MODELING AND SIMULATION OF POLY(LACTIC ACID) POLYMERIZATION

A
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of
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by

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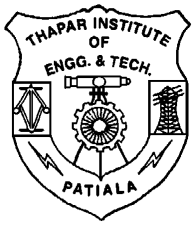

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Dedicated to my father

Late Shri Jagdish Lal Mehta

CERTIFICATE

This is to certify that the thesis entitled "MODELING AND SIMULATION OF POLY(LACTIC ACID) POLYMERIZATION" which is being submitted by Mr. Rajeev Mehta in fulfillment of the requirement for the award of the Degree Doctor of Philosophy in Chemical Engineering, Thapar Institute of Engineering and Technology (Deemed University), Patiala is a record of the candidate's own work carried out by him under our supervision and guidance. The matter embodied in this thesis has not been submitted in part or full to any other University or Institution for the award of any degree.

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(RAJEEV MEHTA)

Abstract

During the past 15 years, a number of aliphatic polyesters have aroused considerable interest due to their biodegradability and biocompatibility. Poly(lactic acid) (PLA) is the main biodegradable polyester of interest, primarily due to its biomedical and pharmacological applications. Since the syntheses of PLA by Carothers in 1932, hundreds of research papers and patents have appeared in the literature. Now large size PLA manufacturing units are being set-up. But, there is a lack of data concerning the rate constants for initiation, propagation and termination steps of PLA polymerization though some data about the apparent rate constant are available. Also, it is extremely difficult to experimentally find the absolute values of different rate constants. Thus, there is a need for mathematical modeling which when used with the readily available experimental data for the average molecular weights, can predict the polymerization rate constants with sufficient accuracy.

This thesis embodies the subject matter resulting out of this study. It is arranged in six different chapters. A brief introduction about the need for non-degradable polymers and a brief history along with the current industrial status of PLA is given in the introduction. Since it is the lactic acid, which starts the PLA lifecycle, its importance is also discussed. Also the future prospects and advantages of PLA are mentioned. This is followed by an introduction to synthesis of PLA by ring-opening polymerization (ROP) of lactide. Focus is then shifted to a discussion of why are mathematical models useful, in general, followed by the need for mathematical modeling of the ring-opening polymerization of PLA. A brief description of the methodology used is also given.

The progress of lactide polymerization has been modeled by assuming a ring opening reaction mechanism comprising of chain initiation, chain propagation, and chain termination. Appropriate differential equations have been developed incorporating the rate controlling reaction(s)/step(s). The resulting differential equations with appropriate boundary conditions were solved using a numerical technique. Effect of unequal reactivity has also been incorporated in the model. The efficacy of model has been tested

by comparing the predicted results on molecular weight and molecular weight distribution with those available in the published literature. The kinetic rate constants have been arrived at, for various PLA polymerization catalysts, by matching the simulated results with the experimental data. The method is extended to quantitatively predict the effect of water present as an impurity in the reactor on the PLA molecular weight.

A mechanistic model to simulate the ring-opening polymerization of PLA for a batch reactor is developed. A number of checks are made to verify the correctness of the solutions in the limiting case of Poisson distribution. Here the molecular weight change as a function of polymerization time, in a homogeneous ring-opening polymerization of PLA, is considered. The results of simulations performed on the model developed in conjunction with the reported experimental data for various catalysts are discussed. The sensitivity of the present technique with respect to k_o, k_p and k_t (rate constants for initiation, propagation and termination by transfer to monomer, respectively) are discussed. The molecular weight of polymer formed is more sensitive to k_p than k_t for shorter reaction time whereas effect of k_t is pronounced for prolonged reaction time. M_n, however, is not very sensitive to k_o. Initiation rate constant has a very peculiar behavior: with a decrease in k_o, the number average molecular weight, M_n, is lower for short reaction time, and as reaction proceeds M_n becomes higher. This interesting result is due to the fact that due to low k_o, the number of initiated chains are less and with the availability of same monomer molecules for the growth of fewer number of chains, the average chain length increases. It is shown that k_o values can be fine-tuned if the polydispersity (M_w/M_n) data is also considered. Based on this methodology, the values of different rate constants for the polymerization of PLA in presence of four catalysts: aluminum isopropoxide, iron trifluoroacetate, iron isobutyrate and zinc lactate are arrived at. A discussion of simulations performed without the assumption of propagation rate constant being chain length independent is also presented.

Above model is applied to the polymerization data in the form of degree of polymerization as a function of monomer-to-initiator ratio. The polymerization data is available in literature for the stannous octoate catalyst for PLLA and PDLLA. Additionally, a second model (Model 2) is developed which considers cationic ring-

opening polymerization mechanism where termination by transfer to polymer and unimolecular termination (first order relative to active species) and intramolecular termination, are considered. The differential equations for the formation and disappearance of the living i-mers P_1, P_2, …P_j, as well as for the consumption of monomer and initiator, along with the formation of deactivated polymer, M_j, for a batch reactor, using above kinetic scheme is written and solved. The typical computing time for Model 1 was 30 min and the Model 2 run took nearly a week. The simulations were matched with the reported data to get the individual rate constants for the ring-opening polymerization of lactide, using stannous octoate as a catalyst. Another objective was to find out if the difference in the degree of closeness of the curves to the experimental points is sufficient to ascribe a polymerization mechanism for the stannous octoate catalyst. However, it is not possible to ascribe a specific mechanism to PLLA and PDLLA polymerization on the basis of experimental data used in modeling. These experimental data points are characterized by poor reproducibility. However, it should be pointed out that for ROP this type of poor reproducibility is expected. The parity plots for the calculated and reported experimental values of average molecular weights show an excellent agreement.

An attempt has also been made to quantify the effect of water as impurity on the polymer molecular weight. The model considers termination by transfer to monomer and by transfer to water. A value of rate constant of chain transfer to water for ionic reaction is taken from the literature and used for the evaluation of rate constants by solving the appropriate differential equations. Although the amount of water present in reaction mixture was not known, simulations reveal that water concentration in the reported data was about 0.5 ppm. It is quantitatively shown that there is a marked decrease in the degree of polymerization in presence of even small concentrations of water in the reaction vessel.

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Nomenclature and Abbreviations

C	Impurity (water) present in reaction kettle (in equation (5.1))
[Co]	Initial water concentration (mol/l)
c	Fraction by which k_j changes as a function of j (dimensionless)
DP_n	Number-average degree of polymerization (dimensionless)
DP_w	Weight-average degree of polymerization (dimensionless)
Gpa	Giga pascals
HIPS	High impact polystyrene
I	Initiator
[I_o]	Initial initiator concentration (mol/l)
j	Number of repeat units in the polymer (dimensionless)
k_{app}	Apparent rate constant (l/mol.min)
k_j	Propagation rate constant for the j^{th} propagation step on a chain (l/mol.min)
k_o	Initiation rate constant (l/mol.min)
k_p	Propagation rate constant (l/mol.min)
k_t	Termination rate constant corresponding to termination by transfer to monomer (l/mol.min)
k_{tc}	Termination rate constant corresponding to termination by transfer to water (l/mol.min)
k_{tp}	Termination rate constant corresponding to termination by transfer to polymer (l/mol.min)
k_{ts}	Termination rate constant corresponding to unimolecular termination (first order relative to active species) and intramolecular termination (min^{-1})
M	Monomer
MD	Machine direction
M_n	Number-average molecular weight
$[M_o]$	Initial monomer concentration (mol/l)
MPa	Mega pascals
M_v	Viscosity-average molecular weight
M_w	Weight-average molecular weight
M_w/M_n	Polydispersity (dimensionless)

MWD Molecular weight distribution

m_j Weight of j-mer (gm)

N_j Number of moles of polymer of j units (dimensionless)

NMR Nuclear magnetic resonance spectroscopy

PCLD Polymer chain length distribution

IR Infra red spectroscopy

n A large integer (dimensionless)

PDLA Poly(D-lactide)

PDLLA Poly(DL-lactide)

PET Poly(ethylene terephthalate)

PLA Poly(lactic acid)

PLLA Poly(L-lactide)

P_1 Activated polymer of one unit

P_j Activated polymer of chain length j

PP Poly(propylene)

ppm Parts per million

psi Pounds per square inch

PVC Poly(vinylchloride)

s Number of chain(s) initiated by an initiator molecule (dimensionless)

T_c Ceiling temperature (^oC)

w Weight of all the molecules in a polymer sample (gm)

w_j Weight-fraction of molecules whose weight is m_j (dimensionless)

τ time variable (dimensionless)

Chapter - 1

Introduction

1.0 Background

A century ago, plastic was one of man's greatest inventions, but today it stands a trifle disgraced as man has realized the menace of this non-degradable resource. For plastic, it is a journey of no return due to its non-perishable nature. Indeed it is a daunting task for man to mitigate the environmental threat posed by plastic.

After its unchallenged applications in the industrial world for over half a century, will plastic be treated with the eco-hazard ignominy merely because it can't be treated? Some of the latest bio-technological inventions seek to answer this question. A clue to one such question can be had by recent research reports by Hardin (http://www.ars.usda.gov/is/pr/2000/000427.htm) from the Agriculture Research Services (ARS), USDA, and the American Agriculture Department, which clearly gives the thumbs-up sign for lactic acid. Lactic acid is the building block of poly(lactic acid) (PLA), which would ultimately be the input for producing biodegradable plastic. The USDA survey indicates that lactic acid can be produced by utilizing agricultural products like cornstarch and fibrous crops residues like the residue from sugarcane industry etc.

Worldwide production of high-volume consumer plastics continues to be dominated by petroleum–based polymers. Two factors have made biodegradable polymers economically attractive. These are (i) environmental and economic concerns associated with waste disposal and (ii) rising costs of petroleum production resulting form the depletion of the most easily accessible reserves. Ease of degradability, versatility and anticipated price/performance of the new generation of polymers, PLA, will enable it to displace a significant volume of fossil fuel-based polymers.

Although degradability of any polymer is commonly termed as being biodegradable, however, according to the European Society for Biomaterials [Williams, 1987] ‘biodegradation’ is a process in which biological agents (enzymes or microbes) play a dominant role in the degradation process. Unlike other biodegradable polymers the degradation of PLA is not biodegradation as it is caused by hydrolytic cleavage of the polymer backbone, with little or no evidence of participation of enzymes. However, PLA is commonly termed as a biodegradable polymer.

The field of biodegradable polymers is a fast growing area of polymer science because of applications of these polymers for temporary surgical and pharmacological applications [Vert et al., 1992]. On the other hand, biopolymers offer a possible alternative to traditional non-biodegradable polymers in a number of bulk applications if recycling is impractical or uneconomical. Composting, which is used for the disposal of food and yard waste, is the most suitable for the disposal of biodegradable materials together with food-contaminated paper [Bastioli, 1998]. In addition, non-degradable polymer products are generally produced from nonrenewable resources such as crude oil and natural gas, while a combination of biodegradability and the application of annually renewable sources offers the chance to make plastics part of a natural cycle [Witt, 1975].

Polylactic acid (PLA) was discovered in 1932 by Carothers (DuPont) who produced a low molecular weight product by heating lactic acid under vacuum. The inability, at this time to increase the molecular weight of the product, led to these studies being abandoned. Subsequent work by DuPont and Ethicon has focused on the manufacture of PLA for medical-grade sutures, implants and controlled drug release applications. More recently, companies, such as Shimadzu and Mitsui Tuatsu in Japan have been producing limited quantities of PLA for "commodity" plastics applications. However, in the absence of the economy of scale these products are still not economically viable. The recent advance in the fermentation of dextrose obtained from corn has dramatically reduced the cost to manufacture the lactic acid monomer necessary to make PLA polymers.

PLA can be manufactured with a wide range of properties, because of lactic acid being chiral with two asymmetric centers existing in four different forms. It can be made into a polymer with molecular weight ranging from a few thousands to over a million. It can be easily converted into film, fiber, spun bond and melt blown products on existing processing equipment.

PLA has practical medical applications as dissolvable sutures, as matrices for drug delivery, and bone fracture internal fixation devices in surgery [Vert et al., 1992]. Other applications include its role as agricultural plant growth promoter, in textiles, and non-woven applications such as fiberfill, crop covers, geotextiles, wipes, diapers, binder fibers, etc. However, the total volume of PLA production remains small compared to

other polymers (e.g. polyethylene reached a global level of 54 million tones in 2001, which can be compared to the figure of about 390,000 tones for PLA which is expected to be produced by 2008).

The major driver for PLA production is its high volume use as fibres. PLA was developed as an alternative binder for cellulosic non-wovens because of its ease of hydrolysis compared to polyvinyl acetate or ethylene-acrylic acid copolymers. Spun-laid and melt-blown non-wovens based on PLA were researched at the University of Tennessee, Knoxville in 1993 [Wandsworth, 1993]. Kanebo (Japan) introduced Lactron® (poly L-lactide) fibre and spun-laid non-wovens in 1994 claiming a capacity of 2000 tons per annum later expanded to 3000 tons per annum. It targeted agricultural applications to start with, and in 1998 was re-launched for apparel end-uses. At that time, Japanese demand for PLA fibres was said to be 500-1000 tons per annum. In order to improve the biodegradability and reduce the cost of the non-wovens, blends with rayon were also developed.

1.1 Lactic Acid – The Raw Material

The present global demand for lactic acid is estimated at 70,000 MT and India is only a minuscule market recording a current demand of 560 MT. Considering the global market trends, agro-based chemicals hold a promising future and the demand for lactic acid is expected to shoot up to 200,000 MT by the end of year 2011. A Netherlands-based company (PURAC) dominating the world in lactic acid production had recently forecast that if the production of biodegradable plastic catches on, the world demand for PLA and lactic acid would shoot up. The company's forecast seems to be turning true. Cargill Dow LLC, a joint venture between two renowned world leaders - Cargill Incorporated and Dow Chemical – has developed a new technology to produce performance polymers entirely from renewable resources - such as natural sugars derived from plants corn, wheat, beets and rice - and use fermentation to create lactic acid (a food additive) and some simple refining steps to create polylactide polymers. What make the lactic acid and its derivatives so endearing is their varied uses other than for biodegradable plastics. According to USDA scientists, "the chemical is commonly used in foods ranging from soda to sausages because it preserves, enhances flavour or imparts desired acidity.

Derivatives of lactic acid such as the solvent ethyl lactate can also be used in manufacturing electronic products, cosmetics, textiles, paints, adhesives, de-inkers and degreasers. Eco-friendly, chlorine-free ethyl lactate could also supplant most of the market for petroleum- derived solvents."

1.2 Future prospects of PLA [http://www.oit.doe.gov/cfm/full article.cfm/id=305]

The economic benefits include an estimated $2 billion/yr of net income that will accrue to the PLA manufacturing value chain in 2020. About $367 million/yr of new revenues will go to the agriculture community for harvesting, collection, and transportation of the feedstock. Energy benefits are estimated to save 202 trillion kJ/yr equivalent of fossil derived fuels in 2020 by the displacement of 8 billion/yr of fossil fuel-based polymers with PLA.

1.3 Advantages of PLA

(a) PLA is made from annually renewable resources. The first generation of PLA is produced from the corn, the cheapest and most widely available fermentable sugar in the world. In other parts of the world, locally available crops such as rice, sugar beets, sugarcane, wheat or sweet potatoes can be used as starch/sugar feedstock. Cargill - Dow is working to develop new conversion technologies to facilitate the use of lignocellulosic biomass feedstocks, such as corn stover (the residue left in the field), grasses, wheat and rice straws, and bagasse (the residue of sugar cane production).

(b) To produce PLA, fewer fossil resources are required. The conventional hydrocarbon polymers use limited reserves of oil and natural gas as their feedstock source. Fossil fuels take millions of years to regenerate. In contrast, the monomer for PLA is derived from annually renewable resources such as corn. Energy from the sun and carbon dioxide from the atmosphere are harnessed in agricultural crops. About one-third of the energy required for PLA is derived from these renewable resources, resulting in PLA utilizing 25-55 percent less fossil fuel than other polymers derived directly from hydrocarbons. This percentage is valid for the "cradle to the factory gate" part of the polymers life cycle.

(c) PLA emits less carbon dioxide because it uses renewable resources as a feedstock. Carbon dioxide is believed to be the most important contributor to global climate change (often referred to, somewhat inaccurately, as "global warming"). Because carbon dioxide is removed from the air when corn is grown, the use of PLA has the potential to emit fewer green house gases compared to competitive hydrocarbon based polymers.

(d) PLA fits into any waste management system with a benefit. At the end of their useful life, PLA products can be disposed of by all traditional waste management methods such as incineration, landfill and mechanical recycling. In addition, PLA products can be composted in industrial composting facilities, thereby providing an alternative means of managing municipal solid waste. Also chemical recycling (is recycling back to the monomer) and anaerobic digestions followed by a composting step are possible future routes.

(e) PLA is produced in environmentally friendly manufacturing processes. As stated before, sustainability is a journey and not an end-point. It is not time yet to declare victory, but PLA is a good start. The fundamental building blocks have been established and we are following a plan for creating an environmentally friendly manufacturing process.

(f) PLA has performance equal to or better than comparable petroleum-based products in many aspects. A product is sustainable only when it has an at least equivalent function as the products it is replacing. PLA meets and often exceeds this requirement.

(g) PLA possesses three major characteristics that make it a potentially attractive biomaterial:

1. It degrades in the body at a rate that can be controlled.
2. Its degradation products are non-toxic, biocompatible, easily excreted entities. PLA undergoes hydrolytic de-esterification to lactic acid, which enters the lactic acid cycle of metabolites. Ultimately it is metabolized to carbon dioxide and water and is excreted.
3. Its rate of degradation can be controlled by mixing it with the PGA polymer.

1.4 Ring-opening polymerization of PLA

Lactide monomers are synthesized by conventional process based on the cyclic compound synthesis through depolymerization of the corresponding oligomers, which are synthesized by polycondensation. This lactide dimer is then used for production of high molecular weight PLA through ring-opening polymerization.

Ring-opening polymerization of lactide can be carried out in melt, bulk, or in solution and by cationic, anionic, and coordination-insertion mechanisms depending on the catalyst. Various types of initiators have been successfully tested, but among them, stannous octoate is usually preferred because it provides high reaction rate, high conversion rate, and high molecular weights, even under rather mild polymerization conditions.

1.5 Why are mathematical models useful?

Mathematical models and their role in science and engineering are points of constant debate, especially when models are employed in an industrial environment. The role of a mathematical model is often misinterpreted; as a result, we frequently blame the model, instead of blaming lack of understanding about a process.

Why, then, are models useful?

1. Models enhance process understanding since they direct further experimentation. They act as the reservoir of one's knowledge about a process, and hence they may reveal interactions in a process that may be difficult, if not impossible, to visualize/predict solely from memory or experience, especially when many factors vary simultaneously. Since a model is a concise, compact form of process knowledge, models enhance transferability of knowledge. In a sense, mathematical modeling is the best way to find out what one does not know about a process.
2. Models are useful for process design, parameter estimation, sensitivity analysis, and process simulation. The significance of these is quite obvious. A valid model allows one to test deviations from process trajectories using a simulator in lieu of running experiments. Cost effectiveness implications are also obvious.

3. Models are useful for process optimization, especially when dealing with highly nonlinear problems such as grade changes/switchovers in batch, semi-batch, and continuous reactors. Extensions to recipe modifications and design are other applications.
4. Models are useful for safety/venting considerations. It is very useful to be able to extrapolated to different operating conditions and anticipate "worst case scenarios" or investigate the possible effects of process factors.
5. Models are useful for optimal sensor selection and testing, sensor location, filtering and inference of unmeasured properties. The trend nowadays in process control is toward "model-based" control, and as the term signifies, application of advanced control techniques may not be possible without a model.
6. Finally, since a model contains process knowledge and is transferable, interactive models are extremely useful for the education and training of new (and old) personnel.

1.6 Need for mathematical modeling of the ROP of PLA

Since the syntheses of PLA by Carothers in 1932, hundreds of research papers and patents have appeared in the literature. Now large size manufacturing units for PLA are being set-up. But, there is lack of data concerning the rate constants for initiation, propagation and termination steps of PLA polymerization except some data about the apparent rate constant. Also, it is extremely difficult to experimentally find the absolute values of different rate constants. Thus, there is a need for mathematical modeling which when used with the readily available experimental data for the average molecular weights, can predict the polymerization rate constants with sufficient accuracy in a short time.

1.7 Present Methodology

The progress of lactide polymerization has been modeled by assuming a ring opening reaction mechanism comprising of chain initiation, chain propagation, and chain termination. Appropriate differential equations have been developed incorporating the rate controlling reaction(s)/step(s). The resulting differential equations with appropriate

boundary conditions were solved using a numerical technique. Effect of unequal reactivity has also been incorporated in the model. The efficacy of model has been tested by comparing the predicted results on molecular weight and molecular weight distribution with those available in the published literature. The kinetic rate constants have been arrived at, for various PLA polymerization catalysts, by matching the simulated results with the experimental data. The method is extended to predict qualitatively the effect of water present as an impurity in the reactor on the PLA molecular weight.

Chapter - 2

Literature Review

2.0 Overview

Substantially large number of research papers and articles related to biodegradable polymers are available in the open literature. In the present chapter a brief review of the relevant literature about the synthesis of PLA, mathematical modeling of polymerization reactions, effect of impurities present during the polymerization on the molecular weight distribution (MWD) of polymers, and the effect of chain length dependent propagation rate constant on the molecular weight are presented.

2.1 Synthesis of PLA

2.1.1 Background

Poly(glycolic acid) (PGA) was synthesized in early 70's [Fruzza and Schmitt, 1971]. It was followed by the synthesis of high-molecular weight poly(lactic acid) (PLA) and copolymers of PLA and PGA [Gilding and Reed, 1981]. These α - polyesters have been investigated for use as sutures and as implant materials for repairing a variety of tissues [Ratner et al., 1996]. 'Vicryl' suture, a blend of PGA (90%) and PLA (10%) was introduced in USA in 1974.

PLA, first synthesized about 70 years ago, has finally arrived as an alternative to PET, HIPS, PVC, and cellulosics in some high-clarity packaging roles. PLA is being used in candy wrap, optically enhanced films, and shrink labels. It's also showing up as the sealant layer in form-fill-seal coextrusions. The novel resin is forging roles in thermoformed cups and containers and is about to appear in single-serve drink bottles. With increasing applications of PLA, considerable attention has been paid on its mechanical properties. A comparison of the mechanical and barrier properties of PLA and some other polymers is given in Tables 2.1, 2.2 and 2.3. Recent developments in the capability to manufacture the monomer economically from renewable feedstock have placed these materials at the forefront of the emerging biodegradable plastics industry. Increasing realization of the intrinsic properties of these polymers, coupled with the knowledge of how such properties can be manipulated to achieve compatibility with

Table 2.1 Properties of biaxial oriented films

(Source: http://www.plasticstechnology.com/articles/200203fa2.html)

	PLA	PP	PET	Nylon	Cellophane
Density, g/cc	1.25	0.9	1.4	1.2	1.45
Haze, %	2.1	1-4	2-5	2-3	1-2
Tensile Str., psi, MD	15,950	27,550 [a]	29,725 [a]	36,250	13,050 [a]
Tensile Mod., psi, MD	478,500	348,000	551,000 [a]	264,625	594,500 [a]
Ultimate Elongation, %, MD	160	110 [a]	140 [a]	125 [a]	23 [a]
Tear, g/mil, MD	15	4-6	18	13	4

MD: Machine direction

[a]: Median of a range of values

Table 2.2 Barrier performances of clear resins

(Source: http://www.plasticstechnology.com/articles/200203fa2.html)

Polymer	MVTR [a]	Oxygen Permeation [b]	CO_2 Permeation [b]
PLA	21	40	183
HIPS	10	300-400	NA
Nylon 6	23	3	NA
PET	1	3-6	15-25
PP	0.7	150	NA
PVC	2	5-20	20-50

[a] :g-mil/100 in.2-day. [b] :cc-mil/100 in.2-day-atm.

Table 2.3 Mechanical properties of PGA and PLA (Source: Engleberg and Kohn, 1991).

Polymer	Glass transition (^{o}C)	Melting temp. (^{o}C)	Tensile strength (MPa)	Flexural modulus (MPa)	Elongation yield (%)	Elongation break (%)
PGA (MW: 50,000)	35	210	n/a	n/a	n/a	n/a
PLA						
PLLA (MW:50,000)	54	170	28	1400	3.7	6.0
PLLA (MW: 1,00,000)	58	159	50	3000	2.6	3.3
PLLA (MW: 3,00,000)	59	178	48	3250	1.8	2.0
PDLLA (MW:20,000)	50	_	n/a	n/a	n/a	n/a
PDLLA (MW:1,07,000)	51	_	29	1950	4.0	6.0
PDLLA (MW: 5,50,000)	53	_	35	2350	3.5	5.0

n/a = not available, (_) = not applicable.

thermoplastics processing, manufacturing, and end-use requirements, have fuelled the technological and commercial interests in PLA products.

2.1.2 Monomer

Synthesis of a polymer begins with its monomer. Monomer of high molecular weight PLA, the lactide, is made from the lactic acid. An important feature of lactic acid is that it exists in two optically active forms L- and D- isomer (Figure 2.1). Fermentation derived lactic acid consists of 99.5% of the L-isomer. Production of the cyclic lactide dimer intermediate results in three potential forms. The D- and L- forms are optically active; the DL- (a mixture of the D- and L- forms) and Meso- form is optically inactive. The ratio of these three forms is readily controlled in the polymerization conditions by judicious selection of the initiator and reaction temperature. Ring opening polymerization of the lactide results in a "family" of polymers containing different isomer ratios and in a range of molecular weights. Polymers with high L- levels can be used to produce crystalline products whereas the higher D- levels (> 15%) result in an amorphous product.

The thermal, mechanical, and biodegradation characteristics of lactic acid polymers are known to depend on the choice and distribution of stereoisomers within the polymer chains. High-purity L- and D- lactides form stereo regular isotactic poly(L-lactide) (PLLA) and poly(D-lactide) (PDLA), respectively. These are semi-crystalline polymers with a high melting point ~ 180°C and a glass transition temperature in the 55-60°C range. The degree of crystallinity depends on many factors, such as molecular weight, thermal and processing history, and the temperature and time of annealing treatments. The *meso*- and DL-lactide, on the other hand, form atactic poly(DL-lactide) (PDLLA), which is amorphous [Thakur et al., 1996]. The mechanical properties and degradation kinetics of the semi-crystalline PLLA are quite different from those of completely amorphous PDLLA. In particular, PLLA is always preferred whenever higher mechanical strength and longer degradation time is required [Fambri et al., 1997].

The PLA lifecycle is shown in Figure 2.2. After formation of PLA oligomers from lactic acid by removal of water, depolymerization of oligomers takes place to give a thermodynamically favored lactide. This monomer is readily polymerized under vacuum

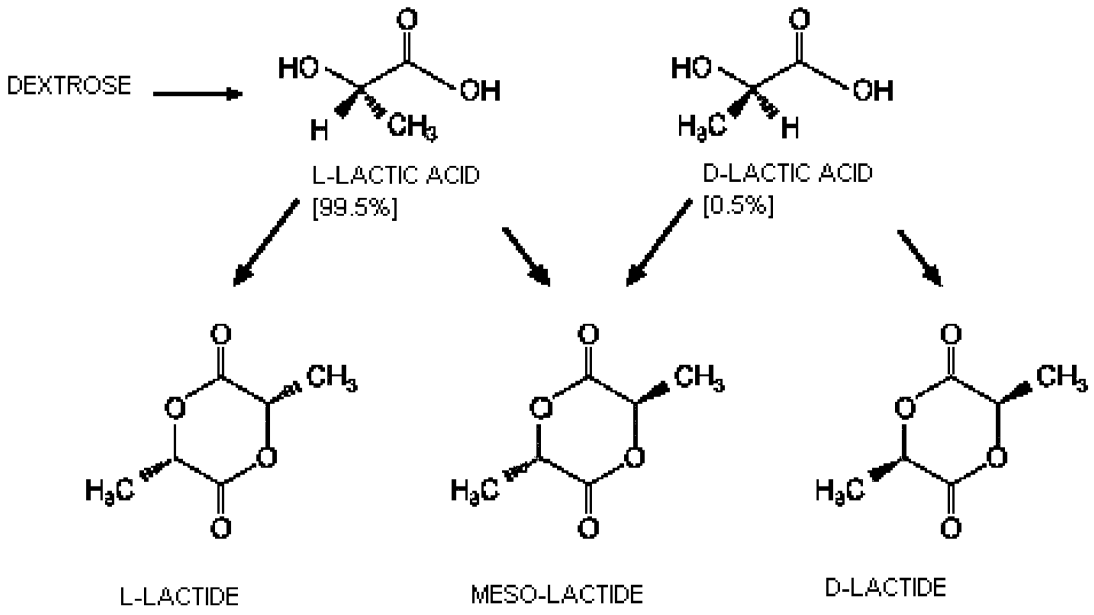


Fig. 2.1 Three different lactides

(Source: http://www.technica.net/NF/NF3/biodegradable.htm)

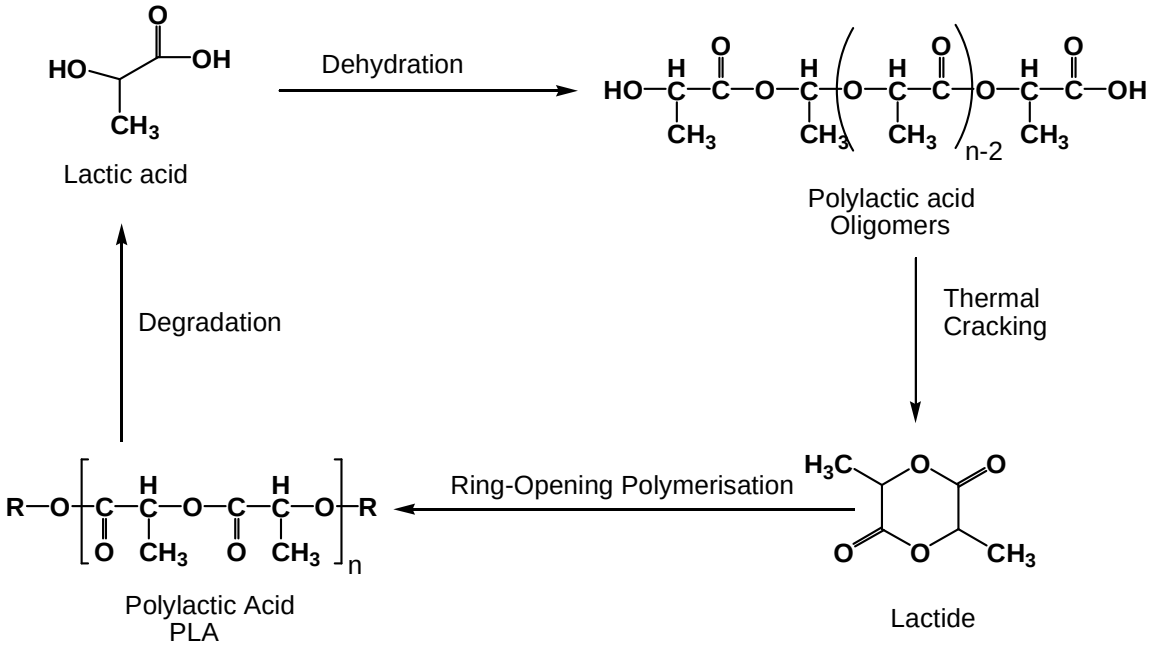


Fig.2.2 PLA lifecycle

distillation. It is used to produce high molecular weight PLA by ring-opening polymerization. The most desired property of the polymer, i.e. degradability, comes in the last step when the high molecular weight PLA degradeds to lactic acid in presence of water.

2.1.3 Synthesis of PLA from Lactic Acid

There are two major routes to produce PLA from the lactic acid monomer (Figure 2.3). The first route involves removal of water of condensation by the use of solvent under high vacuum and high temperature (condensation polymerization). In the other route, water is removed under mild conditions to give an intermediate dimer, the lactide, which on ring-opening polymerization gives high molecular weight PLA.

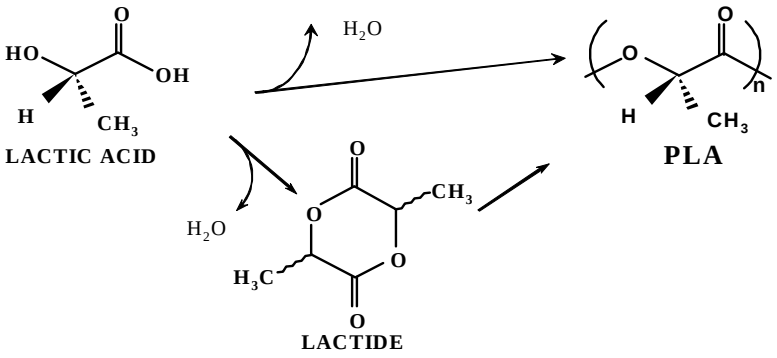


Fig. 2.3 Preparation of PLA

2.1.3.1 Synthesis of low molecular weight PLA by condensation polymerization

Polycondensation of lactic acid is usually performed in bulk by distillation of condensation water, with or without catalyst, while vacuum and temperature are progressively increased. Although, high molecular weight polyesters with good mechanical properties are not easy to obtain, the properties of lactic acid oligomers, which can be further used as intermediates in the synthesis of polyurethanes, can be controlled by the use of different catalysts and functionalization agents, as well as by

varying the polymerization conditions [Gruber et al., 1993a,b; Hiltunen and Seppala, 1998; Hiltunen et al., 1997]. This approach was originally developed by Carothers and is still used by Mitsui Toatsu Chemicals Inc. to manufacture a low to intermediate molecular weight polymer.

Addition of acidic catalysts, such as boric or sulfuric acid accelerates the esterification and transesterification processes, but also catalyzes side reactions at temperatures above 120 ^{o}C. Therefore, polycondensation of aqueous DL-lactic acid never gave M_n's above 3000 [Filachone and Fisher, 1944; Watson, 1948], as against M_n's up to 6500 reported for pure L-lactide. When the precondensates obtained by dehydratization up to 120 ^{o}C are heated to 180 ^{o}C in presence of nonacidic transesterification catalysts, such as PbO, a moderate yield of relatively high-molecular weight PLA may result [Schneider and Wilmington, 1955]. Yet, even the low molecular weight precondensates may be of interest for the preparation of biodegradable glues or lacquers, because the -OH and -COOH end groups allow cross-linking with suitable inorganic or organic multivalent additives [Watson, 1948].

Polycondensation method produces oligomers with average molecular weights several tens of thousands lower than those of PLA synthesized by one-step polycondensation of lactic acid if appropriate azeotropic solvents are employed [Lunt, 1998; http://www.cargilldow.com; Hyon et al., 1997]. This polymer can be used as it is, or can be coupled with isocyanates, epoxides or peroxide to produce polymers having a range of molecular weights. In an alternative method, route two, it is possible to synthesize high molecular weight PLA which finds applications in biomedical and pharmacological areas.

2.1.3.2 Synthesis of high molecular weight PLA by ring-opening polymerization of lactide

Water is removed under mild conditions, without solvent, to produce a cyclic intermediate dimer, referred to as lactide. This monomer is readily purified by vacuum distillation accomplished by heating, again without the need for solvent. By controlling the purity of the dimer it is possible to produce a wide range of molecular weights.

PLA has been produced commercially worldwide since the last decade. The catalyst currently used industrially is stannous octoate (zinc metal has been in use in France). Ring-opening polymerization of lactide can be carried out in melt, bulk, or in solution and by cationic, anionic, and coordination-insertion mechanisms depending on the catalyst [Lofgren et al., 1995; Mercerreyes et al., 1999; Nieuwenhuis, 1992]. The choice of initiator system, co-initiators as chain control agents, catalyst concentration, monomer-to-initiator ratio, and polymerization temperature and time significantly affect the polymer properties. These properties, such as the molecular weight, degree of crystallinity and residual monomer content, in turn affect the physical-mechanical properties and temperature use range of the polylactide and its copolymers [Duda et al., 2000; Grijpma and Pennings, 1991; Kim et al., 1993; Leenslag and Pennings, 1987; Prego et al., 1996; Vert et al., 1995; Vion et al., 1986]. The role of the racemization and the extent of transesterification in the polymerization and copolymerization process are also decisive for the enantiomeric purity and chain microstructure of the resulting polymer [Bero et al., 1990; Chabot et al., 1983; Kasperczyk and Bero, 2000; Kricheldorf and Kreiser, 1987]. Many current PLA polymerization methods employ stannous octoate as the catalyst. It has been shown to be very effective, causes a low degree of racemization at high temperature [Kricheldorf and Serra, 1985], has low toxicity, and is accepted by the US Food and Drug Administration.

A selective summary of literature on PLA synthesis is given in the Table 2.4. Other recent studies include dimeric aluminum chloride complexes of N-alkoxyalkyl- β-ketoimines (activation with propylene oxide)[Doherty et al., 2004], alkoxy-amino-bis (phenolate) Group 3 metal complexes [Cai et al., 2004], aluminum complexes bearing tetradentate bis(aminophenoxide) ligands [Hormnirm et al., 2004], hetero-bimetallic iron(II) alkoxide/aryloxides [McGuinness et al., 2003], stannous octoate and diethanolamine [Li et al., 2003]. β –diiminate ligated magnesium and zinc amides [Chrisholm and Phomphrai, 2003], zinc alkoxide complex [Williams et al., 2003], titanium alkozide [Kim et al., 2003], iron alkoxide [Gibson et al., 2002], 2,6- dimethyl aryloxide [Zhang et al., 2004], calcium coordination complexes [Chrisholm et al., 2003], complexes of Cu, Zn, Co and Ni Schiff base derived from salicylidene and L-aspartic acid [Sun et al., 2002], dizinc-monoalkoxide complex supported by a dinucleating ligand

[Williams et al., 2002], stannous octoate with adducts containing oligomers L-lactide and rac-lactide [Storey et al., 2002], tertiary amines, phosphines and N-heterocyclic carbenes [Connor et al., 2002], alkyl aluminum [Chang and Sun, 2002], aluminum – achiral ligands complexes [Nomura et al., 2002] and lithium chloride [Xie et al., 1999]. In one of the earlier studies, Baker and Smith [2002] documented a procedure of PLA synthesis from racemic materials.

In some of the studies, the monomer (lactide) has been used as received [Stevels et al., 1995] and in others it has been used after recrystallizing it from solutions in solvents like chloroform, ethyl acetate, acetone etc. [Stolt and Sodergard, 1999]. It has been reported that recrystallized L-lactide gives higher intrinsic viscosities than those obtained for the once-recrystallized monomer [Kricheldorf et al., 1998; Kricheldorf and Lee, 1995]. Also, treatment of the reaction kettle with dichlorodimethyl silane (silanizer) favors a higher molecular weight product. The monomer to initiator ratio has varied from 50 to 50,000 in various studies. The operating conditions have also varied considerably. In some cases stirring of the mixture is employed and in others the reaction kettle is sealed and kept in an oven [Schwach et al., 1996; Zhang et al., 1994]. The reaction environment is either air [Kricheldorf and Lee, 1995] or an inert gas [Schwach et al., 1994] or vacuum [Schwach et al., 1996]. The reaction product is dissolved in an appropriate solvent (CH_2Cl_2, $CHCl_3$ or acetone) and precipitated into diethyl ether/ methanol and then filtered and dried. The polymer identification is done by ^{1}H NMR, ^{13}C NMR and FTIR techniques. Characterization of various PLA by NMR [Kasperczyk, 1999] and by IR [Kisher et al., 1998] has been studied. The molecular weights are determined by various ways including measurement of intrinsic viscosity and calculation of M_n by using Mark-Houwink equation [Schindler and Harper, 1979] in chloroform or benzene, Gel permeation chromatography and ^{13}C NMR. The residual solvents are assayed by GC.

Table 2.4 A selective summary of studies on PLA polymerization variables and molecular weight

S.No.	Polymer	Catalyst	Solvent(s)	Reaction Temp. ^{o}C	Reaction time	Molecular weight	Reference
1.	PDLLA PLLA	Al Isopropoxide	Toluene	70-100	Up to 100 hr	M_n>90,000	Dubois et al., 1991
2.	PLLA	Stannous octoate	Glycerol	130	6 hr	DP_n=43-178	Han and Hubbell, 1996
3.	PDLLA PLLA	Stannous octoate	Alcohols	200	60-75 min	M_w<3,50,000	Korhonen et al., 2001
4.	PLLA DLPLA	Stannous octoate	Alcohols, carboxylic acid	130	2-72 hr	M_n<2,50,000	Zhang et al., 1994
5.	PLLA	Stannous octoate	No solvent	130	72 hts.	M_v:=20,000-6,80,000	Hyon et al., 1997
6.	PLLA	Stannous octoate and triphenylamine	No solvent	180-185	7 min	M_n=91,000	Jacobsen et al., 2000
7.	PLLA PDLLA	Stannous octoate and compounds of titanium and zirconium	Toluene	180-235	15-180 min	Mn=40,000-100,000	Rafier et al., 2003
8.	PDLA PLLA PDLLA	Stannous trifluoromethane sulphonate, Scandium(III) trifluoromethane sulfonate	Ethanol	40-65	50-100 hr	DP_n=15-30	Moller et al., 2001
9.	PLLA	Sn substituted mesoporous silica molecular sieve	No slovent	130	72 hr	M_n<36,000	AbdelFattah et al., 1996
10.	PLLA	Mg, Al, Zn, Titanium alkoxides	Methylene chloride	100	-	DP_n<400	Kricheldorf et al., 1998
11.	PLLA	Yttrium tris(2,6-di-teert butyl phenolate) (in toluene)	2-propanol, butanol, ethanol	22	2-5 min	M_n<25,000	Stevels et al., 1995

S.No.	Polymer	Catalyst	Solvent(s)	Reaction Temp. ^{o}C	Reaction time	Molecular weight	Reference
12	PDLLA	Butyl lithium, butyl magnesium (in hexane)	THF	-	30 min	M_n<45,000	Kasperczyk and Bero, 2000
13.	PDLLA	Zn lactate	No solvent	140	96 hr	M_n=212,000	Schwach et al., 1996
14.	PDLLA PLLA	Butylmagnesium, Grignard reagent	Ethers	0-25	4-8 days	M_n<3,00,000	Kricheldorf et al., 1995
15.	PLLA	Potassium naphthalenide	THF, Toluene	40	48-120 hr	M_n<16,000	Stere et al., 1998
16.	PLLA	Complexes of iron with acetic, butyric, siobutyric and dichloroacetic acids	No solvent	170-210.	0.5-25 hr	M_w=1,50,000	Stolt et al., 1999
17.	PDLLA	(Trimethyl triazacyclohexane) praseodymium triflate	No solvent	120-200	18 hr	Mv= 10,000-20,000	Kohn et al., 2003
18.	PDLLA	Lanthanum isopropoxide	Dichloromethane/toluene (70/30)	21	30 min	Mn= 5,300-21,900	Save et al., 2002
19.	PLA (type not specified)	Lead monoxide, lead stearate, basic lead carbonate, antimony trioxide, zinc oxide, cadmium oxide, titanyl stearate, and calcium formate	No solvent	140-180	10-111 hr	IV(in benzene)= 1.21	Schneider et al., 1955

2.1.4 Single-step Reactive Extrusion

In order to make the manufacturing of PLA economically viable, Jacobsen et al. [2000] developed a continuous one-stage process using reactive extrusion technology. This technique requires that the bulk polymerization is close to completeness within a very short time (5-7 min), which is predetermined by the residence time of the extrusion system and that the PLA stability is high enough at the processing temperature. Even though stannous octoate can promote quite fast lactide polymerization, it is also known to have adverse effect on the PLA molecular weight and properties, as a result of back-biting and intermolecular transesterification reactions, not only during the lactide polymerization but also during any further melt processing [Gogolewshi et al., 1993]. The authors showed that the addition of an equimolar amount of a Lewis base, particularly triphenylphosphine onto stannous octoate, significantly enhances the lactide polymerization rate in bulk. Also the influence of process parameters on the final polymer properties was studied. The kinetic effect has been accounted for by coordination of the Lewis base onto the metal atom of the initiator making the insertion of the monomer into the metal alkoxide bond of the initiator easier.

An important task for developing new catalytic systems is to make the catalyst more compatible with the purpose of biomedical applications. Stannous octaote has been one of the most effective catalysts that produces both high yields and high molecular weights. However, like many other catalysts, the cytotoxicity and difficulties in removal of the catalyst from the resulting polymer have limited its utilization in many cases. Additionally, triphenylphosphine is also not likely to be any safer.

2.1.5 Continuous Process for Production of PLA from Lactic acid

A continuous process for manufacture of PLA with controlled optical purity (Figure 2.4) has been described by Gruber et al. [1992, 1993, 1994, 1999, 2001a, b]. The process involves formation of PLA as a low molecular weight condensation product. This is followed by depolymerizing the PLA in a lactide reactor to form crude lactide, which is purified in a distillation system. A purified lactide is then polymerized to form lactide polymers.

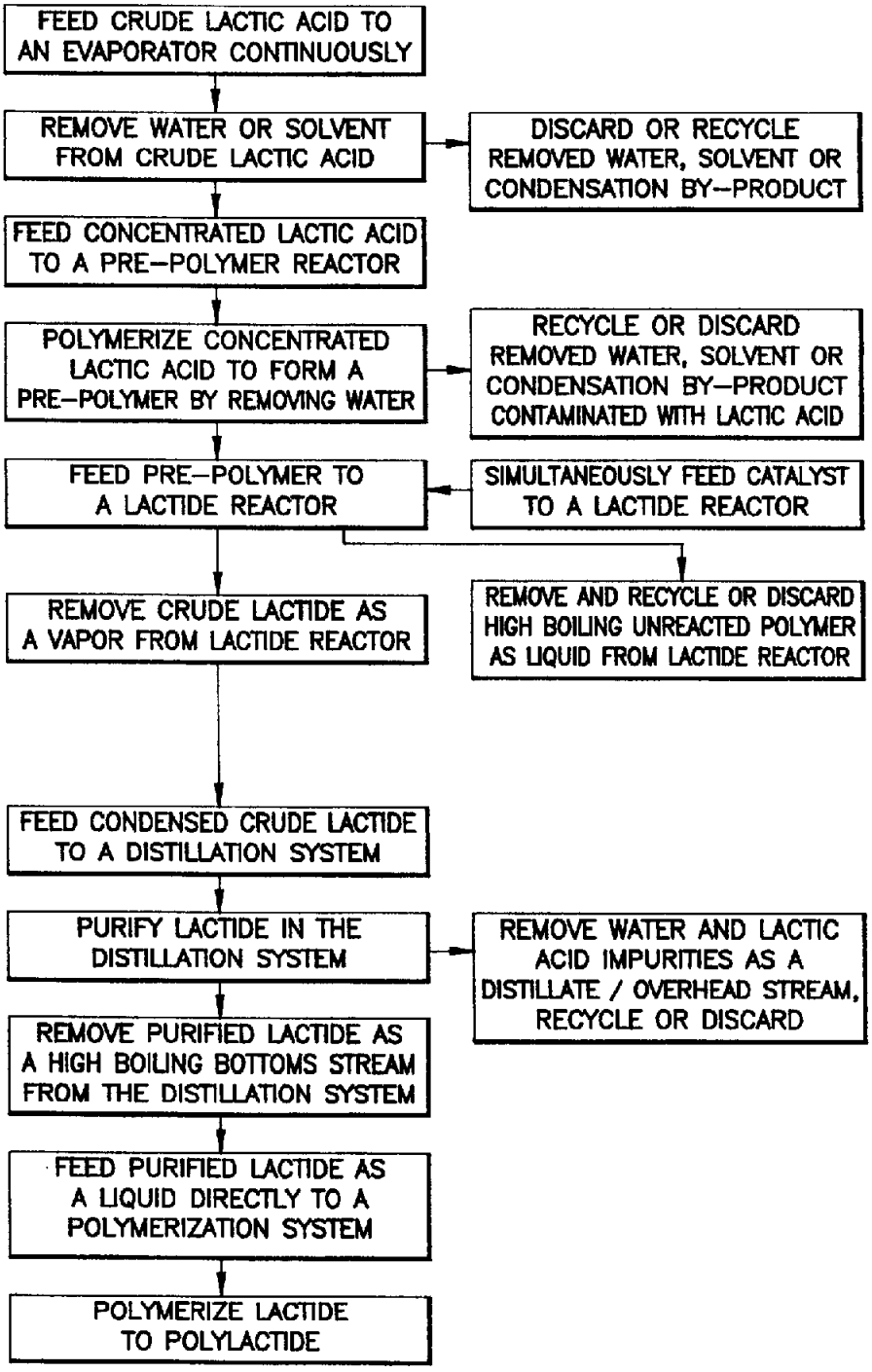


Fig. 2.4 Schematic flow chart of the continuous process for the manufacture of PLA from lactic acid (Source: Gruber et al., 1993).

The crude lactic acid feed is a solution of about 15% lactic acid and about 85% water, and is available commercially. The feed is concentrated by removing water or any other solvent such as methanol, ethanol etc. or hydrolytic medium, which are used as a carrier for the lactic acid, a partial vacuum may be applied in the evaporator. The lactic acid is concentrated to about 99% and transferred to a prepolymer reactor. The prepolymer reactor is essentially a second evaporator system to further remove water or solvent from the lactic acid. It is known that lactic acid undergoes a condensation reaction to form PLA as water is removed. Thus, PLA up to a molecular weight of about 5000 is prepared in the prepolymer reactor. This is transferred to lactide reactor where an appropriate catalyst and process stablizers are added. The mean residence time in the lactide reactor is kept as low as possible. Thus, falling film and thin-film evaporators are used. The lactide is removed continuously from the reactor as vapor. The removal of lactide further drives the depolymerization reaction. The lactide vapors are transferred to a distillation unit for purification. The refined lactide is removed from the distillation system and fed to a polymerization reactor for ring-opening polymerization yielding high molecular weight PLA.

The crude lactic acid feed to this process may be made up of L-lactic acid or D-lactic acid, or combination thereof. The composition of the feed, however, does not translate directly into the polymer during the polymerization. Racemization or conversion of one optical enantiomer to the other may occur. Such racemization is driven by such factors as temperature, pressure, and time at a given temperature or pressure, the presence of catalysts or impurities, and relative concentrations of the two enantiomers at any given time. Amorphous films [Gruber et al., 1996, 1998, 1999, 2001] as well as semi-crystalline films [Gruber et al., 1996, 1998, 2000a, 2000b] can be made from PLA, in a continuous process.

2.1.6 PLA Blends and Composites

A review of the PLA blends has been given by Kylma [2001]. There are two main considerations: miscibility or compatibility, and biodegradability of the second component. Several blend systems containing PLA have been investigated, such as blends of PLA with poly (ε -caprolactone) [Hiljanen-Vainio et al., 1996; Meredith and

Amis, 2000; Tsuji and Ikada, 1996] poly((R)-3-hydroxybutyrate) [Blümm et al., 1995; Koyama and Doi, 1997; Ohkoshi et al., 2000], poly((R)-3-hydroxybutyrate-co-(R)-3-hydroxyvalerate) [Iannace et al., 1994], poly(ethylene oxide) [Nakafuku and Sakoda, 1993; Nijenhuis et al., 1996; Sheth et al., 1997] and poly(vinyl acetate) [Gajria et al., 1996]. Most of the blends have been found to be immiscible with a phase separated morphology. An interesting phenomena in blends of PLLA and PDLA is the formation of a stereocomplex. The PLA stereocomplex is found to possess a racemic crystalline structure, where PDLA and PLLA chains are packed side by side with a D- monomer unit to L- monomer unit in the ratio of 1:1. One of the most interesting findings in PLLA/PDLA stereocomplexation studies is that the melting temperature of the stereocomplex is 230°C, approximately 50°C above that of the corresponding homopolymer. This enantiomeric polymer blend also exhibits substantially higher tensile properties and better thermal stability and hydrolysis resistance than the polylactides from which the blends are prepared [Brochu et al., 1995; Ikada et al., 1987]. An excellent review of the mechanical properties of biodegradable polymers has been prepared by Daniels and co-workers (Figures 2.5 and 2.6) [Daniel et al., 1990]. Their review revealed that unreinforced biodegradable polymers are initially 36% as strong in tension as annealed stainless steel, and 54% in bending, but only 3% as stiff in either test mode. With fiber reinforcement, the highest initial strengths exceeded those of stainless steel. Stiffness reached 62% of stainless steel with nondegradable carbon fibers, 15% with degradable inorganic fibers, but only 5% with degradable polymeric fibers.

Totally bioresobable composite plates have been made from PGA fibers embedded in a PLA matrix. The time evolution of the properties of the PLA can be controlled by making stereo copolymers of D- and L- lactic acid. The number of D-units apparently controls the degradation rate. These composites are bioresorbable, exhibit good biocompatibility with the tissues in which they are implanted, and have adjustable resorption rates, depending on the relative amounts of L- and D- lactic acid units as well as on the quantities of GA and LA repeating units. This concept of bioresorption or biodegradability is an important one in many areas of bioimplants [Boretos and Eden, 1984].

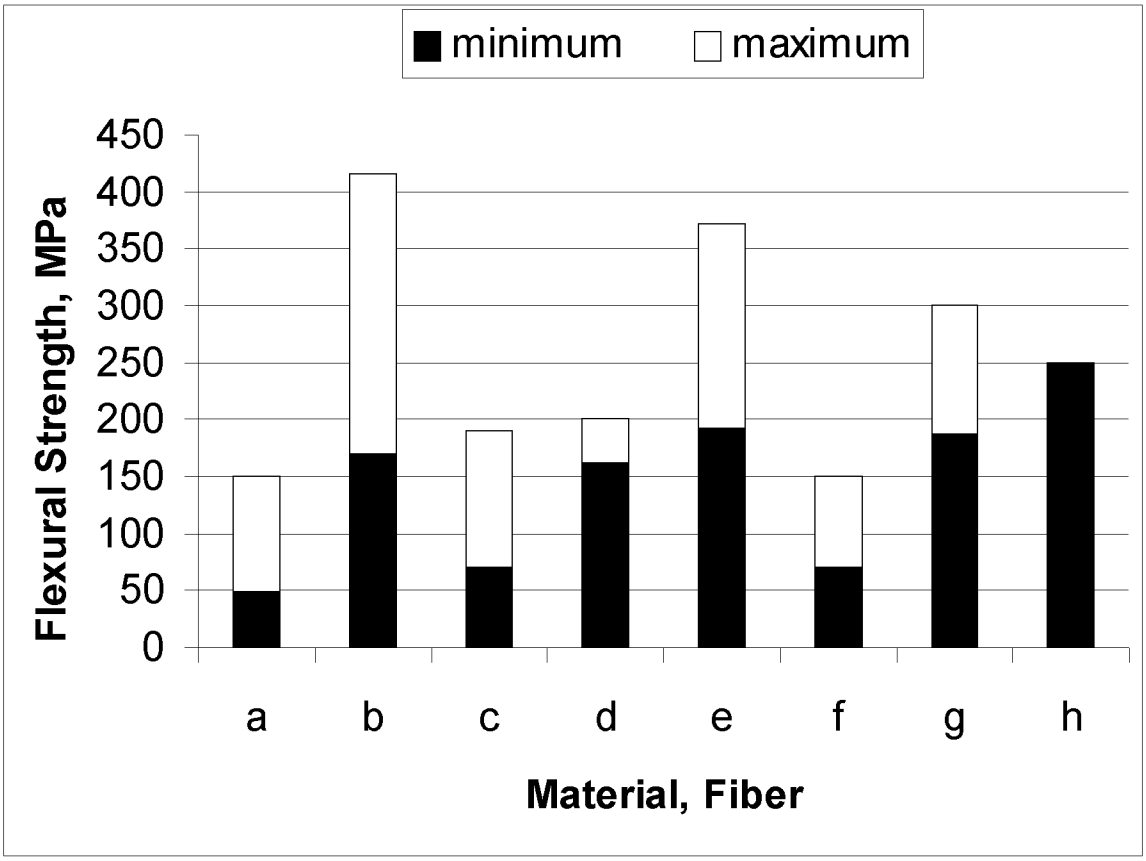


Fig. 2.5 Representative flexural strengths (MPa) of absorbable polymer composites, a-PLA; b-PLA,carbon; c-PLA,inorganic; d-PLA,PLA; e-PGA.PGA; f-PGA/PLA; g-PGA/PLA, carbon; h-PGA/PLA, PGA/PLA (Source: Daniel et al., 1990).

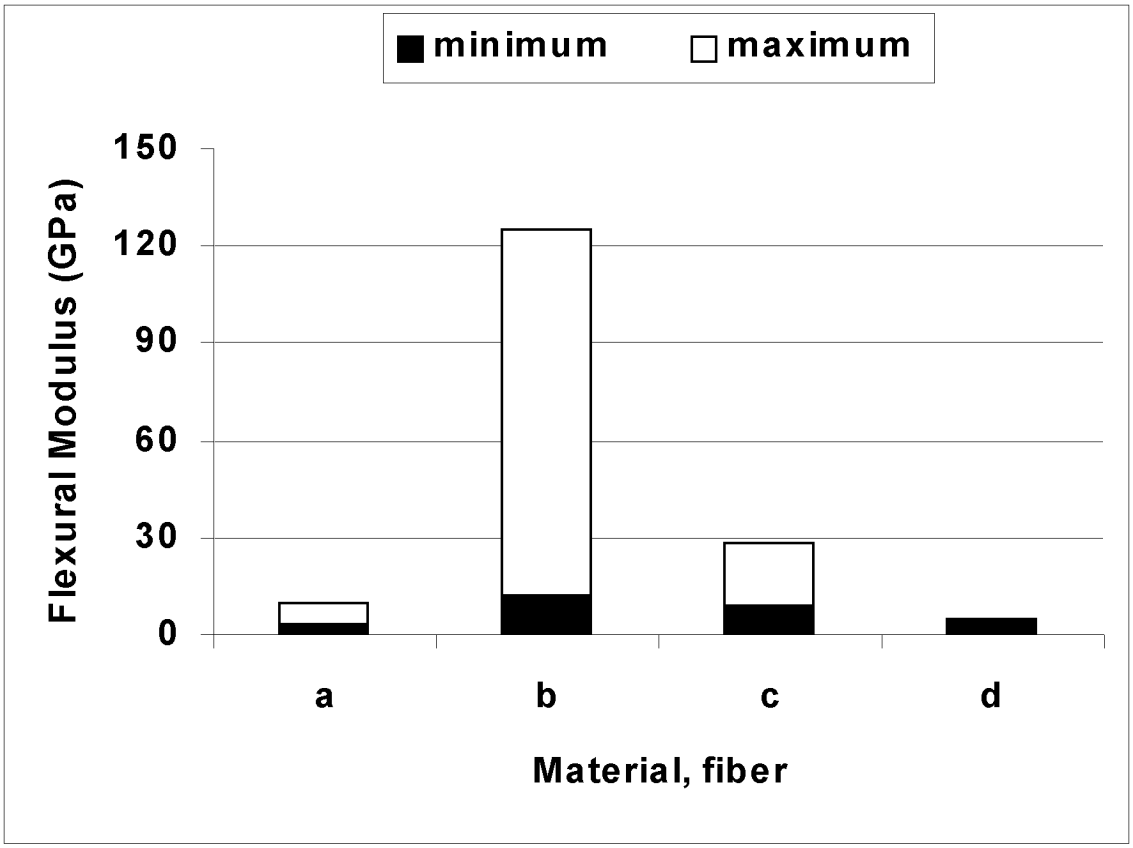


Fig. 2.6 Representative flexural moduli (GPa) of abosorbable polymer composites, a-PLA; b-PLA, carbon; c-PLA, inorganic; d-PLA,PLA (Source: Daniel et al., 1990).

Composites of PLA have been made with jute fibers [Ouchi et al., 2003] and bioactive glass [Roether et al., 2002]. Nano-composites have been made with organo-modified montmorillonites [Paul et al., 2003] and silicates [Maiti et al., 2002; Sinha et al., 2002; Sinha et al., 2003].

2.1.7 Polymerization Mechanism

There has been an increasing interest in the development of simple efficient catalytic systems for the ring-opening polymerization of lactide. Some of the polymerization conditions and the molecular weights of the products are also given in Table 2.4. The mechanism through which the catalyst works has been suggested for some systems. It has been demonstrated that lactone polymerization using aluminum and tin alkoxides proceeds via an insertion mechanism [Barakat et al., 1993; Kricheldorf et al., 1998; Mukaiyama et al., 1983]. Furthermore, when tin halogenides are used as catalysts, it has been proposed that they are actually converted into tin alkoxides, which are the real active species in the polymerization process [Kricheldorf and Sumbel, 1989]. Kricheldorf et al. [1998] suggested that for various metal alkoxides, the ring opening of the lactones involves the cleavage of the acyl-oxygen bond and the alkoxide groups of the initiator form alkyl ester end-groups. Dubois et al. [1991] suggested that the ring opening polymerization using aluminium isopropoxide proceeds through a 'coordination–insertion' mechanism and selective rupture of the acyl-oxygen bond of the monomer, as shown in Figure 2.7. Zhang et al. [1994] studied the effect of hydroxyl and carboxylic acid substances on lactide polymerization in the presence of stannous octoate. Stannous alkoxide, a reaction product between stannous octoate and alcohol, was proposed as the substance initiating the polymerization through coordinative insertion of lactide. Alcohol could affect the polymerization through reactions leading to initiator formation, chain transfer, and transesterification. Carboxylic acids affect the polymerization though a deactivation reaction. Experiments have shown that alcohol increases PLA production rate while carboxylic acid decreases it. The higher the alcohol concentration, the lower is the polymer molecular weight. However, the final molecular weight of PLA is not sensitive to the carboxylic acid concentration.

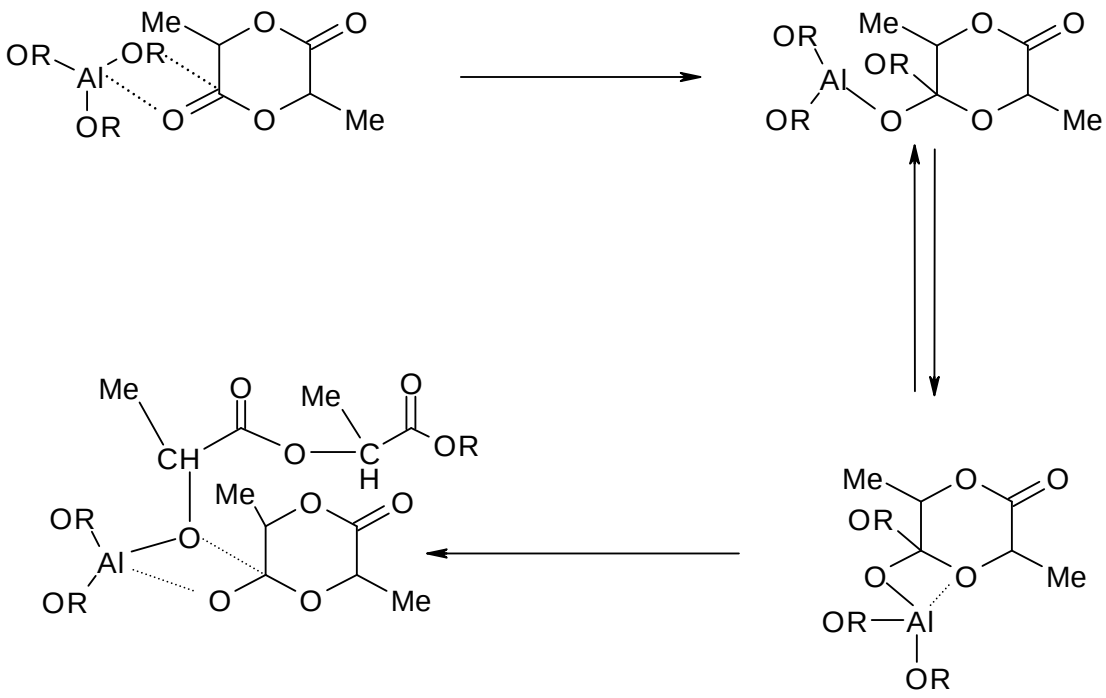
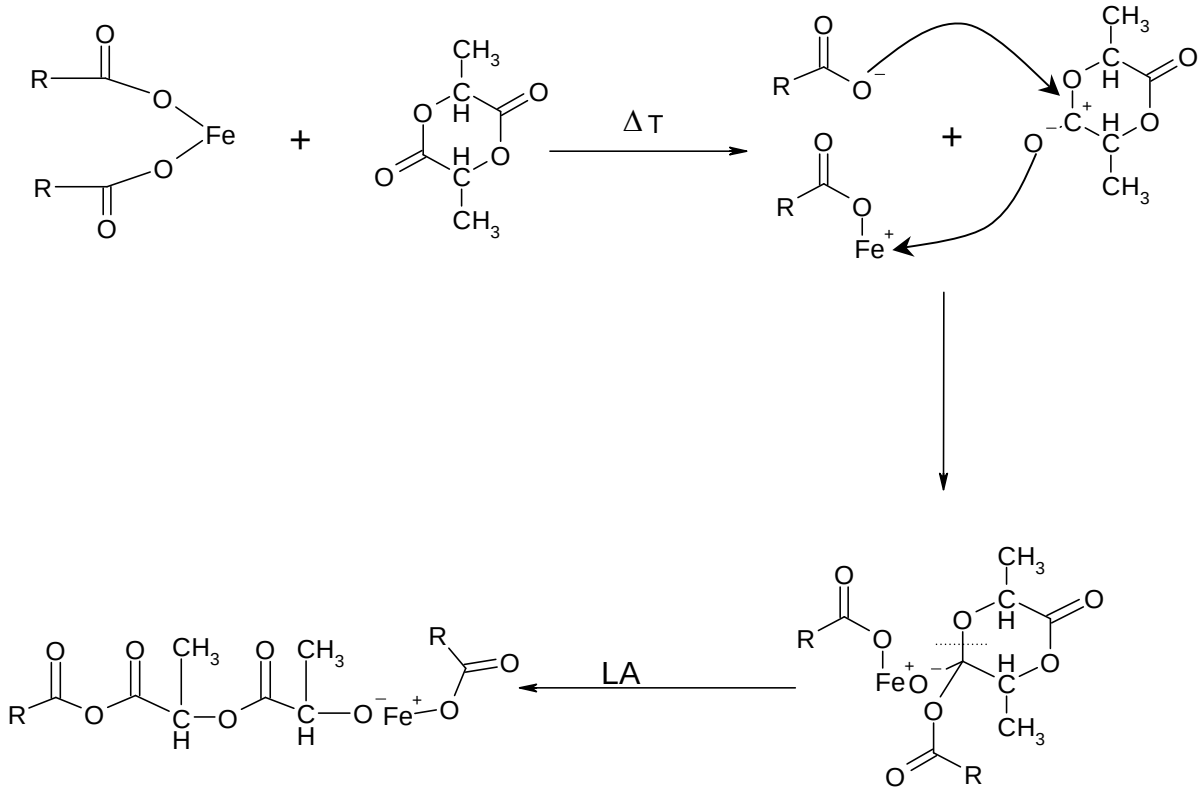


Fig. 2.7 The mechanism of PLA polymerization using Aluminum Isopropoxide as catalyst (Source: Dubois et al., 1991).

Stolt and Sodergard [1999] reported the ring-opening polymerization of L-lactide using different organic monocarboxylic iron complexes. It was observed that the acetate anion as well as the iron, are chemically attached to the polymer chain, and the proposed polymerization mechanism is an anionic type of coordination insertion as described in Figure 2.8.

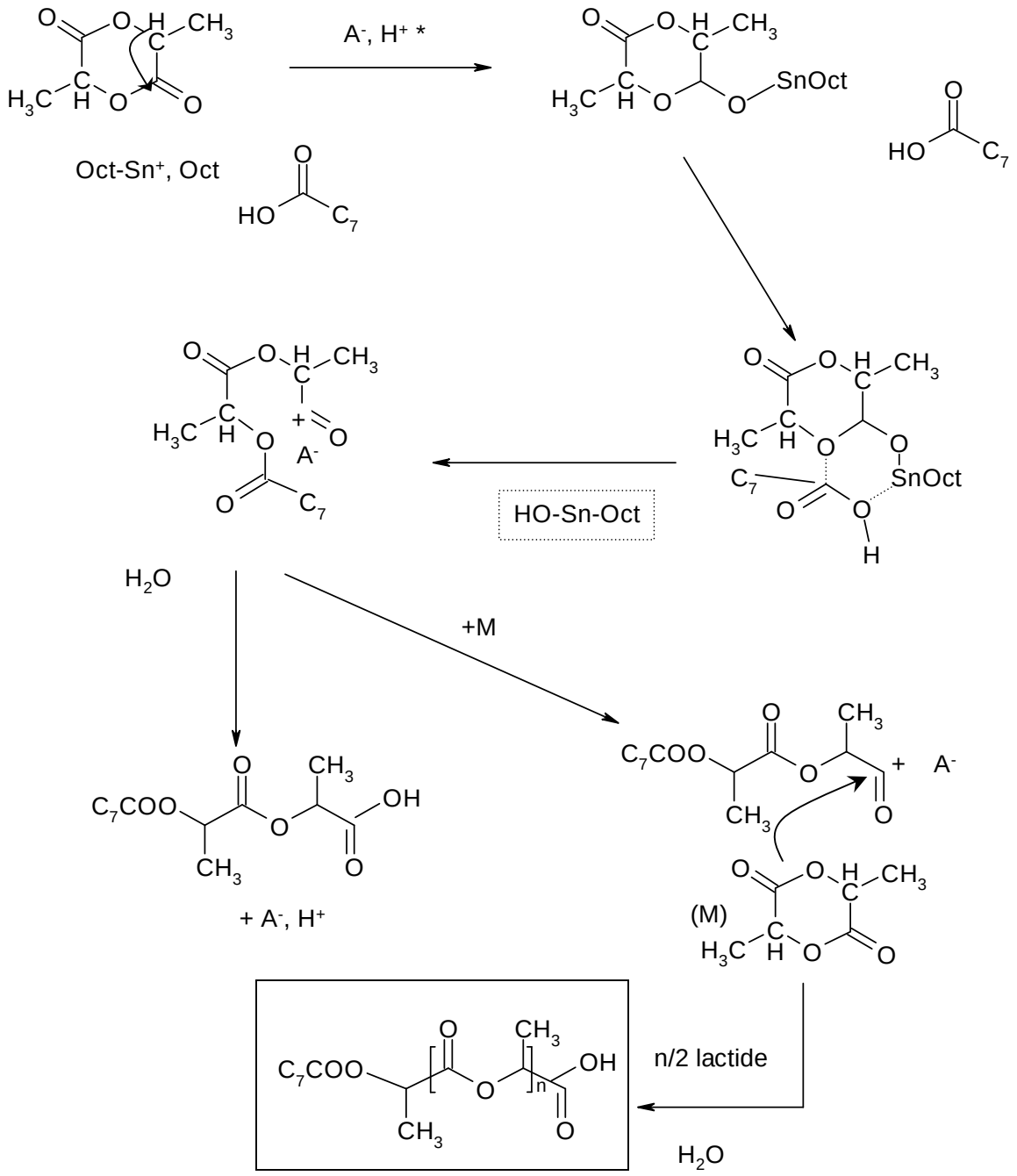
Schwach et al. [1997] reexamined the ring-opening polymerization of PLA in the presence of stannous octoate under conditions allowing for the end-group characterization of growing chains by high-resolution ^{1}H-NMR. For low values of monomer to initiator ratios, the DL-lactide ring was opened to yield lactyl octoate-terminated short chains. A cationic-type mechanism involving co-ordination by octanoic acid was proposed by Schwach et al. [1997] to account for experimental findings (Figure 2.9). In another work [Schwach et al., 1994], the same group studied the bulk polymerization of PLA using stannous octoate and zinc metal as catalysts. A two-level fractional factorial design was used to assess the influence of selected experimental variables with respect to intermolecular transesterification. Within the range of the selected variables, a hierarchy of average effects was established as: polymerization temperature > monomer–to-initiator ratio > polymerization time > initiator > monomer degassing time. The investigation tool used was ^{13}C NMR. In another study Schwach et al. [1998] reported the polymerization of DL- lactide in the presence of zinc metal. The results showed that the polymerization was water sensitive and that only a fraction of zinc was active. A small amount of zinc lactate was present and was proposed to be the actual initiator.

Kricheldorf and Boettcher [1993] studied the polymerization of racemic and meso DL- lactide at 120 ^{o}C in xylene solution or in bulk. Lead oxide (PbO), zinc stearate, antimony (III) 2-ethylhexanoate, and bismuth(III) 2-ethylhexanoate were used as initiators. High yields (greater than or equal to 90%) were obtained only with PbO and Bi(III) 2-ethylhexanoate, but the molecular weights were low in all cases. At higher reaction temperatures, the resulting stereosequences showed an increasing tendency toward randomness. In another study [Kricheldorf and Dunsing, 1985], the same group tested various acidic compounds as potential initiators of the cationic polymerization of



R = CH_3, $CHCl_2$, CF_3, $CH_3(CH_2)_2$, $(CH_3)_2CH$

Fig. 2.8 An anionic type of coordination insertion mechanism for organic monocarboxylic iron complexes as catalysts (Source: Stolt and Sodergard, 1999).



(*) From lactic acid or octanoic acid

Fig. 2.9 Cationic octanoic acid co-initiated mechanism of lactide polymerization in presence of stannous octoate (Source: Schwach et al., 1997).

L-lactide. Regardless of the solvent and temperature, only trifluoromethanesulfonic acid and methyl triflate proved to be useful initiators.

Stannous (II) triflouromethane sulfonate and scandium(III) trifoloromethane sulfonate have also been studied as catalysts for PLA synthesis [Moller et al., 2001]. It was found that polymers of predictable molecular weights and narrow polydispersities could be obtained. The addition of base either as a solvent or as an additive significantly enhanced the polymerization rate with minimal loss to the polymerization control.

Leenslag and Pennings [1987] studied the polymerization of L-lactide as a function of polymerization temperature, time and concentration of catalyst (stannous octoate). PLA with the highest value of intrinsic viscosity (viscosity average molecular weight, $M_v = 10^6$) was synthesized at a low catalyst concentration (0.015 wt%) and at the temperature of 100^{o}C. The M_w/M_n ratios of PLA samples ranged from 2 to 3. The experimental results suggested a nonionic insertion polymerization mechanism. In contrast to this study, using the same catalyst, Hyon et al. [1997] obtained PLA with the maximum molecular weight at a catalyst concentration of 0.05% at 130 ^{o}C. In this study, the decrease in M_v at prolonged polymerization and higher polymerization temperature was attributed to thermal depolymerization of the resultant polylactides. In contrast to this, the drop in M_n in the polymerization using aluminium isopropoxide [Dubois et al., 1991] at higher temperatures and higher monomer-to-initiator ratio was attributed to intra- and inter- molecular transesterification reactions.

Nijenhuis et al. [1992] studied the kinetics and mechanism of L-lactide bulk polymerization using stannous octoate and zinc bis(2,2-dimethyl-3,5-heptanedionate-O,O'). Up to 80% conversion, the rate of polymerization using tin compound was higher than that with zinc-containing catalyst, while at conversions beyond 80%, the latter catalyst gave the higher rate of polymerization. Crystallization of the newly formed polymer has an accelerating effect on the polymerization. The differences in the rate of polymerizations at high conversion for the two catalysts have been suggested to be caused by a difference in crystallinity of the newly formed polymer. It is further suggested that contaminants in the catalyst (such as tin-oxy or tin-hydroxyl contaminants) and the monomer are the true initiators. Initiation as well as polymerization proceeds

through a Lewis acid catalyzed transesterification reaction between an activated lactone and a hydroxyl group.

2.1.8 Thermodynamics: Equilibrium Monomer Conversion

Lactides are six-membered cyclics, and the reversibility of their polymerization could be expected. Polymerization of lactides never reaches 100% conversion, and yields of > 95% require polymerization temperature $\leq 180\ ^{o}C$. Very little experimental data is available on the thermodynamics of the propagation-depropagation steps. Thermodyanamics of L-lactide polymerization in 1,4-dioxane solvent was studied by Duda and Penczek [1990]. The equilibrium concentration of L-lactide, as measured by gel permeation chromatography, decreased from 0.15 mol/l at 133 ^{o}C to 0.06 mol/l at 80^{o}C. The standard thermodynamic parameters, determined on the basis of the temperature dependence of the L-lactide $\leftrightarrow$ PLLA equilibrium position were as follows: enthalpy = -22.9 kJ/mol, entropy = -41.1 J/mol.^{o}C (at 1 mol/l). Negative values of enthalpy and entropy lead to the existence of ceiling temperature, $T_c = 641\ ^{o}C$ (value computed for the bulk polymerization). The relatively high value of polymerization enthalpy compared to that of other six-member monomers was attributed to the bond oppositions and angle distortions in the skew-boat conformation of the L-lactide molecule.

2.2 Mathematical Modeling of Polymerization Kinetics

2.2.1 Modeling Approaches

In order to design a reactor for the production of a polymer, the reactor configuration is optimized such that the polymer product properties such as molecular weight distribution (MWD) are suitable for end use. This MWD is expressed in terms of the distribution function itself or in terms of moments of this distribution.

The first step in modeling polymerization reactors is the postulation of a kinetic mechanism, which governs the set of reactions comprising the polymerizations. For a particular reactor type, say a batch reactor, this mechanism may lead via the mass balance equations to a set governing the evolution of the concentrations of polymer with a given

chain length. These equations might be solved in order to glean the information necessary to understand the polymerization.

There are several ways to solve the mass balance equations. The first is the numerical method. The differential equations form an infinite set. Many attempts have been made for an approximate solution. One way is to replace the discrete variable of infinite range, the polymer chain length, by a continuous variable [Ray, 1972]. The difference – differential equations become partial differential equations. Bamford et al. [1958], Bamford and Jenkins [1960]; Bamford and Tompa [1954] used this procedure in their analysis of vinyl (radical chain growth) polymerization. Zeman and Amundson [1965 a,b] used it extensively to study batch and continuous polymerizations. Analytical solutions were obtained by taking terms from the Taylor series expansion of the activated polymer concentration function. It has been found that the accuracy of approximation is very strongly dependent on the number of terms retained in the Taylor's series expansion, as well as on the polymer chain length [Penczek et al., 1980]. Falkovitz and Segal [1982] concluded that at least a second- order approximation is required in these analyses.

For chain length independent rate constants, the kinetic equations for free radical polymerization have been exactly solved [Kumar and Gupta, 1998; Venkateshwaran and Kumar, 1992]. For chain length dependent rate constants, a series solution has been developed [Sailaja and Kumar, 1995, 1997]. It is shown that the various rate constants can be directly determined from the experimental data on molecular weight distribution. Also, if the monomer concentration as a function of reaction time is known, differential equations describing the generation of activated polymer specie become linear equations with time dependent coefficients and its series solution has been given [Sailaja and Kumar, 1995, 1997] in terms of monomer conversion. The authors have used a technique similar to the finite element method for boundary problems to divide the conversion into subdomains. The size of these steps is decided by a convergence criterion and results were determined at the end of the conversion domain through sequential computation.

Other numerical methods make use of a steady-state assumption (or a stationary state assumption) [Bamford et al., 1958] that the concentration of ions increases

initially, but almost instantaneously reaches a constant, steady state value. This method also assumes that the rate of initiation is equal to the rate of termination. In slower polymerizations, as in the PLA synthesis, the validity of steady-state assumption is not justified.

The steady-state may not be achieved if rate of initiation is greater than rate of termination. The concentration of propagating centers slowly increases throughout the polymerization, reaching a maximum late in the reaction, and then decreases. The expressions derived in the textbooks usually make the assumption of steady-state. The existence of steady-state can be ascertained by measuring the concentration of propagating specie as a function of time. This is certainly not an easy task. It should be mentioned that contrary to these considerations for rate of polymerization, the derivations for the expressions for number average degree of polymerization do not assume steady-state conditions. The ratios of various rate constants can be ascertained by careful experimentation. However, the determination of individual rate constants is a difficult task, as discussed in Section 2.2.3.

The other methods to solve mass balance equations include the discrete transform methods [Abraham, 1970, 1963; Bharucha-Reid, 1960; Feller, 1959; Howe, 1955]. The limitation of the discrete transform methods (including method of moments) is that in complex polymerization mechanism it may not be possible to invert the generating function to give the polymer chain length distribution. Thus it would be difficult to handle the mass balance equations characterized by polymer chain length dependent rate constants. Also, with the advent of gel permeation chromatograph, it has become possible to obtain the experimental determination of the entire polymer chain length distribution (rather than restricted to average molecular weights) [Tirrel et al., 1986, 1996]. In another approach, the mass balance equations are bypassed and a statistical approach is adopted [Case, 1958; Kilkson, 1964; Lopez et al., 1980;Lowry, 1970; Macosko and Miller, 1976; Miller and Macosko, 1978]. The statistical approach has the disadvantage of relying too heavily on intuition and so lacks the methodic reliability of the mass balance approach.

2.2.2 Molecular Weight distributions

1.Number-average molecular weight (M_n):

It is defined as the total weight *w* of all the molecules in a polymer sample divided by the total number of moles present. Thus

$$M_n = \frac{w}{\sum N_j} \tag{2.1}$$

where the summations are over all the different sizes of polymer molecules from $j = 1$ to $j = \infty$ and N_j is the number of moles. The most common methods of measuring M_n are membrane osmometry and vapour pressure osmometry. End-group analysis is also useful for measurements of M_n for certain polymers.

2.Weight-average molecular weight (M_w):

It is defined as:

$$M_w = \sum w_j m_j \tag{2.2}$$

where w_j is the weight-fraction of molecules whose weight is m_j. It is mainly obtained from light scattering measurements. Since the amount of light scattered by a polymer solution increases with molecular weight, this method becomes more accurate for higher polymer molecular weights.

3.Viscosity-average molecular weight (M_v):

Solution viscosity is also useful for molecular-weight measurements. Viscosity like light scattering, is greater for the larger-size polymer molecules than for smaller ones. Solution viscosity measure the M_v defined as:

$$M_v = \left[\sum w_j m_j{}^a\right]^{\frac{1}{a}} = \left[\frac{\sum N_j m_j{}^{a+1}}{\sum N_j m_j}\right]^{\frac{1}{a}} \tag{2.3}$$

where a is a constant. The value of *a* is dependent on the hydrodynamic volume of the polymer and the effective volume of the solvated polymer molecule in solution, and varies with polymer, solvent, and temperature.

More than one average molecular weight is required to reasonably characterize a polymer sample. There is no such need for a monodisperse product for which all three average molecular weights are the same. The situation is quite different for a

polydisperse sample where all the three molecular weights are different. For a polydisperse polymer

$M_w > M_v > M_n$

with the differences between the various average molecular weights increasing as the molecular-weight distribution broadens. For most practical purposes, one usually measures the molecular weight of a polymer sample by measuring M_n and either M_w or M_v.

The ratio of M_w and M_n depends upon the spread of the distribution curve and is often useful as a measure of the polydispersity in a polymer. The characterization of a polymer by M_n alone, without regard to the polydispersity, can be extremely misleading, since most polymer properties such as strength and melt viscosity are determined primarily by the size of the molecules that make up the bulk of the sample by weight.

In addition to the different average molecular weights of a polymer sample, it is frequently desirable and necessary to know the exact distribution of molecular weights. There is usually a molecular-weight range for which any given polymer property will be optimum for a particular application. The polymer sample containing the greatest percentage of polymer molecules of that size is the one that will have the optimum value of the desired property. Since the samples with the same average molecular weight may possess different molecular-weight distributions, information regarding the distribution allows the proper choice of a polymer for optimum performance. These can be found out form a technique known as gel permeation chromatography (GPC) or size exclusion chromatography (SEC).

The distribution of molecular weights in a polymer is generally represented as a set of concentrations of polymer of a given chain length. $[P_j]$ denotes the concentration of polymer of chain length j and its variation with j is the polymer chain length distribution (PCLD). Since the subscript j denotes a set of integer values, $[P_j]$ is therefore a discrete distribution. The number average molecular weight is given as [Tirrel et al., 1986]:

$$M_n = m \frac{\sum_{j=1}^{n} j([P_j]+[M_j])}{\sum_{j=1}^{n} ([P_j]+[M_j])} \qquad (2.4)$$

and the weight average molecular weight as:

$$M_w = m \frac{\sum_{j=1}^{n} j^2([P_j]+[M_j])}{\sum_{j=1}^{n} j([P_j]+[M_j])} \qquad (2.5)$$

where m is the molecular weight of the repeat unit (in the present case for PLA, m=144).

2.2.3 Ring-opening Polymerization of PLA

In ring-opening polymerization, for both D- and L-lactides, initiation results in opening of the ring to form secondary initiator species P_1 [Odian, 1991]. This can be generalized as:

$$M + I \xrightarrow{k_o} P_1 \qquad (2.6)$$

where M is the monomer, I is the initiator and P_1 is the activated polymer of one unit (Figure 2.10). Initiation is characterized by a rate constant k_0. The initiator species grow by successive ring-opening additions of monomer molecules:

$$P_j + M \xrightarrow{k_j} P_{j+1} \quad , \; j=1,2,3,\ldots \qquad (2.7)$$

where P_j is the active polymer chain of j units. The rate constant k_j refers to the jth propagation step on a chain. The nature of the chain-growth process in ring-opening polymerization bears a superficial resemblance to chain polymerization. Only monomer adds to the growing chain in the propagation step. Species larger than monomer do not react with the growing chains. However, ring-opening polymerizations can have the characteristics of either chain or step polymerization or both [Odian, 1991].

The growth of polymer chain continues till its termination or till the monomer is completely consumed. The termination may occur in many ways. Termination by

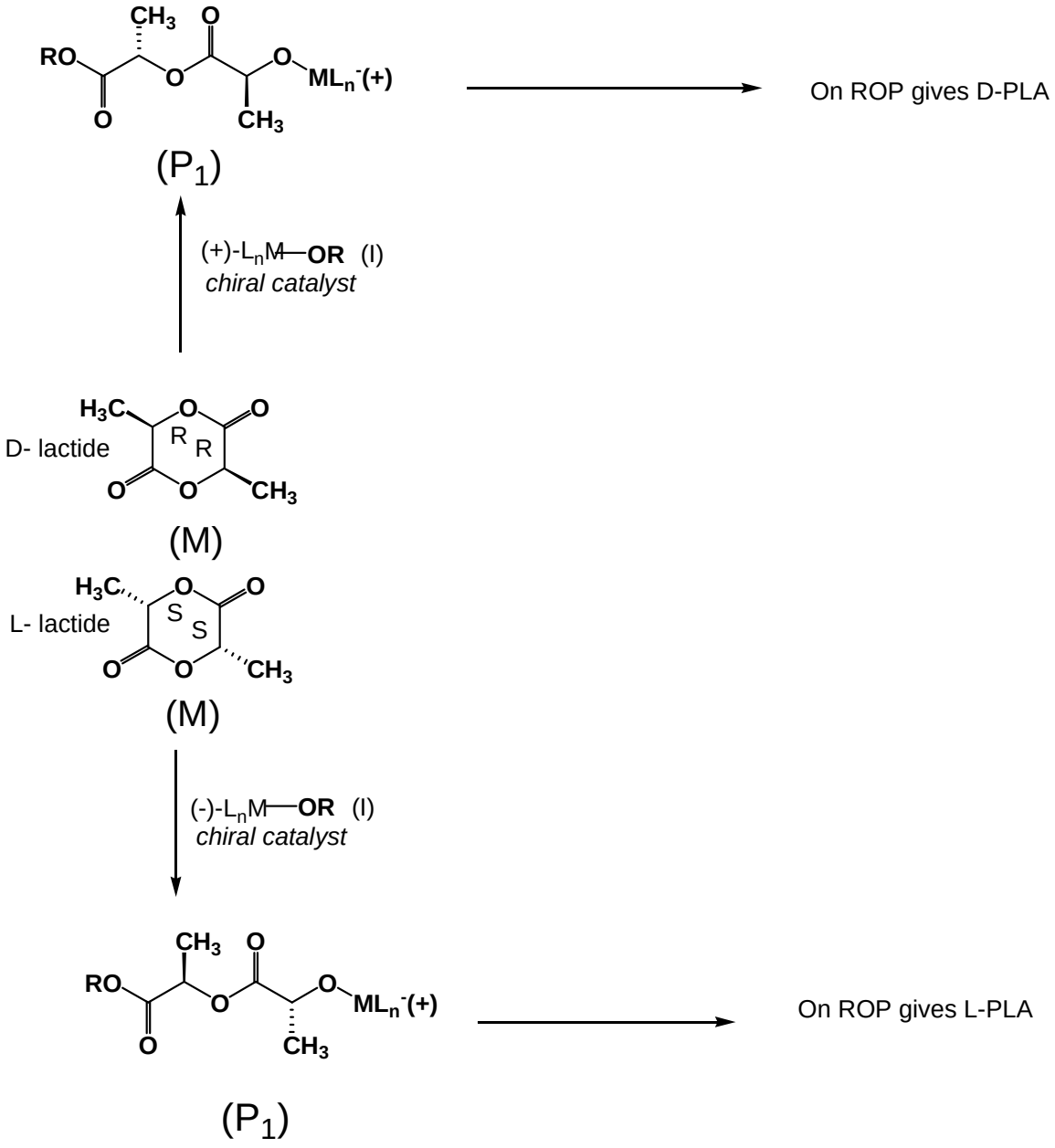


Fig. 2.10 Initiation of L-lactide and D-lactide

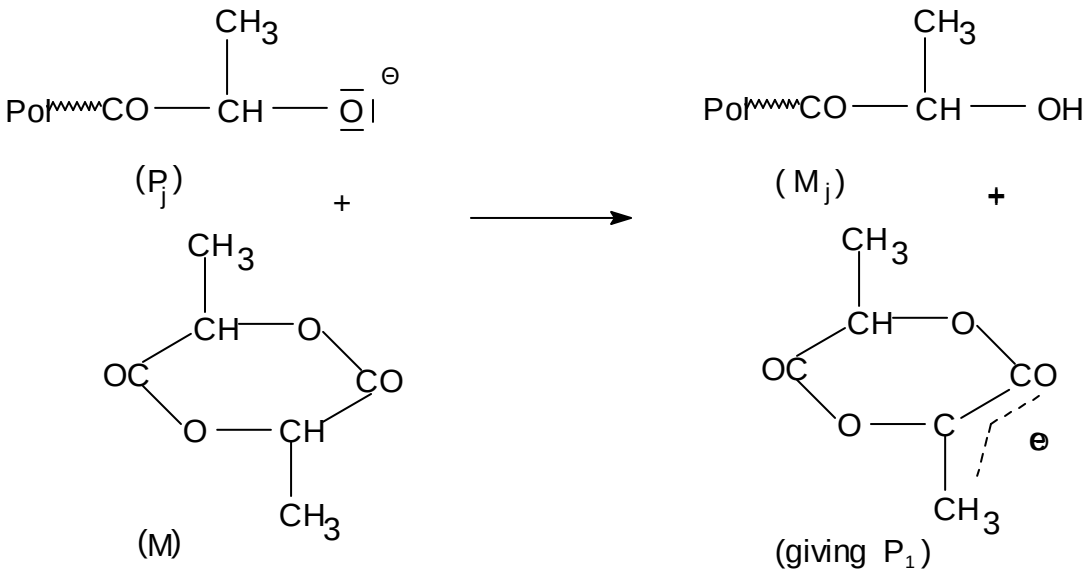


Fig. 2.11 Deprotonation of the monomer in anionic polymerization of PLA (Source: Kricheldorf and Lee, 1995)

transfer to monomer can take place in ring-opening cationic [Penczek et al., 1980] as well as anionic [Kricheldorf and Lee, 1995] polymerizations. The anionic polymerization of lactide proceeds via alkoxide anions, and these anions are basic enough to deprotonate the monomer (Figure 2.11) [Kricheldorf and Lee, 1995]. This deprotonation involves racemization and represents a chain transfer to the monomer with the consequence to reduced molecular weights. Odian [1991] has discussed in detail the mechanism of chain transfer to monomer in the anionic ring-opening polymerization. In the present case, the termination mechanism has been assumed to be the chain transfer to monomer, giving:

$$P_j + M \xrightarrow{k_t} M_j + P_1 \qquad (2.8)$$

In equation (2.8), it is assumed that the charged ring spontaneously forms P_1. Here M_j is the deactivated polymer of j repeat units, which will not participate in any reaction.

Considerable experimental work has also been done by various investigators to study the reaction kinetics of ring-opening polymerization, in general. For a variety of ring-opening polymerization initiated by epoxides, oxetanes, and tetrahydrofuran the propagation rate constant, k_j, is assumed to be constant for all chain lengths (denoted by k_p). The experimentally determined value of k_p (under a number of assumptions) are observed to be in the range of 6 to 0.06 l/mol.min [Dreyfuss and Dreyfuss, 1969, 1976; Ishii and Sakai, 1969; Saegusa and Kobayashi, 1973]. For the ring-opening polymerization of (D, L)-lactide, the apparent rate constant, k_{app}, is defined by the following equation [Dubois et al., 1991]:

$$-\frac{d[M]}{dt} = k_{app}[M][I] \qquad (2.9)$$

where [M] and [I] are monomer and initiator concentrations. Dubois et al [1991] reported its value as 0.6 l/mol.min. Schwach et al. [1996] using zinc lactate as catalyst found k_{app} to be equal to 7.5×10^{-4} l/mole.min. They also found the rate constant to be 8 times higher for stannous octoate compared to that for zinc lactate [Schwach, 1996].

The difficulties in experimental determination of the rate constants are discussed by Odian [1991], and are mentioned herein. Under several assumptions (including the

assumption of steady state i.e. the rate of initiation is equal to the rate of termination) the ratio of rate constants (propagation rate constant/rate constant for termination by transfer to monomer) can be obtained if the variation of number average degree of polymerization with monomer concentration is known. The determination of individual rate constants requires the determination of k_p, a difficult task and one that has not been performed properly. This requires the critical evaluation of the concentration of the propagating species, which should not be taken as equal to the concentration of initiator without any experimental verification (such an assumption holds only if the rate of propagation is much less than the rate of initiation). There are two general methods for the experimental evaluation of this concentration, neither approach being experimentally simple or unambiguous [Odian, 1991]. One method involves short-stopping a polymerizing system by adding a highly effective terminating agent and analyzing the end-groups [Higashimura et al., 1971]. The second method involves UV spectroscopic analysis of the propagating species during polymerization [Sawamoto and Higashimura, 1978].

Evaluation of rate constants by modeling and simulation in conjunction with the experimental results offers several advantages: initiation, propagation and termination rate constants can be evaluated; termination mechanism can be ascertained and lastly chain dependent rate constants can be evaluated.

2.3 Effect of Impurities on the MWD

Various transfer agents present as impurity, solvent or deliberately added to the system, can terminate the growing polymer chain. Water, alcohols, acids, anhydrides and esters have varying chain transfer properties [Mathieson, 1963]. The presence of any of these transfer agents in sufficient concentration results in the termination due to the transfer agents becoming the dominant mode.

Researchers have tried to treat the problem of effect of impurities on the ionic polymerizations analytically. Gold [1957] presented a detailed study of the polymer statistics for a reaction system resembling the ethylene oxide initiator case allowing for the different rates of initiation and propagation. The steady-state assumption was made and an analytical solution is obtained. Nanda and Jain [1967] derived an analytical solution of the problem with the assumption that the impure monomer is added in small

doses to the initiator. This is done such that the reaction of the propagation centers with impurities is essentially completed within the time interval between the consecutive doses. This assumption implies that there would be no accumulation of the monomer or the impurities, even though the rate constants for two processes are different. In another study [Jain and Nanda, 1976] they treated the problem with the steady state assumption and considered the simultaneous effect of chain transfer to monomer and spontaneous chain transfer. Cabrerizo and Guzman [1979] carried out a theoretical study of the effect of a transfer agent on the MWD in living polymer, assuming an infinitely fast initiation and instantaneous reinitiation after the transfer reaction. Expressions for the number – average and weight-average chain lengths are obtained for the three limiting cases: (a) both the monomer and the transfer agent remain at constant concentration, (b) only the concentration of the transfer agent is kept constant, and (c) both concentrations vary with time. Other theoretical studies include Coleman et al. [1963] and Yuan and Yan [1986a, b, 1987].

2.4 Chain length dependent propagation rate constant

The assumption that the propagation rate constant is independent of the chain length has been made in almost all the work in the field. This is partly due to the difficulty in treating the problem analytically or numerically, and also due to lack of experimental data for ionic polymerizations involving chain length dependent rate constants. The possibility that the rate constants are dependent on polymer chain length has been discussed by Zeman and Amundson [1965a, 1965b] and Saidel and Katz [1967]. More recently, Durand and Bruneau [1981], Gandhi and Babu [1978], Gupta and Kumar [1985], Kumar and Gupta [1998] and Gupta et al. [1982, 1979] have analyzed the effect of unequal reactivity in step-growth polymerization. A series solution has been developed [Sailaja and Kumar, 1995, 1997] for anionic polymerization. Nanda and Jain [1968] assumed a linear dependence of the rate constant on the degree of polymerization and obtained the molecular weight distribution for condensation polymerization. In the present work, results are presented for both constant reactivity and a decreasing propagation rate constant with an increasing polymer chain length.

Chapter – 3

Mathematical Modeling of the Poly(lactic acid) Ring-Opening Polymerization Kinetics-1

3.0 Introduction

Since the syntheses of PLA by Carothers in 1932, hundreds of research papers and patents have appeared in the literature. Now large size manufacturing units for PLA are also being set-up. But, there is lack of data concerning the rate constants for initiation, propagation and termination steps of PLA polymerization (except some data about the apparent rate constant, virtually no rate constants are available in literature). Also, it is extremely difficult to experimentally find the absolute values of different rate constants. With this in view, a mathematical modeling was made which when used with the readily available experimental data for the average molecular weights, can predict the polymerization rate constants of various steps with sufficient accuracy in a short time and hence can be used more efficiently for design purposes.

The progress of lactide polymerization has been modeled by assuming a ring opening reaction mechanism comprising of chain initiation, chain propagation, and chain termination. Appropriate differential equations have been developed incorporating the rate controlling reaction(s)/step(s). The resulting differential equations with appropriate boundary conditions were solved using a numerical technique. Effect of unequal reactivity has also been incorporated in the model. The efficacy of model has been tested by comparing the predicted results on molecular weight and molecular weight distribution with those available in the published literature. The kinetic rate constants have been arrived at, for various PLA polymerization catalysts, by matching the simulated results with the experimental data.

In this chapter the equations, which form a mechanistic model to simulate the ring-opening polymerization (ROP) of PLA for a batch reactor, are defined. We consider here the molecular weight change as a function of polymerization time, in a homogeneous ring-opening polymerization of PLA, which has the following properties:

- Each initiator molecule initiates polymer chain(s), at a finite rate.
- Termination occurs by transfer to monomer and is irreversible.
- Concentrations of the reactants may depend upon time but are independent of spatial position with in the reaction vessel, and
- Rate constants are chain length independent.

The results of simulations performed on the model developed in conjunction with the reported experimental data for various catalysts are discussed. The chapter concludes with a discussion of simulations performed without the assumption of propagation rate constant being chain length independent.

3.1 Formulation of the Problem: Mathematical Model 1

The first step in modeling polymerization reactors is the postulation of a kinetic mechanism, which governs the set of reactions comprising the polymerizations. Initiation, propagation and termination reactions are characterized by rate constant k_0 , k_j and k_t, as explained earlier in equations (2.6) to (2.8), respectively.

$$M + I \xrightarrow{k_o} P_1 \qquad (2.6)$$

where M is the monomer, I is the initiator and P_1 is the activated polymer of one unit. The initiator species grow by successive ring-opening additions of monomer molecules:

$$P_j + M \xrightarrow{k_j} P_{j+1} \quad , \; j=1,2,3,\ldots \qquad (2.7)$$

where P_j is the active polymer chain of j units. The rate constant k_j refers to the jth propagation step on a chain. In the present case, the termination mechanism has been assumed to be the chain transfer to monomer, giving:

$$P_j + M \xrightarrow{k_t} M_j + P_1 \qquad (2.8)$$

In equation (2.8), it is assumed that the charged ring spontaneously forms P_1. Here M_j is the deactivated polymer of j repeat units, which will not participate in any reaction.

Mass balance equations for a batch reactor may be written for the above kinetic scheme as follows:

The monomer is consumed in the initiation, propagation and termination reactions. Therefore, the rate of change of monomer concentration can be obtained by adding the rate of consumption of monomer due to all three steps as given in equations

(2.6) to (2.8). The summations in the following equation (3.1) are from a polymer chain of one unit to a chain of *n* units, where, *n* is a very large number.

$$\frac{d[M]}{dt} = -[M]\left\{k_0[I] + \sum_{j=1}^{n} k_j[P_j] + \sum_{j=1}^{n} k_{tj}[P_j]\right\} \qquad (3.1)$$

The change of concentration of initiator *I* is due to its reaction with the monomer lactide only (equation 2.6). Thus, the rate of change of concentration [*I*] is given by:

$$\frac{d[I]}{dt} = -k_0[I][M] \qquad (3.2)$$

P_1 is formed due to initiation of monomer lactide and the termination reaction, and is consumed due to the propagation reaction, hence

$$\frac{d[P_1]}{dt} = k_0[I][M] - k_1[P_1][M] + \sum_{j=2}^{n} k_{tj}[P_j][M] \qquad (3.3)$$

Here, it should be noted that *n* in equations (3.1) and (3.3) represents largest polymer chain with *n* number of repeat units. Theoretically, the value of *n* should tend to infinity. The rate of production of P_j is due to propagation step for P_{j-1} and its consumption is due to propagation step for P_j and the termination reaction. Thus:

$$\frac{d[P_j]}{dt} = [M]\{k_{(j-1)}[P_{j-1}] - k_j[P_j] - k_{tj}[P_j]\}, \; j > 1 \qquad (3.4)$$

The terminated polymer, M_j, is formed due to the initiation reaction, hence

$$\frac{d[M_j]}{dt} = k_{tj}[P_j][M], \qquad j \geq 1 \qquad (3.5)$$

With initial conditions, at t=0

$[M_j]=0$ and $[P_j]=0$, $j \geq 1$ (3.6)

Since no reaction has taken place, therefore concentration of polymer of any chain length is zero. Thus:

$[M]=[M_o]$ (3.7)

If *s* represents number of chains initiated by an initiator molecule, then:

$[I]=[I_o]\times s$ (3.8)

In all of the above equations square brackets represent molar concentrations and subscript *j* appearing with the rate constants indicates chain length dependent values.

3.2 Method of Solution

It is difficult to solve above ordinary differential equations (ODE) given in equations (3.1) to (3.5) along with the boundary conditions (equations 3.6, 3.7 and 3.8) analytically. The differential equations form an infinite set. As discussed earlier (Section 2.2.1), many attempts have been made for an approximate solution with limited success. Now, however, this is possible with the availability of high-speed computers and using the techniques developed in the present research work.

The summation over j in equations (3.1) and (3.5) should continue to infinity, however, it is practically impossible to do so in numerical techniques. In the present work, n=5000 was taken, which is well above the experimentally reported values of degree of polymerization of PLA. It was observed that a value more than this has no effect on the results. In the present work, these equations were solved on a PC using Euler's method with a very small step size. Brief description along with a flow-sheet of the programming technique is given in Appendix A.

For the purpose of comparison with the experimental data, the number average molecular weight, M_n and weight average molecular weight, M_w were also calculated from equations (2.4) and (2.5).

3.3 Simplified Analytical Solution [Tirrel et al., 1986]

To verify the reliability of the proposed technique it is required that the results are compared with the analytical solution of a related problem. A brief and simplified modeling approach, presented by Tirrel et al. [1986], is being used for this purpose and is elaborated in the following paragraphs for the sake of clarity.

If the initiation reaction is very fast then the kinetics of initiation can be neglected. Further, if the termination and transfer are ignored, then the only reaction of interest is the propagation reaction (equation 2.7), leading to a very simple mechanism. The material balances for the various polymer species in a batch reactor given by equations (3.1) to (3.5) then reduce to:

$$\frac{d[M]}{dt} = \sum_{j=1}^{n} k_j [P_j][M] \qquad (3.9)$$

$$\frac{d[P_1]}{dt} = -k_1 \ [P_1][M] \tag{3.10}$$

and

$$\frac{d[P_j]}{dt} = \left\{\left[k_{(j-1)}[P_{j-1}] - k_j[P_j]\right]\right\}[M] \tag{3.11}$$

For the analytical solution of equations (3.9) to (3.11) simultaneously, an assumption of equal reactivity ($k_j = k_p$ for all j) is made. For further simplification of equation (3.11), a dimensionless time variable is defined as

$$\tau = \int_0^t k_p[M]dt \tag{3.12}$$

This leads to the reduction of equation (3.11) to

$$\frac{d[P_j]}{d\tau} = \left[[P_{j-1}] - [P_j]\right] \tag{3.13}$$

with the initial conditions at t=0: $[P_j]$=0 for $j \geq 2$; and $[P_1]=[I_0]\times s$, where $[P_j]$and $[P_1]$are functions of τ only.

One way to solve this equation is sequentially, i.e. starting with P_1, then substituting it into the equation for P_2, and so on. This simple system is also amenable to a direct analytical solution via the Laplace transform. The solution as given by Tirrel et al. [1986] in the form of Poisson distribution is:

$$[P_j] = s[I_0]\frac{\tau^{j-1}e^{-\tau}}{(j-1)!} \tag{3.14}$$

Therefore, Poisson type narrow molecular weight distribution occurs when:

1. The process is free of termination and transfer reactions,
2. The initiation rate is faster than the rate of propagation, and
3. The rate constant of propagation is independent of the degree of polymerization.

If k_p is a function of chain length, then the analytical solution given in equation (3.14) cannot be used. Present approach of comparison is to solve the generalized equations (3.1) to (3.5) numerically by multi-step Euler's method (with k_t equal to zero and a large value of k_o) and compare values of $[P_j]$ with those obtained by

equation (3.14). It was observed that Euler's method, with small step size as discussed in Appendix A is sufficiently accurate for the present purpose. Very close fit between the two curves (Figure 3.1) confirms that the present technique and the computer program developed are stable and capable of giving appropriate results.

Another check for the suitability and reliability of the numerical technique and the computer program developed in the present research work, in the limiting case of Poisson distribution (a large value of k_o and k_t =0), is presented in Figure 3.2. A straight line between the number average degree of polymerization, DP_n, and ($[M_o] - [M]$)/$[I_o]$ is obtained with the slope and the intercept equal to one. This is in agreement with the following equation derived for Poisson distribution [Tirrel et al., 1986]:

$$DP_n = 1 + \frac{[M_o] - [M]}{[I_o]} \qquad (3.15)$$

In Figure 3.2, DP_n (=M_n/m) was calculated by using equations (2.4) where as $[M]$ and $[P_j]$ were determined by solving equations (3.1) to (3.5) corresponding to the situation when there is termination and fast initiation.

To check the material balance equations used in computer programming, Sum of $[P_j]/I_o$ vs. polymerization time was plotted in Figure 3.3. A straight line is obtained even when the ordinate is plotted up to nine decimal places and time up to 150 hr with Δt = 0.01min. This indicates that material balance equations give satisfactory results even after 900000 numbers of iterations. This confirms the accuracy, suitability and reliability of the present numerical technique.

The present numerical technique is applied to the solution reported [Zeman and Amundson, 1965b] by solving the first derivative term in the Taylor series expansion of the activated polymer concentration function. This is discussed in Appendix B and a comparison is shown in Figure B.1.

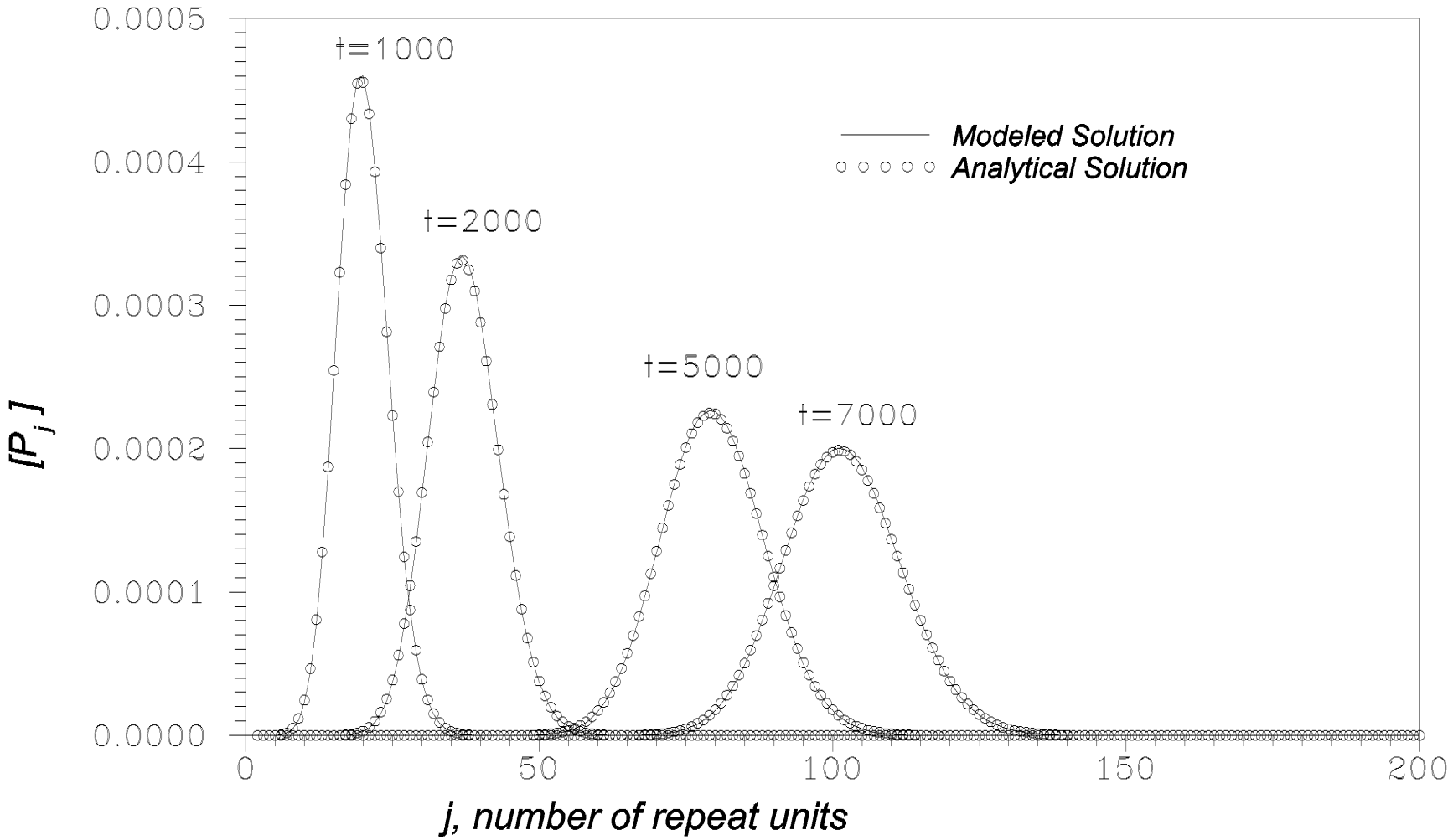


Fig. 3.1 Comparison of numerical and analytical solution for $[P_j]$ vs j as a function of reaction time, t in min.

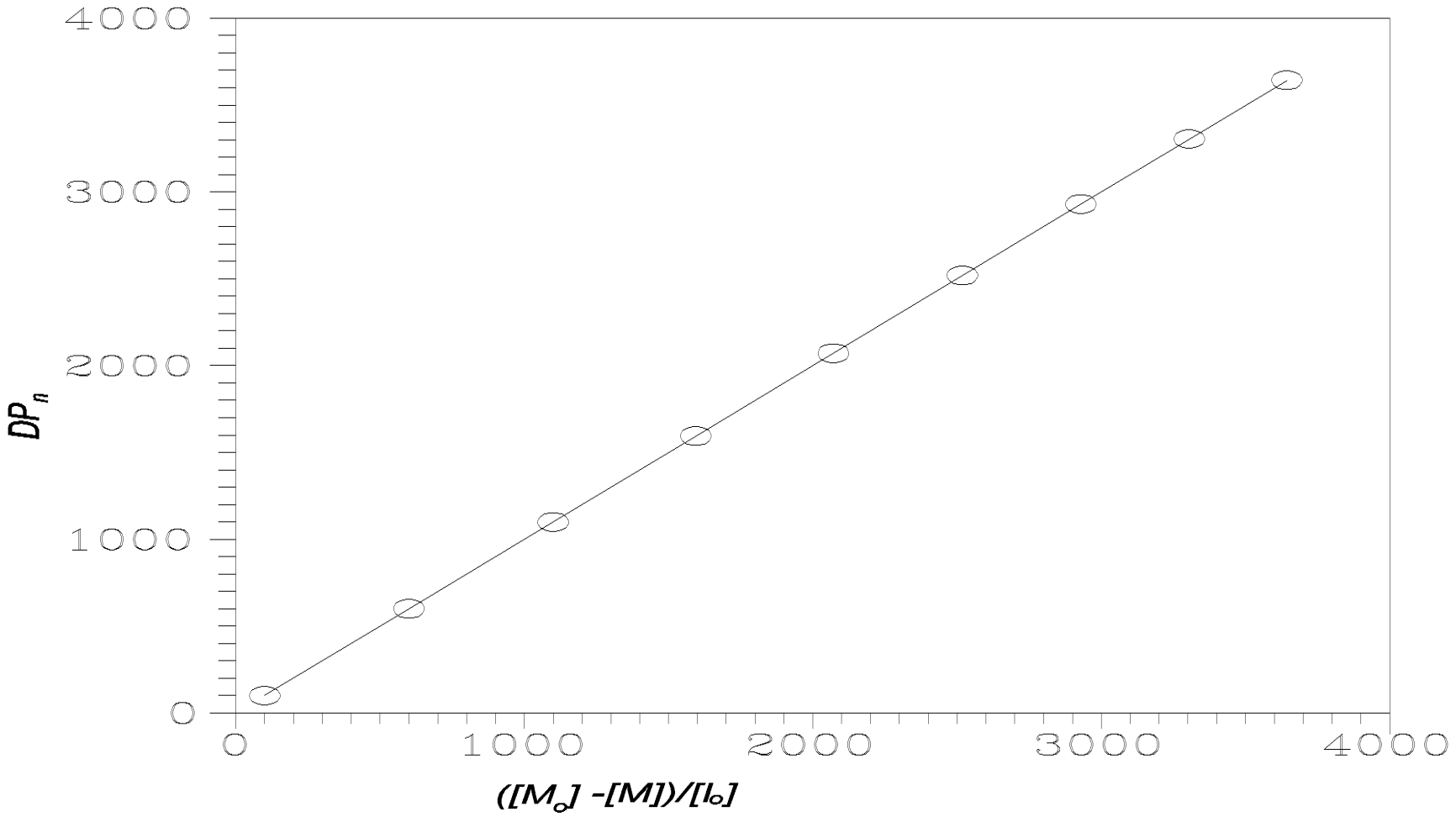


Fig. 3.2 A linear relationship between the degree of polymerization (number average) and $([M_o] - [M])/[I_o]$ obtained by the proposed numerical technique for the limiting case of Poisson distribution

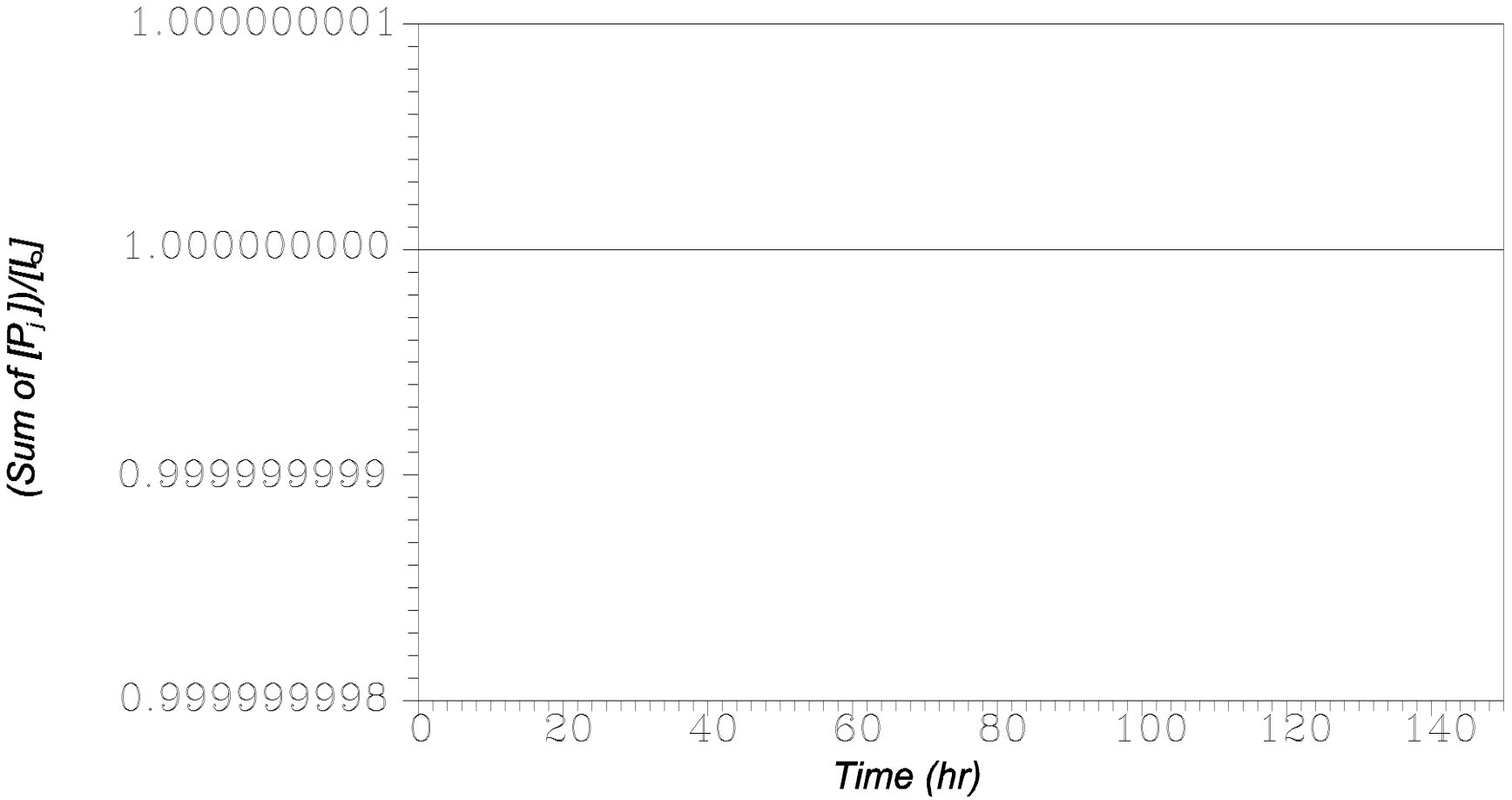


Fig. 3.3 A line of zero slope between the *(Sum of [P_i])/[I_o]* vs.polymerization time obtained by the present numerical technique for the limiting case of Poisson distribution

3.4 Results and Discussion

Figure 3.4 shows the theoretical results obtained in the present work, for normalized number average degree of polymerization as a function of reaction time for different values of propagation rate constant, k_p in the simple case when only propagation reaction is considered (i.e. large k_o and k_t = 0). The value of normalized degree of polymerization for PLA is approximately unity when calculated (by converting experimental M_n data in Figure 3.5 to (DP_n/ 1+M_o/I_o) form) from the data of Dubois et al. [1991] in 50-100 hours reaction time period. Figure 3.4 suggests that the numerical value of k_p in case of polymerization of PLA (for the particular catalyst used) should be of the order of 0.1 l/mol.min. This is so because according to simulated curves as shown in Figure 3.4, the reaction is nearly complete in 50-100 hr for k_p = 0.1 l/mol.min. For other values of k_p it takes either more than 100 hours or the reaction is complete much earlier. This is only an approximate starting point for parameter estimation when initiation and termination kinetics are also considered.

In the present case, however, initiation and termination reactions are also involved. Figure 3.6 demonstrates the effect of k_o, k_p and k_t on the variation of number average molecular weight with time. In this figure, M_n is plotted against time by changing the rate constants k_o, k_p and k_t about the standard value of 0.002, 0.5 and 2.5×10^{-4} l/mol.min, respectively (represented by thick line). These values of rate constants were obtained by fitting experimental data of D, L- lactide polymerization presented by Dubois et al. [1991] (Appendix C). The experimental data for this catalyst and other which have been considered in this work are given in Appendix D. It can be seen from this figure that the molecular weight of polymer formed is more sensitive to k_p than k_t for shorter reaction time whereas effect of k_t is pronounced for prolonged reaction time. In other words, initial slope of the curve is sensitive to k_p and the final slope to k_t. M_n , however, is not very sensitive to k_o.

Initiation rate constant has a very peculiar behavior: with a decrease in k_o, the number average molecular weight, M_n, is lower for short reaction time, and as reaction proceeds M_n becomes higher. This interesting result is because of the fact that due to low k_o, the number of initiated chains are less and with the availability of same monomer molecules

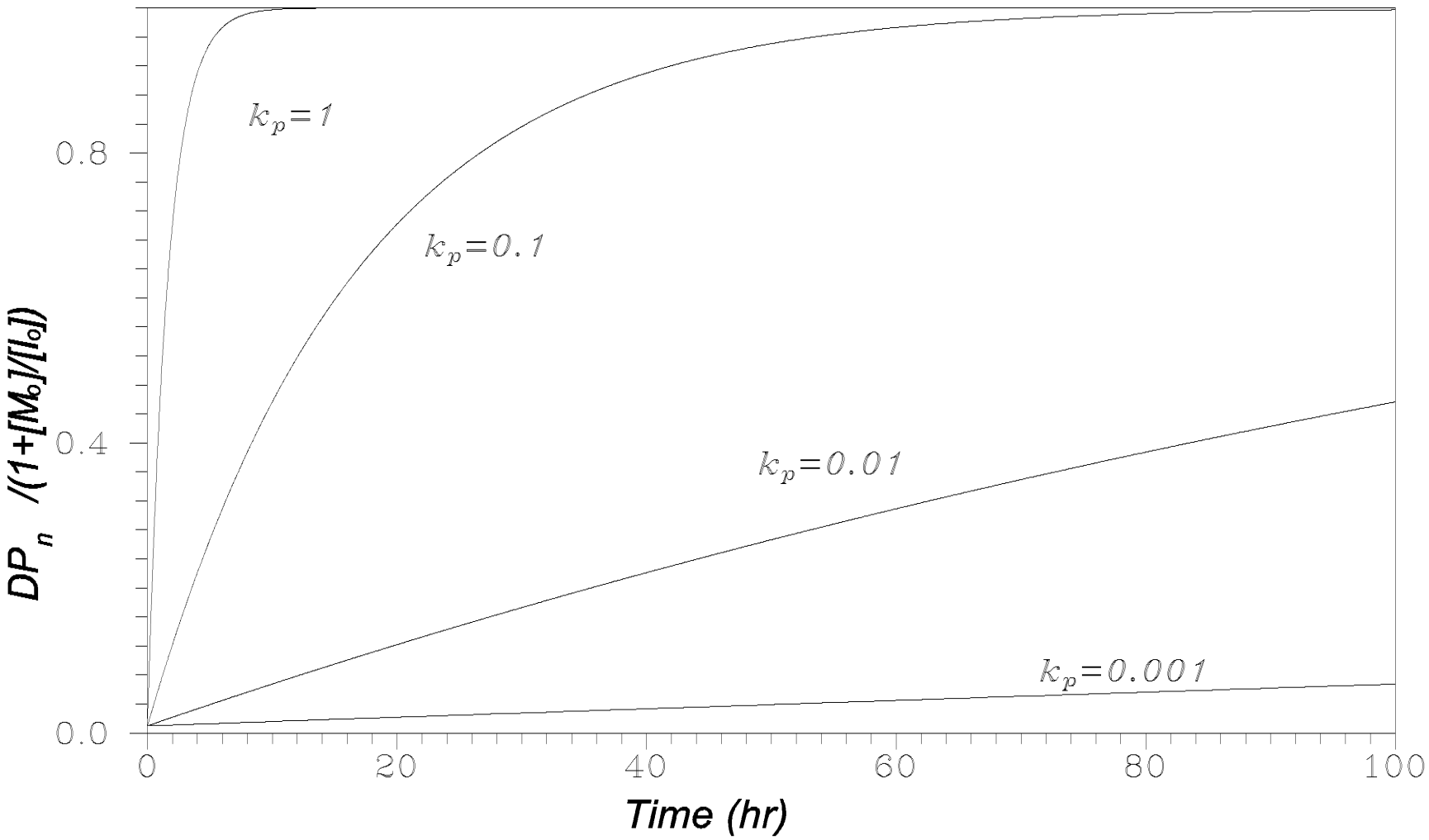


Fig. 3.4 Ratio of degree of polymerization *(DP_n)* and (1+ monomer to initiator ratio *($[M_o]/[I_o]$)*) vs time. The units of k_p are lit/mol.min.

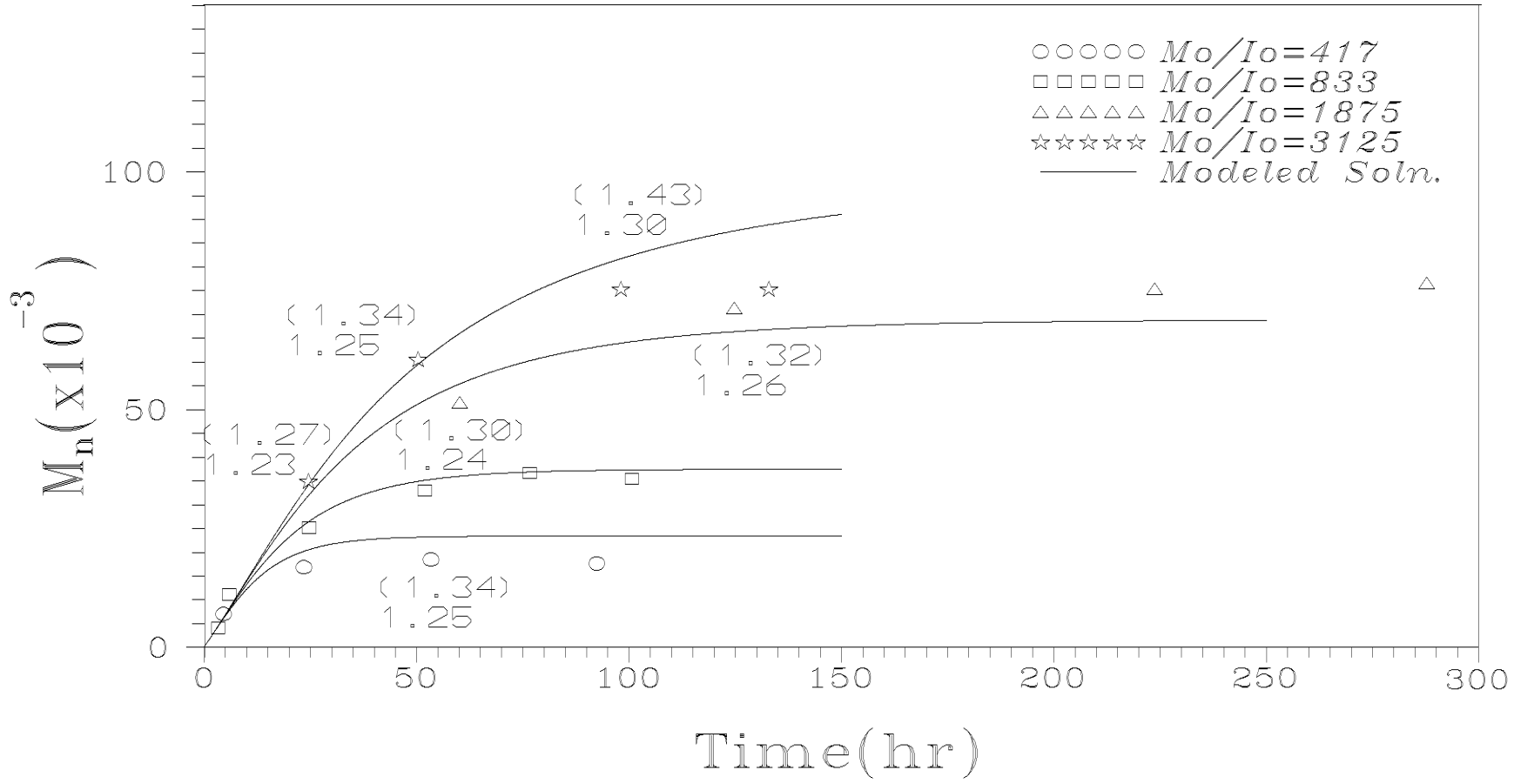


Fig. 3.5 A comparison of experimental [Dubois et al., 1990] and modeling results (number average molecular weight) for the polymerization of (D,L)-lactide, using aluminum isopropoxide catalyst. The solid lines are the solutions obtained from the model and points are the experimental values. The experimental polydispersity of selected points are noted in parentheses and the modeled polydispersity is shown below it.

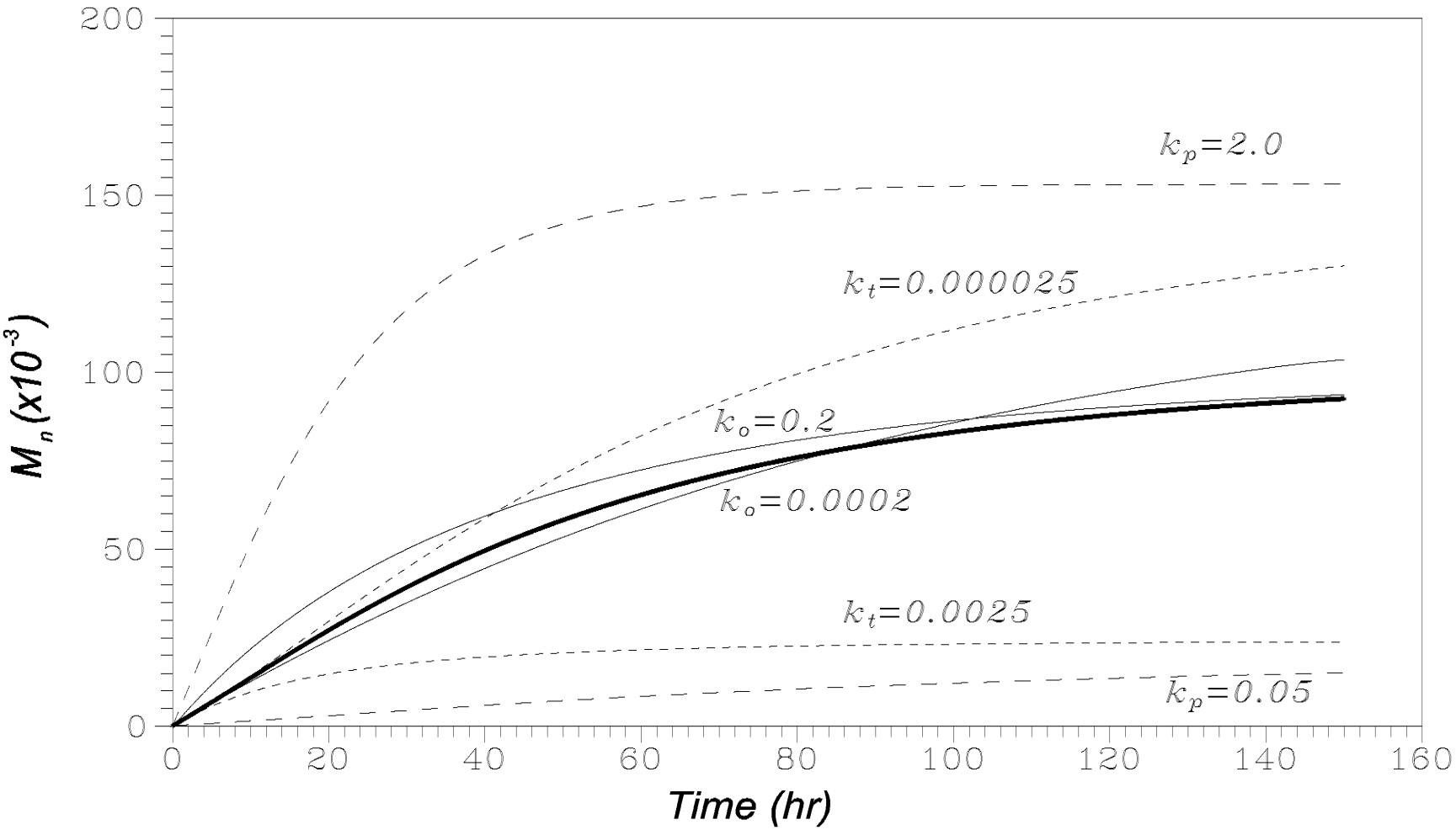


Fig.3.6 M_n vs polymerization time for different k_o, k_p, and k_t (lit/mol.min.). $[M_o]/[I_o]$=3125 (with s=3 in equation (3.8) as each initiator molecule initiates three chains)

for the growth of fewer number of chains, the average chain length increases. It is known termination, affects the molecular weight distribution [Odian, 1991]. Thus, k_o values can be fine-tuned if the polydispersity (M_w/M_n) data is also considered. Figure 3.7 shows variation of polydispersity with the polymerization time as a function of k_o. In Figure 3.8 the same data is re-plotted on a logarithmic time axis, to examine the behavior at lower times. The Poisson distribution curve in the figures corresponds to k_t=0 and a very high value of k_o. At high conversions it is close to one, which is consistent with the following equation [Tirrel et al., 1986] for polydispersity of a Poisson distribution:

$$\frac{M_w}{M_n} = 1 + \frac{\tau}{(1+\tau)^2} \qquad (3.16)$$

where $\tau = \dfrac{([M_o]-[M])}{[I_o]}$

At high conversion, τ approaches $[M_o]/[I_o]$ (which in this case is 3125), and right side of equation (3.16) approaches unity. At low conversion and low reaction times, $[M]$ is close to $[M_o]$ and therefore τ is very small. This increases the value of left side of equation (3.16) to much above unity. As τ increases with monomer conversion, the right side of equation (3.16) starts decreasing and approaches unity. For the curves other than the Poisson distribution curve, the polydispersity again starts to increase with reaction time. This can be explained as follows: the termination and slower initiation leads to a broadening of the MWD. The chains will start and terminate at different time leading to a broad MWD. Hence polydispersity starts increasing with time. Figure 3.9 shows how the polydispersity varies with M_n as a function of k_o. This type of plot is useful in visualizing that given a desired polydispersity and M_n , what value of k_o (and therefore the polymerization catalyst) is required.

The results of M_n and M_w as a function of polymerization time, as reported by Dubois et al. [1991] for different monomer/initiator ratio, are compared with the calculated values in Figure 3.5. In the above-mentioned work, the experimental data on kinetics have been presented in the form of M_n as a function of polymerization time, for PDLLA synthesis using aluminium isopropoxide as the initiator. The molecular weight and molecular weight distribution were determined by using a gel permeation chromatograph operated

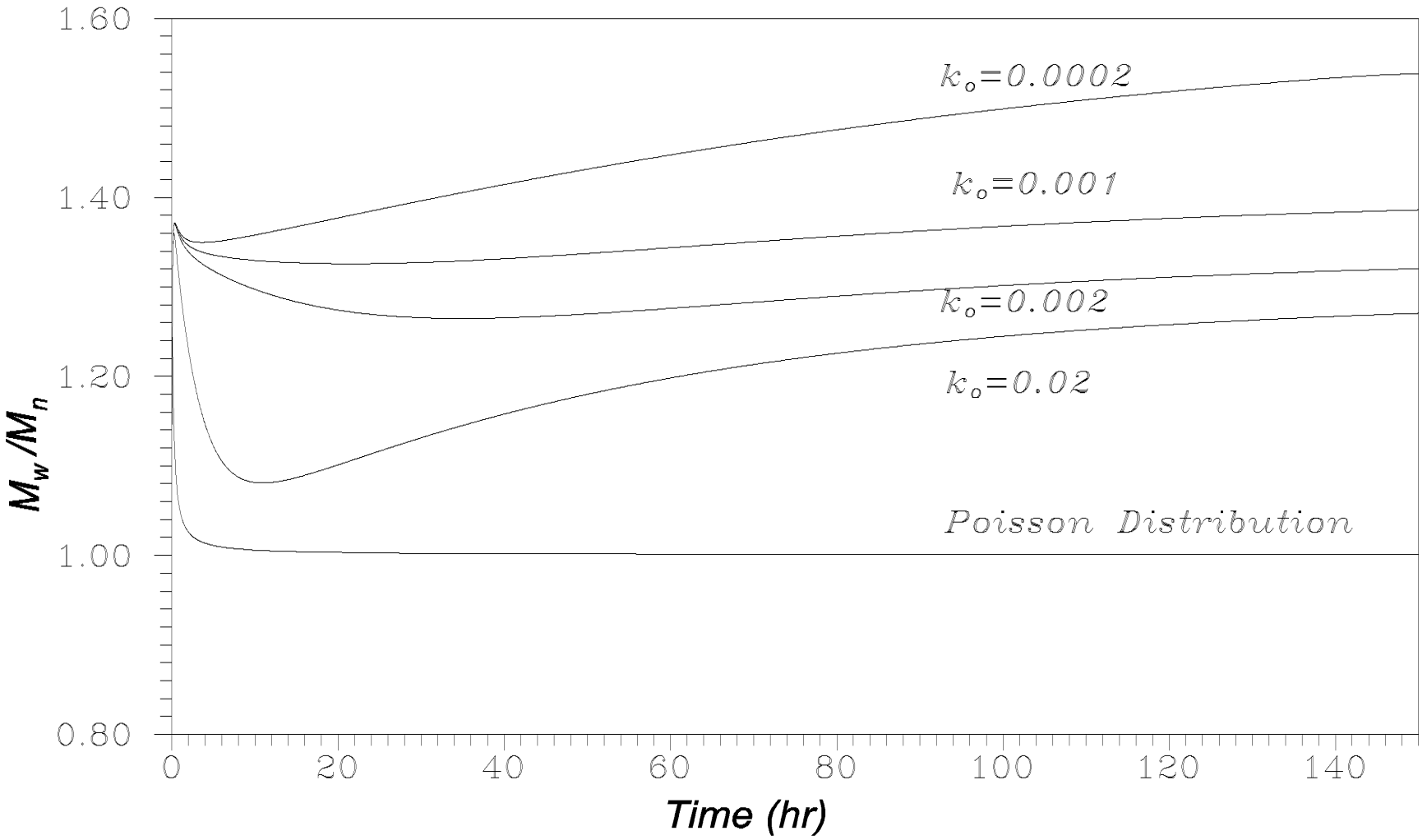


Fig. 3.7 Polydispersity as a function of polymerization time for differentvalues of k_o. k_p=0.5 l/mol.min and k_t=0.00025 l/mol.min and $[M_o]/[I_o]$=3125 (s=3).

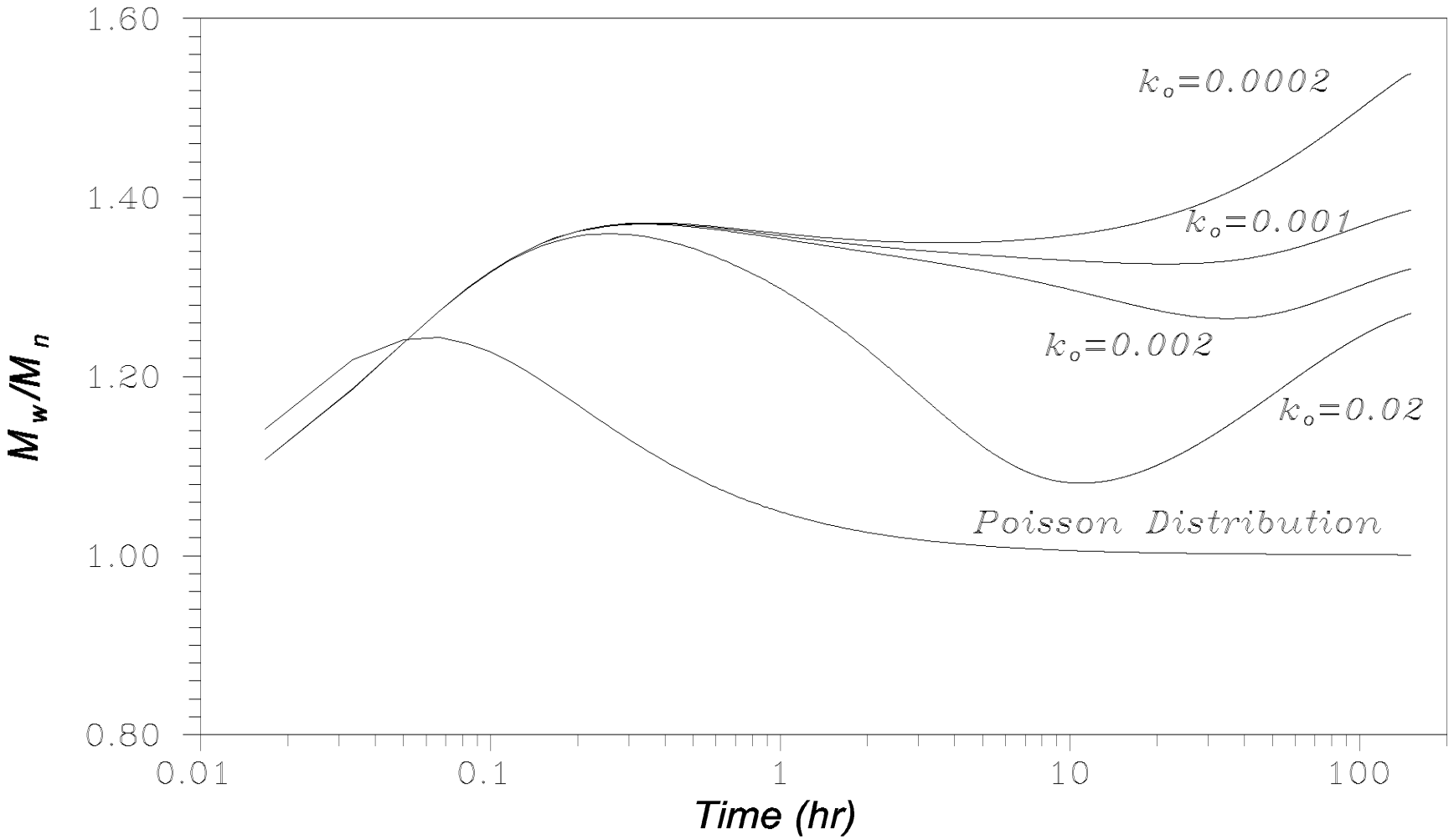


Fig. 3.8 Initial variation of polydispersity as a function of polymerization time for differentvalues of k_o. k_p=0.5 l/mol.min and k_t=0.00025 l/mol.min and $[M_o]/[I_o]$=3125 (s=3).

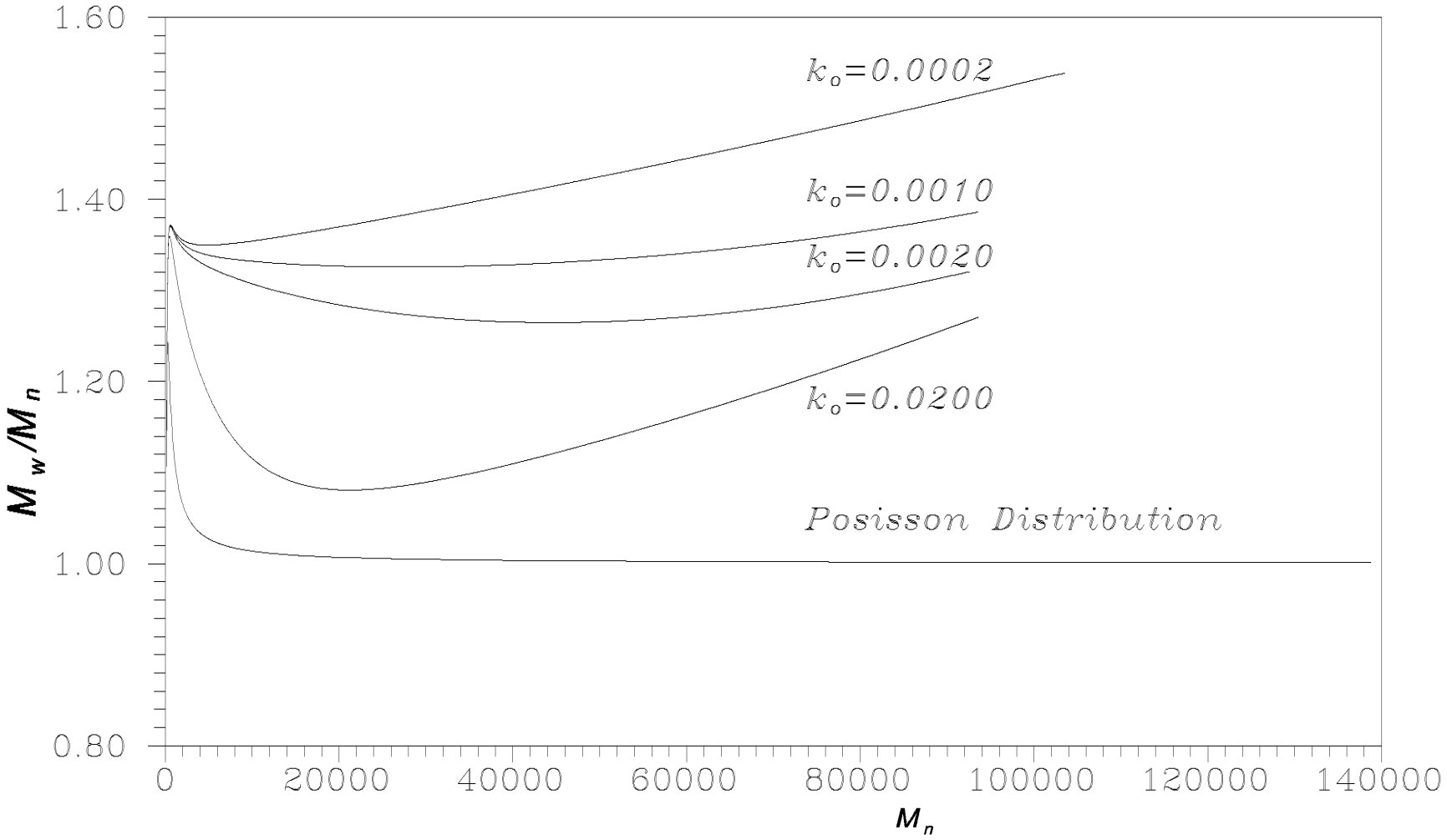


Fig. 3.9 Polydispersity as a function of M_n for different values of k_o. k_p=0.5 l/mol.min and k_t=0.00025 l/mol.min and $[M_o]/[I_o]$=3125 (s=3).

in THF and calibrated with polystyrene standards. After a specified time, the polymerization reaction was stopped and the reaction mixture was washed with water and then precipitated with an excess of methanol. This procedure removed the unreacted monomer, if any, before the sample is analyzed for molecular weight determination. In the present study, the values of experimental monomer/initiator ratio were reduced by a factor of three as an input to the computer program, since each initiator molecule initiates three chains [Dubois et al., 1991]. The close fit between the simulation results and the reported data (Figure 3.5) confirms the validity of this assumption.

The polydispersity values of only a few data points are shown in Figure 3.5 to avoid overcrowding of the figure, however, the detailed listing is given in Table 3.1. The values of polydispersity obtained from the model are slightly lower than the experimental values. This could possibly be due to the transesterification reaction. Dubois et al. [1991] have discussed the occurence of transesterification reaction in PLA synthesis. They have pointed out that polydisperity increases with reaction time due to intermolecular as well as intramolecular transesterification reactions.

The parameters k_o, k_p and k_t were selected from M_n and M_w vs polymerization time curves for different values of rate constant parameters by comparing the simulated and experimental curves. The values of parameters that gave a close fit were chosen. Thus the curve fitting was optimized by line-search and golden-section techniques and model comparison was done by visual assessment. An average simulation took about 30 min for simulating 300 hr polymerization time on a 1.9 GHZ Pentium 4 PC.

The method was also applied for the reported data of PLA synthesis using three other catalysts, namely, iron isobutyrate at 190 ^{0}C, iron trifluoroacetate also at 190 ^{0}C and zinc lactate at 140 ^{o}C.

3.5 Iron Isobutyrate Catalyst for PLA Polymerization

The polymerization procedure for the reported data [Stolt and Sodergard, 1999] involved adding the catalyst to 2 g of monomer (L-lactide) in 5 ml glass ampoules before being sealed under a nitrogen atmosphere. Amount of catalyst used varied between 0.12 and 1.2 wt %, corresponding to molar ratios of approximately 100-1000. The polymerization was carried out at 190^{o}C. After the desired time the polymerization was discontinued by removing the ampoules from the oven, the polymerization products were

Table 3.1 Comparison of experimental polydispersity and calculated polydispersity

$[M_o]/[I_o]$	Time(hr)	Experimental M_w/M_n	Calculated M_w/M_n	% Difference
417	53	1.34	1.25	6.7
	92	1.40	1.25	10.7
833	53	1.30	1.24	4.6
	77	1.50	1.24	17.3
	100	1.65	1.24	25.0
1875	60	1.21	1.24	2.5
	125	1.32	1.26	4.5
	224	1.36	1.27	6.6
3125	24	1.27	1.23	3.1
	50	1.34	1.25	6.7
	100	1.43	1.30	9.1
	133	1.45	1.32	9.0

removed and stored in a desiccator before characterization. Molecular weight and MWD measurements were obtained by size exclusion chromatography (SEC). The mobile phase in the system was tetrahydrofuran and polystyrene standards were used for calibration.

In the present work, the M_n and M_w were calculated as a function of polymerization time, for different monomer/initiator ratio, and were matched with the reported results [Stolt and Sodergard, 1999] as shown in Figure 3.10.

The deviations in predicted and experimental values of M_n and M_w at a fixed value of $[M_0]/[I_0]$ were minimized by adjusting three parameters k_p, k_0, and k_t. by line-search technique followed by golden-section method. To estimate the value of these parameters, an iterative method was adopted in which one parameter was varied at a time (keeping the other two constant). Starting with an initial guess value of all three parameters, a line-search was made (by changing one parameter with a constant increment/decrement) to find a condition where there is minimum deviation in the predicted and experimental values of M_n and M_w for the entire reaction time. Then the value of this parameter was fine tuned between two consecutive values, which were considered during line-search by the method of golden-section. Since the system of equations under consideration is highly nonlinear, on-line graphical observation of reported and predicted data were made after every iteration.

The values of polydispersity obtained from model are slightly lower than the experimental values. Once again, this could be due to the transesterification reaction. The values of the rate constants determined are: k_p=31.5 l/mol.min, k_0=0.02 l/mol.min, and k_t=0.025 l/mol.min. This indicates that the iron isobutyrate catalyst is able to initiate the chains much faster. Also, the chains propagate and terminate at a faster rate.

3.6 Iron Trifluoroacetate Catalyst for PLA Polymerization

The polymerization and characterization procedure for iron trifluoroacetate catalyst for PLA polymerization was the same as enumerated in Section 3.5. In the present work, the method developed is applied to iron triflouroacetate catalyst for PLA polymerization, at 190 ^{0}C [Stolt and Sodergard, 1999]. The results are shown in Figure 3.11. Here, the polydispersity data is not reported in the reference from where

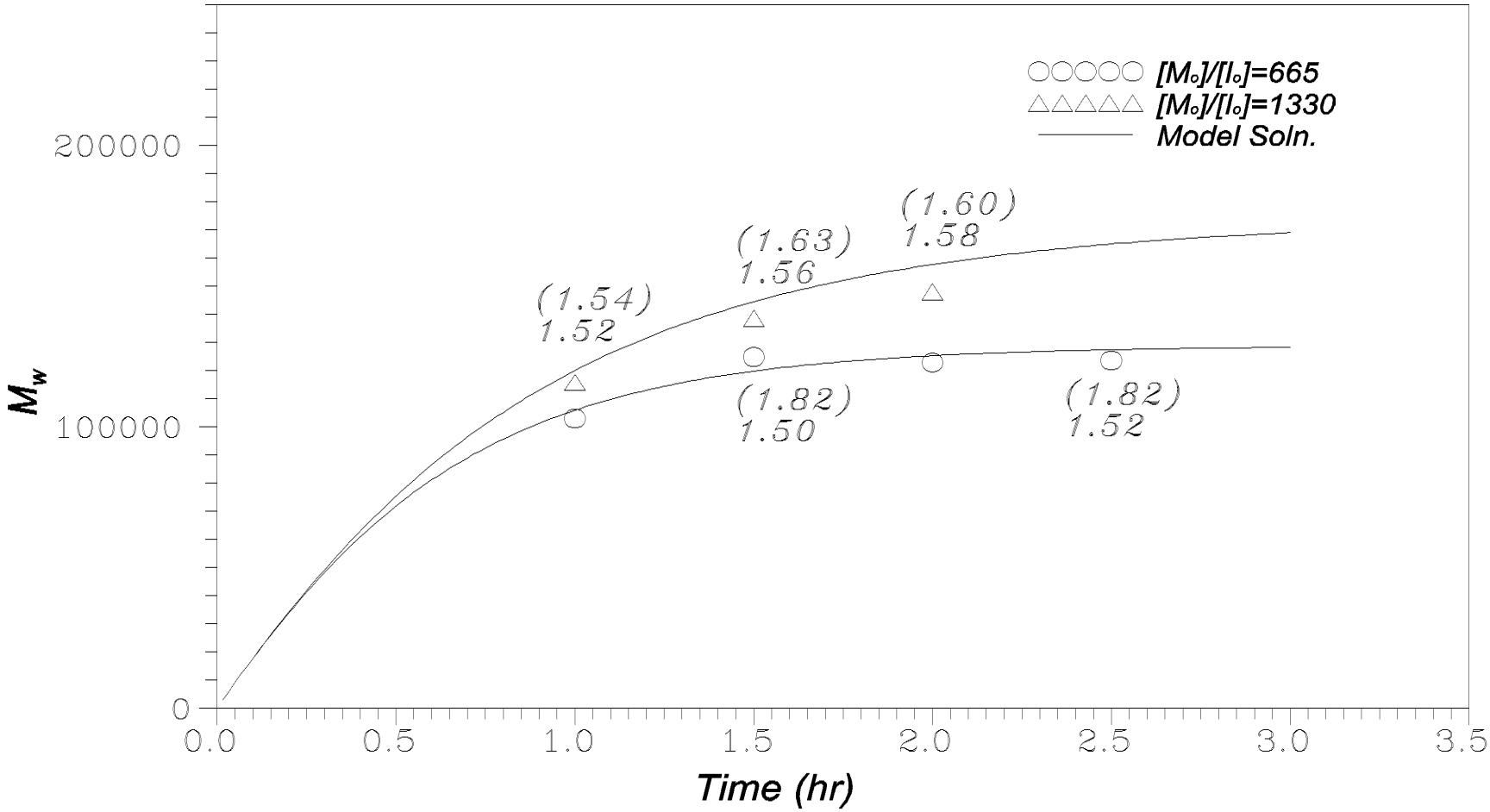


Fig. 3.10 A comparison of experimental [Stolt & Sodergard, 1999] and modeling results (weightr average molecular weight) for the polymerization of L-lactide, using iron isobutyarate catalyst. The solid lines are the solutions obtained from the model and points are the experimental values. The experimental polydispersity of selected points are noted in parentheses and the modeled polydispersity is shown below it.

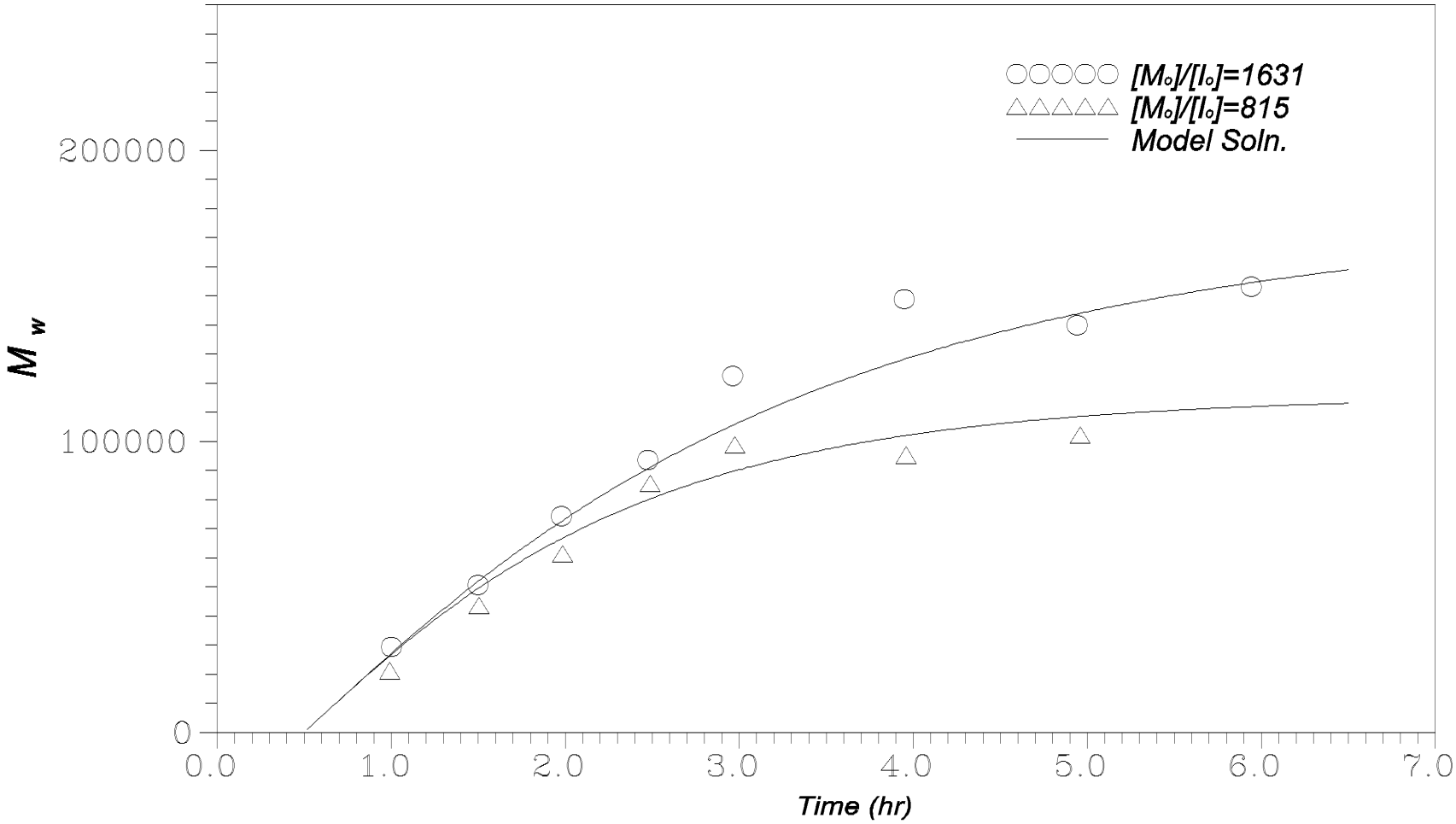


Fig. 3.11 A comparison of experimental [Stolt & Sodergard, 1999] and modeling results (weight average molecular weight) for the polymerization of L-lactide, using iron trifluoroacetate catalyst. The solid lines are the solutions obtained from the model and points are the experimental values.

data have been taken. Thus, the method only yielded the rate constants values for propagation and termination. k_0 could not be ascertained because as discussed before the molecular weight data alone is not sufficient for determining k_0. The values of k_p and k_t determined are 9.5 l/mol.min and 0.006 l/mol.min, respectively.

It is interesting to note that initially it was not possible to curve fit the data for any value of k_p and k_t. However, once the time axis was shifted by 30 min, an excellent fit was obtained for particular k_p and k_t. Stolt and Sodergard [1999] also refers to this induction time as possibly due to the fact that the catalyst has to be thermally activated in the beginning of the polymerization in order to be effective. However, they could not determine this time lag experimentally. From the present research work, we can confidently say that this time lag is 30 mins.

3.7 Zinc Lactate Catalyst for PLA Polymerization

The polymerization procedure for the reported data [Schwach et al., 1998] involved adding a selected amount of monomer with zinc lactate. The feed was then degassed through vacuum/argon cycles applied to the molten mixtures. The flask was cooled and sealed under vacuum. After 24 h of stirring at 140 ^{o}C, the flask was opened and 20 ml of acetone was added. The insoluble residue of catalyst was recovered by filtration and dried under vacuum. Acetone was evaporated from the filtrates and the residues were dried under vacuum. Molecular weights were obtained by size exclusion chromatography (SEC).

The results of the simulation are shown in Figure 3.12. The values of the rate constants determined are: k_p=5.7 l/mol.min, k_0=0.03 l/mol.min, and k_t=0.0050 l/mol.min. It is again interesting to note that initially it was not possible to curve fit the data for any value of k_p and k_t. However, once the time axis was shifted by 4 hrs., an excellent fit was obtained for particular k_p and k_t and this seems to be justified in a manner similar to iron trifluoroacetate catalyst case where the catalyst needed to be thermally activated in order to be effective.

The kinetic rate constants for the four catalysts are summarized in Appendix D. Parity plots for M_n and M_w for the four catalysts considered in this chapter are given at the end of Chapter 4.

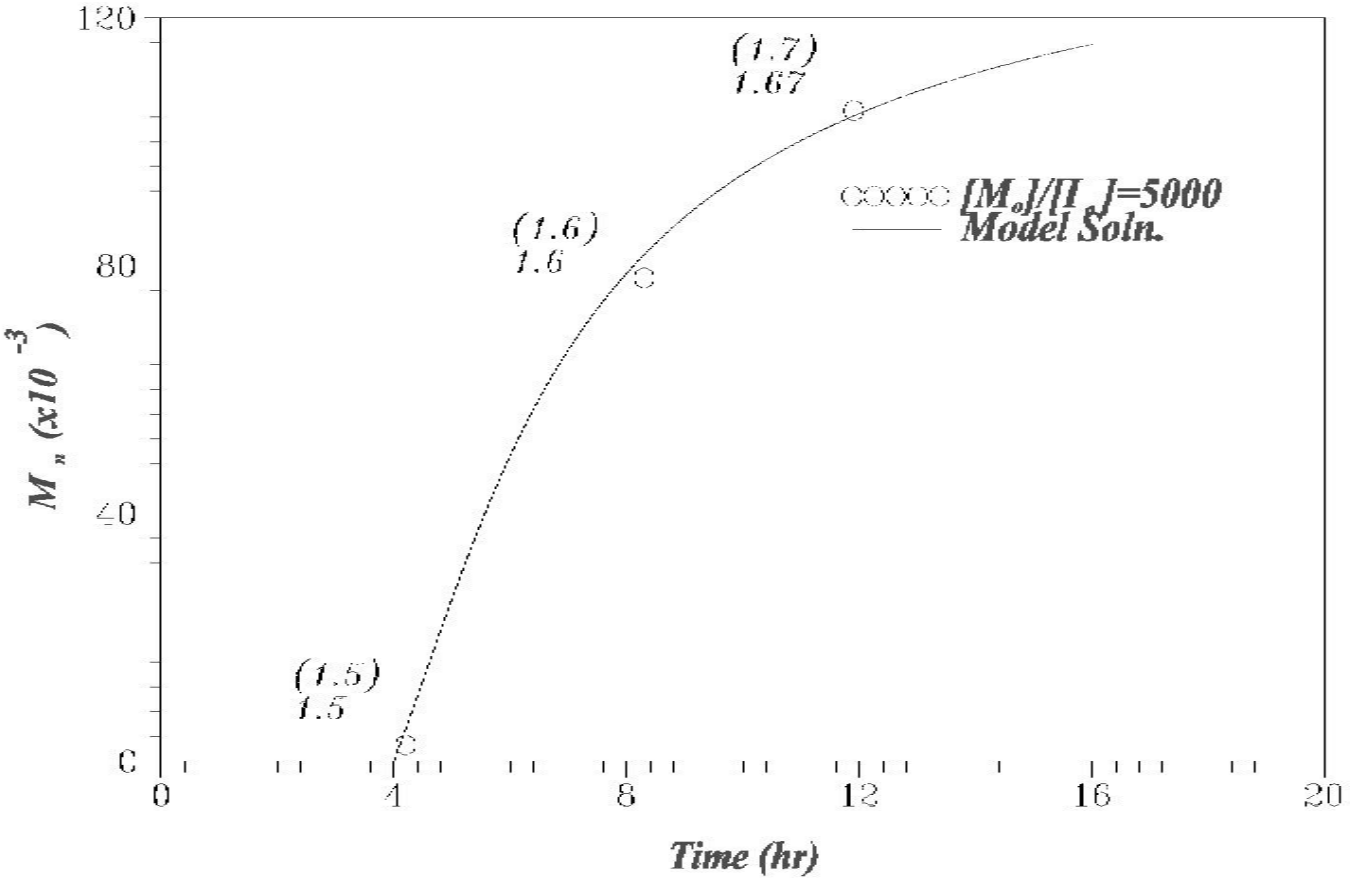


Fig. 3.12 A comparison of experimental [Schwach et al., 1998] and modeling results (numberr average molecular weight) for the polymerization of D,L-lactide, using zinc lactate catalyst. The solid lines are the solutions obtained from the model and points are the experimental values. The experimental polydispersity of selected points are noted in parentheses and the modeled polydispersity is shown below it.

3.8 Chain Length Dependent Propagation Rate Constant

The present method is also extended for simulation of variable propagation rate constant, k_j. Figures 3.13 ($[M_o]/[I_o]$=3125) and 3.14 ($[M_o]/[I_o]$= 417) shows two such typical plots where M_n versus polymerization time when k_j decreases by a constant fraction with increasing chain length, which can be defined by the following equation:

$$k_{j+1} = k_j(1-c) \qquad (3.17)$$

In equation (3.17) the value of c varies from 0 to 1. It is evident that as c increases, the propagation rate constant decreases sharply with a consequent lower molecular weight. At lower values of c, this decrease is only marginal and at c=0, k_j becomes constant.

3.9 Conclusions

During the last decade, PLA have received much attention chiefly due to its bio-medical applications. An attempt has been made towards modeling the polymerization of lactide leading to PLA. In the present thesis, a simple but reliable method is presented, which the use of computers enables the solution of the rate equations corresponding to a scheme involving initiation, propagation and termination. The method is easily extendable for more complex polymerization mechanisms. The simulations can be done in conjunction with the experimental data, to yield individual rate constants. It is possible to obtain unique values for various rate constants if M_n vs time and polydispersity data is available. It should be emphasized that accurate reproducible experimental data is needed for the method to yield accurate rate constants. Also, it is shown that it is possible to treat the problem without the assumption of equal reactivity.

This methodology offers greater opportunity for capturing high, non-equilibrium polymer yield through appropriately timed termination of the polymerization reaction.

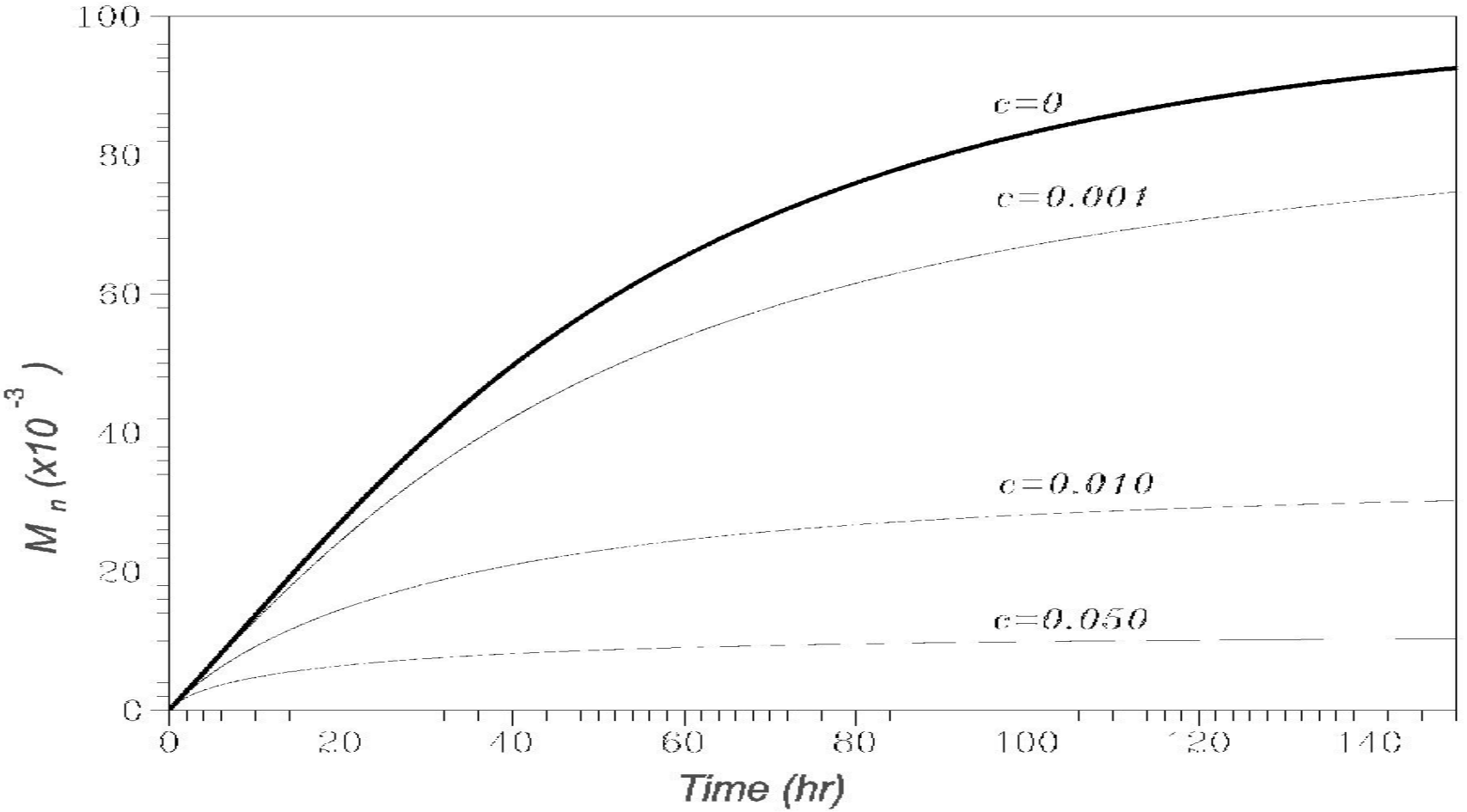


Fig. 3.13 Simulations for M_n vs. polymerization time as a function of chain length parameter c, as defined by equation (3.17). $[M_o]/[I_o]$=3125 (s=3), k_o=0.002 l/mol.min, k_{p1}=0.5 l/mol.min and k_t= 0.00025 l/mol.min

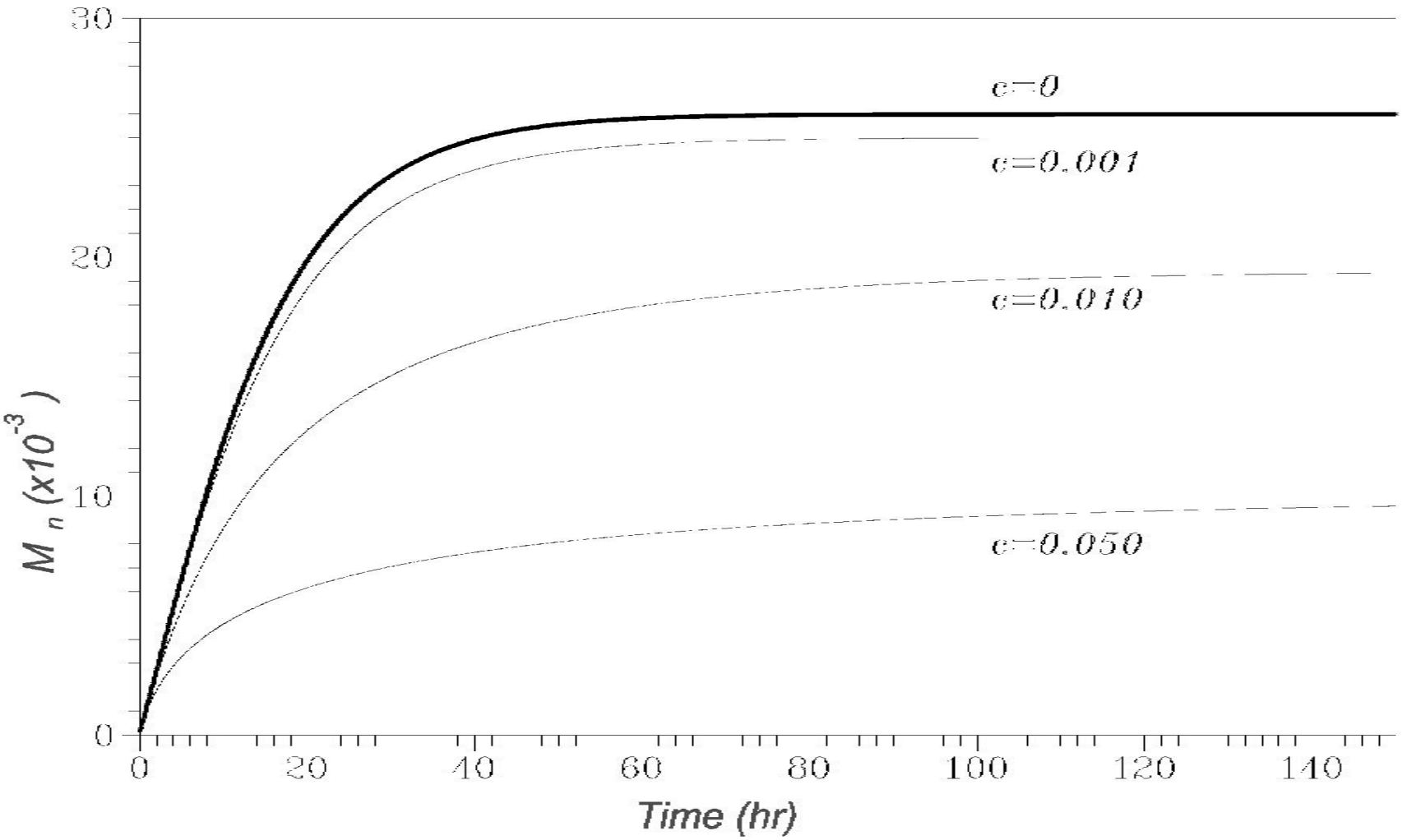


Fig. 3.14 Simulations for M_n vs. polymerization time as a function of chain length parameter c, as defined by equation (3.17). $[M_o]/[I_o]$=417 (s=3), k_p=0.002 l/mol.min, k_{p1}=0.5 l/mol.min and k_t= 0.00025 l/mol.min

Chapter – 4

Mathematical Modeling of the Poly(lactic acid) Ring-Opening Polymerization Kinetics-2

4.0 Introduction

The model developed in Chapter 3 is applied to the polymerization data in the form of degree of polymerization as a function of monomer-to-initiator ratio. The polymerization data is available in literature for the stannous octoate catalyst for PLLA and PDLLA [Eenink, 1987; Zhang et al., 1992]. A second model is formulated which considers cationic ring-opening polymerization mechanism where termination by transfer to polymer and by unimolecular termination (first order relative to active species) and intramolecular termination, are considered. These termination mechanisms have been observed to be present in cationic ring-opening polymerizations, in general [Penczek et al., 1980].

4.1 Formulation of the Problem: Mathematical Model 2

A cationic ring-opening polymerization (ROP) mechanism is developed for PLA polymerization. This differs from Model 1 discussed in chapter 3 with regard to mode of termination reaction. In this case, there are three possible ways through which termination of active chains can take place. It can be assumed that the kinetic scheme can be represented by the following equations:

Initiation and propagation reactions are characterized by a rate constant k_0, as explained earlier in equations (2.6) and (2.7), respectively.

$$M + I \xrightarrow{k_o} P_1 \qquad (2.6)$$

$$P_j + M \xrightarrow{k_j} P_{j+1} \quad , \; j=1,2,3,\ldots \qquad (2.7)$$

The termination by intermolecular chain transfer to active chains P_j and P_m produces an inactive chain M_{j+m}:

$$P_j + P_m \xrightarrow{k_{tp}} M_{j+m} \qquad (4.1)$$

The termination reaction by intermolecular chain transfer to polymer molecule is taken as given by equation (4.1) [Penczek et al., 1980] but there is no reason why similar

transfer to terminated chains also can not take place as shown in the following equation (4.2). The reaction is between a propagating center (the oxonium ion) and an oxygen atom of the ester group of a polymer chain. It is assumed that the inactive product obtained in equations (4.1) and (4.2) do not reinitiate the polymerization of the monomer. Schwach et al. [1997] in their study on ring-opening polymerization of PDLLA, using stannous octoate as a catalyst, have proposed a cationic mechanism involving initiation by octanoic acid (Figure 2.9).

The termination by intermolecular chain transfer to terminated chains M_j produces inactive chain M_{j+m}:

$$P_j + M_m \xrightarrow{k_{tp}} M_{j+m} \tag{4.2}$$

The third case can of unimolecular termination (first order relative to active species) and intramolecular termination given by:

$$P_j \xrightarrow{k_{ts}} M_j \tag{4.3}$$

As discussed in Section 3.1, the differential equations for the formation and disappearance of the living i-mers P_1, P_2, …P_j, as well as for the consumption of monomer and initiator, along with the formation of deactivated polymer, M_j, for a batch reactor, can be written as follows:

$$\frac{d[M]}{dt} = -[M]\{k_o[I] + \sum_{j=1}^{n} k_{pj}[P_j]\} \tag{4.4}$$

$$\frac{d[I]}{dt} = -k_o[I][M] \tag{4.5}$$

$$\frac{d[P_1]}{dt} = k_o[I][M] - k_{p1}[P_1][M] + k_{tp1}[P_1](\sum_{j=2}^{n}([P_j] + [M_j]) \tag{4.6}$$

$$\frac{d[P_j]}{dt} = [M]\{k_{p(j-1)}[P_{j-1}] - k_{pj}[P_j]\} - \sum_{m=1}^{n} k_{tpj}[P_j][P_m] - \sum_{m=1}^{n} k_{tpj}[P_j][M_m] - k_{tsj}[P_j], \quad j>1 \tag{4.7}$$

$$\frac{d[M_j]}{dt} = k_{tsj}[P_j] + \sum_{l=1}^{j-1} k_{tpj}[P_l][P_{j-l}] + \sum_{l=1}^{j-1} k_{tpj}[P_l][M_{j-l}], \quad j > 1 \qquad (4.8)$$

The initial conditions, at t=0, are:

$[M_j]=0$ and $[P_j]=0$, $j \geq 1$ (4.9)

$[M]=[M_o]$ (4.10)

$[I]=[I_o]\times s$ (4.11)

It is subsequently assumed that rate constants are chain length independent. Explanation of equation (4.8) for the time rate change of concentration of M_j is given in Appendix E.

It should be mentioned that Model 1 would be applicable for both anionic and cationic polymerizations, but the Model 2 would be applicable to only cationic polymerizations [Penczek et al., 1980] as the termination mechanisms considered in Model 2 are typical of only cationic ring-opening polymerizations.

4.2 Method of Solution

The method of solution is similar to one outlined in Chapter 3. Equations (4.4) to (4.11) were solved using Euler's method on a PC using Pascal. There was a large difference in the computing time required for running the programs between Model 1 and Model 2. The typical computing time for Model 1 was 30 min on a 1.9 GHz Pentium 4 PC and the Model 2 run took nearly a week on the same PC. The number average degree of polymerization was calculated as a function of monomer-to-initiator ratio and was compared with the reported results [Eenink, 1987; Zhang et al., 1992]. A reaction time of 9000 min was allowed for the polymerization simulations and there was no change in the calculated values even up to 15000 min. Thus, time period of 9000 min (150 hrs) was uniformly used for all the simulations. A check for the reliability of the computer program in the limiting case of Poisson distribution (a large value of k_o and k_t =0) similar to that given in Chapter 3, is presented in Figure 4.1. A straight line between the number average degree of polymerization, DP_n, and $([M_o] - [M])/[I_o]$ is obtained with the slope and the intercept equal to one.

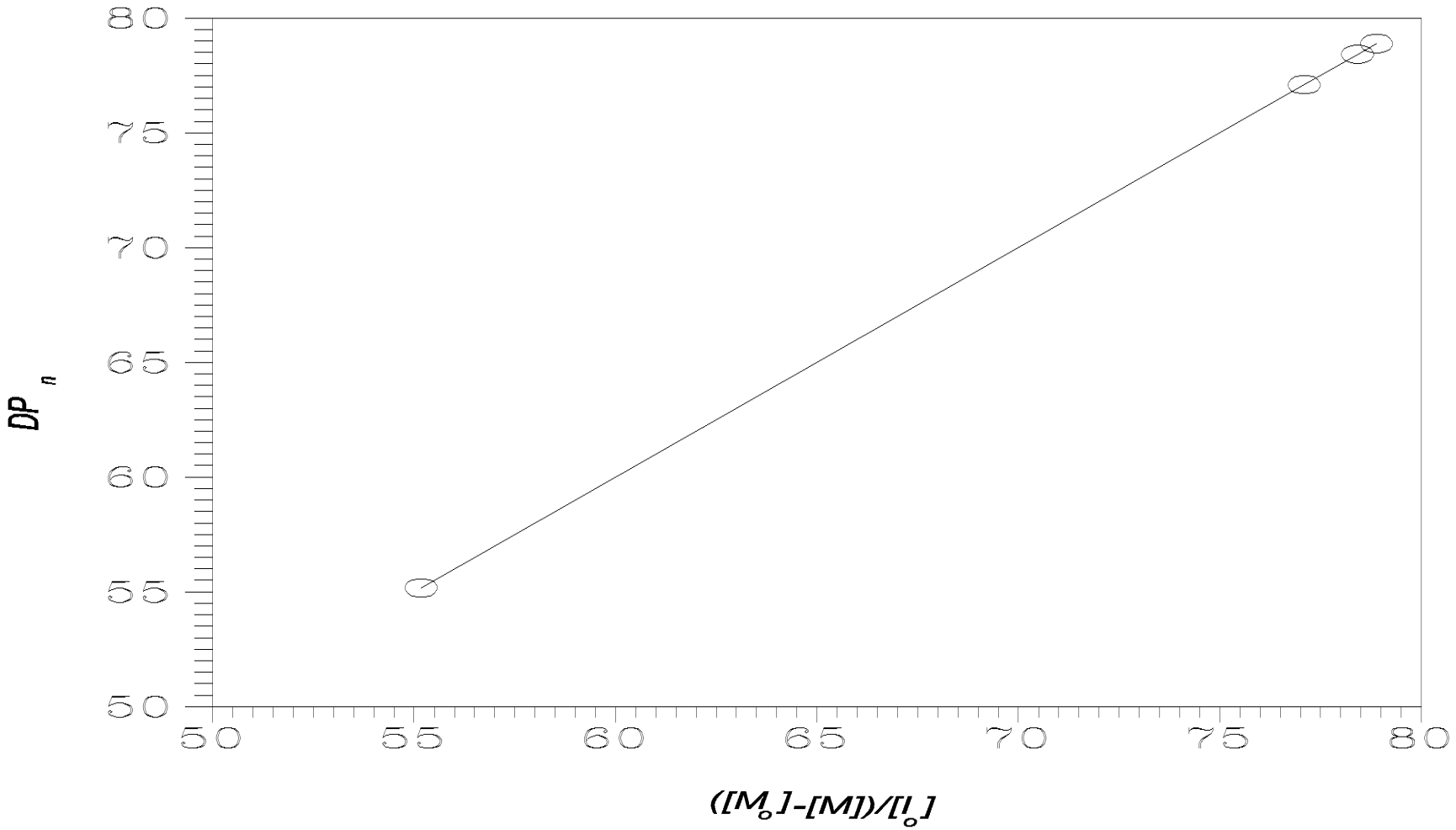


Fig. 4.1 A linear relationship between the degree of polymerization (number average) and *([M₀] - [M])/[I₀]* obtained by the proposed numerical technique for the limiting case of Poisson distribution (for a small value of reaction time).

The results of computer solutions for the Models 1 and 2 are compared with the experimental data in Figure 4.2 for PDLLA [Zhang et al., 1992] and Figure 4.3 for PLLA [Eenink, 1987].

4.3 Results and Discussion

The mathematical modeling tool has been utilized in conjunction with the reported data [Eenink, 1987; Zhang et al., 1992] to get the individual rate constants for the ring-opening polymerization of lactide, using stannous octoate as a catalyst. The values of the rate constants determined are: k_p=0.90 l/mol.min, k_o=0.003 l/mol.min, k_t=1× 10^{-6} l/mol.min, k_{tp}=1× 10^{-6} l/mol.min and k_{ts}=1× 10^{-7} min^{-1}. These rate constants are same for both models (where applicable). It is interesting to note that k_t (rate constant for termination by transfer to monomer) for the first model and k_{tp} (rate constant for termination by transfer to polymer) for the second model, obtained by matching the model curves with the given experimental data, are same. For low values of monomer to initiator ratio both models predict the same curve. At higher monomer-to-initiator ratio, the difference in termination mechanisms comes forth clearly. The termination rate constants are quite small but significant.

The initial portion of the model curves (Figures 4.2 and 4.3) is lower than the corresponding experimental data. According to Zhang et al. [1994] it is stannous alkoxide and not stannous octoate, which is the true initiator that is formed in the presence of alcohol or impurities. The stannous alkoxide concentration would be lower than the added concentration of stannous octoate, and this will explain why the observed degree of polymerization is higher than the monomer-to-stannous octoate molar ratio at low conversion.

Another point that deserves mention is that unlike the experimental points at very high monomer-to-initiator ratio (Figure 4.3), the simulated curves tend to plateau out. A possible explanation is that at higher monomer to initiator ratio initiator concentration is very small. At this concentration even a small amount of impurities (which will vary from one experiment to another) can play havoc with the molecular weight since there are relatively very few growing chains.

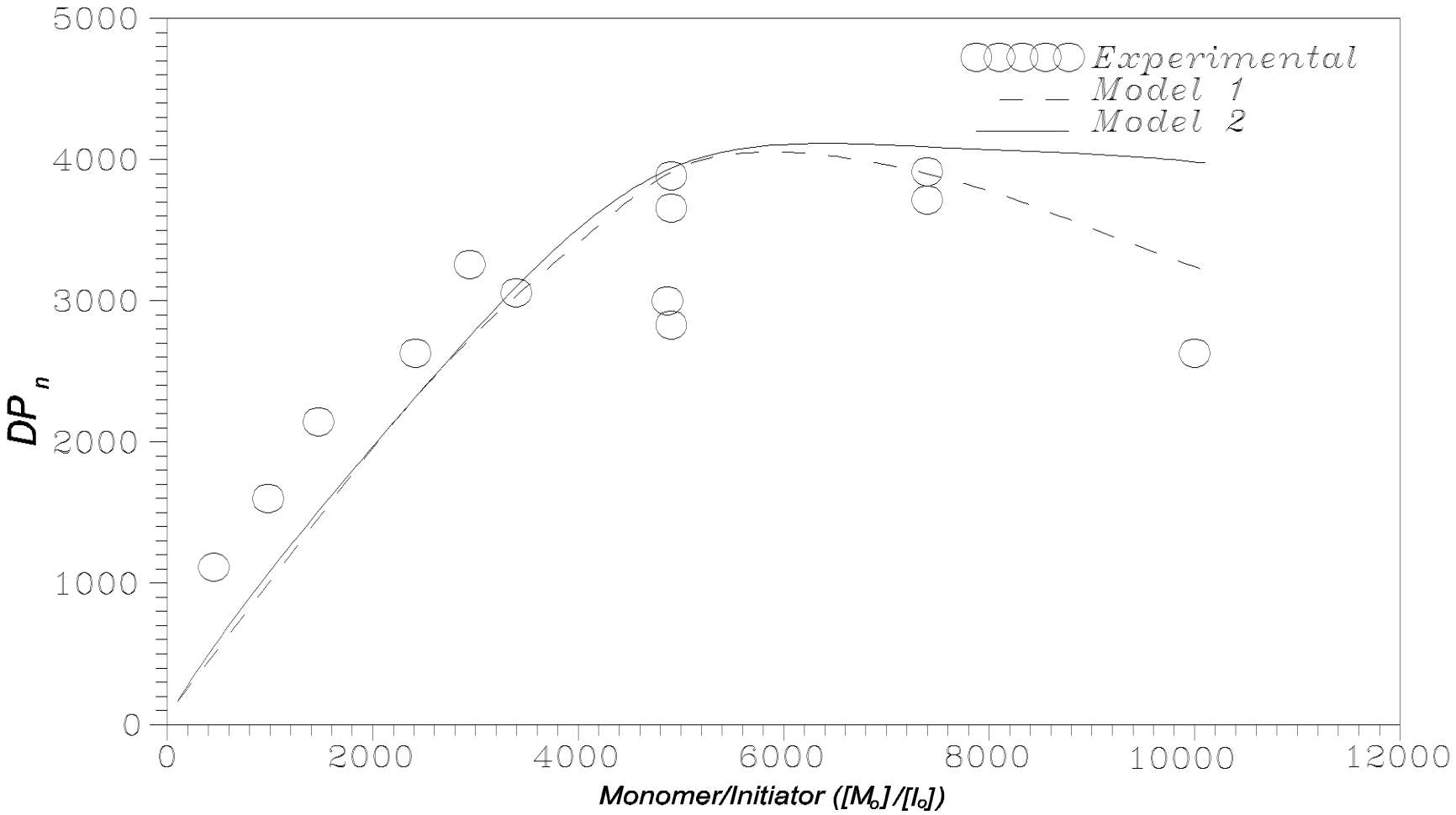


Fig. 4.2 A comparison of experimental [Zhang et al., 1992] and modeling results (number average molecular weight) for the polymerization of D, L-lactide, using stannous octoate catalyst. The solid lines are the solutions obtained from the model and points are the experimental values.

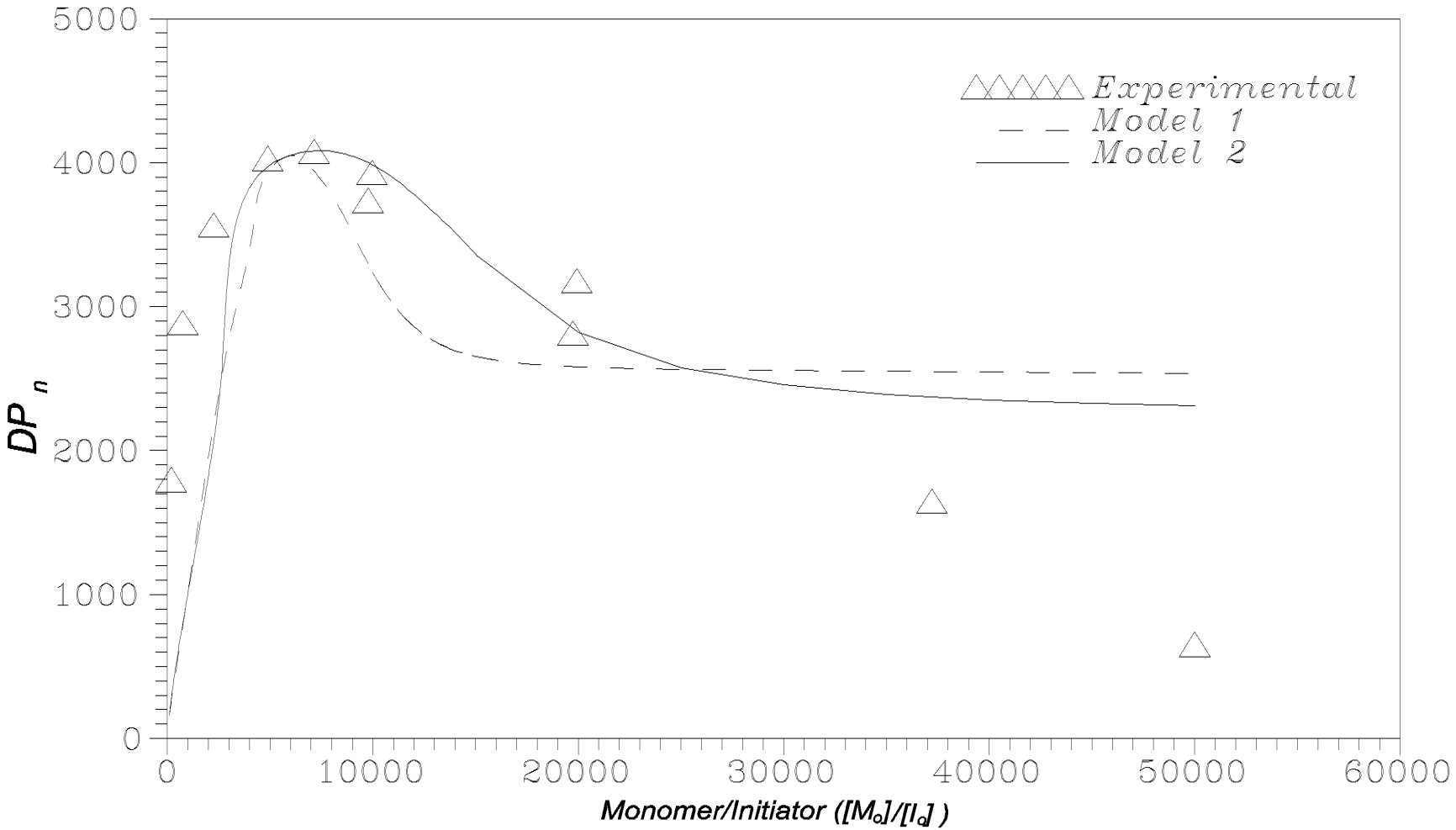


Fig. 4.3 A comparison of experimental [Eenink, 1987] and modeling results (number average molecular weight) for the polymerization of L-lactide, using stannous octoate catalyst. The solid linesare the solutions obtained from the model and points are the experimental values.

At lower values of $[M_0]/[I_0]$ ratio, the initiator concentration $[I_0]$ is considerably high. As the $[M_0]/[I_0]$ ratio increases, for a given $[M_0]$, the number of initiator molecules decreases. So with an increase in $[M_0]/[I_0]$ ratio there is a reduction in the number of chains onto which given monomer molecules can distribute themselves. Thus, the molecular weight increases with an increase in $[M_0]/[I_0]$ ratio. With further increase in $[M_0]/[I_0]$ ratio, the number of initiated chains decreases so much that with the same termination rate constant, there is quick termination of a significant percentage of chains, which results in lowering of molecular weight and peak formation in the curve. For example, taking rather extreme cases for the purpose of illustration, if earlier there were 50,000 number of initiated chains at $[M_0]/[I_0]=1$, then at $[M_0]/[I_0]=25000$ (with same $[M_0]$), there would be two initiated chains. Since monomer is readily available in both cases and the probability of termination by transfer to monomer is same, the chance that one or both the polymer chains gets terminated soon after initiation is high. This would result in a lowering of molecular weight. However, afterwards the curve becomes flat indicating that the termination effect becomes pronounced after chains have reached some minimum size, and further decrease in number of initiated chains should result in lower yields.

The curves in the figures were drawn by matching simulations of Model 1and 2 with the experimental data. The objective was to find out if the difference in the degree of closeness of the curves to the experimental points is sufficient to ascribe a polymerization mechanism for the stannous octoate catalyst. However, it is not possible to ascribe a specific mechanism to PLLA and PDLLA polymerization on the basis of experimental data used in modeling (Figures 4.2 and 4.3). These experimental data points are characterized by poor reproducibility. However, it should be pointed out that for ROP this type of poor reproducibility is expected.

The parity plots for the M_n as well as M_w for all the five catalysts considered (including the four considered in the Chapter 3) are given in Figures 4.4 and 4.5. A summary of the rate constants evaluated for the five catalysts considered is given in Appendix D. Following inferences can be drawn from these results:

1. The values of propagation rate constants are in the range of 0.5 – 31.5 l/mol.min, which are comparable to the values of k_p reported for other ring-opening polymerizations (Odian, 1991). These values are

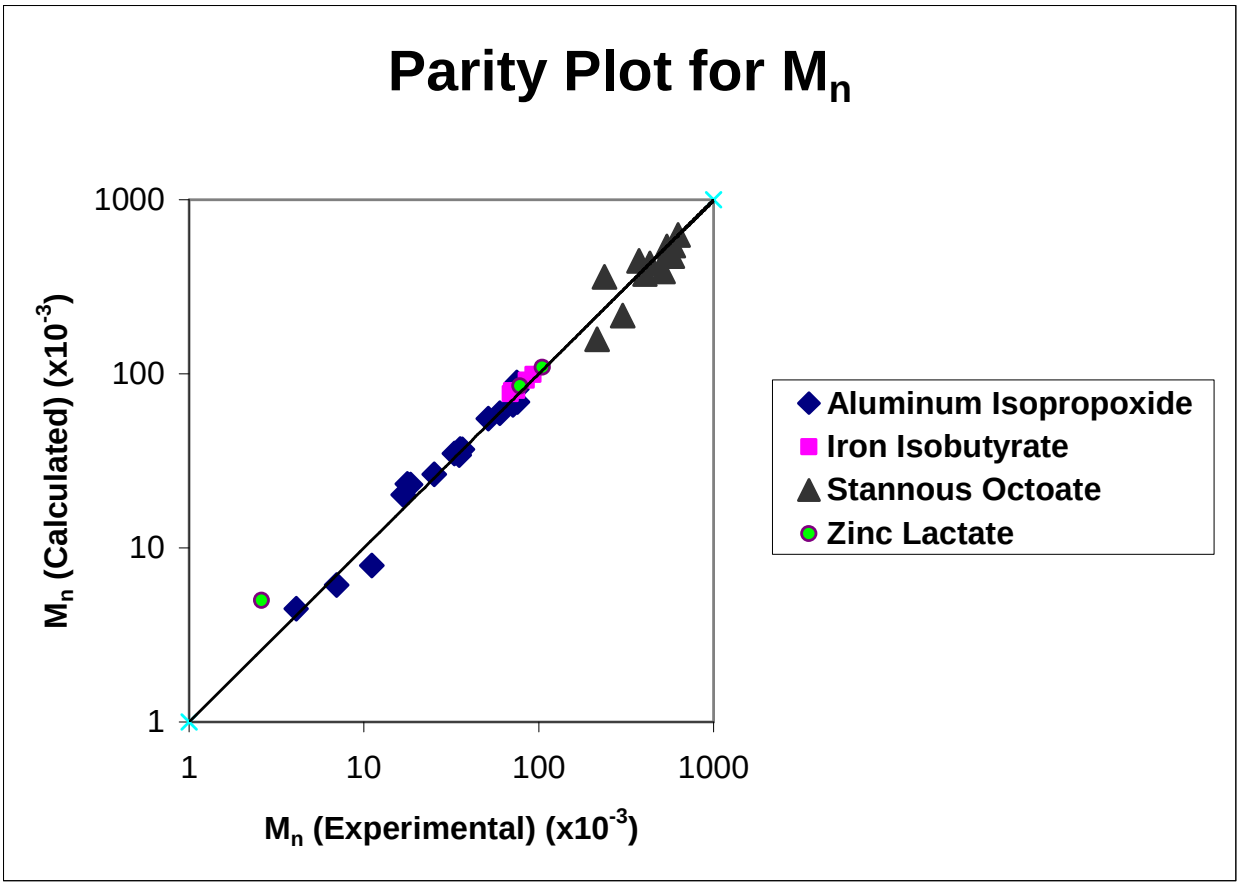


Fig.4.4 Parity plot between the experimental data and the calculated values of M_n for various catalysts.

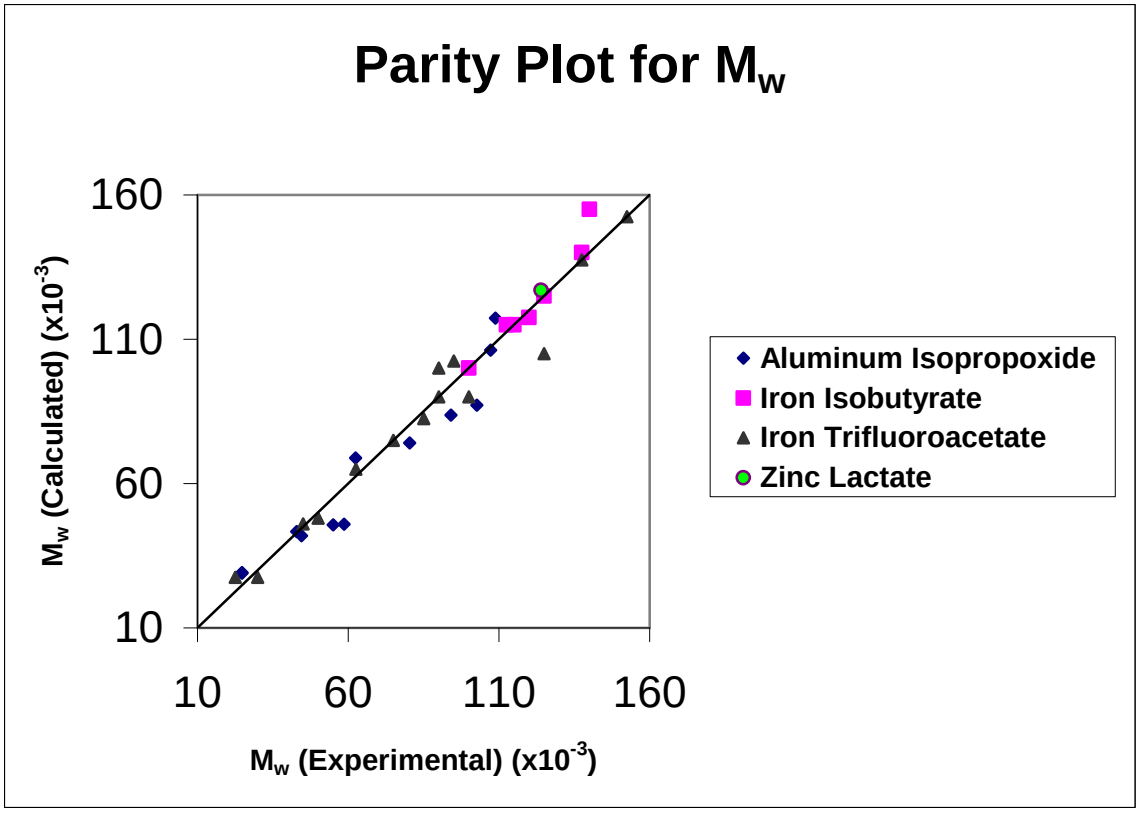


Fig.4.5 Parity plot between the experimental data and the calculated values of M_w for various catalysts.

comparable to the corresponding values for step polymerizations and much smaller than those for various chain polymerizations.

2. The monomer chain transfer termination constant varies greatly for the four catalysts.
3. For the stannous octoate catalyst, the rate constants are same for PDLLA and PLLA.
4. For the cationic mechanism model considered for the stannous octoate catalyst, the values of rate constants for chain transfer to polymer and spontaneous combination and intramolecular termination are very small.

4.4 Conclusions

Modeling the polymerization of lactide as an ionic process, it is possible to follow the experimental data closely. The rate constants for both the mechanisms are same although for the same rate constants, the traces of curves at high monomer-to-initiator ratio are significantly different. The termination rate constants are low but significant. It is not possible to ascribe a particular polymerization mechanism for PLLA and PDLLA for the given experimental data.

It is known that the ROP of DL-lactide by stannous octoate is much more complex to be controlled particularly when one takes into account the facts that traces of water are difficult to remove from lactides and that stannous octoate is always chemically polluted by 2-ethylhexanoic acid. This can be a critical point when the stannous octoate initiator is used as received, as it is often the case in the literature. It is of interest to note that this contaminant is not removed by distillation and, even worse, it gets formed when stannous octoate is allowed to age in a flask. The ROP of lactide initiated by stannous octoate is therefore difficult to investigate. This complexity is likely to be responsible of the fact that, after 30 years of research efforts, one is still ignorant of the exact mechanism of lactide polymerization in the presence of the most popular and industrially used initiator. This is largely due to the fact that part of the initiator is hydrolyzed in the presence of impurities, namely water, octanoic acid, and lactic acid, as deduced from

polymerization at low monomer-to-initiator values. One can argue that the situation might be different in the presence of extremely small amounts of stannous octoate, a point which remains obscure since it is not possible to check the chemical nature of end groups for high molecular weight polymers. However, the proposed model can be used to predict polymerization at very high monomer to initiator ratio and it can be deduced if impurities are playing any significant role under these conditions.

The parity plots for the four catalysts show an excellent agreement between the reported experimental values and the values calculated through the present approach.

Chapter – 5

Mathematical Modeling of the Poly(lactic acid) Ring-Opening Polymerization –Effect of Water as an Impurity

5.0 Introduction

Ionic polymerizations are usually carried out under high vacuum or in an inert atmosphere with rigorously cleaned reagents and glasswares since trace impurities lead to termination of polymerization reaction. Moisture adsorbed on the surface of glassware is usually removed by flaming under vacuum or washing with a active polymer solution. Any moisture present terminates the propagating ions. The remaining ions are not able to usually re-initiate the polymerization and the kinetic chain is broken. Water has an especially negative effect on polymerization, since it is an active chain transfer agent. Presence of even small concentrations of water can greatly limit the polymer molecular weight. The presence of other impurities may not be as much of a problem. Ethanol has a transfer coefficient of about 10^{-3}, its presence would not prevent the formation of high polymer because transfer would be slow, although the polymer would not be living. In impurities, such as water, acids, esters etc., have different chain transfer properties (Mathieson, 1963). The presences of these transfer agents in sufficient concentrations results in transfer to them becoming the dominant mode of termination. Termination by these compounds involves transfer of HO, RO, or RCOO anion or the corresponding cation. Aromatics, ethers, and alkyl halides are relatively weak chain-transfer agents.

Compounds such as amines, triaryl or trialkylphosphines, and thiophene act as inhibitors or retarders in cationic polymerization by converting propagating chains to stable cations that are unreactive to propagation. Agents such as water, alcohol (often with KOH), ammonia, and amines are often used in excess to quench a cationic polymerization.

Traces of water are difficult to remove from lactides and in case of the stannous octoate catalyst, which is industrially used, it is always chemically polluted by 2-ethylhexanoic acid. In this case, part of the initiator is hydrolyzed in the presence of impurities, namely water, octanoic acid, and lactic acid.

In the present work, an attempt is made to quantify the effect of water on the polymer molecular weight during PLA polymerization.

5.1 Formulation of the Problem: Mathematical Model 3

Initiation, propagation and termination by transfer to monomer proceed by the following reactions as discussed before.

$$M + I \xrightarrow{k_o} P_1 \qquad (2.6)$$

$$P_j + M \xrightarrow{k_j} P_{j+1} \quad , \; j=1,2,3,\ldots \qquad (2.7)$$

$$P_j + M \xrightarrow{k_t} M_j + P_1 \qquad (2.8)$$

The model additionally considers termination by transfer to water (impurity) as follows:

Termination by transfer to water can be given by:

$$P_j + C \xrightarrow{k_{tc}} M_j + OH^- / H^+ \qquad (5.1)$$

where M, I and P_j are the monomer (lactide), initiator and active polymer chain of j repeat units, respectively. M_j is the deactivated polymer of j repeat units, which will not undergo propagation. C represents the impurity, water, in equation (5.1). It is assumed that each initiator molecule initiates one polymer chain. The termination mechanism has been assumed to be the chain transfer to monomer and water.

Mass balance equations for a batch reactor may be written for this kinetic scheme as follows:

$$\frac{d[M]}{dt} = -[M]\{k_0[I] + \sum_{j=1}^{n} k_j[P_j] + \sum_{j=1}^{n} k_{tj}[P_j]\} \qquad (3.1)$$

$$\frac{d[I]}{dt} = -k_0[I][M] \qquad (3.2)$$

$$\frac{d[P_1]}{dt} = k_o[I][M] - k_1[P_1][M] + \sum_{j=2}^{n} k_{tj}[P_j][M] - k_{tc1}[P_1][C] \qquad (5.2)$$

$$\frac{d[P_j]}{dt} = [M]\{k_{p(j-1)}[P_{j-1}] - k_{pj}[P_j] - k_{tj}[P_j]\} - k_{tcj}[P_j][C], \qquad j > 1 \qquad (5.3)$$

$$\frac{d[M_j]}{dt} = k_{tj}[P_j][M] + k_{tcj}[P_j][C], \qquad j \geq 1 \qquad (5.4)$$

$$\frac{d[C]}{dt} = -\sum_{j=1}^{n} k_{tcj}[P_j][C] \qquad j \geq 1 \qquad (5.5)$$

Initial conditions, in addition to those in equations (4.9) to (4.11), at t=0, is:

$$[C]=[C_o] \qquad (5.6)$$

where $[C_o]$ is the initial water concentration and $[C]$ is the concentration after time t. It is subsequently assumed that rate constants k_{pj}, k_{tj} and k_{tcj} are chain length independent.

For an ionic polymerization (polymerization of styrene with sodium naphthalene), the chain transfer coefficient of the water, $k_{tr,water}$ (= $k_{t,c}/k_p$), has been reported to be 10 [Szwarc, 1960]. In this work, the same value of chain transfer coefficient has been used.

It should be kept in mind that M represents the cyclic lactide monomer; P_1 is the charged monomer molecule after the lactide monomer ring opens up, and M_1 is the deactivated molecule after the charge on P_1 is no longer present.

5.2 Method of Solution

Researchers have tried to treat the problem of effect of impurities on the ionic polymerizations analytically. Gold [1957] presented a detailed study of the polymer statistics for a reaction system resembling the ethylene oxide initiator case allowing for the different rates of initiation and propagation. The steady-state assumption was made and an analytical solution is obtained. Nanda and Jain [1967] derived an analytical solution of the problem with the assumption that the impure monomer is added in small doses to the initiator. This is done such that the reaction of the propagation centers with impurities is essentially completed within the time interval between the consecutive doses. This assumption implies that there would be no accumulation of the monomer or the impurities, even though the rate constants for two processes are different. In another study [Jain and Nanda, 1976] they treated the problem with the steady state assumption and considered the simultaneous effect of chain transfer to monomer and spontaneous chain transfer. Cabrerizo and Guzman [1979] carried out a theoretical study of the effect of a transfer agent on the MWD in living polymer, assuming an infinitely fast initiation and instantaneous reinitiation after the transfer reaction. Expressions for the number –

average and weight-average chain lengths are obtained for the three limiting cases: (a) both the monomer and the transfer agent remain at constant concentration, (b) only the concentration of the transfer agent is kept constant, and (c) both concentrations vary with time. Other theoretical studies include Coleman et al. [1963] and Yuan & Yan [1986a, b, 1987].

In the present case, equations (3.1), (3.2), (5.2) to (5.5) were solved in a manner similar to that discussed in previous chapters. The number average degree of polymerization was calculated using equation (2.4). Also, as before, the programs were checked for the limiting case of Poisson distribution when there is no termination, and initiation is much faster than propagation.

5.3 Results and Discussion

The mathematical modeling tool has been utilized in conjunction with the reported data [Zhang et al., 1992] to get the individual rate constants for the ring-opening polymerization of lactide, using stannous octoate as a catalyst. The values of the rate constants determined are: k_p=0.90 l/mol.min, k_o=0.003 l/mol.min, k_t=1× 10^{-6} l/mol.min, k_{tc}= 9.0 l/mol.min. The results of computer solutions are shown in Figure 5.1. The water concentration in the experimental reaction vessel is estimated to be 0.5 ppm. The termination rate constant, k_t, is quite small but significant. It limits the maximum PLA molecular weight achievable to about 0.6 million. The effect of increase in water concentration is clearly seen as shifting the entire curve southwards. It is useful to remember that conventional 'dry box' condition usually do not involve moisture level lower than 10^{-3} M [Kennedy, 1976].

It is apparent from Figure 5.1 that once effect of water is considered, the PDLLA polymerization (Zhang et al., 1992) follows the model closely. A possible explanation of the simulated curves in Figure 5.1 is as follows. When a substance like water with a high chain transfer coefficient is present, the termination rate increases drastically. This results in shorter chains and the curves shift downwards with increasing concentration of water. The peaks of the curves also shifts left because the high rate constant result in quick termination of a significant percentage of chains at a lower $[M_0]/[I_0]$ ratio (i.e. higher number of initiated chains for given $[M_0]$).

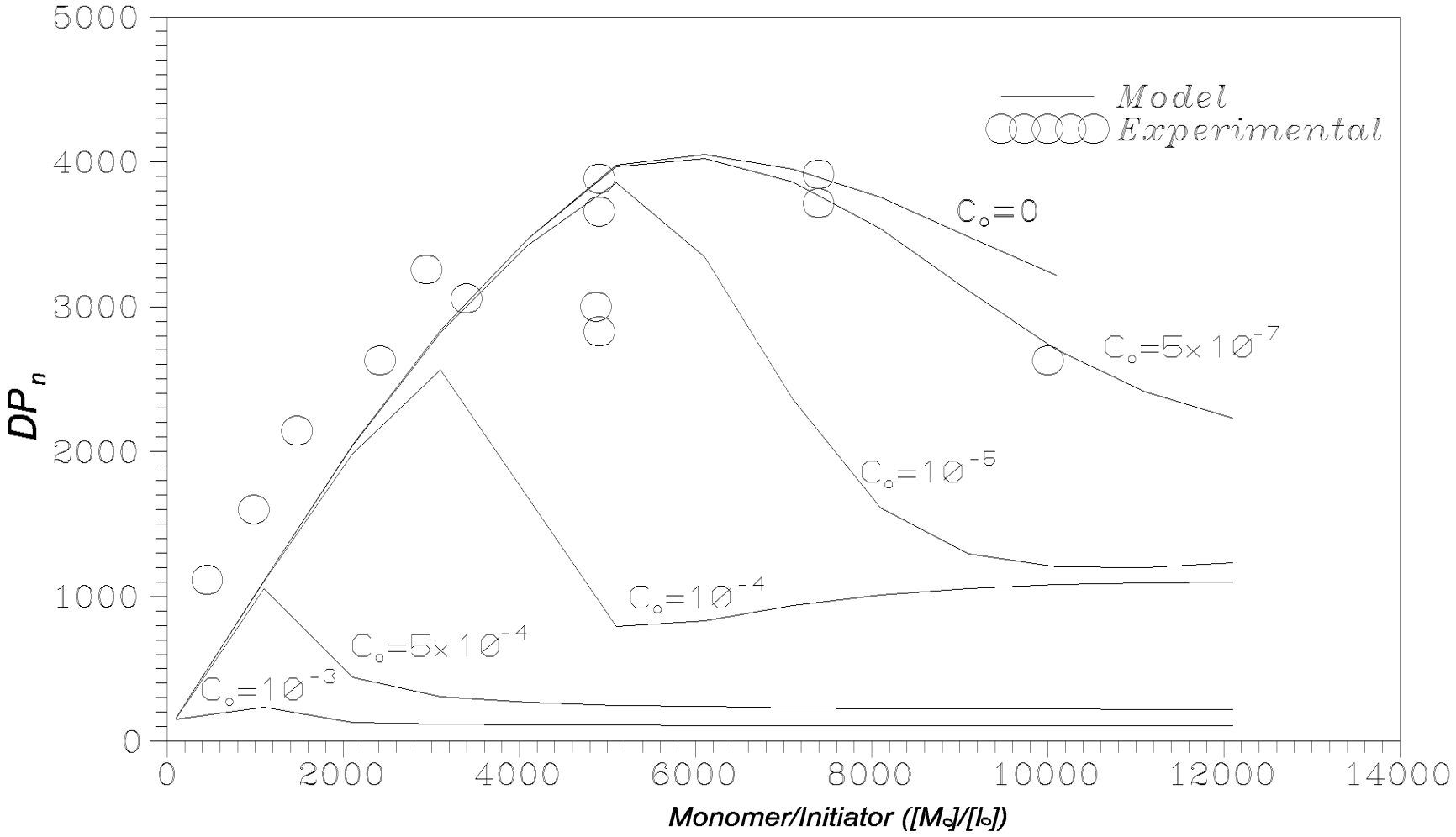


Fig. 5.1 A comparison of experimental [Zhang et al., 1992] and modeling results (DP_n) for the polymerization of (D, L)-lactide. The solid lines are the solutions obtained from the model as a function of initial water concentration, C_o, and the points are experimental values.

5.4 Conclusions

A comprehensive model for ring-opening polymerization of PLA has been developed based on an ionic polymerization mechanism. It was shown that given the range of $[M_0]/[I_0]$ experimental data, it is possible to get rate constants for initiation, propagation and termination by transfer to monomer and water. The method is unique in its simplicity, novelty and efficacy. Simulations reveal that water concentration in the reported data was about 0.5 ppm. It is quantitatively shown that there is marked decrease in the degree of polymerization in the presence of even small concentration of water in the reaction vessel.

Chapter – 6

Conclusions and Recommendations

6.1 Conclusions

On the basis of present modeling approach used for PLA polymerization, the following significant conclusions may be drawn:

1. The progress of lactide polymerization can be modeled by assuming a ring opening reaction mechanism comprising of chain initiation, chain propagation, and chain termination.
2. The simulator developed, based on the solution of differential equations corresponding to the above-mentioned kinetic scheme generates a detailed molecular weight distribution that can be used to estimate average molecular weights (or average degree of polymerization) vs. polymerization time curves. These simulated curves on matching with the reported experimental data (for different catalysts) yields the absolute values of rate constants. The values have been determined for four catalysts, namely, aluminum isopropoxide, iron isobutyrate, iron trifluoroacetate and zinc lactate. Rate constants could be determined by using the molecular weight and the polydispersity vs. polymerization data. An excellent agreement exists between the molecular weight values calculated from the present method and the reported experimental data as borne out by the parity plots.
3. The present method can also be extended to the case where the data is in the form of molecular weight vs monomer-to-initiator ratio. This type of data, available in the literature for stannous octoate catalyst for PLA polymerization, can be used with the simulator. Thus, the values of initiation, propagation and termination by transfer to monomer rate constants were found for stannous octoate catalyzed PLA polymerization.
4. An alternate cationic mechanism can also be considered for stannous octoate catalyzed PLA polymerization, where termination by transfer to polymer and unimolecular termination (first order relative to active species) and intramolecular termination, are considered. The present method yields the absolute values of the rate constants. There is significant difference in the behavior of simulated curves at high monomer-to-initiator ratio for the two models. However, given the poor reproducibility of the experimental data considered in the present work (and likely

to be present in general for these ring-opening polymerizations), it is not possible to choose between the two models.

5. The present method works well without the need of assuming a chain length independent propagation rate constant.
6. It is quantitatively shown that the presence of even trace amount of water can significantly reduce the molecular weight of PLA. As the water concentration is increased, the maximum in the degree of polymerization vs. monomer-to-initiator curves shifts lower and towards left.

6.2 Recommendations for Future Work

The present modeling approach needs further improvement and rigorous testing. For this the following are recommended:

1. Additional data can be collected from the literature and the models developed in this study can be applied to them to generate rate constants for the particular catalysts.
2. The propagation reaction should be made reversible to account for the depropagation reaction. This is expected to lead to a more accurate model.
3. In this study the value of rate constants for stannous octoate catalyzed PLA polymerization have been determined using the data in the form of average molecular weights vs. monomer-to-initiator ratio. It will be interesting to compare these values of rate constants with those obtained for data in the form of average molecular weights vs polymerization time.

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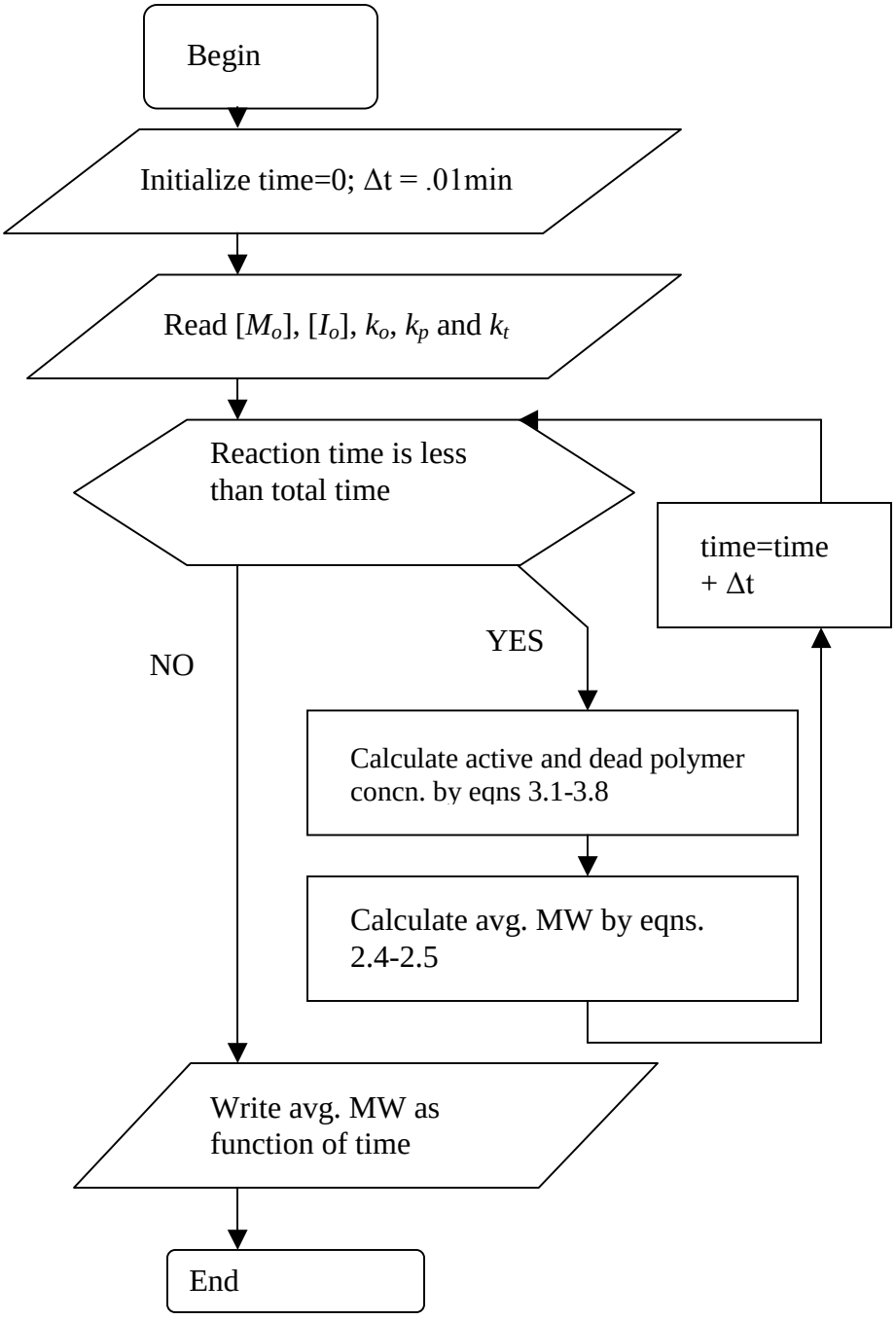
APPENDIX A

Details of the programming technique

A simplified flowchart to calculate the average molecular weights as a function of reaction time as per model 3.1.



Programming technique

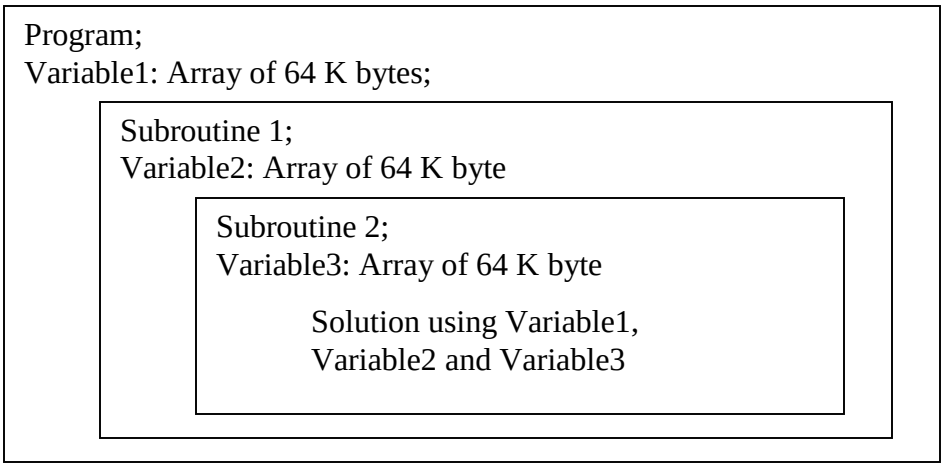
First of all the computer program takes numerical values of all required parameters such as the values of initial monomer concentration, initial initiator concentration and values of rate constants for initiation, propagation and termination etc. The concentrations of active polymer chains and terminated chains as well as rate constants (as a function of chain length) are in the form of arrays of 5000 real numbers.

The differential equations are solved by Euler's method and average molecular weights obtained corresponding to concentration of active and terminated polymer chains. Starting from zero, the time variable is incremented by 0.01 min till it reaches a predefined total reaction time. The time interval was found to be small enough for the present technique.

The program outputs are the values of average molecular weights as a function of polymerization time.

Problem of insufficient memory

When an attempt was made to increase the size of arrays up to 5000 using "Turbo Pascal™" compiler, there was a problem of shortage of memory due to limitation of 64 K bytes stack memory. This is a major bottleneck of making PC based memory-intensive programs. This problem was solved by writing the program by using embedded subroutines as given in figure below. Three set of variables were defined in three different subroutines such that all variables were available to the innermost subroutine as global variables. This approach was successful because each subroutine can have a maximum of 64 K bytes memory.



APPENDIX B

A comparison of the numerical solution of equations (3.1) to (3.6) and the first derivative model solution

In order to check the suitability of the present numerical technique, it was compared to a solution obtained by [Zeman and Amundson, 1965b] for a slightly different kinetic scheme considering only the first derivative term in the Taylor series expansion of the activated polymer concentration analytical function. Their solution is for the following kinetic scheme:

$$M + I \xrightarrow{k_o} P_1 \qquad \text{(B1)}$$

$$P_j + M \xrightarrow{k_j} P_{j+1} \qquad \text{(B2)}$$

$$P_j + M \xrightarrow{k_t} M_j + I \qquad \text{(B3)}$$

Thus the only difference between the present scheme and that considered by Zeman and Amundson is that in equation (B3) an initiator molecule is formed whereas in equation (2.8) P_1 is formed. The comparison is shown in Figure B.1 for the time required for the 99% completion of the reaction. A reasonably good fit is obtained between the two curves. The difference in the two curves may be due to the following reasons:

1. As Zeman and Amundson have observed in their paper, the first derivative model loses a great deal of detail when approximating such sharp distributions.
2. As discussed in the literature review section, it has been found that that the accuracy of approximation is very strongly dependent on the number of terms retained in the Taylor's series expansion, as well as on the polymer chain length [Penczek et al., 1980]. Falkovitz and Segal [1982] concluded that at least a second- order approximation is required in these analyses.
3. The kinetic schemes considered are slightly different.

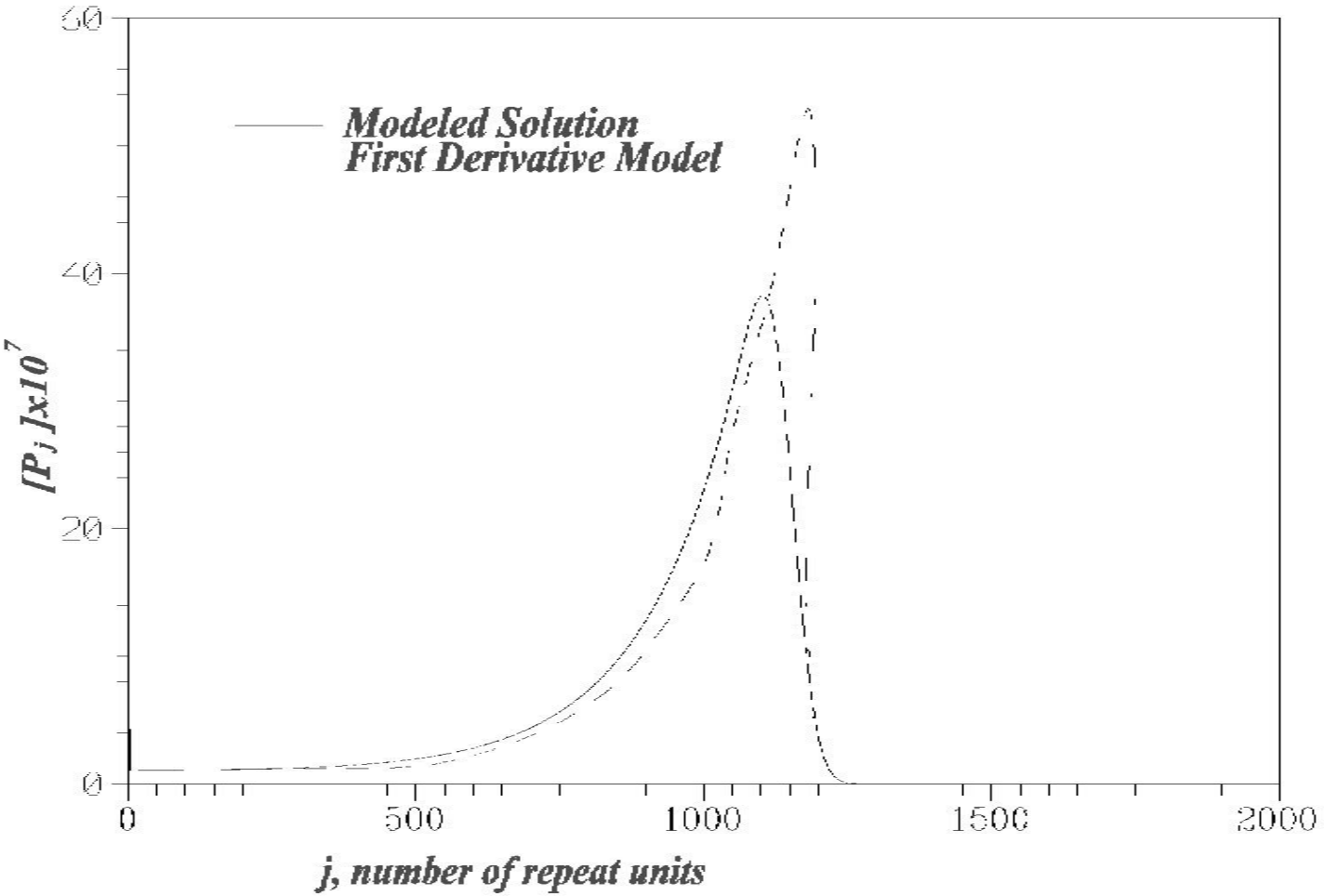


Fig. B.1 Comparison of numerical and first derivative model analytical solution for $[P_j]$ vs j . $[M_o]/[I_o]$=1000 , k_o=62.5 l/mol.hr, k_p=10000 l/mol.hr and k_t= 1.0 l/mol.hr

APPENDIX C

Experimental data for PLA polymerization reported in literature

1. Catalyst: Aluminum isopropoxide [Dubois et al., 1991]

a. $[M_o]/[I_o]=417$

Time, *t* (hr)	4.56	23.4	53.3	92.4
$M_n \times 10^{-3}$	6.99	16.8	18.5	17.7
M_w/M_n	-	-	1.34	1.4

b. $[M_o]/[I_o]=833$

Time, *t* (hr)	3.25	5.84	24.7	52	76.6	100.6
$M_n \times 10^{-3}$	4.1	11.1	25.2	33	36.7	35.5
M_w/M_n	-	-	-	1.30	1.50	1.65

c. $[M_o]/[I_o]=1875$

Time, *t* (hr)	60.13	124.8	223.7	287.7
$M_n \times 10^{-3}$	51.55	71.3	75.5	76.7
M_w/M_n	1.21	1.32	1.36	-

d. $[M_o]/[I_o]=3125$

Time, *t* (hr)	24.5	50.3	98.0	132.9
$M_n \times 10^{-3}$	35	60	75	75
M_w/M_n	1.27	1.34	1.43	1.45

2. Catalyst: Iron isobutyrate [Stolt and Sodergard, 1999]

a. $[M_o]/[I_o]=1330$

Time, *t* (hr)	1	1.5	2.0
$M_w \times 10^{-3}$	11.25	13.75	14
M_w/M_n	1.54	1.63	1.60

b. $[M_o]/[I_o]=665$

Time, *t* (hr)	1	1.5	2.0	2.5
$M_w \times 10^{-3}$	10	12	11.5	12.5
M_w/M_n	-	1.82	-	1.82

3. Catalyst: Iron trifluoroacetate [Stolt and Sodergard, 1999]

a. $[M_o]/[I_o]$=1631

Time, t (hr)	1	1.5	2.0	2.5	3.0	4.0	5.0	6.0
$M_w \times 10^{-3}$	30	50	75	85	125	137.5	135.0	152.5
M_w/M_n	-	-	-	-	-	-	-	-

b. $[M_o]/[I_o]$=815

Time, t (hr)	1	1.5	2.0	2.5	3.0	4.0	5.0
$M_w \times 10^{-3}$	22.5	45	62.5	75	90	90	95
M_w/M_n	-	-	-	-	-	-	-

4. Catalyst: Zinc lactate [Schwach et al., 1998]

$[M_o]/[I_o]$=5000

Time, t (hr)	4.2	8.3	11.9
$M_n \times 10^{-3}$	2.6	78	105
M_w/M_n	1.5	1.6	1.7

5a. Catalyst: Stannous octoate [Zhang et al., 1992] for polymerization of D,L- lactide

$[M_o]/[I_o]$	1000	1500	2400	3400	5000	7500	10100
DP_n	1500	2100	2500	3000	3800	3750	7600

5b. Catalyst: Stannous octoate [Eenink, 1987] for polymerization of L- lactide

$[M_o]/[I_o]$	187	751	2255	4887	7142	4962	9774
DP_n	1796	2888	3567	4029	4077	3932	3737

$[M_o]/[I_o]$	19924	19736	37218	50000
DP_n	3179	2815	1650	655

APPENDIX D

Table D.1 Summary of rate constants determined for various catalysts

S.No.	Polymer	Catalyst	k_o (l/mol.min)	k_p (l/mol.min)	k_t (l/mol.min)
1.	PDLLA	Aluminum Isopropoxide	0.002	0.5	0.00025
2.	PLLA	Iron Isobutyrate	0.020	31.5	0.025
3.	PLLA	Iron Trifluoroacetate	Not Determined	9.5	0.006
4.	PDLLA	Zinc Lactate	0.03	5.7	0.0050
5.	PDLLA, PLLA	Stannous Octoate	0.003	0.9	10^{-6} ---------- $k_{tp}=10^{-6}$ $k_{ts}=10^{-7}$ min^{-1}

APPENDIX E

Explanation of equation (4.8) for the time rate change of concentration of M_j

The equation (4.8) is reproduced below:

$$\frac{d[M_j]}{dt} = k_{ts}[P_j] + \sum_{l=1}^{j-1} k_{tp}[P_l][P_{j-l}] + \sum_{l=1}^{j-1} k_{tpj}[P_l][M_{j-l}], \quad j > 1 \qquad \text{(D1)}$$

The rate of production of terminated polymer M_j is the sum of its production by reactions (4.1) to (4.3). If we write the equations for some values of j, it is easy to verify the equation. This is done below:

For j=2,

$$\frac{d[M_2]}{dt} = k_{ts}[P_2] + \left(k_{tp2}[P_1][P_1]\right) + \left(k_{tp2}[P_1][M_1]\right) \qquad \text{(D2)}$$

For j=3,

$$\frac{d[M_3]}{dt} = k_{ts}[P_3] + \left(k_{tp3}[P_1][P_2] + k_{tp3}[P_2][P_1]\right) + \left(k_{tp3}[P_1][M_2] + k_{tp3}[P_2][M_1]\right) \qquad \text{(D3)}$$

For j=4,

$$\frac{d[M_4]}{dt} = k_{ts}[P_4] + \left(\underline{k_{tp4}[P_1][P_3]} + k_{tp4}[P_2][P_2] + \underline{k_{tp4}[P_3][P_1]}\right) + \left(k_{tp4}[P_1][M_3] + k_{tp4}[P_2][M_2] + k_{tp4}[P_{31}][M_1]\right) \qquad \text{(D4)}$$

For j=5,

$$\frac{d[M_5]}{dt} = k_{ts}[P_5] + \left(k_{tp5}[P_1][P_4] + k_{tp5}[P_2][P_3] + k_{tp5}[P_3][P_2] + k_{tp5}[P_4][P_1]\right) + \left(k_{tp5}[P_1][M_4] + k_{tp5}[P_2][M_3] + k_{tp5}[P_3][M_2] + k_{tp5}[P_4][M_1]\right) \qquad \text{(D5)}$$

The underlined terms in equation (D4) (and several terms in other equations) are numerically equal. But they have to be considered separately because these underlined terms represent different events occurring at the same time to generate a particular terminated polymer chain of four units. The propagating center of a chain of a single repeat unit (P_1) attaches to an ester group in a chain of three units (P_3), as represented by the first underlined term. On the other hand, the second underlined term represents a propagating center of (P_3) being attached to the ester group of (P_1).

List of Publications

PUBLICATIONS

1. **Rajeev Mehta**, V. Kumar, H. Bhunia and S.N. Upadhyay; Synthesis of poly(lactic acid): A review. Journal of Macromolecular Science – Polymer Reviews, 45(4), 325-349, 2005.
2. **Rajeev Mehta**, V. Kumar, S.N. Upadhyay; Mathematical modeling of the poly(lactic acid) ring-opening polymerization kinetics. Polymers-Plastics Technology & Engineering, 2006 (Accepted).
3. **Rajeev Mehta**, V. Kumar, S.N. Upadhyay; Mathematical Modeling of the Poly(lactic acid) Ring-Opening Polymerization using Stannous Octoate as a Catalyst, Polymers-Plastics Technology & Engineering, 2006 (Communicated).

CONFERENCES

1. **Rajeev Mehta**, V. Kumar, S.N. Upadhyay; Mathematical modeling of the poly(lactic acid) ring-opening polymerization kinetics. Conference Proceedings of 'National conference on Catalysis in Energy', IT-BHU, 23-25 Feb. 2006.
2. **Rajeev Mehta** and V. Kumar, Ring-opening poly(lactic acid) polymerization: Synthesis and kinetics . Conference Proceedings of 'National Conference on Materials and Related Technologies', TIET, 313-319, Sept. 2003.
3. **Rajeev Mehta** and V. Kumar, Modeling of the ring-opening poly(lactic acid) polymerization. Conference Proceedings of 'National conference on Polymers and Materials', TTTI, Chandigarh, Feb. 2003.