Copyright Warning & Restrictions

The copyright law of the United States (Title 17, United States Code) governs the making of photocopies or other reproductions of copyrighted material.

Under certain conditions specified in the law, libraries and archives are authorized to furnish a photocopy or other reproduction. One of these specified conditions is that the photocopy or reproduction is not to be "used for any purpose other than private study, scholarship, or research." If a, user makes a request for, or later uses, a photocopy or reproduction for purposes in excess of "fair use" that user may be liable for copyright infringement,

This institution reserves the right to refuse to accept a copying order if, in its judgment, fulfillment of the order would involve violation of copyright law.

Please Note: The author retains the copyright while the New Jersey Institute of Technology reserves the right to distribute this thesis or dissertation

Printing note: If you do not wish to print this page, then select "Pages from: first page # to: last page #" on the print dialog screen



The Van Houten library has removed some of the personal information and all signatures from the approval page and biographical sketches of theses and dissertations in order to protect the identity of NJIT graduates and faculty.

ABSTRACT

PHASE TRANSITIONS OF POLY(L-LACTIC ACID) IN BULK AND IN SOLUTION

by Jing Zhang

Poly(L-lactic acid) (PLLA) has been subject to intensive research in recent years because of its biodegradability. Applications of PLLA, such as porous tissue engineering scaffolds and excipients for controlled release, have been developed in the biomedical and pharmaceutical fields. The crystal structures and morphologies of this semicrystalline polyester are the underlying factors that determine the mechanical and degradation properties of PLLA.

A fundamental understanding of the development of crystal structures and morphologies during the phase transitions of PLLA in bulk and in solution is pursued in this dissertation. Synchrotron wide- and small-angle x-ray scattering (WAXS and SAXS) are adopted as the primary experimental techniques. Crystallization during annealing and drawing in melt-spun PLLA fibers is studied by WAXS with a quantitative evaluation of crystallinity and orientation. This represents the study of phase transitions of PLLA in bulk at temperatures above glass transition temperature (T_g). It is found that chain orientation plays an important role in facilitating the re-crystallization of PLLA during annealing. Upon cooling, the densification of the amorphous phase of PLLA is observed by SAXS. The densification below T_g of PLLA (63°C) is quantified by pycnometry measurements. A nonlinear dependence of the densities of the amorphous phase on temperature with a transition at about 45°C is found from pycnometry measurements. After thermal aging at this temperature, amorphous PLLA samples exhibit maximum excess enthalpies of relaxation. These observations are ascribed to the evolution of the amorphous phase of PLLA towards its equilibrium state via primary nucleation at temperatures below T_g .

The thermally induced phase separations (TIPS) of PLLA in solution are explored by SAXS, WAXS and scanning electron microscopy. A phase diagram of the PLLA/tetrahydrofuran (THF) binary system is established to explain the crystal structures and morphologies in the gels formed during phase separation. A new PLLA crystal form, the δ -form, is identified as a clathrate when PLLA/THF solutions are quenched to temperatures below 10°C. It is proposed that the δ -form crystal has a 4/1 helical chain conformation with THF molecules being incorporated in the interstitial sites of its unit cell. The crystallization kinetics during the gelation of PLLA solutions are studied by *in situ* simultaneous SAXS and WAXS. The Avrami parameters are evaluated from the SAXS invariant Q to determine the nucleation and growth behavior during the crystallization of PLLA in solutions. The dependence of the crystallization kinetics on gelation temperature and concentration is discussed.

PHASE TRANSITIONS OF POLY(L-LACTIC ACID) IN BULK AND IN SOLUTION

by Jing Zhang

A Dissertation Submitted to the Faculty of New Jersey Institute of Technology in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Chemical Engineering

Otto H. York Department of Chemical Engineering

January 2006

Copyright © 2006 by Jing Zhang

ALL RIGHTS RESERVED

APPROVAL PAGE

PHASE TRANSITIONS OF POLY(L-LACTIC ACID) IN BULK AND IN SOLUTION

Jing Zhang

Dr. Jing Wu, Dissertation Advisor
Assistant Professor of Chemical Engineering, NJIT

Dr. Marinos Xanthos, Committee Member Professor of Chemical Engineering, NJIT

Dr. Costas G. Gogos, Committee Member Distinguished Research Professor of Chemical Engineering, NJIT

Dr. Kamalesh K. Sirkar, Committee Member Foundation Professor, Membrane Separations Distinguished Professor of Chemical Engineering, NJIT

Dr. Joshua M. Samon, Committee Member Product Development Project Manager, Ethicon, a Johnson and Johnson Company, Somerville, NJ

Date

Date

Date

Date

Date

BIOGRAPHICAL SKETCH

g Zhang
3

Degree: Doctor of Philosophy

Date: January 2006

Undergraduate and Graduate Education:

- Doctor of Philosophy in Chemical Engineering, New Jersey Institute of Technology, Newark, NJ, 2006
- Master of Engineering in Materials Science and Engineering, Tsinghua University, Beijing, P. R. China, 2001
- Bachelor of Engineering in Polymer Science and Engineering, Tsinghua University, Beijing, P. R. China, 1998

Major: Chemical Engineering

Presentations and Publications:

Jing Zhang and Jing Wu, "The densification of poly(L-lactic acid) amorphous phase," Submitted to Polymer.

Jing Zhang and Jing Wu,

"Crystallinity and orientation in poly(L-lactic acid) fibers during annealing and drawing,"

Proceedings of Society of Plastics Engineers Annual Technical Conference, (ANTEC'05), 1747-1751, 2005, Boston, MA.

Jing Zhang and Jing Wu,

"The gel structure of poly(L-lactic acid),"

American Institute of Chemical Engineers Annual Meeting (AICHE'04), Austin, TX, November, 2004.

Jing Wu and Jing Zhang,

"The amorphous densification of poly(L-lactic acid)," American Institute of Chemical Engineers Annual Meeting (AICHE'03), San Francisco, CA, November, 2003. Jing Wu and Jing Zhang,

"Structure and morphology of poly(L-lactic acid) fibers under hot drawing by insitu synchrotron wide and small angle x-ray scattering," American Physical Society Annual Meeting, Austin, TX, March, 2003.

Chien-Yueh Huang, Lining Zhu, Mu-Ping Nieh, Jing Zhang, Jing Wu,
"Polymeric nano-porous materials prepared via interfacial polymerization in soft ionic liquid,"
American Institute of Chemical Engineers Annual Meeting (AICHE'05), Cincinnati, OH, November, 2005.

Chien-Yueh Huang, Lining Zhu, Jing Zhang, Mu-Ping Nieh, Jing Wu, "Characterization of nano-structures of polyurea synthesized in soft ionic liquids," American Institute of Chemical Engineers Annual Meeting (AICHE'05), Cincinnati, OH, November, 2005.

Chien-Yueh Huang, Lining Zhu, Jing Zhang, Jing Wu, Mu-Ping Nieh, "Nano-structure of polyurea synthesized in room temperature ionic liquids," American Institute of Chemical Engineers Annual Meeting (AICHE'05), Cincinnati, OH, November, 2005. To my beloved family.

ACKNOWLEDGMENT

My greatest appreciation goes to Dr. Jing Wu for his inspirations and countless support, which is the primary reason that this work can be completed. He has been more than an advisor, a friend and a mentor whom I learned so much from. I also would like to express my deepest gratitude to Dr. Marinos Xanthos, whose resourceful suggestions are of great help to my research and life.

Special thanks to Dr. Costas G. Gogos, Dr. Kamalesh K. Sirkar and Dr. Joshua M. Samon for their active participation in my committee and for their kind help on my research proposal and dissertation.

I am really grateful to the Otto H. York Department of Chemical Engineering for providing financial support during my studies at NJIT. Acknowledgements are also given to Dr. Igors Sics and Dr. Lixia Rong at Beamline X27C of National Synchrotron Light Source of Brookhaven National Laboratory, where most of the x-ray scattering experiments of this research were conducted.

Acknowledgement also goes to the following individuals for their help: Ms. Qi Zhang, Mr. Lining Zhu, Dr. Victor Tan, Dr. Zohar Ophir, Mr. Thomas Boland and Mr. Yogesh Gandhi.

Finally, I am indebted to my family, especially to my dear wife, Yan He, for all the unconditional love, support and encouragement that she gave me in the past four years.

TABLE OF CONTENTS

C	Chapter	
1	INTRODUCTION	1
	1.1 Properties and Applications of Poly(L-lactic acid) (PLLA)	3
	1.1.1 Chemical Structures of PLLA	5
	1.1.2 Crystal Structures of PLLA	5
	1.1.3 Applications of PLLA	7
	1.2 The Lauritzen-Hoffman Theory of Polymer Crystallization	9
	1.2.1 Classical Nucleation Theory	10
	1.2.2 Primary Nucleation of Polymer Crystals	11
	1.2.3 Polymer Crystal Growth Modeled by Secondary Nucleation	12
	1.2.4 Critics of the L-H Theory	13
	1.3 Polymer Gels	14
	1.3.1 Physical Gels	15
	1.3.2 Phase Diagram of Polymer Solutions	17
	1.3.3 Gelation via L-C Transition	18
	1.3.4 Gelation via L-L Phase Separation	19
	1.3.5 Gelation via L-C* transition	22
	1.3.6 Kinetics of Phase Separations during Gelation	24
2	EXPERIMENTAL MATERIALS AND TECHNIQUES	24
	2.1 Materials	24
	2.1.1 Poly(L-lactic acid)	24

TABLE OF CONTENTS (Continued)

Cl	Chapter		page
		2.1.2 Solvents	26
	2.2	Sample Preparation	26
		2.2.1 PLLA Melt-spun Fibers	27
		2.2.2 Amorphous PLLA Samples	27
		2.2.3 PLLA Pellets with Different Crystallinities	28
		2.2.4 PLLA Solutions and Gels	28
		2.2.5 Porous PLLA Samples	30
	2.3	Experimental Techniques	30
		2.3.1 Differential Scanning Calorimetry	30
		2.3.2 Thermogravimetric Analysis	30
		2.3.3 Scanning Electron Microscopy	31
		2.3.4 Pycnometry Measurement	31
		2.3.5 X-ray Scattering	33
	2.4	Data Analysis	38
		2.4.1 Crystallinity	38
		2.4.2 Orientation Factor	39
		2.4.3 Data Analysis for Pycnometry Measurement	41
3	CR AN	YSTALLIZATION IN PLLA FIBERS DURING NEALING AND DRAWING	43
	3.1	Introduction	43

TABLE OF CONTENTS (Continued)

С	hapter	Page
	3.2 As-spun Fibers	44
	3.3 The Effects of Constant-length Annealing	47
	3.4 The Effects of Drawing	49
	3.5 Conclusions	52
4	DESIFICATION AND PRIMARY NUCLEATION IN THE AMORPHOUS PHASE OF PLLA	53
	4.1 Introduction	54
	4.2 Densification Amorphous Phase in PLLA	54
	4.3 Effects of Thermal Aging on Primary Nucleation of PLLA	63
	4.4 Conclusions	68
5	CRYSTAL STRUCTURES AND MORPHOLOGIES DEVELOPED DURING TIPS IN PLLA SOLUTIONS	70
	5.1 Introduction	70
	5.2 A New Crystal Form in PLLA/THF Gels: the δ -form	73
	5.3 Phase Diagram of PLLA/THF System	85
	5.4 Conclusions	88
6	KINETICS OF TIPS IN PLLA SOLUTIONS	90
	6.1 Introduction	90
	6.2 Simultaneous SAXS and WAXS during Gelation	92
	6.3 Crystallization Kinetics Revealed by the SAXS Invariant	97
	6.4 Avrami Parameters of PLLA Crystallization in Solutions	100

TABLE OF CONTENTS (Continued)

Chapter		Page
	6.5 Conclusion	107
7	SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH	108
	7.1 Summary	108
	7.2 Recommendations for Future Research	109
	7.2.1 Behavior of the Amorphous Phase of PLLA	109
	7.2.2 Clathrate Crystal Structure	110
A	PPENDIX A: DATA ANALYSIS METHOD	111
A	PPENDIX B: MATLAB SOURCE CODE	118
R	EFERENCES	130

LIST OF TABLES

Tab	Table	
2.1	The properties of the PLLA from Biomer	24
2.2	A list of experimental methods and samples used in this dissertation	26
2.3	The densities of water at different temperatures	33
2.4	The detectors for synchrotron x-ray scattering	34
3.1	PLLA fiber samples by different melt-spinning conditions	44
3.2	The crystallinities and orientation factors of PLLA fibers after annealing	47
3.3	The crystallinities and orientation factors of PLA230 after drawing at 90°C	52
4.1	Results of the lease-square fit of the apparent density data	59
5.1	The five strongest Bragg peaks and their d-spacings of the δ -crystal	77
6.1	The gelation of PLLA/THF solutions at different concentrations and temperatures	92
6.2	The Avrami parameters calculated from SAXS invariants for the gelation in PLLA/THF solutions	106

LIST OF FIGURES

Figure Page		Page
1.1	The life circle and structures of lactic acid, lactide and their polymers	4
1.2	The crystal structure of the PLLA α -form	6
1.3	A schematic drawing of free energy change with increase of nucleus radius	11
1.4	A sketch of a polymer crystal embryo	12
1.5	Different network junctions in polymer gels	16
1.6	The phase diagram of <i>i</i> -PS in trans-decalin	18
1.7	Three types of network morphologies in polymer gels through the L-C phase separation	19
1.8	A schematic phase diagram of L-L phase transition in polymer solutions	20
1.9	The schematic gel morphologies obtained via L-L phase transition	21
2.1	DSC heat flows for the measurements of (a) melting temperature and (b) glass transition temperature of Biomer PLLA	25
2.2	The configuration of the melt-spinning apparatus	27
2.3	The configuration of the equipment setup at beamline X27C	34
2.4	The detectors for x-ray scattering experiments	. 35
2.5	The configuration for the synchrotron simultaneous SAXS/WAXS using a dual-cell setup	37
2.6	The orientation mode of crystalline polymers with an orthorhombic unit cell	. 39
3.1	The 2-D WAXS patterns from PLLA as-spun fibers	44
3.2	The dependence of azimuthal intensities $I(\phi)$ on the azimuthal angle	45
3.3	The evaluation of crystallinity by peak deconvolution from an azimuthal intensity profile from PLA25 fiber	46

LIST OF FIGURES (Continued)

Figure		Page
3.4	The effects of annealing suggested by 2-D WAXS patterns and their 1-D profiles from PLLA fibers	48
3.5	The 2-D WAXS patterns and 1-D profiles from PLA230 fibers drawn to different strains	50
3.6	The azimuthal intensity $I(\phi)$ of the (200) Bragg scattering from PLA230 fiber at different strains	51
4.1	The WAXS patterns from PLA230 fiber (a) annealed at 120°C and (b) at 60°C after ambient cooling from 120°C	55
4.2	The SAXS patterns from the PLA230 fiber as temperature drops from 120°C to 60°C	. 56
4.3	The azimuthal integrated intensity profiles of SAXS patterns from the PLA230 fiber as temperature drops from 120°C to 60°C	57
4.4	The apparent densities of PLLA pellets with two different crystallinities	58
4.5	The densities of the amorphous phase of PLLA at different temperatures below T_g	60
4.6	The excess enthalpies of relaxation of amorphous PLLA after thermal aging at different temperatures	61
4.7	The excess enthalpies of relaxation of amorphous PLLA after thermal aging at 45°C for different time	. 62
4.8	The heat flows of the isothermal DSC experiment at 120°C after thermal aging PLLA at different temperatures	. 64
4.9	The heat flows of the isothermal DSC experiment at 120°C after thermal aging PLLA at temperatures below T _g for different time	. 66
5.1	The SEM images of 10% PLLA/THF gels after freeze-drying	73
5.2	The 2-D WAXS patterns from PLLA/THF gels prepared at different polymer concentrations and gelation temperatures	. 74

LIST OF FIGURES (Continued)

Figu	re	Page
5.3	The 1-D WAXS profiles of PLLA/THF gels	75
5.4	The influence of solvent removal on the WAXS profiles from PLLA crystals	78
5.5	The Chain conformation and packing mode of the δ - crystal of PLLA	80
5.6	The weight loss curve of Sample A during heating in TGA	81
5.7	The 2-D WAXS patterns of the δ - crystal formed in a PLLA fiber	82
5.8	The WAXS profiles of (a) 10% and (b) 15% PLLA/THF gels formed at different temperatures	83
5.9	The SAXS profiles of (a) 10% and (b) 15% PLLA/THF gels formed at different temperatures	84
5.10	A schematic phase diagram of PLLA/THF binary system	87
6.1	The 3-D plots of WAXS profiles recorded during the gelation in PLLA/THF solutions	94
6.2	The 3-D plots of SAXS profiles recorded during the gelation in PLLA/THF solutions	95
6.3	The development of invariant $Q(t)$ during the gelation of 10% PLLA/THF solutions at different temperatures	98
6.4	The development of invariant $Q(t)$ during the gelation of PLLA/THF solutions of different concentrations	99
6.5	The normalized invariant $Q(t)$ during the gelation of PLLA/THF solutions of different concentrations at 0°C	101
6.6	The Avrami plots for the gelation of PLLA/THF solutions of different concentrations at 0°C	103
6.7	A comparison between the experimental data and the Avrami fit for SAXS profile from the 10% PLLA/THF gelled at 0°C	104

NOMENCLATURE

а	Cross-section area of a polymer strand in crystal
A _a	Sum of areas under the amorphous peaks in WAXS
A_c	Sum of areas under the crystalline peaks in WAXS
b	Thickness of the first polymer strand deposited
Ср	Concentration of polymer in solution
е	Direction cosine of the norm of (<i>hkl</i>) plane to axis a
f	Direction cosine of the norm of (hkl) plane to axis b
f _x	Identical to $f_{x,Z}$ when Z is the fiber direction
$f_{\mathbf{x},\mathbf{Z}}$	Orientation factor defined by Eq. 2.1
g	Direction cosine of the norm of (hkl) plane to axis c
ΔG	Free energy change
ΔG_1	Free energy change upon deposition of the first polymer strand
ΔG_{v}	Free energy difference per unit volume
Ι	X-ray scattering intensity
Ι(φ)	Azimuthal intensity of x-ray scattering
k	Crystallization rate constant
l	Length of a polymer strand in crystal
L_B	Bragg spacing of long range order
L_{SD}	Sample-to-detector distance
n	Avrami exponent
PLA	Poly(lactic acid) or Poly(lactide)

PLLA	Poly(L-lactic acid)
q	Scattering vector
Q	SAXS invariant
Qn	Normalized SAXS invariant
r	Radius of sphere liquid nucleus
r*	Critical radius of sphere nucleus
RAP	Rigid amorphous phase
SAXS	Small angle x-ray scattering
t	Time
<i>t</i> _{1/2}	Half-life of crystallization
T _g	Glass transition temperature
v	Number of strands in a polymeric embryonic crystal
V _p	Volumetric capacity
w	Width of the first polymer strand deposited
W	Weight of PLLA pellets
W_1	Total weight of water and pycnometry bottle
<i>W</i> ₂	Total weight of PLLA pellets, water and pycnometry bottle
WAXS	Wide angle x-ray scattering
W _b	Weight of pycnometry bottle
x	Axis of crystal, $x = a$, b or c
Xa	Volumetric ratio of amorphous phase
X _c	Crystallinity
Ζ	Reference direction or the longitudinal direction of fiber

Greek Letters

σ	Surface energy per unit area
$\sigma_{ m s}$	Unit surface energy of lateral interfaces in polymer crystal
σ_{e}	Unit surface energy of end interfaces in polymer crystal
$\phi_{x,Z}$	Angle between crystal axis $x (x = a, b \text{ or } c)$ and direction Z
ϕ	Azimuthal angle
$\phi_{x,Z}$	Angle between crystal axis x and reference direction Z
$\phi_{hkl,Z}$	Angle between the norm of (<i>hkl</i>) plane and direction Z
20	Diffraction angle
λ	Wavelength of x-ray
ρ	Apparent density
$ ho_c$	Density of crystalline phase
$ ho_a$	Density of amorphous phase
$ ho_p$	Apparent density of PLLA pellets
$ ho_w$	Density of water

CHAPTER 1

INTRODUCTION

Poly(L-lactic acid) (PLLA) has been intensively studied in recent years as a biodegradable polymer due to its applications in the biomedical and pharmaceutical fields (Sodergrad and Stolt, 2002; Jacobsen et al., 1999). Since the FDA approval of PLLA as a pharmaceutical excipient in 1979, various PLLA-based products, such as absorbable sutures and controlled-release drug delivery systems, have been developed. More recently, PLLA has been explored as a promising candidate for the application of tissue engineering scaffolds.

Phase transitions in PLLA, such as crystallization and liquid-liquid phase separation, are usually involved in the processing of the PLLA products discussed above. These phase transitions may lead to a variety of crystal structures and nanoscale morphologies, which have been found crucial for the properties of the products. A representative example is the overall degradation rate, which is an important property of PLLA-based biomedical products. It has been found that the rate of degradation of PLLA is greatly dependent on its crystallinity and morphology (Cai, et al., 1996). The closely packed crystalline phase has a higher resistance to water penetration and therefore has a slower rate of degradation than the amorphous phase.

Although a great amount of research on PLLA has been conducted, most of the efforts have been focused on its processing, mechanical and degradation properties. A fundamental understanding of the phase transitions of PLLA in bulk and in solution remains missing. For the phase transitions in the bulk of PLLA, most of the efforts have been focused on the crystallization from melt at temperatures above its glass transition

temperature (T_g) in unoriented systems. There are few reports of PLLA crystallization in oriented systems. The amorphous chains below T_g are usually considered "frozen". The relaxations of the amorphous phase of PLLA towards its equilibrium state at temperatures below T_g have not been explored.

For PLLA solutions, thermally induced phase separation (TIPS) has been widely used to prepare various porous structures. Although theories are well developed for phase separations in solution, there are few explanations on the structure and morphology development during TIPS in PLLA solutions.

Based on literature research and preliminary experimental investigations, the phase transitions in PLLA were selected to be the goal of this dissertation research. Attention is focused on (1) the crystallization of PLLA in oriented systems above T_g , (2) the crystallization of the amorphous phase of PLLA in bulk below T_g and (3) the development of crystal structures and morphologies as well as the kinetics of phase transitions during TIPS in PLLA solutions.

The dissertation is organized as follows. In this chapter, the prior literature on PLLA, the theory on polymer crystallization and polymer gels is reviewed. Detailed literature reviews on the research specific to a chapter will be presented in the introductory section of the corresponding chapter. The experimental techniques and materials used in this dissertation are introduced in Chapter 2. Special attention is paid to synchrotron wide- and small-angle x-ray scattering (WAXS and SAXS), which is capable of probing the atomic structures and nanoscale morphologies of a material system, respectively. In Chapter 3, crystallization in PLLA fiber above its T_g is studied. In Chapter 4, the densification behavior of the amorphous phase of PLLA is studied.

The relaxation of amorphous chains in PLLA is investigated and its effect on the isothermal crystallization of PLLA is discussed based on experimental data.

In Chapter 5, the structural and morphological developments during TIPS in PLLA solutions are explored. During TIPS, solvents are retained in the polymer-rich phase, leading to the formation of polymer gels. A phase diagram is established for the PLLA/THF system and can be used to explain its gelation behavior. The crystal structures of PLLA in gel and their corresponding morphologies are investigated. In Chapter 6, crystallization and the phase transitions in PLLA solutions are monitored by simultaneous synchrotron WAXS and SAXS. The kinetics of phase transitions during gelation are investigated by using Avrami equation. In the end, Chapter 7 concludes this dissertation with a summary and recommendations for future research.

1.1 Properties and Applications of PLLA

Although the first ring-opening polymerization and the synthesis of high molecular weight poly(lactic acid) (PLA) were reported by Carothers et al. as early as 1932 (Carothers et al., 1932), PLA had not been widely used in the next thirty years because its ester bonds are susceptible to hydrolysis, leading to degradation (Sodergrad and Stolt, 2002). The application of PLA as a biodegradable and biocompatible material began in the 1960s, when researchers realized that PLA could be decomposed to nontoxic substances, which can be eliminated by normal metabolic pathways (Kulkarni et al., 1971). Research on the laevorotatory homopolymer of PLA, i.e., PLLA, as a pharmaceutical excipient resulted in the FDA approval for its pharmaceutical applications as a drug delivery material. Subsequent research on PLLA has resulted in a variety of

biomedical applications in the fields of controlled release and tissue engineering. In the latter application, PLLA is fabricated into biocompatible porous matrices to serve as polymeric scaffolds on which cells can attach and develop into tissues (Wong et al., 1997).



Figure 1.1 The life cycle and structures of lactic acid, lactide and their polymers. Source: Jacobsen, S., Degee, P.H., Fritz, H.G., Degee, Ph., Dubois, Ph. & Jerome, R. (1999) Polylactide (PLA)-A new way of production. <u>Polymer Engineering and Science</u>, <u>39</u>, 1311-1319.

1.1.1 Chemistry and Manufacture of PLLA

An introduction to PLA should start from its monomer, lactic acid, which is one of the smallest organic molecules with optical activity. The optical isomers are L(+) and D(-) lactic acid. Since L-lactic acid is found as a metabolic product in mammalian species, so the polymer of L-lactic acid, i.e., PLLA, is usually preferred in biomedical applications. Polymerization of lactic acid can be achieved through two routes: (1) polycondensation of lactic acid into PLA or (2) ring-opening polymerization of lactide, which is a cyclic dimer of two lactic acid molecules, into poly(lactide) (Fukuzaki et al, 1988). When polymerization is carried out by using only the L-isomers, a homopolymer of PLLA can be obtained. It is important to notice that lactic acid, lactide and polylactide starting from the fermentation of biomass, such as corn and sugar. The stereo chemical structures of L-lactic acid, L, L-lactide and their polymers (PLLA) are also displayed.

1.1.2 Crystal Structures of PLLA

As most linear polymers, PLLA is semicrystalline. There have been several studies focused on the crystal structures of PLLA (Miyata and Masuko, 1997; Alemán et al., 2001; Kobayashi et al., 1995; De Santis and Kovacs, 1968; Hoogsteen et al., 1990). Three crystal forms of PLLA, i.e., the α -, β - and γ -form, have been identified. The α -form is the most stable crystalline modification. Its crystal structure assignment was first proposed by De Santis and Kovacs by conformation analysis and molecular transform (De Santis and Kovacs, 1968). Subsequent work by Hoogsteen et al. (Hoogsteen et al., 1990), by Miyata and Masuko (Miyata and Masuko, 1997) and by Kobayashi et al. (Kobayashi et al., 1995) confirmed the initial structural assignment with minor improvements. Its packing mode and the distortion of chain conformation were recently investigated by Alemán, et al. (Alemán et al., 2001). The 10/3 helical conformation of the α -form crystal is shown in Fig. 1.2. The α -form has an orthorhombic or pseudo-orthorhombic unit cell with the following dimensions: a = 10.7 \dot{A} , b = 6.45 \dot{A} , c = 27.8 \dot{A} (De Santis and Kovacs, 1968), or a = 10.7 \dot{A} , b = 6.04 \dot{A} , c =28.7 \dot{A} (Miyata and Masuko, 1997). The β -form is obtained when PLLA fibers are processed at high draw ratios and temperatures (Eling et al., 1982). It has a trigonal unit-cell with a = b = 10.5 \dot{A} and c = 8.8 \dot{A} (Puiggali et al., 2000). The γ -form is the most recent discovery, which can be obtained by epitaxial crystallization on hexamethylbenzene (Cartier et al., 2000), with an orthorhombic unit-cell with a = 9.95 \dot{A} , b = 6.25 \dot{A} and c = 8.8 \dot{A} .



Figure 1.2 The crystal structure of the PLLA α -form. Source: De Santis, P. & Kovacs, A.J. (1968). Molecular conformation of poly(S-lactic acid). <u>Biopolymers, 6</u>, 299-306. (L-lactic acid was named S-lactic acid by the authors of the source paper using the Cahn-Ingold-Prelog system)

The research on PLLA crystals is motivated not only by the interest in the fundamentals of crystallography, but also by the needs arising from the extensive applications of PLLA. Since PLLA is a semicrystalline polymer, the control of its crystal structure, crystallinity and nanoscale morphology is crucial to obtain the desired performance during degradation. It has been found that the amorphous phase of PLLA undergoes hydrolysis or biodegradation at a faster rate than the crystalline phase because water and enzymes can easily penetrate into the loosely packed amorphous region (Sodergard and Stolt, 2002). Other degradable polymers have been blended with PLLA in order to modify its crystallinity or to enhance its mechanical properties (Nakafuku and Takehisa, 2002; Park and Im, 2000). The copolymers of PLLA with another important biodegradable polymer, poly(glycolic acid), have also been extensively investigated (Wang et al., 2001).

1.1.3 Applications of PLLA

Almost all the biomedical and pharmaceutical applications of PLLA originate from its biodegradability. Commercial products of PLLA include VICRYLTM, a remove-free suture developed by Ethicon (Ethicon, 1996), and ReGel[®], a controlled-release drug delivery platform by MacroMed (MacroMed, 2003). The rate of degradation is the most important property of these products. It is controlled by the crystallinity, morphology and blending ratio of PLLA with other components.

Recently, tissue engineering has attracted the attention of many researchers. Fabricating polymers, especially biodegradable and biocompatible polymers, to a highly porous construct as tissue engineering scaffold, has been a challenge for scientists and engineers in the polymer field. As reviewed by Mikos and Temenoff, the methods for preparing porous polymer structures include bonding fibers into nonwoven meshes, solvent casting/particulate leaching, gas foaming, and phase separations (Mikos and Temenoff, 2000). In the phase separation method, PLLA is first dissolved in a solvent which has a relatively high melting point, e.g., 1, 4-dioxane, whose melting point is 11.8°C. Then the phase separation is induced either by a decrease in temperature or by an addition of a nonsolvent. Upon phase transition, a polymer-rich phase emerges, which is a porous gel. The gel is then dried under vacuum for a long period of time to ensure the complete removal of solvents, leaving behind a porous polymer scaffold (Lo et al., 1995; Lo et al., 1996). Two possible phase separation mechanisms, i.e., spinodal decomposition and crystallization, may be involved in this process. They will be further introduced in Chapter 1.3.2. Nam and Park reported that the spinodal decomposition increased the portion of interconnecting pores, which are preferred for tissue engineering scaffolds because the "open" cellular structure facilitates the diffusion of nutrients and tissue growth (Nam and Park, 1999a; Nam et al., 1999b).

Various pairs of PLLA/solvent and different experimental conditions have been attempted by researchers to produce porous structures with different sizes and shapes. Despite the extensive research on the relationship between cellular geometries and experimental conditions, a fundamental understanding of the phase transitions that govern the gelation processes in PLLA solutions is still not available. Fundamental understanding of phase transitions and their implications on the development of crystal structure and morphologies in PLLA solutions are essential for the design of PLLA-based tissue engineering scaffolds. The most recent news on PLA was the commercialization of large-scale production of this polymer, which was resulted from the continuous efforts and developments of related technologies by several companies, such as NatureWorks[®], previously a joint venture of Dow and Cargill. The increase in the scale of production has reduced the cost of PLA remarkably, making this biopolymer highly competitive for plastic consumer product applications. A recent report stated that the market price of PLA was as low as 1\$/lb, which was somewhat higher than petro-based plastics such as PE, PP and PS (Glasbrenner, 2005). As a biodegradable and environmentally friendly plastic, PLA has reasonable mechanical properties to be used for consumer products such as disposable water bottles and milk jars. More importantly, manufacturing of PLA is from natural resources, such as corn, which is annually renewable. A new terminology, biorenewable polymer, was recently coined by the manufacturers of PLA in an effort to promote its applications.

1.2 Lauritzen-Hoffman Theory of Polymer Crystallization

Crystallization is one of the most important phase transformations in polymer systems. It is the process that implements the formation of ordered structures. It has been established that polymer crystallization follows the nucleation and growth mechanism. Modern physics of polymer crystallization commenced in the 1950s due to the discovery of chain-folded lamellar crystals. The Lauritzen-Hoffman theory (L-H theory) on polymer crystallization has been widely accepted and applied to various semicrystalline systems (Lauritzen and Hoffman, 1959; Schultz, 2001a). This theory addresses the nucleation and growth of polymer crystals using the classical nucleation theory and a secondary nucleation process, respectively. The L-H theory is briefly introduced below.

1.2.1 Classical Nucleation Theory

To distinguish the nucleation of semicrystalline polymers from the crystal growth, which is modeled as a secondary nucleation process in the L-H theory, the nucleation process is usually referred to as "primary nucleation". The primary nucleation theory of semicrystalline polymers is derived from the classical nucleation theory on the condensation of vapor to liquid (Schultz, 2001a). A vapor at a temperature below its boiling temperature is considered. The first generated liquid drop or embryo nucleus possesses a large surface to volume ratio. For a spherical liquid nucleus with the radius of r, the change of free energy is

$$\Delta G = 4\pi r^2 \sigma + \frac{4\pi}{3} r^3 \Delta G_{\nu} \tag{1.1}$$

where σ is the surface energy per unit area, and ΔG_{ν} represents the free energy difference between the vapor phase and the liquid phase per unit volume.

The dependence of ΔG on r is schematically shown in Fig. 1.3. It is observed that the nucleus must overcome a critical size r^* to fall into the regime where total free energy drops with increasing r. The critical r^* can be obtained from the corresponding radius where the maximum value of ΔG is found. This is given in Eq. (1.2).

$$r^* = \frac{-2\sigma}{\Delta G_v} \tag{1.2}$$



Figure 1.3 Schematic drawing of free energy change with increase of nucleus radius. Source: Schultz, J. M., Polymer Crystallization: the Development of Crystalline Order in Thermoplastic Polymers, (New York: Oxford University Press, 2001) 141-142.

1.2.2 Primary Nucleation of Polymer Crystals

The primary nucleation theory of polymer chains was developed based on the classical nucleation theory introduced above. A sketch of a polymer embryonic crystal is shown in Fig. 1.4. The nucleus consists of v strands, each with a length l and a cross-section area a. So the cross-sectional area of the nucleus is av and the volume is lav.

Based on this model, a free energy equation similar to Eq. (1.1) can be derived,

$$\Delta G(v,l) = lav\Delta G_v + 2av\sigma_e + Cl\sqrt{av\sigma_s}$$
(1.3)

where C is a constant determined by the shape of the nucleus. With $C = 2\pi^{0.5}$ for a cylinder and C = 4 for a square column, the term $Cl(av)^{0.5}$ gives the lateral area of the nucleus. The symbol σ_s and σ_e are used to denote the unit surface energy of the lateral and the end interfaces, respectively. The lateral interfaces are similar to those in the simple substance, which delineate the molecules in the crystalline and the noncrystalline phases. Across the end interfaces, polymer chains travel from the closely packed

crystalline phase to the loosely packed amorphous phase. Thus, surface energy generated at the "crowded" end interface is extremely high.



Figure 1.4 A sketch of a polymer crystal embryo. Source: Schultz, J. M., Polymer Crystallization: the Development of Crystalline Order in Thermoplastic Polymers, (New York: Oxford University Press, 2001) 144-145

1.2.3 Polymer Crystal Growth Modeled by Secondary Nucleation

In the L-H theory, the growth of polymer crystals is described as the nucleation of a new layer on the growth front. This process is termed secondary nucleation. One strand of a polymer chain is first bound to the chains on the growing layer. The subsequent strands are then fitted into the crystalline registry by chain-folding on the growth front. Obviously, the activation energy involved in the deposition of the first strand is higher than that of the following strands because those strands are bonded to both the substrate

and the strand previously deposited. The energy barrier for the growth of a crystalline layer primarily originates from the deposition of the first strand.

Using a method similar to that introduced in the preceding section, the free energy change upon the deposition of the first strand is given in Eq. (1.4),

$$\Delta G'_{1} = bwl' \Delta G_{v} + 2bw\sigma_{e} + 2bl'\sigma_{s} \tag{1.4}$$

where l' is the strand length. The thickness and width of the strand are represented by b and w, respectively.

1.2.4 Critics of the L-H Theory

The L-H theory of polymer crystallization has survived much criticism ever since its inception (Mandelkern and Haigh, 1998; Strobl, 2000; Muthukumar and Welch, 2001). The early stage mechanism of crystallization was recently questioned by Olmsted et al., who argued that the spinodal decomposition took place even before the appearance of initial crystal structure (Olmsted et al., 1998). This argument was based on the SAXS observation by Imai, Trill and other researchers on several polymer melts (Imai et al., 1994; Trill et al., 1998) as well as their molecular simulations (Olmsted et al., 1998). However, Muthukumar and Welch disagreed with the mechanism of spinodal decomposition by showing that the results of Brownian dynamic simulation match well to the prediction of the nucleation theory at the early stages of crystallization (Muthukumar and Welch, 2001).

The growth stage of polymer crystals is strongly affected by the high surface tension at the melt-crystal interface. The intrinsic metastability of polymers affects the nucleation and growth of polymer crystals. The high surface tensions generated from the density difference between the crystalline and the amorphous phases at the end interfaces force the polymer chains to fold. It is important to note that the formation of chain-extended crystals is possible. Their existence has been demonstrated during the crystallization in polymer gels. Solvent molecules are incorporated into the crystal structure, forming clathrates (Keller, 1995). The longitudinal growth of this crystal becomes possible because the surface tensions at the end interfaces are compensated by the incorporation of solvent molecules into the crystal lattice. Pictorially, a loosely packed crystalline phase is formed, reducing the density difference between the crystalline and liquid phases at the end interface. This leads to the formation of the chain-extended clathrate crystals.

The L-H theory is based on a physical picture of a two-phase model during crystallization, in which amorphous and crystalline phases are the classical end states. More recently, Strobl suggested that there always existed a mesomorphic phase at the crystallization front (Strobl, 2000). Similarly, some researchers identified the crystalline-amorphous interfaces as a distinct phase, namely, the rigid amorphous phase (RAP) (Wunderlich, 2003). RAP was described as the ordered amorphous chains arranged perpendicularly onto the interface of crystal lamellae and amorphous phase, showing a higher order but a lower mobility than the classical amorphous phase. When heated to a temperature above T_g , RAP shows a higher rate of crystallization. Iannece and Nocolais recently reported the formation of RAP in PLLA during cold crystallization at different temperatures (Iannece and Nicolais, 1997). It can be concluded that the argument has focused on the role of the amorphous phase in crystallization, i.e., whether a specific part of the amorphous phase can be isolated from the classical amorphous state,
which is statistically random. Moreover, the behavior of the amorphous phase and its impact on crystallization and other phase transitions are important issues for the properties of PLLA. This subject is studied in Chapters 3 and 4.

1.3 Polymer Gels

Gel is a very broad topic even when limited to polymers. It is hard to give a clear and brief definition of the gel. A gel usually refers to a system that retains a significant amount of liquids and yet keeps its shape under gravity. Gels are liquid-containing resilient solids. The gel state can also be regarded as a transitional state between solution and solid. The ability of shape retention implies the existence of network connection throughout the system. Keller summarized the above characteristics of polymer gels as "fluid-containing, self-supporting disperse systems", in which the "non-fluid" network connecting elements are either individual polymer chains or assemblies of macromolecules (Keller, 1995).

Researchers approach polymer gels from different perspectives, which can be either theoretical or practical. The characterization of the network and the nature of the network junctions have attracted great research efforts. Actually, the mechanism of junction formation is the principle direction in the studies on gels, and can be used to classify polymer gels. Other topics about polymer gels include their mechanical behavior and biological significance. In practice, ultra-strong fibers and various porous structures were produced with gels as intermediaries (Vanderweerdt et al., 1994). Polymer gels can also be used as the biomimetic materials for biomedical engineering (Peppas and Huang, 2002; Yoshida, 2000) or the drug delivery matrix in pharmaceutical products (Uhrich et al., 1999; Fowers et al., 2003).

Based on distinctions in the network junctions, polymer gels can be divided into two basic categories: chemical gels and physical gels. Network junctions in chemical gels are permanent chemical crosslinks, which are irreversible. In physical gels, the junctions are physically associated polymer chains, which can be generated and eliminated under certain physical conditions. Listed in Fig. 1.5 are the network junctions in polymer gels. Physical gels have attracted much research interest due to their reversible nature.



Figure 1.5 Different network junctions in polymer gels. Source: Keller, A. (1995). Introductory lecture aspects of polymer gels. <u>Faraday</u> <u>Discussion, 101</u>, 1-49.

1.3.1 Physical Gels

The network junctions of the physical gels can be generated from phase transitions of polymer solutions, physical associations or entanglements of polymer chains (as

described in Fig. 1.5). Thermodynamically, a physical gel is a metastable system. Although physical gels can remain in the gel state for an extended period of time, ultimately the liquid and solid phases should separate on a macroscopic scale. Most of the research efforts have been focused on the polymer gels formed during phase transitions. One important motivation is that the physical gels are more likely to show "reversible gelation" behavior upon changes in temperature during TIPS.

1.3.2 Phase Diagram of Polymer Solutions

Phase diagrams of polymer solutions based on the data from thermal analysis have been widely used to describe and predict the gelation behavior of polymer/solvent binary systems. Fig. 1.6 shows the phase diagram of isotactic polystyrene (*i*-PS, a typical semicrystalline polymer) in trans-decalin, in which phase transitions at different temperatures and polymer concentrations are drawn. Three phase separation lines are observed in this phase diagram and each of them can give rise to a specific gel.

When the *i*-PS/trans-decalin solution with an initial concentration beyond the critical level $(c_p)_{gel}$ is quenched below the upper most phase separation line, Gel I is obtained through the liquid-crystal (L-C) phase transition. When a liquid-liquid (L-L) phase transition is induced at a low temperature, the formation of gel III takes place. Gel II can be obtained through a liquid-crystalline phase transition mechanism at temperatures between the L-C and L-L lines. In gel II, *i*-PS is found to crystallize into a different crystal structure from the chain-folded lamellar crystal obtained from the L-C transition (Keller, 1995). The corresponding phase separation line is named L-C*.



Figure 1.6 The phase diagram of *i*-PS in trans-decalin. Source: Keller, A. (1995). Introductory lecture aspects of polymer gels. <u>Faraday</u> <u>Discussion, 101</u>, 1-49.

1.3.3 Gelation via L-C Transition

During the gelation of polymer solutions via the L-C phase transition, polymer crystals serve as the network junctions. At a temperature below the L-C phase separation line on the phase diagram, crystallization takes place in the homogenous polymer solution. When the polymer concentration is higher than the critical value $(c_p)_{gel}$, a polymer chain can participate in more than one crystallite, leading to the formation of a network with the crystallites as the network junctions.

One major research interest in polymer gels is the morphology of the crystal junctions and the connections between the junctions. Three types of junctions and the corresponding morphologies can be formed via crystallization (Keller, 1995). In Fig. 1.7(a), junctions are small micelles formed by bundles of chains, with chains connecting through crystals. Fig. 1.7(b) shows the network junctions and connections which are fibrous crystals. In Fig. 1.7(c), crystals are chain-folded lamellae with inter-lamellar chains acting as the interconnecting elements of the network. In (a) and (b) parts of Fig. 1.7, chain-extended crystals instead of chain-folded lamellae are involved in the networks. These two situations are likely to take place in gels of rigid macromolecules, where the rigidity of polymer chains makes folding difficult.



Figure 1.7 Three types of network morphologies in polymer gels through the L-C phase separation. Source: Keller, A. (1995). Introductory lecture aspects of polymer gels. <u>Faraday</u> <u>Discussion, 101</u>, 1-49.

1.3.4 Gelation via L-L Phase Separation

The gelation via L-L phase transition takes place when a system is quenched below the L-L phase separation line. Systems capable to undergo such as gelation can be semicrystalline polymer solutions (e.g., *i*-PS in trans-decalin as shown in Fig. 1.6) or solutions of noncrystallizable polymers [e.g., atactic polystyrene (*a*-PS)].



Figure 1.8 A schematic phase diagram of L-L phase transition in polymer solutions.

A phase diagram of an L-L phase transition is illustrated in Fig. 1.8, in which the binodal and spinodal regions are identified. The gel morphology consequent to L-L phase transitions critically depends on the mode of phase separation. When a polymer solution is quenched into the metastable binodal region, the phase separation takes place via the nucleation and growth mechanism. The gel morphology so obtained is a network consisting of interconnecting spherical particle, which are the polymer-rich phase formed via nucleation and growth during L-L phase transition [Fig. 1.9(a)]. Solvated chains participating in more than one particle serve as the interconnecting elements of the network. When the solution is quenched into the spinodal region, the high driving force of the L-L phase separation results in a bicontinuous morphology, in which the polymer-rich phase and the polymer-poor phase form an interpenetrating network [Fig. 1.9(b)]. Obviously, both the gelation temperature and initial concentration affect the region into which the system is quenched, and the consequent morphology of the gel.



Figure 1.9 The schematic gel morphologies obtained via L-L phase transition. (a) interconnected spherical polymer-rich phase, (b) bicontinuous morphology of the polymer-rich phase (white) and the polymer-poor phase (gray). Source: Source: Keller, A. (1995). Introductory lecture aspects of polymer gels. <u>Faraday</u> <u>Discussion, 101</u>, 1-49.

The spinodal/binodal mechanism of the L-L phase transition can be further complicated by kinetic limitations. A Berghmans point (BP), representing the kinetic limitations of the system, was proposed by Arnauts and Berghmans (Wellinghoff et al., 1979; Arnauts and Berghmans, 1987; Arnauts et al., 1993) to explain the vitrification of the polymer-rich phase. As shown in Fig. 1.8, the T_g of the system is a function of the polymer concentration in the solution. With the increase of the solvent concentration, T_g is depressed. The intersection of the T_g line and the binodal line is called the BP. When the system reaches the BP during the L-L phase transition, the polymer-rich phase is vitrified into the glassy state and the phase separation is impeded.

In most scenarios, due to the kinetic limitations intrinsic to polymers, the polymer-rich phase and the polymer-poor phase can only form separated microdomains and cannot aggregate into two distinct layers in a detectable time scale.

1.3.5 Gelation via L-C* Transition

When an *i*-PS/trans-decalin solution is quenched to temperatures below 50°C but higher than the L-L line, the gelation is implemented by the crystallization of *i*-PS into clathrates. The clathrates are different from the α -form of *i*-PS crystals, which have a chain conformation of 3/1 helix and are usually found in the crystallization of *i*-PS from melt and in the Gel I obtained via the L-C phase transition. The clathrate, on the other hand, has a 12/1 helical conformation with solvent molecules occupying interstitial sites of its unit cell (Atkins et al., 1977; Atkins et al., 1980; De Rudder et al., 2001). The crystallization process for forming the clathrate is conventionally called the L-C* phase transition.

On the morphological scale, the clathrate exhibits itself as a chain-extended crystal. This corresponds to the situation depicted in Fig. 1.7(a) or 1.7(b). This was proved by TEM on the dried *i*-PS/trans-decalin gels which displayed a fine fibrous morphology (Atkins et al., 1984). The chain extension is a direct consequence of the inclusion of solvent molecules in the crystalline registry, which reduces the surface energy at the end interfaces of the system. The formation of the clathrates also has been reported for *s*-PS gels (Daniel and Guerra, 1988; Daniel and Alfano, 2003; Rosa et al., 1999; Van Hooy-Corstjens et al., 2002).

1.3.6 Kinetics of Phase Separations during Gelation

Due to the metastable nature of polymer gels, both thermodynamic driving forces and kinetic limitations take effect in the phase separation during the formation of the gel morphologies. Under this condition, equilibrium phase diagrams of polymer/solvent

systems are insufficient to understand the development of morphology during crystallization and L-L phase transitions. Kinetic effects must also be considered. In addition, even though TEM and SEM can be used to image the gel morphologies, only dried gels representing the end stages of gelation can be observed by these methods. *In situ* experimental techniques, such as Differential Scanning Calorimetry (DSC), WAXS, SAXS, and other spectroscopic techniques are indispensable tools for probing the kinetics of the development of crystal structures and morphologies in polymer gels. Phase transitions during gelation have been investigated by these *in situ* techniques (Van Hooy-Corstjens et al., 2002).

CHAPTER 2

EXPERIMENTAL MATERIALS AND TECHNIQUES

2.1 Materials

2.1.1 Poly(L-lactic acid)

PLLA pellets with no nucleating agents were purchased from Biomer, Germany. The polymer has an average molecular weight (MW) of 130,000 to 140,000 and a MW distribution of 1.95. The melting point of PLLA was determined by DSC using a DSC Q100 from TA Instrument. Virgin pellets were used in the DSC measurements in which a heating rate of 10°C/min was used. The melting point was found to be between 165°C and 167°C. To measure T_g of the sample, the virgin pellets were first melted in the DSC at 200°C and then cooled to -20°C at 20°C/min. The sample was then heated at a rate of 10°C/min in DSC. The T_g was found to be 63°C. The heat flows of these DSC experiments are presented in Fig. 2.1. Other parameters of the PLLA sample were provided by the manufacturer and are listed in Table 2.1.

CAS Registration Number	26680-10-4		
Molecular Weight	130,000-140,000		
Molecular Weight Distribution	1.95		
Density	1.25 g/cm^3		
Thermal Decomposition	250°C		
D-content	~2%		

Table 2.1 The properties of the PLLA from Biomer.

Source: Biomer. (2002). MSDS of Biomer PLLA formulation, Krailling, Germany.



Figure 2.1 DSC heat flows for the measurements of (a) melting temperature and (b) glass transition temperature of Biomer PLLA.

The solvents used in this research include tetrahydrofuran (THF) and ethanol. They were purchased from Sigma-Aldrich and were used as received. Water used for the pycnometry measurement in Chapter 4 was prepared by a Barstead Mega-Pure[®] MP-3A distilled water system.

Chapter	Experimental Techniques	Samples
3	WAXS (Detector: 2-D Mar [®] -CCD)	PLLA melt-spun fibers
	WAXS & SAXS (Detector: 2-D Mar [®] -CCD)	PLLA melt-spun fibers
4	DSC Amorphous PLLA sam	
	Pycnometry density measurement	PLLA pellets
_	WAXS and SAXSPLLA solutions an(Detector: 2-D imaging plates)Porous PLLA sam	
5	SEM	Porous PLLA samples
	TGA	Amorphous PLLA
6	WAXS and SAXS (Detector: 1-D wire detector)	PLLA solutions and gels

 Table
 2.2
 A list of experimental techniques and samples used in this dissertation.

*The amorphous PLLA samples are prepared by a quick quench of PLLA melt. They are samples with a predominant amorphous fraction, and are referred to as amorphous PLLA samples for convenience.

2.2 Sample Preparation

In the experiments performed in this dissertation, both bulk PLLA samples and solution samples were used. The bulk samples include PLLA fibers, pellets and films. Solution samples were prepared for the investigations on the gelation through TIPS. The samples and the corresponding experimental techniques used are listed in Table 2.2. The preparation of these samples is detailed in Chapters 2.2.1 to 2.2.5.

2.2.1 PLLA Melt-spun Fibers

The PLLA fibers were prepared by a melt-spinning apparatus with a shaft driven plunger and a take-up roll equipped with a constant tension controller. The configuration of the melt-spinning apparatus is shown in Fig. 2.2. The PLLA pellets were pre-dried at 80°C under vacuum for three days before melt-spinning. The temperature of the PLLA melt pool was controlled at 182°C. During spinning, the emerging filaments from the spinneret were subject to ambient cooling before being collected by the take-up roll.



Figure 2.2 The configuration of the melt-spinning apparatus.

2.2.2 Amorphous PLLA Samples

The amorphous PLLA samples were prepared by quenching the PLLA melt from 200°C to ambient temperature. PLLA pellets were melted and molded in a film mold on a hot press, followed by quenching with cooling water. Because PLLA has a slow rate of

crystallization, the PLLA film samples prepared in this way exhibited a transparent appearance and no crystalline diffraction peaks can be observed in their WAXS patterns. Therefore, the PLLA samples prepared in this way had a predominant amorphous fraction.

A similar method was used to prepare amorphous PLLA samples in the DSC. The amorphous sample was obtained by quenching the PLLA melt from 200°C to 20°C at a cooling rate of 20°C/min. They were used as the starting materials for subsequent DSC experiments.

2.2.3 PLLA Pellets with Different Crystallinities

PLLA samples with two different crystallinities were prepared for the pycnometry measurement of Chapter 4. The high crystallinity sample was obtained by annealing virgin pellets at 90°C in a vacuum oven for two days; the low crystallinity sample was prepared by quenching the melted PLLA pellets (180°C in a vacuum oven) to -20°C (in a freezer) and then annealing at T_g (63°C) for two days.

2.2.4 PLLA Solutions and Gels

Purified PLLA was prepared for the studies on the phase transitions in PLLA/THF solutions presented in Chapters 5 and 6. Virgin pellets of PLLA were first dissolved in THF at a concentration of 15% by heating and stirring at 60°C. Then 100 ml of the hot solution was dripped into 300 ml ethanol under strong stirring. The white precipitants so obtained were filtered and thoroughly washed with 200 ml ethanol. After overnight drying under vacuum at ambient temperature, the purified PLLA became a white powder

or floccules. The PLLA purified in this way dissolved faster in THF than the virgin pellets and it was used to prepare PLLA solutions of different concentrations.

To prepare PLLA solutions with concentrations ranging from 2% to 15% (wt%), a predetermined amount of PLLA powder was first added into 5 ml THF. The mixture was then stirred with a magnetic stirrer and heated to 60°C, which was slightly lower than the boiling temperature of THF (66°C). The dissolution process usually took 2-3 hours before a clear homogeneous solution could be obtained. The solutions with different concentrations of PLLA in THF were stored in sealed glass vials at room temperature (~20°C) for further use. The maximum dissolvable mass concentration of PLLA in THF was found to be 15%. During storage at room temperature, solutions with concentrations higher than 5% became gels.

The gels of PLLA were prepared by quenching the solutions to a specific temperature. A solution of PLLA in THF was first heated to 50°C to remove possible crystals or gels generated during storage. Then 2-3 ml of PLLA solution was transferred into an aluminum vial and quickly quenched to a predetermined gelation temperature, such as -20°C in a freezer, to induce phase transition and gelation. The sample (wet gel) was maintained at the gelation temperature for one hour to ensure the completion of the gelation process. For real-time x-ray scattering experiments, the gel samples were prepared *in situ* by quenching the solutions in a sample holder.

2.2.5 Porous PLLA Samples

The porous PLLA samples were obtained by removing the solvents from the wet gels through freeze drying at -20°C for 3 days in a freezer. The porous structures (dry gels) were then stored in a desiccator at room temperature for further characterization.

2.3 Experimental Techniques

2.3.1 Differential Scanning Calorimetry

A TA-Q100 DSC instrument equipped with a refrigerated cooling system was used in the DSC measurements. The PLLA samples were melted at 200°C for five minutes and then quenched from the melt to 20°C at a cooling rate of 20°C/min to erase previous thermal histories. The purpose of this process was to obtain the same initial state for all samples. Then two types of DSC experiments were performed. In the thermal aging DSC experiment, samples were aged at 30°C, 45°C or 60°C for 30 minutes. After aging, heating ramps from 0 to 160°C were applied and the heat traces were recorded as a function of temperature. In the isothermal crystallization DSC experiment, after aging at 30°C, 45°C or 60°C, samples were heated rapidly to 120°C for isothermal crystallization and the heat traces were recorded as a function of time. A heating rate of 10°C/min was used unless otherwise specified.

2.3.2 Thermogravimetric Analysis

Thermogravimetric analysis (TGA) was performed with a TA Q50 TGA instrument. Amorphous PLLA films with a thickness about 0.5 mm were prepared by melting and hot-pressing of PLLA pellets, followed by quenching. The amorphous films were then cut into pieces with a size of 0.5×0.5 cm² and hung into the upper level of a sealed vial with drops of THF at the bottom. The vial was kept at -20°C for three days. During the TGA experiment, one of these films was quickly transferred into a TGA sample pan. Weight loss of this sample was recorded as the temperature was increased from ambient to 100°C at a heating rate of 10°C/min and then kept at 100°C until the weight loss showed no change. A nitrogen atmosphere was used during the TGA analysis.

2.3.3 Scanning Electron Microscopy

The porous structures in dried gels of PLLA/THF were observed by Scanning Electron Microscopy (SEM, LEO 1530VP). The porous PLLA samples (dried gels) were carefully fractured and mounted onto an aluminum sample stage using carbon adhesives. Samples were coated with carbon in a Bal-Tec MED 020 sputter coating system under a high vacuum of 2×10^{-5} mbar before SEM observation.

2.3.4 Pycnometry Measurement

A 25 ml pycnometry bottle and a constant temperature water bath were used for pycnometry measurement at a specific temperature. The two types of PLLA pellets with different crystallinities were prepared for the pycnometry measurement as introduced in Chapter 2.2.3. The apparent densities of the two samples were measured by pycnometry at 0°C, 30°C, 45°C and 60°C. For the pycnometry measurement at a specific temperature *T*, the following procedure is applied.

1. Measure the weight of an empty pycnometry bottle (W_b) .

2. Measure the weight of the pycnometry bottle filled with distilled water (W_l) . Before the measurement, the bottle was kept in a water bath at temperature T for 30 minutes. The relationship between W_l and W_b is given by:

$$W_l = \rho_w(T) * V + W_b \tag{2.1}$$

where $\rho_w(T)$ is the density of water at *T*. *V* is the volumetric capacity of the pycnometry bottle.

3. Measure the weight of PLLA pellets (W), which can be expressed as

$$W = \rho_p(T) * V_p \tag{2.2}$$

where $\rho_p(T)$ is the apparent density of the PLLA pellets at T and V_p is the volume of the PLLA pellets.

4. Measure the weight of the bottle which contains the PLLA pellets and is filled with distilled water (W_2). Before the measurement, the air bubbles were carefully removed by stirring and the bottle was kept in the water bath at T for 30 minutes. The relationship between W_2 and W_b is given by:

$$W_2 = \rho_w(T)^* (V - V_p) + \rho_p(T)^* V_p + W_b$$
(2.3)

Eq. (2.3) can be expressed as,

$$W_2 = \rho_w(T) * V + \rho_p(T) * V_p - \rho_w(T) * V_p + W_b$$
(2.4)

Substituting the Eq. (2.1) and (2.2) into (2.4) gives the following expression,

$$W_2 = (W_1 - W_b) + W - \rho_w(T) * V_p + W_b$$
(2.5)

From Eq. (2.5), V_p can be expressed as $V_p = (W_1 + W - W_2)/\rho_w(T)$

With the relationship of $\rho_p(T) = W/V_p$, $\rho_p(T)$ can be expressed as

$$\rho_p(T) = W^* \rho_w(T) / (W + W_1 - W_2)$$
(2.6)

The apparent densities of PLLA pellets at T can be calculated using Eq. (2.6) using measured values of W, W_1 and W_2 and the density of water at T, $\rho_w(T)$, which are listed for 0°C, 30°C, 45°C and 60°C in Table 2.3. For each temperature, the measurement was repeated three times.

Table2.3The densities of water at different temperatures.

Temperature(°C)	0	30	45	60
Density (g/ml)	0.99987	0.99567	0.99025	0.98324
We and D.O. Antila	NIL & Davian	WIL (1002)	Handhaalt of Cl	amaistan and

Source: Weast, R.C., Astle, M.J. & Beyer, W.H. (1983), <u>Handbook of Chemistry and</u> <u>Physics</u>, Boca Raton: CRC Press, Inc., F-11.

2.3.5 X-ray Scattering

Synchrotron WAXS and SAXS are powerful and indispensable tools for probing atomic structures and nanoscale morphologies, respectively. In this dissertation, WAXS and SAXS experiments were performed at the Advance Polymer Beamline (X27C) of National Synchrotron Light Source in Brookhaven National Laboratory. Strong incident x-ray beam generated from the synchrotron radiation of an electron accelerator was monochromatized by a double-multilayer (silicon/tungsten) monochromator and collimated by a three-pinhole collimation system. The beamline can be customized to collect one-dimensional (1-D) or two-dimensional (2-D) scattering signals. These setups can be used to probe the unoriented and oriented systems, respectively.

A typical configuration of the beamline X27C is given in Fig. 2.3. It is the setup for collecting 1-D scattering profiles from fiber samples.



Figure 2.3 Configuration of the equipment setup at beamline X27C. Source: Retrieved Sep. 24 2005 from the world wide web: http://www.bnl.gov/nsls/x27c.

One of the crucial elements of a SAXS/WAXS setup is the detectors used. Three types of detectors were used in this dissertation. They are a 2-D Mar[®]-CCD detector [Fig. 2.4(a)] and 2-D imaging plate detectors and the 1-D wire detectors [Fig. 2.4(b)]. Table 2.4 lists the specifications of these detectors. All the scattering data collected were subject to background, absorption and scattering volume corrections. The experimental procedures for probing oriented and unoriented systems are discussed in the following sections.

Detector	Туре	Model	Original Data Format	Frame-to-Frame Mode	Application
Mar [®] -CCD	2-D	Mar [®] -CCD	Scattering Pattern	Automated	0
Imaging Plate	2-D	Fuji BAS 2500	Scattering Pattern	Manual	O, W&S
Wire	1 - D	EMBL^{*}	Scattering Profile	Automated	W&S

Table2.4The detectors for synchrotron x-ray scattering.

*EMBL: European Molecular Biology Laboratory

** O: the detector can register orientation information of a sample, W&S: the detector can register WAXS and SAXS simultaneously.



(a)



(b)

Figure 2.4 The detectors for x-ray scattering experiments: (a) the 2-D Mar[®]-CCD detector and (b) the 1-D EMBL wire detectors. Source: Retrieved Sep. 24 2005 from the world wide web: http://www.bnl.gov/nsls/x27c.

2.3.5.1 SAXS and WAXS from Oriented Systems In Chapter 3 and 4, polymer fibers are studied by SAXS and WAXS. During the experiment, a single filament of PLLA fibers was mounted vertical to the horizontal plane and to the x-ray beam. Fibers were subject to various thermal and mechanical stimuli when SAXS or WAXS scattering patterns were collected by the 2-D Mar[®]-CCD detector. The mechanical stimuli were imposed by a modified Instron 4410 tabletop stretching unit and the temperature of the filament was controlled by an environmental chamber. The wavelength of the incident x-ray beam used for the scattering experiments in Chapter 3 and 4 was 1.366 Å

2.3.5.1 SAXS and WAXS from PLLA Gels and Solutions The PLLA solution/gel samples are also probed by SAXS and WAXS in Chapter 5 and 6. The samples were first placed into a copper sample cell, whose windows are subsequently sealed by Kapton[®] films. The copper sample cell was then mounted onto a ruler-like sample holder for scattering experiments.

For the *in situ* WAXS/SAXS studies on the gelation processes of PLLA solutions, a dual-cell setup was used. The cells were made from stainless steel and the temperature of each cell could be controlled independently by a temperature controller. Cell 2 was carefully configured into the position of the incident x-ray beam to ensure that the sample in Cell 2 can be irradiated by x-rays. A hole was cut on each side of Cell 2 to allow the passage of x-rays. During an experiment, the ruler-like sample holder was "jumped" rapidly from Cell 1 into Cell 2 by a pneumatic pump and x-ray scattering from the sample was collected subsequently. The experimental setup is schematically shown in Fig. 2.5. The sample-to-detector distances (L_{SD}) for the WAXS and SAXS experiments are calibrated by standards of aluminum oxide and silver behenate, respectively. The values of L_{SD} are usually on the order of 100 mm (for WAXS) and 1500 mm (for SAXS). Related calculation procedures, such as the calibration of L_{SD} , are discussed in Appendix B. The wavelength of incident x-ray for the scattering experiments in Chapter 5 and 6 was 1.371 Å.



Figure 2.5 The configuration for the synchrotron simultaneous SAXS/WAXS using a dual-cell setup.

To perform an *in situ* scattering experiment, about 0.1 ml of the PLLA/THF solution was quickly transferred into the copper sample cell and sealed with Kapton[®] films. Since solution samples prepared with concentrations above 5% would gel at the ambient temperature, pre-heating was necessary to ensure that there was no gel remained in polymer solutions. The copper sample cell was then fixed into the ruler-like sample holder and inserted into the Cell 1, whose temperature was set at 40°C. At this

temperature, the PLLA/THF sample remains as a homogeneous solution. To collect SAXS/WAXS from the gels, the sample holder was jumped move rapidly, by a pneumatic pump, into Cell 2, which had been set to a designated gelation temperature. At the same time, the x-ray beam was turned on and data collections began. The 1-D wire detectors were used to record the *in situ* simultaneous WAXS/SAXS from the gelation process. The frame time for signal integration of each profile was two seconds and there was a minor interval (5 microseconds) between each frame.

For the characterization of samples at ambient temperature, a copper sample holder containing a dry or wet gel sample was directly inserted into Cell 2 at room temperature for scattering experiments. To collect SAXS and WAXS profiles from static samples, imaging plate detectors were used. The use of imaging plates leads to a high signal-to-noise ratio and a high resolution in the reciprocal space.

2.4 Data Analysis

The data analysis methods for x-ray scattering and pycnometry data are introduced in this section. The analysis is implemented by programs written in MATLAB[®], which are presented in Appendix A and B.

2.4.1 Crystallinity

2-D WAXS patterns were first reduced to 1-D profiles by integrating over the azimuthal angles from 0° to 360° for diffraction angles from 5° to 25°. The integrated value at a given diffraction angle was normalized by the number of pixels contributing to the integration. The 1-D profiles were then deconvoluted into individually indexed

Gaussian peaks and amorphous halos by a least-square fitting procedure. The overall crystallinity index is given by $X_c = A_c / (A_a + A_c)$, where X_c is the crystallinity, A_c and A_a are the areas under the crystalline and amorphous peaks, respectively.



Figure 2.6 The orientation mode of crystalline polymers with an orthorhombic unit cell.

2.4.2 Orientation Factors

The orientation mode of crystalline polymers with an orthorhombic unit cell in the Cartesian coordinate system is shown in Fig. 2.6. The orientation factor of a crystal axis x (x = a, b or c) with respect to a reference direction Z is defined as,

$$f_{x,Z} = \frac{1}{2} \left(3 \left\langle \cos^2 \phi_{x,Z} \right\rangle \right) - 1$$
 (2.7)

where $\langle cos^2 \phi_{x,Z} \rangle$ is the mean-square cosine of the angle between the axes and Z. In case of uniaxially orientated polymer fibers, $f_{x,Z}$ is the orientation factor of the crystal axis x with respect to the fiber axis Z. When $f_{x,Z} = 1$, the axis x is parallel to the direction Z, when $f_{x,Z} = 0$, the orientation of the axis x with respect to Z is random and when $f_{x,Z} = -0.5$, the axis x is perpendicular to Z. Usually, the fiber axis is chosen as the Z direction. Orientation factors $f_{a,Z}$, $f_{b,Z}$, and $f_{c,Z}$ are simply denoted f_a , f_b , and f_c .

It is known that for an orthorhombic crystal (Alexander, 1969a),

$$f_a + f_b + f_c = 0 (2.8)$$

It has also been proved that,

$$e^{2}\langle\cos^{2}\phi_{a,Z}\rangle + f^{2}\langle\cos^{2}\phi_{b,Z}\rangle + g^{2}\langle\cos^{2}\phi_{c,Z}\rangle = \langle\cos^{2}\phi_{hkl,Z}\rangle$$
(2.9)

where e, f and g are the direction cosines of the norm of (hkl) plane to the axes a, b and c, respectively (Alexander, 1969a).

The relationship of $\langle \cos^2 \phi_{hkl,Z} \rangle$, the azimuthal intensity $I(\phi)$ and the azimuthal angle ϕ is given by,

$$\left\langle \cos^2 \phi_{hkl,Z} \right\rangle = \frac{\int\limits_{0}^{\pi/2} I(\phi) \sin^2(\phi) \cos \phi \, d\phi}{\int\limits_{0}^{\pi/2} I(\phi) \cos(\phi) \, d\phi}$$
(2.10)

The two strongest diffraction peaks of the PLLA α -crystal, i.e., (200) and (203), can be used to evaluate the orientation factors. For (hkl) = (200), Eq. (2.10) can be simplified with e = 1 and f = g = 0,

$$\langle \cos^2 \phi_{a,Z} \rangle = \langle \cos^2 \phi_{200,Z} \rangle$$
 (2.11)

For (*hkl*) = (203), geometrical relationships give $e^2 = 0.75$, $f^2 = 0$ and $g^2 = 0.25$. So Eq. (2.9) reduces to,

$$0.75\left\langle\cos^{2}\phi_{a,Z}\right\rangle + 0.25\left\langle\cos^{2}\phi_{c,Z}\right\rangle = \left\langle\cos^{2}\phi_{203,Z}\right\rangle$$
(2.12)

Using azimuthal profiles of the (200) and (203) diffractions, the orientation factors f_a and f_c are obtained by the following procedure: (1) Determine $\langle \cos^2 \phi_{200,Z} \rangle$ and $\langle \cos^2 \phi_{203,Z} \rangle$ by using Eq. (2.10), (2) Determine $\langle \cos^2 \phi_{a,Z} \rangle$ and $\langle \cos^2 \phi_{c,Z} \rangle$ by using Eq. (2.11)

and (2.12), (3) Determine f_a and f_c by using Eq. (2.7). The value of f_b can be evaluated from Eq. (2.8). In this way, the orientation of crystallites in PLLA fibers can be obtained.

2.4.3 Data Analysis for Pycnometry Measurement

Assuming a two-phase model for semicrystalline polymers, the relationship correlating measured apparent density ρ , crystallinity X_c , the density of the amorphous phase ρ_a and the density of the crystalline phase ρ_c , is given by the following equation (Alexander, 1969c):

$$X_c = \frac{\rho_c}{\rho} \frac{(\rho - \rho_a)}{(\rho_c - \rho_a)} \tag{2.13}$$

Since the pycnometry measurements were conducted at temperatures below T_g of PLLA, it was reasonable to assume that the crystallinities of the samples remained constant during the course of measurement. It is further assumed that ρ_a is a function of temperature, while ρ_c is not. This assumption is justified, as the thermal expansion coefficients of crystals are orders of magnitude lower than those of the corresponding glasses.

By measuring the apparent densities $\rho_1(T_i)$ and $\rho_2(T_i)$ at T_i for the two PLLA pellets samples whose crystallinities are X_{c1} and X_{c2} , respectively, Eq. (2.13) gives,

$$X_{c,1} = \frac{\rho_c}{\rho_1(T_i)} \frac{\rho_1(T_i) - \rho_a(T_i)}{\rho_c - \rho_a(T_i)}$$
(2.13a)

$$X_{c,2} = \frac{\rho_c}{\rho_2(T_i)} \frac{\rho_2(T_i) - \rho_a(T_i)}{\rho_c - \rho_a(T_i)}$$
(2.13b)

Since measurement were conducted at four temperatures with $T_i = 0^{\circ}$ C, 30° C, 45° C and 60° C, equations (2.13a) and (2.13b) lead to eight equations. There are seven unknowns in these equations. They are the four densities of amorphous phase $\rho_a(T_i)$ at $T_i = 0^{\circ}$ C, 30° C, 45° C and 60° C, the two crystallinities, X_{c1} and X_{c2} , and the density of crystalline phase ρ_c . These unknowns can be determined by a least-square fit using the eight equations.

CHAPTER 3

CRYSTALLIZATION IN PLLA FIBERS DURING ANNEALING AND DRAWING

3.1 Introduction

As discussed in Chapter 1, PLLA has been studied extensively in recent years as a promising biodegradable material. Towards this end, extensive investigations have been conducted to study the crystallization of PLLA in unoriented systems (Mano et al., 2004). However, there are few reports in the open literature on the crystallization of PLLA in oriented systems. Fiber is one of the most important oriented systems. PLLA fibers are extensively used in various biomedical applications. In this chapter, the crystallization of PLLA fibers during annealing and drawing is studied.

Melt-spinning is the most economical method to produce PLLA fibers. To obtain the desired mechanical properties, drawing has to be employed as a post-spinning treatment to induce their crystallization and orientation. Previous studies showed that both the mechanical and biodegradation properties of PLLA fibers are strongly dependent on the crystallinity and morphology, which are in turn determined by the spinning and drawing conditions (Fambri et al., 1997; Suesat et al., 2003; Schmack et al., 1999). Although qualitative assessments of these parameters by x-ray diffraction and birefringence have been reported (Mezghani and Spruiell, 1997), quantitative results are not available. Quantitative evaluations on the effects of various thermal and mechanical conditions on the structure development in PLLA fibers are conducted in this chapter. Attentions is focused on the crystallization of PLLA above its T_g . The experimental technique employed is *in situ* WAXS.

43

Sample	Plunger speed (mm/min)	Take-up roll speed (rpm)	Fiber Diameter (µm)	Crystallinity	fa	f_b	f_c
PLA230	3.5	155	230	0%*	_	-	-
PLA100	2.5	400	100	6.5%	-0.32	-0.44	0.76
PLA25	2.5	650	25	12.5%	-0.38	-0.45	0.83

 Table
 3.1
 PLLA fiber samples by different melt-spinning conditions.

*No crystalline scattering observed in WAXS

3.2 As-spun Fibers

Fig. 3.1 shows the 2-D WAXS patterns from the as-spun fibers prepared under the spinning conditions listed in Table 3.1. Prepared at the lowest take-up speed and the fastest plunger speed, sample PLA230 is amorphous with no signs of crystallinity as suggested by Fig. 3.1(c). Only a broad amorphous halo can be observed. Orientated crystals are observed in samples PLA100 and PLA25, which are prepared at higher take-up speeds. It can be qualitatively observed that PLA25, which is prepared at the highest take-up speed, has a higher degree of orientation than PLA100.



Figure 3.1 The 2-D WAXS patterns from PLLA as-spun fibers (a) PLA25, (b) PLA100, (c) PLA230.

The orientation factors of these fibers are calculated using the method presented in Chapter 2.4.2. The azimuthal intensity profiles of PLA25 and PLA100 are extracted from the (200) and (203) Bragg rings on their 2-D WAXS patterns and are shown in Fig. 3.2.



Figure 3.2 The dependence of azimuthal intensities $I(\phi)$ on the azimuthal angle. Left, (200) plane diffraction; Right, (203) plane diffraction.

The orientation factor f_c in PLA25 is found to be 0.83, suggesting that the *c* axis of the unit cell, which is also the polymer chain direction, is highly orientated along the fiber axis. The values of f_a and f_b of PLA25 are close to -0.5, indicating that both of these two axes are almost perpendicular to the fiber axis. Comparing with PLA25, fiber PLA100 is less orientated with an orientation factor $f_c = 0.76$. For both fibers, the values of f_b are closer to -0.5 than those of f_a . Similar observation was reported by Kitao et al. for the melt-drawn LDPE fibers, which also has an orthorhombic crystal unit cell (Kitao et al., 1973).

Fig. 3.3 shows the indexing and the evaluation of crystallinity for PLA25 by peak deconvolution of its 1-D scattering profile, which is obtained from azimuthal integration of the corresponding 2-D pattern. From the indexed scattering peaks, it can be

identified that the PLLA crystal is in its α -form. The crystallinity of the fiber with the highest orientation (PLA25) is found to be 12.5%. Prepared at a lower take-up speed, PLA100 has a crystallinity of 6.5%. No crystallinity is observed in the sample of PLA230, which was prepared at the lowest take-up speed. The low crystallinity in the as-spun fibers can be explained by the intrinsic slow rate of crystallization of PLLA. Post-spinning treatments including annealing or drawing above T_g are usually necessary to enhance the crystallinity and orientation of PLLA fibers.



Figure 3.3 The evaluation of crystallinity by peak deconvolution from an azimuthal intensity profile from PLA25 fiber.

3.3 The Effects of Constant-length Annealing

PLLA fibers were subject to constant-length annealing above its T_g for five minutes. The development of crystallization can be clearly observed in Fig. 3.4, in which the 2-D WAXS patterns for the fibers and their corresponding 1-D profiles from fibers before and after annealing are compared. The (200) and (203) Bragg peaks become stronger at higher temperatures. As shown in Fig. 3.4(a-d), PLA230 sample was annealed at 90°C, 105°C and 120°C. A higher annealing temperature results in a higher crystallinity in the fiber. This is evident from the increase in the intensity of crystalline diffraction peaks in the 1-D profiles. At 120°C, the crystallization is highly developed. Even some weak diffraction peaks can be observed.

Raw Fiber	Annealing Temperature (°C)	Crystallinity	fa	fb	fc
PLA230	120	40.7%	-0.06	-0.12	0.18
PLA230	105	27.0%	-0.11	-0.18	0.28
PLA230	90	21.5%	-0.09	-0.13	0.22
PLA100	90	40.2%	-0.47	-0.10	0.57
PLA25	90	42.8%	-0.45	-0.25	0.70

 Table
 3.2
 The crystallinities and orientation factors of PLLA fibers after annealing

The (e) to (h) parts of Fig. 3.4 illustrate the development of crystallinity in PLA100 and PLA25 when they are annealed at 90°C. As shown in Table 3.2, after annealing for 5 minutes, an increase in crystallinity is found in sample PLA230, which displays no crystallinity in its as-spun state. The increase in crystallinity is dependent on the annealing temperature. At 120°C, a crystallinity of 40.7% is obtained, while at 90°C, only half of this value can be reached. Compared with PLA230, which was prepared with the lowest take-up speed, PLA25 and PLA100 show a higher tendency to crystallize during annealing. High crystallinities of 42.8% and 40.2% are achieved in PLA25 and PLA100 even at a moderate annealing temperature of 90°C, respectively. It appears that a high density of primary nucleation developed in these fibers is responsible for these phenomena.



Figure 3.4 The effects of annealing suggested by 2-D WAXS patterns and their 1-D profiles from PLLA fibers: (a) as-spun PLA230, (b) PLA230 annealed at 90°C, (c) PLA230 annealed at 105°C, (d) PLA230 annealed at 120°C, (e) as-spun PLA100, (f) PLA100 annealed at 90°C, (g) as-spun PLA25, (h) PLA25 annealed at 90°C.

When the orientation factors are examined (Table 3.2), the f_c of the crystals in the sample PLA230 after annealing is found to be around 0.2. The crystals formed during annealing derive their orientations from the original orientation of the amorphous phase. Another interesting observation in Fig. 3.4(b-d) is that the (200) scattering ring from the annealed PLA230 is concentrated on both the meridian and equator. This indicates that the newly formed crystals by annealing have two preferred orientations, longitudinal and radial. In other words, crystals with c-axis perpendicular to the fiber direction are also formed during the annealing of PLA230. Slight deorientation can be observed in the highly oriented fibers under annealing conditions. The f_c of PLA25 drops from 0.83 to 0.70 and the f_c of PLA100 drops from 0.76 to 0.57. By constant-length annealing, the crystallinity can be increased significantly without losing too much in crystalline orientation.

3.4 The Effects of Drawing

To produce fibers with desired properties, drawing at temperatures above T_g has been used as a primary post-spinning treatment. The drawing of a single PLLA filament under a constant strain rate was studied by *in situ* WAXS. PLA230 fiber was fully annealed at 90°C and then was subjected to drawing at a strain rate of 0.5 mm/min. Fig. 3.5 shows the change in 2-D patterns and the corresponding 1-D profiles during drawing. It suggests an increase in the intensity of the (200) peaks upon drawing. Similarly to the results presented in Chapter 3.3, one can find that the (200) intensity is concentrated on both the equator and the meridian after annealing. With increasing strain, the scattering intensity of (200) on the meridian diminishes. This is probably due to a drawing induced orientation.



Figure 3.5 The 2-D WAXS patterns and 1-D profiles from PLA230 fibers drawn to different strains. (a) 0%, (b) 9%, (c) 17%, (d) 25%, (e) 34%.

This observation is more evidently illustrated in Fig. 3.6, where the azimuthal intensity profiles $I(\phi)$ of the (200) scattering at different strains are displayed. The equator corresponds to $\phi = 0^{\circ}$ and the meridian corresponds to $\phi = 90^{\circ}$. With increasing strain, the crystals with their *c*-axis oriented in the radial direction are eliminated as suggested by the gradual increase in the azimuthal intensities at $\phi = 90^{\circ}$.


Figure 3.6 The azimuthal intensity $I(\phi)$ of the (200) Bragg scattering from PLA230 fiber at different strains.

The computational results of the crystallinity and orientation factors of the PLA230 fiber drawn at 90°C are listed in Table 3.3. The crystallinity increases from 19.7% (strain = 0%) to 36.6% (strain = 34%). Since the sample had been fully annealed at 90°C before drawing, the gain of 17% crystallinity after drawing is ascribed to the drawing process. As the maximum achievable crystallinity is about 40% by annealing (Table 3.2), the attainment of a crystallinity of 36.6% at a strain of 34% shows the important role of drawing on PLLA crystallization. A high crystallinity can be achieved in PLLA fibers by moderate drawing at temperatures above T_g , e.g., 90°C.

Correspondingly, the orientation factors are also affected in drawn fibers. Specifically, the f_c increases from 0.08 to 0.22 as the fiber is drawn at a strain of 34%, indicating the development of orientation.

Strain	Crystallinity	fa	f_b	f_c
0	19.7%	-0.03	-0.06	0.08
9%	31.8%	-0.03	-0.05	0.08
17%	33.4%	-0.08	-0.08	0.16
25%	35.7%	-0.10	-0.09	0.19
34%	35.8%	-0.12	-0.10	0.22

Table 3.3 The crystallinities and orientation factors of PLA230 after drawing at 90°C

3.5 Conclusions

The development of crystallinity and orientation is quantitatively evaluated from *in situ* 2-D WAXS when PLLA fibers are subject to various thermal and mechanical treatments. Crystallization and crystal orientations in as-spun fibers are strongly dependent upon the take-up speeds of spinning. When the melt-spun fibers are heated above T_g , further crystallization is induced. It is shown that the induced crystallinity critically depends upon the initial orientation of the fibers. The effect of drawing above T_g on the crystallinity and orientation is also investigated, which suggests that drawing can remarkably induce crystallization in PLLA fibers.

CHAPTER 4

DENSIFICATION AND PRIMARY NUCLEATION IN THE AMORPHOUS PHASE OF PLLA

4.1 Introduction

As most linear polymers, PLLA is semicrystalline. Three crystal forms of PLLA, the α -, β - and γ -form, have been identified. The crystal structures of the three crystal forms have been successfully analyzed (De Santis and Kovacs, 1968; Puiggali et al., 2000; Cartier et al., 2000). While the crystal structures of PLLA and its crystallization kinetics have been well studied, the properties of the amorphous phase in PLLA and its role in crystallization and phase transitions remain unknown. In fact, most of the investigations on the behavior of amorphous phase were performed based on noncrystalline polymers. There are few investigations on the properties of thermal aging on the crystallization of PLLA are not well understood although the excess enthalpies of relaxations of PLLA below its T_g were reported (Cai et al., 1996). From this perspective, an investigation of the behavior of amorphous PLLA and its role on the crystallization of unoriented bulk material were initiated.

There have been several reports on the abnormal behavior of densities of the amorphous phase in semicrystalline polymers. Griffith et al. reported that the density of the amorphous phase in poly(4-methyl-pentene-1) could exceed that of the crystalline phase (Griffith and Ranby, 1960). Using synchrotron SAXS, Barnes reported that the scattering contrast of syndiotactic polystyrene (*s*-PS) could change drastically as a function of temperature. This behavior was ascribed to the difference in thermal

expansion rates between the amorphous and crystalline phases of s-PS (Barnes and Bras, 2003).

In this chapter, the densities of the crystalline and amorphous phases of PLLA were investigated by synchrotron WAXS, SAXS and pycnometry. Experimental results suggest that there is a nonlinear dependence of the density of amorphous phase in PLLA on temperature with a transition at about 45°C. Combining DSC data, this behavior is ascribed to the primary nucleation below T_g . The kinetic and dynamic origins of this behavior are discussed.

4.2 Densification of Amorphous Phase in PLLA

The 2-D WAXS were used to characterize the melt-spun fiber PLA230, which was introduced in Chapter 3.2, at two conditions, (a) annealing at 120°C for five minutes and (b) annealing at 60°C after ambient cooling from 120°C. Their WAXS patterns are shown in Fig. 4.1(a) and 4.1(b), respectively. Little change is observed between the two WAXS patterns. This suggests that there is little difference in crystallinity upon ambient cooling from 120°C to 60°C. The crystallinity evaluation for 1-D profiles azimuthally integrated from Fig. 4.1(a) and 4.1(b) via the peak deconvolution (as shown in Fig. 3.3) was conducted. The crystallinities so evaluated are (a) 47% and (b) 46%, respectively. Also observed in Fig. 4.1(a) and 4.1(b) is the constancy in 2 θ locations of the corresponding diffraction peaks. This suggests that the unit cell dimensions of PLLA at 60°C and 120°C are the same. Therefore, the density of the crystalline phase of PLLA can be regarded as a constant in this temperature range.



Figure 4.1 The WAXS patterns from PLA230 fiber (a) annealed at 120°C and (b) at 60°C after ambient cooling from 120°C.

The 2-D SAXS pattern from the PLA230 fiber annealed at 120°C is shown in Fig. 4.2(a). It has two meridional lobes. Combining the crystalline peaks in Fig. 4.1(a) and the meridional lobes in Fig 4.2(a), it can be concluded that PLLA crystallizes into the α -form crystal with a chain-folded lamellar morphology at 120°C. The (b) to (f) parts of Fig. 4.2 show the real-time SAXS patterns from the same fiber during ambient cooling from 120°C to 60°C. The most striking observation from these patterns is that the two lamellar lobes on the meridian disappear as temperature decreases from 120°C to 60°C. This is further demonstrated in Fig. 4.3, in which 1-D integrated azimuthal intensities of Fig. 4.2(a) to 4.2(f) are plotted against the scattering vector *q*.



Figure 4.2 The SAXS patterns from the PLA230 fiber as temperature drops from 120° C to 60° C: (a) at 120° C, (b) at 98° C, (c) at 83° C, (d) at 72° C, (e) at 65° C, (f) at 60° C.

Obviously, the disappearance of the meridional lobes on the SAXS patterns upon ambient cooling cannot be ascribed to the destruction of lamellar morphology since the corresponding WAXS patterns at 120°C and 60°C [Fig. 4.1(a) and 4.1(b)] suggest the stability of the crystalline phase. The disappearance of the lamellar lobes can only be explained by the loss of electron density contrast between the amorphous and crystalline phases as temperature decreases from 120°C and 60°C. Since the densities of the crystalline phase can be regarded as constant in this temperature range, the loss of SAXS contrast should originate from the densification of the amorphous phase as temperature decreases.



Figure 4.3 The azimuthal integrated intensity profiles of SAXS patterns from the PLA230 fiber as temperature drops from 120°C to 60°C.

The loss of electron density contrast makes PLLA transparent to x-ray at low q (0.1 to 1 nm⁻¹). This leads to the disappearance of the lamellar scattering peak as well as the diminished scattering intensity at q around 0.1 nm⁻¹ in Fig 4.3. Similar densification behavior was observed in poly(4-methyl-pentene-1) by Griffith (Griffith and Randy, 1960) and by Litt (Litt, 1963) and in syndiotactic polystyrene by Barnes and Bras, who used a similar argument to interpret their SAXS results (Barnes and Bras, 2003).

Motivated by this result from PLLA fibers, efforts were made to determine if the same densification behavior existed in an unoriented PLLA system. According to our knowledge, there are no reports on the density of the amorphous phase of PLLA in the open literature. It was decided to conduct pycnometry measurements to deduce the dependence of the amorphous phase density of PLLA on temperature. The pycnometry measurements were conducted at 0°C, 30°C, 45°C and 60°C for PLLA pellet samples with high and low crystallinity, respectively. The sample preparation and experimental procedure for the pycnometry measurement can be found in Chapter 2.2.3 and Chapter 2.3.4, respectively.



Figure 4.4 The apparent densities of PLLA pellets with two different crystallinities.

The experimentally measured apparent densities of the two samples at 0° C, 30° C, 45° C and 60° C are shown in Fig. 4.4. For the sample with a higher crystallinity, a rather linear dependence of density on the temperature can be observed. This is expected because thermal expansion coefficients usually have a linear dependence on temperature. However, a different densification behavior is observed for the pellet sample with a lower crystallinity. The dependence of density on the temperature shows a nonlinear relationship with a transition temperature at about 45° C. Since a constant density of the crystalline phase can be assumed in the temperature range of 0° C to 60° C, the increase of apparent density upon cooling should be interpreted as the densification of the amorphous phase.

Density of Amorphous Phase (g/cm ³)			Density of Crystalline	Low Crystallinity	High Crystallinity	
0°C	30°C	45°C	60°C	Phase (g/cm^3)	(PLLA-L)	(PLLA-H)
1.254	1.243	1.237	1.227	1.283	9.7%	38.2%

 Table
 4.1
 Results from the least-square fit of the apparent density data.

The experimentally measured apparent densities were analyzed by the procedure described in Chapter 2.4.3. The results are tabulated in Table 4.1, which includes the densities of the amorphous phase at 0°C, 30°C, 45°C and 60°C, the density of the crystalline phase and the crystallinities of the two samples. The density of the crystalline phase is found to be 1.283 g/cm³, which is very close to the value reported by Miyata and Masuko, which is 1.285 g/cm³ (Miyata and Masuko, 1997). The densities of the amorphous phase increase from 1.227 g/cm³ to 1.254 g/cm³ as temperature decreases from 60°C to 0°C. A plot of the density of the amorphous phase with respect to

temperature is given in Fig. 4.5, where the nonlinear densification of the PLLA amorphous phase is clearly shown. Two distinct regions can be identified with a transition temperature around 45°C. From 60°C to 45°C, a faster rate of increase in the density of the amorphous phase is observed, while from 45°C to 0°C, a slower but linear densification is obtained.



Figure 4.5 The densities of the amorphous phase of PLLA at different temperatures below T_g .

The densities of solids are determined by two factors, (a) the average structure or molecular packing of the solids, and (b) the extent of thermal expansion. Except for crystalline solids of simple substances, there is no theoretical treatment on the densities of amorphous polymers in the open literature. Nevertheless, the dependence of thermal expansion coefficients on temperature can be regarded linear for most amorphous polymers below T_g . Therefore, the nonlinear behavior of the density of the amorphous phase in PLLA around 45°C suggests that there is a detectable change in the average amorphous structure of PLLA around this temperature.

To test this argument, a thermal aging DSC experiment was conducted (Chapter 2.3.1). Shown in Fig. 4.6 are the heat traces from heating ramps of PLLA, which had been previously aged at 30°C, 45°C and 60°C for 30 minutes. The heat trace from a non-aged sample was also measured. For each heat trace, an endothermic peak (i.e., the excess enthalpy of relaxation) just above T_g is illustrated. It is observed that the excess enthalpies of relaxation reach the maximum in the sample aged at 45°C.



Figure 4.6 The excess enthalpies of relaxation of amorphous PLLA after thermal aging at different temperatures.

The existence of the excess enthalpies of relaxation can be interpreted as the energy necessary to destroy certain "ordered" local structures formed during thermal aging below T_g . Above T_g , the ordered structures are destroyed due to the increase in chain mobility, leading to the observation of an endothermic peak. From Fig. 4.6, it appears that the extent of the formation of the ordered local structure reaches its maximum when amorphous PLLA is aged at 45°C and increases with increasing aging time (Fig. 4.7). Assuming the ordered local structure has a higher density than the amorphous phase, this argument can be used to explain the density transition around 45°C. A maximum excess enthalpy of relaxation around 40°C was also observed by Cai and co-workers (Cai et al., 1996).



Figure 4.7 The excess enthalpies of relaxation of amorphous PLLA after thermal aging at 45°C for different time.

4.3 Effects of Thermal Aging on Primary Nucleation of PLLA

After associating the density anomaly and the excess enthalpies of relaxation to the ordered local structure, the immediate next question is: "what is the ordered local structure in the amorphous phase?" Since PLLA is crystallizable, it is highly likely that the ordered structures are the primary nuclei developed in the amorphous phase. In other words, even at a temperature below its T_g , PLLA continues to evolve towards its equilibrium structure (i.e., the crystalline phase) via primary nucleation.

To test this argument, DSC is used to probe the isothermal crystallization of amorphous PLLA (Chapter 2.2.2) after thermal aging. After aging at 30°C, 45°C or 60°C for 30 minutes, samples were jumped to 120°C for isothermal crystallization. A non-aged sample was also measured in the isothermal crystallization experiment. Traces of the heat flows during the isothermal crystallizations were recorded as a function of time and are shown in Fig. 4.8. It is observed that the sample aged at 45°C leads to the fastest rate of crystallization.

The heat traces of the isothermal crystallizations from samples aged at different temperatures for different aging time are compared in Fig. 4.9(a) to 4.9(c). As shown in Fig. 4.9(a) and 4.9(c), the aging time is immaterial to the rate of crystallization for samples aged at 60°C and 30°C. For samples aged at 45°C [Fig. 4.9(b)], a shorter aging time leads to a faster rate of crystallization.

Thermal aging below T_g and its implications on crystallization were previously explored for isotactic polystyrene (*i*-PS) (Cheng and Lotz, 2005). It was found that extended aging time greatly increased the overall rate of crystallization when *i*-PS was heated rapidly to a temperature above its T_g . The increase in overall rate of crystallization was ascribed to the increase in primary nucleation density.



Figure 4.8 The heat flows of the isothermal DSC experiment at 120°C after thermal aging PLLA at different temperatures.

The DSC data of this work also suggest that the thermal aging of PLLA below its T_g can influence the overall rate of crystallization. If this behavior is associated to the change in primary nucleation density during thermal aging, the present data suggest that there is an optimal temperature around 45°C, at which the rate of primary nucleation is the fastest. Aging at other temperatures produces lower nucleation densities, which leads to a slower rate of crystallization (Fig. 4.8). This is consistent with the maximum enthalpy relaxation found in the sample aged at 45°C (Fig. 4.6). However, at 45°C, the

effect of aging time on the rate of crystallization is rather counter-intuitive and the trend is exactly opposite to that of *i*-PS reported by Cheng and Lotz (Cheng and Lotz, 2005). Longer aging time should produce a higher density of primary nuclei as suggested by the excess enthalpy of relaxation data shown in Fig. 4.7. However, as shown in Fig 4.9(b), longer aging times (240 and 480 minutes) lead to a slower rate of crystallization than shorter aging times (30 and 120 minutes). This behavior may be explained by a self-poisoning argument, i.e., the high nucleation density produced during the extended aging time leads to a slower rate of crystallization due to the lack of available amorphous chain to sustain a faster growth rate as the system is almost consumed by the existence of primary nuclei. Such a self-poisoning effect was also observed in polymer gels (Keller, 1995).

It is interesting to note that 45°C appears to be a critical temperature for thermal aging of PLLA below its T_g . At this temperature, the excess enthalpies of relaxation are much larger than those at other temperatures. This is also supported by the data of Cai and co-workers (Cai et al., 1996). The overall rate of crystallization in samples aged at 45°C is larger than those aged at other temperatures. In addition, samples aged at other temperatures (i.e., 30°C and 60°C) have little change in the rate of crystallization when compared with the non-aged amorphous sample (Fig. 4.8); their rate of crystallization is almost independent upon aging time [Fig. 4.9(a) and 4.9(c)]. Therefore, 45°C appears to be the temperature at which the system is sensitive to thermal aging.



Figure 4.9 The heat flows of the isothermal DSC experiment at 120°C after thermal aging PLLA at temperatures below T_g for different time at (a)45°C, (b)60°C, and (c)30°C.

One can certainly try to interpret this behavior from a kinetic perspective using an argument of the competition between thermodynamic driving forces and kinetic limitations. However, this explanation still cannot fully explain why the system is sensitive to thermal aging at 45°C but almost insensitive to thermal aging at other temperatures.

To explain these phenomena, one has to face the question on how a semicrystalline system evolves towards its equilibrium state (i.e., the crystalline phase) via primary nucleation below T_g when large-scale thermal fluctuations are frozen (Cheng and Lotz, 2005).

Recently, the significance of Terahertz (THz) dynamics in polymer crystallization was recognized, by noting that the nucleation and growth of polymer crystals are implemented by non-bonded interchain motions, and concerted and de-localized intrachain vibrational motions (Wu, 2005). These motions are low frequency collective modes involving many atoms, residing in the THz frequency regime. Although one of the THz modes, the longitudinal acoustic mode, has been investigated for semicrystalline polymers for many years, the significance of THz dynamics in polymer crystallization was not recognized until recently (Wu, 2005).

It was also found that irradiating poly(trimethylene terephthalate) films with a monochromatic free electron laser (FEL) with a wavelength of 71 cm⁻¹ could induce crystallization at about 5°C degrees below T_g . This suggested that the activation of the mode at 71 cm⁻¹ induced crystallization (Wu, 2005).

The thermal aging experiment conducted in this work is not too distant from the FEL irradiation experiment discussed above. During aging, thermal energies are input

into the system. Although the exact value of the most probable input energy is not known, it should be on the scale of kT. For T = 45°C, kT = 220 cm⁻¹, which is in the THz regime. Our data then suggest that an input of a distribution of THz energy corresponding to aging at 45°C is much more effective for inducing primary nucleation. It is likely that a specific THz mode of PLLA is important in initiating primary nucleation and the fundamental frequency of this mode is close to the most probable energy of T=45°C. Therefore, thermal aging at 45°C can excite this mode effectively, leading to the formation of primary nuclei, while aging at other temperatures cannot.

4.4 Conclusions

In summary, the density of the amorphous phase of PLLA is found to be closely dependent upon the temperature. At 60°C, the contrast between the crystalline and amorphous phase disappears as suggested by the disappearance of SAXS lamellar lobe. This is because the density of the PLLA amorphous phase increases as temperature decreases and is approaching to that of the crystalline phase at 60°C. The density of the amorphous phase of PLLA was measured at temperatures below its T_g . A nonlinear dependence of the density of amorphous phase in PLLA on temperature was found with a transition temperature at about 45°C. This is also the temperature at which the thermally aged amorphous PLLA exhibits the maximum excess enthalpies of relaxation. Thermal aging at this temperature also influences the isothermal crystallization behavior greatly when the system is subsequently jumped to 120°C. This can be interpreted by a change in primary nucleation density due to the thermal aging below T_g . It is suggested

that a specific THz mode, which corresponds to the most probable thermal energy of 45° C, is important in initiating primary nucleation of PLLA below its T_g .

CHAPTER 5

CRYSTAL STRUCTURES AND MORPHOLOGIES DEVELOPED DURING TIPS IN PLLA SOLUTIONS

5.1 Introduction

The fabrication of three-dimensional (3-D) porous structures from biodegradable polymers has been a subject of intensive research due to its application as tissue engineering scaffolds. A polymer matrix with a high porosity and an appropriate pore size can serve as the artificial extracellular scaffolds for cell growth. How to fabricate polymers, especially biodegradable and biocompatible polymers, into a highly porous structures has been a challenging and fascinating topic for scientists and engineers in the polymer field. As reviewed by Mikos (Mikos and Temenoff, 2000) and Liu (Liu and Ma, 2004), several fabrication methods, including solvent casting/particle leaching, nonwoven fiber bonding, electro-spinning, gas foaming, emulsion freeze drying and thermally induced phase separation (TIPS), have been developed to prepare polymer scaffolds to fulfill the requirements of tissue engineering and cell cultures.

Recently, the technique of using TIPS to fabricate porous structures from the biodegradable/biocompatible polymers has attracted much attention (Zhang and Ma, 2000; Lo et al., 1995; Lo et al., 1996). In this approach, a polymer solution is first prepared. Heating is almost always needed either to accelerate the dissolution process or to keep the polymer solution from phase separation. The solution is then quenched to a lower temperature to induce phase separation, which usually leads to gelation. Subsequently, the solvent is removed from the gel by freeze-drying, and a porous polymer matrix is fabricated (Nam and Park, 1999a; Nam et al., 1999b). The porous

70

structure and the morphology of the scaffolds depend on the selection of polymer, solvent and the polymer concentration as well as the details of TIPS. Generally, TIPS can lead to the following desired features, including open-cellular porous structure, controllable pore size, good mechanical properties and mild operation conditions. Porous structures of PLLA fabricated by TIPS in its solutions have been reported by Zhang et al. (Zhang et al., 2004), Lo et al. (Lo et al., 1995; Lo et al., 1996) and Nam et al. (Nam and Park, 1999; Nam and Yoon, 1999). Gelation of polymer solutions during TIPS is always involved, leading to the formation of a polymer-rich phase, which is a solvent-containing 3-D network. Keller reviewed the gelation process and suggested that either the liquid-liquid (L-L) phase transition or the liquid-crystal (L-C) phase transition is responsible for the formation of physical gels (Keller, 1995). The characteristics of the polymer matrix, such as its crystal structure and morphology, critically depend on the mechanism of phase separation. The performance of the scaffolds during cell cultures is ultimately determined by porous structures.

Contrary to the intensive efforts on the fabrication of the porous polymer scaffolds, the fundamentals on the development of crystal structures and morphologies during scaffolds fabrication are not well understood. The phase morphology and crystal forms are important factors that affect the degradation rate. The fundamental understanding of phase transitions in PLLA solutions, including the phase separation mechanism and its consequent crystal structures and morphologies, is important in controlling the performance of the scaffold.

In this chapter, the crystal structures of PLLA gels and their porous matrices fabricated through TIPS are examined by WAXS and SAXS. PLLA/THF wet gels with

different concentrations were prepared at various phase separation temperatures. The corresponding porous matrices (dry gels) were then obtained by solvent removal via freeze-drying. The formation of a new crystal form of PLLA, the δ -form, is discovered when the PLLA/THF solutions are quenched to a low temperature, e.g., -20°C. When the gelation of PLLA/THF solutions was induced at a higher temperature, e.g., 20°C, only the α -form of PLLA formed. The polymorphism of PLLA can be explained by the existence of two liquid-crystal phase transformations of the PLLA/THF solutions. After the removal of solvent THF, the transformation from the δ -form to the α -form was observed, suggesting the presence of THF is important on the stability of the δ -form. A clathrate structure is proposed, in which THF molecules are incorporated into the unit cell of the δ -form. Combined WAXS and SEM on the dried gels show that the porous PLLA matrix with underlying α -crystal structure exhibits a lamellar morphology, while the matrix with underlying δ -crystal exhibits a fibrillar network. The SAXS data suggest that the δ -form is chain-extended.



(a)



(b)

Figure 5.1 The SEM images of 10% PLLA/THF gels after freeze-drying. Gelation temperatures, (a) 20° C, (b) -20° C. (scale bar at left-bottom: one μ m)

5.2 A New Crystal Form in PLLA/THF Gels: the $\delta\mbox{-form}$

The SEM micrographs of typical PLLA 3-D porous structures obtained via the TIPS process are shown in Fig. 5.1. The concentrations of the two solutions subject to TIPS

are both 10%. The gelation temperature of Fig. 5.1(a) is 20°C and that of Fig. 5.1(b) is -20° C. From Fig 5.1(a), one finds that flake-like lamellae form an open cellular porous morphology, whose pore size is on the scale of 1 µm. In Fig. 5.1(b), an interconnecting fibrous network of PLLA with a pore size of about 1 µm is observed. Apparently, the gelation temperature affects the phase separation process and the morphology. These intriguing observations on difference in the morphology due to the differences in gelation temperature motivated the following studies.



Figure 5.2 2-D The 2-D WAXS patterns from PLLA/THF gels prepared at different polymer concentrations and gelation temperatures: (a) 15%, 20°C, (b) 10%, 20°C, (c) 15%, -20°C, (d) 10%, -20°C.

The gelation of PLLA in THF solutions was studied by WAXS and SAXS. WAXS data indicate that crystallization of PLLA takes place during gelation. Fig. 5.2 shows the 2-D WAXS patterns of PLLA wet gels in THF with a polymer concentration are both 10%. The gelation temperature of Fig. 5.1(a) is 20°C and that of Fig. 5.1(b) is -20° C. From Fig 5.1(a), one finds that flake-like lamellae form an open cellular porous morphology, whose pore size is on the scale of 1 µm. In Fig. 5.1(b), an interconnecting fibrous network of PLLA with a pore size of about 1 µm is observed. Apparently, the gelation temperature affects the phase separation process and the morphology. These intriguing observations on difference in the morphology due to the differences in gelation temperature motivated the following studies.



Figure 5.2 2-D The 2-D WAXS patterns from PLLA/THF gels prepared at different polymer concentrations and gelation temperatures: (a) 15%, 20°C, (b) 10%, 20°C, (c) 15%, -20°C, (d) 10%, -20°C.

The gelation of PLLA in THF solutions was studied by WAXS and SAXS. WAXS data indicate that crystallization of PLLA takes place during gelation. Fig. 5.2 shows the 2-D WAXS patterns of PLLA wet gels in THF with a polymer concentration are both 10%. The gelation temperature of Fig. 5.1(a) is 20°C and that of Fig. 5.1(b) is -20° C. From Fig 5.1(a), one finds that flake-like lamellae form an open cellular porous morphology, whose pore size is on the scale of 1 µm. In Fig. 5.1(b), an interconnecting fibrous network of PLLA with a pore size of about 1 µm is observed. Apparently, the gelation temperature affects the phase separation process and the morphology. These intriguing observations on difference in the morphology due to the differences in gelation temperature motivated the following studies.



Figure 5.2 2-D The 2-D WAXS patterns from PLLA/THF gels prepared at different polymer concentrations and gelation temperatures: (a) 15%, 20°C, (b) 10%, 20°C, (c) 15%, -20°C, (d) 10%, -20°C.

The gelation of PLLA in THF solutions was studied by WAXS and SAXS. WAXS data indicate that crystallization of PLLA takes place during gelation. Fig. 5.2 shows the 2-D WAXS patterns of PLLA wet gels in THF with a polymer concentration of 10% or 15% and with a gelation temperature of -20° C or 20° C. The strong scattering rings observed in Fig. 5.2(a) and 5.2(b) indicate that the α -crystal is formed at 20° C. In Fig. 5.2(c) and (d), WAXS patterns from gels that were obtained at a low gelation temperature of -20° C are shown. Two scattering rings close to the center appeared on the WAXS patterns. This observation indicates that a different crystal form other than the α -crystal is obtained at -20° C.



Figure 5.3 The 1-D WAXS profiles of PLLA/THF gels (Integrated from data shown in Fig. 5.2).

The difference in the location of the diffraction peaks can be clearly observed in Fig. 5.3, in which 1-D intensity profiles obtained by azimuthal integration of the 2-D patterns is Fig. 5.2 are shown. The PLLA samples gelled at 20°C displayed the scattering peaks of the α -form, including the strongest peaks at 20 = 14.9° and the second strongest peak at 20 = 17.1°. These peaks are indexed to be peaks of (200) plane and (203) plane, respectively. The scattering from the solvent can be observed as a diffusive

halo, overlapping with the scattering peaks of PLLA crystals. PLLA/THF solutions gelled at -20°C show scattering peaks remarkably different from those of the α -crystals formed at 20°C. The x-ray scattering peaks of the α -form cannot be observed in parts (c) and (d) of Fig. 5.3. Instead, two new strong scattering peaks are found at $2\theta = 10.1^{\circ}$ and 12.7°, along with several other weak peaks. These peaks cannot be indexed by the published crystal polymorphs of PLLA (i.e., the α -, β - and γ - forms). Therefore, a new crystal form, hereafter referred to as the δ -form, is obtained in PLLA/THF gels when gelation temperature is -20°C.

As reviewed in Chapter 1.6, clathrate structures form in *i*-PS solution. It is suspected that the δ -form of PLLA is also a clathrate with solvent molecules participating in its unit cell. In order to further investigate the role of solvent molecules in the unit cell of the δ -form, samples A, B and C was prepared.

Sample A was prepared by the absorption of cold THF vapor into PLLA. An amorphous PLLA film (described in Chapter 2.2.2) was placed into the upper level of a sealed vial containing drops of THF liquid at the bottom and the vial was kept at -20°C for 3 days. Sample B was a freeze-dried product of Sample A. And Sample C was prepared by the cold-extraction of THF from a wet gel (15% PLLA/THF at -20°C) containing δ -crystal, followed by freeze-drying. Cold-extraction of THF was performed by rinsing a 2 ml wet gel in 20 ml ethanol at -20°C for two days. Ethanol is a nonsolvent to PLLA but is miscible with THF. To ensure the total extraction of THF, the solvent was replaced by new ethanol every 6 hours.

The WAXS pattern of Sample A is shown in Fig. 5.4, in which only the δ -form peak is found. The diffraction peaks from the δ -crystals in Sample A are stronger than

those from the wet gels as shown in Fig. 5.2(c) and 5.2(d). This is because that there are more δ -crystals in Sample A than those in the wet gels of the same scattering volume. In addition, the interference of the scattering halo from the excess THF in the wet gels is eliminated. In this way, more diffraction peaks from the δ -crystals can be observed. The five strongest Bragg peaks and their corresponding d-spacings of the δ -crystal are listed in Table 5.1 ($\lambda = 1.371 \text{ Å}$).

Peak	Diffraction angle (2θ)	d-spacing (Å)		
1	10.1	7.87		
2	12.7	6.36		
3	16.2	4.88		
4	18.3	4.33		
5	20.0	3.97		

Table 5.1 The five strongest Bragg peaks and their d-spacings of the δ -crystal.

Part B of Fig. 5.4 is the WAXS profile from Sample B which obtained by freeze-drying of Sample A. Strong diffraction peaks of the δ -form are still present but another strong peak at $2\theta = 14.9^{\circ}$ emerges. It is the (200) diffraction peak of the α -form. This observation suggests that a δ to α transition takes place at -20°C during freeze-drying. The α -crystal cannot be generated from the amorphous phase because the WAXS of Sample A suggests that only δ -crystal can be obtained in the condition of -20°C with THF present. It appears that a part of the δ -crystals transform to the α -crystal upon losing THF molecules. Sample C was prepared by cold-extraction and freeze-drying of a PLLA/THF wet gel containing δ -crystals. The corresponding WAXS profile from sample C is shown in part C of Fig. 5.4. It only displays the diffraction peaks from the α -crystal and no traces of the diffraction peaks from the δ -crystal can be



Figure 5.4 The influence of solvent removal on the WAXS profiles from PLLA crystals. (A) amorphous PLLA crystallized in THF vapor at -20°C, (B) sample A freeze-dried, (C), sample C from wet gel (15%, -20°C) by cold-extraction and freeze-drying.

Another interesting characteristic of the δ -crystal can be observed when Sample A is subject to extension. The characteristic peaks of the δ -form disappear and only scattering of the orientated α -form crystal can be captured by WAXS even at a low draw ratio of 50%. Thus the δ -form structure is destroyed by extension. This observation suggests that the chain conformation of the δ -form should be somewhat "more helical", i.e., having a shorter period and larger gyration, than the 3/1 helix of the α -form. This feature also provides more interstitial sites for the incorporation of THF molecules into

the unit cell of the δ -form. From these experiments, it is suggested that the participation of the THF molecules in the δ -form is crucial for its stability. Thus, it is highly likely that the δ -form is a clathrate with THF participation in its unit cell. The chain conformation and the packing of the δ -form are simulated in *Cerius2*[®] and are given in Fig. 5.5. The repeat of the helix is found to be 8.58 Å. THF molecules are accommodated in the interchain spaces between helical layers of PLLA chains. To accommodate the THF molecules, each polymer chain has to shift one half of a helical repeat from its adjacent chains to form the interstitials. The top view of a single PLLA chain in δ -form is given in Fig. 5.5(b), showing the arrangement of four monomer units in one helical period.

To determine the ratio between the monomer units and the solvent molecules in the δ -crystal, TGA was used (Rosa et al., 1999; Tsutsui et al., 1999). TGA was performed on Sample A, which was assumed to have the maximum absorbed amount of THF. After the absorption of THF for an extended period of time at -20°C, Sample A was quickly transferred into a TGA sample pan, which is subsequently heated at 10°C/min to 100°C and then kept isothermal at 100 °C for 20 minutes (as discussed in Chapter 2.3.3). The curve of weight loss versus time is given in Fig. 5.6, showing an average weight loss of 20%. Since the monomer unit of PLLA has the same molecular weight as THF, the weight loss of 20% suggests that the ratio between the numbers of the repeating units and THF is 4:1. These data lead to the proposal of a packing mode of the δ -form, whose top view is shown in Fig. 5.5(c).



Figure 5.5 The chain conformation and packing mode of the δ - crystal of PLLA. (a) side view with the clathrate THF molecules, (b) top view of a single chain, (c) top view of the packing mode: O, PLLA, \bullet , THF.

As illustrated in Fig. 5.5(c), four PLLA chains create a column of interstitial sites for THF molecules. Correspondingly, each PLLA helix is surrounded by four guest THF molecules. Since there are four monomer units in one helix, the ratio of the repeating unit of PLLA to THF in this packing mode is 4:1. TGA was also used by Rosa (Rosa et al., 1999) and Tsutsui (Tsutsui et al., 1999) to determine the clathrate structure of syndiotactic polystyrene with various solvents (Rosa et al., 1999).



Figure 5.6 The weight loss curve of Sample A during heating in TGA.

The proposed chain conformation in Fig. 5.5(a) is supported by WAXS patterns from the orientated δ -crystals obtained via absorption of cold THF in PLLA fiber. Using the same procedure for preparing Sample A, Sample D was prepared by placing an orientated PLLA melt-spun fiber (PLA100, as described in Chapter 3.2) in cold THF vapor to induce the formation of the δ -crystal. The 2-D WAXS pattern from Sample D was recorded with the fiber axis vertical. In Fig. 5.7, weak δ - diffraction peaks and moderate α - diffraction peaks are both observed and indexed. The (200) scattering peaks of the α -form are located on the equator. Four scattering rings of the δ -form crystal are concentrated around the equator and are identified to be the peaks of δ -1, δ -2, δ -3 and δ -5 as listed in Table 5.1. Obviously, these peaks represent crystal planes with indices of (hk0) when an orthorhombic lattice is assumed. The strongest evidence supporting the proposed 4/1 helix conformation is from the peak δ -4, which is concentrated on the meridian of the 2-D pattern. The δ -4 peak represents a (00*I*) plane perpendicular to the chain direction. The d-spacing of δ -4, 4.33 Å, matches to one half of the proposed helical repeat, which is 4.29 Å.



Figure 5.7 The 2-D WAXS patterns of the δ - crystal formed in a PLLA fiber.

The interchain distance in the δ -crystal can also be estimated from the corresponding value of the α -form. The chain-chain distance in α -form is 6.25 Å (De

Santis and Kovacs, 1968). With a more helical conformation and the incorporation of solvent molecules in the unit cell, the interchain distance in the δ -crystal should be larger. It is likely that the d-spacing of the peak δ -1, which is 7.9 Å, represents the interchain distance in the δ -crystal.



Figure 5.8 The WAXS profiles of (a) 10% and (b) 15% PLLA/THF gels formed at different temperatures. (Δ : 20°C, +: 10°C, \Diamond : 0°C, ×: -10°C)



Figure 5.9 The SAXS profiles of (a) 10% and (b) 15% PLLA/THF gels formed at different temperatures (Δ : 20°C, +: 10°C, \Diamond : 0°C, ×: -10°C)
5.3 Phase Diagram of PLLA/THF System

Upon establishing that the δ-form is a clathrate, *in situ* WAXS and SAXS experiments from PLLA/THF wet gels at different gelation temperatures were conducted to establish a phase diagram of the PLLA/THF solution. This experiment employs the dual-cell setup presented in Chapter 2.3.1. During the experiment, PLLA/THF gels were melted in Cell 1 at 40°C to obtain a homogeneous solution. The sample holder was pneumatically "jumped" into Cell 2, which was set to a specific gelation temperature, to induce phase separation. The WAXS and SAXS profiles were registered simultaneously by two 1-D wire detectors.

Fig. 5.8 shows the WAXS profiles of the PLLA/THF systems after 30 minutes of The gelation process can be considered gelation at the temperatures of interest. completed after 30 minutes. Fig. 5.8(a) shows the WAXS profiles from a 10% polymer solution, while Fig. 5.8(b) shows those from a 15% solution. From both parts of Fig 5.8, it is observed that at low gelation temperatures of 10°C, 0°C and -10°C, only the diffraction peaks of the δ -form can be observed, while at a high gelation temperature of 20°C, only the characteristic diffraction peaks of the α -form can be observed. These results match well with the L-C and L-C* transitions shown in Fig. 1.6, suggesting that the phase separation behavior of PLLA/THF are similar to that of i-PS/trans-decalin From these data, the L-C* transition line of a PLLA/THF solution can be system. located anywhere between the 10°C and 20°C for the polymer concentrations of 10% and Since the gelation of PLLA/THF can not be induced above 30°C, the L-C line 15%. may be located anywhere between 20°C and 30°C.

The corresponding SAXS profiles are shown in Fig. 5.9. The SAXS profiles from the 10% and 15% PLLA/THF gels look rather similar. At the high gelation temperature of 20°C, at which the existence of the α -form is detected by WAXS, a peak at $q = 0.023 \ A^{-1}$ is observed. This suggests that the PLLA α -crystals form a lamellar morphology in the gel with a long period of 27.3 nm. The corresponding morphology is flake-like, which is shown in Fig. 5.1(a). No obvious peak can be observed from the SAXS profiles when the gelation temperature is at or below 10°C. At these conditions, the δ -form crystal is formed as suggested by WAXS. Therefore, it is inferred that the δ -form exists as a chain-extended crystal, and the corresponding morphology of the gels is fibrillar as suggested by Fig. 5.1(b)

A phase diagram summarizing the above discussions is illustrated in Fig. 5.10, in which both the SEM and WAXS results are also shown. The two liquid-crystal phase separation lines, L-C and L-C* are drawn. A L-L phase separation line may exist at the even lower temperatures, which is plotted as a dotted line in Fig. 5.10.

When gelation of the PLLA/THF solutions takes place through the L-C phase transition, PLLA crystallizes into its α -form crystal, which is proved by the WAXS data. As has been discussed before, α -form is the most stable crystalline modification of PLLA. During the phase transition in the PLLA solutions at higher temperatures (e.g., 20°C), polymer chains have enough time to adjust their conformations into the crystal structure of the lowest energy. As expected from the gel morphology proposed by Keller (Keller, 1995), the chain-folded growth of the PLLA α -crystal results in the flake-like morphology [Fig. 1.7(c)], which is supported by the SEM image [Fig. 5.1(a)] and SAXS data (Fig. 5.9).



Polymer concentration (%)

Figure 5.10 A schematic phase diagram of PLLA/THF binary system.

When a solution is quenched to the temperatures below the L-C* line, because of the high rate of phase separation, the system is trapped into a metastable state. The new δ -form crystal observed by WAXS data is suggested to be a clathrate. Correspondingly, the chain-extended growth of crystals and the fibrous morphology, as proposed in Fig. 1.7(b), are suggested by the SEM image [Fig. 5.1(b)] and SAXS data (Fig. 5.9). Without chain-folding, the δ -form crystalline phase has to find a way to release the surface tension on the end interfaces as polymer chains travel from the crystalline region to the amorphous region in the chain-extended crystals. This is explained by the clathrate structure of δ -crystals, in which solvent molecules reduce the packing density of chains in PLLA crystals. Therefore, the density difference between the crystalline phase and the amorphous phase is reduced and surface tensions on the end interfaces are alleviated. A similar mechanism was reported for s-PS gels (Daniel and Guerra, 2002; Daniel et al., 2003). The crystals of s-PS with a chain-extended morphology were also found to be clathrate.

5.4 Conclusions

Previous research on the fabrication of porous structures of PLLA via TIPS has been focused on correlating operational conditions and pore geometries. This investigation focused on the underlying crystal structures and morphologies of PLLA/THF gels. By using synchrotron WAXS and SAXS, wet and dry gels of PLLA in THF formed during TIPS were examined. The effect of gelation temperature on the phase separation mechanism, crystal structure and phase morphology is elucidated. The α -form crystal of PLLA was observed in the PLLA/THF gel at 20°C when gelation was induced through the L-C phase transition, which led to a flake-like morphology. A new crystal form, the δ -form, was found in PLLA/THF gels at temperatures below 10°C. A clathrate structure is assigned to the δ -form and the gelation below 10°C follows the L-C* transition. Its chain-extended morphology is also suggested by SAXS and SEM.

The PLLA chains in the δ -form clathrate are proposed to be in a 4/1 helical conformation, with a half helical repeat of 4.3 \mathring{A} . This is supported by WAXS pattern from the orientated δ -form crystal in the PLLA fiber sample. THF molecules are incorporated into the interstitial sites of the unit cell. Each interstitial site is bound by two helical layers and by four PLLA chains. This entails that the ratio between the numbers of the repeating units of PLLA and THF molecules in the unit cell is 4:1. This

ratio is substantiated by the TGA measurement. A d-spacing of 7.9 \mathring{A} is likely to be an interchain distance in the δ -crystal.

CHAPTER 6

KINETICS OF TIPS IN PLLA SOLUTIONS

6.1 Introduction

In Chapter 5, the effects of temperature and concentration on the crystallization of PLLA in THF were investigated. Two crystal polymorphs and their morphologies were identified by SAXS, WAXS and SEM. It is desirable to further investigate the kinetics of the development of crystal structures and morphologies during TIPS, which was largely unexplored. In this chapter, the effects of experimental conditions on the kinetics of TIPS in PLLA/THF solutions are studied. The kinetic parameters are evaluated from the experimental data.

Melt crystallization and cold crystallization of PLLA and its copolymers at temperatures above T_g have been thoroughly investigated for unoriented systems. With its relatively low rate of crystallization, PLLA can be prepared to have a wide range of crystallinity from 0 to 40% (Zhang and Wu, 2005). Earlier studies on the crystallization kinetics of PLLA were performed through hot stage microscopy, by which the spherulitic growth was measured (Vasanthakumari and Penning, 1983). Differential scanning calorimetry (DSC) was also used to study the crystallization of PLLA (Ohtami et al., 2003). Mano et al. reported their work on cold crystallization of PLLA studied by simultaneous SAXS and WAXS, through which the development of morphology and crystallization of PLLA was examined and the kinetic parameters were evaluated. It was suggested that the nonisothermal cold crystallization of the PLLA followed a 3-D growth. Wang (Wang et al., 2001) and Cho (Cho et al., 2003) reported the application

of time-resolved WAXS and SAXS to study the melt crystallization of PLLA copolymers. By calculating scattering invariant Q and crystallinity X_c , the temperature, at which the highest rate of crystallization rate takes place, was determined. In other related works on polymer gels, *in situ* SAXS and WAXS were applied to study the phase separation behavior of syndiotactic polystyrene (*s*-PS) gels (Rastogi et al., 1998). The *s*-PS/solvent systems showed a similar phase diagrams to that of the PLLA/THF system. A solvent-participated clathrate crystal polymorph was also found in *s*-PS gels.

This chapter aims at investigating the kinetics of TIPS in PLLA/THF solutions at different concentrations and temperatures. The development of crystal structure and morphology in the gelation process was probed in real time by the simultaneous synchrotron WAXS and SAXS. Because of the use of brilliant synchrotron x-rays, scattering data can be collected in a very short time interval, e.g., one second per frame. The early stages of the structure development during gelation can be captured by this technique. To illustrate the development of structures on the atomic scale and nanoscale, 3-D plots of the WAXS and SAXS profiles are given. The invariant *Q* evaluated from SAXS is used to examine the Avrami behavior of the gelation process.

6.2 Simultaneous SAXS and WAXS during Gelation

A list of samples and experimental conditions used in this chapter is given in Table 6.1. The visual observations on the gelation of these samples were also recorded. During the simultaneous WAXS and SAXS on gelation, the maximum experimental time was 20 minutes after a sample cell was quickly moved into Cell 2 from Cell 1 in the dual-cell setup described in Chapter 2.3.1. If a sample still remained a clear solution after 20 minutes, it was considered as not gellable.

 Table 6.1
 The gelation of PLLA/THF solutions at different concentrations and temperatures.

Concentration Temperature	2%	5%	10%	15%
-20°C	Gel	Gel	gel	-
0°C	×	Gel	gel	gel
20°C	×	×	×	gel

gel : gelation takes place within 20 minutes

× : gelation doesn't take place with 20minutes

- : sample not examined

3-D plots of WAXS and SAXS intensity profiles from the PLLA/THF system gelled at -20°C, 0°C and 20°C are shown in Fig. 6.1 and 6.2, respectively. The crystallization process is illustrated by the time-resolved WAXS data. In Fig. 6.1(a), the WAXS profiles from the 10% PLLA/THF solution after quenching from 40°C to -20°C are shown. At the onset of the gelation, the WAXS profiles are characterized by a broad halo from the THF solvent, centered around $2\theta = 17.5^{\circ}$. No crystalline scattering peaks can be observed. After 20 seconds, two diffraction peaks of the δ -crystal can be observed at $2\theta = 10.1^{\circ}$ and 12.7° . The development in intensities of the diffraction peaks is completed in 30 seconds and the intensities of the peaks remain constant for the rest of the experiment. This suggests a fast rate of formation of the δ -crystals.

The WAXS profiles of 10% PLLA/THF gelled at 0°C are given in Fig. 6.1(b). In this case, PLLA crystallizes into the δ -form but the rate of crystallization is much lower because a higher gelation temperature (0°C) is applied. Diffraction peaks of the δ -form become evident at about 100 seconds and the development of intensity continues for another 200 seconds. When the gelation temperature is increased to 20°C, the crystallization of PLLA from solution becomes extremely slow. For the 10% PLLA/THF solution gelled at 20°C, the sample has to stand still for 60 minutes before a gel can be obtained. During the experimental period of 20 minutes, no diffraction peak can be observed in WAXS after quenching the solution to 20°C. Fig. 6.1(c) shows the WAXS on the gelation of the 15% PLLA/THF solution at 20°C. With a higher concentration of PLLA, the crystallization in the 15% solution is faster than that in 10% solution. As expected from the PLLA/THF phase diagram proposed in Chapter 5, the α -crystal of PLLA is obtained in this situation. This is evident by the development of the strong diffraction peak at $2\theta = 14.9^\circ$, i.e., the (200) peak of α -crystal.



Figure 6.1 The 3-D plots of WAXS profiles recorded during the gelation in PLLA/THF solutions. (a) 10% PLLA/THF gelled at -20°C, (b) 10% PLLA/THF gelled at 0°C, (c) 15% PLLA/THF gelled at 20°C.



Figure 6.2 The 3-D plots of SAXS profiles recorded during the gelation in PLLA/THF solutions. (a) 10% PLLA/THF gelled at -20°C, (b) 10% PLLA/THF gelled at 0°C, (c) 15% PLLA/THF gelled at 20°C.

The development of morphology during the gelation of PLLA/THF solutions is illustrated by the *in situ* SAXS profiles shown in Fig. 6.2. The SAXS profiles of the 10% PLLA/THF solution gelled at -20°C are given in Fig. 6.2(a). Several flat profiles are observed at the early stages of the gelation, indicating little density fluctuation in the system. Then a fast growth of the SAXS intensity is observed at the early stages. This is because the driving force of crystallization is higher when the solution is quenched to -20°C. The development of scattering intensity at low momentum transfers (q < 0.04 $Å^{-1}$) suggests the development of density fluctuations on a length scale greater than 15 nm. Since no obvious scattering peak can be observed in these SAXS profiles, there is no long-range periodic order.

A similar conclusion can also be drawn for Fig. 6.2(b), in which the SAXS profiles of 10% PLLA/THF gelled at 0°C are shown. Only a very weak shoulder at $q \sim 0.016 \ A^{-1}$ in the intensity profile can be observed, which suggests a very weak periodic order. The development of the intensity at low q (q < 0.04 A^{-1}) takes place at about 100 seconds after quenching and then develops at a slower rate than that of the -20°C quenching. Comparing Fig. 6.2(b) to Fig. 6.1(b), similar patterns of intensity development are found in the SAXS and WAXS profiles. This suggests that the crystallization of PLLA is the primary process that is responsible for the morphology development probed by SAXS. The similar observations and conclusions can be found in Fig. 6.2(a) and 6.1(a).

When the concentration of PLLA is increased to 15% and the gelation temperature is increased to 20°C, the corresponding SAXS profiles [Fig. 6.4(c)] show the development of a lamellar morphology, which is usually found in melt crystallized

semicrystalline polymers. A predominant peak at $q \sim 0.023 \text{ Å}^{-1}$ is observed. This corresponds to a long periodic order of 27.3 nm. This peak is much stronger than the weak shoulders found in Fig. 6.2(a) and 6.2(b). This peak grows simultaneously with the diffraction peak of α -form in the WAXS of Fig. 6.3(c). During gelation, the intensity of this SAXS peak develops, and yet its position remains constant, indicating a stable long-range order in the α -crystal lamellae.

The 3-D WAXS and SAXS profiles provide a qualitative depiction of the process of crystallization and morphology development during gelation. Quantitative analysis is discussed in the following sections.

6.3 Crystallization Kinetics Revealed by the SAXS Invariant

In the analysis of SAXS data, the invariant Q(t) is used to represent the total density contrast of a system (Alexander, 1969c). It is given by,

$$Q(t) = \int_0^\infty q^2 I(q,t) dq \tag{6.1}$$

By using Eq. (6.1), the invariant Q(t) at a given time of phase separation can be calculated. Fig. 6.3 shows Q(t) vs. time for 10% PLLA/THF solutions when the gelation temperatures are -20°C and 0°C. The development of the total density fluctuation or phase separation is clearly illustrated in the S-shaped curves. Each curve can be divided into three stages. An induction stage can be identified at the early stages of the phase separation. At this stage, the values of Q(t) are low. The length of this period is determined by the gelation temperature. A short induction period, which is less than 20 seconds, is found when the gelation temperature is -20°C. At 0°C, the induction period is extended to approximately 100 seconds. The growth stage is the second stage after induction. Q(t) increases during this stage, suggesting the development of density contrast. The duration of the growth stage is also affected by the gelation temperature. A lower gelation temperature results in a shorter growth stage. The last stage is the plateau period, where phase separation is completed and the invariant Q(t) levels off. Fig. 6.3 illustrates how the gelation temperature affects the duration of each stage during phase separation.



Figure 6.3 The development of invariant Q(t) during the gelation of 10% PLLA/THF solutions at different temperatures.

The dependence of the invariant Q(t) on the PLLA concentration is investigated by comparing the Q(t) curves from the gels prepared by the same gelation temperature but at different concentrations. Fig. 6.4(a) shows the gelation kinetics for PLLA/THF solutions at 0°C. One observes that the sample with the highest concentration of 15% shows the shortest induction period and growth period, while the phase separation in the 5% sample is much slower and cannot be completed within 20 minutes. Thus, with the same depth of quench, the phase separation kinetics in PLLA/THF solutions is dependent upon the concentrations of PLLA. The solution with a higher concentration of PLLA entails a faster rate of crystallization.



Figure 6.4 The development of invariant Q(t) during the gelation of PLLA/THF solutions of different concentrations. (a) at 0°C, (b) at -20°C.

Fig 6.4(b) shows the gelation kinetics in PLLA/THF solutions at -20°C. It is interesting to observe that the Q(t) curves of the samples with different concentrations at this low temperature show virtually the same trend. The phase separations are completed within 50 seconds. The induction and growth stages are estimated to be 20 seconds and 30 seconds, respectively, for sample of all concentrations. This observation indicates that when the gelation temperature is low enough, such as -20°C, the rate of phase separation in PLLA/THF solutions is primarily determined by the gelation temperature. The effect of concentration on phase separation, which can be observed at the moderate temperatures, e.g., 0°C, is suppressed by a predominant thermodynamic driving force for crystallization at -20°C.

6.4 Avrami Parameters of PLLA Crystallization in Solutions

For all the invariant Q(t) curves shown in Fig. 6.3 and 6.4, the Avrami behavior of the crystallization is evident. Avrami equation has been widely used to describe the kinetics of isothermal crystallization and phase separation (Zhang et al., 2004). The traditional Avrami equation correlates crystallinity X_c to the time of crystallization. It is given by,

$$1 - X_c(t) = \exp\left(-kt^n\right) \tag{6.2}$$

where k is the crystallization rate constant, which is dependent on the rate of nucleation and growth. The Avrami exponent is denoted by n, which is related to the nature of nucleation and to the geometry of the crystal growth (Cakmak et al., 1998). From $X_c(t)$, the Avrami parameters can be evaluated by using the following procedure. Taking the natural logarithm on both sides of the Avrami equation gives rise to

$$ln[1-X_{c}(t)] = -kt^{n}$$
(6.3)

To transform Eq. (6.3) into a linear equation, another logarithm is taken on the both sides of Eq. (6.3), which gives,

$$ln\{-ln[1-X_{c}(t)]\} = ln(k) + nln(t)$$
(6.4)

By fitting the left hand side of Eq. (6.4) again ln(t), parameters n and ln(k) can be found from the slope and intercept of the fitted line, respectively.

Although the development of crystallinity can be clearly observed from the WAXS profiles obtained from the PLLA/THF solution during gelation, it is rather difficult to separate the intensities from the polymer crystals and those from the solvent. This is because an unknown portion of the PLLA is still dissolved in THF and the amount of this portion of the polymer keeps changing during the gelation.



Figure 6.5 The normalized invariant Q(t) during the gelation of PLLA/THF solutions of different concentrations at 0°C.

The kinetics of crystallization are usually studied by DSC and real time WAXS, whose data are analyzed the Avrami equation. Data from other experimental techniques have also been used to evaluate the Avrami parameters. Zhang and co-workers evaluated the Avrami behavior of PLLA cold-crystallization by infrared spectroscopy (Zhang et al., 2004). Lee et al. reported their attempt in applying the Avrami equation to analyze invariant Q(t) (Lee and Im, 2005). This approach was suggested as the "reminiscent of Avrami-type crystallization kinetics" (Talibuddin et al., 1998). During this analysis, a normalized invariant $Q_n(t)$ is used. It is given by,.

$$Q_n(t) = [Q(t) - Q_{min}] / (Q_{max} - Q_{min})$$
(6.5)

where Q_{max} and Q_{min} are the maximum and minimum values of an experimental Q(t) curve, respectively. Q_{max} and Q_{min} are usually obtained from the plateau and the induction stage of a Q(t) curve, respectively.

The normalized $Q_n(t)$ is proportional to the Avrami equation with a proportional constant k_i ,

$$Q_n(t) = k_1 [1 - exp(-kt^n)]$$
(6.6)

Based on their calculations, Lee and Im (Lee and Im, 2005) suggested that the parameter k_1 was very close to 1, so k_1 is assumed to be unity in the following analysis and Eq. (6.6) reduces to,

$$1 - Q_n(t) = \exp(-kt^n) \tag{6.7}$$

Similarly to the operation performed in Eq. (6.2) to (6.4), natural logarithm is taken twice on both sides of Eq. (6.7), giving rise to

$$ln \{-ln[1-Q_n(t)]\} = ln(k) + nln(t)$$
(6.8)

Accordingly, the Avrami parameters of n and k are obtained from the slope and the intercept of a linear fit of $ln \{-ln[1-Q_n(t)]\}$ against ln(t). This is shown in Fig. 6.6 using the data presented in Fig. 6.5.



Figure 6.6 The Avrami plots for the gelation of PLLA/THF solutions of different concentrations at 0°C.

The different rates of crystallization in the PLLA/THF solutions of various concentrations at 0°C are clearly visualized in Fig. 6.6. The extracted Avrami parameters (n and k, for the 10% PLLA/THF solution gelled at 0°C) are used to simulate the Avrami curve using Eq. (6.7). This simulated curve matches well with the experimental data. This is shown in Fig. 6.7.



Figure 6.7 A comparison between the experimental data and the Avrami fit for SAXS profile from the 10% PLLA/THF gelled at 0°C (Discrete point: experimental data; solid line: Avrami curve).

The Avrami parameters (i.e., Avrami exponent *n*, crystallization rate constant *k* and half-life $t_{1/2}$) are listed in Table 6.2 for the samples studied in this chapter. The half-life $t_{1/2}$ is another important parameter for the crystallization kinetics and can be expressed as,

$$t_{1/2} = \left(\frac{\ln 2}{k}\right)^{1/n}$$
(6-9)

The effects of concentration and temperature on the kinetics of gelation are suggested by the Avrami parameters listed in Table 6.2. When the lowest gelation temperature -20° C is used, the Avrami parameters (*n* and *k*) for samples with different

concentrations (10%, 5% and 2%) are almost the same, indicating that the sensitivity of the crystallization kinetics on the polymer concentration is suppressed by a predominant thermodynamic driving force. For the gels obtained at -20°C, the Avrami exponent $n \sim$ 4 suggests a spherical growth and a homogeneous nucleation (Schultz, 2000b). For the samples with various concentrations (15%, 10% and 5%) gelled at 0°C, where the δ -form crystal is generated, the half-life time $t_{1/2}$ increases remarkably with decreasing concentration. Differences in the nucleation types of the three samples are suggested by their different Avrami exponents. As the concentration decreases from 15% to 10% and 5%, n increases from 2.0 to 3.4 and 3.9, indicating an increase in growth dimensionality. The value of n = 2 in the 15% sample suggests the heterogeneous nature of nucleation and a 2-D growth (Zhang et al., 2004), while higher values of n suggesting that the system is approaching a homogeneous nucleation and a 3-D growth in 10% and 5% solutions (Mano et al., 2004). The effect of gelation temperature on the samples with the same concentration can be illustrated by the gelation of the 10% solutions at 0°C and -20°C. The difference of gelation temperature results in, not only a different rate of crystallization (k and $t_{1/2}$), but also a different nucleation behavior as suggested by n.

In the solution of the lowest polymer concentration (i.e., 5%), the nucleation behavior is almost independent of the gelation temperature. This is observed from the little difference in n for the 5% solutions in Table 6.2. In this case, the rate of crystallization is still dependent upon the gelation temperature. This suggests that k is more dependent upon the temperature than n does, particularly at the low concentrations. This explains why some expected gelations, such as those from the 10% solution at 20°C and the 2% solution at -20°C (Table 6.1), can not be observed within the experimental time scale, which is 20 minutes. The gelation can only take place in a long time after quenching.

PLLA Concentration (mass ratio)	Gelation temperature (°C)	N	k (s ⁻ⁿ)	t _{1/2} (s)
15% —	0	2.0	2.55 E-4	34
	20	1.8	3.43 E-5	155
10% —	-20	4.1	6.84 E-7	24
	0	3.4	2.97 E-9	226
5%	-20	4.1	1.39 E-7	35
	0	3.9	9.87 E-14	1589
2%	-20	4.1	1.86 E-7	33

Table 6.2 The Avrami parameters calculated from SAXS invariants for the gelation in PLLA/THF solutions.

The α -crystals of PLLA is obtained in the 15% solution gelled at 20°C. The Avrami exponent *n*, equal to 1.8, suggests a two-dimensional growth and a heterogeneous nucleation. The rate of crystallization is affected by the high gelation temperature or the low thermodynamic driving force, giving a longer half-life than for the sample with the same concentration but gelled at 0°C.

Avrami parameters, especially the exponent n, have been widely used to describe the kinetics of polymer crystallization, but it should be noted that the interpretation of their physical meaning is not singular in literature. Most of the research on kinetics was based on melt or bulk crystallization. The interpretation of the Avrami exponent of the crystallization in solution should also consider information obtained from structural characterization.

6.5 Conclusions

The kinetics of thermally induced gelation in PLLA/THF solutions is studied by *in situ* simultaneous synchrotron WAXS and SAXS. Crystallization is responsible for the gelation via TIPS in PLLA/THF solutions. Qualitative observation on the development of crystallization and morphology can be achieved by using the 3-D plots of the WAXS and SAXS profiles. The invariant Q from SAXS data is used to represent the overall density contrast of the system and is used to track the crystallization kinetics.

The Avrami behavior of the gelation is quantitatively analyzed by evaluating the crystallization rate constant k and the Avrami exponent n. The effects of concentration and temperature on the nature of the nucleation and growth of crystals during gelation are discussed. When crystallization gives rise to the clathrate δ -crystal, a high concentration of PLLA is likely to induce a heterogeneous nucleation while a low gelation temperature almost always leads to a homogeneous nucleation and a 3-D growth.

The two factors, i.e., the concentration of a polymer solution and the gelation temperature, determine the thermodynamic driving force of the phase transition. Generally, a high polymer concentration and a low gelation temperature entail a high thermodynamic driving force for crystallization and can induce a fast rate of crystallization. Among the two factors, temperature plays a more critical role. A deep quench to -20°C can suppress the effect of concentration.

CHAPTER 7

SUMMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

7.1 Summary

The phase transitions of PLLA in bulk and in solution and the development of crystal structures and morphologies were studied in this dissertation. Crystallization and orientation in PLLA fibers subject to various thermal and mechanical treatments are studied by WAXS. This represents the effort in elucidating the crystallization behavior in orientated PLLA systems at temperatures above T_g . It is shown that crystallization and orientation development in PLLA fibers critically depend upon annealing temperature and drawing. The importance of the amorphous phase of PLLA on crystallization is further investigated by studying its relaxation at temperatures below T_g . A noticeable densification upon cooling is observed by SAXS and pycnometry. A nonlinear densification transition at about 45°C is also observed. This is also the temperature at which the maximum excess enthalpies of relaxation are observed. These results suggest that the system is evolving towards its equilibrium via primary nucleation at temperatures below Tg, which explains the observed higher rate of isothermal crystallization after aging at 45°C.

Efforts were also undertaken to study the phase transitions in PLLA solutions. A phase diagram consisting of two types of liquid-crystal phase transitions is developed to interpret the crystallization and morphology developed during TIPS in PLLA solutions. Besides the flake-like morphology formed during the L-C transition in which chain-folded α -crystals of PLLA are obtained, a chain-extended clathrate crystal, the

 δ -form, with a fibrillar morphology was shown to be formed when PLLA crystallizes in THF solutions at temperatures below 10°C. This new clathrate δ -crystal of PLLA is reported for the first time. A chain conformation of a 4/1 helix is proposed for the δ -crystal. Kinetic studies on the gelation in PLLA/THF solutions suggest an Avrami behavior.

7.2 Recommendations for Future Research

PLLA has been intensively studied for its application as a biodegradable polymer in the biomedical and pharmaceutical fields. Research presented in this dissertation has been focused on the fundamentals of the PLLA phase transitions in bulk and in solution. The observations of the primary nucleation of the amorphous phase of PLLA below T_g in bulk and the formation of the clathrate δ -crystal in PLLA/THF solutions have opened two interesting research directions for PLLA, in which future research should be conducted.

7.2.1 Behavior of the Amorphous Phase of PLLA

A locally ordered conformation which is closely related to primary nuclei has been proposed in this research to explain the densification of the amorphous phase of PLLA, the excess enthalpies of relaxation and the isothermal crystallization behavior after thermal aging. More research is needed to uncover the structural evolution during amorphous densification. This can be achieved by applying correlation function analysis on the ultra-high angle x-ray diffraction data and spectroscopies.

It is a conventional wisdom that the amorphous chains are "frozen" at temperatures below T_g , and aging below T_g has little influence on the properties of a polymer. The phenomenon of densification in PLLA amorphous phase suggests the importance of thermal histories below T_g . Thus, further investigation on how PLLA evolves towards its equilibrium state via primary nucleation and its implications on the properties of PLLA should be conducted. A practical implication of this behavior is that such aging and structure evolution actually takes place in implants made from PLLA. At the body temperatures of 36-37°C, the amorphous phase of PLLA continues to evolve towards its crystalline state via primary nucleation. In a closely related study, Cai et al. reported the effects of physical aging on the enzymatic degradation of PLLA, showing that the thermally aged PLLA (at 37°C) gave an obviously lower rate of degradation. How do the subtle changes in the amorphous phase affect long-term implants made from PLLA? More efforts should be undertaken along this direction.

7.2.2 Clathrate Crystal Structure

A new crystal form, the δ -crystal, with a fibrillar morphology has been observed in PLLA/THF gels and their dried porous structures. It contributes to a fundamental understanding of the morphology development during the fabrication of the PLLA-based scaffolds for tissue engineering. Further efforts in solving the crystal structure of the δ -form should be undertaken. The challenges lie in the growth of orientated δ -form crystals or single crystals. Also, the impact of the new δ -crystal and its fibrillar morphology on the performance of porous PLLA scaffolds for tissue engineering should be examined.

APPENDIX A

DATA ANALYSIS METHODS

WAXS and SAXS data collected in the experiments of this dissertation were saved in data files of different formats. These data files were then imported and processed by programs written in Matlab[®]. Three different detectors were used, including the 2-D Mar[®]-CCD, 2-D imaging plates and 1-D wire detectors. This entails that data were stored in various formats. The Matlab[®] programs written to process these data are listed in Appendix B.

The Matlab[®] version and operation systems are:

MATLAB[®] Version 6.5.0.180913a (R13)

MATLAB[®] License Number: 227700

Operating System: Microsoft Windows 2000 Version 5.0 (Build 2195: Service Pack 4)

MATLAB®	Version 6.5	(R13)
Filter Design Toolbox	Version 2.2	(R13)
Image Processing Toolbox	Version 3.2	(R13)
MATLAB [®] Compiler	Version 3.0	(R13)
Optimization Toolbox	Version 2.2	(R13)
Signal Processing Toolbox	Version 6.0	(R13)
Symbolic Math Toolbox	Version 2.1.3	(R13)
Wavelet Toolbox	Version 2.2	(R13)

A.1 Data Analysis from the Mar[®]-CCD Detector

A.1.1 Data Format

Original data from the Mar[®]-CCD detector is stored in the '*tiff*' format as 2-D images of 1024×1024 pixels. Data are saved as 1024×1024 floating point matrices after imported by Matlab[®].

A.1.2 Center Determination

The geometric center of the image, (512.5, 512.5), is usually not the center of the scattering pattern, at which the incident beam impinges the detector. The center of a scattering pattern is determined by Polar Image Processor (Version 2.5.4, Stonybrook Technology & Applied Science, Inc.) from the scattering patters of standard samples, i.e., silver behenate for SAXS and aluminum oxide for WAXS. Their strong scattering rings in the 2-D patterns are used to find the image center. Since the Mar[®]-CCD detector is fixed in one position during an experimental period, the center remains the same for all the data images obtained by the same experimental configuration.

A.1.3 Azimuthal Integration

To perform intensity related calculation, 1-D wide-angle diffraction profiles are usually needed. These 1-D WAXS profiles, e.g., $I vs. 2\theta$ curves, are obtained by integrating over the azimuthal angles of the corresponding 2-D WAXS patterns from 0° to 360°. The integrated value at a given diffraction angle is then normalized by the number of pixels contributing to the integration.

A.1.4 Calibration

Any point on a scattering pattern can be indexed by the distance or pixel number (P_1) from the center of the pattern. To convert the pixel number to diffraction angle 2θ for WAXS or scattering vector q for SAXS, calibration is needed based on the known peaks of standard samples. First, the sample to detector distance (L_{SD}) is calculated as:

$$L_{SD} = 0.158 P_1 / tan (2\theta_1) \text{ (mm)}$$

where P_I is the pixel number of a scattering peak from a standard sample, $2\theta_I$ is the corresponding scattering angle of the peak, which can be calculated from the known d-spacing and the wavelength of the incident x-ray. The pixel resolution of the Mar[®]-CCD detector is 0.158 mm. With the L_{SD} evaluated, the conversion of the pixel number P to 2θ can be achieved by the following two equations,

 $2\theta = \arctan(0.158P/L_{SD})$

For SAXS, since 2θ is small, $\theta = 1/2 \cdot 2\theta = 1/2 \cdot \tan(2\theta) = 1/2 \cdot 0.158 P/L_{SD}$

Therefore,

$$q = 4\pi \sin\theta/\lambda = 4\pi\theta/\lambda = 2*0.158\pi P/(L_{SD}*\lambda)$$

The values of 2θ and q are saved as two single-column Excel files, respectively, to be used in data analysis.

A.1.5 Background, Absorption and Scattering Volume Correction

The background (air), sample absorption and scattering volume correction is performed by using the following equation:

$$data_corrected = \frac{raw_data / IC1}{a / b} - \frac{BKG}{BKG_IC1}$$

where BKG is the scattering intensity matrix of the air background, IC1 and BKG_IC1 are the integrated intensities of the incident x-ray beam for the sample and the air background, respectively. The sample transmission a and air transmission b are defined as, a = IC1/IC2 and $b = BKG_IC1/BKG_IC$. IC2 and BKG_IC2 are the integrated intensities of the primary x-ray beam after it travels through the sample or the empty sample holder, respectively.

A.1.6 Peak Deconvolution

Peak deconvolution for 1-D WAXS profiles is performed by using a least-square fitting procedure. Diffraction peaks and an amorphous halo are assumed to be Gaussian-type peaks, which can be describe as,

$$y(x) = A_1 \exp\left\{-0.5\left[\frac{(x-A_2)}{A_3}\right]^2\right\}$$

where A1, A2 and A3 are the Gaussian parameters, representing the height, position and width of the peak, respectively. Initial guess of the parameters are needed before the curve-fitting.

A.2 Data Analysis from Imaging Plates

A.2.1 Data Format

Data from imaging plates is stored in the 'uint16' format (Unsigned 16-bit integer). The data is imported as a 2-D 2000×2500 matrix. The original data are usually reduced to a smaller frame by retaining the center position of the image. The frame is then saved and analyzed.

A.2.2 Center Determination

Because an imaging plate needs to be removed from its holder and scanned after the registration of the scattering intensity from a sample, the center of each scattering pattern is different and has to be determined individually. To find the center of a scattering pattern, an initial guess is needed. Then a horizontal and a vertical intensity profiles through the guessed center are obtained. If the intensity distribution of each profile is symmetric about the center, the guessed center is the true center of the pattern. Otherwise, another guess is tested by this procedure until the true center is found.

A.2.3 Azimuthal Integration

See Chapter A.1.3.

A.2.4 Calibration

The calibration of data from imaging plates uses the same method for Mar[®]-CCD (as described in Chapter A.1.4), except the pixel resolution is 0.1 mm.

A.2.5 Background, Absorption and Scattering Volume Correction

See Chapter A.1.5.

A.3 Data from 1-D Wire Detector

A.3.1 Data Format

The data from two 1-D wire detectors are given in the ASCII format with two columns and 1024 rows, representing the 1024 pixels of the wire detector. Column one is the pixel number and column two is the intensity values. Pixels 1 to 512 are reserved for the SAXS detector and Pixels 513 to 1024 are reserved for the WAXS detector. Two 1-D detectors are usually used for simultaneous scattering experiments, in which multiple frames of scattering profiles are registered continuously for a sample under certain thermal or mechanical stimuli. Each frame (i.e., each 1-D profile) is saved as an individual file. When the data are imported by Matlab[®], the profiles from the same sample are loaded and combined into one data matrix, in which each row corresponds to a scattering intensity profile and each column represents a pixel number.

A.3.2 Calibration

The pixel resolution of the 1-D detectors is unknown; therefore the calibration of the 1-D data is different from the procedure for the Mar[®]-CCD and imaging plates. For WAXS, the diffraction angle 2θ of any pixel P can be evaluated from the following equation,

$$\tan 2\theta = \frac{P - P_1}{P_1 - P_2} (\tan 2\theta_1 - \tan 2\theta_2) + \tan 2\theta_1$$

where P_1 and P_2 are the pixel numbers of the diffraction peaks of the WAXS standard, aluminum oxide, and $2\theta_1$ and $2\theta_2$ are the corresponding diffraction angles calculated from the known d-spacings of the standard and the x-ray wavelength..

For SAXS, the position of main beam is first determined by,

$$SP_0 = SP_1 - (SP_2 - SP_1)$$

where SP_1 and SP_2 are the pixel numbers of the first and second order scattering peaks of the SAXS standard, silver behenate. SP_0 is the pixel position of the incident x-ray beam on the detector. The distance between SP_0 and SP_2 is twice of that between SP_0 and SP_1 . Assuming the pixel resolution is ΔP , the scattering vector q of a corrected pixel number P, i.e., the physical pixel number minus SP_0 , can be obtained as follows,

In the small angle scattering geometry, $2\theta = tan2\theta = P\Delta P/L_{SD}$

So,
$$\theta = P \Delta P / (2L_{SD})$$

Then,
$$q = \frac{4\pi\theta}{\lambda} = \frac{4\pi}{\lambda} \cdot \frac{P\Delta P}{2L_{SD}} = \frac{2\pi P}{\lambda} \cdot \frac{\Delta P}{L_{SD}}$$

The constant $\Delta P/L_{SD}$ can be evaluated from the known q and P for the SAXS standard, silver behenate.

A.3.3 Background, Absorption and Scattering Volume Correction

See Chapter A.1.5.

APPENDIX B

MATLAB[®] SOURCE CODES

The Matlab[®] codes used in this dissertation are listed in this chapter. Lines starting with a percentage sign, i.e., "%", are comments. The "filename" and "directory" in the codes should be adjusted before running. The "Program Code" is the Matlab[®] code that can be run directly, while the "Function Code" is called by the "Program Code".

B.1 Program Code for importing Mar[®]-CCD data

% This file is a code that calls jw_bres_circle_azi.m % extract an 1-D azimuthal profile of an image matrix data from MarCCD,

clear clc close all

%specify directory for image data dir = 'c:\jingzhang\NSLS-DATA-aug2002\doing'; cd (dir);

%specify MarCCD data file name fileName = 'sPLA120C01.0001.img'; BKGfile = 'sPLA120C01.0004.img'; savefile = 'sPLA120C_0001.mat'

% Giving the IC1, IC2, BKG_IC1, BKG_IC2 IC1 = 37.22293; BKG_IC1 = 37.22293; scale factor =0.956;

%total number of columns TOTAL_COL = 1024; TOTAL_ROW = 1024;

%xCenter is column center center_col = 524;

%yCenter is row center center_row = 523;

%specify radius of the circle you want to extract %SPECIFY IN THE UNIT OF DEGREE total_radius = 499;

```
start angle = 0;
end angle = 359;
angle resolution = 1;
% Importing MarCCD date file in tif format
image matrix = imread(fileName, 'tif');
BKG matrix = imread(BKGfile, 'tif');
%%%%%%%%%%% Background Correction
                                                  final_matrix = (double(image_matrix)/IC1)/(a/b)-(BKG_matrix/BKG_IC1)
% Load q and two theta for SAXS and WAXS
q = xlsread('C:\jingzhang\NSLS-DATA-aug2002\matlab\q.xls');
two_theta = xlsread ('c:\jingzhang\NSLS-DATA-aug2002\matlab\two_theta.xls');
%check center postion and radius postion
if((center col + total radius \geq TOTAL COL) || (center col - total radius \leq 0) || (center row +
total_radius >= TOTAL_ROW ) || (center_row - total_radius <= 0));
   disp('Combination of center coordinate and the radius is out of the image range')
end:
for radius = 1:total radius;
[cordn, counter] = jw_bres_circle_azi(radius);
%%%%%NOTE THAT you can only use the cordn array with its subscript
%%%%from 1 to counter
%The following are coordinate transformation
%col_cordn is x-dimension (or the first column) of the cordn array
col_cordn = cordn(1:counter, 1) + center_col;
%row_cordn is y-dimension (or the second column) of the cordn array
row cordn = -cordn(1:counter, 2) + center row;
total = 0;
    for j=1:1:counter;
         azi profile(j) = final matrix ( row cordn(j), col cordn(j) );
        total = total + double (azi_profile(j));
        x = cordn(j,2);
        y = cordn(j,1);
        azi_degree_index(j) = 180*atan(y/x)/pi;
        if x < 0:
             azi degree index(j) = 180 + azi_degree_index(j);
         else if (y < 0) && (x \ge 0);
             azi degree index(j) = 360 + azi degree index(j);
        end;
```

end;

final(radius) = total / counter;
end;

% Plot the 1-D scattering profile figure; plot (q, final); %plot (two theta, final);

% Save the 1-D profile save(savefile, 'final');

B.2 Function Code for Generating Coordinates on the Circle with Certain Radius

%This files extracts an azimuthal profile of a circle %centered at (0,0) with a radius = radius %RETURN: the (x,y) coordinate and the number of points.

function [cordn, counter] = jw_bres_circle_azi(radius)

%the size of the first octant: starting from positive y axis in the first quandrant %initially set the octantSize using the following equation %Then keep track of the octantSize by counting using "octantCounter" octantSize = round((radius/sqrt(2)) +3); octantCounter = 1; %the subscript starts from the "1", different than C, which starts from zero

%keeping track of (x,y) coordinate in the first octant octantArray = zeros(octantSize, 2);

%keeping track of (x,y) coordinate that is returned %initially set its size using the following equation %Then keep track of the its size by counting using "counter" cordn = zeros(octantSize*8, 2); counter = 1; %counting how many points are extracted.

```
%%%This first point on the positive y axis
x = 0;
y = radius;
%p and p0 are variables used in the algorithm.
p0 = 1 - radius;
p = p0;
```

```
%special flag for the Line 45 degree
line45 = 0;
```

```
cordn(counter, 1) = x;
cordn(counter, 2) = y;
counter = counter + 1;
```

else

```
%The code within while is the core of Bresenham algorithm.
%%obtain the first octant starting from y axis
while (y > x)
if( p < 0 )
p = p + 2 * x + 3;
x = x + 1;
```

120
```
p = p + 2 * x - 2 * y + 5;
         y = y - 1;
         x = x + 1;
    end %end of if -- else
    octantArray(octantCounter,1) = x;
     octantArray(octantCounter, 2) = y;
     octantCounter = octantCounter + 1;
     cordn(counter, 1) = x;
    cordn(counter,2) = y;
     counter = counter + 1;
end %%end of while
%decrement one to reflect the real array index/size
octantCounter = octantCounter - 1;
%double check the last point
if octantArray(octantCounter,1) > octantArray(octantCounter,2)
    %simple ignore that point
    octantCounter = octantCounter - 1;
    counter = counter - 1;
elseif octantArray(octantCounter,1) == octantArray(octantCounter,2)
    %for counter keep that point, so do NOT decrement counter
    %and set special flag
    line45 = 1:
    mirrorPointX = octantArray(octantCounter,1);
    mirrorPointY = octantArray(octantCounter,1);
    %for octantArray --> ignore that point
    octantCounter = octantCounter -1;
else %if octantArray(octantCounter,1) < octantArray(octantCounter,2), there must be an error
    disp('ERROR ERROR ERROR ERROR ERROR ERROR ERROR')
end
%%second octant above positive x axis
for i = octantCounter:-1:1
     cordn(counter, 1) = octantArray(i, 2); %swap y to be the new X
     cordn(counter,2) = octantArray(i,1); %swap x to be the new Y
     counter = counter + 1;
end
%%process the point on the positive x-axis
cordn(counter,1) = radius;
cordn(counter,2) = 0;
counter = counter + 1;
%%third octant below positive x axis
for i = 1 : 1: octantCounter
    cordn(counter,1) = octantArray(i,2); %swap y to be the new X
    cordn(counter,2) = -octantArray(i,1); %swap x to be the new -Y
    counter = counter + 1;
end
```

121

```
%%process the point on the 45 degree line
if line 45 == 1
     cordn(counter, 1) = mirrorPointX;
     cordn(counter, 2) = -mirrorPointY;
     counter = counter + 1;
end
%%fourth octant to the right of negative y axis
for i = octantCounter:-1:1
     cordn(counter, 1) = octantArray(i, 1); %x to be the new X
     cordn(counter,2) = -octantArray(i,2); %-y to be the new Y
     counter = counter + 1;
end
%%process the point on the negative y-axis
cordn(counter, 1) = 0;
cordn(counter,2) = -radius;
counter = counter + 1;
%%fifth octant to the left of negative y axis
for i = 1: 1: octantCounter
     cordn(counter,1) = -octantArray(i,1); %-x to be the new X
     cordn(counter,2) = -octantArray(i,2); %-y to be the new Y
     counter = counter + 1;
end
%%process the point on the 45 degree line
if line 45 == 1
     cordn(counter, 1) = -mirrorPointX;
     cordn(counter, 2) = -mirrorPointY;
     counter = counter + 1;
end
%%sixth octant below the negative x axis
for i = octantCounter:-1:1
     cordn(counter, 1) = -octantArray(i, 2); %-y to be the new X
     cordn(counter,2) = -octantArray(i,1); %-x to be the new Y
     counter = counter + 1;
end
%%process the point on the negative x-axis
cordn(counter,1) = -radius;
cordn(counter,2) = 0;
counter = counter + 1;
%%seventh octant above the negative x axis
for i = 1 : 1 : octantCounter
     cordn(counter, 1) = -octantArray(i, 2); %-y to be the new X
     cordn(counter,2) = octantArray(i,1); %x to be the new Y
     counter = counter + 1;
end
%%process the point on the 45 degree line
if line 45 == 1
    cordn(counter, 1) = -mirrorPointX;
```

```
cordn(counter, 2) = mirrorPointY;
```

```
counter = counter + 1;
end
%eighth octant near positive y axis*/
for i = octantCounter : -1 : 1
    cordn(counter,1) = -octantArray(i,1); %-x to be the new X
    cordn(counter,2) = octantArray(i,2); %y to be the new Y
    counter = counter + 1;
end
```

```
counter = counter - 1;
```

B.3 Program Code for Peak Deconvolution

% This is the script m-file that perform least square curve fitting based % on gaussian peaks by calling function jz_gussian_fit % for 1-D WAXS profiles from MarCCD

clear close all

```
% Specify dir and file name
dir = 'c:\jingzhang\NSLS-DATA-aug2002\work';
cd (dir);
filename='PLA25m.mat';
savefile='PLA25m.mat';
```

% Giving Initial Guess of Gaussian Parameters
% Every 3 parameters are for one Gaussian Peak: Height, Position, Width
% The first two peaks are the two amorphous halos
% The last but two and one parameters are slope and intercept for baseline
% The last parameter is the number of peaks

coeff0 = [3.3673 13.641 3.3197 0.71838 19.411 2.025 4.8796 14.481 0.13878 1.793 14.623 0.41074 1.1945 16.538 0.16618 0.08195 20.165 0.41314 0.094113 19.46 0.31423 0.18501 21.563 0.18746 0.036769 0.41207 8];

% import the WAXS or SAXS data from speicified .mat file load (filename); xdata_origin = xlsread ('two_theta.xls');

% Cut data and two_theta data = final(82:438); vxx = xdata_origin(82:438);

% Call jz_fit_gaussian function for curve-fitting [parameters, intt, IB] = jz_fit_gaussian(vxx',data,coeff0);

```
% Pick the base line parameters and peak number
m = length (parameters);
base1 = parameters(m-2);
base2 = parameters(m-1);
peak = parameters (m);
```

```
% Generate the profile for each fitted gaussian peak
% by calling function jz gaussian_1
for n = 1:peak;
    m = 3*(n-1)+1;
    y(n,1:length(vxx)) = base1.*vxx' + base2 + jz_gaussian_1(vxx',parameters(m:m+2));
end
% Calculate the sum of all gaussian peaks
% by calling function jz gaussian sum
curvefit = jz gaussian_sum(parameters,vxx');
% Calculate residue
residue = curvefit - data;
% Plot the fitted peaks
figure
plot (vxx,data,'r-',vxx,curvefit,'b-.',vxx,residue,'g--');
hold on;
plot (vxx,y(1,1:length(vxx)),'k:',vxx,y(2,1:length(vxx)),'k:',vxx, y(3,1:length(vxx)),
'k:',vxx,y(4,1:length(vxx)),'k:',vxx,y(5,1:length(vxx)),'k:',vxx,y(6,1:length(vxx)),'k:',vxx,y(7,1:length(vxx)),'
k:',vxx,y(8,1:length(vxx)),'k:');
legend ('Original Data Curve', 'Overall Fitted Curve', 'Residue', 'Fitted Gassian Peaks', 2);
xlim([5,25]);
```

```
xlabel ('2\Theta (degree)');
ylabel ('intensity (a.u.)');
```

% Calculate areas of crystalline peaks and all peaks for crystallinity Ac = (intt(3)+intt(4)+intt(5)+intt(6)+intt(7)+intt(8)) A = (intt(1)+intt(2)+intt(3)+intt(4)+intt(5)+intt(6)+intt(7)+intt(8)); ratio = Ac/A;

save (savefile, 'final', 'xdata_origin', 'vxx', 'data', 'curvefit', 'y', 'parameters', 'intt', 'IB', 'ratio', 'coeff0')

B.4 Function Code for Total Fitted Curve Calculation

```
function gauss = jz_gaussian_sum(coeff,xdata)
```

gauss = g + base1.*xdata + base2;

```
peak = coeff(length(coeff));

base1 = coeff(length(coeff)-2);

base2 = coeff(length(coeff)-1);

a = zeros(length(xdata));

g = a(1,1:length(xdata));

for n = 1:peak;

m = 3*(n-1)+1;

gau(n,1:length(xdata)) = jz_gaussian_1 (xdata,coeff(m:m+2));

g = g + gau(n,1:length(xdata));

end
```

B.5 Function Code for Least-Square Curve Fitting

% This is the function that perform curve fitting based on Gaussian peak

function [parameters, integrals, IB] = jz_fit_gaussian(vxx,v,coeff)

```
% Use lsqcurvefit to perform nonlinear curve fit
opt = optimset('LevenbergMarquardt', 'on', 'MaxFunEvals', 100000,'MaxIter', 10000);
[parameters,resnorm,exitflag] = lsqcurvefit(@jz_gaussian_sum,coeff,vxx,v,[],[],opt);
```

```
% Pick total number of peak
peak = coeff(length(coeff));
k=1;
% Integration of peaks
for n = 1:peak;
```

% Determine the width of gaussian peak, if peak is too narrow, the % inegration width is limited to 10, otherwise use the whole 2theta range.

```
if coeff(k+2) < 0.23;
    t1 = coeff(k+1)-5;
    t2 = coeff(k+1)+5;
else;
    t1=vxx(1); t2=vxx(length(vxx));
end
```

```
% Integration of peak area by numerical integration
% by calling jz_gaussian_1
integration_all = quadl(@jz_gaussian_1,t1,t2,[],[],coeff(k:k+2));
```

```
% Calculate the rectangular area
first_y_val = jz_gaussian_1(t1,coeff(k:k+2));
last_y_val = jz_gaussian_1(t2,coeff(k:k+2));
rectangle_area = (t2-t1) * (first_y_val + last_y_val)/2;
```

```
% Peak area by substract total area - rectangular area integrals(n) = integration_all - rectangle_area;
```

```
% Calculate the peak width
modeled_y_vals = jz_gaussian_1(vxx,coeff(k:k+2));
IB(n) = integrals(n)/max(modeled_y_vals);
```

```
k = k+3;
end
```

B.6 Function Code for Single Gaussian Peak Calculation

% This is the functional form of Gaussian function.

```
function gaussian = jz_gaussian_1(xdata,coeff)
a1 = coeff(1); a2 = coeff(2); a3 = coeff(3);
gaussian = a1.*exp(-0.5*((xdata-a2)/a3).^2);
```

Program Code for Reading Imaging Plate Data

% This is the m-file that read a imaging plates data % by calling Fun_IP_opener to read imaging plates data

% Specify dir dir = 'c:\jingzhang\NSLSDATA_April2004\PLA'; cd (dir);

% Specify fileName filename='50-0_W.img'; savename='50-0-W.mat';

% Import data by calling function IP_opener image matrix = Fun_IP_opener(dir, filename);

% Plot the data matrix figure; imagesc(image_matrix);

save (savename, 'image_matrix');

B.7 Function Code for Importing Imaging Plates Data

% This function read intensity data from imaging plate % convert them into linear scale; and return the image matrix

function image_matrix= Fun_IP_operner(dir_data,filename)
cd(dir_data);

%open big-endian file [fid message]=fopen(filename, 'r', 'b');

%the imaging plates used in X27C, Fujifilm is 2000*2500 (200mm*250mm) %read unsigned int matrix of 2000*2500 %imaging plates always use unsigned int, i.e., 'uint16' [image_matrix, count] = fread(fid, [2000,2500], 'uint16'); fclose(fid);

B.8 Program Code for Finding Center of Imaging Plates

% This program is to use image plate data (already saved as matrix of m
% file) to find center of image with out obvious peaks
% by estimate a center, X or Y scan lines are plotted across the estimated
% center. After taking a X-scan at certain Y, the profile is folded a certain X
% value (X_fold) and the two half-profiles are ploted and overlap. Changing X_fold point
% in a range of X near the center until a X_fold value is found where the 2
% half-profiles are the same. Then X center is found. Y center found in the
% same way.

% Specify dir

dir = 'c:\jingzhang\NSLSDATA_April2004\PLA'; cd (dir); % Specify fileName filename='50-0 W.mat'; % Initial guess of center x1 = 1175;y1 = 1006;% Generate pixels for x-axis and y-axis $x_axis = (1:1:2500);$ $y_axis = (1:1:2000);$ % Load image plate file, data in variable of 'image_matrix' load (filename,'-mat'); % Initial X scan on guessed center x_scan = image_matrix(1004, :); figure; plot (x_axis, x_scan); % X scan on moved x center and folding/overlay for n = x1-10:x1+10;figure; plot (1:n, x_scan(1:n),'b'); hold on; for k = 1:2500-n;m(k) = n+(k-1)-2*(k-1);end plot (m, x scan(n:2499),'r'); hold off; title(['X CENTER: ',int2str(n)]); xlim ([0,n+10]); $yy = max(x_scan(1:n));$ ylim ([0.5*yy,1.05*yy]); m=0; end % Initial Y scan on guessed center y_scan = image_matrix(:, 1176); figure; plot (y_axis, y_scan); % Y scan on moved x center and folding/overlay for n = y1-10:y1+10;figure; plot (1:n, y_scan(1:n),'b'); hold on; for k = 1:2000-n;m(k) = n+(k-1)-2*(k-1);end plot (m, y_scan(n:1999),'r'); hold off; title(['Y CENTER: ',int2str(n)]);

```
xlim ([0,n+10]);
xx = max(y_scan(1:n));
ylim ([0.4*xx,1.05*xx]);
m=0;
end
```

B.9 Program Code for Reading Multi-frame 1-D Wire Detector Data

```
% This program is used to load the group of single 1-D intensity data
% the name list has been generated and saved as txt file
% the program load the 1-D file by following the name list and store the
% data into a matrix
% Specify dir
dir = 'C:\jingzhang\BNL2005\1-D\THF-15-RT';
cd (dir);
% Specify the list of 1-D file names and par file names
listfile = 'list.txt';
parlist = 'parlist.txt';
% Specify the Background file name and par file name
BKGfile = 'C:\jingzhang\BNL2005\1-D\BKG AND STANDARD\BKG1D4-60S001.swx';
BKGic = 'C:\jingzhang\BNL2005\1-D\BKG AND STANDARD\BKG1D4-60S001.par';
% Specify save file name
savefile = 'THF-15-RT.mat';
% Load 1-D file into matrix
% by picking up the 1-D filename from namelist file and then load the file into a
% matrix (1024*total lines)
i = 0;
fid=fopen(listfile);
while 1
     tline = fgetl(fid);
     if ~ischar(tline), break, end
     i = i+1;
     temp = load (tline, '-ascii');
     raw_data(:,i) = temp(:,2);
end
fclose(fid);
% total frames of 1-D files
row = i;
% load the q and 2theta
two theta = xlsread ('2theta.xls');
q = xlsread ('q.xls');
% pick up the IC1 and IC2 of 1-D filename from parfile name list file and then load the file into a
% matrix (1024*total lines)
i = 0;
fid=fopen(parlist);
```

```
while 1
    tline = fgetl(fid);
    if ~ischar(tline), break, end
    j =j+1;
    [temp1,temp2,temp3]=textread(tline,'%s %f %s', 'delimiter','\t');
    IC (j,1) = temp2(11);
    IC (j,2) = temp2(12);
end
fclose(fid);
```

```
% read Backgroud file
temp = load (BKGfile, '-ascii');
BKG = temp(:,2)/30;
% read Background par file
[temp1,temp2,temp3]=textread(BKGic,'%s %f %s', 'delimiter','\t');
BKG_IC(1) = temp2(11);
BKG_IC(2) = temp2(12);
```

```
% Background correction
for n = 1: row;
a = IC(n,2)/IC(n,1);
b = BKG_IC(2)/BKG_IC(1);
data_corrected (:, n)= raw_data(:,n)/IC(n,1)/(a/b)-(BKG/BKG_IC(1));
end
```

```
% Separate the corrected data into SAXS and WAXS data
% based on the SAXS center determined
SAXS = data_corrected(40:512,:);
WAXS = data_corrected(513:1024,:);
```

```
% 3-D plot of the SAXS data vs. q and time
figure;
for m = 1:row;
time = zeros([1,473])+2*(m-1);
plot3(q,time, SAXS(:,m),'b');
hold on;
```

```
end
```

```
% 3-D plot of the SAXS data vs. 2theta and time
figure;
for m = 1:row;
time = zeros([1,512])+2*(m-1);
plot3(two_theta,time, WAXS(:,m),'b');
hold on;
end
```

```
save (savefile, 'WAXS', 'SAXS');
```

REFERENCES

- Alemán, C., Lotz, B. & Puiggali, J. (2001). Crystal structure of the α-form of poly(L-lactide). <u>Macromolecules</u>, 34, 4795-4801.
- Alexander, L.E. (1969a). X-ray Diffraction Methods in Polymer Science. New York: John Wiley and Sons Inc., 241-247.
- Alexander, L.E. (1969b). X-ray Diffraction Methods in Polymer Science. New York: John Wiley and Sons Inc., 291-293.
- Alexander, L.E. (1969c). X-ray Diffraction Methods in Polymer Science, Chapter 3: Degree of Crystallinity in Polymers. New York: Wiley-Interscience, 188-192.
- Arnauts, J. & Berghmans, H. (1987). Amorphous thermoreversible gels of atactic polystyrene. <u>Polymer Communications, 28</u>, 66-68.
- Arnauts, J., Berghmans, H. & Koningsveld, R. (1993). Structure formation in solution of atactic polystyrene in trans-decalin. <u>Makromolekulare Chemie, 194</u>, 77-85.
- Atkins, E.D.T., Isaac, D.H., Keller, A. & Miyasaka, K. (1977). Analysis of anomalous x-ray diffraction effects of isotactic polystyrene gels and its implications for chain conformation and isomeric homogeneity. <u>Journal of Polymer Science: Polymer</u> <u>Physics Edition, 15</u>, 211-26.
- Atkins, E.D.T., Isaac, D. H. & Keller, A. (1980). Conformation of polystyrene with special emphasis to the near all-trans extended-chain model relevant in polystyrene gels. Journal of Polymer Science: Polymer Physics Edition, 18, 71-82.
- Atkins, E.D.T., Hill, M.J., Jarvis, D.A., Keller, A., Sarhene, E. & Shapiro, J.S. (1984). Structural studies on gels from isotactic polystyrene. <u>Colloid Polymer Science</u>, 262, 22-45.
- Balta-Calleja, F.J. & Vonk, C.G. (1989). <u>X-Ray Scattering of Synthetic Polymers</u>. Amsterdam: Elsevier, 154-155.
- Barnes, J.D. & Bras, W. (2003). Temperature-dependent three-dimensional small-angle scattering in semicrystalline polymers. Journal of Applied Crystallography, 36, 664-668.
- Beberdt, F. & Berghmans, H. (1994a). Phase behavior of syndiotactic Polystyrene-o-xylene. Polymer, 35, 1694-1704.

- Beberdt, F. & Berghmans, H. (1994b). Phase behavior of syndiotactic polystyrene-decalin. <u>Polymer, 34</u>, 2192-2201.
- Berghmans, M., Thijs, S., Cornette, M., Berghmans, H., De Schryer, F.C., Moldenaers, P. & Mewis, J. (1994). Thermoreversible gelation of solutions of syndiotactic poly(methyl methacrylate) in toluene: a two-step mechanism. <u>Macromolecules, 27</u>, 7669-7676.
- Cai, H., Dave, V., Gross, R.A. & McCarthy, S.P. (1996). Effects of physical aging, crystallinity, and orientation on the enzyme degradation of poly(Lactic acid), Journal of Polymer Science Part B: Polymer Physics, 34, 2701-2708
- Cakmak, M., Teitge, A., Zachmann, H.G. & White, J.L. (1998). On-line small-angle and wide-angle x-ray scattering studies on melt-spinning poly(vinylidene fluoride) tape using synchrotron radiation, <u>Journal of Polymer Science Part B: Polymer Physics</u>, 31, 371-381.
- Carothers, W.H., Dorough, G.L. & Van Natta, F.J. (1932). Polymerization and ring formation X: Reversible polymerization of six-membered cyclic esters. Journal of <u>American Chemical Society</u>, 54, 761-762.
- Cartier, L, Okihara, T, Ikada, Y, Tsuji, H., Puigali, J. & Lotz, B. (2000). Epitaxial crystallization and crystalline polymorphism of polylactides. <u>Polymer, 41</u>, 8909-8919.
- Chatani, Y. & Nakamura, N. (1993). Coiled-coil molecular model for isotactic polystyrene gels. <u>Polymer, 34</u>, 1644.
- Cheng, Z.D. & Lotz, B. (2003). Nucleation control in polymer crystallization: structural and morphological probes in different length- and time-scales selection processes. <u>Philosophical Transaction of the Royal Society A, 361</u>, 517-537.
- Cho, J., Baratian, S., Kim, J., Yeh, F., et al., (2003). Crystallization and structure formation of poly(L-lactide-co-meso-lactide) random copolymer: A time-resolved wide- and small-angle x-ray scattering study, <u>Polymer, 44</u>, 711-717.
- Daniel, C. & Guerra, G. (2002). Clathrate phase in syndiotactic polystyrene gels. <u>Macromolecules, 35</u>, 2243-2251.
- Daniel, C., Alfano, D., Guerra, G. & Musto, P. (2003). Physical gelation of syndiotactic polystyrene in the presence of large molar volume solvents induced by volatile guests of clathrate phases, <u>Macromolecules</u>, 36, 1713-1716.
- De Rudder, J., Berghmans, H., Roels, T. & Jacobs, A. (2001). The gelation mechanism of solutions of isotactic polystyrene in cis-decalin. Colloids and Surfaces A: <u>Physicochemical and engineering aspects, 183-185</u>, 313-326.

- De Santis, P. & Kovacs, A.J. (1968). Molecular conformation of poly(s-lactic acid). <u>Biopolymers, 6</u>, 299-306.
- Eling, B., Gogolewski, S. & Pennings, A.J. (1982). Biodegradable materials of poly(L-lactic acid) 1. Melt-spun and solution-spun fibers. <u>Polymer, 23</u>, 1587-1593.
- Ethicon Inc. (1996). <u>VICRYL (Polyglactin 910)</u> Suture Essential Product Information, Somerville: Ethicon Inc., 1-5.
- Fambri, L., Pegoretti, A., Fenner, R., Incardona, S.D. & Migliaresi, C. (1997) Biodegradable fibres of poly(L-lactic acid) produced by melt spinning. <u>Polymer. 38</u>, 79-85.
- Fowers, K.D., Baudys, M., Rathi, R. & Shih, C. Thermally reversible gelling materials for safe & versatile depot delivery. <u>Drug Delivery Technology</u>, 3, 30-34.
- Fukuzaki. H., Yoshida, M., Asano, M., Fukuzaki, H. & Kaetsu, I. (1988). Direct copolymer of L-lactic acid with δ-valerolactone in the absence of catalysts. <u>European Polymer Journal, 24</u>, 1029-1036.
- Gilding, D.K. & Reed, A.M. (1979). Biodegradable polymers for use in surgery-polyglycolic/poly(lactic acid) homo- and copolymer: 1. Polymer, 20, 1459-1464.
- Giordano, R.A., Wu, B.M., Borland, S.W., Cima, L.G., Sachs, E.M., & Cima, M.J. (1996). Mechanical properties of dense polylactic acid structures fabricated by three dimensional printing. Journal of Biomaterials Science, Polymer Edition, 8, 63-75.
- Glasbrenner, B.S. (2005). Plastics in the environment: responsibility the next big thing. A keynote presentation at <u>Society of Plastics Engineers Annual Technical</u> <u>Conference</u> (ANTEC'05), Boston, MA.
- Griffith, J.H. & Ranby, B.G. (1960). Dilatometric measurements on poly(4-methyl-1-pentene) glass and melt transition temperatures, crystallization rates, and unusual density behavior. Journal of Polymer Science, 44, 369-381.
- Guenet, J. M., McKenna, G. B., (1998). Thermoreversible gelation of isotactic polystyrene: thermodynamic and phase diagrams. <u>Macromolecules, 21</u>, 1752-1756
- Hagan, S.A., Coombes, A.G.A., Garnett, M.C., Dunn, S.E., Davies, M.C., Illum, L., Davis, S.S., Harding, S.E., Purkiss, S., Gellert, P.R. (1996).
 Polylactide-poly(ethylene glycol) copolymers as drug delivery system: 1.
 Characterization of water dispersible micelle formation systems. Langmuir, 12, 2153-2161.

- Hikmet, R.M., Callister, S. & Keller, A. (1988). Themalreversible gelation of atactic polystyrene: Phase transformation and morphology. <u>Polymer, 29</u>, 1377-1388.
- Hoogsteen, W, Postema, A.R., Pennings, A.J., Brinke, G.T. & Zugenmaier, P. (1990). Crystal structure, conformation, and morphology of solution-spun poly(L-lactide) fibers. <u>Macromolecules</u>, 23, 634-642.
- Hua, F.J., Kim, G.E., Lee, J.D., Son, Y.K. & Lee, D.S. (2002). Macroporous poly(L-lactide) scaffold 1. Preparation of a macroporous scaffold by liquid-liquid phase separation of a PLLA-dioxane-water system. Journal <u>Biomedical Material</u> <u>Research, 63</u>, 161-167.
- Hua, F.J., Do Nam, J., Lee, D.S. (2001). Preparation of a macroporous poly(L-lactide) scaffold by liquid-liquid phase separation of a PLLA/1,4-dioxane/water ternary system in the presence of NaCl. <u>Macromolecular Rapid Communication, 22</u>, 1053-1057.
- Ho, M-H. Kuo, P-Y., Hsieh, H-J., Hsien, T-Y., Hou, L-T., Lai, J-Y. & Wang, D-M. (2004). Preparation of porous scaffolds by using freeze-extraction and freeze-gelation methods. <u>Biomaterials</u>, 25, 129-138.
- Iannace, S. & Nicolais, L. (1997). Isothermal crystallization and chain mobility of poly(L-lactide). Journal of Applied Polymer. Science, 64, 911-919.
- Imai, M., Kaji, K. & Kanaya, T. (1994). Structure Formation of poly(ethylene terephthalate) during the induction period of crystallization: 3. Evolution of density fluctuations to lamellar crystal. <u>Macromolecules</u>, 27, 7103-7108.
- Jacobsen, S., Degee, P.H., Fritz, H.G., Degee, Ph., Dubois, Ph. & Jerome, R. (1999) Polylactide (PLA)-A new way of production. <u>Polymer Engineering and Science</u>, 39, 1311-1319.
- Kalb, B & Pennings, A.J. (1980). General crystallization behaviour of poly(L-lactic acid). <u>Polymer, 21</u>, 607-612.
- Keller, A. (1995). Introductory lecture aspects of polymer gels. <u>Faraday Discussion, 101</u>, 1-49.
- Kitao, T., Ohya, S., Furukawa, J. & Yamashita, S. (1973). Journal Polymer Science: <u>Polymer Physics Edition, 6</u>, 1091-1109.
- Kobayashi, J., Asahi, T., Ichiki, M., Oikawa, A., Suzuki, H., Watanabe, T., Fukada, E. & Shikinami, Y. (1995). Structure and optical properties of polylactic acids. <u>Journal of</u> <u>Applied Physics</u>, 77, 2957-2973.

- Kulkarni, R.K., Moore. E.G., Hegyeli, A.F. & Leonard, F. (1971). Biodegradable poly(lactic acid) polymers. Journal of Biomedical Material Research, 5, 169-81.
- Kunz, M., Drechsler, M. & Moller, M. (1995). On the structure of ultra-high molecular weight polyethylene gels. <u>Polymer, 36</u>, 1331-1339.
- Lauritzen, J.I.& Hoffman, J.D. (1959). Formation of polymer crystals with folded chains from dilute solution. Journal of Chemical Physics, 31, 1680-1681.
- Lee, W.D.& Im, S.S. (2005). Crystallization behavior of P(EN-co-ET) copolyesters: crystallization Kinetics and Morphology Revealed by DSC, Time-resolved SAXS Analysis, and TEM, Journal of Polymer Science: Part B: Polymer Physics, 43, 805-816.
- Litt, M.J. (1963). Poly(4-methylpentene): X-ray measurement of crystal density and observation of structural anomaly. Polymer Science, 1, 2219-2224.
- Liu, X. & Ma, P.X. (2004). Polymeric scaffold for bone tissue engineering, <u>Annals of</u> <u>Biomedical Engineering</u>, 32, 477-486.
- Lo, H., Kadiyala, S., Guggino, S.E. & Leong, K.W. (1996). Poly(L-lactic acid) foams with cell seeding and controlled-release capacity. <u>Journal Biomedical Material</u> <u>Research, 30</u>, 475-484.
- Lo. H., Ponticiello, M.S. & Leong, K.W. (1995). Fabrication of controlled release biodegradable foams by phase separation. <u>Tissue Engineering, 1</u>, 15-28.
- MacroMed Inc. (2003). <u>ReGel[®]: Injectable Gel Depot</u>. Sandy: MacroMed Inc. Retrieved April 28, 2004 from the World Wide Web: http://www.macromed.com/regel.htm
- Mandelkern, A.R.G. & Haigh, J.A. (1998) Crystallization kinetics of high molecular weigh n-alkanes. <u>Macromolecules</u>, 31, 765-768.
- Mano, J.F., Wang, Y., Viana, J.C., Denchev, Z. & Oliveira, M.J. (2004). Cold crystallization of PLLA studied by simultaneous SAXS and WAXS, <u>Macromolecular</u> <u>Materials and Engineering</u>, 289, 910-915.
- Marquardt, D.W. (1963). Journal of the Society for Industrial and Applied Mathematics. <u>11</u>, 431-441.
- Metters, A.T., Anseth, K.S. & Bowman, C.N. (2000). Fundamental studies of a novel, biodegradable PEG-b-PLA hydrogel. <u>Polymer, 41</u>, 3993-4004.
- Mezghani, K & Spruiell, J.E. (1997). High speed melt spinning of poly(L-lactic acid) filaments. Journal of Polymer Science: Part B: Polymer Physics, 36, 1005-1012.

- Mikos, A.G. & Temenoff, J.S. (2000). Formation of highly porous biodegradable scaffolds for tissue engineering, <u>Electronic Journal of Biotechnology [online]</u>, 3, http://www.ejbiotechnology.info/content/vol3/issue2/full/5/index.html
- Miyata, T. & Masuko, T. (1997). Morphology of poly(L-lactide) solution-grown crystals. Polymer, 38, 4003-4009.
- Muthukumar, M. & Welch, P. (2001). Modeling polymer crystallization from solutions. <u>Polymer, 41</u>, 8833-8837.
- Nakafuku, C. & Takehisa, S. (2004). Glass transition and mechanical properties of PLLA and PDLLA-PGA copolymer blends. Journal of Applied Polymer Science, 93, 2164-2173.
- Nam, Y.S. & Park, T.G. (1999a). Porous biodegradable polymeric scaffolds prepared by thermally induced phase separation. <u>Journal of Biomedical Material Research</u>, 47, 8-17.
- Nam, Y.S., Yoon, J.J. & Park, T.G. (1999a). Biodegradable polymeric microcellular foams by modified thermally induced phase separation method. <u>Biomaterials</u>, 20, 1783-1790.
- Ohtami, Y., Okumura, K. & Kawaguchi, A. (2003). Crystallization behavior of amorphous poly(L-Lactide), Journal of Macromolecular Science, Part B: Physics, B42, 875-888.
- Olmsted, P.D., Poon, W.C.K., McLeish, T.C.B., Terrill, N. J. & Ryan, A. J. (1998). Spinodal-assisted crystallization in polymer melts. <u>Physical Review Letters</u>, 81, 373-376.
- Okihara, T., Tsuji, M., Kawaguchi, A., Katayama, K., Tsuji, H., Hyon, S.H. & Ikada, Y. (1991). Crystal structure of stereocomplex of poly(L-lactide) and poly(D-lactide). Journal of Macromolecular Science, Physics, 30, 119-140.
- Park, S.Y., Han, D.K. & Kim, S.C. (2001). Synthesis and characterization of star-shaped PLLA-PEO block copolymers with temperature-sensitive Sol-Gel transition behavior. <u>Macromolecules</u>, 34, 8821-8824.
- Park, J.W. & Im, S.S. (2000). Biodegradable polymer blends of poly(L-lactic acid) and gelatinized starch. Polymer Engineering and Science, 40, 2539-2550.
- Peppas, N.A. & Huang, Y. (2002). Polymers and gels as molecular recognition agents. Pharmaceutical Research, 19, 578-587.
- Puiggali, J., Ikada, Y., Tsuji, H., Cartier, L., Okihara, T. & Lotz, B. (2000). The frustrated structure of poly(L-lactide). <u>Polymer, 41</u>, 8921-8930

- Rastogi, S., Goossens, J.G.P. & Lemstra, P.J. (1998) An in situ SAXS/WAXS/Raman spectroscopy study on the phase behavior of syndiotactic polystyrene (sPS)/solvent: Compound formation and solvent (dis)ordering. <u>Macromolecules</u>, 31, 2938-2998.
- Reed, A.M. & Gilding, D.K. (1981). Biodegradable polymers for use in surgery poly(glycolic)/poly(lactic acid) homo and copolymers: 2. in vitro degradation. <u>Polymer, 22</u>, 494-498.
- Reeve, M.S., McCarthy, S.P., Downey, M.J. & Gross, R.A. (1994). Polylactide stereochemistry: effect on enzymic degradability. <u>Macromolecules, 27</u>, 825-831.
- Roels, T., Beberdt, F. & Berghmans, H. (1994). Solvent quality and phase stability in syndiotactic polystyrene. <u>Macromolecules, 27</u>, 6216-6220.
- Rosa, C.D., Rizzo, P., Ballesteros, O.R., Petraccone, V. & Guerra, G. (1999). Crystal structure of the clathrate-form of syndiotactic polystyrene containing 1,2-dichloroethane, <u>Polymer, 40</u>, 2103-2110.
- Schmack, G., Tandler, B., Vogel, R., Beyreuther, R., Jacobsen, S. & Fritz, H-G. (1999). Biodegradable fibers of poly(l-lactic acid) produced by high-speed melt spinning and spin drawing. Journal Polymer Science, 73, 2785-2797.
- Schultz, J.M. (2001a). <u>Polymer Crystallization: the Development of Crystalline Order in</u> <u>Thermoplastic Polymers</u>. New York, Oxford University Press, 140-169.
- Schultz, J.M. (2001b). <u>Polymer Crystallization: the Development of Crystalline Order in</u> <u>Thermoplastic Polymers</u>. New York, Oxford University Press, 179-180
- Sodergrad, A. & Stolt, M. (2002). Properties of lactic acid based polymers and their correlation with composition. <u>Progress in Polymer Science, 27</u>, 1123-1163.
- Strobl, G. (2000). From the melt via mesomorphic and granular crystalline layers to lamellar crystallites: a major route followed in polymer crystallization. <u>European</u> <u>Physical Journal E: Soft Matter, 3</u>, 165-183.
- Suesat, J., Philips, D.A.S., Wilding, M.A. & Farrington, D.W. (2003). The influence of yarn-processing parameters on the tensile properties and structure of poly(l-lactic acid) fibres. <u>Polymer, 44</u>, 5993-6002.
- Talibuddin, S., Runt, J., Liu, L-Z. & Chu, B. (1998). Microstructure development and crystallization of poly(ethylene oxide) and melt-miscible PEO blends, <u>Macromolecules</u>, 31, 1627-1634.

- Terrill, N.J., Fairclough, P.A., Towns-Andrews, E., Komanschek, B.U. Young, R.J. & Ryan, A.J. (1998). Density fluctuation: the nucleation event in isotactic polypropylene crystallization. <u>Polymer</u>, <u>39</u>, 2381-2385.
- Tsutsui, K., Katsumata, T., Yamamoto, Y., Fukatsu, H., Yoshimizu, H., Kinoshita, T. & Tsujita, Y. (1999). The structure organization in syndiotactic polystyrene film induced by toluene vapour sorption, <u>Polymer, 40</u>, 3815-3819.
- Uhrich, K.E., Cannizzaro, S.M., Langer, R.S. & Shakesheff, K.M. (1999). Polymeric systems for controlled drug release. <u>Chemical Review</u>, 99, 3181-3198.
- Vandeweerdt, P., De Cooman, R., Berghmans, H. & Meijer, H. (1994). Gel spinning of porous poly(methyl methacrylate) fibers. <u>Polymer, 35</u>, 5141-5143.
- Van Hooy-Corstjens, C.S.J., Magusin, P.C.M.M., Rastogi, S. & Lemstra, P.J. (2002). A comparative study on gels and clathrates of syndiotactic polystyrene: Solvent mobility in polymer – solvent compounds. <u>Macromolecules</u>, 35, 6630-6637.
- Vasanthakumari, R. & Pennings, A.J. (1983). Crystallization kinetics of poly(L-lactic acid), <u>Polymer, 24</u>, 175-178.
- Wang, Z.-G., Wang, X., Hsiao, B. S., Andjelic, S. Jamiokowski, D., McDivitt, J., Fischer, J., Zhou, J. & Han, C.C. (2001). Time-resolved isothermal crystallization of absorbable PGA-co-PLA copolymer by synchrotron small-angle X-ray scattering and wide-angle X-ray diffraction. <u>Polymer, 42</u>, 8965-8973.
- Wellinghoff, S.T., Shaw, J. & Baer. E. (1979). Polymeric materials from the gel state: the development of fringed micelle structure in a glass. <u>Macromolecules</u>, 12, 932-939.
- Wong, W.H. & Mooney, D.J. (1997). <u>Synthetic biodegradable polymer scaffolds</u>. Boston: Birkhauser, 54-55.
- Wu, J., Schultz, J.M., Yeh, F., Hsiao, B. & Chu, B. (2000). In-situ simultaneous synchrotron small- and wide-angle x-ray scattering measurement of poly(vinylidene fluoride) fibers under deformation. <u>Macromolecules</u>, 33, 1765-1777.
- Wu, J., Schultz, J.M., Samon, J.M., Pangelinan, A.B., & Hoe, C.H. (2001a). In situ study of structure development in poly(trimethylene terephthalate) fibers during stretching by simultaneous synchrotron small- and wide-angle x-ray scattering. <u>Polymer, 42</u>, 7141-7151.
- Wu, J., Schultz, J.M., Samon, J.M., Pangelinan, A.B., & Hoe, C.H. (2001b) In situ study of structure development during continuous hot-drawing of poly(trimethylene terephthalate) fibers by simultaneous synchrotron small- and wide-angle x-ray scattering. <u>Polymer, 42</u>, 7161-70.

- Wunderlich, B. (2003). Reversible crystallization and rigid amorphous phase in semicrystalline macromolecules. <u>Progress in Polymer Science, 23</u>, 384-450.
- Yoshida, R. (2000). Design and construction of self-oscillating biomimetic polymer gels. <u>Maku, 25</u>, 287-289.
- Zhang, J. & Wu, J. (2005). Crystallinity and orientation development in poly(L-lactic acid) fibers during annealing and drawing. <u>Proceeding of Annual Technical</u> <u>Conference (ANTEC2005)</u>, 1747-1751.
- Zhang, J., Tsuji, H., Noda, I. & Ozaki, Y. (2004). Structural changes and crystallization dynamics of poly(L-lactide) during the cold-crystallization process investigated by infrared and two-dimensional infrared correlation spectroscopy, <u>Macromolecules</u>, 37, 6433-6439.
- Zhang, R. & Ma, P.X. (2000). Synthetic nano-fibrillar extracellular matrices with predesigned macroporous architectures, Journal of Biomedical Materials Research, 52, 430-438.
- Zwiers, R.J.M., Gogolewski, S, & Pennings, A.J. General crystallization behaviour of poly(L-lactic acid) PLLA: 2. Eutectic crystallization of PLLA. Polymer, 24, 167-174.