.8 ppm was attributed to the \( C_{2,3,5} \) carbons of the \( \beta \)-CD and the PPO block. The cross sections of the 2D WISE spectrum at this frequency did not show both the narrow and broad lines. This was strong evidence that the PPO block does reside inside the cavity of the \( \beta \)-CD, and its line-width changes from 2.5 kHz in the pure copolymer shown in Figure 4.5 to 37 kHz after the PPO block is complexed with \( \beta \)-CD.

Figure 4.7 2D WISE spectrum of the inclusion complex of \( \beta \)-CD/EPE77 the contour plot and projections (a), cross sections at the frequency of the 107.7 ppm of \( C_1 \), 85.1 ppm of \( C_4 \), 76.8 ppm of \( C_{2,3,5} \), 74.4 ppm of a \( CH_2 \) from the PEO block, and 64.4 ppm of \( C_6 \) (b).
The proton line-width at half maximum corresponding to the carbon group from pure EPE77 block copolymer and β-CD/EPE77 inclusion complex respectively is shown in Table 4.2. From Table 4.2, based on the higher resolution of the $^{13}$C projection of the 2D spectra shown in Figure 4.5a, the proton line-width of the PEO block in the complexes can be observed directly from the cross sections of the 2D WISE spectrum at the chemical shift of carbon resonance of this block at 74.4 ppm. Figure 4.7b shows that the proton full-width at half-height of the PEO block in the complexes was 3.3 kHz, which is very similar to the value of the PEO block in the pure EPE77 copolymer (which is 2.8 kHz shown in Table 4.2). This value was more than ten times smaller compared to the proton full-width at half-height of the PPO block in the complexes (at 37 kHz shown in Table 4.2). Therefore, this technique provided direct experimental evidence for the complexation of β-CD with PEO-β-PPO-β-PEO, that the PPO block was placed inside of the cavity of the β-CD, and that the PEO block was not involved in this inclusion process within the cavity of the β-CD.

Table 4.2 Proton line-widths (kHz) at half-maximum corresponding to the carbon group for EPE77 and β-CD/EPE77.

<table>
<thead>
<tr>
<th>Sample</th>
<th>a (PEO)</th>
<th>c,d (PPO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPE77</td>
<td>2.8</td>
<td>2.5</td>
</tr>
<tr>
<td>β-CD/EPE77</td>
<td>3.3</td>
<td>37</td>
</tr>
</tbody>
</table>
We are also interested in the morphology of the complex system on a smaller scale. That is whether or not the intermolecular interaction of the complex system is on the molecular level. In order to further investigate this characteristic of the system, cross polarization kinetics must be performed. Quantitatively, the dependence of the magnetization, \( M(t) \) as a function of the contact time \( t \) may be written as:

\[
M(t) = M_0 [1 - \exp(-\lambda t)] \exp(-t/T_{\rho H})
\]

where \( \lambda = 1 + \frac{T_{CH}}{T_{1\rho C}} - \frac{T_{CH}}{T_{1\rho H}} \). \( M(t) \) denotes the magnetization at contact time \( t \), which is proportional to the peak intensity of particular resonance in the \(^{13}\)C CP/MAS spectra. \( M_0 \) denotes the initial equilibrium magnetization, \( T_{CH} \) is the cross polarization time, \( T_{1\rho C} \) is the carbon spin-lattice relaxation time in the rotating frame, and \( T_{1\rho H} \) is the proton spin-lattice relaxation time in the rotating frame. Very often, in rigid polymeric materials, \( T_{CH} \ll T_{1\rho C} \) and \( T_{1\rho H} \), and eq. 1 can be simplified to:

\[
M(t) = M_0 [1 - \exp(-t/T_{CH})] \exp(-t/T_{1\rho H})
\]

Note that for the resonances caused by the mobile PPO blocks, Eq. 2 is not valid to treat the data. Figure 4.8 shows the intensity profiles of the methyl group of the PPO blocks before and after complexation with the \( \beta \)-CD. While it is impossible to fit the data for PEO-\( b \)-PPO-\( b \)-PEO due to the mobility of the methyl group, the intensity of the methyl group of the PPO blocks after complexation can be fitted using Eq. 2. \( T_{CH} \) values based on the fitting results for \( \beta \)-CD and the \( \beta \)-CD/EPE77 inclusion complex are listed in Table 4.3. This result indicates that the PPO blocks are included in the cavity of the \( \beta \)-CD. The rigidity of the methyl group of the PPO blocks increased after complexation. Therefore, the fitting of the intensity profiles of the resonance with variable contact time is only valid for the rigid resonance. This observation is consistent with the results of the line-
width investigation of the spectra as shown in Figure 4.3. Finally, the cross polarization time $T_{CH}$ of all of the resonances of the $\beta$-CD decreased after complexion with the PEO-$b$-PPO-$b$-PEO copolymers. This is strong evidence of the formation of the inclusion complexes between the $\beta$-CD and PEO-$b$-PPO-$b$-PEO copolymer.

Table 4.3 Values of $T_{CH}$ ($\mu$s) determined from curve fitting the variable contact time.

<table>
<thead>
<tr>
<th>Sample</th>
<th>CH$_3$-(PPO)</th>
</tr>
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<tbody>
<tr>
<td>EPE46</td>
<td>N/A (&gt;5000)</td>
</tr>
<tr>
<td>EPE77</td>
<td>N/A (&gt;5000)</td>
</tr>
<tr>
<td>EPE146</td>
<td>N/A (&gt;5000)</td>
</tr>
<tr>
<td>$\beta$-CD/EPE46</td>
<td>856.5</td>
</tr>
<tr>
<td>$\beta$-CD/EPE77</td>
<td>702.5</td>
</tr>
<tr>
<td>$\beta$-CD/EPE146</td>
<td>787.7</td>
</tr>
</tbody>
</table>
Figure 4.8 Plots of $M(t)$ of $^{13}$C CP/MAS spectra of the methyl resonance of the PPO blocks versus the contact time for the EPE46 copolymer (a), $\beta$-CD/EPE46 inclusion complex (b), EPE77 copolymer (c), $\beta$-CD/EPE77 inclusion complex (d), EPE146 copolymer (e), and $\beta$-CD/EPE146 inclusion complex (f). The symbols represent experimental data and the solid red lines represent the best fitting results based on equation 2.
4.3 Stoichiometry of Inclusion Complexes

The average number of threaded β-CDs in the inclusion complexes was determined via $^1$H NMR spectroscopy in DMSO-d$_6$ since the inclusion complexes were completely dissociated into their components in polar solvents. As shown in Figure 4.9 for β-CD/EPE46, a comparison between the integral intensities of the H$_1$ proton peak of β-CDs and the methyl protons of the PPO blocks shows that the molar ratio of PO units to β-CD was identified to be about 3:1. This ratio was maintained in all three inclusion complex samples. Based on the molar ratio, the average number of β-CDs threaded onto the PPO block was about 13, and it was only dependent on the molecular weight of the PPO blocks. Theoretically, it is assumed that based on size matching, two PO repeat units can accommodate one threaded β-CD; whereas, Harada et al. observed that the ratio of monomer unit to cyclodextrin increased with an increase in the PPO molecular weight.$^{59,68,69}$ Their observations differ because the inclusion complexes start to precipitate out from aqueous solution when they become more hydrophobic with increasing intermolecular hydrogen bonding after threading more and more β-CDs. The precipitation occurs before the β-CDs can completely cover the PPO blocks.
In this chapter, we have used 2D ROESY solution NMR and 1D and 2D solid-state NMR to elucidate the formation, dynamics and structure of inclusion complexes of PEO-\(b\)-PPO-\(b\)-PEO with \(\beta\)-CD (a schematic process of inclusion complexation is shown in Figure 4.10). In 2D ROESY experiments, the cross peaks between protons H\(_3\) and H\(_5\) in the cavity of \(\beta\)-CDs and the methyl protons of the PPO blocks indicate that the \(\beta\)-CDs can thread onto PEO-\(b\)-PPO-\(b\)-PEO copolymers and form inclusion complexes in aqueous solution. 2D wide-line separation (WISE) NMR experiments provided clear evidence that broad lines appeared for the PPO blocks after forming inclusion complexes; whereas, the PEO blocks maintained the narrow line results, indicating that \(\beta\)-CDs only thread onto the PPO blocks. The high efficiency of cross-polarization and spin diffusion
experiments in $^{13}$C solid-state NMR showed that the mobility of PPO blocks dramatically decreases after $\beta$-CD complexation, indicating that they are selectively incorporated onto the PPO blocks. The hydrophobic cavities of $\beta$-CD restrict the PPO block mobility, which is evidence of the formation of inclusion complexes in the solid state. The stoichiometry of inclusion complexes was studied using $^1$H NMR. The molar ratio of PO units to $\beta$-CD was about 3:1 for three inclusion complexes, and it indicated that the total number of threaded $\beta$-CDs was only dependent on the molecular weight of the PPO blocks.

Figure 4.10 The schematic inclusion complex of $\beta$-CD with PEO-$b$-PPO-$b$-PEO.
CHAPTER V

SUPRAMOLECULAR STRUCTURE OF $\beta$-CYCLODEXTRIN AND
POLY(ETHYLENE-OXIDE)-BLOCK-POLY(PROPYLENE OXIDE)-BLOCK-
POLY(ETHYLENE OXIDE) INCLUSION COMPLEXES

5.1 Identification of the Supramolecular Crystal Structure of Self-Assembled Inclusion Complexes

Figure 5.1 exhibits a set of 1D WAXD powder patterns observed for the self-assembled inclusion complexes, pure EPE77, and hydrated $\beta$-CD at room temperature in a $2\theta$ range from 3° to 35°. In the pure copolymer system, the PEO blocks crystallized to form a monoclinic structure with $a = 0.805$ nm, $b = 1.304$ nm, $c = 1.948$ nm and $\beta = 125.4^\circ$. Therefore, in the WAXD of EPE77 (Figure 5.1a), there are two prominent reflection peaks at $2\theta = 19^\circ$ assigned as the (120) reflection and at $2\theta = 23^\circ$ which is attributed to several overlapped reflections. The hydrated $\beta$-CD (Figure 5.1e and insert image) was reported to have a herringbone packing structure when it is complexed with water guest molecules. Its crystal structure possesses a monoclinic unit cell with $a = 2.126$ nm, $b = 1.031$ nm, $c = 1.512$ nm and $\beta = 112.3^\circ$ with a space group of $P2_1$. The diffraction patterns of the three self-assembled $\beta$-CD/EPE inclusion complexes shown in
Figures 5.1b, 5.1c and 5.1d are quite different from the WAXD of the hydrated β-CD and pure copolymer. These differences indicate that the inclusion complexes form a different crystal structure. Furthermore, the other reflections observed in Figure 5.1b, 5.1c, and 5.1d reveal that the inclusion complex is in a three dimensionally ordered crystal in the solid state. However, 1D WAXD powder patterns do not provide structural symmetry and unit cell lattices due to the lack of dimensionality of these reflections. Therefore, it is insufficient for complete structure determination.

![WAXD powder diffraction patterns](image)

Figure 5.1 WAXD powder diffraction patterns for the EPE77 triblock copolymer (a), the β-CD/EPE46 inclusion complexes (b), the β-CD/EPE77 inclusion complexes (c), the β-CD/EPE146 inclusion complexes (d), the hydrated β-CD (e).
In order to accurately determine the supramolecular crystal structure of self-assembled inclusion complexes, a 2D WAXD fiber pattern from oriented crystals is required. The oriented single supramolecular crystal mats possess 2D WAXD fiber patterns as shown in Figure 5.2. These WAXD fiber patterns exhibit diffractions not only on the equator and the meridian, but also in quadrants (Figures 5.2a, 5.2b and 5.2c). After crystallographic analysis, it was found that the diffraction spots which are on the meridian in the low-angle region ($2\theta < 5^\circ$) do not belong to the supramolecular crystal structure. Additionally, through small angle x-ray scattering (SAXS) experiments, the results show that SAXS patterns are on the meridian as well (Figure 5.3). The diffractions in SAXS patterns, showing 1$^{\text{st}}$, 2$^{\text{nd}}$ and...etc ordered peaks, are found to corresponded with the diffraction patterns in low-angle region ($2\theta < 5^\circ$) from 2D WAXD experiments (Figure 5.2), in which they only show higher ordered peaks. These ordered diffractions with characteristic ratios of 1:2:3:4:5... are attributed to the alternating layers formed by stacking the supramolecular structures on top of each other during sedimentation (schematic shown in Figure 5.4), indicating the stacking direction of supramolecular single crystals is along the sedimentation direction. Additionally, the higher ordered peaks gradually disappear with increasing composition of inclusion complexes as shown in Figure 5.3. The results may be due to the fact that there is an increasing irregular thickness of alternating layers or/and the surface roughness of the supramolecular crystal structure with increasing length of tethered PEO blocks. Nevertheless, the diffraction pattern in Figure 5.2c also includes the PEO crystal diffraction and will be discussed later. At this moment, we exclude those diffractions attributed to the PEO crystal and alternating layers.
Figure 5.2 2D WAXD fiber diffraction patterns for the supramolecular structure of the β-CD/EPE46 inclusion complexes (a), the β-CD/EPE77 inclusion complexes (b), and the β-CD/EPE146 inclusion complexes (c). The ring diffraction pattern at $2\theta = 28.46^\circ$ is attributed to the standard sample of silicon powder.
Figure 5.3 2D SAXS patterns of the $\beta$-CD/EPE46 inclusion complex (a), the $\beta$-CD/EPE77 inclusion complex (b), and the $\beta$-CD/EPE146 inclusion complex (c).

Figure 5.4 Schematic of alternating layers formed though stacking of supramolecular single crystals on the top each other in the $\beta$-CD/EPE46 inclusion complex system.
For the inclusion complex crystals, we can identify that the $c^*$-axis is on the meridian and that the $b^*$-axis is on the equator, yet the $a^*$-axis is 21°-tilted away from the equator. Therefore, the (00$l$) planes are on the meridian and the (0$k$0) planes are on the equator. Using the reciprocal lattice method and refinement procedure, the unit cell for the supramolecular crystal structure of $\beta$-CD/EPE46 (Figure 5.2a) is monoclinic with $a = 1.91$ nm, $b = 2.43$ nm, $c = 1.57$ nm and $\beta = 111^\circ$ and one crystal unit cell contains four inclusion complex molecules. The experimentally observed and calculated diffraction angles ($2\theta$) and $d$-spacing values of the crystal lattice are listed in Table 5.1. The space group is $C_2$ symmetry determined based on the relationships among diffraction spot intensities and the systematic distinctions. It is noteworthy that crystal structures for $\beta$-CD/EPE77 (Figure 5.2b) and $\beta$-CD/EPE146 (Figure 5.2c) also show an almost identical monoclinic space group $C_2$ with $a = 1.91$ nm, $b = 2.43$ nm, $c = 1.57$ nm, $\beta = 111^\circ$ (Table 5.2), and $a = 1.90$ nm, $b = 2.44$ nm, $c = 1.57$ nm, and $\beta = 111^\circ$ (Table 5.3), respectively.
Table 5.1. Crystallographic parameters of supramolecular structure of \( \beta \)-CD/EPE46 inclusion complexes.

<table>
<thead>
<tr>
<th>(hkl) plane</th>
<th>(2\theta) (degree)</th>
<th>d-spacing (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>expt(^a)</td>
<td>calc(^b)</td>
</tr>
<tr>
<td>(001)</td>
<td>6.02</td>
<td>6.02</td>
</tr>
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\(^a\) Experimental values observed in Figure 5.2a. \(^b\) Calculated based on the monoclinic unit cell of \(a = 1.91\) nm, \(b = 2.43\) nm, \(c = 1.57\) nm, \(\alpha = 90^\circ\), \(\gamma = 90^\circ\), \(\beta = 111^\circ\).
Table 5.2. Crystallographic parameters of supramolecular structure of $\beta$-CD/EPE77 inclusion complexes.

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\(^a\) Experimental values observed in Figure 5.2b. \(^b\) Calculated based on the monoclinic unit cell of \(a = 1.91\) nm, \(b = 2.43\) nm, \(c = 1.57\) nm, \(\alpha = 90^\circ\), \(\gamma = 90^\circ\), \(\beta = 111^\circ\).
Table 5.3. Crystallographic parameters of supramolecular structure of β-CD/EPE146 inclusion complexes.

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*a Experimental values observed in Figure 5.2c. b Calculated based on the monoclinic unit cell of a = 1.90 nm, b = 2.44 nm, c = 1.57 nm, α = 90°, γ = 90°, β = 111°.
The supramolecular crystal structure can be further confirmed by the SAED experiments obtained from the supramolecular single crystal in TEM. Figure 5.5a shows an SAED pattern of the [103] zone, and the $c^*$-axis of the single crystal is parallel to the electron beam, indicating the $ab$-plane of this crystal lies on the copper grid surface. On the basis of the determined monoclinic structure from 2D WAXD, the electron diffraction pattern with the [001] zone (Figure 5.5b) can be obtained by tilting clockwise 21° around the $b^*$-axis. In Figure 5.5b, the odd-numbered diffraction spots on the $(0k0)$ axis are extinct; therefore, the diffraction spots on the meridian that remain are the (020), (040), and (060) diffractions with a $d$-spacing of 1.21 nm between the neighboring (020) planes. Along the $a^*$-axis, a pair of weak diffraction spots with a $d$-spacing of 0.89 nm is assigned as the (200) diffraction since the odd-numbered diffraction spots are also extinct. The $\gamma^*$-angle between the $a^*$ and the $b^*$ axes is 90°, which is consistent with the $\gamma$-angle calculated based on the 2D WAXD results. The 2D unit cell assignment of the $ab$-plane is, therefore, found to agree well with the structure determined via the 2D WAXD experiments.
From the results of the 2D WAXD fiber patterns, the supramolecular single crystal structure obtained from other PEO-\(b\)-PPO-\(b\)-PEO copolymers with \(\beta\)-CD (\(\beta\)-CD/EPE46 and \(\beta\)-CD/EPE146) also possesses the identical crystal structure. Based on previous results provided from the nuclear magnetic resonance experiments, the threaded \(\beta\)-CD molecules in both of these systems are located around the PPO blocks. The only difference is the molecular weights of the PEO blocks are different in these two systems. Therefore, we can conclude that in these supramolecular single crystals, the PPO blocks with threaded \(\beta\)-CDs are the building blocks, and they are closely packed to form the lamellar single crystals. The PEO blocks are attached to the lamellar crystal surfaces, acting as tethered chain molecules. Only closely-packed supramolecular single crystals having long range order can exhibit diffractions in WAXD and SAED patterns (Figures 5.2 and 5.5). In addition, the finding of PEO crystal diffraction patterns (Figure 5.2c)
indicates that supramolecular structures are not affected or destroyed when PEO crystallization occurs on their surfaces.

5.2 Crystallographic Simulation of Inclusion Complex Molecular Packing

The supramolecular building block packing in the single crystal can be verified via computer calculation. To build up this structure with four inclusion complexes with the $C_2$ space group, basic unit cell parameters according to the experimental data deduced from the 2D WAXD and SAED results are used. Since the tethered PEO blocks do not take part in the supramolecular single crystals, we excluded them in this computer calculation. Only the PPO blocks and threaded $\beta$-CDs are involved in this simulation. Figure 5.6 presents a series of the supramolecular building block packing schemes along different zones. These schemes are used to generate the calculated 2D WAXD fiber pattern and the [001] zone SAED pattern as shown in Figures 5.7a and 5.7b. These schemes show the best fits with the experimental results. The computer simulation shown in Figure 5.6 reveals that one threaded $\beta$-CD on the PPO polymer chain occupies two chemical repeating units of PPO, since one $\beta$-CD possesses a height of 0.75 nm and the length of two PPO chemical repeating units is 0.71 nm in its free energy minimized conformation of an extended PPO chain. Furthermore, as shown in Figure 5.6a, the $\beta$-CDs are suggested to be in a tail-to-tail arrangement along the extended PPO chain (the $c$-axis in the crystal) to form a 1D column as the building block to construct the supramolecular single crystals. This type of columnar building block has been frequently observed in the cases when $\beta$-CDs formed channel-type inclusion complexes with guest
molecules.\textsuperscript{143-150} In the columnar building blocks, $\beta$-CDs tend to arrange into the thermodynamically most stable tail-to-tail dimers (a motif of the column) because in such a dimer arrangement, the inter-$\beta$-CD hydrogen bonds between the secondary hydroxyls are preferentially formed. However, $\beta$-CDs are not stacked in a straight line when viewing along the $b$-axis, but rather, form an inclined column as shown in Figure 5.6a. The explanation for the inclined column structure could be attributed to a cooperation of interactions resulting from hydrogen bonding between $\beta$-CDs as well as spatial fitting between $\beta$-CDs and the atactic PPO chain. Note that the atactic PPO chain does not possess a conformational regularity and that it is selectively included in the inner-cavity of $\beta$-CDs. The overall PPO block conformation in the single crystals is a balance between the need to minimize intramolecular steric interaction of the PPO itself and space filling the $\beta$-CD cavity by maximizing the PPO-$\beta$-CD physical interactions. The distance between $\beta$-CD and PPO has been investigated to be less than 0.4 nm as evidenced by 2D ROESY experimental results. The conformation of the PPO chain contains both \textit{trans} and \textit{gauche} configurations. As a result, the PPO chain is disordered within the cavity of $\beta$-CDs and does not contribute to the crystallographic symmetry.
Figure 5.6 The molecular packing schemes based on computer simulation. The channel-type structure composed of four symmetric related inclusion complexes viewed along the $b$-axis (a), the molecular packing in the crystal lattice viewed along the [001] zone (b), viewed along the [010] zone (c), and viewed along the [100] zone (d). The molecular packing schemes of (b), (c) and (d) contain four unit cells along each projection plane.
Figure 5.7 Computer calculated 2D WAXD fiber pattern (a) and SAED pattern of the [001] zone (b) which are the best fits with the experimental 2D WAXD (Figure 5.2) and SAED diffraction patterns (Figure 5.3b).

On the basis of quantitative analysis of the 2D WAXD fiber patterns as shown in Figure 5.2, it is observed that the intensity of the diffraction for the (002) spot is stronger than that of the (001) spot. In addition, the diffraction spots of the (150), (240), (132), (112), (310), and (330) planes also possess strong diffraction intensities. From the computed packing scheme in the crystal lattice, it has been determined that the (002) planes are located on the secondary hydroxyls of the β-CDs compared with the (001) planes. Only the primary hydroxyl groups are located on the (001) planes. Therefore, the (002) plane possesses a higher number of atoms and thus, contributes to a stronger electron density. On the other hand, the stronger intensities on the (150), (240), (132), (112), (310), and (330) diffractions are due to the fact that the hydroxyl groups and/or the glycosidic oxygen atoms of β-CD are largely located on these planes.
5.3 Crystal Morphology of the Supramolecular Structure of Inclusion Complexes

Figure 5.8a shows a supramolecular single crystal morphology observed in TEM, and its corresponding SAED pattern from the [001] zone. The observed morphology under TEM was lozenge-shaped. Based on the [001] zone SAED pattern, the \( b^* \)-axis points toward the acute angle, while the \( a^* \)-axis is toward the obtuse angle with respect to this crystal morphology. The acute angle is estimated to be \( \sim 73^\circ \), which matches the acute angle between the (110) and the (\( \bar{1} \)10) planes calculated based on the computer simulation (Figure 5.8b). Therefore, the observed lozenge-shaped supramolecular single crystal is bounded by four (110) planes. From the crystallographic point of view, for a monoclinic unit cell with \( \beta = 111^\circ \) to construct a lozenge-shaped single crystal, the necessary condition is that this single crystal must align the long axis of this columnar building block parallel to the \( c \)-axis as shown in the computer simulation (Figure 5.6a) and a flat crystal surface that is parallel to the \( a^*b \)-plane (Figure 5.6b). Note that the size of the supramolecular single crystal along the \( c \)-axis (Figure 5.6c) is limited by the length of the PPO block that can accommodate the threaded \( \beta \)-CDs along the chain direction.\(^{46,47}\) Furthermore, the existence of the PEO blocks as tethered chains on both sides of the single crystal surfaces does not allow crystal development along the [001] direction. Hence, the supramolecular crystal can only grow along \( a^* \)- and \( b \)-axes, resulting in the lozenge-shaped lamellar single crystal morphology (Figure 5.8a).
Figure 5.8 TEM bright field morphology image and SAED pattern of the [001] zone (inset) for a single supramolecular crystal of \( \beta \)-CD/EPE77 inclusion complexes (a), and the resultant crystal morphology based on computer simulation (b).

5.4 Proposed Mechanisms of the Formation of the Supramolecular Structure

According to SAXS experiments (Figure 5.3), the lamellar thicknesses of the supramolecular single crystals can be calculated based on the first ordered peaks, which position at 13.2nm (q=0.475nm\(^{-1}\)), 13.6nm (q=0.462nm\(^{-1}\)), and 9.1nm (q=0.692nm\(^{-1}\)), for \( \beta \)-CD/EPE46, \( \beta \)-CD/EPE77, and \( \beta \)-CD/EPE146, respectively. Based on the previous NMR results (Figure 4.9), it revealed that 13 \( \beta \)-CDs in average threaded onto the PPO block to construct a single inclusion complex chain. If the PPO segment in the supramolecular single crystal is fully extended, the thickness should be, at least, 10 nm regardless of the tethered PEO blocks. However, the assumption of extended chain model
only supports for β-CD/EPE46 and β-CD/EPE77 systems (Figure 5.9a), but not in β-CD/EPE146. The thinner thickness found in β-CD/EPE146 indicated the possibility of which the supramolecular single crystal in this system is formed by once-fold chain of inclusion complexes (Figure 5.9b). With this configuration the lamellar thickness of the supramolecular single crystals of β-CD/EPE146 is therefore half of the thickness of the supramolecular single crystals formed by extended chain. The driving force of the once-fold chain in β-CD/EPE146 may come from the need to avoid the high reduced tethering density of tethered PEO blocks, which is unfavorable for the crystallization process of the inclusion complexes. The reduced tethering density is calculated according to $$\bar{\sigma}^{\text{PEO}} = \frac{1}{S} \pi (R_g)^2$$, where S is the surface area for a single tethered PEO block and $$R_g$$ is the radius of gyration of the PEO block. The S was calculated by $$S = \frac{ab}{2}$$ in units of square nanometer per tethered chains. The a and b are dimensions of unit cell of supramolecular crystal structure at ambient condition (Table 5.4). The calculated values of reduced tethering density of tethered PEO blocks are shown in Table 5.5. In the case of extended chain in β-CD/EPE146, the $$\bar{\sigma}^{\text{PEO}}$$ is 11, which is approaching the highly stretched region ($$\bar{\sigma} = 14.3$$). In order to keep away from high reduced tethering region, the inclusion complexes fold once and aggregate in “anti-parallel” packing to form the supramolecular crystal (Table 5.5 and Figure 5.9b). By doing so, the reduced tethered density can be decreased to 5.5 (only half of reduced tethering density of extended chain model). Through combined results of SAXS experiments and reduced tethering density calculation, the proposed mechanisms of the formation of the supramolecular crystal in different systems are schemed in Figure 5.9.
Table 5.4 Dimensional parameters of the supramolecular structure of inclusion complexes at ambient temperature.

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Table 5.5 Radius of gyration\textsuperscript{153} and reduced tethering density of tethered PEO blocks in different inclusion complex systems.

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Figure 5.9 Proposed mechanisms of the formation of the supramolecular single crystal for β-CD/EPE46 inclusion complexes, β-CD/EPE77 inclusion complexes (a), and β-CD/EPE146 inclusion complexes (b).
5.5 Thermal Stability of the Supramolecular Structure of Inclusion Complexes

Differential scanning calorimetric (DSC) analysis of the supramolecular structures at heating rate of 10 °C/min are shown in Figure 5.10. Note that thermal behaviors recorded in the DSC measurements shown in Figure 5.10 represent that thermal history of supramolecular structure aggregated from water medium. A broad endothermic peak around 100 °C for three inclusion complex systems is related to evaporation of water molecules (Figure 5.10). In addition, a broad endothermic peak around 40 °C in β-CD/EPE77 (Figure 5.10b) and a sharp endothermic peak at 52 °C in β-CD/EPE146 (Figure 5.10c) indicates the melting of the PEO crystal in the supramolecular structure. The observed endothermic peak at higher temperature (~170 °C) in both β-CD/EPE77 and β-CD/EPE146 systems is corresponded to transition of supramolecular structure (Figure 5.10b and 5.10c), from ordered crystal structure to less-ordered or disordered structure, whereas there is no transition peaks of supramolecular structure found in β-CD/EPE46 (Figure 5.10a). The absent endothermic peak of transition in β-CD/EPE46 inferred that supramolecular structure is gradually degraded with the increase of the temperature.
To further study these phase behaviors, the 2D WAXD patterns of the supramolecular structures were recorded during the heating process. When temperature is elevated to 80°C, the obtained 2D WAXD patterns showed that the diffractions of β-CD/EPE46 (Figure 5.11a) not only decrease but also change in comparison with the diffraction pattern at ambient temperature (Figure 5.2a), while the diffraction patterns of other two systems (Figure 5.11b and 5.11c) remain almost unchanged. The dimensional parameters of the supramolecular structure for different inclusion complex systems at ambient temperature and at 80°C are shown in Table 5.4 and Table 5.6, respectively.
Figure 5.11 2D WAXD fiber diffraction patterns for the supramolecular structure of β-CD/EPE46 inclusion complexes (a), β-CD/EPE77 inclusion complexes (b), and β-CD/EPE146 inclusion complexes (c) at 80°C. The ring diffraction pattern at 2θ=28.46° is attributed to standard sample of silicon powder.
The slight changes of dimensions found for supramolecular structure in both \( \beta \)-CD/EPE77 and \( \beta \)-CD/EPE146 result from the thermal expansion. On the other hand, the \( a \)-axis dimension of supramolecular structure has shrunk 10\% in \( \beta \)-CD/EPE46 (Table 5.4 and 5.6). The shrinkage may be due to the fact that inclusion complexes pack closer once certain amount of water molecules, which are solvated in interstices among inclusion complexes along \( a \)-axis, removed at elevated temperature. The preserved crystal structure at elevated temperature for both \( \beta \)-CD/EPE77 and \( \beta \)-CD/EPE146 systems is believed that higher reduced tethering density of tethered PEO blocks in these two systems acts as a “lock” (Table 5.5), and, thus, retains the integrity of supramolecular structure until the temperature is above 170° C. As the samples are heated up to 200° C, only a few of diffractions are observed in 2D WAXD patterns for three inclusion complex systems, indicating that ordered supramolecular structure turns into less-ordered or disordered

<table>
<thead>
<tr>
<th>Sample</th>
<th>( a ) (nm)</th>
<th>( b ) (nm)</th>
<th>( c ) (nm)</th>
<th>( \alpha ) (°)</th>
<th>( \beta ) (°)</th>
<th>( \gamma ) (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta )-CD/EPE46</td>
<td>1.71</td>
<td>2.47</td>
<td>1.57</td>
<td>90</td>
<td>115</td>
<td>90</td>
</tr>
<tr>
<td>( \beta )-CD/EPE77</td>
<td>1.95</td>
<td>2.43</td>
<td>1.57</td>
<td>90</td>
<td>111</td>
<td>90</td>
</tr>
<tr>
<td>( \beta )-CD/EPE146</td>
<td>1.98</td>
<td>2.43</td>
<td>1.58</td>
<td>90</td>
<td>110</td>
<td>90</td>
</tr>
</tbody>
</table>
structure (Figure 5.12). The remaining diffractions are possibly attributed to structural characteristic of β-CD molecule and/or less-ordered structure of inclusion complexes.

Figure 5.12 2D WAXD fiber diffraction patterns for β-CD/EPE46 inclusion complexes (a), β-CD/EPE77 inclusion complexes (b), and β-CD/EPE146 inclusion complexes (c) at 200°C. The ring diffraction pattern at 2θ=28.46° is attributed to standard sample of silicon powder.
In summary, supramolecular crystal structures are formed via self-assembly of a series of β-CD/PEO-\(b\)-PPO-\(b\)-PEO inclusion complexes. On the basis of 2D WAXD fiber patterns and SAED patterns, the crystal structure was determined to be the same for all the inclusion complex systems studied. Each crystal unit cell contains four inclusion complex building blocks. The \(C_2\) space group was determined based on the relationship among diffraction spot intensity and systematic extinctions. Through computer simulation of the supramolecular structure utilizing the Cerius\(^2\) software, the packing of inclusion complexes in the crystal lattice was investigated. The simulated 2D WAXD fiber patterns and SAED patterns agreed well with experimental results. The observation of crystal morphology from TEM and combined with [001]-zone SAED patterns indicate that the supramolecular crystal structures are lozenge-shaped and bound by four (110) planes. Through combined results of 2D WAXD, SAXS and reduced tethering density calculation, mechanisms of the formation of the supramolecular single crystal were proposed. With observations of phase behaviors of supramolecular structure based on DSC and 2D WAXD experiments, it is speculated that the tethered PEO blocks play an important role in the formation and stabilization of supramolecular crystal structure.
6.1 Crystallization Behavior and Crystal Orientation of PEO Blocks on the Supramolecular Structure

Figure 6.1 shows a set of DSC traces at a heating rate of 10 °C/min for three inclusion complex systems after removal of previous thermal history. Only a single endothermic peak at ~56°C, corresponding to the melting peak of PEO crystals, is observed in the β-CD/EPE146 system (Figure 6.1c), while there are no endothermic peaks in DSC thermal trace for the other two systems. For the β-CD/EPE46 inclusion complex, the molecular weight of the PEO blocks (< 2000 g/mol) in this composition is too low to crystallize at room temperature. In addition, due to the restrained mobility of the PEO chains by the supramolecular structure, PEO cannot crystallize in the β-CD/EPE77 system. Meanwhile, even though the PEO blocks still can crystallize in the β-CD/EPE146 inclusion complex, the crystallinity of the PEO blocks was severely
decreased (only about 20%) in comparison with PEO crystallization in the EPE146 triblock copolymer (the crystallinity of PEO is about 90%) shown in Figure 6.2.

Figure 6.1 DSC heating thermal diagram at 10 °C/min for β-CD/EPE46 inclusion complexes (a), β-CD/EPE77 inclusion complexes (b), β-CD/EPE146 inclusion complexes (c).

Temperature(°C)

Figure 6.1 DSC heating thermal diagram at 10 °C/min for β-CD/EPE46 inclusion complexes (a), β-CD/EPE77 inclusion complexes (b), β-CD/EPE146 inclusion complexes (c).
On the basis of DSC results (Figure 6.1), PEO blocks only can crystallize in the β-CD/EPE146 system. As a result, the following investigation of the crystallization temperature-dependent PEO crystal orientations on the supramolecular structure surface was systematically carried out through PEO crystallization from the melt state (80°C) in the β-CD/EPE146 system at different isothermal crystallization temperatures ($T_c$). From previous results in chapter 5 (Figure 5.11 and Table 5.6), it showed that the supramolecular structures of β-CD/EPE146 persist at 80°C even though the cell dimensions have been slightly changed due to thermal expansion.
Through 2D WAXD patterns, the PEO crystal orientations with respect to the supramolecular structure at different \( T_c \) were observed. Figure 6.3a shows diffraction patterns when the samples were quenched in liquid N\(_2\). This pattern exhibits two major isotropic rings with regards to the PEO crystal \( d \)-spacings of 0.463 nm (red arrow marked) and 0.390 nm (blue arrow marked). The inner ring with a \( d \)-spacing of 0.463 nm is indexed as (120), while the outside ring consists of overlapped (\( \bar{1}32 \)), (032), (\( \bar{2}12 \)), (112), (\( \bar{1}24 \)), (\( \bar{2}04 \)), and (004) diffraction planes with \( d \)-spacing of 0.390 nm. These isotropic ring patterns indicate a random PEO crystal orientation on the supramolecular structure (schematic shown in Figure 6.3b). During the liquid N\(_2\) quenching process, a large number of homogeneous nucleation sites are created. The primary nucleation density is so high that little crystal growth is needed to complete crystallization. The sizes of the PEO crystals generated are correspondingly small and are not affected by the surroundings.
Figure 6.3 2D WAXD fiber diffraction patterns for PEO crystallized on the supramolecular structure of β-CD/EPE146 inclusion complexes when quickly quenched into liquid N₂ (a), schematic of random PEO crystal orientation on the supramolecular structure (b).

The WAXD patterns shown in Figure 6.4 and 6.5 were recorded when the samples were quickly quenched from 80°C (melt state of PEO blocks) to $T_c$ between -60 and 40°C. From these experiments, two types of diffraction patterns were found. When samples were isothermally crystallized at $T_c = -40°C$ for 2 hrs, the 2D WAXD pattern shown in Figure 6.4a exhibits two pairs of the (120) diffraction arcs (red circle marked diffractions) along the equator and meridian, while the blue circle marked diffractions at $\theta = 23°$ ($d$-spacing = 0.390nm) belong to the mixed diffractions of other PEO crystal planes. The azimuthal profile of the (120) diffractions (Figure 6.4b) reveals that (120) planes of PEO crystals are at $\theta = 0°$, 90°, 180°, and 270°. This diffraction pattern can be explained using a [421] uniaxial pattern with [421] along the meridian direction. From
this uniaxial pattern, it is deduced that the $c$-axis of the PEO crystal possesses an approximately homogenous orientation on the surface of the supramolecular structure (the $c$-axis of the crystals is perpendicular to the basal surface normal of the supramolecular single crystal) as demonstrated in Figure 6.5c.

Figure 6.4 2D WAXD fiber diffraction patterns of PEO crystallized at $T_c = -40^\circ$C on the supramolecular structure of $\beta$-CD/EPE146 inclusion complexes (a), azimuthal profile of the (120) diffraction planes of the PEO crystals (b), schematic of the homogenous PEO crystal orientation (c).

Figure 6.4 2D WAXD fiber diffraction patterns of PEO crystallized at $T_c = -40^\circ$C on the supramolecular structure of $\beta$-CD/EPE146 inclusion complexes (a), azimuthal profile of the (120) diffraction planes of the PEO crystals (b), schematic of the homogenous PEO crystal orientation (c).
The 2D WAXD patterns shown in Figure 6.5, which are diffraction patterns when PEO was crystallized at \( T_c = 0^\circ C \) (Figure 6.5a) and \( T_c = 30^\circ C \) (Figure 6.5b), are almost identical. Again, the red circle marked diffractions are attributed to the (120) planes at \( 2\theta = 19^\circ \) (\( d \)-spacing = 0.463 nm), while the blue circle marked diffractions at \( 2\theta = 23^\circ \) (\( d \)-spacing = 0.390 nm) belong to the mixed diffractions of several PEO crystal planes. In the both patterns, only one pair of the (120) diffraction arcs (red circle marked diffractions) is located along equator (at \( \theta = 90^\circ \) and \( 270^\circ \)). The azimuthal scan is shown in Figure 6.5c. These WAXD patterns are consistent with diffraction patterns in which the \( c \)-axis of the PEO crystals is oriented parallel to the normal of the supramolecular structure (homeotropic crystal orientation) as illustrated in Figure 6.5d.
Figure 6.5 2D WAXD fiber diffraction patterns of PEO crystallized at $T_c = 0^\circ$C (a), and at $T_c = 30^\circ$C (b). The azimuthal profile of the (120) diffraction planes of PEO crystals (c), and a schematic of the homeotropic PEO crystal orientation (d).

The summary of the $c$-axis orientation changes with respect to $T_c$ is shown in Figure 6.6. Two crystal orientations were found throughout the crystallization temperature range ($T_c = -60 \sim 40^\circ$C). Namely, the $c$-axis of PEO crystals is perpendicular to the basal surface normal of the supramolecular structure when the $T_c$ is below $-35^\circ$C (Figure 6.4 and Figure 6.6). On the other hand, the $c$-axis of PEO is parallel to the normal
of supramolecular crystal structure when the $T_c$ is higher than -35 °C (Figure 6.5 and Figure 6.6). In addition, when the samples were quenched to LN$_2$ from the PEO melt, a random $c$-axis orientation is found (Figure 6.3).

Figure 6.6 PEO crystal orientation changes on the supramolecular structure of $\beta$-CD/EPE146 inclusion complexes as a function of isothermal crystallization temperature ($T_c$).

Figure 6.7 shows $T_m$ and crystallinity of the PEO blocks in the $\beta$-CD/EPE146 inclusion complex system with isothermal crystallization temperature ($T_c$). The results shows $T_m$ only changes with $T_c$ when $T_c > 10^\circ$C, and $T_m$ keeps around 53°C when $T_c \leq 10^\circ$C. Meanwhile, the crystallinity shows irregular changes with $T_c$ (roughly in the range between 24 ∼ 33%) when $T_c \leq 10^\circ$C. The observations of constant $T_m$ and irregular crystallinity of PEO crystals when $T_c \leq 10^\circ$C can be explained as such: In the low $T_c$
range, the PEO blocks grow imperfect crystals (less stable crystal) due to poor chain mobility. Those imperfect crystals tend to recrystallize or reorganize to form a more stable crystal during the heating process in DSC experiments. As a result, the observed $T_m$ and crystallinity of PEO crystals when $T_c \leq 10^\circ C$ cannot be related to the actual crystallization behavior of PEO with respect to $T_c$.

![Figure 6.7 The melting temperature and crystallinity changes with isothermal crystallization temperature ($T_c$) observed by DSC.](image)
As mentioned in the background section, the change of PEO crystal orientation is mostly observed under confined environment. Accordingly, the finding of the crystal orientation change in our system implies that PEO crystallization may be affected by the confined effect. This confined environment was introduced by the means of stacking supramolecular crystal structures during sedimentation based on previous SAXS results. On the basis of studies regarding crystal orientation change up to now, the dominant factors which influence the origin of PEO crystal orientation change have been suggested to be due to anisotropic density (thermal) fluctuations and maximization of crystallinity.\textsuperscript{154-159} From the viewpoint of critical nucleus formation, the density (thermal) fluctuations are required to overcome the nucleation barrier in polymer crystallization. Under a confining geometry, the nucleus’s ability to overcome the barrier in the parallel or perpendicular directions relies on the density (thermal) fluctuation differently, which is an anisotropic density (thermal) fluctuation effect. Recent theoretical studies\textsuperscript{158,160,161} and experimental investigations\textsuperscript{162-164} reveal that anisotropic density (thermal) fluctuation may influence the preference of chain orientation in primary crystal nucleation. However, the subsequent crystal growth determines the final crystal orientation in order to maximize crystallinity. Hence, it is suggested that the orientation of the PEO crystals within a confined geometry is due to the consequence of interplay between the need to grow larger crystals and the nucleation density. Therefore, the observed orientation change of PEO crystals with respect to the surface of the supramolecular structure can be explained by the following. When the crystallization temperature ($T_c$) is lower ($T_c \leq -35^\circ$C), the nucleation density is relatively higher, and the crystal growth dimensions are limited not only by confined geometry, but also by an impingement of neighboring
crystals in which the c-axis of the PEO crystals preferentially grow parallel to the supramolecular structure’s basal surface. On the other hand, a decrease of nucleation density with increasing $T_c$ (when $T_c > -35^\circ C$) leads to homeotropic crystal orientation since PEO crystals tend to have a two dimensional growth at low nucleation density. As in the case of samples quenched in LN$_2$, the nucleation density is so high that little crystal growth is necessary for crystallization (almost zero dimensional crystal growth), leading to random crystal orientation.

To summarize, the DSC experimental results revealed that the tethered PEO blocks can crystallize on the supramolecular structures when their molecular weights are high enough. The crystallization of PEO blocks in inclusion complex systems is greatly depressed due to restraint of PEO chain mobility by the supramolecular structure. Using 2D WAXD experiments, the PEO crystal orientation changes with respect to the surface of the supramolecular structure have been found to be dependent upon crystallization temperature ($T_c$). Two crystal orientations are found throughout crystallization temperatures ($T_c = -60 \sim 40^\circ C$). When the $T_c$ is below -35℃, the c-axis of the PEO crystals was observed to be perpendicular to the basal surface normal of the supramolecular structure. On the other hand, the c-axis of PEO is parallel to the normal when the $T_c$ is higher than -35 °C. In addition, when the samples were quenched in LN$_2$ from the PEO melt, the random c-axis orientation of PEO was found. It is believed that the introduction of the confined effect via sedimentation of supramolecular structures and, hence, the interplay between primary nucleation density and need to achieve high crystallinity during crystallization, lead to PEO crystal orientation differences with respect to $T_c$.  

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CHAPTER VII

SUMMARY

To gain insight into supramolecular structure formation via self-assembly of inclusion complexation, a series of inclusion complexes of β-cyclodextrin (β-CD) with poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-b-PPO-b-PEO) copolymers was prepared. The inclusion complexes between the PEO-b-PPO-b-PEO copolymers and β-CDs formed in aqueous solution and were detected by 2-D ROESY. The differences in resonance peaks from $^{13}$C solid-state NMR indicated that β-CDs possess different molecular packing (columnar structure) from pure β-CDs (herringbone structure) after forming complex. Wide-Line Separation (WISE) NMR experiments provided clear evidence that showed broad lines appeared for the PPO blocks after forming inclusion complexes, whereas the PEO blocks still remained the narrow line, revealing that β-CDs only thread onto the PPO blocks. The finding of molar ratio of PPO unit to β-CD is identical (3:1) in all inclusion complex systems, providing additional proof that β-CDs are only selectively threaded onto the PPO blocks. The high efficiency of cross-polarization and spin diffusion showed that the mobility of PPO blocks dramatically decreases after β-CD complexation, and thus, exhibited that β-CDs are tightly incorporated onto the PPO blocks. The fact that β-CD can form a site-selective
complex with the PPO blocks, but not the PEO blocks, is attributed to steric fitting and hydrophobic (and/or van der Waals) interaction.

On the basis of bright-filed and selected area electron diffraction (SAED) TEM and two-dimensional (2D) wide angle X-ray diffraction (WAXD) experiments, the supramolecular crystal structure was observed and determined to be a monoclinic lattice for all inclusion complex systems. Each crystal unit cell contained four inclusion complexes. The space group was identified to be $C_2$ symmetry based on the relationship among diffraction spot intensity and systematic extinctions. With the help of computer simulation, the packing of inclusion complexes in the crystal lattice could be achieved. The simulated 2D WAXD fiber patterns and SAED patterns agreed well with the experimental results. The results suggested that the PPO blocks with threaded $\beta$-CDs are the building blocks, and they are closely packed to construct the crystal structure. In addition, the building block was proposed to possess an inclined columnar structure. The explanation for that could be attributed not only to favored tail-to-tail $\beta$-CDs arrangement, which is thermodynamically most stable, but also to the cooperative interactions resulting from hydrogen bonding between $\beta$-CDs as well as spatial fitting between $\beta$-CDs and the atactic PPO chain. Observations of the morphology in TEM combined with the [001]-zone SAED patterns indicated that the supramolecular crystals are lozenge-shaped, bound by four (110) planes. Through combined results of 2D WAXD, SAXS and reduced tethering density calculation, mechanisms of the formation of the supramolecular single crystal were proposed. With observations of phase behaviors of the supramolecular structure based on DSC and 2D WAXD experiments, it is speculated that the tethered
PEO blocks play an important role in the formation and stabilization of the supramolecular crystal structure.

By varying the molecular weight of tethered PEO blocks, the crystallization behavior and crystal orientation of PEO were investigated. The DSC experimental results revealed that the tethered PEO blocks can only crystallize on the supramolecular structures when their molecular weights are high enough. The crystallization of the PEO blocks in inclusion complex systems is greatly hampered due to the depression of the PEO chain mobility by the supramolecular structure. The PEO crystal orientation changes with respect to the surface of the supramolecular structure depends upon crystallization temperature \( T_c \), based on 2D WAXD experiments. Three different \( c \)-axis orientations of the PEO crystals were observed with respect to supramolecular structure depending upon crystallization temperature \( T_c \). When the \( T_c \) is below -35°C, the \( c \)-axis of the PEO crystals is perpendicular to the basal surface normal of supramolecular structure. On the other hand, the \( c \)-axis of the PEO crystals is parallel to the normal of supramolecular crystal structure when the \( T_c \) is higher than -35 °C. In addition, when the samples were quenched to LN\(_2\) from PEO melt, the \( c \)-axis of the PEO crystals is randomly oriented on the supramolecular structure. It is believed that cooperative interplay among confined geometry, primary nucleation density, and the need to achieve high crystallinity, lead to the PEO crystal orientation differences with respect to \( T_c \).
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