ABSTRACT

MALIK, RAVISH. Computer Simulation of Protein-like Copolymers (PLCs). (Under the direction of Dr. Carol K. Hall and Dr. Jan Genzer.)

This thesis describes a computational investigation, using discontinuous molecular dynamics and kinetic Monte Carlo simulation, aimed at the development of protein-like copolymers (PLCs) as compatibilizing agents for polymer blends, and as “drug” delivery agents.

Protein-like copolymers (PLCs) represent a new type of functional copolymer, that exhibit large-scale compositional heterogeneities and long-range statistical correlations along the co-monomer sequence. The concept of PLCs was first introduced by Khokhlov and coworkers who demonstrated using computer simulations that random copolymers with tunable monomer sequences (RCPs) could be generated by adjusting the compactness of a parent homopolymer composed of component A, and then converting exposed segments on the exterior of the coil into B segments by reacting them with specific chemical species in the surrounding solution.

We employed two computer simulation methods to investigate the role of PLCs as interfacial compatibilizers for a polymer blend containing two immiscible homopolymers. We used large-scale equilibrium discontinuous molecular dynamics (DMD) simulations to explore the effect of compatibilizer co-monomer sequence distribution on miscibility and interfacial characteristics of two incompatible homopolymers. Kinetic Monte Carlo (MC) simulations were used to study the phase separation dynamics of immiscible polymer blends compatibilized by PLCs. The effectiveness of PLCs to act as compatibilizers was compared
with those of diblock, simple linear gradient, random, and alternating copolymers. The simulations indicated that for the chain lengths considered PLCs were better compatibilizers than alternating and random copolymers, acted at par with simple linear gradient copolymers, but were not as good as diblocks.

We employed kinetic Monte Carlo to investigate how adding \( \approx 4.92\% \) PLCs composed of segments of type C and D to an immiscible asymmetric A/B binary polymer blend containing 80\% homopolymers of type A and 20\% homopolymers of type B affected the phase separation dynamics. The ability of PLCs to slow down the phase separation process depended sensitively on the interaction energy between the PLCs and homopolymers, the PLC chain length, and the PLC chemical composition. PLCs compatibilized the binary blend more effectively as the attractive interaction between the PLC blocks and homopolymers increased. Nominal improvement in compatibilization of the binary blend was achieved with increasing PLC chain length. For a given interaction energy and chain length C/D PLCs with composition around \( 0.3 \leq x_c \leq 0.5 \) (where \( x_c \) is the mole fraction of the C component in the PLC) acted as the most effective compatibilizers. The growth of phase-separated domains followed a dynamical scaling law for both the A/B binary blend and PLC compatibilized A/C-D/B ternary blend in the late stages of phase separation. The universal scaling functions were nearly independent of the interaction energy, PLC chain length, and PLC chemical composition. The phase-separated domains grew with dynamical self-similarity irrespective of the type of PLC added to the binary
blend, although the type of PLC significantly altered the growth rate of the phase-separated domains.

We also used kinetic Monte Carlo simulation to explore the role of PLCs as “drug” carriers. We examined the assembly of PLCs and delineated the conditions conducive to drug encapsulation. The effects of changes in the system volume fraction, PLC composition, and the strength and range of the interaction between the hydrophobic component of the PLC and the drug on the encapsulation efficiency was explored by performing cluster analysis and evaluating the density profiles of the PLC copolymer segments and those of the drugs. The presence of drug facilitated easier coil-to-globule transition for the PLCs. The interaction strength between the hydrophobic component of the PLC and the drug acted as a coupling parameter that determined whether the system encapsulated or whether the PLCs and drugs aggregated separately.
Computer Simulation of Protein-like Copolymers (PLCs)

by
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DEDICATION

To my father, Dipak Malik, my mother, Ritu Malik, my sister, Bhavana Malik, and my grandmother Sheila Malik. Your affection, sacrifice and support were vital.
BIOGRAPHY

Ravish Malik was born on May 25, 1981 in Chhattisgarh, India. He is the son of Dipak and Ritu Malik and has an elder sister, Bhavana. He moved to Mumbai, MH for five years to pursue primary school, and moved back to Bhilai, CG to attend Delhi Public School. He graduated with a scholar gold medal in June 1999. He attended the Indian Institute of Technology (IIT), Kanpur and earned his B.Tech. in Chemical Engineering in May 2004. After working as a research associate under the guidance of Dr. J.P. Gupta and Dr. Sanjay Gupta at ACMS/CHE, IIT Kanpur, he joined a leading pharmaceutical company Dr Reddy’s Laboratories (NYSE: APD) as a junior project manager in the projects department. He came to Raleigh, NC in August 2005 to pursue a doctorate in chemical engineering at North Carolina State University. He received his M.S. in chemical engineering in December 2007 and defended his PhD in July 2011. While pursuing his PhD he also received a M.S. in financial mathematics (focus on statistics) in December 2010. He will join the PhD career development program at Air Products where his first assignment will be at the computational modeling center under the guidance of Dr Sanjay Mehta.
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CHAPTER ONE

Introduction

1.1 MOTIVATION

Protein-like copolymers (PLC) represent a new type of functional copolymers that exhibit large-scale compositional heterogeneities and long-range statistical correlations between co-monomer units\textsuperscript{1-35}. PLCs represent a cross between block copolymers and random copolymers. They function effectively as block copolymers because they self assemble into unique structures, recognize patterns on surfaces, and act as compatibilizers and interfacial agents. Yet PLCs possess the advantages of random copolymers in that they are easy to fabricate and exhibit tailorable characteristics. Previous studies have demonstrated the effect of co-monomer sequence distribution on the solution and interfacial behavior of copolymers\textsuperscript{4,5,9,10,16,19,36-65}.

Khokhlov and co-workers\textsuperscript{1,2,4} used computer simulation to reveal that random copolymers with tunable co-monomer sequence distributions could (cf. Figure 1.1a), in principle, be generated by adjusting the size (compactness or collapse) of a parent homopolymer made of A segments and converting selected A segments on the homopolymer’s outer periphery into B segments by reacting those segments with other
chemical species in the surrounding solution. Coils that were fully expanded exhibited a random distribution (cf. **Figure 1.1b**) of the “colored” species, while macromolecules that were collapsed possessed random-blocky “protein-like” (cf. **Figure 1.1c**) co-monomer sequences since only monomers that were present on the periphery of the collapsed coil underwent “coloring.” Khokhlov and co-workers also explored the assembly of PLC’s in bulk and at interfaces using molecular simulation and theory, and evaluated various thermodynamic characteristics including coil-to-globule transition and phase behavior\(^1,4-7,9,10,15-19,21,27,28,62,63,66\).

![Figure 1.1](image)

**Figure 1.1** a) Schematic illustrating the method of forming random copolymers by “coloring” homopolymer coils. Depending on the collapse of the parent homopolymer, the resulting random copolymer possesses either (b) random or (c) blocky distribution of monomer units\(^1,2,4\).

Since the introduction of the coloring scheme for preparing PLCs suggested by Khokhlov and co-workers\(^1,2,4,8,18\), several experimental studies have been conducted aimed at synthesizing random copolymers with tunable monomer sequence distributions (RCPs)\(^15,28,58,65,67-71\). Genzer and coworkers\(^65\) synthesized poly(styrene-\textit{co}-4-bromostyrene) (PBr\(_x\)S) RCPs by brominating polystyrene (PS) in solvents with varying degree of solubility. **Figure 1.2** depicts a schematic representation of the experimental “coloring” scheme of Genzer and coworkers for PS in good and poor solvents. While bromination below the theta
temperature (\textit{i.e.}, poor solvent condition) of the parent homopolymer resulted in the formation of blocky PBr$_x$S RCPs, bromination above the theta temperature (\textit{i.e.}, good solvent condition) produced “truly” random PBr$_x$S RCPs. Genzer and coworkers also established that the sequence distribution of 4-BrS in PBr$_x$S PLCs had a profound effect on interfacial properties (\textit{i.e.}, adsorption and desorption$^{65,72}$) and bulk properties (\textit{i.e.}, coil dimension in solution, and solution viscosity$^{73}$).

\textbf{Figure 1.2} (top) PS bromination leading to PBr$_x$S formation, (middle) bromination of parent PS in either good solvent (T$>\theta$, PS chains expanded), or poor solvent (T$<\theta$, PS chains collapsed) conditions, (bottom) PBr$_x$S copolymers with random or random-blocky monomer sequence distributions are generated depending on the solvent quality$^{65}$. 
PLCs could play a significant role in emerging areas important to interfacial chemistry. This idea is based on the expectation that PLCs will behave at surfaces the way that biomolecules do in that they can “recognize” and bind selectively to surfaces with particular chemical patterns and can discriminate between various surface chemical motifs\(^74\). Computer simulation studies and theoretical approaches\(^46\) have demonstrated that in order to achieve pattern recognition, exact control of the monomer sequence distribution is not required. Instead, only statistical matching of distributions on the chain to those on the substrate is needed. PLCs show promise in applications as efficient and inexpensive adhesion promoters with tailored characteristics, polymeric nanoparticles for drug delivery, thin film stabilizers, “seeds” for organizing non-polymeric inclusions, chromatographic separation devices, and compatibilizers for polymer blends.

Computer simulations have proved to be an indispensable tool in studying complex polymeric systems. On the one hand, computer simulations of polymers reaffirm findings from theorists and experimentalists and further extend that knowledge. On the other hand, computer simulations attempt to answer questions that are difficult to answer via experiments. In doing so, the simulator must construct a model of a polymer which contains both the short-range features found in monomeric or atomistic systems and the long-range features, which arise, by definition, from the molecular weight of the polymer in question\(^75-78\). Other features, such as side chains, backbone angles, time scales, charges and solvent qualities, that is, all of the complexities found in nature, must be considered if one is to investigate highly complex (and ultimately, more interesting) systems\(^79-82\). Fortunately, the processing capability of modern computers grows
increasingly more powerful each day, allowing one to advance the collective knowledge about polymers.

This Ph.D. dissertation describes computational research aimed at supporting the development of protein-like copolymers as compatibilizers for immiscible polymer blends, and as “drug” delivery agents. We employ discontinuous molecular dynamics (DMD) simulations to understand the role of PLCs as compatibilizers for immiscible polymer blends from a thermodynamic equilibrium perspective. We also use lattice Monte Carlo (MC) simulations based on the bond fluctuation model to study the dynamics of phase separation of immiscible polymer blends in the presence of PLCs. We also utilize lattice MC simulations to access the viability of PLCs as “drug” delivery agents.

1.2 OVERVIEW

This section provides a summary of the Ph.D. dissertation. All chapters supply their own literature review and references.

In Chapter 2 we describe the results of DMD computer simulations aimed at understanding the role of PLCs as compatibilizing agents for a polymer blend containing two incompatible homopolymers (A/B). The effectiveness of PLCs to act as compatibilizers is compared to that of block, alternating and random copolymers at low copolymer concentration (≈0.66%). PLCs localize at the A/B interface and are oriented preferentially parallel to it, judged by comparing the parallel and perpendicular components of the radius of
gyration ($\langle R_g^2 \rangle > \langle R_g^3 \rangle$). At lower temperatures PLCs possess higher interfacial width than random and alternating copolymers as they penetrate the A/B interface more than random and alternating copolymers with the same chemical composition; the PLCs are very efficient at making multiple connection points across the A/B interface. The average fraction of crossings for PLCs is as high as 80% of the number of junction points, i.e. the number of bonds between A and B monomers in the A-B copolymer. PLCs are likely to outperform random and alternating copolymers as efficient interfacial stabilizers.

In Chapter 3 we present the results of kinetic MC simulations aimed at exploring the effect of copolymer sequence distribution on the dynamics of phase separation of an immiscible A/B binary homopolymer blend. Diblock, alternating, random, PLCs, and simple linear gradient copolymers having equal number of A and B segments, with identical chemical composition and chain length are considered as compatibilizers. All copolymers irrespective of their sequence retard the process of phase separation by migrating to the biphasic A/B homopolymer interface, thereby minimizing the interfacial energy and promoting adhesion between the homopolymer-rich phases. As expected, diblock copolymers perform the best; each block of the A-B block copolymer penetrates the energetically favorable homopolymer-rich phase making entanglements with the homopolymers. Alternating copolymers lie at the interface and PLCs, simple linear gradient and random copolymers weave back and forth across the interface. The weaving and penetration is more pronounced for PLCs than for simple linear gradient and random copolymers. Judging by the contact analysis, extension and orientation of the copolymers at
the interface, and structure factor calculations, it is evident that for the chain lengths considered in our computer simulations, PLCs are not as good as diblocks but are better compatibilizers than alternating and random copolymers, and are on par with simple linear gradient copolymers.

In Chapter 4 we use kinetic MC simulation based on the bond fluctuation model to investigate how adding $\approx 4.92\%$ PLCs to an immiscible binary polymer blend affects the dynamics of phase separation. PLCs slow down effectively the process of phase separation in binary A/B blends by migrating to the biphasic interface, thereby reducing the interfacial tension. The ability of PLCs to retard effectively the process of phase separation depends sensitively on the interaction energy between the PLCs and homopolymers, and the PLC chain length. PLCs compatibilize the binary blend more effectively with increasing attractive interaction between the PLC blocks and the homopolymers. Nominal improvement in compatibilization of the binary blend is achieved with increasing PLC chain length. The growth of phase-separated domains follows a dynamical scaling law for both the binary blend and PLC compatibilized ternary blend in the late stages of phase separation. The universal scaling functions are nearly independent of the interaction energy and PLC chain length. Thus the phase-separated domains grow with dynamical self-similarity irrespective of the type of PLC added to the binary blend, although the type of PLC significantly alters the growth rate of the phase-separated domains.

In Chapter 5 we use kinetic MC simulation based on the bond fluctuation model to investigate how adding $\approx 4.92\%$ 70-mer PLC made of C and D segment to an immiscible asymmetric A/B binary polymer blend containing 80% homopolymers of type A and 20%
homopolymers of type B affects the phase separation dynamics. The segments of type C (or D) possess attractive interactions with segments of homopolymer A (or B). The ability of PLCs to retard effectively the phase separation process depends sensitively on the composition of PLCs. PLCs with composition around $0.3 \leq x_c \leq 0.5$ (where $x_c$ is the mole fraction of the C component in the PLC) are most effective in compatibilizing the A/B binary blend. The universal scaling functions for the growth of phase-separated domains in PLC compatibilized blends during the late stages of phase separation are nearly independent of the PLC composition.

In Chapter 6 we explore the utilization of protein-like copolymers (PLCs) as vehicles for the transportation of “drugs” to their intended targets and as a means of increasing drug solubility. We perform kinetic Monte Carlo simulations on systems containing PLCs and model drug molecules in order to understand how PLCs assemble and what system conditions encourage good encapsulation. In this chapter, we detail the effect of system volume fraction, PLC chemical composition, strength and range of the interaction between hydrophobic segments on the PLC and drug molecules on the encapsulation efficiency. The density profiles of the hydrophobic, hydrophilic, and the drug segments within the PLC globule are calculated to gauge the encapsulation efficiency. We find that the presence of drug in the system affects the conditions at which the PLC coil to globule transition occurs. We also find that the interaction strength between hydrophobic component of the PLC and the drug acts as a coupling parameter that determines whether the system encapsulates or whether the copolymer and drug aggregate separately. Our results can be used by experimentalists as a framework for optimizing drug encapsulation.
In Chapter 7 we make suggestions for future work on PLCs as compatibilizers, as nanoparticles for drug delivery, as agents to disperse inorganic fillers in fabrication of polymeric nanocomposites, and as surface-based probes for pattern recognition.

In Appendix A we describe advanced statistical analyses to characterize the distribution of block lengths in 10000-mer PLCs, and quantify the long-range correlations along the PLC sequence. We propose an iterative coloring scheme to generate PLCs as an alternative to Khokhlov’s instantaneous coloring algorithm.

Chapters 2, 3, 4, 5, and 6 are based on the following publications.


Chapter 4: Malik, R., Hall, C. K. & Genzer, J. “Phase Separation Dynamics for a Polymer Blend Compatibilized by Protein-like Copolymers: a Monte Carlo Simulation”, *Macromolecules (submitted)*.

Chapter 5: Malik, R., Hall, C. K. & Genzer, J. “Effect of Protein-like Copolymers Composition on the Phase Separation Dynamics of a Polymer Blend: a Monte Carlo Simulation”, *Soft Matter (to be submitted for publication)*.

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CHAPTER TWO

Protein-like Copolymers (PLCs) as Compatibilizers for Homopolymer Blends

2.1 INTRODUCTION

Polymer blending represents a cost effective method for formulating new soft materials. The properties of polymer blends can be fine-tuned by varying the composition and the types of polymers that are mixed. However, polymer blending is challenging because polymers are usually chemically incompatible. Because the low entropic gain upon mixing cannot compensate the enthalpic losses due to unfavorable interactions, most polymer blends tend to macro-phase separate, thereby limiting their potential applications. Macromolecular compatibilizers are typically added to overcome these difficulties. They segregate preferentially at the interface between the two immiscible homopolymers, thereby reducing interfacial tension and increasing structural integrity and homogeneity leading to improved stability and mechanical strength of the interface. While block copolymers have been used readily to improve the properties of immiscible polymer interfaces, a few studies suggested that random copolymer may, under certain circumstances, act as effective compatibilizing
agents as well. In this paper we discuss how the compatibilization efficacy of random copolymers can be tuned by adjusting the co-monomer sequences.

Protein-like copolymers (PLCs) represent a new class of functional copolymer that exhibits large-scale compositional heterogeneities and long-range correlations along the co-monomer sequence\textsuperscript{1-3}. The concept of PLCs was first introduced by Khokhlov and coworkers\textsuperscript{2,3} who used computer simulations to demonstrate that random copolymers with tunable monomer sequences could be generated by adjusting the compactness of a parent homopolymer composed of component A, and then converting exposed segments on the polymer surface into B segments by reacting them with other species in the surrounding solution. In a series of papers, Khokhlov and co-workers explored the assembly of such simulated PLCs in the bulk and at interfaces and evaluated various thermodynamic characteristics\textsuperscript{1-12}.

The sequence along the copolymer compatibilizer has a profound effect on the phase behavior and interfacial characteristics of the blend to be compatibilized. Dadmun\textsuperscript{13} used lattice Monte Carlo (MC) simulations based on the bond fluctuation model (BFM) to explore the effect of copolymer sequence distribution on the interfacial structure and miscibility of a compatibilized polymer blend containing a copolymer and two homopolymers. Dadmun considered block, alternating, random, random-alternating and random-block copolymer sequences as compatibilizers. His results suggest that alternating and block copolymers represent the best interfacial modifiers while random copolymers are the worst interfacial modifiers. Dadmun also reported that the departure of copolymer sequence from a purely random copolymer (i.e., random-alternating or random-block sequence) has a profound effect
on the performance of the copolymer as an interfacial stabilizer. Using the BFM MC approach, Kamath and Dadmun\textsuperscript{14} further explored the effect of the copolymer chain architecture on the dynamics of a binary blend formed by dispersing AB copolymers in a homopolymer A. They considered random, random-blocky, block, and alternating AB copolymer sequences and found that random and random-blocky copolymers are ideal compatibilizers as they move rapidly through the matrix phase within which they distribute uniformly. Using lattice MC simulations Ko et al.\textsuperscript{15} examined the effect of compatibilizer sequence distribution on the phase separation dynamics of binary blends. They established that block copolymers possessed the best ability to retard the phase separation while random compatibilizers outperformed alternating copolymers. Balazs and DeMeuse\textsuperscript{16} extended the formalism of Flory-Huggins theory and calculated the effect of the copolymer sequence on the phase diagrams for homopolymer A / homopolymer B / copolymer AB ternary systems at different copolymer concentrations. They reported that diblock copolymers were not always the optimal thermodynamic compatibilizers for a blend. Lyatskaya et al.\textsuperscript{17} employed numerical self-consistent mean field methods to calculate the reduction in interfacial tension upon adding copolymer compatibilizers of varied sequence to a binary blend. Their study revealed that for a fixed copolymer molecular weight, block copolymers were the best interfacial compatibilizers, but longer random copolymers outperformed shorter block copolymers in reducing the interfacial tension between incompatible homopolymer phases.

Since the introduction of the coloring scheme for preparing PLCs suggested by Khokhlov and co-workers\textsuperscript{1-3,18,19}, several experimental studies have been conducted aimed at synthesizing random copolymers with tunable monomer sequence distributions (RCPs)\textsuperscript{20-28}. 
Recently Genzer and coworkers\textsuperscript{28} synthesized poly(styrene-\textit{co}-4-bromostyrene) (PBr\textsubscript{x}S) RCPs by brominating polystyrene (PS) in solvents with varying degree of solubility. While bromination below the theta temperature of the parent homopolymer resulted in the formation of blocky PBr\textsubscript{x}S RCPs, bromination above the theta temperature resulted in the formation of random PBr\textsubscript{x}S RCPs. Genzer \textit{et al} also found that the sequence distribution of 4-BrS in PBr\textsubscript{x}S PLCs has a profound effect on interfacial properties (i.e., adsorption and desorption\textsuperscript{28,29}) and bulk properties (i.e., coil dimension in solution and solution viscosity\textsuperscript{30}).

To this point most experimental and theoretical research on compatibilizers has focused on the performance of block, random, alternating, random-blocky and random-alternating copolymers as compatibilizers for incompatible homopolymers blends. The use of PLCs as potential compatibilizers for immiscible homopolymers blends has not been explored. Since for a given degree of polymerization and composition, PLCs are blockier than random, alternating, random-blocky and random-alternating copolymers\textsuperscript{6} they are more likely to form entanglements with homopolymer rich phases. They are also more likely to weave back and forth across the interface, binding the two homopolymers phases together, and thus acting as effective compatibilizers for incompatible binary blends. This work focuses on utilizing PLCs as interfacial compatibilizers.

In this paper we present the results of discontinuous molecular dynamics (DMD) computer simulations aimed at supporting the development of PLCs as compatibilizing agents for a polymer blend containing two incompatible homopolymers. The DMD simulations are performed on an incompatible binary blend containing 530 38-mers of homopolymer A and 530 38-mers of homopolymer B, mutually immiscible, to which a small
number (≈0.66%) of 38-mers containing equal number of A and B monomers in the copolymer are added. Diblock, alternating, random, and PLCs made of A and B units are considered as copolymer compatibilizers. Initially the ternary blend system is equilibrated at high temperature and slowly cooled so that the homopolymers phase separate and the A-B copolymers end up localizing at the interface. The density profiles and the orientation of the different copolymers at the interface are evaluated in order to investigate the mechanism by which the copolymers stabilize the interface. To establish the efficacy of the various copolymer sequences the interfacial width of the binary (no-copolymer) as well as the ternary (compatibilized) blend is calculated. Since it is difficult to assess directly the number of entanglements made by the copolymer compatibilizer with the respective homopolymer phases, the average number of crossings made by the copolymer across the interface is calculated and used as a proxy for the number of copolymer-homopolymer entanglements. The design of the DMD simulation is inspired by the work of Dadmun$^{13}$ on the effect of the copolymer sequence distribution on the interfacial characteristics and miscibility of a blend containing two homopolymers. Following Dadmun’s$^{13}$ work very few copolymer chains were added to the compatibilized blend so that the incompatible homopolymers would phase separate, leading to the formation of a interface, and the copolymers would migrate to the interface. However, our work goes beyond that of Dadmun$^{13}$ as we have explored PLCs as potential compatibilizers and compared their performance to block, alternating, and random copolymers. Since it is easier to delineate the copolymer sequence effects for longer chains we have used 38-mer (close to the entanglement length$^{31,32}$) polymer chains; both the copolymers and homopolymers employed in Dadmun’s$^{13}$ work were 10-mers. To gain better
insight into the weaving effect of various copolymer sequences we have estimated the average number of crossings made by the various copolymer sequences across the interface, the average crossing length and the normalized number of crossings.

Highlights of our results are as follows. The two incompatible homopolymers A and B in the compatibilized blend phase separate upon annealing; the copolymers migrate to the A/B interface regardless of the copolymer sequence. The width of the density profile for block (A-b-B) copolymers across the interface is largest followed by those for A-B PLCs, random (A-co-B) and alternating (A-alt-B) copolymers. The interfacial width of the ternary (compatibilized) blend for the various copolymer sequences is higher than the binary (no-copolymer) blend. The interfacial width of the block copolymer compatibilized blend is highest followed by PLCs, random and alternating copolymer compatibilized blends. The radius of gyration of the copolymer perpendicular \( \langle R_g^2 \rangle_\perp \) and parallel \( \langle R_g^2 \rangle_\parallel \) to the interface is evaluated and presented. Block copolymers stretch most across the interface while alternating copolymers stretch least across the interface. PLCs stretch more across the interface than random copolymers at \( T^* \leq 2 \), where \( T^* \) is a reduced temperature. Alternating copolymers stretch most along the interface while block copolymers stretch least along the interface. Random copolymers stretch more along the interface than PLCs at \( T^* < 4 \). The average number of crossings across the interface made by different copolymers is calculated. Alternating copolymers make the most number of crossings, followed by random, PLCs and block copolymers. The average crossing length for block copolymers is highest followed by those for PLCs, random and alternating copolymers. To estimate the efficiency of the knitting effect of the copolymer; the average number of crossings across the interface is
normalized by the number of junction points, i.e., the number of bonds between A and B spheres in the AB copolymer. Apart from block copolymers, PLCs are very efficient in making multiple crossings across the interface compared to the other copolymer sequences investigated. The average number of crossings across the interface is as high as 80% of the total number of junction points for the PLCs, which suggests that high molecular weight PLCs might be very efficient in stabilizing the interface.

In the next section, we describe the DMD method and the generation of PLCs via the instant coloring procedure of Khokhlov and co-workers. The following section presents the simulation results for various copolymer sequences. The final section concludes with a short summary of the results and a discussion.

### 2.2 MODEL AND METHOD

The binary blend system consists of 530 38-mers of A chains and 530 38-mers of B chains. The ternary (compatibilized) blend consists of the binary blend plus 7 38-mers of copolymer chains containing monomers of types A and B with composition \( x_A = x_B = 0.5 \). The chain lengths for the homopolymer/copolymer are chosen as 38 since it is close to the entanglement length of the polymer chains present in the blend.\(^{31,32}\) The number of copolymer chains is chosen to be low (7 or \( \approx 0.66\% \)) to prevent compatibilization and to ensure the formation of an interface in the copolymer blend system at low reduced temperature after equilibrium is attained. Because in the phase-separated “compatibilized” blend the
copolymers are likely to be present at the interface, we can make inferences about the relative efficiency of the copolymers by calculating several properties discussed later in this section. The copolymers and homopolymers are modeled as flexible chains of nearly-tangent spheres.

In order to increase computational efficiency we have chosen to have the two components A and B repel each other instead of having attractive A-A and attractive B-B interactions. Therefore, the A-A and B-B interactions are modeled using a hard sphere potential while the incompatibility between A and B components is modeled as a repulsive square-shoulder potential of strength $\varepsilon_{AB}$ which extends to an intermolecular separation $\lambda\sigma$ with $\lambda=1.5$. The resulting potentials are:

\[
U_{AA}(r) = U_{BB}(r) = \begin{cases} 
\infty & \text{if } r \leq \sigma \\
0 & \text{if } r > \sigma 
\end{cases} 
(2.1)
\]

\[
U_{AB}(r) = \begin{cases} 
\infty & \text{if } r \leq \sigma \\
\varepsilon_{AB} & \text{if } \sigma < r \leq \lambda\sigma \\
0 & \text{if } r > \lambda\sigma 
\end{cases} 
(2.2)
\]

The packing fraction, $\eta = \pi N \sigma^3/(6V)$, for the pure as well as compatibilized blend is set to $\eta=0.35$, where N is the number of spheres in the simulation box, and V is the volume of the simulation box.

In a DMD computer simulation, particles experience collisions when they encounter a discontinuity in the potential such as the boundary of a hard sphere, square well or square shoulder potential. Between collisions, particles move along linear trajectories, making the simulation technique faster than traditional MD simulations. The post-collision velocities can be found by solving the collision dynamics equations. In order to treat chains of spheres effectively, Rapaport created bonds by restricting the distance between adjacent spheres.
along a chain to lie between $\sigma$ and $\sigma(1+\delta)^{33,34}$. Bellemans later extended this model so that the distance between adjacent spheres is allowed to lie between $\sigma(1-\delta/2)$ and $\sigma(1+\delta/2)$, making the average bond length $\sigma^{35}$. The temperature of the system and, concordantly, the total kinetic energy are held constant throughout the DMD simulation. To regulate temperature, we employ a heat bath in the form of an Andersen thermostat$^{36}$, which allows the temperature to fluctuate about an average system temperature, $T^* = k_B T / \epsilon_{AB}$. This is accomplished by having spheres collide stochastically with “ghost” particles, which then change the spheres’ velocity.

In order to characterize statistically the different types of AB copolymer sequences used as compatibilizers we need to introduce the uniformity factor developed by Dadmun$^{13}$. The uniformity factor for component A is defined as:

$$U_A = \left[ \sum_{l=1}^{L-1} s_l \right] + 1 / (L_A - 1)$$

(2.3)

where $s_l$ is 1 if the $l$-th and $(l+1)$-st sphere are type A, -1 if the $l$-th sphere is type A and the $(l+1)$-st sphere is B type and 0 if the $l$-th sphere is B type regardless of the type of $(l+1)$-st sphere. Here $L$ is the total number of monomers in the copolymer and $L_A$ is the total number of A spheres in the copolymer. By definition, compositionally symmetric (50% A, 50% B) alternating copolymers have uniformity factor -1, symmetric block copolymers have uniformity factor 1 and symmetric random copolymers have uniformity factor 0. The uniformity factor for symmetric PLCs should lie roughly halfway between those for random and block copolymers.
The symmetric random AB copolymer was generated using the following algorithm. Starting with a homopolymer A, spheres were picked randomly and changed to type B if the sphere chosen was of type A. This process was repeated till the desired composition was achieved and the uniformity factor for components A and B in the random AB copolymer sequence was reduced to zero.

The symmetric AB 38-mer PLCs were generated via a simulation-based instantaneous coloring procedure originally proposed by Khokhlov et al.\textsuperscript{1-3}. A 38-mer A chain with square well interactions (well width $\lambda_{AA}=1.5$) between non adjacent A spheres was initialized in a random coil configuration. Figure 2.1a shows the initial configuration. DMD simulations were performed on the 38-mer A chain at a low reduced temperature $T^*=k_B T/|\epsilon_{AA}|=1.0$. The simulation box was chosen big enough (box length 15) so that the isolated chain did not interact with its periodic images. The chain collapsed to a globular conformation after about 1 million DMD moves. Figure 2.1b shows a snapshot of the resulting globular conformation. The spheres in the final globular conformation were sorted in order of their distance from the center of the globule. The 19 spheres farthest from the center were colored to be B as depicted in Figure 2.1c. The coloring procedure resulted in the creation of an AB PLC with composition $x_A = x_B = 0.5$. After the coloring procedure the AB PLC was relaxed. Figure 2.1d shows a snapshot of the symmetric AB 38-mer PLC generated via the instantaneous coloring procedure. Figure 2.2 illustrates the four copolymer sequences considered (a) block, (b) random, (c) alternating and (d) PLCs.
DMD simulations were performed on the binary and ternary blend systems. The simulations on the blend systems were started in a random configuration at the desired packing fraction. Both blend systems were relaxed at an initial high temperature $T^*=20$ and then annealed slowly in steps of $\Delta T^*=1$ till $T^*=1$ was achieved. At each temperature DMD simulations were performed for 6 billion moves to allow for sufficient equilibration of the system.

The morphology and interfacial characteristics of the blend were characterized via the following measures: 1) the density profiles of homopolymers A and B and the copolymer with respect to the interface, 2) the interfacial width of the binary (no-copolymer) and the ternary compatibilized blend, 3) the radius of gyration of the copolymer perpendicular to the interface, $\langle R_g^2 \rangle_\perp$, 4) the radius of gyration of the copolymer parallel to the interface, $\langle R_g^2 \rangle_\parallel$, 5) the shape anisotropy of the copolymer coil, defined here as $\langle R_g^2 \rangle_\parallel - \langle R_g^2 \rangle_\perp$, 6) the average number of crossings made by the copolymer across the interface, $<N_t>$, 7) the average length of a crossing made by the copolymer across the interface, and 8) the normalized number of crossings made by the copolymer across the interface, $<L_t>$.

We use the density profiles of homopolymer A, homopolymer B, and copolymer AB to calculate the interfacial width of the binary (no-copolymer) as well as the ternary (compatibilized) blend utilizing the approach developed by Helfand and coworkers$^{37-40}$. Under the Helfand approach the interfacial width for the binary and ternary blend is defined by the following formulas:

$$w_{AB} = \int_{-\infty}^{\infty} \Phi_A(x)\Phi_B(x)dx \quad (2.4)$$
\[ w_{ABC} = \int_{-\infty}^{\infty} \{ \Phi_A(x)\Phi_B(x) + \Phi_A(x)\Phi_C(x) + \Phi_B(x)\Phi_C(x) \} dx \]  \hspace{1cm} (2.5)

where \( w_{AB}, w_{ABC} \) is the interfacial width of the binary (no-copolymer) and ternary (compatibilized) blend respectively. \( \Phi_A(x), \Phi_B(x), \Phi_C(x) \) are local volume fractions of the homopolymer A, homopolymer B, copolymer AB respectively and \( x \) in the direction perpendicular to the A/B interface.

The radius of gyration of the copolymer perpendicular and parallel to the interface is defined by the following formulas:

\[
\langle R^2_g \rangle_\perp = \frac{\sum_{i=1}^{N} \sum_{j=1}^{L} \sum_{k=1}^{L} (r(i,j)_\perp - r(i,k)_\perp)^2}{2(L)^2 N} \]  \hspace{1cm} (2.6)

\[
\langle R^2_g \rangle_\parallel = \frac{\sum_{d=1}^{2} \sum_{i=1}^{N} \sum_{j=1}^{L} \sum_{k=1}^{L} (r(i,j)_\parallel - r(i,k)_\parallel)^2}{4(L)^2 N} \]  \hspace{1cm} (2.7)

Here \( r(i,j)_\perp \) is the position of the \( j \)-th monomer on the \( i \)-th copolymer chain along the direction perpendicular to the interface and \( r(i,j)_\parallel \) is the position of the \( j \)-th monomer on the \( i \)-th copolymer chain along the direction parallel to the interface, \( N \) is the number of copolymer chains, \( L \) is the number of spheres in a single copolymer chain, \( d \) refers to the two directions parallel to the interface in the phase separated regime of the compatibilized blend. Equations (2.6) and (2.7) for \( \langle R^2_g \rangle_\perp \) and \( \langle R^2_g \rangle_\parallel \) are mathematically equivalent to the formula for the radius of gyration involving the center of mass. The anisotropy of the copolymer chain is characterized by the parameter \( \alpha \) which is defined to be:

\[ \alpha = \langle R^2_g \rangle_\parallel - \langle R^2_g \rangle_\perp \]  \hspace{1cm} (2.8)

The average number of crossings, \( <N_t> \) at a given temperature is calculated by locating the interface in the phase separated compatibilized blend after equilibrium is
attained, calculating the number of times a copolymer chain intersects the interface followed by averaging over all the copolymer chains. The average length of the crossing \(<L_i>\) across the interface for a copolymer is defined as: \(<L_i> = \frac{L}{\langle N_i \rangle + 1}\), where \(L\) is the length of the copolymer and \(\langle N_i \rangle\) is the average number of crossings across the interface made by the copolymer.

The system properties for both the binary and ternary blend systems were averaged over five runs starting from uncorrelated random initial configurations. The results for ternary blends compatibilized by PLCs or random copolymer were averaged over ten different copolymer sequences for a given initial configuration. Thus, fifty simulations were performed for ternary blends compatibilized by either PLCs or random copolymer. The error bars depicted for each graph represent the sample standard deviations of the properties calculated and plotted on the graphs.

### 2.3 RESULTS AND DISCUSSION

Snapshots of the symmetric binary blend system are shown in Figure 2.3. Figure 2.3a shows that the binary blend is homogeneous at initial high temperature \(T^*=20\). After the binary blend is annealed to low temperature \(T^*=1\), the two incompatible homopolymers have phase separated, forming an interface (cf. Figure 2.3b). Snapshots of the ternary blend with PLCs as the compatibilizing agent are shown in Figure 2.4. Specifically, Figure 2.4a demonstrates that the compatibilized blend is initially homogeneous at \(T^*=20\). After
lowering the system temperature to $T^*=1$, the two incompatible homopolymers have phase separated, forming an interface with PLCs localized at the interface (cf. Figure 2.4b). Similar trends are observed for the other compatibilized blend systems containing block, alternating and random copolymers. In order to locate the direction of phase separation, the concentration distribution of components A and B along the three directions are regularly monitored during the simulation of the binary and ternary blend systems. At high temperatures the components A and B in the blend are distributed uniformly. At lower temperatures as the phase separation occurs, the concentration distribution of components A and B along the direction of phase separation is non-uniform, unlike those in the other two directions. Once the direction of phase separation has been established for the blend systems in the phase separated regime, the interface can be located by calculating the gradient of the concentration distribution of components A and B along the direction of phase separation.

Figure 2.5 shows the density profiles of the two homopolymers and copolymer from the four compatibilized blends with $\approx 0.66$ % (a) block, (b) random, (c) alternating and (d) PLCs at $T^*=1$ along the direction of phase separation. All copolymer sequences end up localizing at the interface, thereby stabilizing the interface. None of the copolymer sequences act as thermodynamic compatibilizers as intended, i.e., they are unable to prevent the phase separation of the incompatible homopolymers as the amount of copolymer added is intentionally very low ($\approx 0.66$ %). Due to the periodic boundary conditions there are two interfaces present in the system. The width of the density profile for block copolymers across the interface is highest followed by those for PLCs, random, and alternating copolymers. The wider the density profile of the copolymer across the interface, the more the copolymer
penetrates the homopolymer-rich phases leading to entanglements and better interfacial strength. **Figure 2.6** shows the interfacial width of the binary (no-copolymer) and ternary (compatibilized) blend as a function of the reduced temperature. The interfacial width of the compatibilized blend for the various copolymer sequences is higher than the binary blend which clearly shows that all the four copolymer compatibilizers act as effective interfacial stabilizers. The interfacial width of block copolymers is highest followed by PLCs, random, and alternating copolymers.

In order to act as an effective interfacial modifier, a copolymer compatibilizer must migrate to the interface and weave across the interface thus promoting adhesion between the immiscible phases by knitting them together. Thus an ideal copolymer compatibilizer is one which maximizes the number of entanglements it makes with the homopolymers on either side of the interface. Since it is difficult to quantify directly the number of entanglements made by the copolymer with the homopolymer, an alternative way is to look at the orientation of the copolymer with respect to the interface via the radius of gyration parallel and perpendicular to the interface and the average number of crossings made by the copolymer across the interface. If the copolymer is stretched sufficiently perpendicular to (and spaced well parallel across) the interface, thus making numerous crossings across the interface, it is more likely to form entanglements with the homopolymers and act as an effective interfacial modifier.

The orientation of the copolymer at the interface depends upon the sequence of the copolymer and the temperature. **Figure 2.7a** shows the radius of gyration of the copolymer perpendicular to the interface \( \langle R_g^2 \rangle_\perp \) versus the reduced temperature for the four copolymer
compatibilizers. Block copolymers stretch most across the interface while alternating copolymers stretch least. PLCs penetrate the interface more than random copolymers at T*≤2. The reason for this switching behavior between PLCs and random copolymer is unclear. Thus block copolymers stabilize the interface by penetrating into the homopolymer phase on either side of the interface, allowing the formation of entanglements and the reduction of unfavorable contacts. Figure 2.7b shows the radius of gyration of the copolymer parallel to the interface \( \langle R_g^2 \rangle \parallel \) versus the reduced temperature for the four copolymer compatibilizers. Alternating copolymers stretch most along the interface while block copolymers stretch least. Random copolymers stretch more along the interface than PLCs at T*<4. The reason for this switching behavior between PLCs and random copolymer is unclear. At any given temperature \( \langle R_g^2 \rangle \perp \) is greater than \( \langle R_g^2 \rangle \parallel \) for the block copolymer, which implies that the block copolymer volume is shaped like a cylinder driven into the interface. Since the diblock copolymer barely covers the interface each of the two blocks of the diblock copolymer adopt a mushroom type configuration. At a given temperature for alternating, random and PLCs, \( \langle R_g^2 \rangle \parallel \) is greater than \( \langle R_g^2 \rangle \perp \) which suggests that copolymer volumes for these sequences are shaped like a pancake.

The preferred orientation of the copolymer with respect to the interface can be characterized by the anisotropy as measured by the parameter \( \alpha \) defined earlier. Figure 2.7c shows a plot of \( \alpha \) versus the reduced temperature for the four copolymer sequences. Anisotropy increases as temperature decreases for all the four copolymer compatibilizers, revealing that as the thermal fluctuations decrease the copolymers adopt a preferred lower
energy configuration at the interface. Alternating copolymers are most anisotropic, while block copolymers are least anisotropic. Random copolymers are more anisotropic than PLCs at $T^* \leq 3$. The reason for this switching behavior between PLCs and random copolymer is unclear.

Figure 2.8 depicts the side view of the simulation box parallel to the interface (left panel) as well as the top view of the simulation box perpendicular to the interface (right panel) for each of the four compatibilized blends with $\approx 0.66\%$ copolymer after equilibrium has been attained at $T^*=1$. Block copolymers (Figures 2.8a, 2.8b) orient preferentially perpendicular to the interface penetrating the homopolymer phases on either side of the interface. Alternating copolymers (Figures 2.8e, 2.8f) prefer to lie parallel to the interface. Random copolymers (Figures 2.8c, 2.8d) and PLCs (Figures 2.8g, 2.8h) also prefer to lie parallel to the interface although to a lesser degree than alternating copolymers.

Since the primary mechanism for interfacial compatibilization of the immiscible homopolymer blends containing random, alternating and PLC is knitting across the interface, the average number of crossings made by the different copolymers across the interface is an important factor in determining the relative performance of the copolymer sequences as effective compatibilizers. Figure 2.9a depicts the average number of crossings across the interface as a function of the reduced temperature for the four copolymer sequences. Alternating copolymers make the highest average number of crossings across the interface followed by random, PLCs, and block copolymers. These findings are consistent with the fact that alternating copolymers stretch most along the interface (i.e., $\langle R_g^2 \rangle_\parallel$ is high) and have the highest number of junction points for a given degree of polymerization and composition.
of the copolymer, i.e., the number of bonds between A and B spheres in the AB copolymer. Block copolymers make a single crossing across the interface as they have just one junction point. Random copolymers make more crossings across the interface than PLCs as they have a higher number of junction points than PLCs. At $T^* = 1$ the average length of the crossing for the different copolymers is: block ($38/2 \approx 19$), alternating ($38/14.5 \approx 2.6$), random ($38/11.5 \approx 3.3$) and PLCs ($38/8 \approx 4.8$). Apart from diblock copolymers, PLCs have the highest average crossing length. When the average number of crossings across the interface is normalized by the number of junction points in the copolymer an interesting trend arises. Figure 2.9b shows the normalized number of crossings across the interface versus the reduced temperature for the four copolymer sequences. Apart from diblock copolymers, PLCs are very efficient in making multiple crossings across the interface compared to any other copolymer sequences. The average number of crossings across the interface for PLCs is as high as 80% of the number of junction points for the PLC, which suggests that high molecular weight PLC might be very efficient in stabilizing the interface.

Our results are in good agreement with the lattice Monte Carlo simulations of Dadmun\textsuperscript{13} for block, random and alternating copolymers. The simulation results from Dadmun’s work on random-block (uniformity factor of 0.5) copolymers cannot be extended directly to PLCs for comparison as random-block copolymers have a sequence distribution different than PLCs. Moreover the copolymer chains used (10-mer) in Dadmun’s work were shorter (below the entanglement length) and it is certainly easier to detect sequence effects accurately for longer copolymer chains. Further support for this is Khokhlov’s\textsuperscript{6} demonstration that random-block copolymers (whose block length obeys a Poisson
distribution) are statistically different from PLCs (which obey Levy flight statistics for the block length), despite having the same composition and average block length (or uniformity factor) for both types of copolymers. Although we have conducted the computationally intensive simulations for only one copolymer concentration (≈0.66% at which the copolymers barely saturate the interface), we believe that the general trends amongst the various copolymer sequences hold true even at higher copolymer concentrations. Further studies of blends with higher copolymer concentrations are in progress and will be the subject of future publications.

2.4 CONCLUSION

We have performed discontinuous molecular dynamics simulations aimed at supporting the development of protein-like copolymers (PLCs) as compatibilizing agents for a polymer blend containing two incompatible homopolymers. The results are compared to those for systems with block, alternating and random copolymers acting as compatibilizers. As the compatibilized blend was annealed from high to low temperature the two incompatible homopolymers phase separated and the copolymers migrated to the interface. None of the added copolymers prevented the phase separation because the amount of copolymer added (≈0.66 %) was intentionally too low. We calculated the density profiles of the copolymer and homopolymers in the compatibilized blend along the direction of phase separation. The width of the density profile for block copolymers across the interface was
highest followed by those of PLCs, random, and alternating copolymers. The wider the density profile of the copolymer across the interface, the more the copolymer penetrates the homopolymer-rich phases leading to entanglements and better interfacial strength. We also calculated the interfacial width of the binary (no-copolymer) and ternary (compatibilized) blend. The interfacial width of the compatibilized blend for the various copolymer sequences is higher than the binary blend which clearly shows that all the four copolymer compatibilizers act as effective interfacial stabilizers. The interfacial width of block copolymers is highest followed by PLCs, random, and alternating copolymers.

The orientation of the copolymer at the interface depended upon the sequence of the copolymer. The radii of gyration of the copolymer perpendicular ($\langle R_g^2 \rangle_\perp$) and parallel ($\langle R_g^2 \rangle_\parallel$) to the interface were monitored. Block copolymers stretched most across the interface while alternating copolymers stretched least. PLCs stretched more across the interface than random copolymers at $T^* \leq 2$. Alternating copolymers stretched most along the interface while block copolymers stretched least. Random copolymers stretched more along the interface than PLCs at $T^* < 4$. The reason why the orientation of PLCs relative to random copolymers switches as we reduce the temperature is unclear.

To gain deeper insight into the interfacial behavior and relative compatibilizing efficiency of the various copolymer sequences, the average number of crossings across the interface made by different copolymers was calculated. Since alternating copolymers have the highest number of junction points across the interface they make the largest average number of crossings, followed by random, PLCs, and block copolymers. The average crossing length for block copolymers was highest followed by those for PLCs, random, and
alternating copolymers. The average number of crossings across the interface was normalized by the number of junction points to estimate the efficiency of the knitting effect of the copolymer. Apart from block copolymers, PLCs were very efficient in making multiple crossings across the interface compared to the other copolymer sequences. The average number of crossings across the interface for PLCs was as high as 80% of the number of junction points for the PLC, which suggests that high molecular weight PLCs might be very efficient in stabilizing the interface.

The results of our simulation are in good agreement with the Monte Carlo simulations of Dadmun\textsuperscript{13} for block, random, and alternating copolymers. In a nutshell, sequence distribution in copolymer compatibilizers plays an important role in the way that these copolymers orient at the interface. PLCs penetrate the interface more than random and alternating copolymers at lower reduced temperatures and are very efficient in making multiple crossings across the interface. PLCs can be synthesized and tuned\textsuperscript{28} easily and hence they might be useful as potential compatibilizers and adhesion promoters for incompatible homopolymer blends. The contrast in the performance between PLCs and random copolymers as compatibilizers would be even better for longer chains but the simulations become too computationally intensive for us to perform. A study of the dynamics of phase separation of PLC compatibilizers in blends is under way in our laboratory using kinetic lattice Monte Carlo (BFM) simulations.
2.5 FIGURES

Figure 2.1 Snapshots illustrating instantaneous coloring procedure to generate 38-mer AB PLC (A = red, B = dark blue) with composition $x_A = x_B = 0.5$: (a) random configuration of 38-mer A chain, (b) collapsed globular configuration of the A chain, (c) 19 spheres farthest from the center of the globule are colored to type B, and (d) relaxed chain configuration of the resulting AB PLC.
Figure 2.2 Sequences of 38-mer AB copolymers \( (A = \text{red}, B = \text{dark blue}) \) with composition \( x_A = x_B = 0.5 \): (a) block, (b) random (one sequence realization), (c) alternating, and (d) PLC (one sequence realization).
Figure 2.3 Simulation snapshots of the binary blend in: (a) initial configuration at $T^*=20$, and (b) phase separated configuration at $T^*=1$. 
Figure 2.4 Simulation snapshots of PLC compatibilized blend in: (a) initial configuration at $T^*=20$, and (b) phase separated configuration at $T^*=1$. 
Figure 2.5 Density profiles for the homopolymers (red and blue lines) and copolymer (black lines) in the compatibilized blend at $T^*$=1: (a) block, (b) random, (c) alternating, and (d) PLC.
Figure 2.6 Interfacial width versus the reduced temperature of the binary (no-copolymer) and ternary (compatibilized) blend.
Figure 2.7 (a) Radius of gyration of the copolymer perpendicular to the interface versus the reduced temperature, (b) Radius of gyration of the copolymer parallel to the interface versus the reduced temperature, and (c) Anisotropy of the copolymer, $\langle R_g^2 \rangle - \langle R_g^2 \rangle_{\perp}$, versus the reduced temperature for the different copolymer sequences.
Figure 2.8 Simulation snapshots of the compatibilized blend after equilibrium has been attained at $T^*=1$: (a) block (side view of the simulation box parallel to the interface), (b) block (top view of the simulation box perpendicular to the interface), (c) random (side view), (d) random (top view), (e) alternating (side view), (f) alternating (top view), (g) PLC (side view), and (h) PLC (top view).
Figure 2.9 (a) Average crossings made by the different copolymer types across the interface versus the reduced temperature, and (b) Normalized average crossings (average crossings made by the different copolymer types across the interface divided by the number of junction points in the copolymer) versus the reduced temperature.
2.6 REFERENCES


CHAPTER THREE

Effect of Copolymer Compatibilizer Sequence on the Dynamics of Phase Separation of Immiscible Binary Homopolymer Blends

3.1 INTRODUCTION

Polymer blends represent an effective route to formulating novel soft materials because their properties can be tuned by varying the composition and types of polymers that are mixed. Polymer blending is, however, challenging because the constituent polymers are often immiscible; the entropic gain upon mixing cannot compensate for the enthalpic losses due to unfavorable interactions. As a consequence most polymer blends tend to macro-phase separate, thereby limiting their utility. Compatibilizers are typically added to overcome these difficulties. They segregate preferentially at the interface between the immiscible homopolymers, reducing interfacial tension and increasing structural integrity and homogeneity, thereby leading to improved stability and mechanical strength of the interface.

In this study we investigate the effects of copolymer compatibilizer sequence on the dynamics of phase separation in immiscible binary homopolymer blends. While diblock copolymers have come to be viewed as the compatibilizer of choice, their tendency to microphase separate at higher copolymer loading\textsuperscript{1-5} has led to utilization of other copolymer
sequences as compatibilizers. Here we consider diblock, protein-like, simple linear gradient random, and alternating copolymers with particular focus on the relative merits of the first three. Gradient copolymers have been proposed as an alternative to diblock copolymers as compatibilizers because they do not microphase separate easily at higher copolymer loading. Protein-like copolymers (PLCs) might also serve effectively as compatibilizers as was suggested by our recent computer simulations studies of the equilibrium properties of PLCs, diblock, random, and alternating copolymer compatibilizers. More recently we explored the dynamics of phase separation in an immiscible binary blend compatibilized by PLCs and found that PLCs succeeded in slowing down the process of phase separation.

Protein-like copolymers (PLCs) represent a new class of functional copolymers that exhibit large-scale compositional heterogeneities and long-range correlations along the co-monomer sequence. The concept of PLCs was first introduced by Khokhlov and coworkers who employed computer simulations to demonstrate that random copolymers with tunable monomer sequences could be generated by adjusting the compactness of a parent homopolymer composed of monomers A, and then converting those segments exposed to the outer periphery of the collapsed coil into B units by reacting the original A monomers with other chemical species present in the surrounding solution. Gradient copolymers are novel copolymers whose composition changes gradually along the chain from one species to the other. They are synthesized routinely via several polymerization methods, most frequently by controlled free radical polymerization.
The co-monomer sequence along the copolymer compatibilizer is expected to play an important role in governing the phase behavior and interfacial characteristics of the immiscible polymer blend to be compatibilized. This was demonstrated by Ko et al.\textsuperscript{7} who used lattice MC simulations to explore the effect of compatibilizer sequence distribution on the phase separation dynamics of immiscible binary blends. They considered diblock, alternating, random, random-alternating, and random-block copolymer sequences as compatibilizers. Their simulation results suggested that diblock copolymers were best at retarding the phase separation followed by random-block, random, random-alternating, and alternating copolymers. Ko et al.\textsuperscript{7} did not consider PLCs and gradient copolymer sequences.

In this work, we use kinetic Monte Carlo simulation based on the bond fluctuation model (BFM)\textsuperscript{33} to investigate the effects of the copolymer compatibilizer sequence on the phase separation dynamics of an immiscible binary blend of homopolymers to which diblock, random, alternating, PLCs, and simple linear gradient copolymer are added.

The binary system contains 9736 20-mers of homopolymer A and 2434 20-mers of homopolymer B. The blends are compatibilized by adding 180 70-mer copolymers containing equal numbers of A and B monomers in the copolymer. Diblock, protein-like, simple linear gradient, random, and alternating copolymers made of A and B units are considered as copolymer compatibilizers. Both the binary blend (A/B) and ternary blend (A/B/A-co-B) are mixed uniformly in the initial state. Phase separation between homopolymers A and B is induced by introducing positive pairwise interaction energies between monomer A and B units. As the immiscible polymer blend phase separates, homopolymer A-rich and homopolymer B-rich domains start to form and grow with time.
This process is retarded in the compatibilized blend as the copolymers localize to the biphasic A/B interface between the two homopolymers, minimizing the unfavorable interactions and interfacial tension.

To establish the efficacy of the various copolymer sequences and monitor the process of phase separation, the normalized numbers of contacts between segments A-A (\(\langle n_{AA}(t)\rangle/\langle n_{AA}(0)\rangle\)), B-B (\(\langle n_{BB}(t)\rangle/\langle n_{BB}(0)\rangle\)), and A-B (\(\langle n_{AB}(t)\rangle/\langle n_{AB}(0)\rangle\)) are recorded where \(t=0\) refers to the initial homogenous state and \(t\) refers to time elapsed after the phase separation commences. The extent of penetration of copolymers into the homopolymer-rich phase over time is monitored by recording the fraction of contacts made by the copolymer segments, \(A'\) and \(B'\), with the two different homopolymer segments A and B, \(f_{AA}(t)\), \(f_{AB}(t)\), \(f_{BA}(t)\), and \(f_{BB}(t)\). The degree of copolymer chain expansion with time is monitored by evaluating the normalized radius of gyration \(\langle R_g^2(t)\rangle/\langle R_g^2(0)\rangle\) of the copolymer. The dynamics of phase separation in both the binary and the ternary blend is monitored using the time dependent collective structure factor, \(S(q,t)\). The conformation of the different copolymers at the interface is evaluated in order to investigate the mechanism by which the copolymers stabilize the interface.

Highlights of our results are as follows. In the ternary compatibilized blend all copolymers irrespective of their sequence localize to the biphasic interface between the two immiscible homopolymers, minimizing the unfavorable enthalpic interactions and interfacial tension, thereby retarding the process of phase separation. Diblock copolymers are the most effective compatibilizers followed by PLCs and simple linear gradient (which have similar
effectiveness), random, and alternating copolymers. This ranking is based on ranking their performance according to the following criteria: an ideal compatibilizer should maximize the normalized number of contacts between A-B segments, minimize the normalized number of contacts between B-B segments, stretch the most at the interface and maximize the number of energetically favorable contacts between the copolymer-homopolymer segments $A'-A$ and $B'-B$. In addition, based on the structure factor $S(q,t)$ calculations, diblock copolymers slow down the phase separation most effectively followed by PLCs and simple linear gradient copolymers (which perform similarly), random, and alternating copolymers. The conformation of the copolymers at the interface differs from type to type with the diblock copolymers penetrating the energetically-favorable homopolymer-rich phase and forming entanglements with the homopolymers, the alternating copolymers laying at the interface, and the PLCs, simple linear gradient and random copolymers weaving back and forth across the interface. The weaving is more pronounced for PLCs than for the random copolymers but similar to that of simple linear gradient copolymers.

In the next section, we describe the MC method and the generation of simple linear gradient copolymers and PLCs via the instant coloring procedure of Khokhlov and co-workers. The following section presents the simulation results for various copolymer sequences. The final section concludes with a short summary of the results and a discussion.
3.2 MODEL AND METHOD

The A/B binary blend system consists of 9736 20-mers of type A and 2434 20-mers of type B. The ternary (compatibilized) blend contains the binary blend plus 180 70-mer copolymer chains (≈4.92% of total number of segments in the ternary blend system) each of which consists of monomers of types A and B with composition $x_A = x_B = 0.5$, where $x_i$ is the mole fraction of component $j$. The copolymer sequences considered include: diblock (A-b-B), PLC (A-plc-B), simple linear gradient (A-slg-B), random (A-ran-B), and alternating (A-alt-B). The polymers are modeled as self-avoiding walks on a three-dimensional cubic lattice. The phase separation of homopolymer chains A and B is induced by introducing positive repulsive pairwise interaction energy between A and B units $\varepsilon_{AB} = \varepsilon_{AB}/k_B T = 0.5$, where $k_B$ is the Boltzmann constant and $T$ is the absolute temperature, in both the binary and ternary blend systems. The interaction energies between identical segments are set to zero ($\varepsilon_{AA} = \varepsilon_{BB} = 0$). Additionally the interaction energies between each segment type and the empty sites on the lattice are set to zero. To calculate the energy of the system we need to decide on a range of the interactions; this is usually reported in terms of the number of nearest neighbors to any site that experience an interaction. The MZCCL (the eighteen vectors obtained by all the sign inversions and permutation of the two vector families $P(1,0,0) \cup P(1,1,0)$ between segments assuming one of the segments is located at $(0,0,0)$) interaction range was chosen.
The lattice Monte Carlo (MC) simulations are based on the three-dimensional bond fluctuation model (BFM)\textsuperscript{33} and are performed in the NVT canonical ensemble. We chose the BFM to model the dynamics of phase separation in polymer blends since it has been utilized previously\textsuperscript{34-37} to predict the properties of dense polymer melts. In the BFM each monomer represents a Kuhn segment and occupies eight sites on a simple cubic lattice. Successive monomers along the chain are connected via a predetermined set of bond vectors. In order to avoid bond crossing and monomer overlap, the bond vectors are derived from all possible permutations and sign inversions of the following six vector families:

$P(2,0,0) \cup P(2,1,0) \cup P(2,1,1) \cup P(2,2,1) \cup P(3,0,0) \cup P(3,1,0)$. For example, all possible permutations and sign inversions of the vector family $P(2,0,0)$ yield the following six distinct bond vectors: $(2,0,0)$, $(-2,0,0)$, $(0,2,0)$, $(0,-2,0)$, $(0,0,2)$, and $(0,0,-2)$. Repeating this process for all of the six vector families leads to a total of 108 bond vectors and 87 bond angles. Thus, the model possesses some of the flexibility associated with an off-lattice model while maintaining the advantages associated with working on a lattice, such as integer arithmetic and parallelization\textsuperscript{38}. The MC algorithm is executed in the following manner. First a monomer unit is chosen at random and translated by one lattice spacing in a direction chosen randomly out of the six possible directions. Next a check is made to verify that the resulting move does not violate the excluded volume and bond constraints set forth by the BFM. If it does, the move is rejected and the monomer is restored to its original position. If all of the BFM constraints are satisfied, the Metropolis sampling rule is applied, \textit{i.e.}, the move is accepted with a probability equal to $\min(1, \exp(-\Delta E/k_B T))$, where $\Delta E$ is the energy.
change due to the move. The MC simulations are performed on a simple cubic lattice of 
$L \times L \times L$ sites with $L=80$. The volume fraction, $\phi = N/L^3$, for the pure as well as 
compatibilized blend is set to $\phi = 0.5$, where $N$ is the number of beads in the simulation 
box. Periodic boundary conditions are imposed in all three directions ($x$, $y$, and $z$) to 
overcome the limitation of finite system size.

In order to characterize statistically the different types of AB copolymer sequences 
used as compatibilizers we introduce the uniformity factor developed originally by 
Dadmun$^{11}$. The uniformity factor for component A is defined as:

$$U_A = \left\{ \frac{1}{N_C} \sum_{n=1}^{N_C-1} s_n + 1 \right\} \frac{1}{N_{typeA}}$$

(3.1)

where $s_n$ is 1 if the $n$-th and ($n+1$)-st sphere are type A, -1 if the $n$-th sphere is type A and 
the ($n+1$)-st sphere is type B and 0 if the $n$-th sphere is B type regardless of the type of ($n+1$)-
st sphere. Here $N_C$ is the total number of monomers in the copolymer and $N_{typeA}$ is the total 
number of A monomer segments in the AB copolymer. By definition, compositionally 
symmetric (i.e., 50% A, 50% B) alternating copolymers possess uniformity factor -1, 
symmetric diblock copolymers have uniformity factor 1, and random copolymers have 
uniformity factor 0. The uniformity factor for symmetric PLCs and simple linear gradient 
copolymers should lie roughly halfway between those for random and diblock copolymers.

The symmetric random A-B copolymer was generated using the following algorithm. 
Starting with a homopolymer A, segments were picked randomly and changed to type B if 
the segment chosen was of type A. This process was repeated till the desired composition
was achieved and the uniformity factor for components A and B in the random AB copolymer sequence was reduced to zero.

The simple linear gradient A-B copolymer was generated using the multiblock model proposed recently by Jiang et al. Using this approach the gradient copolymer chain of length \( N_C \) is segmented into \( Y \) intervals of equal lengths \( \Delta l = N_C / Y \). Each interval is viewed as a mini A-B diblock sequence, whose composition is specified via the local gradient distribution function \( g(l) \). The \( j^{th} \) interval \( (j = 0,1,2,\ldots,Y-1) \) begins with an A block in the range \([j\Delta l, (j + F_j)\Delta l]\), followed by a B block in the range \([(j + F_j)\Delta l, (j + 1)\Delta l]\), where \( F_j \) is the fraction of A blocks in the \( j^{th} \) interval. For a specified \( g(l) \), \( F_j \) is defined by the following equation:

\[
F_j = Y \int_{j\Delta l}^{(j+1)\Delta l} g(l) dl
\]  

where the local gradient distribution function \( g(l) \) for a simple linear gradient copolymer is defined by the following equation:

\[
g(l) = 1 - l / N_C
\]

We chose the linear concentration profile over the non-linear hyperbolic tangent concentration profile for gradient copolymers as it would lead to a more fair comparison amongst the various copolymer sequences considered as compatibilizers. The “tanh-gradient” copolymer with non-linear hyperbolic tangent local concentration profile is described by the following equation:
\[ g(l) = \frac{1}{2} \left[ 1 - \tanh \left\{ \lambda \left( \frac{l}{N_c} - \frac{1}{2} \right) \right\} \right] \] (3.4)

where \( \lambda \) is a parameter. In the above equation when \( \lambda \to \infty \) we recover the concentration profile of a diblock copolymer while for \( \lambda \to 0 \) the concentration profile corresponds to that of a random copolymer. There is no value of \( \lambda \) at which the “tanh-gradient” copolymer concentration profile reduces to that of the simple linear gradient copolymer. For large values of \( \lambda \) the “tanh-gradient” copolymer is blockier than PLCs; as a result it is likely that such copolymers would outperform PLCs as compatibilizers. However, the tendency to microphase separate also increases with increasing \( \lambda \). In contrast, for \( \lambda \to 0 \) the “tanh-gradient” gradient copolymer is less blocky than PLCs and is likely to underperform PLCs as a compatibilizer. This is why we chose to work with simple linear gradient copolymers.

The symmetric AB PLCs were generated via a simulation-based instantaneous coloring procedure originally proposed by Khokhlov et al.\(^{24-26}\). A detailed description of our implementation of Khokhlov’s coloring procedure to generate 70-mer AB PLCs via discontinuous molecular dynamics (DMD) simulation can be found in our previous work\(^{22}\). To prepare the symmetric AB 70-mer PLC, a 70-mer A chain with square well interactions between non-adjacent A monomer segments was initialized in a random coil configuration. \textbf{Figure 3.1a} shows a snapshot of a sample initial configuration. DMD simulations were performed on the A chain at a low reduced temperature till the A macromolecule collapsed to a globular conformation as shown in \textbf{Figure 3.1b}. The segments in the final globular conformation were sorted in order of their distance from the center of the globule. The 35 segments of type A farthest from the center were colored to be B as depicted in \textbf{Figure 3.1c}.
The coloring procedure resulted in the creation of a 70-mer AB PLC with a composition $x_A = x_B = 0.5$. After the coloring procedure, the configuration of the AB PLC was relaxed. **Figure 3.1d** displays a snapshot of a symmetric AB 70-mer PLC generated via the instantaneous coloring procedure. **Figure 3.2** illustrates the five copolymer sequences considered (a) diblock, (b) PLC (one sequence realization), (c) simple linear gradient, (d) random (one sequence realization), and (e) alternating.

MC simulations are performed on the binary (A/B) and ternary (A/B/A'-B') blend systems. The simulations on the blend systems are started in a random configuration at the desired volume fraction. Initially the blend systems are mixed uniformly; once the interactions are switched on and MC simulations have been performed for 100,000 Monte Carlo steps (MCS), the systems demix sufficiently into homopolymer A-rich and homopolymer B-rich phases. In each MCS, all segments in the system are moved once on average.

The dynamics of phase separation is monitored by evaluating: 1) the normalized number of nearest-neighbor contacts between segments A-A ($\langle n_{AA}(t) \rangle / \langle n_{AA}(0) \rangle$), B-B ($\langle n_{BB}(t) \rangle / \langle n_{BB}(0) \rangle$), and A-B ($\langle n_{AB}(t) \rangle / \langle n_{AB}(0) \rangle$) where $t = 0$ refers to the initial homogenous state and $t$ refers to time elapsed after the phase separation commences, 2) the fraction of PLC A nearest-neighbor contacts that are to homopolymer segments A segments, $f_{AA}(t)$, and similarly $f_{AB}(t)$, $f_{BA}(t)$, and $f_{BB}(t)$, 3) the copolymer chain expansion ratio, i.e., the normalized copolymer radius of gyration $\langle R_g^2(t) \rangle / \langle R_g^2(0) \rangle$, 4) the spherically-
averaged time-dependent collective structure factor $S(q, t)$ for the binary blend and for the ternary compatibilized blends, and 5) the conformation of the copolymers at the interface at the end of the simulation.

The fraction of PLC A nearest-neighbor contacts that are to homopolymer segments A segments is defined to be:

$$f_{AA}(t) = \langle n_{AA}(t) / (n_{AA}(t) + n_{AB}(t)) \rangle$$

where $A'$ and $B'$ refer to the A and B segments of the AB copolymer, respectively, and $n_{AA}(t)$, and $n_{AB}(t)$ denote the nearest-neighbor contacts between segments $A' \sim A$ and $A' \sim B$, respectively, at time $t$. Similarly $f_{AB}(t)$, $f_{BA}(t)$, and $f_{BB}(t)$ can also be defined.

The copolymer chain expansion ratio, $\langle R_g^2(t) \rangle / \langle R_g^2(0) \rangle$ is calculated, where $\langle R_g^2(t) \rangle$ is defined by the following equation:

$$\langle R_g^2(t) \rangle = \sum_{i=1}^{N_{copolymer}} \sum_{j=1}^{N_C} \{r_{i,j}(t) - r_{i,m}^m(t)\}^2 / \{N_{copolymer} N_C \}$$

with $\langle R_g^2(t) \rangle$ equal to the copolymer radius of gyration at time $t$. Here $r_{i,j}(t)$ is the position of the $j$-th monomer on the $i$-th copolymer chain at time $t$ and $r_{i,m}^m(t)$ is the position of the center of mass of the $i$-th copolymer chain at time $t$, $N_{copolymer}$ is the number of copolymer chains.

The time-dependent collective structure factor for both the binary and ternary blend systems is calculated to follow the time evolution of the long-range ordering. The structure factor represents the Fourier transform of the pair correlation function and is defined by the following equation:
\[
S(q,t) = \left( \frac{1}{L^3} \sum_{j} \left( \exp(iq \cdot r_j) (\phi^A_j(t) - \phi^B_j(t)) - \langle \phi^A_j - \phi^B_j \rangle \right) \right)^2
\]

where the scattering vector \( q \) is given by \( q = \frac{2\pi n}{L} \) with \( n \) equal to a positive integer vector, \( i.e., \ n=(n_x,n_y,n_z) \), the local concentration variable \( \phi^A_j(t) \) (or \( \phi^B_j(t) \)) at time \( t \) is equal to one if lattice site \( j \) is occupied by an A (or B) segment and zero otherwise. The outer angular bracket \( \langle \ldots \rangle \) denotes a thermal statistical average. The contribution from the copolymer chains to the collective structure factor is neglected since we are interested principally in the phase separation of homopolymers A and B, and the copolymer compatibilizer loading \( \approx 4.92 \% \) is small relative to the homopolymers. To improve the statistics in \( q \)-space the collective structure factor is averaged spherically as follows:

\[
\Delta S(q,t) = \sum_{q \in \left\{ \frac{\Delta q}{2} \| q \leq \frac{\Delta q}{2} \right\}} \frac{S(q,t)}{m(q,\Delta q)}
\]  

where

\[
m(q,\Delta q) = \sum_{q \in \left\{ \frac{\Delta q}{2} \| q \leq \frac{\Delta q}{2} \right\}} 1
\]

denotes the number of lattice points in a spherical shell of radius \( q \) with \( \Delta q \) as the shell thickness. In scattering experiments on real immiscible polymer blends, the intensity of scattered radiation, which is related to the structure factor \( S(q,t) \) is small initially (for all values of the scattering vector or scattering angle \( q \)) as the homopolymers are mixed.
uniformly. As the phase separation progresses, a distinct peak in the structure factor \( S(q^*, t) \) develops at a scattering vector \( q^* \). Physically, at time \( t \), \( 1/q^* \) represents a measure of the characteristic length scale in the blend while \( S(q^*, t) \) is proportional to the difference in concentrations of the constituent homopolymers in the polymer blend.

We also determine the conformation of the copolymers at the interface at the end of the simulation. To do so we move along a copolymer chain and for a given copolymer segment we calculate the difference between the number of nearest-neighbor contacts of that copolymer segment with homopolymer segment A and with homopolymer segment B, \( \langle N_A - N_B \rangle \). If \( \langle N_A - N_B \rangle \) is large and positive it implies that the copolymer segment resides preferentially in the homopolymer A-rich phase, while a small and negative value of \( \langle N_A - N_B \rangle \) signifies that the copolymer segment lies preferentially in the homopolymer B-rich phase.

The system properties for both the binary and ternary blends were averaged over five simulation runs starting from uncorrelated random initial configurations. The results for ternary blends compatibilized by PLCs or random copolymers were averaged over five different copolymer sequences for a given initial configuration. Thus, 50 simulations were performed for ternary blends compatibilized by either PLCs or random copolymers. The errors which represent the sample standard deviations of the properties calculated were within 5%. We chose not to represent the errors bars, which are relatively small, on the plots for the sake of clarity.
3.3 RESULTS AND DISCUSSION

Snapshots of the asymmetric binary blend system at various times during the demixing process are presented in Figure 3.3. Specifically, Figure 3.3 shows the binary blend (a) initially, (b) at a very early stage in the simulation (5k MCS), (c) halfway through the simulation (50k MCS), and (d) at the end of the simulation (100k MCS). As the phase separation progresses, homopolymer A-rich and homopolymer B-rich domains begin to form and grow. Figure 3.4 shows the ternary A/B/A’-B’ blend compatibilized with the PLC (a) initially, (b) at a very early stage in the simulation (5k MCS), (c) halfway through the simulation (50k MCS), and (d) at the end of the simulation (100k MCS). Comparison of Figures 3.3 and 3.4 provides a simple visual comparison of how the presence of the PLC compatibilizer retards the phase separation of the A/B binary blend. In the PLC-compatible ternary blend, homopolymer A-rich and homopolymer B-rich domains form and grow as was the case for the pure binary blend; this time, however, the PLCs migrate to the A/B biphasic interface, reducing unfavorable contacts, minimizing interfacial energy and binding the two homopolymer phases together. Similar behavior is observed for the ternary blends compatibilized by diblock, simple linear gradient, random, and alternating copolymers.

The process of phase separation in both binary and ternary blends is accompanied by a change in the number of A-A, B-B, and A-B contacts with time. We expect the number of A-A, and B-B contacts to increase and the number of A-B contacts to decrease with
increasing phase separation time. In Figure 3.5a we plot the normalized number of B-B contacts \( \langle n_{BB}(t) / n_{BB}(0) \rangle \) versus time. The \( \langle n_{BB}(t) / n_{BB}(0) \rangle \) is lowest for diblock copolymers followed by those for PLCs and simple linear gradient copolymers (which are similar), random, and alternating copolymers. The \( \langle n_{BB}(t) / n_{BB}(0) \rangle \) for all the ternary blends compatibilized by various copolymer sequences is lower than those for the binary (i.e., no-copolymer) blend, indicating that all copolymers act effectively as compatibilizers. In Figure 3.5b we plot the normalized number of A-B contacts \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) versus time, where, for clarity, time is restricted to the latter half of the simulation. The \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) is highest for diblock copolymers followed by those for PLCs and simple linear gradient copolymers (which are similar), random, and alternating copolymers. The \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) for all the ternary blends compatibilized by various copolymer sequences is higher than those for the binary (i.e., no-copolymer) blend. Note that the higher the value of \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) or the lower the value of \( \langle n_{BB}(t) / n_{BB}(0) \rangle \) the greater the extent of mixing between the two immiscible homopolymers. Copolymers, which maximize \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) or minimize \( \langle n_{BB}(t) / n_{BB}(0) \rangle \), are effective compatibilizers and hence, based on this criteria, diblocks are the best compatibilizers followed by PLCs and gradient (which are similar), random, and alternating copolymers.

As the phase separation evolves in ternary compatibilized blends, the copolymers migrate to the biphasic interface between the two homopolymers and penetrate the homopolymer-rich phases. To monitor the extent of penetration of copolymers into the
homopolymer-rich phases, we record the fraction of PLC A nearest-neighbor contacts that are to homopolymer segments A segments \( f_{AA}(t) \) and similarly, \( f_{AB}(t) \), \( f_{BA}(t) \), and \( f_{BB}(t) \). In Figure 3.6a we plot \( f_{AA}(t) \) versus phase separation time. The \( f_{AA}(t) \) increases with time, as expected, for diblock, PLC and simple linear gradient copolymers since the interaction between components \( A' (A' \) refers to the component A on the AB copolymer) and A is favorable. However, \( f_{AA}(t) \) decreases with time for alternating and random copolymers. The increase in \( f_{BB}(t) \) with increasing time for all copolymer sequences as shown in Figure 3.6b. A plausible reason for this counterintuitive behavior for random and alternating is that they are pushed preferentially into the homopolymer B-rich phase (minor phase) at the biphasic interface. The \( f_{AA}(t) \) and \( f_{BB}(t) \) are highest for diblock copolymers followed by those for PLCs and simple linear gradient copolymers (which are similar), random, and alternating copolymers; concordantly, diblocks are the best compatibilizers followed by PLCs and gradient (which are similar), random, and alternating copolymers.

Figure 3.7 displays the copolymer chain expansion ratio, or normalized radius of gyration \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \), as a function of time. The \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \) increases for all copolymer sequences with increasing time as expected. An effective copolymer compatibilizer is likely to exhibit a relatively high chain expansion since this would signify greater stretching and entanglement formation with the homopolymer-rich phases. Diblock copolymers stretch most as they have the highest \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \) followed by PLCs and simple linear gradient copolymers (which are similar), random, and alternating copolymers.
To quantify the extent of phase separation in both the binary and ternary compatibilized blends, we determine the spherically-averaged time-dependent collective structure factor $S(q,t)$. Figure 3.8 shows a plot of $S(q,t)$ as a function of the scattering vector for both the binary and ternary (i.e., compatibilized) blends. Initially $S(q,t)$ is small for all cases as the blend is homogeneous. With increasing phase separation time a distinct peak develops and the location of the peak shifts towards smaller values of the scattering vector, signifying the growth in size of the phase-separated domains. This behavior is also observed in light scattering experiments on real polymer blends\textsuperscript{40-50}. An efficient compatibilizer would suppress the height of the peak in $S(q,t)$ and shift it to higher values of the scattering vector. The structure factor for the binary blend without any copolymer compatibilizer is shown in Figure 3.8a. The $S(q,t)$ for the diblock, PLC, simple linear gradient, random, and alternating copolymer compatibilized blends are shown in Figures 3.8b through 3.8f, respectively. Based on the $S(q,t)$ calculations, diblock copolymers are most effective in slowing down the process of phase separation because they have the smallest $S(q,t)$, followed by PLCs and simple linear gradient copolymers (which are similar), random, and alternating copolymers. All copolymers irrespective of their sequence slow down the phase separation in compatibilized blends in comparison to the binary blend (no-copolymer).

Figure 3.9 depicts the simulation snapshots for each of the five compatibilized blends with \( \approx 4.92\% \) copolymer at the end of the simulation. Each block of the diblock copolymer (Figure 3.9a) penetrates the homopolymer-rich phases on either side of the interface.
Alternating copolymers (Figure 3.9c) prefer to lie at the interface. Random copolymers (Figure 3.9b), PLCs (Figure 3.9d), and simple linear gradient copolymers (Figure 3.9e) weave back and forth across the biphasic interface binding the two homopolymer rich phases together.

To establish the conformation of the copolymers at the interface and the mechanism by which they stabilize the interface, we calculate the difference between the number of nearest-neighbor contacts of that copolymer segment with homopolymer segment A, and with homopolymer segment B, \( \langle N_A - N_B \rangle \) for each copolymer segment along the copolymer chain at the end of the simulation. Figure 3.10 depicts \( \langle N_A - N_B \rangle \) along the copolymer chain for various copolymer sequences. A large and positive value of \( \langle N_A - N_B \rangle \) for a particular copolymer segment indicates that the copolymer segment lies in the homopolymer A-rich phase. A small and negative value of \( \langle N_A - N_B \rangle \) for a particular copolymer segment indicates that the copolymer segment lies in the homopolymer B-rich phase. From the data in Figure 3.10 it is evident that each block of the diblock copolymer penetrates the energetically favorable homopolymer-rich phase (i.e., A’ penetrates A and B’ penetrates B) making entanglements with the homopolymers. Alternating copolymers lie at the interface as the value of \( \langle N_A - N_B \rangle \) is close to zero. PLCs, simple linear gradient and random copolymers weave back and forth across the interface. The weaving and penetration across the interface is pronounced for PLCs in comparison to random copolymers, while that of gradient copolymers are on a par with the behavior seen in PLCs. This analysis is useful because we
do not have to make any a priori assumptions about the flatness of the biphasic interface between the two homopolymers.

It is of interest to compare our results with the lattice MC simulations of Ko et al.\textsuperscript{7}, who reported that diblock copolymers were the best compatibilizers followed by random-block, random, random-alternating, and alternating copolymers. The relative compatibilization performance of diblock, random, and alternating copolymers as suggested by our simulations are in good agreement with the results of Ko et al.\textsuperscript{7}. The simulation results from Ko et al.’s work on random-block (uniformity factor of 0.5) copolymers cannot be equated with those of PLCs for comparison purposes because random-block copolymers have a sequence distribution that is different from that of PLCs. Khokhlov and coworkers\textsuperscript{51} have demonstrated that random-block copolymers (whose block length obeys a Poisson distribution) are statistically different from PLCs (which obey Levy flight statistics for the block length), despite having the same composition and average block length (or uniformity factor) for both types of copolymers. Our results on the performance of PLCs as compatibilizers relative to those of diblock, random, and alternating copolymers are consistent with our previous work involving DMD simulations\textsuperscript{22}.

As mentioned several times earlier, the compatibilizing performance of simple linear gradient copolymers, which have a highly ordered sequence, is on a par with that of PLCs. One plausible reason for this is that the degree of blockiness of PLCs is comparable to that of simple linear gradient copolymers. Another plausible reason is that unlike PLCs, simple linear gradient A-B copolymers possess long blocks of type A adjacent to short blocks of type B on the one end of the copolymer and vice versa on the other end of the copolymer,
and the long blocks of type A prefer to penetrate the homopolymer A-rich phase. While doing so, they drag successfully along the short adjacent blocks of type B leading to higher interfacial energy and poor weaving across the biphasic interface.

Although we have presented results only for copolymer concentration of \( \approx 4.92\% \), computer simulations for higher copolymer loadings, \( i.e., \approx 19.69\% \), have also been performed. The trends amongst the various copolymer sequences observed at \( \approx 4.92\% \) copolymer concentration also hold true for the higher copolymer concentration \( \approx 19.69\% \). Interestingly the diblock did not microphase separate even at this higher copolymer concentration, most likely because the homopolymers in our simulations are much shorter than the diblock copolymers. Previous studies\(^{52-58}\) on diblock-copolymer compatibilized ternary polymer blends have shown that for microphase separation of diblock to occur, the diblock concentration must be high (\( \approx 20\% \)), the effective interaction strength parameter must be large (\( \chi_{AB}L_{copolymer} > 10.5 \)), and the homopolymers must be much longer than each block of the diblock copolymer. We chose to perform kinetic MC simulations on ternary polymer blends with short (20-mer) homopolymer chains because working with very long homopolymer chains (relative to the copolymers) would require a bigger simulation box to minimize the finite size effects, and this would have been too computationally demanding. It would be interesting to study the compatibilization effectiveness of various copolymer sequences in immiscible binary polymer blends at high copolymer concentrations with very long homopolymers relative to the copolymer as it is likely that the diblock as well as simple linear gradient copolymers might microphase separate easily, unlike PLCs. PLCs might thus
be the most effective compatibilizers. Self-consistent field theory (SCFT) studies of compatibilized blends with higher copolymer concentrations and very long homopolymers relative to the copolymer chain lengths are in progress and will be the subject of future publications.

3.4 CONCLUSIONS

We presented the results of kinetic Monte Carlo simulations aimed at exploring the effect of co-monomer sequence in copolymer compatibilizers on the dynamics of phase separation of incompatible A/B binary homopolymer blends. Diblock, PLCs, simple linear gradient, random, and alternating copolymers made of equal numbers of A and B segments and identical chain lengths were considered as compatibilizers. In binary blends the process of phase separation was accompanied by the formation and growth of homopolymer B (minor homopolymer phase) rich domains dispersed in a matrix of homopolymer A (major homopolymer phase). In ternary compatibilized blends all copolymers irrespective of their sequence retarded the process of phase separation by migrating to the biphasic interface between the two incompatible homopolymers, thus minimizing the interfacial energy and promoting adhesion.

The normalized number of nearest neighbor contacts between homopolymer segments A and B or between B and B were recorded to monitor the process of phase separation. For all the blend systems the number of A-B contacts decreased with time while
the number of the B-B contacts increased with time, indicating the demixing of the blend. Diblock copolymers maximized the normalized number of A-B contacts and minimized the normalized number of B-B contacts, followed by PLCs and simple linear gradient copolymers (which were similar), random, and alternating copolymers. The fraction of PLC contacts with homopolymer segments, \( A' - A \) and \( B' - B \), were recorded to monitor the extent of penetration of copolymers into the homopolymer rich phase. The fraction of \( A' - A \) contacts increased with time for all sequences except random and alternating copolymers, while the fraction of \( B' - B \) contacts increased for all copolymer sequences. A plausible explanation for this counterintuitive behavior for random and alternating copolymers is that they are pushed preferentially into the homopolymer B-rich phase (minor phase) at the biphasic interface. Diblock copolymers maximized the fraction of \( A' - A \), and \( B' - B \) contacts followed by PLCs and simple linear gradient copolymers (which were similar), random, and alternating copolymers.

We calculated the time-dependent collective structure factor \( S(q,t) \) for all the blend systems to monitor the dynamics of phase separation. Diblock copolymers were most effective in slowing down the process of phase separation as they had the smallest \( S(q,t) \), followed by PLCs and simple linear gradient copolymers (which were similar), random, and alternating copolymers. All copolymers irrespective of their sequence succeeded in slowing down the phase in immiscible binary polymer blends.

Diblock copolymers stretched the most at the interface as deduced from the highest chain expansion ratio followed by PLCs and simple linear gradient copolymers (which were
similar), random, and alternating copolymers. The chain expansion ratio increased with time for all copolymer sequences.

We monitored the orientation of the copolymers at the interface by evaluating the difference between the number of nearest-neighbor contacts of that copolymer segment with homopolymer segment A and with homopolymer segment B at the end of the simulation for each copolymer segment along the copolymer chain. No assumption was made about the flatness of the interface. Each block of the diblock copolymer penetrated the homopolymer rich phase on either side of the interface. Alternating copolymers preferred to lie at the interface. Random, PLCs and simple linear gradient copolymers weaved back and forth across the interface, binding the two homopolymer rich phases together. The weaving and penetration was more pronounced for PLCs than for random or simple linear gradient copolymers.

Our results are in good agreement with the lattice Monte Carlo simulations of Ko et al.\textsuperscript{7} for diblock, random, and alternating copolymers. Our results on the performance of PLCs as compatibilizers relative to those of diblock, random, and alternating copolymers are in excellent agreement with our previous work involving DMD simulations on PLCs\textsuperscript{22}. A surprising result of our work is the compatibilizing ability of PLCs observed here in on a par with that of simple linear gradient copolymers, which have received a great deal of attention as potential alternatives to diblock copolymers for use as compatibilizers\textsuperscript{12-21}. Compared to diblock and gradient copolymers, which are synthesized via controlled free radical polymerization\textsuperscript{14,27-32}, PLCs are relatively easy to prepare via the coloring reaction described by Genzer and coworkers\textsuperscript{59}. PLCs thus have real potential as compatibilizers for immiscible
polymer blends. In a nutshell, the copolymer sequence plays a dominant role in determining its ability to effectively act as a compatibilizer for immiscible blends.
Figure 3.1 Snapshots illustrating instantaneous coloring procedure to generate 70-mer A-B PLC (A = dark blue, B = light pink) with composition $x_A = x_B = 0.5$: (a) random configuration of 70-mer A chain, (b) collapsed globular configuration of the A chain, (c) 35 spheres farthest from the center of the globule are colored to type B, and (d) relaxed chain configuration of the resulting A-B 70-mer PLC.
Figure 3.2 Sequences of 70-mer A-B copolymers (A = dark blue, B = light pink) with composition $x_A = x_B = 0.5$: (a) diblock, (b) PLC (one sequence realization), (c) simple linear gradient, (d) random (one sequence realization), and (e) alternating.
Figure 3.3 Simulation snapshots of the A/B binary blend (A = light blue, B = red) at time: (a) $t=0$ (initial configuration), (b) $t=5k$ MCS (early stage configuration), (c) $t=50k$ MCS (halfway configuration), and (d) $t=100k$ MCS (final configuration).
Figure 3.4 Simulation snapshots of the PLC compatibilized A/B/A’-B’ blend (A = light blue, B = red, A’ = dark blue, B’ = light pink) at time: (a) $t=0$ (initial configuration), (b) $t=5k$ MCS (early stage configuration), (c) $t=50k$ MCS (intermediate configuration), and (d) $t=100k$ MCS (final configuration).
Figure 3.5 Normalized contacts for copolymer compatibilized blends with phase separation time: (a) B-B contacts $\langle n_{BB}(t) \rangle / \langle n_{BB}(0) \rangle$ and (b) A-B contacts $\langle n_{AB}(t) \rangle / \langle n_{AB}(0) \rangle$. 
Figure 3.6 Fraction of the nearest-neighbor contacts between the copolymer and homopolymer segments with phase separation in ternary compatibilized blends: (a) $f_{AA}(t)$ and (b) $f_{BB}(t)$. 
Figure 3.7 Copolymer normalized radius of gyration $\frac{<R_g^2(t)>}{<R_g^2(0)>}$ with phase separation time for ternary compatibilized blends.
Figure 3.8 Evolution of $S(q,t)$ with phase separation time for: (a) binary blend (no copolymer), (b) diblock copolymer ternary blend, (c) PLC ternary blend, (d) gradient copolymer ternary blend, (e) random copolymer ternary blend, and (f) alternating copolymer ternary blend.
Figure 3.9 Simulation snapshots of the binary blend compatibilized by various copolymer sequences at the end of the simulation: (a) diblock, (b) PLC, (c) simple linear gradient, (d) random, and (e) alternating.
Figure 3.10 Orientation of the copolymers at the interface at the end of the simulation.
3.6 REFERENCES


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CHAPTER FOUR

Phase Separation Dynamics for a Polymer Blend Compatibilized by Protein-like Copolymers: a Monte Carlo Simulation

4.1 INTRODUCTION

Macro-phase separation in polymer blends limits their applicability as adhesives, interfacial stabilizers, coatings, membranes, ion-exchange systems, and functional materials for biomedical applications\(^1\). To arrest the process of phase separation in immiscible polymer blends, macromolecular compatibilizers are typically added. They localize at the interface between the immiscible homopolymers, thereby reducing interfacial tension and slowing down the process of phase separation, leading to finer domain dispersion and improved mechanical strength of the interface. Our recent computer simulation results suggest that protein-like copolymers (PLCs) could be used effectively as compatibilizers for immiscible homopolymer blends and might represent an attractive alternative to block, random, and alternating copolymer compatibilizers from a thermodynamic point of view\(^2\). In this study we investigate the dynamics of phase separation of an immiscible polymer blend in the presence of PLCs as compatibilizers.
Protein-like copolymers represent a new class of functional copolymers that exhibit large-scale compositional heterogeneities and long-range correlations along the co-monomer sequence\(^3\). The concept of PLCs was first introduced by Khokhlov and coworkers\(^3\)-\(^5\) who used computer simulations to demonstrate that random copolymers with tunable monomer sequence distributions could be generated by adjusting the compactness of a parent homopolymer composed of component A, and then converting exposed segments on the polymer coil surface into B segments by reacting them with other species in the surrounding solution.

In order to control the morphology and properties of immiscible polymer blends, it is necessary to understand the mechanisms that govern the phase separation dynamics. These have been explored extensively both theoretically\(^6\)-\(^13\) and experimentally\(^12,14-25\). Particular attention has been paid to the impact of diblock compatibilizers on phase separation dynamics in immiscible polymer blends\(^26-34\). Diblock copolymers are popular as compatibilizers due to their effectiveness in reducing the interfacial tension and increasing the mechanical strength of immiscible interfaces; these are affected in part by having the copolymer blocks entangle within the respective homopolymers. However, since diblock copolymers themselves microphase separate easily at higher copolymer loading\(^35-38\), other copolymer sequences have been considered\(^34,39,40\). This possibility has stimulated experimental and theoretical research on the dynamics of phase separation of immiscible homopolymers blends in the presence of random, alternating, random-blocky, random-alternating, and gradient copolymers\(^41-45\) as possible interfacial compatibilizers.
The dynamics of phase separation of immiscible homopolymers blends in the presence of PLCs as compatibilizers has not yet been explored. In this work, we use kinetic Monte Carlo (MC) simulation to investigate how adding protein-like copolymer (PLC) to an immiscible binary blend of homopolymers affects the phase separation dynamics. The effects of the pairwise interaction parameters between the homopolymers and the PLC blocks (which may be chemically different) and the effects of variation in the PLC chain length on the phase separation dynamics in immiscible blends are examined.

Kinetic MC simulations based on the bond fluctuation model are performed on an immiscible binary blend containing 9736 20-mers of homopolymer A and 2434 20-mers of homopolymer B, to which \( \approx 4.92\% \) PLCs containing equal numbers of C and D monomers is added. Both the binary blend (A/B) and ternary blend (A/B/C-plc-D) are mixed uniformly in the initial state. Phase separation between homopolymers A and B is induced by introducing positive pairwise interactions between monomer A and B units. As the immiscible polymer blend phase-separates, A-rich and B-rich homopolymer domains start to form and grow. This process is retarded in the compatibilized blend as the PLCs localize to the biphasic interface between the two homopolymers minimizing the unfavorable interactions and reducing the interfacial tension. The process of phase separation is monitored by recording the number of contacts between segments of A - A (\( \langle n_{AA}(t) \rangle \)), B - B (\( \langle n_{BB}(t) \rangle \)), and A - B (\( \langle n_{AB}(t) \rangle \)). The extent of penetration of PLCs into the homopolymer-rich phase over time is monitored by recording the fraction of contacts made by the PLC segments with homopolymer segments \( f_{CA}(t) \), \( f_{CB}(t) \), \( f_{DA}(t) \), and \( f_{DB}(t) \). The extent of PLC chain expansion with time is
recorded by evaluating the normalized radius of gyration \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \) of the PLC. The dynamics of phase separation in both the binary and the ternary blend is measured using the time dependent collective structure factor \( S(q,t) \). To gauge the compatibilization effectiveness of various PLC types (as characterized by PLC-homopolymer interaction strength parameters and the PLC chain length), the dynamic scaling exponent associated with \( q_i(t) \), the first moment of the structure factor at time \( t \), is calculated for the late stages of phase separation. To demonstrate the existence of self-similarity amongst the phase separated structures developed at various times during the late stages of phase separation in both the binary and ternary blends, the structure factor \( S(q,t) \) is scaled in terms of a characteristic length parameter \( 1/q_i(t) \) and scaling function \( F(x) \), and the time invariance of \( F(x) \) is tested in the late stages of phase separation. The universality of the scaling function is verified for various types of ternary blends compatibilized by PLCs.

Highlights of our results are as follows. C-plc-D copolymers effectively compatibilize the blend by migrating to the biphasic interface between the immiscible homopolymers, thereby reducing the unfavorable interactions between the immiscible homopolymers. The ability of PLCs to retard effectively the process of phase separation depends sensitively on the interaction energy between the PLCs and homopolymers, and the PLC chain length. PLCs compatibilize the A/B blend more effectively as the attractive interaction between the PLC C (or D) segments and homopolymers A (or B) increases. Marginal improvement in compatibilization of the A/B blend is achieved with increasing PLC chain length. The phase-separated structures developed at various times during the late stages of phase separation
exhibit self-similarity in both the binary and ternary blends, i.e., the morphology change with time involves only an increase in the size of phase-separated domains and not any change in the interfacial structure. As a consequence the late stage structure factor \( S(q, t) \) can be rewritten in terms of a characteristic length parameter \( 1/q(t) \) and a time-invariant scaling function \( F(x) \). \( F(x) \) is universal as it is nearly independent of the PLC-homopolymer interaction strength parameters, and the PLC chain length for PLC compatibilized ternary blends during the late stages of phase separation.

In the next section, we describe the MC method and the generation of PLCs via the instant coloring procedure of Khokhlov and co-workers. The following section presents the simulation results for dynamics of phase separation of immiscible binary blends in the presence of PLC sequences. The final section concludes with a short summary of the results and a discussion.

### 4.2 MODEL AND METHOD

The A/B binary blend system consists of 9736 20-mers of type A and 2434 20-mers of type B. The ternary (compatibilized) blend contains the binary blend plus protein-like copolymer chains (\( \approx 4.92\% \) of total number of segments in the ternary blend system) containing monomers of types C and D having compositions \( x_c = x_d = 0.5 \). The PLCs and homopolymers are modeled as self-avoiding walks on a three dimensional bond-fluctuation cubic lattice. The chain length of the PLC compatibilizer is varied to be 30, 50, and 70.
segments, while the amount of PLCs added to the binary blend is held fixed. The phase separation of homopolymer chains A and B is induced by introducing positive repulsive pairwise interaction energy between A and B segments \( \varepsilon_{AB} = \frac{\varepsilon_{AB}}{k_B T} \approx 0.5 \) in both the binary and ternary blend systems. Since the symmetric C-D PLC compatibilizer is composed of segments that are chemically different from the homopolymer units, one must specify ten monomer-monomer interaction parameters: \( \varepsilon_{AB}, \varepsilon_{AC}, \varepsilon_{AD}, \varepsilon_{BC}, \varepsilon_{BD}, \varepsilon_{CD}, \varepsilon_{AA}, \varepsilon_{BB}, \varepsilon_{CC}, \varepsilon_{DD} \). The values of \( \varepsilon \) are listed in Table 4.1. The interaction energies between the segments of homopolymer A and the segments of type C (\( \varepsilon_{AC} \)) on the C-D PLC, and between the segments of homopolymer B and the segments of type D (\( \varepsilon_{BD} \)) on the C-D PLC are both chosen to be negative, so that C-D PLCs become effective compatibilizing agents for the immiscible A/B binary blend. The strengths of the interaction energies \( \varepsilon_{AC} = \varepsilon_{BD} \) are varied to be -0.1, -0.2, and -0.5. The interaction energies \( \varepsilon_{AD}, \varepsilon_{BC}, \) and \( \varepsilon_{CD} \) are all set equal to 0.5, to discourage miscibility between their corresponding segments. The interaction energies between identical segments are set to zero (\( \varepsilon_{AA} = \varepsilon_{BB} = \varepsilon_{CC} = \varepsilon_{DD} = 0 \)). Additionally the interaction energies between each segment type and the empty sites are set to zero.
Table 4.1 Matrix of Interaction Parameters

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>0.5</td>
<td>varied to be 0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>0.5</td>
<td>varied to be 0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>0</td>
<td>varied to be 0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
<td>0</td>
<td>varied to be 0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

The lattice MC simulations are based on the three-dimensional bond fluctuation model (BFM) performed in the NVT ensemble. We chose the BFM to model the dynamics of phase separation in polymer blends since it has been utilized previously to predict the properties of dense polymer melts successfully. In the BFM each monomer represents a Kuhn segment and occupies eight sites on a simple cubic lattice. Successive monomers along the chain are connected via a predetermined set of bond vectors. In order to avoid bond crossing and monomer overlap, the bond vectors are derived from all possible permutations and sign inversions of the following six vector families: $P(2,0,0) \cup P(2,1,0) \cup P(2,1,1) \cup P(2,2,1) \cup P(3,0,0) \cup P(3,1,0)$. For example, all possible permutations and sign inversion of the vector family $P(2,0,0)$ yield the following six distinct bond vectors: $(2,0,0), (-2,0,0), (0,2,0), (0,-2,0), (0,0,2), \text{ and } (0,0,-2)$. Repeating this
process for all the six vector families leads to a total of 108 bond vectors and 87 bond angles. Thus, the model possesses some of the flexibility associated with an off-lattice model while maintaining the advantages associated with working on a lattice, such as integer arithmetic and parallelization. The MC algorithm is executed in the following manner. First a monomer unit is chosen at random, and translated by one lattice spacing in a direction chosen randomly out of the six possible directions. Next a check is done to verify that the resulting move does not violate the excluded volume and bond constraints set forth by the BFM. If it does, the move is rejected and the monomer is restored to its original position. If all the BFM constraints are satisfied, the Metropolis sampling rule is applied i.e. the move is accepted with a probability equal to $\min(1, \exp(-\Delta E / k_B T))$, where $\Delta E$ is the energy change due to the move, $k_B$ is the Boltzmann constant and $T$ is the temperature. The lattice MC simulations are performed on a simple cubic lattice of $L^3$ sites with $L = 80$. The volume fraction, $\phi = N/L^3$, for the pure as well as compatibilized blend is set to $\phi = 0.5$, where $N$ is the number of occupied sites in the simulation box. Periodic boundary conditions are imposed in all three directions ($x$, $y$, and $z$) to overcome the limitation of finite system size.

The symmetric C-D PLCs were generated via a simulation-based instantaneous coloring procedure originally proposed by Khokhlov et al. A detailed description of our implementation of Khokhlov’s coloring procedure to generate C-D PLCs (with chain lengths 30, 50, and 70) via discontinuous molecular dynamics (DMD) simulation can be found in our previous work. To prepare the symmetric C-D 70-mer PLC, a 70-mer C chain with square well interactions between non adjacent C monomer segments was initialized in a random coil
configuration. Figure 4.1a shows a snapshot of a sample initial configuration. Discontinuous molecular dynamics simulations \(^2\) were performed on the C chain at a low reduced temperature till the C chain collapsed to a globular conformation as shown in Figure 4.1b. The segments in the final globular conformation were sorted in order of their distance from the center of the globule. The 35 segments of type C farthest from the center were colored to be D as depicted in Figure 4.1c. The coloring procedure resulted in the creation of a 70-mer C-D PLC with a composition of \(x_c = x_d = 0.5\). After the coloring procedure, the configuration of the C-D PLC was relaxed. Figure 4.1d shows a snapshot of a sample C-D 70-mer PLC generated via the instantaneous coloring procedure.

MC simulations were performed on the binary and ternary blend systems. The simulations on the blend systems were started in a random configuration at the desired volume fraction. Initially the blend systems were uniformly mixed, but once the interactions were turned on MC simulations were performed for 100,000 Monte Carlo steps (MCS); the systems demix sufficiently into homopolymer A-rich and homopolymer B-rich phase for us to consider this a phase separated system. In each MCS, all beads in the system are moved once on average.

To monitor the dynamics of phase separation the following measures are used: 1) the normalized number of nearest-neighbor contacts between segments of A-A (\(\langle n_{AA} (t) \rangle / \langle n_{AA} (0) \rangle\)), B-B (\(\langle n_{BB} (t) \rangle / \langle n_{BB} (0) \rangle\)), and A-B (\(\langle n_{AB} (t) \rangle / \langle n_{AB} (0) \rangle\)) where \(t\) is the time elapsed since the start of the phase separation, 2) the fraction of the nearest-neighbor contacts between the PLC and homopolymer segments \(f_{CA} (t), f_{CB} (t), f_{DA} (t), \) and \(f_{DB} (t),\)
3) the PLC chain expansion ratio, i.e., the normalized PLC radius of gyration \( \langle R_g^2(t) \rangle / \langle R_g^2(0) \rangle \), 4) the time-dependent collective structure factor for the binary blend and the ternary compatibilized blends, 5) the first moment of the structure factor vs. time, 6) the scaling exponent, which is obtained from the slope of the first moment of the structure factor vs. time during the later stage of phase separation, and 7) the scaling function during the late stages of phase separation.

The fraction of contacts made by the C segments of the C-D PLC with homopolymer segments A, \( f_{CA}(t) \) is defined by the following equation:

\[
f_{CA}(t) = \langle n_{CA}(t) / (n_{CA}(t) + n_{CB}(t)) \rangle
\] (4.1)

where \( n_{CA}(t) \), and \( n_{CB}(t) \) refer to the nearest-neighbor contacts between segments of C-A and C-B respectively at time \( t \). Similarly \( f_{CB}(t) \), \( f_{DA}(t) \), and \( f_{DB}(t) \) can also be defined.

The PLC chain expansion ratio, \( \langle R_g^2(t) \rangle / \langle R_g^2(0) \rangle \) where \( \langle R_g^2(t) \rangle \) is defined by the following equation:

\[
\langle R_g^2(t) \rangle = \frac{\sum_{i=1}^{N_{PLC}} \sum_{j=1}^{n_{segment}} \{ r_{i,j}(t) - r_{i}^{cm}(t) \}^2}{n_{PLC} n_{segment}}
\] (4.2)

In equation (4.2) \( \langle R_g^2(t) \rangle \) is the PLC radius of gyration at time \( t \) while \( \langle R_g^2(0) \rangle \) is the PLC radius of gyration initially. \( r_{i,j}(t) \) is the position of the \( j \)-th monomer on the \( i \)-th PLC chain at time \( t \) and \( r_{i}^{cm}(t) \) is the position of the center of mass of the \( i \)-th PLC chain at time \( t \), \( N_{PLC} \) is the number of PLC chains, \( n_{segment} \) is the number of spheres in a single PLC chain.
The time-dependent collective structure factor for both the binary and ternary blend systems is evaluated to monitor the time evolution of the long-range ordering. The structure factor is the Fourier transform of the pair correlation function and is defined by the following equation:

\[
S(q,t) = \left\langle \left( \sum_{r_j} \exp(i\mathbf{q} \cdot \mathbf{r}_j) \left( \phi^A_j(t) - \phi^B_j(t) - \langle \phi^A_j - \phi^B_j \rangle \right) \right)^2 \right\rangle / L^3
\]  

(4.3)

where \( L \) is the box length, the scattering vector \( \mathbf{q} \) is defined as \( \mathbf{q} = 2\pi \mathbf{n}/L \) where \( \mathbf{n} \) represents a positive integer vector, i.e. \( \mathbf{n} = (n_x, n_y, n_z) \), the local concentration variable \( \phi^A_j(t) \) (or \( \phi^B_j(t) \)) at time \( t \) is equal to one if lattice site \( j \) is occupied by an A (or B) segment and zero otherwise, and the outer angular bracket \( \langle \ldots \rangle \) denotes a thermal statistical average. The contribution from the PLC chains to the collective structure factor is neglected since we are principally interested in the phase separation of homopolymers A and B, and the PLC compatibilizer loading (≈4.92%) is small relative to the homopolymers. To improve the statistics in \( q \) space the collective structure factor is spherically averaged as follows:

\[
S(q,t) = \sum_{q \left( \frac{\Delta q}{2} \right) \leq q \leq q + \frac{\Delta q}{2}} S(q,t) / m(q,\Delta q)
\]  

(4.4)

where

\[
m(q,\Delta q) = \sum_{q \left( \frac{\Delta q}{2} \right) \leq q \leq q + \frac{\Delta q}{2}} 1
\]  

(4.5)
denotes the number of lattice points in a spherical shell of radius \( q \) with \( \Delta q \) as the shell thickness. In light-scattering experiments on real immiscible polymer blends the intensity of light scattered or the structure factor \( S(q,t) \) is small initially (for all values of the scattering vector or scattering angle \( q \)) as the homopolymers are uniformly mixed, but a distinct peak in the structure factor \( S(q^*,t) \) develops at a scattering vector \( q^* \) as the phase separation occurs. Physically at time \( t \), \( 1/q^* \) is a measure of the characteristic length scale in the blend while \( S(q^*,t) \) is a measure of the difference in concentrations of the constituent homopolymers in the polymer blend.

We evaluate the first moment \( q_l(t) \) of the structure factor \( q_l(t) = \sum_q q S(q,t) / \sum_q S(q,t) \).

The inverse of \( q_l(t) \) is a measure of the average domain size of the phase-separated domains in both the binary and ternary blends. It is well known that \( q_l(t) \) is time invariant in the early stage of phase separation where Cahn’s linearized theory\(^6,53\) is applicable. In the late stages \( q_l(t) \) decreases with increasing phase separation time due to growth in the size of the phase-separated domains. The time dependence of \( q_l(t) \) in the later stage of phase separation is characterized by the following power law\(^9\) equation:

\[
q_l(t) \sim t^{-\alpha}
\]

(4.6)

where \( \alpha \) is the scaling or dynamical exponent whose value depends on the mechanism of domain growth. Although the scaling exponent is generally a function of phase separation time and temperature, it tends to reach 1/3 for \( t \to \infty \) when long-range hydrodynamic interactions are absent\(^54\), which is the case in our simulation. When long-range hydrodynamic
interactions are significant\textsuperscript{55,56} $\alpha = 1$. We obtain the scaling exponent from the slope of the log-log plot of $q_i(t)$ versus time in the late stages of phase separation for both the binary and ternary blends. The scaling exponent is useful for comparing the compatibilization effectiveness of various types of PLCs based on the values of the interaction energies and chain length. The smaller the value of the scaling exponent in a PLC compatibilized blend, the more effective the PLC is a compatibilizer. A smaller value of the scaling exponent implies a higher value of the slope in the log-log plot of $q_i(t)$ versus time during the late stages of phase separation, which, in turn, implies a higher value of $q_i(t)$ or smaller domain size (since scattering vector and length scale are inversely related) of phase-separated structures, and hence slower phase separation.

Phase-separated structures developed at various times during the late stages of phase separation in binary polymer blends exhibit self-similarity\textsuperscript{24,57}, i.e., the morphology change with time involves only an increase in the size of the phase-separated domains but not a change in the interfacial structure. If self-similarity exists between the phase-separated structures developed at various times during the late stages of phase separation for a demixing polymer blend, the structure factor can be rewritten in terms of a single time-dependent length parameter $1/q_i(t)$ and the scaling function $F(x)$ as described by the following equation:

$$S(q,t) = \left[\frac{1}{q_i(t)}\right]^3 F(x)/G$$  \hspace{1cm} (4.7)

where $x = q/q_i(t)$ is the reduced scattering vector, $F(x)$ is the scaling function, and $G$ is an arbitrary normalization constant. If the scaling law as described by equation (4.7) holds for
the binary polymer blend during the late stages of phase separation; the scaling function \( F(x) \) becomes independent of time during the late stages of phase separation. The scaling law for immiscible binary blends described above has also been shown to hold for binary blends compatibilized by diblock copolymers in the late stage of phase separation\textsuperscript{29-31} with the normalization constant \( G = (\pi \sum_{q} q^2 S(q,t))^{-1} L \), where \( L \) is the length of the simulation box. We test the validity of the scaling law as described in equation (4.7) for binary blends compatibilized by PLCs.

The properties for both the binary and ternary blend systems were averaged over five runs starting from uncorrelated random initial configurations. The results for ternary blends compatibilized by PLCs were averaged over three different copolymer sequences for a given initial configuration (five different initial configurations) and set of interaction energy parameters (\( \varepsilon_{AC} = -0.1, \varepsilon_{AC} = -0.2 \), and \( \varepsilon_{AC} = -0.5 \)) and chain lengths (30, 50, and 70 mers). Thus, 135 simulations were performed for ternary blends compatibilized by PLCs.

### 4.3 RESULTS AND DISCUSSION

Snapshots of the asymmetric binary blend system are shown in Figure 4.2 at various times during the demixing process. Figure 4.2 shows the binary blend (a) initially, (b) at a very early stage in the simulation (5k MCS), (c) halfway through the simulation (50k MCS), and (d) at the end of the simulation (100k MCS). As the phase separation progresses
homopolymer A-rich and homopolymer B-rich domains begin to form and grow. Figure 4.3 shows the ternary PLC compatibilized blend (a) initially, (b) at a very early stage in the simulation (5k MCS), (c) halfway through the simulation (50k MCS), and (d) at the end of the simulation (100k MCS). Comparison of Figures 4.2 and 4.3 gives a sense of how the presence of PLC compatibilizer retards the phase separation of the binary blend. In the ternary blend, homopolymer A-rich and homopolymer B-rich domains form and grow as was the case for the binary blend but this time the PLCs migrate to the biphasic interface between the two homopolymers, reducing unfavorable contacts, minimizing interfacial energy, and binding the two homopolymer phases together.

The process of phase separation in both binary and ternary blends is accompanied by a change in the number of A-A, B-B, and A-B contacts with time. We expect the number of A-A, and B-B contacts to increase and the number of A-B contacts to decrease with phase separation time. Figure 4.4 shows a plot of the normalized number of A-B contacts \( \langle n_{AB}(t) / n_{AB}(0) \rangle \) with phase separation time. The time has been restricted to the latter half of the simulation for clarity. In Figure 4.4a the PLC chain length is fixed to be 70 while the interaction energy is varied. As the strength of the favorable interaction energy between the PLC blocks and homopolymers increases, the normalized number of A-B contacts increases, implying an increase in the effectiveness of PLCs as compatibilizers. In Figure 4.4b the interaction energy is fixed to be \( \varepsilon_{AC} = \varepsilon_{BD} = -0.5 \) while the PLC chain length is varied. As the PLC chain is increased from 30 to 70 the normalized number of A-B contacts increases.
marginally, implying a nominal improvement in compatibilization effectiveness with increasing PLC chain length.

As the phase separation evolves in blends compatibilized by PLCs, the PLCs migrate to the biphasic interface between the two homopolymers to penetrate both homopolymer-rich phases. To monitor the extent of penetration of PLCs into the homopolymer-rich phases we monitor the fraction of the contacts between the PLC and homopolymer segments $f_{CA}(t)$, $f_{CB}(t)$, $f_{DA}(t)$, and $f_{DB}(t)$. Since the interaction between components C and A is favorable we expect $f_{CA}(t)$ to increase with time. Figure 4.5 shows a plot of the $f_{CA}(t)$ with phase separation time. In Figure 4.5a the PLC chain length is fixed to be 70 while the interaction energy is varied. As the strength of the favorable interaction energy between the PLC blocks and homopolymers increases, $f_{CA}(t)$ increases, implying the increase in effectiveness of PLCs as compatibilizers. In Figure 4.5b the interaction energy is fixed to be $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$ while the PLC chain length is varied. As the PLC chain length is increased from 30 to 70, $f_{CA}(t)$ increases marginally implying a nominal improvement in compatibilization effectiveness with increasing PLC chain length.

Figure 4.6 depicts the PLC chain expansion ratio or normalized radius of gyration with phase separation time. In Figure 4.6a the PLC chain length is fixed to be 70 while the interaction energy is varied. In Figure 4.6b the interaction energy is fixed to be $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$ while the PLC chain length is varied. The performance of PLCs as compatibilizers improves with increasingly favorable interaction energies between the PLC
blocks and homopolymers and with PLC chain length. One would expect the effective PLC compatibilizers to have a higher PLC chain expansion ratio as they are likely to stretch more forming engagements with the homopolymers-rich phases in comparison to ineffective PLC compatibilizers. However, we do not observe this trend here. We do not have a good explanation for this anomaly; it will be the subject of further investigation.

To quantify the extent of phase separation in both the binary and ternary compatibilized blends, we determine the spherically-averaged time-dependent collective structure factor \( S(q,t) \). Figure 4.7 shows a plot of \( S(q,t) \) versus the scattering vector for both the binary and PLC compatibilized ternary blends. Initially as the blend is homogeneous \( S(q,t) \) is small for all cases. With increasing phase separation time a distinct peak develops and the location of the peak shifts towards smaller values of the scattering vector, signifying the growth in size of the phase-separated domains. This behavior is also observed in light scattering experiments on real polymer blends. An efficient compatibilizer would suppress the peak of \( S(q,t) \) and shift it to higher values of the scattering vector. The structure factor for the binary blend without any PLC compatibilizer is shown in Figure 4.7a. In Figure 4.7b the PLC chain length is fixed to be 70 while the interaction energy is varied. As the strength of the favorable interaction energy between the PLC blocks and homopolymers increases, the peak in \( S(q,t) \) is suppressed, implying an increase in effectiveness of PLCs as compatibilizers. In Figure 4.7c the interaction energy is fixed to be \( \varepsilon_{AC} = \varepsilon_{BD} = -0.5 \) while the PLC chain length is varied. As the PLC chain is
increased from 30 to 70 the peak of $S(q,t)$ is suppressed marginally implying a nominal improvement in compatibilization effectiveness with increasing PLC chain length.

To gain further insight into the time evolution of the structure factor in the late stage of phase separation we evaluate the first moment of the structure factor $q(t)$. The inverse of $q(t)$ is a measure of the average size of the phase-separated domains in both the binary and ternary compatibilized blends. Figure 4.8a shows a log-log plot of $q(t)$ versus time for the binary polymer blend. In the early stage of phase separation $q(t)$ is time invariant, as predicted by Cahn’s linearized theory$^{6,53}$. In the late stages of phase separation, $q(t)$ decreases with time due to growth in the size of the phase-separated domains. Since $q(t)$ in the late stage of phase separation can be characterized by a power law$^9$, we obtain the scaling exponent $\alpha = 0.311$ from the slope of the plot in the late stage of phase separation. Our value is reasonably close to the theoretically accepted value of $\alpha = 1/3$ for a binary blend under the asymptotic limit ($t \to \infty$) when long-range hydrodynamic interactions are insignificant$^{54}$, which is the case in our simulation. In Figure 4.8b we plot the scaling exponent for the ternary blend compatibilized by PLCs of different chain lengths and interaction energies. The scaling exponent values shown are evaluated over roughly identical time intervals in order to make fair comparison between the phase separation processes. The smaller the value of the dynamic scaling exponent, the more effective the PLC is as a compatibilizer for the immiscible binary blend. A smaller value of the scaling exponent implies a higher value of the slope in the log-log plot of $q(t)$ versus time during the late stages of phase separation,
which implies a higher value of \( q(t) \) or smaller domain size (since scattering vector and length scale are inversely related) of phase-separated structures, and hence slower phase separation. The scaling exponent analysis gives us a quick way to compare all of the nine ternary blend systems (3 PLC chain lengths, and 3 values of the interaction energies); unlike the other analyses that we presented before in which the PLC interaction energy is held fixed while the PLC chain is varied and vice versa. Longer PLC chains which exhibit strong interaction with homopolymers are most effective in slowing down the process of phase separation in immiscible binary blends as they lead to smaller values of the dynamical scaling exponent.

To test the applicability of dynamical scaling laws in the late stage of phase separation in binary polymer blends compatibilized by PLCs, we evaluate the scaled structure factor as described earlier in the method and model section. Figure 4.9 shows a plot of the scaled structure factor, \( F(x) = G[q_1(t)]^3 S(q,t) \), versus the reduced scattering angle \( x = q / q_1(t) \) at various times in the late stages \((t \geq 80k \text{ MCS})\) of phase separation for a binary blend compatibilized by 70-mer PLC with interaction energy \( \varepsilon_{AC} = \varepsilon_{BD} = -0.5 \). Since the scaled structure factors at various times in the late stages of phase separation all fall on a single master curve, this establishes the existence of dynamical self-similarity amongst the growing phase-separated structures in the blend compatibilized by PLCs. Figure 4.10 shows a plot of the scaled structure factor at the end of the simulation (100k MCS) for the ternary A/B/C-plc-D blend compatibilized by various types of PLCs at various values of the interaction energies between the PLC blocks and homopolymers and the PLC chain length.
In Figure 4.10a the PLC chain length is fixed to be 70 and the interaction energy is varied. In Figure 4.10b the interaction energy is fixed to be $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$ while the PLC chain length is varied. It is evident from Figures 4.10a and 4.10b that the scaled structure factor is nearly independent of both the interaction energy $\varepsilon_{AC} = \varepsilon_{BD}$ as well as the PLC chain length for all values of the reduced scattering angle explored by the simulation. This behavior implies universality of the scaled structure factor which means that the phase-separated domains in the ternary compatibilized blend grow with dynamical self-similarity irrespective of the type of PLC added.

4.4 CONCLUSIONS

We have performed kinetic Monte Carlo simulations aimed at understanding the effect of adding \( \approx 4.92\% \) protein-like copolymer (PLC) on the dynamics of phase separation of a polymer blend containing two immiscible homopolymers A and B, where the C-plc-D copolymer used consists of blocks chemically different from the homopolymers. The ability of PLCs to effectively retard the process of phase separation depends sensitively on the interaction energy between the PLCs and homopolymers, and the PLC chain length.

We have evaluated the number of nearest-neighbor contacts, the time-dependent collective structure factor, the first moment of structure factor, and the dynamical scaling exponent to monitor the process of phase separation and gauge the effectiveness of various
types of PLCs as characterized by the PLC-homopolymer interaction strength parameters and the PLC chain length. The effectiveness of PLCs as compatibilizers improves with increasingly favorable interaction energies between the PLC segments and homopolymers and with the PLC chain length. There is a limit to the enhancement in performance of PLCs as compatibilizers attained as the PLC chain length increases. Contrary to our expectation the effective PLC compatibilizers (long PLC chains with strong interactions with homopolymers) do not stretch as much as the less effective PLC compatibilizers (short PLC chains with weak interactions with homopolymers). We do not have an explanation for this anomaly and this will be subject of future investigation.

The process of phase separation in binary polymer blends compatibilized by PLCs obeys scaling laws during the late stage which implies the existence of self-similarity between the phase-separated structures developed at various times, i.e. the morphology change with time involves only an increase in the size of the phase-separated domains but not a change in the interfacial structure. To the best of our knowledge no experiments have been performed on using PLCs as compatibilizers for immiscible polymer blends. Light-scattering experiments on the dynamics of phase separation in blends compatibilized by PLCs are needed to validate our findings. It is interesting to note that scaling laws which hold for blends compatibilized by diblock \textsuperscript{29-31} copolymers also hold for PLC compatibilized blends.

The scaling functions in PLC compatibilized blends are universal as they are nearly independent of the interaction energy and the PLC chain length. Thus the phase-separated domains grow with dynamical self-similarity irrespective of the type of PLCs added to the
binary blend, although the type of PLC significantly alters the growth rate of the phase-separated domains.

Our work has practical implications for optimizing the performance of PLCs as compatibilizers for immiscible blends with respect to the PLC chain length and attractive interactive interaction energy between the PLC blocks and homopolymers. Optimizing the performance of PLCs as compatibilizers with respect to the composition of PLCs and the case of PLCs with repulsive interactions with homopolymers will be subject of future work.
4.5 FIGURES

Figure 4.1 Snapshots illustrating instantaneous coloring procedure to generate 70-mer CD PLC (C = dark blue, D = light pink) with composition $x_c = x_D = 0.5$: (a) random configuration of 70-mer C chain, (b) collapsed globular configuration of the C chain, (c) 35 spheres farthest from the center of the globule are colored to type D, and (d) relaxed chain configuration of the resulting CD 70-mer PLC.
Figure 4.2 Simulation snapshots of the A/B binary blend (A = light blue, B = red) at time:
(a) $t=0$ (initial configuration), (b) $t=5k$ MCS (early stage configuration), (c) $t=50k$ MCS
(halfway configuration), and (d) $t=100k$ MCS (final configuration).
Figure 4.3 Simulation snapshots of the A/B/C-plc-D ternary blend (A = light blue, B = red, C = dark blue, D = light pink) compatibilized by 70-mer PLC with $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$ at time: (a) $t=0$ (initial configuration), (b) $t=5k$ MCS (early stage configuration), (c) $t=50k$ MCS (intermediate configuration), and (d) $t=100k$ MCS (final configuration).
Figure 4.4 Normalized A-B contacts $\langle n_{AB}(t) \rangle / \langle n_{AB}(0) \rangle$ with phase separation time: (a) interaction energy $\varepsilon_{AC}$ varied (70-mer PLC), and (b) PLC chain length varied (fixed interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$).
Figure 4.5 Fraction of C-A contacts $f_{CA}(t)$ with phase separation time: (a) interaction energy $\varepsilon_{AC}$ varied (70-mer PLC), and (b) PLC chain length varied (fixed interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$).
Figure 4.6 PLC chain expansion ratio or normalized radius of gyration $\left< R_g^2(t) \right> / \left< R_g^2(0) \right>$ with phase separation time: (a) interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.1$, and (b) PLC chain length varied (fixed interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$).
Figure 4.7 Evolution of $S(q,t)$ with phase separation time for: (a) binary A/B blend, (b) ternary A/B/C-plc-D blend - interaction energy $\varepsilon_{AC}$ varied (70-mer PLC), and (c) ternary A/B/C-plc-D blend - PLC chain length varied (fixed interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$).
Figure 4.8 (a) $q(t)$ with phase separation time for A/B binary blend, and (b) scaling exponent for the ternary A/B/C-$plc$-D blend.
Figure 4.9 Scaling function in the late stage of phase separation for a binary blend compatibilized by 70-mer PLC with interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$. 
Figure 4.10 Scaling function in the late stages of phase separation for ternary A/B/C-plc-D blend: (a) interaction energy $\varepsilon_{AC}$ varied (70-mer PLC), and (b) PLC chain length varied (fixed interaction energy $\varepsilon_{AC} = \varepsilon_{BD} = -0.5$).
4.6 REFERENCES


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CHAPTER FIVE

Effect of Protein-like Copolymers Composition on the Phase Separation Dynamics of a Polymer Blend: a Monte Carlo Simulation

5.1 INTRODUCTION

This paper is part of a series designed to explore the possibility that protein-like copolymers could be useful as compatibilizing agents for polymer blends. Protein-like copolymers (PLCs) are a new class of functional copolymers whose block length sequence distribution obeys Levy flight statistics in contrast to traditional random-block copolymers, whose block length obeys a Poisson distribution \(^1-^3\). PLCs can be prepared in the laboratory by adjusting the compactness of a parent homopolymer “A” (by exposing it to poor solvent) and then reacting exposed segments on the outer surface with other species in the surrounding solution, turning them into distinctly different segments, “B”\(^4\). Thus far we have shown via computer simulations that (PLCs) could be an attractive alternative to diblock, random, alternating, and simple linear gradient copolymer compatibilizers from thermodynamic equilibrium\(^5\) and kinetic\(^6\) points of view. We also found that the dynamics of phase separation in ternary PLC compatibilized blends depends sensitively on the interaction energy between the PLC blocks and the homopolymers, and on the PLC chain length\(^7\). In this
paper we investigate the effect of PLC composition on the dynamics of phase separation of an immiscible polymer blend in the presence of PLCs as compatibilizers.

In order to control the morphology and properties of immiscible polymer blends through the use of compatibilizers it is necessary to understand the mechanisms that govern the phase separation dynamics. Particular attention has been paid to the impact of diblock compatibilizers on phase separation dynamics in immiscible polymer blends because diblock copolymers are already being used as compatibilizers.

The effect of diblock copolymer composition on the phase separation dynamics of an A/B asymmetric polymer blend was explored by Kim et al. using Monte Carlo simulations. Their simulations suggest that diblocks with composition similar to that of the asymmetric blend are optimal compatibilizers when the copolymers are much longer than the homopolymers and that symmetric diblocks are optimal compatibilizers when the copolymers are shorter than the homopolymers. Thomas and Prud’homme performed experiments to study the compatibilization effect of PS-b-PMMA diblock copolymers on an asymmetric immiscible polymer blend containing 70% PS and 30% PMMA where the PS-b-PMMA diblocks were much longer than either the PS or PMMA homopolymers. Their experiments suggest that symmetric diblock copolymers were optimal compatibilizers for the asymmetric blend. Since these two groups were working on different cases it is hard to draw any general conclusions from their reports. Nevertheless it would be of interest to verify if the optimal PLC composition for asymmetric blends follows trends similar to those observed for diblocks.
In this work, we use kinetic Monte Carlo simulations to investigate the effect of PLC composition on the phase separation dynamics of an immiscible blend compatibilized by \(\approx4.92\%\) PLCs. The simulations are performed on an asymmetric immiscible binary blend comprised of 9736 20-mers of homopolymer A and 2434 20-mers of homopolymer B. The ternary PLC compatibilized blend consists of the binary blend plus 420 30-mer PLCs composed of monomers of type C and D, which have favorable interaction with homopolymers A and B, respectively. The binary blend and PLC compatibilized ternary blends are homogeneous initially. Introduction of a positive pairwise interaction energy between segments of type A and B leads to the phase separation of homopolymers A and B. The phase separation of the immiscible polymer blend is accompanied by the formation and growth of homopolymer A-rich and homopolymer B-rich domains. However in the ternary compatibilized blend the phase separation is retarded as the PLCs preferentially segregate between the two homopolymers, minimizing the interfacial tension and unfavorable interactions. The process of phase separation is monitored by recording the normalized number of contacts between segments A and B \((n_{AB}(t))/\langle n_{AB}(0) \rangle\). The extent of penetration of PLCs into the homopolymer-rich phase over time is monitored by recording the fraction of contacts made by the PLC segments with homopolymer segments \(f_{CA}(t), f_{CB}(t), f_{DA}(t),\) and \(f_{DB}(t)\). The extent of PLC chain expansion with time is monitored by evaluating the normalized radius of gyration \(\langle R_g^2(t) \rangle/\langle R_g^2(0) \rangle\) of the PLC. The conformation of PLCs at the interface is evaluated in order to quantify the weaving ability of PLCs. The dynamics of phase separation in both the binary and the ternary blends is measured using the time...
dependent collective structure factor $S(q, t)$. To gauge the compatibilization effectiveness of PLCs with different compositions; the dynamic scaling exponent associated with $q(t)$, the first moment of the structure factor versus time, is calculated for the late stages of phase separation. To corroborate the existence of self-similarity amongst the phase separated structures at different times during the late stages of phase separation, the structure factor $S(q, t)$ in both the binary and ternary blends is scaled in terms of a characteristic length parameter $1/q(t)$ and scaling function $F(x)$, and the time independence of $F(x)$ during the late stages of phase separation is tested. The universality of the scaling function is tested for ternary blends with different PLC compositions.

Highlights of our results are as follows. C-plc-D copolymers irrespective of their composition segregate preferentially between the immiscible homopolymers, minimizing the unfavorable interactions and leading to compatibilization of the immiscible binary blend. The ability of PLCs to effectively retard the process of phase separation depends sensitively on the PLC composition. PLCs with composition around $0.3 \leq x_c \leq 0.5$ are most effective in compatibilizing the asymmetric A/B blend (80% A, 20% B). PLCs penetrate and weave back and forth across the interface between the phase separated domains; this weaving effect is more pronounced for PLCs with composition $x_c \leq 0.5$. The optimal diblock compatibilizer composition suggested by the work of Kim et al.\textsuperscript{13} of $x_c = 0.8$ does not apply to our PLCs, but the optimal PLC composition based on the experiments of Thomas and Prud’homme\textsuperscript{17} of $x_c = 0.5$ is closer to our optimal diblock copolymer composition. As we have already seen in previous work\textsuperscript{7}, the phase-separated structures developed at different times during the late
stages of phase separation exhibit self-similarity (i.e. the morphology change with time only involves an increase in the size of phase separated domains but no change in the interfacial structure) in both the binary and ternary blends. Thus the structure factor $S(q,t)$ can be rewritten in terms of a characteristic length parameter $1/q_i(t)$ and a time-invariant scaling function $F(x)$. Here we show that $F(x)$ is universal meaning it is nearly independent of the PLC composition for the binary blends compatibilized by PLC during the late stages of phase separation.

In the next section, we describe the MC method and the generation of PLCs via the instantaneous coloring procedure of Khokhlov and co-workers. The following section presents the simulation results for the effect of PLC composition on the dynamics of phase separation of immiscible binary blends compatibilized by PLCs. The final section concludes with a short summary of the results and a discussion.

5.2 MODEL AND METHOD

The A/B binary blend system consists of 9736 20-mers of type A and 2434 20-mers of type B. The ternary (compatibilized) blend contains the binary blend plus protein-like copolymer chains ($\approx 4.92\%$ of total number of segments in the ternary blend system) containing monomers of type C and D. The composition of PLC chains added is varied from $x_c = 0.1$ to $x_c = 0.9$ in steps of 0.1. The PLCs and homopolymers are modeled as self-avoiding walks on a three dimensional cubic lattice. The phase separation of homopolymer chains A
and B is induced by introducing positive repulsive pairwise interaction energy between A and B segments $e_{AB} = e_{AB}/k_BT = 0.5$ in both the binary and ternary blend systems. Since the C-D PLC compatibilizer is composed of segments that are chemically different from the homopolymer units, one must specify ten monomer-monomer interaction parameters: $e_{AB}, e_{AC}, e_{AD}, e_{BC}, e_{BD}, e_{CD}, e_{AA}, e_{BB}, e_{CC}, e_{DD}$. The values of $e$ used are listed in Table 5.1. The interaction energies between the segments of homopolymer A and the segments of type C ($e_{AC}$) on the C-D PLC, and between the segments of homopolymer B and the segments of type D ($e_{BD}$) on the C-D PLC are both chosen to be negative, so that the C-D PLCs become effective compatibilizing agents for the immiscible A/B binary blend. The strengths of the interaction energies $e_{AC}$, $e_{BD}$ are both set equal to -0.5. The interaction energies $e_{AD}$, $e_{BC}$, and $e_{CD}$ are all set equal to +0.5, to discourage miscibility between their corresponding segments. The interaction energies between identical segments are set to zero ($e_{AA} = e_{BB} = e_{CC} = e_{DD} = 0$). Additionally the interaction energies between each segment type and the empty sites are set to zero. To calculate the energy of the system we need to decide on a range of the interactions; this is usually reported in terms of the number of nearest neighbors to any site that experience an interaction. The MZCCL (the eighteen vectors obtained by all the sign inversions and permutation of the two vector families $P(1,0,0)\cup P(1,1,0)$ between segments assuming one of the segments is located at $(0,0,0)$) interaction range was chosen.
Table 5.1 Matrix of Interaction Parameters

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<tr>
<td>B</td>
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The lattice MC simulations are based on the three-dimensional bond fluctuation model (BFM) performed in the NVT ensemble. We chose the BFM to model the dynamics of phase separation in polymer blends since it has been utilized previously to predict the properties of dense polymer melts successfully. In the BFM each monomer represents a Kuhn segment and occupies eight sites on a simple cubic lattice. Successive monomers along the chain are connected via a predetermined set of bond vectors. In order to avoid bond crossing and monomer overlap, the bond vectors are derived from all possible permutations and sign inversions of the following six vector families: \( P(2,0,0) \cup P(2,1,0) \cup P(2,1,1) \cup P(2,2,1) \cup P(3,0,0) \cup P(3,1,0) \). For example, all possible permutations and sign inversions of the vector family \( P(2,0,0) \) yield the following six distinct bond vectors: (2,0,0), (-2,0,0), (0,2,0), (0,-2,0), (0,0,2), and (0,0,-2). Repeating this process for all the six vector families leads to a total of 108 bond vectors and 87 bond angles.
Thus, the model possesses some of the flexibility associated with an off-lattice model while maintaining the advantages associated with working on a lattice, such as integer arithmetic and parallelization. The MC algorithm is executed in the following manner. First a monomer unit is chosen at random, and translated by one lattice spacing in a direction chosen randomly out of the six possible directions. Next a check is done to verify that the resulting move does not violate the excluded volume and bond constraints set forth by the BFM. If it does, the move is rejected and the monomer is restored to its original position. If all the BFM constraints are satisfied, the Metropolis sampling rule is applied, i.e. the move is accepted with a probability equal to \( \min(1, \exp(-\Delta E/k_B T)) \), where \( \Delta E \) is the energy change due to the move, \( k_B \) is the Boltzmann constant and \( T \) is the temperature. The lattice MC simulations are performed on a simple cubic lattice of \( L \times L \times L \) sites with \( L = 80 \). The volume fraction, \( \phi = N/L^3 \), for the pure as well as compatibilized blend is set to \( \phi = 0.5 \), where \( N \) is the number of occupied sites in the simulation box. Periodic boundary conditions are imposed in all three directions (\( x \), \( y \), and \( z \)) to overcome the limitation of finite system size.

The 30-mer C-D PLCs with varying compositions were generated via a simulation-based instantaneous coloring procedure originally proposed by Khokhlov et al.\(^1\)\(^-\)\(^3\). A detailed description of our implementation of Khokhlov’s coloring procedure to generate C-D PLCs via discontinuous molecular dynamics (DMD) simulation can be found in our previous work\(^5\).

MC simulations were performed on the binary and ternary blend systems. The simulations on the blend systems were started in a random uniformly-mixed initial
configuration at the desired volume fraction. After the interactions were turned on and 100,000 Monte Carlo steps (MCS were performed, the systems demix sufficiently into homopolymer A-rich and homopolymer B-rich phase for us to consider this a phase separated system. In each MCS, all beads in the system are moved once on average.

To monitor the dynamics of phase separation the following measures are used: 1) the normalized number of nearest-neighbor contacts between segments A and B \( \left( \frac{\langle n_{AB}(t) \rangle}{\langle n_{AB}(0) \rangle} \right) \) where \( t \) is the time elapsed since the start of the phase separation, 2) the PLC chain expansion ratio, i.e., the normalized PLC radius of gyration \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \), 3) the time-dependent collective structure factor for the binary blend and the ternary compatibilized blends, 4) the first moment of the structure factor vs. time, 5) the scaling exponent, which is obtained from the slope of the first moment of the structure factor vs. time during the later stage of phase separation, and 6) the scaling function during the late stages of phase separation.

The PLC chain expansion ratio, \( \frac{\langle R_g^2(t) \rangle}{\langle R_g^2(0) \rangle} \) is calculated where \( \langle R_g^2(t) \rangle \) is defined by the following equation:

\[
\langle R_g^2(t) \rangle = \frac{1}{N_{PLC}^n_{segment}} \sum_{i=1}^{N_{PLC}^n_{segment}} \sum_{j=1}^{n_{segment}} \left( r_{i,j}(t) - r_{i}^{cm}(t) \right)^2 / \left\{ N_{PLC}^n_{segment} \right\}
\]

In equation (5.1), \( \langle R_g^2(t) \rangle \) is the PLC radius of gyration at time \( t \) while \( \langle R_g^2(0) \rangle \) is the PLC radius of gyration initially. \( r_{i,j}(t) \) is the position of the \( j \)-th monomer on the \( i \)-th PLC chain
at time $t$ and $r_i^{cm}(t)$ is the position of the center of mass of the $i$-th PLC chain at time $t$, $N_{PLC}$ is the number of PLC chains, $n_{segment}$ is the number of spheres in a single PLC chain.

We determine the conformation of the PLCs at the interface at instant in time at the end of the simulation for a single PLC sequence. To do so we move along a PLC chain and for a given PLC segment we calculate the difference between the number of nearest-neighbor contacts of that PLC segment with homopolymer segment A and with homopolymer segment B, $\langle N_A - N_B \rangle$. The $\langle N_A - N_B \rangle$ is averaged over five different initial random configurations of the ternary PLC compatibilized blend for a single PLC sequence at an instant in time at the end of the simulation i.e., at 100k MCS. If $\langle N_A - N_B \rangle$ is large and positive it implies that the PLC segment resides preferentially in the homopolymer A-rich phase, while a small and negative value of $\langle N_A - N_B \rangle$ implies that the PLC segment lies preferentially in the homopolymer B-rich phase.

The time-dependent collective structure factor for both the binary and ternary blend systems is calculated to monitor the time evolution of the long-range ordering. The structure factor is the Fourier transform of the pair correlation function and is defined by the following equation:

$$S(q,t) = \left\langle \left| \sum_{r_j} \left( e^{i\mathbf{q} \cdot \mathbf{r}_j} \right) (\phi_A^i(t) - \langle \phi_A^i \rangle) \right|^2 \right\rangle / L^3 \quad (5.2)$$

where the scattering vector $\mathbf{q}$ is given by $\mathbf{q} = 2\pi \mathbf{n} / L$ with $\mathbf{n}$ equal to a positive integer vector, i.e., $\mathbf{n} = (n_x, n_y, n_z)$, the local concentration variable $\phi_A^i(t)$ (or $\phi_B^i(t)$) at time $t$ is equal to
1 if lattice site \( j \) is occupied by an A (or B) segment and 0 otherwise. The outer angular bracket \( \langle \ldots \rangle \) denotes a thermal statistical average. The contribution from the PLC chains to the collective structure factor is neglected since we are interested principally in the phase separation of homopolymers A and B, and the CD PLC compatibilizer loading (\( \approx \)4.92 \%) is small relative to the homopolymers. To improve the statistics in \( q \)-space the collective structure factor is averaged spherically as follows:

\[
S(q, t) = \sum_{q\left(\frac{\Delta q}{2}\right) \leq q \leq q + \left(\frac{\Delta q}{2}\right)} S(q, t) / m(q, \Delta q)
\]

where

\[
m(q, \Delta q) = \sum_{q\left(\frac{\Delta q}{2}\right) \leq q \leq q + \left(\frac{\Delta q}{2}\right)} 1
\]

denotes the number of lattice points in a spherical shell of radius \( q \) with \( \Delta q \) as the shell thickness. In light-scattering experiments on real immiscible polymer blends, the intensity of light scattered, which is related to the structure factor, \( S(q, t) \) is small initially (for all values of the scattering vector or scattering angle \( q \) as the homopolymers are mixed uniformly. As the phase separation progresses, a distinct peak in the structure factor \( S(q^*, t) \) develops at a scattering vector \( q^* \). Physically, at time \( t \), \( 1/q^* \) is a measure of the
characteristic length scale in the blend while \( S(q^*, t) \) is proportional to the difference in concentrations of the constituent homopolymers in the polymer blend.

We evaluate the first moment \( q_1(t) \) of the structure factor \( q_1(t) = \sum_q q S(q, t) / \sum_q S(q, t) \). The inverse of \( q_1(t) \) is a measure of the average domain size of the phase-separated domains in both the binary and ternary blends. It is well known that \( q_1(t) \) is time invariant in the early stage of phase separation where Cahn’s linearized theory\(^{25,26}\) is applicable. In the late stages \( q_1(t) \) decreases with increasing phase separation time due to growth in the size of the phase-separated domains. The time dependence of \( q_1(t) \) in the later stage of phase separation is characterized by the following power law\(^{27}\) equation:

\[
q_1(t) \sim t^{-\alpha}
\]  

(5.5)

where \( \alpha \) is the scaling or dynamical exponent whose value depends on the mechanism of domain growth. Although the scaling exponent is generally a function of phase separation time and temperature, it tends to reach 1/3 for \( t \to \infty \) when long-range hydrodynamic interactions are absent\(^{28}\), which is the case in our simulation. When long-range hydrodynamic interactions are significant\(^{29,30}\) \( \alpha = 1 \). We obtain the scaling exponent from the slope of the log-log plot of \( q_1(t) \) versus time in the late stages of phase separation for both the binary and ternary blends. The scaling exponent is useful for comparing the compatibilization effectiveness of various types of PLCs based on the values of the interaction energies and chain length. The smaller the value of the scaling exponent in a PLC compatibilized blend, the more effective the PLC is as a compatibilizer. A smaller value of the scaling exponent
implies a higher value of the slope in the log-log plot of $q(t)$ versus time during the late stages of phase separation, which, in turn, implies a higher value of $q(t)$ or smaller domain size (since scattering vector and length scale are inversely related) of phase-separated structures, and hence slower phase separation.

Phase-separated structures developed at various times during the late stages of phase separation in binary polymer blends exhibit self-similarity\textsuperscript{31,32}, i.e., the morphology change with time involves only an increase in the size of the phase-separated domains but not a change in the interfacial structure. If self-similarity exists between the phase-separated structures developed at various times during the late stages of phase separation for a demixing polymer blend, the structure factor can be rewritten in terms of a single time-dependent length parameter $1/q(t)$ and the scaling function $F(x)$ as described by the following equation:

$$S(q,t) = \left[1/q(t)\right]^3 F(x)/G$$ \hspace{1cm} (5.6)

where $x = q/q(t)$ is the reduced scattering vector, $F(x)$ is the scaling function, and $G$ is an arbitrary normalization constant. If the scaling law as described by equation (5.6) holds for the binary polymer blend during the late stages of phase separation, the scaling function $F(x)$ becomes independent of time during the late stages of phase separation. The scaling law for immiscible binary blends described above has also been shown to hold for binary blends compatibilized by diblock copolymers in the late stage of phase separation\textsuperscript{11-13} with the normalization constant $G = (\pi \sum_q q^2 S(q,t))^{-1} L$, where $L$ is the length of the simulation.
box. We test the validity of the scaling law as described in equation (5.6) for binary blends compatibilized by PLCs.

The properties for both the binary and ternary blend systems were averaged over five runs starting from uncorrelated random initial configurations. The results for ternary blends compatibilized by PLCs were averaged over three different copolymer sequences for a given initial configuration (five different initial configurations) for each of the nine PLC chain compositions. Thus, 135 simulations were performed for ternary blends compatibilized by PLCs. The errors which represent the sample standard deviations of the properties calculated were within 4%. We chose not to represent the errors bars on the density profile plots for clarity.

5.3 RESULTS AND DISCUSSION

Figure 5.1 shows a plot of the normalized number of A-B contacts \( \langle n_{ab}(t)/n_{ab}(0) \rangle \) with phase separation time over the latter half of the simulation. A higher value of \( \langle n_{ab}(t)/n_{ab}(0) \rangle \) for an immiscible polymer blend is indicative of greater mixing amongst the constituent homopolymers A and B. The normalized number of A - B contacts decreases with time for all blend systems as they phase separate as expected. The PLCs with composition \( x_c \leq 0.5 \) are more effective in slowing down the process of phase separation than PLCs with composition \( x_c > 0.5 \) as they lead to a higher value of \( \langle n_{ab}(t)/n_{ab}(0) \rangle \). PLCs with
composition around $0.3 \leq x_c \leq 0.5$ are the best compatibilizers as they lead to the highest value of $\langle n_{AB}(t) / n_{AB}(0) \rangle$ for the blends they compatibilize. The $\langle n_{AB}(t) / n_{AB}(0) \rangle$ is higher for the PLC compatibilized ternary blends than for the binary (no-copolymer) blend which implies that all PLCs irrespective of composition act as compatibilizers.

**Figure 5.2** is a plot of the PLC chain expansion ratio or normalized radius of gyration versus phase separation time. PLCs with composition around $0.3 \leq x_c \leq 0.5$ have the highest chain expansion ratio. PLCs with extreme compositions like $x_c = 0.2$ or $x_c = 0.8$ have a lower chain expansion ratio. We expect PLCs with a higher chain expansion ratio to be effective as they are likely to stretch more and form engagements with the homopolymers-rich phases on either side of the interface.

To establish the conformation of the PLCs at the interface and the mechanism by which they stabilize the interface, we calculate the difference between the number of nearest-neighbor contacts of that PLC segment with homopolymer segment A, and with homopolymer segment B, $\langle N_A - N_B \rangle$ for each PLC segment along the PLC chain at an instant in time at the end of the simulation for a single PLC sequence. The $\langle N_A - N_B \rangle$ presented is averaged over five different initial random configurations of the ternary PLC compatibilized blend for a single PLC sequence at an instant in time at the end of the simulation *i.e.*, at 100k MCS. **Figure 5.3** depicts $\langle N_A - N_B \rangle$ along the PLC chain for various PLC compositions. A large and positive value of $\langle N_A - N_B \rangle$ for a particular PLC segment indicates that the PLC segment lies in the homopolymer A rich-phase. A small and negative value of $\langle N_A - N_B \rangle$ for a
particular PLC segment indicates that the PLC segment lies in the homopolymer B rich-phase. All PLCs irrespective of the composition stabilize the interface by weaving back and forth across the interface. The weaving is more pronounced for PLCs with composition $x_c \leq 0.6$ than PLCs with composition $x_c > 0.6$. PLCs with composition around $0.3 \leq x_c \leq 0.6$ are most effective in knitting across the interface binding the two homopolymer rich phases together. This analysis is useful because we do not have to make any a priori assumptions about the flatness of the biphasic interface between the two homopolymers.

To quantify the extent of phase separation in both the binary and ternary compatibilized blends, we determine the spherically-averaged time-dependent collective structure factor $S(q,t)$. Figure 5.4 shows a plot of $S(q,t)$ versus the scattering vector for both the binary and PLC compatibilized ternary blends. Initially as the blend is homogeneous $S(q,t)$ is small for all cases. With increasing phase separation time a distinct peak develops and the location of the peak shifts towards smaller values of the scattering vector, signifying the growth in size of the phase-separated domains. This behavior is also observed in light scattering experiments on real polymer blends$^{31-41}$. An efficient PLC compatibilizer would be expected to suppress the peak of $S(q,t)$ and shift it to higher values of the scattering vector. The structure factor for the binary blend without any PLC compatibilizer is shown in Figure 5.4a. Figures 5.4b through Figures 5.4f depict the $S(q,t)$ for the PLC compatibilized ternary blends with PLC composition varying from $x_c = 0.1$ to $x_c = 0.9$, respectively. PLCs with composition $x_c \leq 0.5$ suppress the peak in $S(q,t)$ effectively and are better compatibilizers than PLCs with composition $x_c > 0.5$. PLCs with composition
around $0.3 \leq x_c \leq 0.5$ are the best compatibilizers as they retard the process of phase separation by the greatest extent.

To gain further insight into the time evolution of the structure factor in the late stage of phase separation we evaluate the first moment of the structure factor $q_1(t)$. The inverse of $q_1(t)$ is a measure of the average size of the phase separated domains in both the binary and ternary compatibilized blends. We obtain the scaling exponent from the slope of the log-log plot of $q_1(t)$ versus time in the late stages of phase separation for both the binary and ternary blends. **Figure 5.5** shows the scaling exponent for the ternary blend compatibilized by PLCs with varying composition. The scaling exponent values shown are evaluated over roughly identical time intervals in order to make a fair comparison between the phase separation processes. The smaller the value of the dynamic scaling exponent, the more effective the PLC is as a compatibilizer for the immiscible binary blend. This is because a smaller value of the scaling exponent implies a higher value of the slope in the log-log plot of $q_1(t)$ versus time during the late stages of phase separation, which in turn implies a higher value of $q_1(t)$ or a smaller domain size (since scattering vector and length scale are inversely related), and hence slower phase separation. PLCs with composition $x_c \leq 0.5$ are more effective compatibilizers than PLCs with composition $x_c > 0.5$ as they lead to smaller values of the dynamical scaling exponent. PLCs with composition around $0.3 \leq x_c \leq 0.5$ are the best compatibilizers.

**Figure 5.6** shows a plot of the scaled structure factor at the end of the simulation (100k MCS) for the ternary A/B/C-plc-D blend compatibilized by PLCs with varying PLC
compositions. It is evident from Figure 5.6 that the scaled structure factor is nearly independent of PLC composition for all values of the reduced scattering angle explored by the simulation. This behavior implies universality of the scaled structure factor which means that the phase-separated domains in the ternary compatibilized blend grow with dynamical self-similarity irrespective of the PLC composition.

It is of interest to make comparisons between optimal compatibilizer composition for PLCs and diblock copolymers. The optimal diblock compatibilizer composition suggested by the work of Kim et al.\textsuperscript{13} of $x_c = 0.8$ does not apply to our PLCs, but the optimal PLC composition based on the experiments of Thomas and Prud'homme\textsuperscript{17} of $x_c = 0.5$ is closer to our optimal diblock copolymer composition. The optimal PLC compatibilizer composition based on our simulations is around $0.3 \leq x_c \leq 0.5$ which does not match the optimal diblock compatibilizer of either groups but it is closer to the optimal diblock compatibilizer composition based on the experiments of Thomas and Prud’homme\textsuperscript{17}.

We do not yet have a good physical explanation for why the optimal PLC compatibilizer composition in our simulations is around $0.3 \leq x_c \leq 0.5$. This will be the subject of future publications. It is also interesting to note that scaling laws which hold for blends compatibilized by diblock\textsuperscript{11-13} copolymers also hold for PLC compatibilized blends irrespective of the PLC composition.
5.4 CONCLUSIONS

We have performed kinetic Monte Carlo simulations aimed at understanding the effect of adding 4.92% protein-like copolymer (PLC) on the phase separation dynamics of a polymer blend containing two immiscible homopolymers A and B, where the C-plc-D copolymer used consists of blocks that are chemically different from the homopolymers. The ability of PLCs to effectively retard the process of phase separation depends sensitively on the PLC composition.

Nearest-neighbor contacts, extent of penetration of PLCs into the homopolymer rich-phases, PLC chain expansion ratio, conformation of the PLCs at the interface, time-dependent collective structure factor, first moment of structure factor, and dynamical scaling exponent were used to monitor the process of phase separation and gauge the effectiveness of various PLC compositions. PLCs with composition \( x_c \leq 0.5 \) are more effective compatibilizers than PLCs with composition \( x_c > 0.5 \). PLCs with composition around \( 0.3 \leq x_c \leq 0.5 \) are the best compatibilizers.

The scaling functions in PLC compatibilized blends are universal as they are nearly independent of the PLC composition. Thus the phase-separated domains grow with dynamical self-similarity irrespective of the composition of PLCs added to the binary blend, although the PLC composition significantly alters the growth rate of the phase-separated domains.
Our work has practical implications in that it allows us to optimize the performance of PLCs as compatibilizers for immiscible blends by choosing the best PLC composition. Optimizing the performance of PLC compatibilizers exhibiting repulsive interactions with homopolymers will be subject of future work.
Figure 5.1 Normalized A-B contacts $\langle n_{AA}(t) \rangle / \langle n_{AA}(0) \rangle$ with phase separation time.
**Figure 5.2** PLC chain expansion ratio or normalized radius of gyration $\langle R_g^2(t) \rangle / \langle R_g^2(0) \rangle$ with phase separation time.
Figure 5.3 Conformation of the PLCs at the interface at 100k MCS for a single PLC sequence.
Figure 5.4 Evolution of $S(q,t)$ with phase separation time for: (a) binary A/B blend, and ternary A/B/C-$plc$-D blend with PLC composition $x_c$: (b) 0.1, (c) 0.3, (d) 0.5, (e) 0.7, (f) 0.9. Note the scale change for (e) and (f).
Figure 5.5 Scaling exponent for the ternary A/B/C-\textit{Plc}-D blend with varying PLC composition.
Figure 5.6 Scaling function in the late stages of phase separation for ternary A/B/C-plc-D compatibilized blend with varying PLC composition.
5.6 REFERENCES


Hashimoto, T., Itakura, M. & Shimidzu, N. Late Stage Spinodal Decomposition of a Binary Polymer Mixture .2. Scaling Analyses on Qm(Tau) and Im(Tau). *Journal of Chemical Physics* **85**, 6773-6786 (1986).


CHAPTER SIX

Exploring the Potential for Using Protein-like Copolymers as Drug Delivery Devices

6.1 INTRODUCTION

Two important problems associated with cancer chemotherapy are that anti-tumor drugs may be poorly soluble in the bloodstream and that they attack the body in an untargeted fashion, killing healthy cells as well as diseased cells\textsuperscript{1,2}. Research in recent years has focused on using nanotechnology to solubilize these drugs and to make them more selective for cancer cells\textsuperscript{3}. Encapsulation increases drugs’ solubility, and functionalization allows them to be targeted to the tumor\textsuperscript{4}. We seek to provide a theoretical framework that describes the encapsulation of “drugs” by a potential new drug delivery carrier, protein-like copolymers (PLCs), focusing in particular on the drugs’ effect on PLC globule formation and aggregation.

Protein-like copolymers (PLCs) represent a new class of functional copolymers that exhibit large-scale compositional heterogeneities and long-range correlations along the co-monomer sequence\textsuperscript{5-7}. The concept of PLCs was first introduced by Khokhlov and coworkers\textsuperscript{5,6} who used computer simulations to demonstrate that random copolymers with
tunable monomer sequences could be generated by adjusting the compactness of a parent homopolymer composed of component A, and then converting exposed segments on the polymer surface into B segments by reacting them with other species in the surrounding solution. Our recent computer simulations suggest that the sequence along the PLC plays a dominant role in its interfacial behavior\textsuperscript{8-11}.

The use of polymeric nanoparticles for targeted drug delivery is not new. The polymeric nanoparticles currently being used or investigated for use as drug delivery devices include polymeric biodegradable nanoparticles, liposomes, polymeric micelles, and dendrimers. These nanoparticle-based drug delivery devices can be divided roughly into two classes, multi-molecule carriers meaning nanoparticles created via the assembly of groups of molecules such as polymeric biodegradable nanoparticles, polymeric micelles and liposomes, and single-molecule carriers such as dendrimers. Biodegradable polymeric nanoparticles\textsuperscript{12,13} can be fabricated in a wide range of sizes and varieties and have drawn considerable attention because they provide steady drug release for weeks, yet do not accumulate in the body. Liposomes\textsuperscript{14} are small water-filled vesicles surrounded by a bilayer synthesized from non-toxic phospholipids and cholesterol. Since they are natural materials, they are considered low toxicity drug delivery carriers that can circulate in the blood stream for a long time. Polymeric micelles\textsuperscript{15} are nanoscale polymeric structures that are physiologically stable in biological environment, and thus can deliver drugs securely to the targeted location. They are suitable carriers for water-insoluble drugs as they have a hydrophobic core. A potential disadvantage of polymeric micelles is that they can dissociate into free chains below the critical micelle concentration, causing sudden release of the drug.
Dendrimer-based nano-scale drug delivery systems have been proposed as an alternative to polymeric micelle nanoparticles. Dendrimers are synthetic, highly branched, spherical, mono-disperse macromolecules of nanometer dimensions prepared by an iterative\textsuperscript{16-18} synthetic methodology. The core–shell architecture of dendrimers with hydrophobic internal cavities\textsuperscript{19} and modifiable surface functionality\textsuperscript{20}, grows linearly in diameter as a function of the added generations and exponentially with respect to the surface groups. These characteristics, along with water solubility, are some of the features that make them attractive for biological and drug-delivery applications\textsuperscript{21-31}. The drug payload can be physically entrapped within the dendrimer or chemically attached to the surface. Unlike polymeric micelles, dendrimers do not dissociate as they are covalently bound.

Our interest in using protein-like copolymers for drug delivery was sparked in part by their resemblance to dendrimer-based nano-delivery systems. Like dendrimers they can function as unimolecular drug containers in which the payload is physically entrapped. However, unlike dendrimers whose stationary branched configuration serves as a sponge for drug molecules, PLCs could adsorb or release drug molecules as they undergo a coil globule transition in response to an external stimuli. The coil to globule transition can be induced by immersion in a poor solvent, change in pH or reducing the temperature below the theta temperature; the globule so formed will adopt a structure with a dense hydrophobic core surrounded by a loose hydrophilic corona, making it highly soluble in aqueous medium. We suggest exploiting the coil to globule transition of PLCs to encapsulate drugs. While our main focus is on single PLCs we also consider the multi-PLC case to see if there are any opportunities for drug encapsulation in concentrated PLC systems.
In this paper we use kinetic Monte Carlo (MC) computer simulations based on the bond fluctuation model to investigate the behavior of a model PLC-solvent system in the presence of model “drug” molecules with the objective of assessing the potential of PLCs as nano-scale drug or solute carriers. Although we will refer to the solute molecules in this paper as “drug” molecules we should point out that we have made no attempt to build in any drug-like features; our drug molecules are intended to represent any type of molecular solute that could be absorbed or encapsulated by a PLC. MC simulations are performed on both single and multi chain 100-mer PLC systems to mimic low and high PLC concentration respectively. The single chain PLC system consists of one 100-mer PLC, and 400 drug molecules while the multi-chain PLC system consists of 20 100-mers PLCs, and 8000 drug molecules. The solvent is implicit for both the single and multi PLC chain systems. We explore the impact that the hydrophobic drug particles have on the ease with which the PLCs undergo the coil to globule transition. We also vary the system density, PLC composition, and the strength and range of the interaction between the hydrophobic segments on the PLC and the drug to demonstrate how each of these variables affects the drug encapsulation ability of the system. We use visual analysis of the simulation snapshots to determine if the PLCs succeed in encapsulating drugs. We also present profiles for the hydrophobic (H), hydrophilic (P), and drug segments within the PLC to quantify the encapsulation efficiency of HP PLCs.

Highlights of our results are as follows. We find that the presence of drug in systems with low PLC concentration makes it easier for the PLCs to undergo a coil to globule transition below the theta temperature while encapsulating drugs. The interaction strength
\( \varepsilon_{HH} \) (between H-H segments) must be stronger than \( \varepsilon_{HD} \) (between H-D segments) and \( \varepsilon_{DD} \) (between D-D segments) for successful drug encapsulation by PLCs. For single PLC chain systems the interaction range extending to the nearest twenty six neighbors is optimal for encapsulation while for multi PLC chain systems the interaction range extending to the nearest eighteen or twenty six neighbors is optimal for drug encapsulation. A PLC composition of \( x_H = 0.5 \) is optimal for encapsulation for both single and multi-PLC systems. We also find that the interaction strength between the hydrophobic segments on the PLC and drug acts as a coupling parameter that determines whether the system encapsulates or whether the copolymer and drug aggregate separately.

In the next section, we describe the MC method and the generation of PLCs via the instant coloring procedure of Khokhlov and co-workers\(^5,6\). The following section presents the simulation results for PLC nanoparticles as carriers for solubilizing drugs (or solute) molecules. The final section concludes with a short summary of the results and a discussion.

### 6.2 MODEL AND METHOD

The single PLC chain system consists of 400 drug (D) molecules and a single 100-mer PLC containing monomers of types H (hydrophobic) and P (hydrophilic). The composition of the PLC is varied to be \( x_H = 0.3 \), \( x_H = 0.4 \), \( x_H = 0.5 \), and \( x_H = 0.7 \). The multi-PLC chain system consists of 8000 drug molecules and 20 100-mers PLCs containing monomers of types H and P with composition \( x_H = 0.5 \). In both the single and multi-chain...
PLC systems the voids (V) or unoccupied lattice sites play the role of an implicit solvent. PLCs are modeled as self-avoiding walks on a three-dimensional cubic lattice. The values of the various interaction energies $\varepsilon_{ij}$ between segments of type $i$ and $j$ are listed in Table 6.1. The interaction energies $\varepsilon_{VV}$, $\varepsilon_{VH}$, $\varepsilon_{VP}$, $\varepsilon_{HH}$, $\varepsilon_{HP}$, $\varepsilon_{PP}$ are held fixed; their values are closely related to those used in the work of Khokhlov et al$^{5,6}$ on generating PLCs. To account for the fact that the drug molecules will be hydrophobic in aqueous medium we set $\varepsilon_{VD} = 0.3$ and choose only negative values for $\varepsilon_{DD}$. The interaction energies $\varepsilon_{HD}$ and $\varepsilon_{DD}$ are varied. To calculate the energy of the system we need to decide on a range of the interactions; this is usually reported in terms of the number of nearest neighbors to any site that experience an interaction. Three different interaction ranges are considered assuming one of the segments is located at $(0,0,0)$: SZCCL (the six vectors obtained by all sign inversions and permutations of the vector family $P(1,0,0)$ between segments), MZCCL (the eighteen vectors obtained by all the sign inversions and permutation of the two vector families $P(1,0,0) \cup P(1,1,0)$), and LZCCL (the twenty-six vectors obtained by all the sign inversions and permutation of the vector families $P(1,0,0) \cup P(1,1,0) \cup P(1,1,1)$).
The lattice Monte Carlo simulations are based on the three-dimensional bond fluctuation model (BFM) performed in the NVT ensemble. In the BFM each monomer represents a Kuhn segment and occupies eight sites on a simple cubic lattice. The drug or the solute molecule also occupies eight sites on a simple cubic lattice. Successive monomers along the chain are connected via a predetermined set of bond vectors. In order to avoid bond crossing and monomer overlap, the bond vectors are derived from all possible permutations and sign inversions of the following six vector families: \( P(2,0,0) \cup P(2,1,0) \cup P(2,1,1) \cup P(2,2,1) \cup P(3,0,0) \cup P(3,1,0) \). For example, all possible permutations and sign inversions of the vector family \( P(2,0,0) \) yield the following six distinct bond vectors: \((2,0,0), (-2,0,0), (0,2,0), (0,-2,0), (0,0,2), \) and \((0,0,-2)\). Repeating this process for all six vector families leads to a total of 108 bond vectors and 87 bond angles. Thus, the model has some of the flexibility associated with an off-lattice model while

<table>
<thead>
<tr>
<th>( \varepsilon_{ij} )</th>
<th>V (Void)</th>
<th>H</th>
<th>P</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>V (Void)</td>
<td>0</td>
<td>0.3</td>
<td>-0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>H</td>
<td></td>
<td>-1.0</td>
<td>0.0</td>
<td>( \varepsilon_{HD} ) varied</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.0</td>
<td>0.0</td>
<td>( \varepsilon_{DD} ) varied</td>
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Table 6.1 Matrix of Interaction Parameters
maintaining the advantages associated with working on a lattice, such as integer arithmetic and parallelization\textsuperscript{34}.

The MC algorithm is executed in the following manner. First a unit is chosen at random, and translated by one lattice spacing in a direction chosen randomly out of the six possible directions. Next a check is done to verify that the resulting move does not violate the excluded volume and bond constraints (if the selected unit is a monomer on a polymer chain) set forth by the BFM. If it does, the move is rejected and the unit is restored to its original position. If all the BFM constraints are satisfied, the Metropolis sampling rule is applied, i.e. the move is accepted with a probability equal to $\min(1, \exp(-\Delta E / k_B T))$, where $\Delta E$ is the energy change due to the move, $k_B$ is the Boltzmann constant and $T$ is the temperature. The lattice Monte Carlo (MC) simulations are performed on a simple cubic lattice of $L \times L \times L$ sites, where $L = 50$ for both single and multi PLC chain systems. The volume fraction, $\phi = N / L^3$, for the single PLC chain system is set to $\phi = 0.004$, and for the multi PLC chain system is set to $\phi = 0.08$, where $N$ is the number of segments including drug molecules in the simulation box. Periodic boundary conditions are imposed in all three directions ($x$, $y$, and $z$) to overcome the limitation of finite system size.

The HP PLCs were generated via a simulation-based instantaneous coloring procedure originally proposed by Khokhlov et al.\textsuperscript{5-7}. A detailed description of our implementation of Khokhlov's coloring procedure to generate 100-mer HP PLCs via discontinuous molecular dynamics (DMD) simulation can be found in our previous work\textsuperscript{8}. 
To gauge the effectiveness of different PLC-drug systems and understand the role of various parameters on the drug encapsulation efficiency the following measures are used: 1) visual analysis of simulation snapshots, and 2) density profiles of the hydrophobic (H), hydrophilic (P) segments, and drug (D) segments within the PLC globule that is formed.

Visual analysis of simulation snapshots, although empirical, allows us to identify those cases in which a PLC has successfully encapsulating drug molecules. If the HP PLCs are effective in encapsulating drugs they are likely to adopt a globular conformation with a dense drug-containing hydrophobic core and a surrounding hydrophilic corona.

To quantify the performance of PLCs as drug carriers we evaluate the density profiles for the hydrophobic (H), hydrophilic (P), and drug (D) segments within the HP PLC globule that is formed during the coil to globule transition in the presence of drug molecules at low PLC concentration. The density profile of any component across a drug/PLC aggregate is determined by finding the aggregate’s center of mass, calculating the number of component sites in a spherical shell at evenly spaced distances from the center of mass and then dividing by the volume of the shell. The density profiles were averaged over time during the last 0.001 fraction of the simulation.

Kinetic MC simulations were performed on the single and multiple chain PLC-drug systems. The simulations were started in a random configuration at the desired volume fraction. The appropriate interactions were switched on and MC simulations were performed for 2,000,000 Monte Carlo steps (MCS). In each MCS, all beads in the system are moved once on average. The system properties for both the single and multi-chain PLC systems were averaged over five runs starting from uncorrelated random initial configurations, and
over three PLC sequences for a given initial configuration. The errors which represent the sample standard deviations of the properties calculated were within 3%. We chose not to represent the errors bars on the density profile plots for clarity.

6.3 RESULTS AND DISCUSSION

We first report the results on the PLC-drug systems involving single 100-mer PLC chain. Figure 6.1 shows simulation snapshots for a single chain PLC-drug system with $x_H = 0.5$, and interaction strengths $\varepsilon_{HD} = -1$ and $\varepsilon_{DD} = -1$. Figure 6.1a shows a snapshot of a typical initial configuration in which both the PLCs and drug molecules are randomly mixed. Figures 6.1b through 6.1d show the PLC-drug system at the end of the simulation with interaction ranges (b) SZCCL (nearest six neighbors), (c) MZCCL (nearest eighteen neighbors), and (d) LZCCL (nearest twenty six neighbors). Comparison of Figures 6.1b through 6.1d gives a sense of how the interaction range affects the ability of the PLCs to undergo a coil to globule transition while encapsulating drugs. The short ranged SZCCL interaction (cf. Figure 6.1b) leads to weak collapse of the PLC chain, with no drug encapsulation at all. The medium ranged MZCCL interaction (cf. Figure 6.1c) leads to good collapse of the PLC chain, but the drug encapsulation is weak. The long ranged LZCCL interaction (cf. Figure 6.1d) leads to strong collapse of the PLC chain, with excellent drug encapsulation which is desirable. The single-chain PLC system shown in Figure 6.1d can be
considered an ideal drug carrier as it succeeds in encapsulating a large amount of drug ($\approx 12\%$ of the 400 drug molecules loaded) in its hydrophobic core.

**Figure 6.2** shows simulation snapshots for a single chain 100-mer PLC-drug system with PLC composition $x_H = 0.5$, and interaction range LZCCL at interaction strengths (a) $\varepsilon_{HD} = -0.1327$ and $\varepsilon_{DD} = -0.0663$, (b) $\varepsilon_{HD} = -1$ and $\varepsilon_{DD} = -0.2653$, and (c) $\varepsilon_{HD} = -1.5$ and $\varepsilon_{DD} = -1$. In (c) we chose strong H-D interaction relative to the H-H or D-D interaction in the hopes of boosting up the drug encapsulation efficiency of the single-chain PLC system.

In **Figure 6.2a** the PLC undergoes a coil to globule transition but the drug molecules do not get encapsulated due to the weak H-D interaction relative to the H-H interaction. In **Figure 6.2b** the drug molecules get encapsulated due to the strong H-D interaction but the PLC does not undergo a coil to globule transition completely due to the weak D-D interaction, for reasons which will be explained below. In **Figure 6.2c** the drug molecules get encapsulated due to the very strong H-D interaction relative to the H-H and D-D interactions but the PLC does not undergo coil to globule transition completely. The PLC’s failure to undergo coil-to-globule transition despite the strong H-H interaction is counterintuitive. A plausible reason is as follows; the strong H-D interactions cause the drugs to aggregate around the H blocks of the HP PLC screening the H-H interactions while the weak D-D interactions prevent the drugs from acting as a bridge between the H segments. Thus the D-D interaction relative to the H-H interaction must be strong enough for the drugs to act as a bridge between the H segments thereby promoting the PLC coil-to-globule transition. Thus it is apparent that in
order for the PLC to undergo a coil-globule transition and for drugs to be encapsulated the condition $\epsilon_{HH} \geq \epsilon_{HD} \geq \epsilon_{DD}$ must be satisfied.

**Figure 6.3** shows simulation snapshots for a single chain 100-mer PLC-drug system with interaction strengths $\epsilon_{HD} = -1$ and $\epsilon_{DD} = -1$, and interaction range LZCCL at (a) $x_H = 0.3$, (b) $x_H = 0.5$, and (c) $x_H = 0.7$. As seen in **Figure 6.3a**, if the hydrophobic content of the HP PLC is below 50%, i.e., $x_H < 0.5$ then the PLC has a large hydrophilic corona which enhances the PLC solubility and is desirable but the amount of drug encapsulated by the PLC is low which is undesirable. As seen in **Figure 6.3c**, if the hydrophobic content of the HP PLC is above 50%, i.e., $x_H > 0.5$ then the amount of drug encapsulated by the PLC is high which is desirable but the PLC has a small hydrophilic corona which limits the solubility of the PLC and is undesirable. Thus it is apparent that the PLC composition $x_H = 0.5$ is optimal for drug encapsulation and solubility of the HP PLCs.

So far we have relied on visual analysis of simulation snapshots which, although empirical, is useful as it provides physical insight into the workings of the single chain 100-mer PLC-drug system. We now present the results of the density profiles of the hydrophobic (H), hydrophilic (P), and drug (D) segments of within the PLC globule for the single chain 100-mer HP PLC-drug system. **Figure 6.4** depicts the density profiles respectively for the H, P, and D segments within the PLC globule for the single-chain 100-mer PLC system shown in **Figure 6.1d**. Since the PLC shown in **Figure 6.1d** underwent a coil-to-globule transition while successfully encapsulating drugs in its hydrophobic core, the densities for segments H and D are very high near the center of mass of the PLC globule and tail off at distances away
from the globule’s center. The density of P segments at distances near the globule’s center is negligible and increases with increasing distance from the globule’s center while peaking at distances near the outer periphery of the HP PLC globule. These behaviors are what one would expect.

We now report the results for PLC-drug systems involving multi 100-mer PLC chains, in an effort learn what would happen at higher PLC concentrations. In the multi-chain system we have three possibilities: (1) individual chains undergo a coil to globule transition while encapsulating drugs, (2) many PLCs aggregate to form large clusters with drugs encapsulated or (3) both phenomena happen simultaneously. This makes the analysis of the density profiles harder to interpret.

Figure 6.5 shows simulation snapshots at the end of the simulation for the multi-chain 100-mer PLC-drug system with PLC composition $x_H = 0.5$, and interaction strengths $\varepsilon_{HD} = -1$ and $\varepsilon_{DD} = -1$ with interaction ranges (a) SZCCL (nearest six neighbors), (b) MZCCL (nearest eighteen neighbors), and (c) LZCCL (nearest twenty six neighbors). Comparison of Figures 6.5a through 6.5c gives a sense of how the interaction range affects the ability of the system to encapsulate drugs. The short ranged SZCCL interaction (cf. Figure 6.5a) does not lead to collapse of the PLCs to a globular conformation, and no drug encapsulation. Both the medium ranged MZCCL (cf. Figure 6.5b) and long ranged LZCCL (cf. Figure 6.5c) interactions cause the PLCs to aggregate and form large clusters which encapsulate drugs. Thus it is necessary to have the either MZCCL or LZCCL interaction range for satisfactory drug encapsulation.
Figure 6.6 shows simulation snapshots for a multi chain 100-mer PLC-drug system with PLC composition \( x_H = 0.5 \), and interaction range MZCCL at the end of the simulation for interaction strengths (a) \( \varepsilon_{HD} = -0.5 \) and \( \varepsilon_{DD} = -0.5 \), (b) \( \varepsilon_{HD} = -0.75 \) and \( \varepsilon_{DD} = -0.75 \), and (c) \( \varepsilon_{HD} = -1 \) and \( \varepsilon_{DD} = -1 \). In Figure 6.6a the drugs are dispersed uniformly unlike the other two systems which have stronger H-D and D-D interactions. The condition \( \varepsilon_{HH} \geq \varepsilon_{HD} \geq \varepsilon_{DD} \) must still be satisfied in the multi chain PLC systems to encapsulate drugs, however lower values of the interaction energies \( \varepsilon_{HD} \) and \( \varepsilon_{DD} \) favor uniform drug dispersion which is undesirable.

6.4 CONCLUSIONS

We presented the results of kinetic Monte Carlo (MC) simulations aimed at supporting the development of protein-like copolymers as nanoparticles for drug (or solute) delivery. We considered both the single and multi chain PLC based systems to mimic low and high PLC concentrations, respectively. Unoccupied lattice sites played the role of an implicit solvent for both the single and multi chain PLC systems. We performed visual analysis of the simulation snapshots to determine if the PLCs succeeded in encapsulating drugs. We quantified the encapsulation efficiency of PLC based systems by performing cluster analyses to evaluate the density and composition profiles of the hydrophobic (H), hydrophilic (P), and the drug (D) segments within the cluster.
The presence of drug molecules in the system made it easier for the PLCs to undergo a coil to globule transition which is important for drug encapsulation especially for systems with low PLC concentration. Weak D-D interactions caused the PLCs to collapse partially while weak H-D interactions hindered the process of drug encapsulation. The following condition $\varepsilon_{HH} \geq \varepsilon_{HD} \geq \varepsilon_{DD}$ must be satisfied for successful drug encapsulation by the PLCs. The longest interaction range considered, LZCCL, was optimal for drug encapsulation in the single PLC chain systems, while the medium and long interaction ranges MZCCL and LZCCL proved optimal in multi PLC chain systems. PLCs with composition $x_H = 0.5$ proved optimal for enhanced drug encapsulation and solubility for both the single and multi chain PLC systems. In multi chain PLC systems, weak interaction between H-D and D-D segments lead to uniform drug dispersion which is undesirable.

PLCs share common features with dendrimers such as their ability to adopt hydrophobic core-hydrophilic shell architectures below the theta temperature, allowing them to form unimolecular micelles with high drug encapsulation capacity and excellent solubility in solution. PLCs could also prove useful in encapsulating drugs at low polymer concentrations where polymeric-micelle-based drug carriers might become unstable as they are below the critical micelle concentration. In a nutshell PLCs have real potential as nanoparticles for drug delivery. Alternate routes to drug delivery via PLCs would be the subject of future publications.

It is difficult to validate our work due to the lack of prior experimental and theoretical research on PLCs as nano-scale carriers for drugs (or solute) molecules. In this paper we
have mainly discussed the drug encapsulation process by the PLCs. The release of drugs could be accomplished by altering the pH or solubility of the solution, or changing the temperature which would cause the PLC globules to either undergo inversion or expansion to a coil like conformation. Alternate routes to drug-delivery via PLCs exist which we have not explored in this paper. As an example complementary PLC polyelectrolyte sequences could also be used to form ionic complexes with the drug molecules. We could also utilize the coil to globule transition of a homopolymer below the theta temperature (poor solvent conditions) to encapsulate drugs first and then perform the coloring process suggested by Khokhlov and coworkers to create modified PLCs with enhanced solubility in solution.
Figure 6.1 Simulation snapshots of the single 100-mer HP PLC chain drug (D) system (H = light blue, P = red, D = green): (a) initially, and at the end of the simulation with interaction range (b) SZCCL, (c) MZCCL, and (d) LZCCL.
Figure 6.2 Simulation snapshots of the single 100-mer HP PLC chain drug (D) system at the end of the simulation with interaction strength (a) $\varepsilon_{HD} = -0.1327$ and $\varepsilon_{DD} = -0.0663$, (b) $\varepsilon_{HD} = -1$ and $\varepsilon_{DD} = -0.2653$, and (c) $\varepsilon_{HD} = -1.5$ and $\varepsilon_{DD} = -1$. 
Figure 6.3 Simulation snapshots of the single 100-mer HP PLC chain drug (D) system at the end of the simulation with PLC composition (a) $x_H = 0.3$, (b) $x_H = 0.5$, and (c) $x_H = 0.7$. 
Figure 6.4 Density profile of the H, P, and D segments for the single-chain 100-mer HP PLC drug system with PLC composition $x_H = 0.5$, interaction strength $\varepsilon_{HD} = \varepsilon_{DD} = -1$, and LZCCL interaction range.
Figure 6.5 Simulation snapshots of the multi chain 100-mer HP PLCs drug (D) system at the end of the simulation with interaction range (a) SZCCL, (b) MZCCL, and (c) LZCCL.
Figure 6.6 Simulation snapshots of the multi chain 100-mer HP PLCs drug (D) system at the end of the simulation with interaction strength (a) $\varepsilon_{HD} = \varepsilon_{DD} = -0.5$, (b) $\varepsilon_{HD} = \varepsilon_{DD} = -0.75$, and (c) $\varepsilon_{HD} = \varepsilon_{DD} = -1$. 
6.6 REFERENCES


Malik, R., Hall, C. K. & Genzer, J. Phase Separation Dynamics for a Polymer Blend Compatibilized by Protein-like Copolymers: a Monte Carlo Simulation. *Macromolecules (to be submitted).*


Malik, R., Hall, C. K. & Genzer, J. Effect of Protein-like Copolymers Composition on the Phase Separation Dynamics of a Polymer Blend: a Monte Carlo Simulation. *Soft Matter (to be submitted for publication).*


CHAPTER SEVEN

Future Work

We have performed molecular-level computer simulations aimed at supporting the development of protein-like copolymers as compatibilizers for immiscible polymer blends, and as “drug” delivery agents. In this chapter we suggest possible directions for future work based upon our findings in Chapters 2 through 6.

7.1 INVESTIGATE THE COMPATIBILIZATION EFFECTIVENESS OF LONG PLCs

We performed DMD simulations on 38-mers in Chapter 2 and kinetic MC simulations on 70-mers in Chapter 3 to gauge the compatibilization effectiveness of various copolymer sequences for immiscible polymer blends from thermodynamic and kinetic points of view, respectively. We chose to work with 20-mers, 38-mers, and 70-mers as the simulations were relatively fast. It would, however, be of interest to look at much longer chains because this would allow us to truly pinpoint the differences between random-block (Poisson distribution of block lengths), random, PLC, and simple linear gradient copolymers as compatibilizers. In addition, we should be able to observe the microphase separation in
binary blends compatibilized by diblock or gradient copolymers that occurs at high copolymer concentrations (≈20%) when the homopolymers are much longer than the copolymer and the effective interaction strength parameter is large (χ_{AB}L_{copolymers} > 10.5 for the diblocks and χ_{AB}L_{copolymers} > 29.5 for the gradient copolymers). Since computer simulations involving multi-chain systems containing chains longer than 100 are computationally challenging, we suggest that self consistent field theory (SCFT) methods be utilized instead. In the future, we plan to investigate the compatibilization effectiveness of various 300-mer copolymer sequences for immiscible binary blends containing homopolymers with chain lengths varying between 100 and 300 using the 1-D SCFT model developed by Balazs and coworkers\(^1\) based on the Scheutjens–Fleer theory\(^2\).

### 7.2 INVESTIGATE THE ROLE OF HAMS AS COMPATIBILIZERS

We suggest that kinetic MC simulations as described in Chapter 3 be performed to investigate the dynamics of phase separation of immiscible binary polymer blends compatibilized by HAMS (i.e., heteropolymers with adjustable monomer sequences) to obtain a more realistic picture of PLCs as compatibilizers than those presented in Chapter 3.

The computational approach developed by Khokhlov and coworkers\(^3,4\) for generating PLCs is practically infeasible because the parent homopolymer globule is assumed to be in a frozen state and the coloring reaction is assumed to be instantaneous. A more realistic scheme was recently presented by Strickland et al.\(^5\) who performed DMD simulations to
generate AB HAMS or heteropolymers with adjustable monomer sequences. (Genzer has also referred to these as RCPs\(^6\) or random copolymers with tunable monomer sequences). They accounted for the conformation fluctuations with time of the parent homopolymer A, the presence of explicit reactant molecules which cause the segments of type A to change to segments of type B, and the different solubilities of segments A and B in the implicit solvent. They chose to name the AB sequences as HAMS instead of PLCs (the latter name was originally coined by Khokhlov and coworkers\(^3,4\)).

While PLCs are on a par with simple linear gradient copolymers we would expect HAMS to perform poorly compared to gradient copolymers as they are less blocky than PLCs.

7.3 SIMULATE DYNAMICS OF PLCs IN A HOMOPOLYMER MATRIX

We suggest that kinetic MC simulations be used to explore the dynamics of PLCs in a homopolymer matrix. The ability of a copolymer compatibilizer to migrate quickly to the biphasic interface between the immiscible homopolymers without forming aggregates determines ultimately its effectiveness as a compatibilizer. Hence it would be of interest to compare the diffusion of PLCs in a homopolymer matrix to that of other copolymer sequences like diblock, gradient, random, and alternating and to test if the PLCs form aggregates in the homopolymer matrix.
7.4 SIMULATE PLC COMPATIBILIZERS WITH REPULSIVE INTERACTIONS

We suggest that kinetic MC simulations be performed to investigate the phase separation dynamics of an immiscible A/B polymer blend in the presence of C-plc-D copolymers having repulsive interactions with the immiscible homopolymers. The motivation for this investigation is the following. The binary blend consists of incompatible homopolymers A and B, while the PLCs might be composed of monomers of type C and D, which are, in general, different chemically from the homopolymer segments. Ideally, one would want the segments C and D of the C-plc-D copolymer to possess attractive interactions with homopolymers A and B, respectively, for effective compatibilization. Block copolymers with repulsive interactions between the blocks and the homopolymers have been shown to retard the phase separation dynamics of immiscible homopolymer blends. It is worthwhile to explore if PLCs also exhibit similar behavior.

7.5 INVESTIGATE ALTERNATIVE ROUTES FOR DRUG-DELIVERY VIA PLCs

In Chapter 6 we performed lattice MC simulations to provide a proof of concept that PLCs could be used to encapsulate or release “drugs” (or solutes) via a coil-to-globule transition under varying solvent conditions. There are, however, additional routes to “drug” delivery via PLCs. For instance, one could also use polyelectrolyte PLCs to encapsulate drugs. One set of the PLCs would have permanent positive charged groups, while the other
set would have temporary negative charged groups (depending on the acidity conditions). Tuning the acidity of the polyelectrolyte PLCs mixture should result in the formation (or breakup) of the ionic complex between the two PLCs, encapsulating (or releasing) the drug. Alternatively, temperature variation might lead to the coil-to-globule transition for either one or both of the PLCs, resulting in the breakup of the polyelectrolyte complex and causing the drug to be released. Computer simulations could reveal how the charge distribution along the PLC polyelectrolyte, drug size, size of the ion complex, PLC chain length, PLC concentration, and changes in temperature or acidity conditions could affect the mechanism and dynamics of the drug uptake or release. It must be pointed out that working with charged polymers is computationally intensive as one must account for the long-range Cumbic interactions using methods like the particle-mesh Ewald\(^8\) summation. We also suggest that the coil to globule transition of a homopolymer below the theta temperature (poor solvent conditions) be utilized to encapsulate drugs first followed by the coloring process suggested by Khokhlov\(^3,4\) and coworkers to create modified PLCs with enhanced solubility in solution.

### 7.6 INVESTIGATE THE ROLE OF PLCs AS DISPERSING AGENTS

We suggest that computer simulations be used to assess the potential of PLCs as dispersing agents for inorganic fillers during the formation of polymeric nanocomposites. We could simulate the A/B/C\(-plc\)-D (A is the homopolymer matrix, B is the inorganic filler, and C\(-plc\)-D is the PLC copolymer composed of segments of type C and D) ternary system to
understand the role of PLCs as dispersing/compatibilizing agents. A sample simulation snapshot for the polymer nanocomposite is shown in Figure 7.1. Computer simulations will be used to understand the role of PLC loading, filler loading, interactions between the various segments and PLC chain length on the extent of dispersion of the inorganic filler in the homopolymer matrix.

7.7 SIMULATE SURFACE BASED HAMS PROBES

Genzer and coworkers proposed that nanoporous silica (NPS) functionalized with HAMS brushes could be utilized to develop novel tailorable chromatographic stationary phases for separating pharmaceutical and biological macromolecules. The overall idea for such a method is shown pictorially in Figure 7.2. They suggested two methods for creating NPS functionalized with HAMS brushes. In the “grafting onto” technique PBrS HAMS would be made in solution and then grafted onto NPS, while in the “grafting from” method they would be synthesized directly on the NPS. We suggest that simulations be used to investigate the “grafting onto” and “grafting from” self assembly of HAMS brushes to gain insight into how the two methods impact the brush conformation, monomer sequence distribution, density profile, interfacial characteristics, and the separation capacity of these HAMS brushes. We suggest that the “grafting onto” HAMS brushes be modeled as an impenetrable flat surface located in the $x-y$ plane at $z=0$, with HAMS copolymers attached to one side of the surface at the desired surface grafting density. Periodic boundary
conditions would be applied only in the $x$ and $y$ directions; the height of the simulation box should be much higher than the length or width of the simulation box. The model for the “grafting from” HAMS brushes will be similar to the “grafting onto” HAMS brushes except that the HAMS will no longer be attached to the surface, and the surface will have attractive interactions with one of the monomers of the HAMS copolymer in the bulk.

7.8 SIMULATE HAMS SOLUTION PHASE BEHAVIOR

The Genzer group has studied the phase behavior of PBr$_x$S HAMS in cyclohexane in detail using turbidity and SANS measurements. Figure 7.3 shows a schematic of the phase diagram for random and blocky HAMS. The effect of HAMS sequence, HAMS composition, and HAMS $^1$H/$^2$D isotopic substitution on the phase diagram (in the temperature HAMS mole fraction plane) has been elucidated. Molecular simulation could provide insight into the solution phase behavior of HAMS, the key differences between the phase behavior of random and blocky HAMS sequences, and the precise mechanism for phase separation of the HAMS. The phase behavior of the HAMS solution could be simulated using off-lattice Monte Carlo in the grand canonical $\mu VT$ ensemble (chemical potential, volume, and temperature fixed but particle insertions and deletions allowed) and that periodic boundary conditions be applied.
Figure 7.1 Simulation snapshot of the ternary A/B/C-\textit{plc}-D polymer nanocomposite, where A is the homopolymer matrix, B the inorganic filler, and C-\textit{plc}-D is the dispersing agent (A = light pink, B = dark blue, C = red, D = light blue).
Figure 7.2 Schematic showing pictorially the application of HAMS as smart stationary phase in liquid chromatography. Two random copolymers (1 & 2) enter the mobile phase and interact with the stationary phase comprising silica beads with grafted HAMS. By monitoring the signal in the eluent, recognition events can be monitored. For instance, the top portion of the cartoon illustrates the situation with no molecular recognition between the analyte and the stationary phase. In contrast, in the bottom portion we depict a situation where copolymer 2 recognizes its complementary HAMS counterpart and hence elutes at much longer times than copolymer 1.
Figure 7.3 Schematic diagram illustrating possible conformational changes in random-blocky (b-PBr₅S, blue line), and random (r-PBr₅S, blue line) HAMS as a function of the 4-BrS content in PBr₅S⁹.
7.10 REFERENCES


APPENDIX A.

Generation of PLCs or HAMS (Heteropolymers with Adjustable Monomer Sequences) and their Statistical Characterization

A.1 TYPES OF COPOLYMERS BASED ON SEQUENCE DISTRIBUTION

Based on the sequence of the hydrophobic (H) and hydrophilic (P) units, a two-letter HP linear copolymer may be classified in the following ways:

1] Random copolymer: The H and the P monomeric units are distributed randomly along the copolymer. A random copolymer is generated by randomly picking a bead along a chain and assigning it type H. This is repeated until the desired composition of the H component is reached. The remaining beads are labeled as P. Thus to generate a random copolymer only the composition of the HP copolymer must be specified.

2] Random Block copolymer: The distributions of the lengths of the H and P component blocks in a random block copolymer follow the Poisson distribution. The probability of the finding an H block along the random block copolymer sequence with length $L_H$ is

$$P(L_H) = \exp(-\lambda) \left( \frac{L_H}{\lambda} \right)^{\lambda} / L_H !$$  \hspace{1cm}  (A.1)
where \( L_H \) is the length of the H component block and \( \langle L_H \rangle \) is the average length of the H component block. Since \( L_H \) can only take discrete values and follows the Poisson distribution it is a discrete or stochastic random variable. Thus the composition and average block length of one of the components in a HP copolymer must be fixed to completely specify the Poisson distribution of the random block copolymer. A Poisson process is a stochastic process utilized for modeling random events in time that occur to a large extent independently of one another. The Poisson distribution can be sampled via the Poisson process\(^1\).

3] Alternating Block copolymer: An alternating block copolymer is most generally represented as \( (H_xP_y)_n H_uP_v \), where \( x \) is the block length of the H component, \( y \) is the block length of the P component, \( n \) is the number of times the pattern \( H_xP_y \) is repeated, \( u \) is the number of H beads present in the last H block, and \( v \) is the number of P beads present in the last P block. The H (or P) component block length is fixed for an alternating block copolymer. To generate an alternating block copolymer the average block length for the H (or P) component and the composition of the HP copolymer must be specified. Since the average block length of the H component is specified, the total number of blocks is determined. The number of blocks for the H and P components is the same. Next the block length for the P components is established. Sometimes to attain the desired HP copolymer composition, H (or P) beads at the end of the alternating block sequence must be added or deleted.
HAMS or Protein like copolymer: Govorun et al.$^{2}$ showed that the probability distribution of the length of the H (or P) component blocks in HAMS follow Lévy Flight Statistics. One of the unique statistical properties exhibited by protein like copolymers is the presence of long range correlations along the sequence when compared to random block, random and alternating block copolymer$^{2-4}$.

A.2 PREPARATION OF HAMS VIA INSTANTANEOUS COLORING PROCEDURE

Following the instantaneous coloring algorithm of Khokhlov et al.$^{5,6}$, two-letter HP 10000-mer HAMS with different hydrophobic/hydrophilic compositions were generated. The hydrophobic homopolymer was modeled as a square well chain of length 10000, bead diameter $\sigma$, well width $\lambda_{HH}\sigma$, and well depth $\epsilon_{HH}$. DMD was used to collapse a 10000-mer hydrophobic (H) homopolymer to a globular conformation at a given reduced temperature $T^* \equiv k_B T / \epsilon_{HH}$ and packing fraction $\eta \equiv \pi N \sigma^3 / (6V)$ where $T$ is the absolute temperature, $k_B$ is the Boltzmann constant, $N$ is the number of beads in the simulation box, and $V$ is the volume of the simulation box. The collapse of an initially random coil homopolymer was simulated using DMD at a low reduced temperature $T^* = 1.0$, low packing fraction $\eta = 0.006$, $\lambda_{HH} = 1.5$, $\sigma = 1$, and $\epsilon_{HH} = 1$. The temperature was maintained constant during the collapse by utilizing the Andersen thermostat$^{7,8}$. Figure A.1 shows the various stages of collapse, while Figure A.2a shows the final globular conformation of the collapsed
homopolymer. Next the beads in the final globular conformation were sorted in order of their distance from the center. A fraction of the beads determined by the composition of the desired HP HAMS were colored to be hydrophilic (P). After the coloring procedure, the different interaction potentials were set at $\varepsilon_{HH} = 1$, $\varepsilon_{HP} = 0$ and $\varepsilon_{PP} = 0$ and the HAMS copolymer was relaxed. Figure A.2b and Figure A.2c show pictures of the 10000-mer HAMS at $x_H = 0.5$ in a collapsed and open chain conformation respectively. The H beads are red and the P beads are blue.

A.3 STATISTICAL CHARACTERIZATION OF HAMS

Six HP copolymers each 10000-mers long with the same composition $x_H = 0.5$ but with different statistical distributions - HAMS, random, regular alternating, diblock, random block and alternating block copolymers were generated. The average block length of the H component was set at 15 for the HAMS, random block and alternating block copolymers. To bring out the statistical differences between HAMS, random, random block and alternating block copolymers, the following calculations were performed on six different types of copolymers:

A] Uniformity Factor Calculation: A Uniformity Factor $^9$, defined to be:

$$U_H = \left( \frac{\sum_{n=1}^{N-1} x_n}{N_H} + 1 \right) / (N_H - 1)$$

(A.2)
was calculated. Here, \( s_n \) is 0 if the \( n \)-th bead is P type, 1 if the \( n \)-th & \((n+1)\)th bead are type H, and -1 if the \( n \)-th bead is type H & the \((n+1)\)th bead is P type. \( N \) is the total number of monomers in the copolymer and \( N_H \) is the total number of H beads in the copolymer. The uniformity factor helps to distinguish between various copolymer sequences. Values are displayed in Table A.1. As expected symmetric random copolymers have uniformity factor close to zero. Symmetric regular alternating copolymers with uniformity factor -1 and symmetric diblock copolymers with uniformity factor 1 represent the two extremes. In terms of the uniformity factor, HAMS are comparable to random block and alternating block copolymers with the same composition and chain length.

<table>
<thead>
<tr>
<th>Type of 10000-mer copolymer ( ( x_H = 0.5 ) )</th>
<th>Uniformity Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>-0.0004</td>
</tr>
<tr>
<td>HAMS (average block length 15)</td>
<td>0.8670</td>
</tr>
<tr>
<td>Random Block (average block length 15)</td>
<td>0.8686</td>
</tr>
<tr>
<td>Alternating Block (average block length 15)</td>
<td>0.8666</td>
</tr>
<tr>
<td>Regular Alternating (average block length 1)</td>
<td>-1</td>
</tr>
<tr>
<td>Diblock Copolymer</td>
<td>1</td>
</tr>
</tbody>
</table>

B] **Sequence Map Comparison:** To facilitate a visual comparison of the various types of sequences, a one dimensional map of the sequence along the chain was prepared with the hydrophilic (type P) beads signified by a \(-1\) and the hydrophobic beads (type H) beads
signified by a +1. **Figure A.3** compares the sequence map for a HAMS sequence to those for random, random block (same average block length), and an alternating block (same average block length) copolymer, each 10000-mers long with composition $x_H = 0.5$. **Figure A.3** only shows the first 1000 monomer units along the copolymer chain for clarity. Clearly from **Figure A.3**, the HAMS copolymer differs from the others in that it has very long stretches of either H or P units.

C] **Frequency Distribution**: The frequency distribution for the length of the hydrophobic block of HAMS was compared to those for random and random block copolymers (same average block length) each 10000-mer long with the same composition $x_H = 0.5$. **Figure A.4** shows a comparison of the frequency distributions. The $x$ axis of the plot is truncated at 50, although it extends to 10000. It is interesting to note that HAMS possess very long H blocks (as long as 250 units with a finite non-zero probability) as compared to random and random block copolymers. Govorun et al.\(^2\) showed that the probability distribution for the length of the H (or P) component block in HAMS follow Lévy Flight statistics.

D] **Sample Skewness and Kurtosis**: As we have seen the uniformity factors for HAMS, random and alternating block HP copolymers with the same composition and average block length are almost identical. A more appropriate calculation for distinguishing between the different sequence types is sample skewness and kurtosis. The sample skewness of the
distribution is a measure of the departure from symmetry about the mean of the distribution. Sample skewness can be positive (or negative) indicating that most of the distribution lies to the left (or right) side of the mean. Sample kurtosis is a measure of the peakedness of a distribution compared to the standard normal distribution. The standard normal distribution has a mean of zero and a variance equal to one. The sample kurtosis can be positive (or negative) indicating that a distribution is more (or less) peaked compared to the standard normal distribution. Since both the sample skewness and kurtosis are estimators of the true or population skewness and kurtosis, respectively, they can be unbiased (mean of the sample skewness and kurtosis equals the population skewness and kurtosis respectively) or biased (mean of the sample skewness and kurtosis is not equal to the population skewness and kurtosis respectively).

Sample skewness (biased and unbiased) and kurtosis (biased and unbiased) are mathematically formulated in this section. Let $x_i$ denote the length of an H block present in an HP copolymer sequence, and $n$ denote the total number of different lengths of the H block present in the HP copolymer sequence. The average block length of the HP copolymer sequence is defined as:

$$\langle x \rangle = \frac{1}{n} \sum_{i=1}^{n} x_i / n$$  \hspace{1cm} (A.3)

The biased sample skewness $g_1$ is defined by equation (A.4) while the unbiased sample skewness $G_1$ is defined in terms of biased sample skewness by equation (A.5).
\[ g_1 = \frac{\sqrt{n} \sum_{i=1}^{n} (x_i - \langle x \rangle)^3}{\left( \sum_{i=1}^{n} (x_i - \langle x \rangle)^2 \right)^{3/2}} \]  
(A.4)

\[ G_1 = \frac{\sqrt{(n-1)n}}{n-2} g_1 \]  
(A.5)

The biased sample kurtosis \( g_2 \) is defined by equation (A.6) while the unbiased sample kurtosis \( G_2 \) is defined by equation (A.7).

\[ g_2 = \frac{n \sum_{i=1}^{n} (x_i - \langle x \rangle)^4}{\left( \sum_{i=1}^{n} (x_i - \langle x \rangle)^2 \right)^2} - 3 \]  
(A.6)

\[ G_2 = \frac{(n+1)(n-1)n}{(n-2)(n-3)} \frac{\sum_{i=1}^{n} (x_i - \langle x \rangle)^4}{\left( \sum_{i=1}^{n} (x_i - \langle x \rangle)^2 \right)^2} - 3 \frac{(n-1)^2}{(n-2)(n-3)} \]  
(A.7)

Table A.2 lists the biased as well as the unbiased sample skewness for various copolymer sequences. The distribution of length of the H blocks is most positively skewed for HAMS sequence when compared to any other copolymer sequence. Table A.3 lists the biased as well as the unbiased sample kurtosis for various copolymer sequences. The distribution of length of the H blocks in HAMS has the highest kurtosis (biased as well as unbiased) when compared to any other copolymer sequence. Since distribution for the length
of the H blocks exhibits positive sample kurtosis (both unbiased as well as biased) it is leptokurtic or super Gaussian.

Table A.2 Sample Skewness for H component (biased and unbiased)

<table>
<thead>
<tr>
<th>Type of 10000-mer copolymer $x_n = 0.5$</th>
<th>Sample Skewness (Biased)</th>
<th>Sample Skewness (Unbiased)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>2.047</td>
<td>2.048</td>
</tr>
<tr>
<td>Random Block (average block length 15)</td>
<td>0.368</td>
<td>0.369</td>
</tr>
<tr>
<td>HAMS (average block length 15)</td>
<td>4.378</td>
<td>4.398</td>
</tr>
</tbody>
</table>

Table A.3 Sample Kurtosis for H component (biased and unbiased)

<table>
<thead>
<tr>
<th>Type of 10000-mer copolymer $x_n = 0.5$</th>
<th>Sample Kurtosis (Biased)</th>
<th>Sample Kurtosis (Unbiased)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>5.299</td>
<td>5.312</td>
</tr>
<tr>
<td>Random Block (average block length 15)</td>
<td>0.783</td>
<td>0.813</td>
</tr>
<tr>
<td>HAMS (average block length 15)</td>
<td>25.224</td>
<td>25.625</td>
</tr>
</tbody>
</table>

E] **Monitoring Correlations Along the Sequence:** The differences between the various copolymers can be characterized by the differences between the correlation of the H and P segments along the chain. Random, random block and alternating block copolymers have a
characteristic correlation length over which their sequences are correlated. HAMS don’t have any characteristic correlation length, i.e., HAMS sequences are correlated over the entire length. Thus HAMS exhibit long range correlations in their sequences. Below we describe our implementation of two ways of monitoring correlation along sequences:

**E.1] Long Range Correlations Measure using Dispersion Analysis**

The long-range correlations of HAMS sequences along the chain were analyzed using a method developed by Stanley and coworkers. A computer generated HP copolymer sequence is transformed into an assembly of +1 (for H beads) and −1 (for P beads) as in Figure A.3. A window of length \( l \) is slid along the copolymer sequence step by step, summing the plus and minus ones within the window at each step. This sum, \( \alpha(l) \), is a new discrete random variable whose value depends on the location \( i \) of the sliding window along the copolymer sequence. \( \alpha(l) \) has a unique distribution, whose sample mean \( \langle \alpha(l) \rangle \) is determined by the overall HP composition, and whose dispersion or sample variance \( D^2(l) \) is defined as:

\[
D^2(l) = \frac{\sum_{i=1}^{N-l+1} (\alpha_i(l) - \langle \alpha(l) \rangle)^2}{N-l+1}
\]  

(A.8)

\( D(l) \) is the sample standard deviation of the discrete random variable \( \alpha(l) \) and is defined by the following equation:

\[
D(l) = \sqrt{D^2(l)}
\]

(A.9)
Long range correlations are present (i.e. there is no characteristic correlation length scale) when $D(l)$ obeys a power law $D(l) \propto l^\beta$ with $\beta > \frac{1}{2}$ for large $l$.

The slope $\beta$ for various copolymer sequences is calculated from the plot of $\log_{10}\{D(l)\}$ versus $\log_{10}\{l\}$ as shown in Figure A.5. In determining the slope, $\log_{10}\{l\}$ greater than 2 was utilized. The HAMS that we generated via the instantaneous coloring procedure exhibited $\beta \sim 0.8$, thus indicating the presence of long range correlations, unlike our random ($\beta \sim 0.5$), and random-block ($\beta \sim 0.5$) copolymers. The rapid change in slope for alternating block copolymer at about $\log_{10}(15j)$, for $j = 1, 2, 3,...$ indicates the presence of a characteristic correlation length scale for the alternating block copolymer.

**E.2] Long Range Correlations Measure using Detrended Fluctuation Analysis (DFA)**

Another method of detecting the power law long range correlations along the HP copolymer sequence is the detrended fluctuation analysis (DFA) developed by Peng et al. Following is Peng et al.'s DFA algorithm:

a] A one dimensional random walk along the HP copolymer sequence is performed. When an H bead is encountered the walker moves a unit step forward, and when a P bead is encountered the walker moves a unit step backward. Thus at any location $i$, along the copolymer chain there is a unique value $y(i)$ due to the random walk. Figure A.6 shows a plot of $y(i)$ versus $i$ for four different HP copolymer statistics (all 10000-mers long, $x_H = 0.5$ , with average block length of 15 in case of HAMS, alternating block and random block). Please note that all four walks are performed independently for each type of copolymer.
b) Next the copolymer sequence in divided into $n$ non-overlapping boxes and a linear
least squares fit is performed on the $y(i)$ data in each box. If $N$ denotes the number of
beads of the copolymer, then the length of each non-overlapping box $l$ is defined as $l = N/n$
. The ordinate of the straight line segments arising from the linear fit is denoted by $y_i(i)$.

Figure A.7 shows the plot of $y_i(i)$ as well as $y(i)$ versus $i$ for HAMS HP copolymer for a
box length of 1000.

c) The detrended walk is obtained by subtracting $y_i(i)$ from the original walk $y(i)$.

d) The detrended function $F_d(l)$ is defined by the following equation:

$$F_d(l) = \sqrt{\frac{\sum_{i=1}^{N} [y(i) - y_i(n)]^2}{N}}$$  \hspace{2cm} (A.10)

Generally, $F_d(l)$ shows the same behavior as $D(l)$. The presence of long range correlation
(i.e. the absence of a characteristic correlation length scale) is detected by power law
$F_d(l) \propto l^\beta$ with $\beta > \frac{1}{2}$ for large $l$. Figure A.8 shows the plot of \(\log_{10}\{F_d(l)\}\) versus
$\log_{10}\{l\}$ for four different types of copolymer sequences with the same composition and
average block length. For large $\log_{10}\{l\}$ greater than 3, HAMS have the greatest slope,
$\beta \sim 0.87$, while random, and random block copolymers have $\beta \sim 0.5$, and alternating
block has $\beta \sim 0.0$. Additionally random block and alternating block copolymers display a
crossover in the slope at around $\log_{10} 15$ indicating the presence of a characteristic length of
15 (note that the average block length for these is 15) which indicates the absence of long range correlations, unlike HAMS.

F] **Segmentation of Sequences:** A 40000-mer copolymer was generated by stitching together random (10000-mer), alternating block (10000-mer, average block length 15), random block (10000-mer, average block length 15) and HAMS (10000-mer, average block length 15) copolymers all with the same composition \( x_H = 0.5 \). The 40000-mer copolymer was laid down starting at one end and wound back and forth. 200 beads were laid before a turn and there are 50 turns per copolymer sequence as depicted by Figure A.9. To identify different types of sequences present in the 40000-mer copolymer the following computations were carried out:

1] **Segmentation Function**

Segmentation function developed by Gusev et al.\(^{12}\) was used to segment the 40000-mer HP copolymer sequence. The segmentation function, \( S(k, L, x) \) is defined as:

\[
S(k, L, x) = f_L^H \ln(f_L^H) + (1 - f_L^H) \ln(1 - f_L^H) - \sum_{i=1}^{L-1} \sum_{j=1}^{L-1} P_{ij}^k(k) \ln(P_{ij}^k(k))
\]  

(A.11)

where \( L \) is the length of the sliding window along the position \( x \) of the copolymer chain, \( f_L^H \) is the fraction of H beads within the window \( L \), \( k \) is the length of another sliding
window which moves step by step within the window of length \( L \), \( i \) refers to starting bead in a segment of length \( k \) (\( i = +1 \) corresponds to H type bead while \( i = -1 \) corresponds to P type bead), \( j \) refers to last bead of the segment of length \( k \) (\( j = +1 \) corresponds to H type while \( j = -1 \) corresponds to P type). \( P^i(k) \) is the joint probability that a segment of \( k \) units has a beginning at unit \( i \) and an end at unit \( j \). Thus we have four distinct \( P^i(k) \)'s.

Figure A.10 shows two different views of the segmentation function in three dimensions. \( L = 3000 \) was chosen for the calculation. It is clear that \( S(k, L, x) \) is extremely sensitive to the copolymer sequence. Visual analysis allows judgment on some features of various copolymer sequences. \( S(k, L, x) \) is constant for random copolymer sequence, oscillatory for random block copolymer sequence, extremely oscillatory for alternating block copolymer sequence, increases monotonically to a constant value for HAMS.

2] **Trans-Information Function**

Trans-information or mutual information function\(^{13-16}\) was used to segment the 40000-mer HP copolymer sequence. The trans-information function, \( I(k, L, x) \) is defined by the following equation:

\[
I(k, L, x) = \sum_{i=\pm 1} \sum_{j=\pm 1} P^{ij}(k) \log_2 \left[ \frac{P^{ij}(k)}{\left( \sum_{j=\pm 1} P^{ij}(k) \right) \left( \sum_{i=\pm 1} P^{ij}(k) \right)} \right] 
\]  
(A.12)
where \( L \) is the length of the sliding window along the position \( x \) of the copolymer chain, \( k \) is the length of another sliding window which moves step by step within the window of length \( L \), \( i \) refers to starting bead in a segment of length \( k \) (\( i = +1 \) corresponds to H type bead while \( i = -1 \) corresponds to P type bead), \( j \) refers to last bead of the segment of length \( k \) (\( j = +1 \) corresponds to H type while \( j = -1 \) corresponds to P type), \( P_{ij}(k) \) is the joint probability that a segment of \( k \) units has a beginning at unit \( i \) and an end at unit \( j \). Thus we have four distinct \( P_{ij}(k) \)'s. 

\[
\sum_{j=-1,+1} P_{ij}(k) \text{ is the probability that a segment of length } k \text{ units begins at unit } i, \quad \sum_{i=-1,+1} P_{ij}(k) \text{ is the probability that a segment of } k \text{ units ends at unit } j.
\]

Figure A.11 shows the trans-information function in three dimensions. \( L = 3000 \) was chosen for the calculation. Trans-information function is extremely sensitive to the copolymer sequence. Visual analysis allows judgment on some features of sequence statistics. It is zero for random copolymer sequence, oscillatory for random block copolymer sequence, extremely oscillatory for alternating block copolymer sequence, decreases monotonically to a constant value for HAMS.

3] **Shannon Divergence Measure**

In addition to the segmentation function and trans-information function entropic segmentation\textsuperscript{17-20} based on Jensen-Shannon divergence measure\textsuperscript{17} was utilized to locate the
boundaries of various sequences within the 40000-mer HP copolymer. Jensen-Shannon divergence measure $C(l_1, l_2)$ is defined by the following equation:

$$C(l_1, l_2) = H(L) - \left[ \frac{l_1}{L} H(l_1) + \frac{l_2}{L} H(l_2) \right]$$  \hspace{1cm} (A.13)

$$H(l_i) = -\sum_n P^i(n) \ln(P^i(n))$$  \hspace{1cm} (A.14)

$$H(l_2) = -\sum_n P^{i2}(n) \ln(P^{i2}(n))$$  \hspace{1cm} (A.15)

$$H(L) = -\sum_n P^L(n) \ln(P^L(n))$$  \hspace{1cm} (A.16)

$$P^L(n) = \frac{l_1}{L} P^i(n) + \frac{l_2}{L} P^{i2}(n)$$  \hspace{1cm} (A.17)

where $L$ is total length of the sequence (40000 in this case), $l_i$ is the cutting point position ($0 \leq l_i \leq L$) such that $l_1 + l_2 = L$, $H$ is Shannon’s entropy defined by equations (A.14) through (A.16). $P^i(n)$, $P^{i2}(n)$, and $P^L(n)$ are the probabilities of finding a uniform block of length $n$ of either H or P type in a frame of length $l_1$, $l_2$, and $L$ respectively.

**Figure A.12** depicts the Jensen Shannon divergence (JSD) measure as a function of the cutting point position. Clearly the well defined maxima at the concatenation points between random, alternating block, and random block statistics helps locate the boundaries between sequences. The maximum at the concatenation points between random block and HAMS statistics is not sharp. Although JSD does not help identify the kind of statistics involve unlike the segmentation or trans-information function it definitely helps in locating
the boundaries between sequences. Thus segmentation function, trans-information function and Jensen-Shannon divergence measure are complementary.

**A.4 MODIFIED ITERATIVE COLORING ALGORITHM FOR GENERATION OF HAMS**

Since the instantaneous coloring algorithm for generating HAMS\textsuperscript{5,6} would be impossible to implement experimentally, in 2002 Chertovich et al.\textsuperscript{21} proposed a sequential coloring scheme for generating HAMS via lattice Monte Carlo simulations. In these simulations a bead is picked from amongst the beads farthest from the center of mass of the collapsed hydrophobic (H) globule and changed to hydrophilic (P) with a new interaction potential. The globule is then allowed to relax for a fixed time before the next bead is colored. I implemented Chertovich’s sequential coloring scheme using DMD but ended up making copolymers that were more diblock than HAMS. In Chertovich’s coloring scheme, the H beads present at the surface of the collapsed globule are transformed into P beads while H beads present within the core of the collapsed globule are neglected. To account for the coloring of the H beads in the core as well as on the surface of the collapsed globule I modified Chertovich’s\textsuperscript{21} sequential coloring approach by introducing an additional stochastic coloring parameter, $\gamma$ ($0 < \gamma < 1$), which determines the frequency with which an H bead is picked up from the surface or the core of the collapsed globule for coloring. A large value of $\gamma$ will favor the coloring of an H bead present at the surface of the globule while a lower
value of $\gamma$ will favor the coloring of an H bead present in the core of the globule. The various steps involved in the new sequential coloring algorithm to generate HAMS are as follows:

1] A hydrophobic homopolymer chain is collapsed to a globular conformation by switching on a uniform strong attraction between the monomer units.

2] The hydrophobic beads present at the surface or the core of the collapsed globule are colored to hydrophilic sequentially one at a time according to the scheme listed below in (3). After a particular hydrophobic bead is colored to hydrophilic, the HP copolymer chain is relaxed for a fixed number of steps equal to the relaxation time for the copolymer chain. The normalized end-to-end distance squared autocorrelation function, $C_{R^2}$ is defined by the following equation:

$$C_{R^2}(t') = \frac{\langle R^2(t')R^2(0) \rangle - \langle R^2 \rangle^2}{\langle R^4 \rangle - \langle R^2 \rangle^2}$$  \hspace{1cm} (A.18)

where $R^2$ is the square of the magnitude of the end to end vector, $\langle ... \rangle$ denotes a time average. $C_{R^2}(t')$ for a copolymer chain decays as the copolymer chain relaxes. The number of simulation steps required for $C_{R^2}(t')$ to decay to zero is used as the relaxation time for the copolymer chain.

3] The emerging HP HAMS copolymer should have a core-shell microstructure, with the core consisting mostly of H beads, and the shell consisting mostly of P beads. At each coloring step a random number, $r$ ($0 < r < 1$) is generated. The particular H
bead to be colored is chosen by comparing $r$ to $\gamma$, according to one of the following schemes:

**Scheme I** ($r > \gamma$): Pick an H bead located at the surface of the hydrophobic core of the emerging HP HAMS copolymer.

**Scheme II** ($r < \gamma$): Pick an H bead located at the surface of the shell of the emerging HP HAMS copolymer.

Thus on an average, Scheme I is implemented $1 - \gamma$ times while Scheme II is implemented $\gamma$ times.

4] The coloring of H to P beads is terminated when the desired composition of the HP HAMS copolymer is reached.

The new sequential coloring algorithm was implemented for a 120-mer collapsed hydrophobic homopolymer using DMD in the canonical ensemble (NVT) at $T^* = 1.0$, $\eta = 0.006$, $\lambda_m = 1.5$, $\varepsilon_{mm} = 1$, $\varepsilon_{mp} = 0$, and $\varepsilon_{pp} = 0$. The number of DMD events needed for relaxing the copolymer chain prior to coloring an H bead to a P bead was determined by calculating the end-to-end distance squared autocorrelation function (defined by equation (A.18)) using a shift register algorithm. Figure A.13 depicts the normalized end-to-end distance squared autocorrelation function for a collapsed 120-mer H globule versus the number of DMD events. Since the normalized end-to-end distance squared autocorrelation function decays to zero after 55 million DMD events, 80 million DMD events were used for the chain relaxation. Figure A.14 shows snapshots of the 120-mer HAMS generated via the new sequential coloring algorithm with composition varying from $x_p = 0.1$ to $x_p = 0.9$. These
HAMS have a core shell microstructure, with a dense hydrophobic core surrounded by long dangling hydrophilic loops. The radius of gyration $\langle R_g^2 \rangle$ or the size of the globule increases with increased coloring of the collapsed globule as shown in Figure A.15. The hydrophobic core size decreases while the hydrophilic shell increases with increased coloring.

The blockiness of the HAMS generated via sequential coloring procedure as well as the long range correlations along the sequence is sensitive to the stochastic coloring parameter ($\gamma$). Figure A.16 top and bottom show a comparison of the average length of the H block for a 120-mer HAMS generated via sequential coloring procedure to that generated using the instantaneous coloring procedure with composition $x_H = 0.3$ and $x_H = 0.7$, respectively, as a function of $\gamma$. Data is shown for three different simulation runs. Since the fluctuation in the average block length is large, the relationship between the average block length and $\gamma$ can’t be established. Longer chains and more simulation runs (meaning more computer time) would be required to establish the trend between the average block length and $\gamma$.

Figure A.17 top and bottom show the dispersion analysis for the 120-mer HAMS prepared via the sequential coloring procedure to the instantaneous coloring procedure with composition $x_H = 0.3$ and $x_H = 0.7$ respectively. Judging from the differences between the slopes of the various plots in Figure A.17, the value of the stochastic coloring parameter determines the strength of the long range correlations along the HP HAMS copolymer sequence.
Figure A.1 10000-mer homopolymer chain conformation ($\eta = 0.006$) at various stages of collapse: 0, 10 million, 20 million, 30 million, 90 million, 3 billion DMD events respectively.
Figure A.2 (a) Collapsed 10000-mer globule, (b) HAMS $x_\eta = 0.5$ prepared via instantaneous coloring procedure ($\eta = 0.006$), (c) prepared HAMS opened up.
Figure A.3 Sequence map for four different 10000-mer copolymer sequences with $x_H = 0.5$ and average block length 15.
Figure A.4 Frequency distribution for different 10000-mer copolymer sequences with \( x_p = 0.5 \). The \( x \) axis of the plot has been truncated at 50 for visual clarity although it extends to 10000.
Figure A.5 Dispersion analysis for HAMS, random, random-block and alternating block copolymers sequences each 10000-mer with $x_H = 0.5$. 
Figure A.6 Independent one-dimensional random walk for: HAMS, random, random-block and alternating block 10000-mer copolymer sequences with $x_H = 0.5$. 
Figure A.7 One dimensional random walk for 10000-mer HAMS with $x_{hf}=0.5$, and average block length 15 along with linear least squares fit for window length 1000.
Figure A.8 DFA for HAMS, random, random-block and alternating block 10000-mer copolymer sequences $x_H = 0.5$. 
Figure A.9 40000-mer HP copolymer sequence obtained by stitching random, alternating block, random-block and HAMS copolymers in series.
Figure A.10 Segmentation function for 40000-mer HP copolymer sequence obtained by stitching random, alternating block, random-block and HAMS in series (two different views).
Figure A.11 Trans-information function for 40000-mer HP copolymer sequence obtained by stitching random, alternating block, random-block and HAMS copolymers in series.
Figure A.12 Jensen Shannon divergence measure for 40000-mer HP copolymer sequence obtained by stitching random, alternating block, random-block and HAMS copolymers in series.
Figure A.13 Normalized end to end distance squared autocorrelation function for 120-mer homopolymer.

\[ C_{\text{EE}}(t') = \frac{\langle R^2(t')R^2(0) \rangle - \langle R^2 \rangle^2}{\langle R^2 \rangle - \langle R^2 \rangle^2} \]
Figure A.14 Snapshots of 120-mer long HAMS prepared via sequential coloring procedure with composition varying from $x_p = 0.1$ (a) through $x_p = 0.9$ (i) in increasing steps of 0.1.
Figure A.15 Radius of gyration for 120-mer HAMS (prepared via sequential coloring algorithm) with increased coloring (increasing P composition).
Figure A.16 Average block length versus stochastic coloring parameter for various 120-mer HAMS with composition: (top) $x_H = 0.3$, (bottom) $x_H = 0.7$. 
Figure A.17 Dispersion analysis for 120-mer HAMS generated via instantaneous coloring as well as sequential coloring procedure (for various stochastic coloring parameters) with composition: (top) $x_H = 0.3$, (bottom) $x_H = 0.7$. 
A.6 REFERENCES


