Satya Prakash Dubey

Mathematical modelling and simulation of continuous, highly precise, metal/eco-friendly polymerization of Lactide using alternative energies for reaction extrusion

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Full time PhD

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This thesis is submitted in partial fulfilment of the requirements for the degree of PhD

(NB. This section can be removed if the award of the degree is based solely on examination of the thesis)

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Dedicated to my Hero

(Dr. Avul Pakir Jainulabdeen "A. P. J." Abdul Kalam)

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This work is just a small drop in the ocean of knowledge and information created by celebrated authors whose published work has been consulted and referred in this Doctoral research thesis.

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Satya Dubey

ABSTRACT

Polylactic acid (PLA) is one of the most promising bio-compostable and biodegradable thermoplastic made from renewable sources. PLA, is typically obtained by polymerising lactide monomer. The technique mainly used for ring opening polymerization (ROP) of Lactide is based on metallic/bimetallic catalyst (Sn, Zn, and Al) or other organic catalysts in suitable solvent. However, the PLA synthesized using such catalysts may contain trace elements of the catalyst, which may be toxic. In this work, reactive extrusion experiments using stannous octoate $Sn(Oct)_2$ and tri-phenyl phosphine $(PPh)_3$ were considered to perform ROP of lactide monomer using ultrasound as an alternative energy (AE) source for activating and/or boosting the polymerization. Mathematical model of ROP of lactide, was developed to estimate the impact of reaction kinetics and AE source on the polymerization process.

Ludovic® software, a commercial code was used. It was adopted for the simulation of continuous reactive extrusion of PLA. Results from experiments and simulations were compared to validate the simulation methodology. Results indicate that the application of AE source in reaction process boost the PLA formation rate. Result obtained through Ludovic simulation and experiments were validated. It was shown that there is a case for reducing the residence time distribution (RTD) in Ludovic due to the 'liquid' monomer flow in the extruder. This change in the parameters resulted in validation of the simulation. However, it was concluded that the assumption would have to be established by doing further validations.

The simulation model includes the details of kinetics of reactions involved with in the process and helps to upscale the reaction output. This work also estimates the usefulness and drawbacks of using different catalysts as well as effect of alternative energies and future aspects for PLA production.

Keywords: alternative energy; bio-degradable; reactive extrusion; metal/non-metal catalyst; eco-friendly; mathematical modelling; ring opening polymerization (ROP)

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***Abbreviations*:**

PLA, Poly Lactic Acid;
PLLA, Poly Levo Lactic Acid;
LA, Lactic Acid; L-LA, Levo Lactic Acid;
DL-LA, Dextro, Levo Lactic Acid;
CA, Cellulose acetate;
PA, Polyamide;
PBS, Poly-butylene succinate;
PP, Poly-propylene;
PU, Poly-urethane;
PET, Polyethylene terephthalate;
HIPP, High impact polystyrene;
PVC, Poly vinyl chloride;
ROP, Ring opening polymerization;
UFDA, U.S. Food and Drug Administration;
AE, alternative energy;
OMt-K10, Montmorilloniate-K10;
DMAP, Di-alkyl-amino-pyridine;
PPY, Polypyrrole;
NHC, N-heterocyclic carbine;
bvp4c, Boundary Value Problems;
MINDO, Modified Intermediate Neglect of Differential Overlap;
MO, Molecular orbital;
µ- Microwave
B3LYP, Becke 3-Parameter (Exchange), Lee, Yang and Parr (correlation; density functional theory);
US, Ultrasound;
PCL, poly (ε-caprolactone);
Rex, Reactive extrusion
LRP, living free radical polymerization;

1 INTRODUCTION

1.1 **Background**

The use of polymers has increased exponentially in the past 4-5 decades. Polymers cover the wide range of applications such as consumer products, medical equipment, packaging, drugs, clothes, household, stuff etc. An average American family produces more than 3,000 kg/year of harmful waste [1],[2]. Sven Jacobsen et al. [23] mentioned in an article that in the case of plastic waste, US alone produced 35 million tonnes of consumer polymers in 1998 whereas the corresponding figure of Europe and Asia were 34 million tonnes and 25 million tonnes respectively. This has resulted in the production of large amounts of waste, and plastic waste disposal is now one of the major challenges of the present time. This has prompted scientists to look closely at bio-based and biodegradable polymers such as cellulose acetate (CA), polyamide (PA), poly-butylene succinate (PBS), poly-lactic acid (PLA), poly-propylene (PP), poly-urethane (PU) etc. comes in the existence [1].

1.2 **Advantages of Polymers**

The major factors to judge the quality and suitability of polymers depend on its degradability and availability of its basic constituent material (monomers). There are several advantages of using petrochemical-based polymers such as (a) low cost and high-speed production; (b) good heat sustainability; (c) good barrier properties and (d) high mechanical performance. On the other hand, several disadvantages include: (a) rise in oil and gas prices during recent decades; (b) declining oil and gas resources; (c) environmental concerns for their degradation or incineration and global warming; (d) consumer toxicity risks due to the monomers or oligomers migrating to edible materials and (e) uneconomical costs and cross-contaminations in their recycling [2]-[4].

1.3 **Conventional Catalysis process and alternatives**

Use of metallic or bimetallic catalysts for the synthesis of bio-polymers helps to achieve industrial scale throughput. However, these metal catalysts were proven to be carcinogenic in nature and harmful to the environmental (toxicity and hazardousness) [1],[6],[7],[8]. Hence, research efforts need to be directed to replace use of such catalysts from the production process. There are some studies that reported on the production of biopolymer using some organic/metal-free catalysts by Dalko et al. [3], Kamber et al. [4], Wang et al. [5]. However, the throughput production reported through these works was very less (2-5) kg/hr, which is less than that of typically obtained for using metallic catalyst at industrial scale production.

1.4 **Poly-Lactic acid (PLA) bio-polymer**

Biodegradable polymers emerged as an important alternative to traditional polymers such as polyethylene terephthalate (PET), high impact polystyrene (HIPP) and poly vinyl chloride (PVC) [5]-[8]. In the field of biopolymers, PLA emerged as a promising polymer because of its property as a compostable, biodegradable thermoplastic [8] made from renewable sources such as corn starch, sugarcane and chips. Poly-Lactic acid (PLA) was discovered in 1932 by Carothers (at DuPont) [6], [7].

Commercial use of PLA has increased in in last 15 years because of its biodegradable and biocompatible nature and extensive use in the field of medical and clinical consumer products [1], [18], [21], [30]. The market for biodegradable and the common consumable polymer such as PET, HIPP and PVC, which is useful for household products, was approximately around 200,000 tonnes in 2005, of which PLA was 100,000 tonnes. Lactic acids are the major component of the food-related application in the USA and cover 85% of the commercial products.

1.5 Synthesis of PLA: Use of metallic catalyst and non-metallic catalysts

For PLA synthesis, Ring opening polymerization (ROP) of Lactide (LA) monomer is one of the preferred methods. In the literature, the technique mainly developed for ROP of LA is based on metal and the bimetallic catalyst like (Sn, Zn and Al) [7],[8],[9],[10] in the suitable solvent and has proven to be an effective way to produce PLA. These processes lead to throughputs in the range of (30-40) kg/hr, making production scalable and cost effective. Although the metallic catalysts ensure the industrial level of production, Traces of metallic catalyst are often found in the processed PLA. This limits the use of PLA in the field of medicine and food packaging [6-7].

Replacing the metallic catalysts with non-metallic catalysts or some other metal free source is the most natural solution. However, such a switch makes the production ‘inefficient’ because of low activation energy of non-metallic catalysts like cyclic carbonates etc. [11]. As a result, the throughput obtained from such a process is well below the requirements for industrial scale production (30-40) kg/hr. In addition, any reaction mechanism that uses these catalysts will have to be studied and reaction rate kinetics etc. for the ROP process will need to be established. Further, in order to scale such process from lab scale production to industrial scale output, a mathematical model encompassing the continuous reactive extrusion process of PLA needs to be generated.

Using non-metallic catalysts to process PLA (or other bio-polymers) is an active area of research. Projects InnoREX, MAPSYN and altergo [97], [110], [111] are active in this area. Project InnoREX was one such attempt.

1.6 **Project InnoREX**

- Aim: To develop a novel reactor concept using alternative energies for the continuous, highly precise, metal-free polymerization of LA.
- Objectives: The demand for biobased polymers is growing fast. According to the current state of the art, metal-containing catalysts are needed to improve the polymerization rate of lactones, posing a hazard to health and the environment. In InnoREX, metal-containing catalysts will be replaced by eco-friendly catalysts. These have been shown to efficiently control the polymerization of lactide, but their activity must still be improved to meet industrial standards. This will be achieved by the low-intensity but the highly-targeted application of alternative energies (microwaves, ultrasound, laser light). These energies increase catalyst activity and enable precise control of the

reaction by exciting only small parts of the reaction mixture without response time.

The study reported in this thesis is inspired from the objectives of the project InnoREX.

1.7 **Research strategy and guideline**

The main aim of the current research is to develop, explain and analyse the reaction kinetics of ROP process formation of PLA by using eco-friendly catalyst and alternative energy source (Microwave, Laser and Ultrasound source). The PhD thesis briefly introduces the related scientific state-of-art via a literature review, methodology, application of different techniques and tools.

In the following chapters, the author will set up the area of research by giving the details of the state-of-the-art by highlighting the most significant attempt made so far in the field of ROP of LA as (chapter 2). Based on that identification of the gap in literature has been highlighted which are used as a key focus of this research work to contribute knowledge and fulfil the gap by providing significant and detailed research strategy.

Chapter 3, gives the methodology of the research and a justification for using that approach. Followed by Chapter 4 and Chapter 5, which enlightened the complete mechanism of details of initial extrusion reaction parameters, considering the impact of AE source in the mechanism and their use to develop the mathematical simulation model, which were used as an initial input for Ludovic simulator. Through Ludovic, proper consideration of environment of extrusion process including the impact of AE source were considered to validate the result of both experimental and theoretical extrusion process.

Chapter 6, details the attempt made to replace the conventional metallic catalyst with alternative eco-friendly catalyst and its impact on the reaction mechanism by calculating the reaction parameters involved. The reaction process mentioned in this chapter, is based on batch process reaction and experimental data based on this reaction has been used to perform simulation process and further on validation of both theoretical and experimental results has been concluded. Chapter 7, highlights the need for sensitivity analysis of the developed reaction mechanism and its modelling through mathematical simulation. Chapter 8, and chapter 9, contributed in terms of the conclusion and recommendation of the further research work based on the finding of current research work.

2 LITERATURE REVIEW

2.1 **Overview**

[1]The terms polymer and monomers were derived from the Greek roots poly (many), mono (one) and mers (units). Polymers are very large molecules made when many smaller molecules join together, end to end. The smaller molecules are called monomers. The monomers from which the polymers are constructed are reflected in the repeating structural unit of the simplest polymer [12]. For example, Polyethylene is the out-come of repeating structural unit of monomer(s) called ethene (ethylene) and the corresponding linear polymer is called high-density polyethylene (HDPE). See *Figure 1*

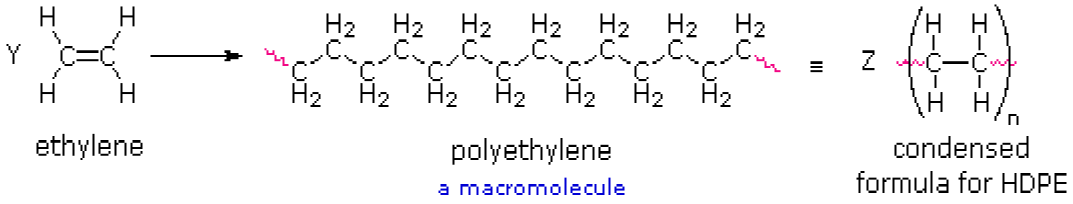

Figure 1: Polymerization of Alkenes [11]

2.1.1 **Classification of Polymers**

Based on features like monomer source, structure, physiochemical and polymerization, polymers can be classified as shown in *Figure 2*

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1. All the details in this chapter were taken from [1] "Chronological Review of The Catalytic Progress Of Polylactic Acid Formation Through Ring Opening Polymerization." (**International Research Journal of Pure and Applied Chemistry**)". 2016 - Volume 12, issue 3, DOI: 10.9734/IRJPAC/2016/27469

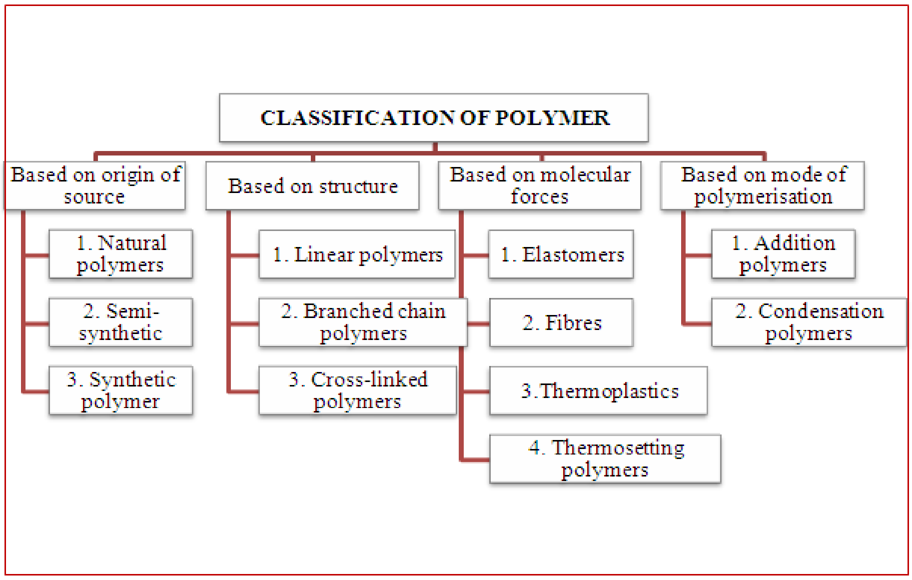

Figure 2-Classification of Polymers [13]

2.1.2 **Types of polymerization**

Monomers link together to form polymers mainly by two reaction mechanisms [14]

(a) Addition polymerization

(b) Condensation polymerization.

The mechanism of polymerization affects the physical and chemical properties and uses of the polymer.

(i) **Addition Polymerization**: Unsaturated monomers link in a way that the repeated unit has the same composition as the monomer. In addition-polymerization, monomers react to form a polymer without the formation of by-products. It is also known as chain-growth polymerization. A special case of chain-growth polymerization leads to living polymerization. Aromatic compounds support addition polymerization.

$$n\,(CH_2{=}CH_2) \longrightarrow (-CH_2\text{-}CH_2-)_n$$

(ii) **Condensation Polymerization**: Condensation polymerization is a process in which water or some other substance separates during the combination of two or more monomer molecules. The terms condensation and step-growth polymerization are often used synonymously. A condensation polymer is the preferred way for the polymerization of aliphatic compounds. See *Figure 3*

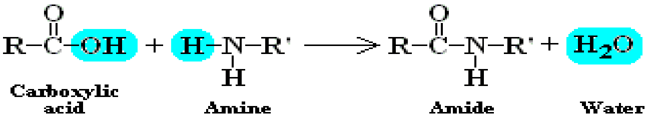

Figure 3: Typical condensation of carboxylic acid and amine [14]

2.1.2.1 **Ring opening Polymerization**

Ring-opening polymerization (ROP) is a special case of chain growth polymerization, which in general follows the step-growth polymerization trend by the addition of monomers step-by-step [15]. The polymerization process begins with the opening of the cyclic ring of monomers such as cyclic ether, amides (lactams) and esters (lactones). The process catalysed by the initiator or other species to create an active centre where further cyclic monomers attack to form a larger polymer chain through ionic propagation. Once the process started by the initiator, monomers keep adding to the active polymer chain and increasing the chain length. A wide variety of cyclic monomers have been successfully polymerized by using ROP such as cyclic olefin, amines, sulphides etc. The suitability of polymerization of cyclic monomer depends on both thermodynamic and reaction kinetic factors [11].

2.2 **Thermo-dynamics of ROP of Cyclic Monomers**

The thermodynamic factors play a very significant role in determining the relative stability of cyclic monomer and linear polymer structures during the conversion of cycloalkanes to the corresponding linear polymer [11], [13]. The Ring opening polymerisation is thermodynamically favourable to all except the 6-membered ring. The order of thermodynamically favoured cyclic structure is 3> 4> 8> 5> 7. The defined trend is because of bond angle strain in 3 and 4-membered rings, eclipsed conformational strain in the 5-membered ring and trans-annular strain in 7 and 8-membered rings. Thermodynamic parameters do not guarantee the polymerization of the cyclic monomer as in the case of a 6-membered ring. Polymerization also requires a favourable kinetic pathway to open the ring and undergo reaction. The existence of a heteroatom in the ring provides a suitable site for nucleophilic or electrophilic attack by an initiator and resulting in further propagation by opening the ring. Such monomers polymerise, since both thermodynamic and kinetic factors are favourable [11].

Polymerization Mechanism:

1. Cationic polymerization: Is a process in which a cationic initiator transfers charge to monomers which become reactive. It is a type of chain growth polymerization.
2. Anionic polymerization: In anionic polymerization, the active centres are the anion. It is a type of addition polymerization.

The basic difference between cationic and anionic polymerization is that addition of monomer to cationic polymerization is possible until the end site is active to accept another monomer and then terminate but in the case of anionic polymerization, it is considered as living polymerization with no termination step involved. ROP is generally started by the attack of ionic (anionic or cationic) initiator on the cyclic ring monomer to create an active site for further addition of monomer(s). The reaction involves the nucleophilic attack of the monomer on the oxonium ion. See *Figure 4*

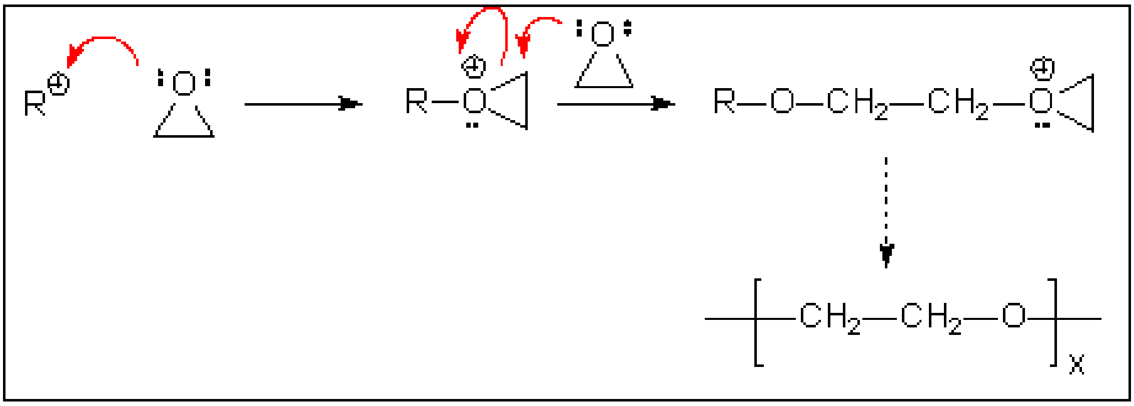

Figure 4: Mechanism of ROP [16]

In the case of active species determination, Kricheldorf et al. [9] reported that tin halogenides, the suitable catalyst for ROP of LA is actually converted into tin alkoxide and behaves as real active species. For different metal alkoxide, the ROP of Lactones involves the rupture of acyl-oxygen bond and further the alkoxide groups of initiators create alkyl ester end groups [10]. Several ring-opening polymerizations proceed as living polymerizations and polymer molecular weight increases linearly with conversion and ratio of monomer to initiator [7]. ROP is the preferred way of polymerization because of the higher polymer molecular weight property.

2.3 **Poly Lactic Acid (PLA)**

2.3.1 **PLA material and its importance**

Lactic acid, which is the basic building unit of PLA, was first isolated from sour milk in 1780 by the Swedish chemist Scheele and was produced commercially by 1881[16]. The two common monomer(s), which polymerize to synthesise PLA, are Lactic acid and Lactide. PLA is aliphatic polyester and its building unit Lactide is normally extracted from the renewable sources such as corn starch, sugarcane and chips [17]. Lactide as a monomer unit for PLA has two enantiomers D and L Lactide. It has the various application such as buffering agent, acidic flavouring agent and bacterial inhibitor in several processed foods. Because of easy degradability, versatility and anticipated price PLA should be able to displace a significant volume of fossil fuel-based polymers [18]. Also due to the good mechanical property of PLA [30], [31] it is one of the polymers widely accepted in the medical sector and packaging material [17], [18]. PLA can be easily recycled, incinerated or landfilled for disposal in-soil degradation after use. Due to their biocompatibility and mechanical properties, PLA and their copolymers are widely used in tissue engineering for function restoration of impaired tissues (33). In order to enhance the application, it is necessary to understand the link between PLA materials and the manufacturing process. PLA provides a closed natural recycling route as its monomers are extracted from plants and crops which are then polymerised and processed into a packaging material and at the end-of-life degrade in soil.

2.3.2 **Mechanisms for Polymerization of LA**

The most common and efficient way to obtain PLA is the ROP of Lactide with suitable metal catalysts (Tin, Zinc, aluminium) in the suitable solvent [20]-[22]. An alternative way to produce PLA is the direct condensation of lactic acid monomer [16]. In general, it is the least expensive route, but in a solvent-free system, it is difficult to attain high molecular weights (30-50 kg/hr). To get the higher molecular weight, use of other coupling agents or esterification-promoting agents are required, which increases cost and complexity [21]. Normally, the entropically favoured Lactide monomers are produced at the temperature below 200^{o}C [22]. Based on cost and reaction time, ROP is the preferred route for large-scale industrial production. See *Figure 5*

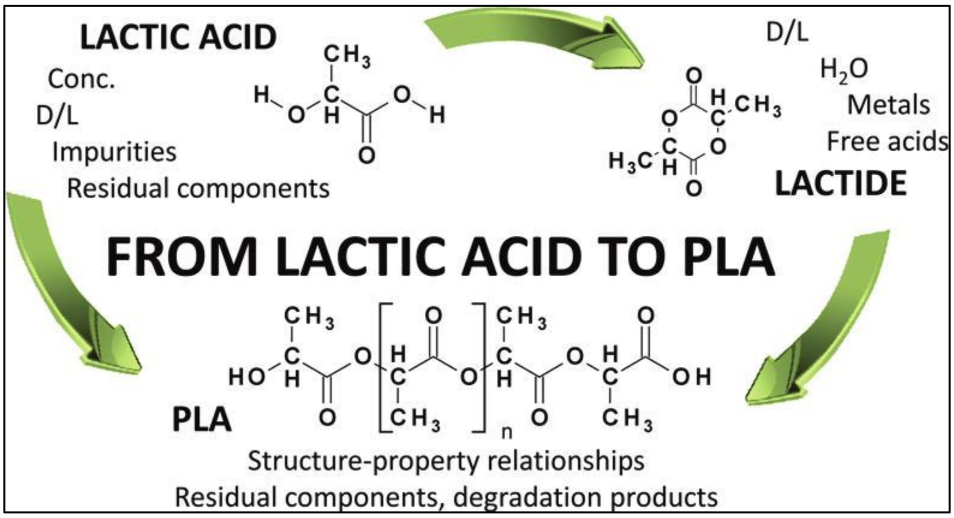

Figure 5: ROP of Lactide and Lactic acid monomer to form PLA polymer [24]

For the production of PLA by ROP at high throughput at industrial scale, many different catalysts (Aluminium isopropoxide, Zinc lactate and Stannous octoate) [23] were studied to enhance the reaction productivity. Among them, tin octoate- $Sn(Oct)_2$, approved by the U.S. Food and Drug Administration (UFDA), is the most widely used [25].

2.3.3 **PLA processing: current trend**

Currently, PLA processing is based on batch process and reactive extrusion, [25],[26]. The selection of initiator system, catalyst concentration, monomer-to-initiator ratio, polymerization time and temperature change the property of the polymer. Initially, the ROP of LA was carried out in Batch Process, which contains several vessels to mix the initiator and catalyst with monomer at certain temperature [22]. The commonly used solvent for the batch process is Toluene. The current trend for the production of PLA at commercial level mostly supports reactive extrusion or twin-screw extruder technology [26] see *Figure 6.* For reactive extrusion polymerization, the purified form of Lactide is used. A mixture of D or L-Lactide acid, stabiliser and catalytic system is transferred continuously into a nitrogen purged material feeding unit. The crystalline powdery type PLA was mixed with the catalyst such as stannous octoate dissolved in toluene. It was extracted later from the mixture, using a vacuum. The design of the screw widely influences the degree of mixing of PLA with other components and degree of mixing has the huge impact on ROP of LA [27].

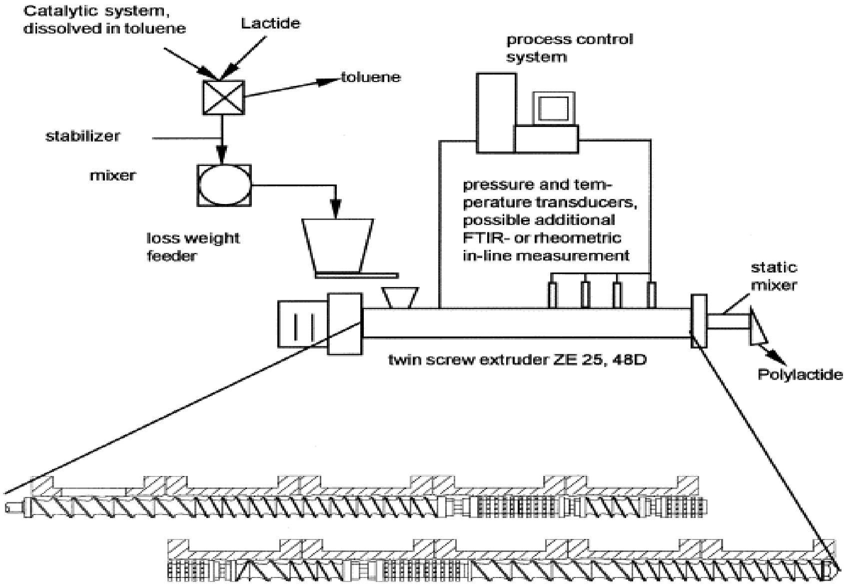

Figure 6: Twin Screw Extruder [27]

For the production of PLA, the optical purity of the reagent lactic acid is crucial because the small amount of enantiomer impurity changes the properties such as crystallinity or biodegradation rate of polymerization. Another factor, which affects the properties of the polymer, is the detection and removal of impurities during reaction because impurities can easily change the intermediate reaction and product [28], [29], [79].

2.4 **Chronological progress in PLA research**

2.4.1 **Synthesis of PLA from Lactide**

Use of the metal catalyst in a suitable solvent for the synthesis of PLA has been the standard practice for decades and has also resulted in industrial scale production at manufacturing units such as Nature work (USA, Blair) (10), Purac (Netherlands) (34), Synbra (Netherlands) etc. Dubois et al [7] in 1991 reported mechanism of ROP of LA using batch process and aluminium isopropoxide as catalyst in toluene solvent. Others like Witzke et al. [31] reported reversible kinetics of L-Lactide in oven-dried container using stannous octoate $Sn(Oct)_2$ as a catalyst in toluene solvent [8].

2.4.2 **Demerits of conventional method**

Jennifer et al. [32] reported that $Sn(Oct)_2$ used in the polymerisation of PLA is an irritant to the eyes, respiratory system and skin. Because of the different reaction stages involved in the polymerization of PLA, impurity formation and side products are almost a certainty. Although Lactic acid and Lactide are non-toxic in nature, the use of $Sn(Oct)_2$ or another metal catalyst is also very toxic and hazardous [29] for the environment.

Apart from the catalyst, the reaction time is also an important factor, which decides the production cost and quality of commercial PLA. Mehta et al. [33] reported the variation of number average molecular weight of PLA with the time scale of 0-150 hours by using the experimental data of Dubois [7] batch process.

2.4.3 **Theoretical Modelling for LA Polymerization**

To implement the effect of metal/metal-free catalyst in the reaction mechanism, a proper understanding of reaction kinetics is needed. It is necessary to develop a theoretical mathematical model to check the suitability of parameters (time, concentration, temperature and rate constants) in reaction mechanism for PLA polymerization. Yu et al. [8],[34] and Mehta et al. [29], [33], detailed the basics of ROP process and reaction stages involved during the polymerization of LA performed in batch process experiment. For the estimation of monomer conversion and average molecular weight along the extruder, Puaux et al. and Banu et al. [25],[26] reported the theoretical model to simulate the reaction process.

2.4.4 Reaction mechanisms for PLA formation using metal/non-metal catalysts

Kamber et al. [4], Enders et al.[19], Csihony et al. [24] etc. performed a very detailed review on existence and importance of organo-catalytic ring opening polymerization. The work examined several methods for the ROP of polymers such as Cationic, Anionic, Enzymatic and other organic Ring-Opening Polymerization. The initial verification of the reaction mechanism used for understanding of ROP of LA is mentioned below *Figure 7*

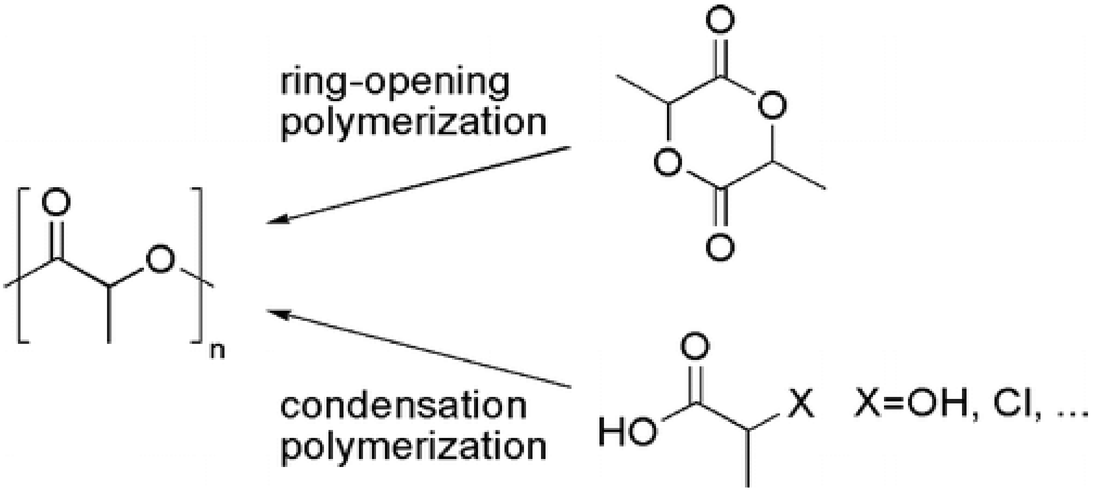

Figure 7: PLA Formation routes [4]

The proposed mechanism works well but in terms of the formation of PLA through Lactide and lactic acid but in the context of reaction stage details, especially intermediate step, which describe the molecular weight distribution and the molecular weight of the macromolecules, was unclear. Once polymerization reaction starts, it proceeds through different stages and goes on to the final stage with certain molecular weight. In terms of the details of the different reaction stages involved with in the reaction process, step growth or chain growth processes becomes significant. [37]-[40].

2.4.5 **Different Synthesis Mechanisms of PLA**

Details of several mechanisms, such as Coordination-Insertion Mechanism, Activated Monomer Mechanism and Monomer-Activated Mechanism versus Chain End-Activated Mechanism is mentioned below in *Figure* 8

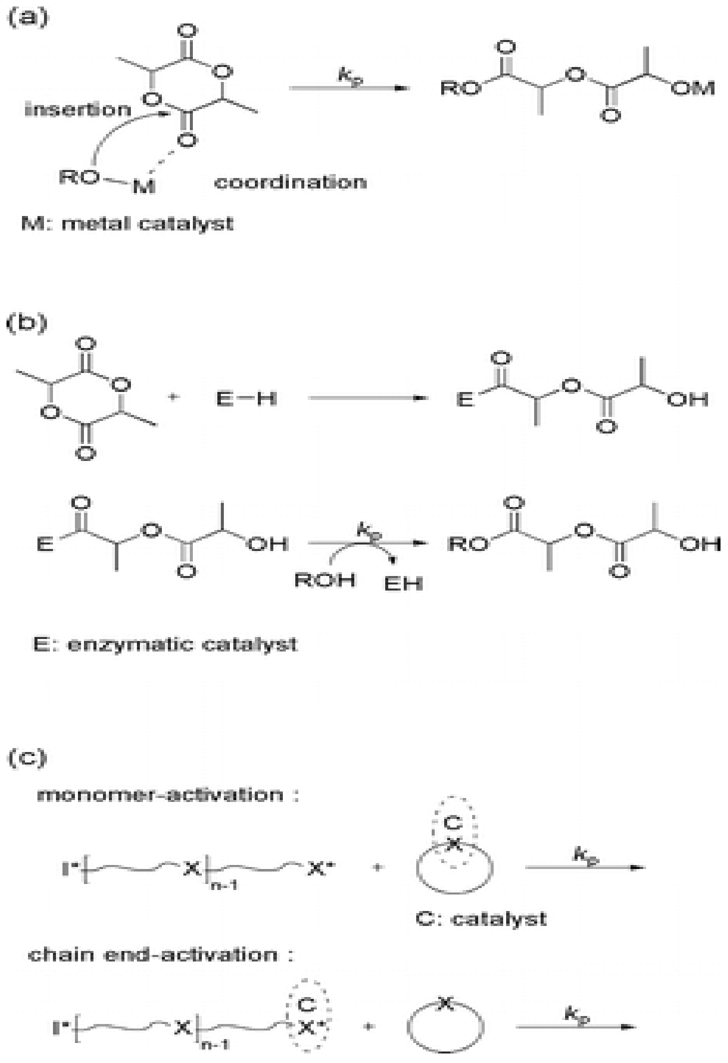

Figure 8: Different Mechanism [4]

In general, the ROP of lactides follows the coordination-insertion mechanism [39]. The coordination-insertion mechanism shows better production yield and faster reaction times [40]. There is also an alternative classification for enzymatic ROP's known as an activated-monomer mechanism. In this process, the enzymes react with monomer and activate the monomer to enhance the polymer-chain addition process [38]. Kobayashi et al. [38], first introduced the field of enzyme-catalysed ring-opening polymerization, with the application of a lipase catalyst for

ROP of lactones. Enzymes show an effective stereo reaction and are extracted from renewable resources that can be easily recycled. To define the role of catalyst, classification of the catalytic process of ROP reactions by chain end-activated or monomer-activated mechanism is useful.

2.4.6 **Metal-free/Organic ligand catalysis for PLA synthesis**

Several other ligands in organic and non-metallic catalysts are also capable of starting ROP of LA, such as Pyridine, Phosphine and Carbenes [40]-[42], [53]. In 2001, the first organo-catalyst, basic amines such as DMAP and PPY as trans-esterification catalysts, were applied to the living ROP of LA [3], [4]. DMAP was used successfully not only for trans-esterification but also for many other organic transformations such as alkylation, acylation, and nucleophilic substitutions etc. [44]. Because of these properties, DMAP was the subject of several reviews [43],[45]-[49], [50], [52], [54], [62]. The mechanism for ROP of LA using Pyridine such as DMAP (di-alkyl-amino-pyridine) is mentioned below *Figure* 9

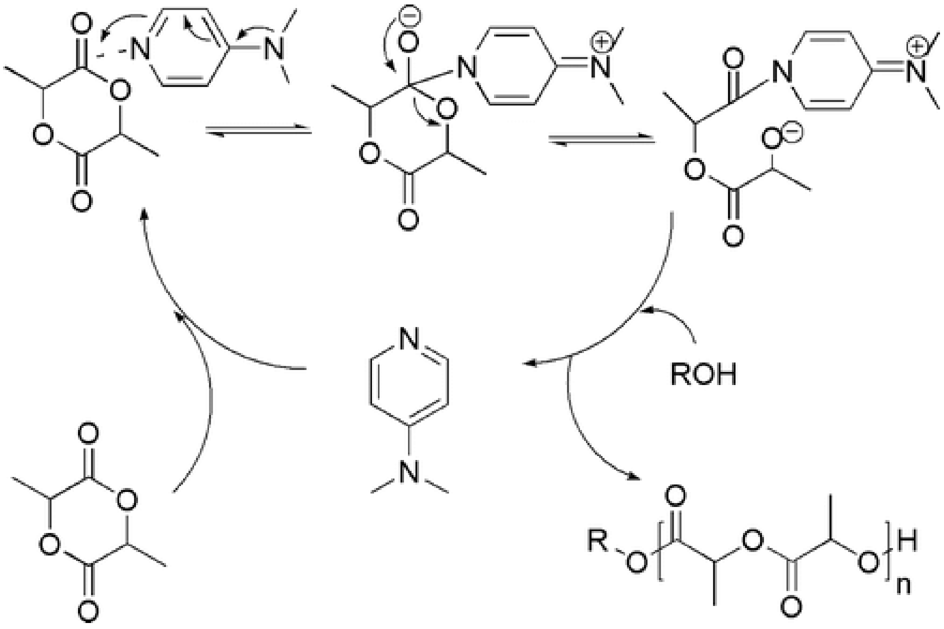

Figure 9: DMAP acylation mechanism [4]

In this series, phosphines are also commonly known ligands in organometallic chemistry and homogenous catalysis. Phosphines are capable to mediate the variety of organic transformation including acylation reactions [44]. Several tertiary phosphines, were used for trans-esterification catalysts of the ROP of LA [40]. In the presence of alcohol especially benzyl alcohol, phosphines were found to be the effective catalyst for ROP process of LA [24]. The phosphine catalysed polymerization process in CH_2Cl_2 or toluene was slower and requires high temperature (90°C -100°C) in comparison to those catalysed by DMAP. Phosphine catalyst activity for LA polymerization in decreasing order is following: $P(n\text{-}Bu)_3 > P(tert\text{-}Bu)_3 > PhPMe_2 > Ph_2PMe > PPh_3 > P(MeO)_3$. For nucleophilic-mechanism the suitability is based on more basic and nucleophilic-alkyl-substituted phosphines for the effective LA polymerization catalysts [45] [46]. The mechanism is shown below in *Figure 10*

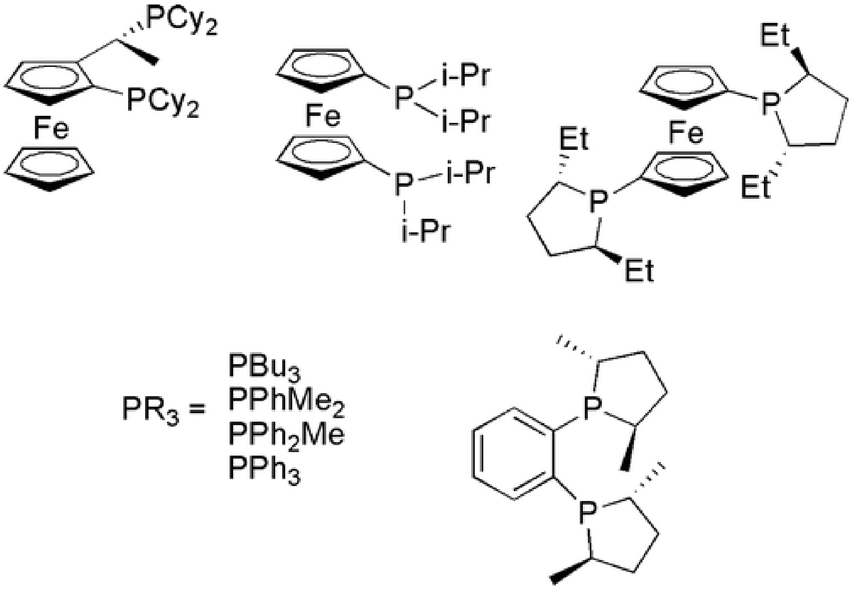

Figure 10: Phosphine Catalysis mechanism [4]

Breslow introduced the use of carbenes as the catalyst for polymerization. The work explained the idea that deprotonated thiazolium or imidazolium salts can act as the nucleophilic catalyst [47]. Breslow's studies generated curiosity in several groups to investigate the application of stabilised carbenes as nucleophilic organic catalyst [46], [48]. For trans-esterification reaction, the high reactivity of N-heterocyclic carbenes was considered for the de-polymerization reactions of thermoplastics [50]. Polyesters PCL and poly-(glycolide) with high molecular weight were obtained using NHC catalyst. By using NHC-catalyst the commercially important polyester poly-(ethylene terephthalate) (PET) was prepared [52]. Two mechanisms were proposed for trans-esterification reactions using NHC-catalysis: a nucleophilic mechanism to create acyl imidazolium intermediates [41] and the other is an alcohol-activation mechanism where hydrogen bonding between the carbenes and the alcohol release the alcohol group toward the nucleophilic attack [54] and stabilises the tetrahedral intermediate [53]. The high reactivity of NHC supports the catalysis of ROP process of lactones. Different varieties of carbenes were investigated such as unsaturated imidazolylidene, saturated imidazolylidene and triazolylidene and were found to be effective for ROP [54]. The activity and selectivity of the ROP polymerization depend on the nature of the carbene and the monomer. The reaction rate reported is close enough to those of the most active metal catalysts for ROP of Lactide [53], [56], [57]. Higher nucleophilicity and basicity of NHCs compared to DMAP are responsible for the higher reaction rates. In the mechanism of polymerization of the Lactones using carbene catalysis, the termination can be started by deactivation of the carbene with the addition of acetic acid, CO_2 or $CS_{2,}$ which later forms the zwitterionic species [58] and removed from the polymer by the precipitation process. The formation of a zwitterionic intermediate is the key feature of the nucleophilic mechanism. Nucleophilic attack of the carbene on the lactones generates zwitterionic species, followed by ROP of tetrahedral intermediate to create the acyl-imidazolium alkoxide zwitterions [59]. Mechanism of NHC catalysed ROP and formation of zwitterion are mentioned below in *Figure 11* & *Figure 12*

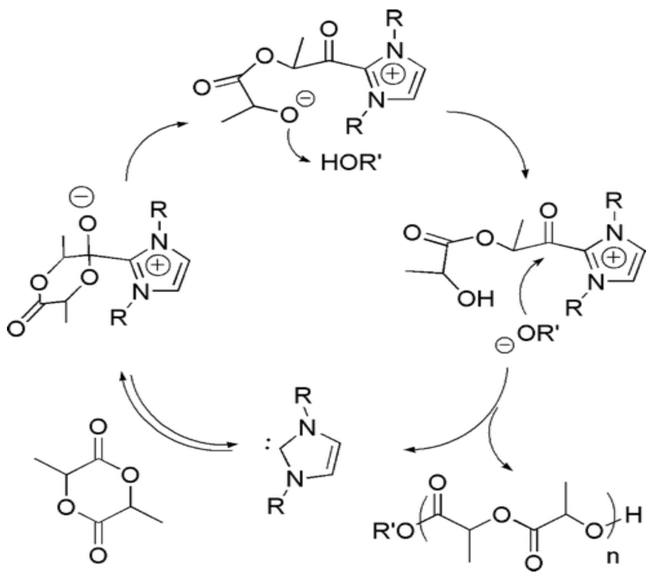

Figure11: Nucleophilic Monomer-Activated Mechanism for ROP [4]

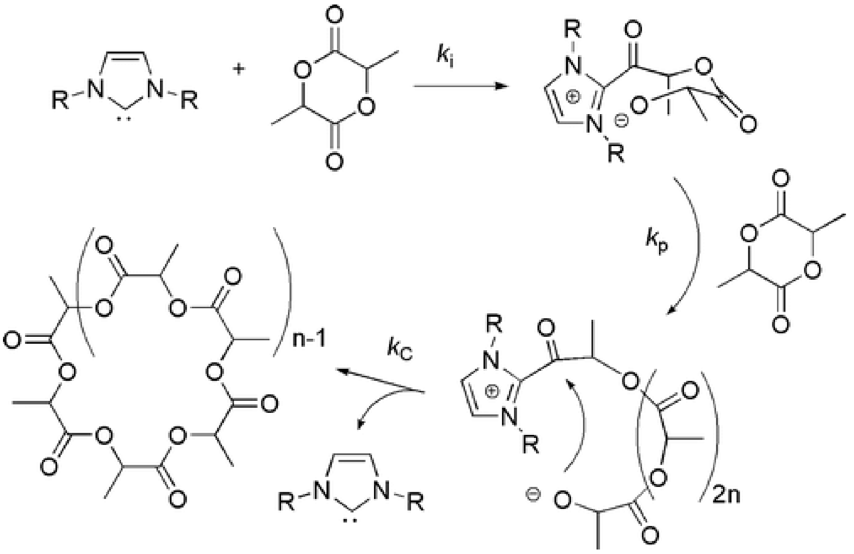

Figure12: Zwitterionic Polymerization of LA to Cyclic [4]

Recently in 2013, Wang et al [5]. used N-heterocyclic carbine, an organic catalyst, as a nucleophilic catalyst to produce PLA [48]. They investigated the influence of temperature, monomer/initiator molar ratio, monomer/catalyst molar ratio, monomer concentration, as well as polymerization time [5]. In comparison with another catalyst especially metal catalysts, carbine catalysts [19], [24], [60] are inexpensive, highly active and nontoxic in nature. In the search of a reliable alternative to metal catalysts, imidazolium-based carbenes, a special kind of NHC were shown to be superior organo-catalysts for polymerization [61]. Several reported methods define the suitability of carbene catalyst to exclude the complexity of isolating sensitive carbene complex and to provide details of polymerization process [48], [50], [58] [60]-[65]. Parameters such as monomer/initiator molar ratio ([M]/[I]), monomer/catalyst molar ratio ([M]/[C]) and monomer concentration affect the molecular weight and poly-dispersity of polymerization process significantly. Both the monomer conversion and molecular weight of PLLA increase with the increase of Lactide concentration up to a saturation point then start decreasing. The decrease in molecular weight at higher concentration happens because the active monomer chain centre cannot react with the monomer owing to the increase in the systems viscosity. The monomer/initiator [LLA]/[I] molar ratio was examined in detail. It was observed that the molar ratio was relatively critical to prepare high yield and high molecular weight polymer. Because of the availability of few active centres in the polymerization system, the polymerization process could not continue with decreasing initiator amount. Yet increasing initiator content can lead to many and short polymeric chains, thus decreasing the molecular weight of PLLA. The amount of catalyst also affects the formation of active species directly and the monomer conversion. Due to the large number and shorter polymeric chains produced, the molecular weight of PLLA decreased when more catalyst was in the reaction. Further polymerization temperature and time also significantly affect the ROP of LLA. It was also found that higher temperature enhances the rate of intermolecular trans-esterification and thermal degradation reaction and causes the decrease in molecular weight of PLLA, whereas below 15°C the polymerization reaction proceeds slowly.

2.5 ROP through Alternative Energies (Microwave, Ultrasound & Laser) Incorporation

A large number of reactions, either organic or inorganic, show the significant increase in reaction speed under microwave irradiation compared with conventional heating. Application of microwave heating to process chemical reactions has received increasing attention in the past few years. Due to its qualities such as high efficiency, the capability of uniform heating and reduced reaction time, a large number of chemical reactions, both organic and inorganic, undergo a significant increase in reaction speed due to microwave irradiation compared to the general methods for heat-irradiation such as furnace chamber and LASER heating etc. Cheng et al. [71] and Li et al [72] investigated the microwave-assisted radical polymerization of styrene with a faster polymerization rate in comparison to conventional heating. The first microwave-irradiated polymerization of D,L- lactide was reported by Liu et al. [73],[74].

The combination of microwave heating technology and living free radical polymerization (LRP) help to increase the rate and effectiveness of reaction [74]. However, there are very few studies that report on implementing microwave heating to LRP (microwave-assisted LRP).

In the literature, it has also been heavily debated that the increase in reaction rate not only arises from thermal effects but also from non-thermal ''microwave effects'' [71-74]. The effect of microwave irradiation in step-growth polymerizations are the most investigated polymerization reactions in the field of ROP process. A large amount of data is available in case of polyamides and polyimides, poly-ethers and polyesters. e.g. production of artificial polyamides were derived from amino acids and nylon salts through above process [74],[75]. Wiesbrock et al. introduced the technique to polymerize amino acids having composition x-aminoacetic acid, $H_2N(CH_2)xCOOH$ by using domestic microwave oven [74].

2.5.1 **Ring-Opening Polymerizations of aliphatic polyesters**

Aliphatic polyesters are biodegradable polymers. Albert et al. [76] introduced the microwave-assisted ring-opening polymerization of ε-caprolactone, utilising mono-modal microwave reactor. Mostly the microwave-assisted polymerizations were facilitated utilizing catalyst and the most common catalyst used is stannous octoate [$Sn(Oct)_2$] [73],[77]. Zhuo and co-workers investigated the microwave-assisted ring-opening polymerization of ε-caprolactone using stannous octoate [$Sn(Oct)_2$] as the catalyst and maleic acid as initiator [77], they found increase in molecular weight up to maximum irradiation times of 135 min (360 W). Koroskenyi and McCarthy also reported the increase in polymerization rates of microwave-assisted polymerization kinetics of ε-caprolactone [78].

2.5.2 **Microwave assisted ROP of monomers**

Microwave-assisted polymerization due to its capability of direct heating, high-temperature homogeneity, reaction rate enhancement and energy savings, has become a fast-growing field of polymer research [77],[79]. Apart from ring-opening polymerization of ε-caprolactone, microwaves were used to successfully polymerize several other cyclic monomers. Scola and co-workers [79] reported the formation of nylon-6 with the ω-caproic acid-initiated polymerization of ε-caprolactam. Schubert and co-workers made a detailed investigation with the microwave-assisted living cationic ROP of 2-ethyl-2-oxazoline [80]. They performed the polymerization up to 200°C in acetonitrile and found that the polymerization was accelerated by a factor of 400 by keeping the living character of the polymerization.

2.5.2.1 **Microwave-assisted ROP of poly-lactide**

Microwave assisted ROP of Lactide monomer emerged as a possible environmentally friendly alternative to chemical synthesis of PLA. This technique supports the polymerization process by providing homogeneous heating [73]. Zhang et al. successfully synthesised the D,L-lactic acid by using ethanol , ZnO, $SnCl_2$ and Cat-A as catalyst applying continuous microwave irradiation in less than an hour. A yield of 36% was reported upon complete synthesis [78]. On the other hand, compared to conventional heating with the same experimental setup, the negligible non-thermal effect of microwave irradiation was revealed. Based on chemical bonding studies, lactide molecule contains two polar carbonyl groups which provide a suitable site of dielectric heating by absorbing microwaves, because of this fact Liu et al. [73] investigated the ROP of D,L-lactide (DLLA) considering micro-wave irradiation for PLA synthesis. The rough reaction scheme of microwave-assisted ROP of lactide is in *Figure 13*

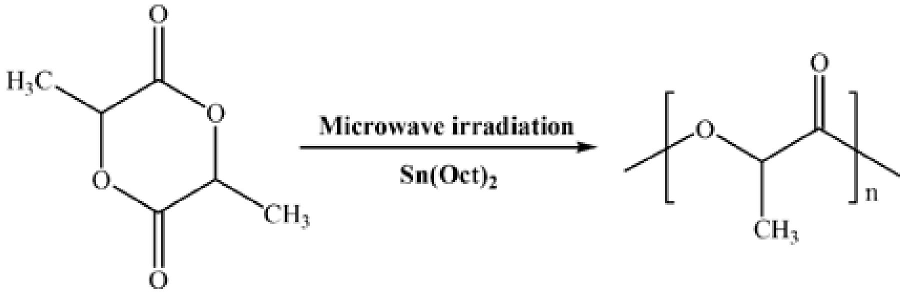

Figure 13: Microwave-assisted ring-opening polymerization of Lactide [73]

The source 2.45 GHz of microwave energy has been used as a pulse source to irradiate the mixture for short times. Further, the weight ratio of the precipitate of polymer to the monomer was considered to determine the yield of the conversion of the amount of lactide into PLA. The precipitate obtained was verified as P-DLLA by means of 1 H NMR spectroscopy and GPC test, which were similar to those of an authorised PLA specimen. By measuring the weight average molecular weight (M_w) and yield of the resultant P-DLLA at varied time intervals, the effect of microwave energy on the ROP of DLLA was investigated at different power levels (170, 255, 340, and 510 W). With the help of detailed investigation, Liu et al. proposed that the rate of polymerization step and the chain propagation of PDLLA were enhanced significantly by an increase in microwave power up to certain extent of temperature.

2.5.3 **Ultrasound/Ultrasonic facilitated ROP of poly-Lactide**

In the case of ROP of Lactide monomer, there is a lack of information in the literature. Ultrasonic sources were used to investigate the effect of several other poly Lactide substituents like (d,l-lactide-co-glycolide) and hydroxyapatite (PLGA/HAp) composite [81]. The processing of the PLGA and the PLGA/HAp composite with ultrasonic irradiation or ultra-sonification shows significant changes in the molar mass and molecular properties. Other similar studies on the controlled assembly of poly (d,l-lactide-co-glycolide)/hydroxyapatite core–shell nanospheres using ultrasonic irradiation were also reported.

Jevtić et al. [82] first reported the use of Ultrasound source as a thermal energy source for degradation of the PLA chain. Intense and targeted Ultrasound source to separate the PLA chain from poly lactide-co-glycolic acid was one of the first attempts to use an AE source for polymer chain separation. Price et al. [83] investigated the application of ultrasound source for the ROP synthesis of cyclic lactones. Dubey et al. [84] also reported ROP of LA through reactive extrusion process using $Sn(Oct)_2$ and Ultrasound source as AE.

Photo-initiated free radical polymerizations have been used over the last five decades and have the significant role in the detailed explanation of the free radical polymerizations process kinetics. Absorption of UV beam in the reaction creates the cleavage in the bond between several species and facilitates the conditions for breaking the bond and initiate polymerization. The surface graft polymerizations initiated by UV irradiation exhibit several features such as fast reaction rate, low cost of processing, simple equipment, easy industrialisation etc. [85]. The detailed mechanism of surface grafting polymerization is in *Figure 14* [86],[87].

In literature, the use of Ultrasound source is reported as an energy source for degradation of PLA chain. Work based on separation of PLA chain with their complex substituents called poly lactide-co-glycolic acid using intense and targeted Ultrasound has also been reported in literature because of which, Ultrasound would be used as a relevant future AE source for ROP process to provide considerable bond breaking energy to initiate the polymerization reaction.

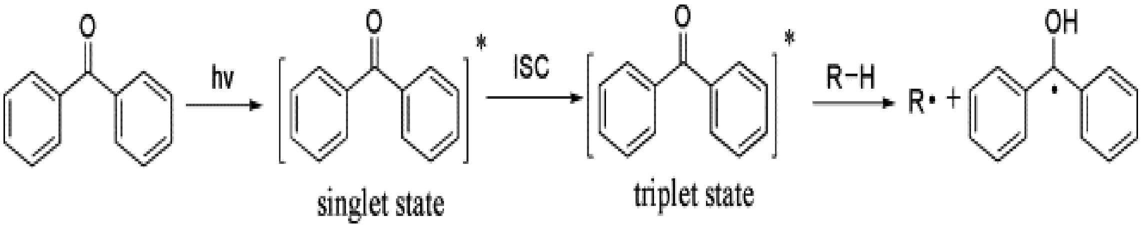

Figure 14: Photo-grafting polymerization through UV radiation [86]

2.6 ROP through Continuous Reactive Extrusion

There are several polymer-processing techniques like melt blending, polymerization, branching, grafting and functionalization. Reactive extrusion (REx) is a cost effective method for these techniques [89], [90] because of its low cost production and processing techniques. Important features of extrusion polymerization are as following

- Melt processing can be carried out in the solvent free medium. So, the product can be easily isolated.
- There is a continuous process, which starts from monomer and gets completed with the formation of polymer or final product.
- Residence time and residence time distribution can be controlled
- Several extrusion streams can be incorporated while running process

There are several benefits of the extruders in different applications such as deciding the grade of the mixing, proper control and higher conversion output. The geometry of the screw in the extruder control its effectiveness [89]. The screw size, geometry and rotating speed of the screw in the extruder control the residence time, power input and the scale of mixing to form the melt.

Various types of high molecular weight biodegradable polymers are prepared by ROP of a cyclic ester such as poly(ε-caprolactone) (PCL), polylactides (PLAs) and other aliphatic–aromatic poly-condensates as poly(butylene adipate-co-terephtalate). By using reactive extrusion for ROP of several polymers at the industrial level, it is possible to have control over polymerization, which is required to achieve desired molecular weights and suitable functional end groups [88].

Apart from PCL and PLAs, there are several other biodegradable aliphatic polyesters, for which traditional poly-condensation method is used. E.g. poly-(alkylene succinate) designed by Showa Denko, trademarked

Bionolle® [88]. However, due to relatively poor mechanical properties and high cost compared to other polymers (polyethene and polypropylene), the biodegradable co-polyesters are still not very popular. It is possible to combine these biodegradable polymers with cheap inorganic (silicate type particles) or organic fillers (starch granules) to reduce the cost and to optimise the properties of aliphatic polyesters [91], [92].

2.6.1 **ROP of poly (ε-caprolactone) PCL through reactive extrusion**

The bulk polymerization of ε-caprolactone in the presence of aluminium-sec-butanoxide $Al(OsecBu)_3$, an aluminium alkoxide catalyst or initiator, significant enough to initiate fast and restrictive ROP of lactones [88] was performed in a co-rotating twin-screw extruder with screw diameter of 30 mm and having a length-to-diameter (L/d) ratio of 15 [90]. Several heating and cooling chambers were designed with in the extruder barrel to control the melt temperature. To avoid the non-significant contamination of lactone initiator and processing polyester chains with moisture, PCL and $Al(OsecBu)_3$ (in anhydrous toluene solution) were continuously purged with nitrogen flow into the opening feed throat of the twin-screw extruder. It was found that PCL was completely converted into polyester chains with a yield ~ 99% within a maximum residence time of 2 min. The scheme of the extrusion process for ROP of poly (ε-caprolactone) PCL through reactive extrusion is in *Figure 15* [89].

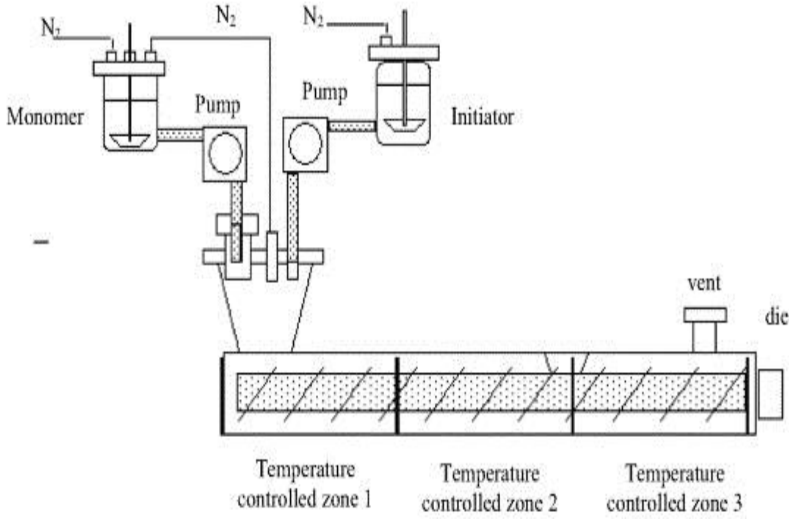

Figure 15: Co-rotating twin-screw extruder for PCL polymerization [89]

2.6.1.1 **ROP of LA using continuous extrusion reaction**

The current trend for commercial production of PLA supports the use of a continuous single-stage process reactive extrusion or twin screw extruder technology as it satisfies both kinetic and thermal stability requirements [26], [27], [84]. For reactive extrusion polymerization, the use of purified form of lactide is very significant. A mixture of D or L-Lactide acid, stabiliser and the catalytic system is transferred continuously into a nitrogen purged material feeding unit [5]. The crystalline powdery type LA is mixed with the catalyst such as stannous octoate dissolved in toluene. It is extracted later from the mixture using the vacuum. Design of the screw geometry greatly influences the degree of mixing of PLA with other components which in turn has a huge impact on ROP of LA *Figure 16*

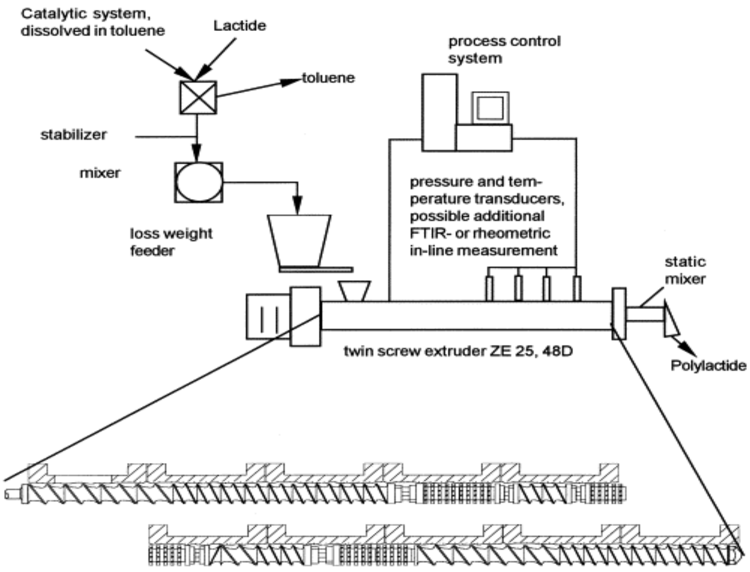

Figure16: Twin Screw Extruder [27]

The lactide ROP proceeds through the ‘coordination–insertion’ mechanism by involving the cleavage of the particular oxygen-acyl cyclic ester monomer. It has been reported that the presence of one equimolar Lewis base such as tri-phenylphosphine along with 2-ethylhexanoic tin (II) salt ($Sn(Oct)_2$), significantly improves the lactide polymerization rate. For the production of PLA the optical purity (D and L type) of the reagent, lactic acid is crucial because small amounts of enantiomer impurities change the properties such as crystallinity or degradation rate of the polymer. Another factor, which affects the properties of the polymer, is the detection and removal of impurities during the reaction as impurities can easily change the intermediate reactions and products [26], [93]-[95], [100]-[102].

2.7 Theoretical modelling for ROP process kinetics

In the literature, several reaction mechanisms were proposed to describe the ROP process. To explain the importance of reaction parameters (monomer concentration, temperature, rate constants), a reaction mechanism was formulated in the form of ordinary differential equations (ODE). Various theoretical models were proposed to explain the data from the experiments [8], [25], [26], [29], [33], [84]. Mathematical tools such as Polymath, Mathematica, and Matlab etc. are able to solve the ODEs and obtain the reaction rate constants k_0, k_j and k_t. To verify the experimental results, different groups adopted different mathematical techniques. These are explained in brief in the following section

2.7.1 Mathematical techniques to solve ODEs

- Banu et al. [26] applied the least square method in their mathematical model to verify the reactive extrusion experimental work of ROP of LA using tin octoate catalyst. The procedure based on boundary value estimation function ''bvp4c'' (MATLAB).
- Tanaka et al. [96] proposed the theoretical method for the polymerization of pyrrole by using the Semi-empirical molecular orbital (MO) at the MINDO/3 level of approximation which is a quantum chemical method to calculate the electron correlation effect normally for Zn, Al-containing compounds.
- Ryner et al. [65] used the hybrid density functional method B3LYP a quantum chemistry calculation using Gaussian software to calculate

the geometries and energies, which govern the thermo-dynamical properties of ROP of LA.

- Yu. et al. [8], [34] numerically solved the rate kinetics equation with the help of method of moments to verify the experimental work using tin-octoate as the metallic catalyst. The method of moments is a technique for calculating estimators of the parameters that is based on matching the sample moments with the corresponding distribution moments.
- Mehta et al. [29], [33] solved the ODE rate equation by using multiple-step Euler method and verified the model with the help of Dubois et al 1991 experimental report, which considered Aluminium isopropoxide as catalyst.
- Dubey et.al covered the details of mathematical modelling of polymerization of PLA based on five-stage reaction mechanism using MATLAB to solve ODE’s. [84]
- Dubey et al. [103] also revealed the reaction kinetic details of ROP process for PLA formation by considering the combination of the metal catalyst and AE source in the extrusion reaction process, which is one of its own kind of innovative work in this field.

2.8 Gaps in Literature

Based on detailed literature survey and analysis of available work, the shortcomings and lack of knowledge in the field of research and industrial manufacturing of PLA in large volume are as follows:

- Lack or limited theoretical and mathematical modelling for ROP process for PLA formation
- Use of non-metal catalyst/organic catalyst for high molecular weight PLA processing (30 kg/h)
- Reactive extrusion time for PLA processing from hours to minutes (20-0.2) hrs
- Impact of alternative energy input (Laser, Microwave, Ultra-sound) on the reaction mechanism
- Mathematical simulation of suitable reaction mechanism considering alternative energy sources and non-metal catalyst
- Details of reaction rate kinetics and reaction procedure including material mixing and residence time distribution
- Lack of understanding of kinetics of effective reaction mechanisms in continuous reactive extrusion (Ludovic software) for large-scale simulation of PLA extrusion process

2.9 **Aim & Objectives of the Research Project**

The study aims to validate the computer simulations for ROP of Lactide by using non-metal catalyst and alternative forms of energy in both batch and continuous (reaction) processes. Thus, the main aim of the study can be split into two as follows

- develop and validate the mathematical model and numerical simulation code for reaction of ROP of Lactide monomer in a batch process using eco-friendly catalyst and alternative sources of energy

- integrate the validated simulation code with Ludovic Software to validate the simulation process for the continuous reactive extrusion of Lactide monomer in the presence of eco-friendly catalysts and alternative energies

Objectives

I. Develop a mathematical model to simulate the ROP (batch) process and validate the code by comparing the output with results of experiments through literature data
II. Selection of simulation technique for the modelling of the reaction mechanism
III. Simulation of most suitable reaction mechanism (rate kinetics) reported in literature and its implementation (numerical code)
IV. Simulation of experimental data based on (Metal/metal-free) catalyst and with or without AE source in batch process
V. Based on validation of Ludovic simulated extrusion result with actual extrusion experiment result, modification of mathematical model

3 METHODOLOGY

The methodology defined in this chapter came about as a result of the study of the state-of-the-art of reaction kinetics of ROP. Comprehensive literature survey and background study was performed to establish the basic principles of ROP process for LA formation. This resulted in an estimation of most suitable reaction mechanism and mathematical model for the rate kinetics of the reaction mechanism. *Figure 17* depicts a flowchart of the methodology.

In the literature, several reaction mechanisms based on the three-stage reaction by Mehta et al. [33] to five stage reactions by Yu et al. [34], Banu et al. and Jacobsen et al. [23] were reported. The three-stage reaction mechanism focused mainly on initiation of monomer, propagation of monomer (addition to chain) and at the end termination of the polymer chain. This mechanism is based on batch process and is one of the benchmark mechanisms for the ROP of LA.

As reported earlier in this section, Yu et al. [34], Banu et al. and Jacobsen et al. [23] found that rate kinetics of ROP of lactide monomer were not just dependent on initiation, propagation and termination, but also on side reactions. The five-stage reaction mechanism, which considers side reactions, such as intermediate reactant, product and their impact on reaction output, emerged as the most suitable method to define the ROP of LA.

3.1 **Selection of mathematical tool**

Now once the suitable reaction mechanism is finalised, which covers all the possible reaction stages, next step was to select most appropriate mathematical tool to formulate/convert mechanism in terms of mathematical equations.

The five-stage rate kinetics of ROP of lactide monomer finalised can be expressed in terms of sets of ODEs. For that several methods were investigated which were used in literature. Such as Euler's method, Moment method, least square fit method and MATLAB. The most suitable tool had to be based on several factors such as ease of define variables, accurate calculations, in-built debugging tool, ease of coding and least time for convergence etc. Table I. shows the comparison of several mathematical tools.

Table I Comparison of different mathematical tools

S.N0	**Polymath**	**Mathematica**	**Matlab**
1	Differential equation solver(ODE, NLDE, Algebraic)	Differential equation solver(ODE, NLDE)	Preferred Ordinary Differential equation solver
2	Script declaration	Mathematical variable declaration	Easy variable declaration/initialization
3	Suitable for algebraic expressions	Algebraic expressions and vectors	Simple handling of vectors and matrices
4	Complex Plotting function, Excel Spreadsheet	Plotting function exist	High-quality built-in plotting functions
5	Least availability of debugging tool	Editing and debugging tools available	Strong built-in editing and debugging tools
6	Scripted coding	Unique symbolic language, and advanced code	Quick and easy coding

Based on the features of MATLAB in Table I such as simple handling of vectors and matrices, easy variable declaration, easy coding and expertise, it seems to be the most suitable method to solve the rate equations and verify the validity of the model with experimental data. In MATLAB the RK-4 method was used because of its accuracy and efficiency (with regards to time) in solving the linear ordinary differential equations (i), (ii), (iii), (iv) and (v) reported by Mehta et al. [33]

Methods such as multiple-step Euler's method and Multiple-step Heun's method also suitable to solve linear equations but RK-4, is a method to integrate ordinary differential equations by considering a trial step at the midpoint of an interval, which truncate the error “ε“(difference between the real solution and the solution obtained with the numerical method) lower than the one obtained by other methods. For example, in RK4 ε is proportional to Δt^5 (where Δt is the size of the step, in this work for simulation Δt varies from .01 to.05 sec) meanwhile in forward Euler’s method ε is proportional to Δt^2.minimize lower-order error terms.

The procedure for applying for 4th order Runge-Kutta method in a system of “n” differential equations is the following:

- The formula for calculating the next step will be:

  $y_{i,j+1} = y_{i,j} + \frac{\Delta t}{6} \cdot \left[k1_{i,j} + 2 \cdot k2_{i,j} + 2 \cdot k3_{i,j} + k4_{i,j}\right]$..........(A)

  Where $y_{i,j}$ is the value of variable “i” after “j” steps in time (t)

- And the parameters k1, k2, k3 and k4 are assessed for each variable “i” in each time step “j” using these expressions (*i-iv*):

  $k1_{i,j} = f_i\left(t, y_{1,j}, y_{2,j}, y_{3,j}, \dots, y_{n,j}\right)$.................................. (*i*)

$$k2_{i,j} = f_i\left(t + \frac{\Delta t}{2}, y_{1,j} + \frac{\Delta t}{2} \cdot k1_{i,j}, \dots, y_{n,j} + \frac{\Delta t}{2} \cdot k1_{n,j}\right)\dots\dots\dots (ii)$$

$$k3_{i,j} = f_i\left(t + \frac{\Delta t}{2}, y_{1,j} + \frac{\Delta t}{2} \cdot k2_{i,j}, \dots, y_{n,j} + \frac{\Delta t}{2} \cdot k2_{n,j}\right)\dots\dots\dots (iii)$$

$$k4_{i,j} = f_i(t + \Delta t, y_{1,j} + \Delta t \cdot k3_{i,j}, \dots, y_{n,j} + \Delta t \cdot k3_{n,j})\dots\dots\dots (iv)$$

For more details, please refer to Appendix-1.3

3.2 Methodology building process

In addition to the selection of suitable reaction mechanism (Five-stage) and a mathematical tool to convert it into a mathematical model, alternative analysis techniques of other research methodology, like the ones used in project MAPSYN and altergo [110-111] were also considered before finalising the methodology used in this research.

The aim of the project MAPSYN is to combine different innovative energy efficient chemical reaction processes, assisted with novel microwave, ultrasonic and plasma systems, up to the manufacturing scale. The application of alternative energy sources was studied individually for both micro-reactor and flow reactor systems (i.e. continuous not batch processes) [110].

For project altergo, the aim is to overcome the existing problems towards implementation of alternative energy technologies for intensified chemical manufacturing. The methodology was exemplified for three alternative energy technologies, namely ultrasound, microwave, and non-thermal plasma applied to different areas of advanced pharmaceutical synthesis and green fuels and bulk chemicals synthesis [111].

3.3 Suitability of selected Methodology

The methodology depicted in *Figure 17* and *Figure 18*, has several advantages, which are missing in the literature:

- Methodology explains the step by step progress of research strategy
- It details the several trials taken to formulate the reaction mechanism
- Most suitable mathematical tool selection and its application
- Transition of batch process simulation data to perform continuous reactive extrusion simulation through Ludovic®
- Consideration of AE source in the experiment and its proper implementation in simulation process for up-scaling strategy
- Simulation of data based on eco-friendly catalyst system
- Validation of experiment vs simulation model result

The primary task was to understand different stages reported in literature involved in ROP with conventional metal catalysts. Then the reaction rate kinetics in the form of mathematical differential equations were formed. The validation of the model for reaction rate kinetics of ROP of lactide monomer with conventional catalyst was done by comparing the output of the model with experimental data from the literature. The second step was to implement alternative, non-metal catalyst based reaction data and calculate its effect on the theoretical model.

Different catalysts based on their efficiency, directly affect the reaction parameters such as rate and time [44], [46]. Metal catalysts tend to sustain the ROP reaction at high temperatures; on the other hand, organic catalysts tend to sustain them at low temperature. Implementation of alternative energy (to increase temperature) will be the option to facilitate the polymerization process. The effect of AE on corresponding reaction rate kinetics was considered in the reaction mechanism modelling.

The details of the methodology are described as a flow chart below in *Figure 17 & Figure 18*. The flow chart highlights the progress of the research method starting with detailed literature survey for ROP process considering suitable reaction mechanism available and its modelling through different mathematical tools. Further, on validation of the developed theoretical model result with the experimental one, which is mainly based on metal-based catalyst and AE source consideration through the reactive extrusion process.

The final validation was made by consideration of Ludovic software, which incorporates the data generated through mathematical modelling as an input and provide result by considering thermo-mechanical environment simulation same as in twin screw extruder barrel experiment.

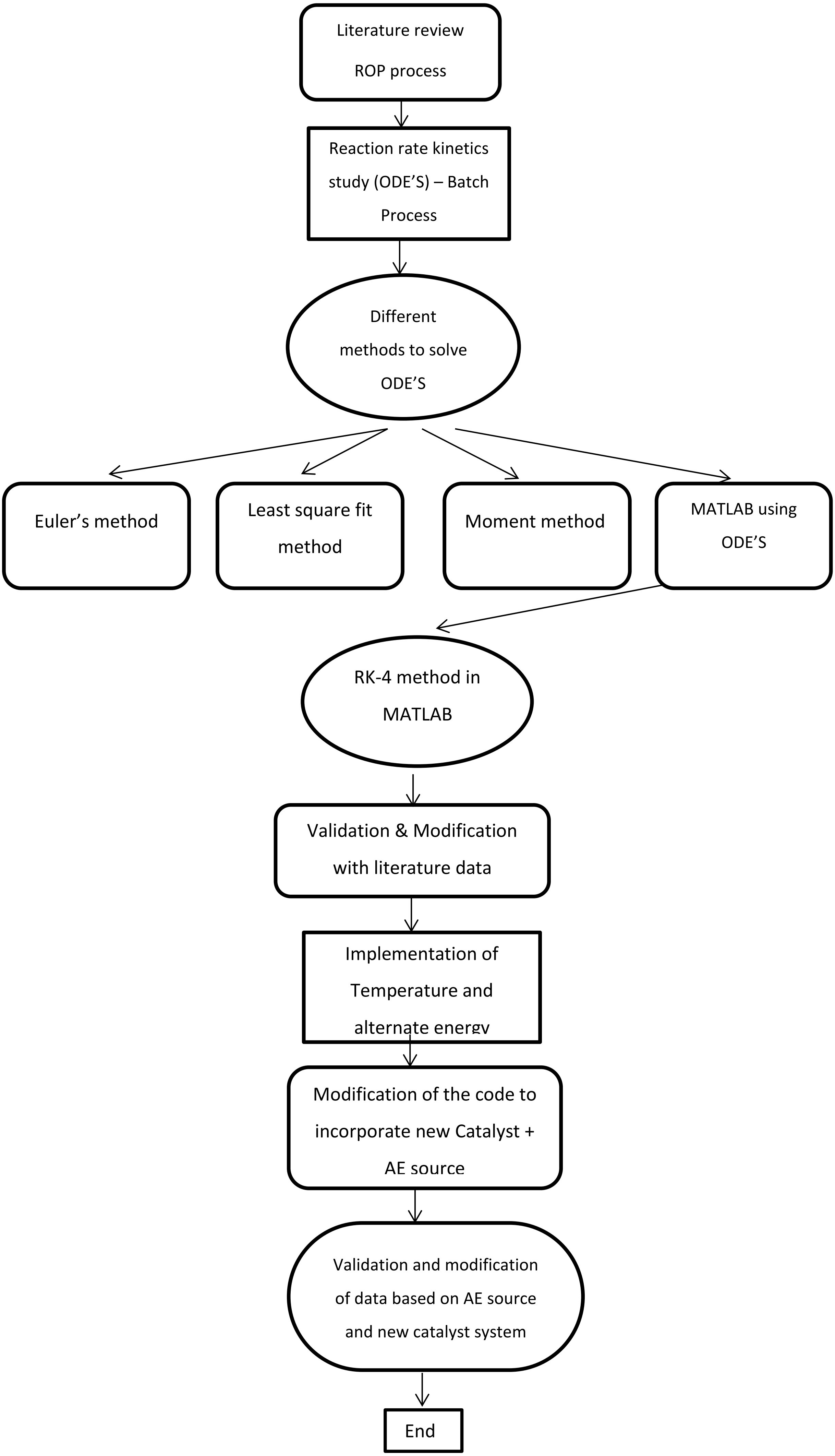

Figure 17 Flowchart of research Methodology

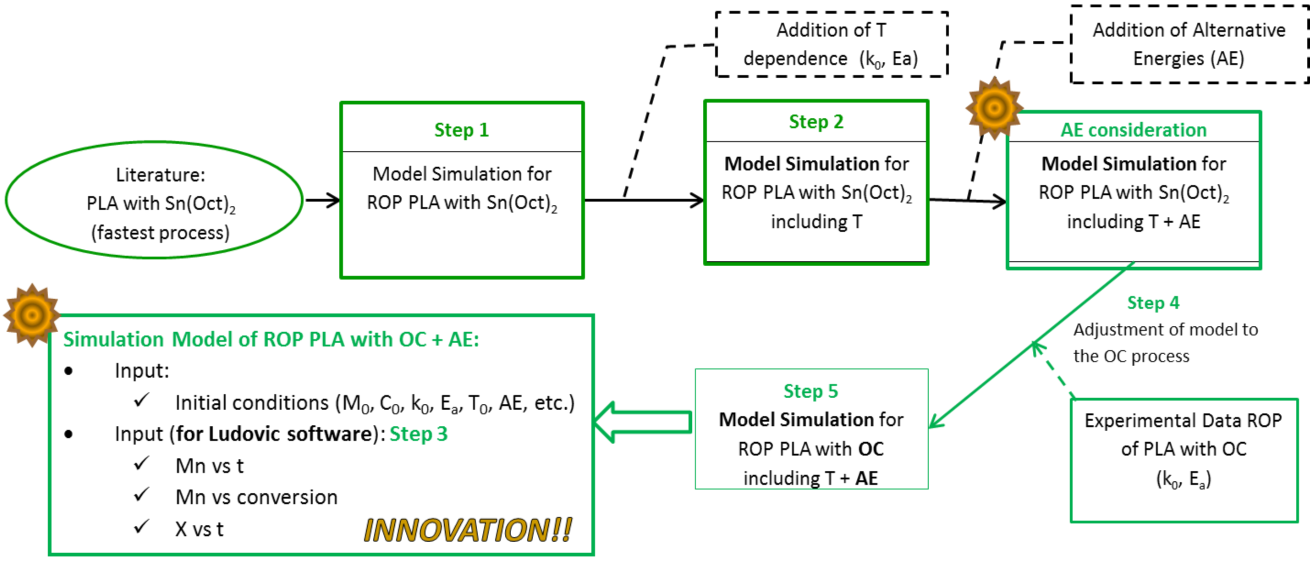

Figure 18 Flowchart of project Methodology

Further details regarding the details of working with Ludovic software and incorporation of mathematical model data into Ludovic, to fulfil the desired gap in the literature with proper research and validation were described as separately in chapters 4,5 & 6.

4 Mathematical Modelling for Continuous Reactive Extrusion of Poly (lactic acid) formation kinetics -1

4.1 Introduction

[2]The production of the large amount of waste is one of the major challenges at the present time, and polymers represent 70% of global waste [1],[23]. Because of massive consumption, problems such as decomposition and recycling of the used polymers were raised. As an alternative, bio-based and/or bio-degradable polymers such as cellulose acetate (CA), polyamide (PA), poly-butylene succinate (PBS), poly-lactic acid (PLA), poly-propylene (PP), poly-urethane (PU) etc. have raised interest [2]. PLA is a possible solution to these problems as it is compostable, the biodegradable thermoplastic polymer made from renewable sources [3].

The conventional method of synthesis of PLA is ROP process based on metal (Sn, Al, Zn) catalysis of Lactide monomer using suitable co-catalyst such as dodecanol and solvent toluene, water etc. [8], [9], [10]. However, one of the main limitations for the application of PLA is the presence of traces of toxic metal catalyst in the final product. A safe and efficient production process need to be developed to avoid potential hazards and toxicity. To overcome the issue of toxicity and health hazards, several

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[2] All the details of this chapter are taken from the published work by Dubey[1], S.P.; Abhyankar, H.A.; Marchante, V.; Brighton, J.L.; Bergmann, B. Mathematical modeling for continuous reactive extrusion of poly lactic acid formation by ring opening polymerization considering metal/organic catalyst and alternative energies. World Acad. Sci. Eng. Technol. Int. J. Chem. Nuclear Mater. Metall. Eng.. **(Vol:9, No:2, 2015)**

groups have been investigating the production of PLA using non-metal/organic catalyst [5]-[9].

It has also been found that alternative energy sources (LASER, Ultrasounds, Microwaves) could be a prominent option to facilitate the ROP of lactide monomers [71], [74], [83].

The implementation of metal-free catalyst and suitable application of alternative energy source in the ROP of LA may result in the complete replacement of the metal catalysts from the conventional process and production of considerable amount (128–152) kDa of PLA [104].

To overcome the issue of trace catalyst present in the final product while processing the ROP of LA at the commercial level, more safer and efficient mechanism is needed to produce PLA at large scale in an environment friendly conditions.

The impact of activity of several metal/non-metal catalysts on the reaction mechanism of ROP of LA was considered in this work. The state of the art of modelling several reaction mechanisms proposed in literature was done in chronological order. Based on investigation of kinetic model reported by Witzke et al., Mehta et al., Banu et al. and Yu et al. [8],[25], [26], [31], [33] the most suitable mathematical models explaining the reaction mechanisms were modelled in the form of first order ordinary differential equations (ODE) to get the reaction output by comparing molecular weight and conversion with time. Matlab with RK-4 method was finalised for the mathematical modelling. The analysis of simulation model explains the impact of several reaction parameters like concentration, rate constants, time etc. significantly. To consider the scale of production at the commercial level, the data created by the mathematical model (variation of conversion rate and molecular weight with time and temperature) has been used in Ludovic® [98] software. The isothermal curves (data) generated as an output from the ODE is then used as input in Ludovic® software. Ludovic® then uses the data to process actual extruder reaction conditions by considering the screw length, screw speed and viscosity parameter.

4.2 **Materials and Methods**

4.2.1 **Materials Details**

ROP of lactide was performed at Fraunhofer, ICT lab [107]. As an initial test L-lactide monomer (Sigma-Aldrich) and stannous octoate $Sn(Oct)_2$ (Sigma-Aldrich) as the catalyst to initiate the reaction process were mixed in the presence of tri-phenyl phosphine $(PPh)_3$ (Sigma-Aldrich), using toluene (Sigma-Aldrich) as a solvent.

4.2.2 **Experimental Process**

The extrusion reaction was performed using a co-rotation twin-screw extruder (Leistritz 27 HP). The extruder used has a diameter 27 mm and a length of 52 L/D. Ultrasound was applied with a specialised extruder block with the sonotrode being mounted at 25D (Ultrasound Sonification device UIP2000hdT, Hielscher Ultrasonics GmbH). Monomer and catalysts, were premixed under inert gas atmosphere and fed into main feed. To evaluate the influence of the rotation speed experiments, were conducted at 40, 75, 150, 300, 600 and 1000 rpm, while all remaining process parameters have been kept constant. The same initial conditions were used in all the cases, which are shown in Table II. In addition, to optimize the reaction process of ROP of lactide through reactive extrusion, several tests were made. The details of experimental reaction parameters are mentioned in the Table II.

TABLE II

REACTION PARAMETER

Symbol	PARAMETER	Value(Unit) [a]
M_0	Initial concentration of monomer	8.326 (mol/L)
C_0	Initial concentration of catalyst	0.008 (mol/L)
D_0	Initial concentration of co-catalyst	0.008 (mol/L)
T_0	Initial temperature	50 °C
M	Monomer mass	(1.2-2.5) ṁ / kg/
RPM	Rotation speed	(40-1000) rotation/min

4.3 Mathematical Modelling and Simulation of Reaction Kinetics of ROP of Lactide

4.3.1 Learning and trial to model the reaction mechanism

The initial investigations provided satisfactory results compared to literature Mehta et.al. [33] but further detailed studies discloses the fact of several other reaction stages such as trans-esterification and chain scission. These two side reactions influence the molecular weight and conversion factor significantly.

To overcome the issue of influence of side reaction on the output, reaction mechanism proposed by Yu et al. [8], [34] were investigated which consider all the relevant stages possible in the ROP of lactide by using $Sn(Oct)_2$ as a catalyst and 1-dodecanol as co-catalyst in the batch process.

The stages and reaction mechanism adopted is following:

Activation of catalyst:

$$\mathrm{C} + \mathrm{D}_i \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} \mathrm{R}_i + \mathrm{A} \text{ .... (1)}$$

Propagation

$$R_i + M \underset{k_d}{\overset{k_p}{\rightleftarrows}} R_{i+1} \text{ .... (2)}$$

Chain Transfer

$$R_i + D_j \underset{k_s}{\overset{k_s}{\rightleftarrows}} R_j + \mathrm{D_i} \text{ .... (3)}$$

Trans-Esterification

$$R_j + R_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + R_i \text{.......... (4)}$$

$$R_j + D_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + D_i \text{ .... (5)}$$

$$R_j + G_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + G_i \text{ .... (6)}$$

Non-radical Radom Chain scission

$$R_j \overset{k_{de}}{\longrightarrow} R_{i-k} + G_k \text{..................} (7)$$

$$D_i \overset{k_{de}}{\longrightarrow} D_{j-k} + G_k \text{..................} (8)$$

$$G_i \overset{k_{de}}{\longrightarrow} G_{i-k} + G_k \text{...................} (9)$$

Where: ka1, ka2: Activation rate coefficients, kp, kd: Propagation rate coefficients, ks: Chain-transfer rate coefficient, Kte: Trans-esterification rate coefficient, Kde: Random chain scission reaction rate coefficient.

C: catalyst, Sn(Oct)$_2$, A: octanoic acid (OctOH) produced by catalyst, Ri: Active polymer chain with length i, Di: Dormant polymer chain with length i, M monomer,

In the above-proposed mechanism, reaction 1 represents the activation of catalyst (C), reaction 2 represents the propagation stage of monomer and reaction 3 signifies the chain termination part of the reaction. The reactions (4-6) are side reactions known as intermolecular trans-esterification. Similarly, reactions (7-9) are side reaction called Non-radical random chain scission, which mostly occurs at higher reaction temperatures.

In order to model the above reaction mechanism, reaction stages (1-9) were transformed into first order ordinary differential equations. The differential equations were designed to consider the influence of each reaction parameter such as rate constants, concentration variation with time and concentration of catalyst, co-catalyst and Lactide monomer.

4.3.2 **Mathematical Modelling of Reaction Mechanism**

The present developed model considered the Yu et al. proposed mechanism by adding additional steps, which govern more precise mechanism of ROP of LA. The formulation and mechanism again formulated as an input file for Matlab considering all the rate equation as an ordinary differential equation. With the help of Yu et al. proposed initial parameter details, the model is verified at different concentration ratio and time interval, which shows a comparable variation of parameters as reported. For details, see Appendix –A1.1.

Mathematical equations based on above reaction mechanism, which shows variation of several parameters with time are following:

Equations

- $\frac{d[C]}{dt} = -ka1 \cdot [C] \cdot \sum_{i=0}^{n}[D_i] + ka2 \cdot \sum_{i=0}^{n}[R_i] \cdot [A] = -ka1 \cdot [C] \cdot D_T + ka2 \cdot R_T \cdot [A]$................(10)
- $\frac{d[A]}{dt} = ka1 \cdot [C] \cdot \sum_{i=0}^{n}[D_i] - ka2 \cdot \sum_{i=0}^{n}[R_i] \cdot [A] = ka1 \cdot [C] \cdot D_T - ka2 \cdot R_T \cdot [A]$...............(11)
- $\frac{d[M]}{dt} = -kp \cdot [M] \cdot \sum_{i=0}^{n-1}[R_i] + kd \cdot \sum_{i+1}^{n}[R_i]$........(12)
- $\frac{d[R_0]}{dt} = ka1 \cdot [C] \cdot [D_0] - ka2 \cdot [R_0] \cdot [A] - kp \cdot [M] \cdot [R_0] - ks \cdot [R_0] \cdot \sum_1^n[D_j] + ks \cdot [D_0] \cdot \sum_1^n[R_j] - kte \cdot [R_0] \cdot \sum_1^n[R_j] - kte \cdot [R_0] \cdot \sum_1^n[D_j] - kte \cdot [R_0] \cdot \sum_1^n[G_j] + kte \cdot \sum_{i+1}^{n}[R_j] \cdot \sum_0^n[R_k] + kde \cdot \sum_1^n[R_j] \ldots\ldots\ldots\ldots..$ (13)

- $\frac{d[R_i]}{dt} = ka1 \cdot [C] \cdot [D_i] - ka2 \cdot [R_i] \cdot [A] - kp \cdot [M] \cdot \sum_1^n[R_i] + kd \cdot \sum_{i+1}^{n}[R_i] - ks \cdot [R_i] \cdot \sum_1^n[D_j] + ks \cdot [D_i] \cdot \sum_1^n[R_j] - kte \cdot [R_i] \cdot \left(\sum_1^n[R_j] + \sum_1^n D_j + \sum_1^n G_j\right) + kte \cdot \sum_{i+1}^{n}[R_j] \cdot (\sum_1^n[R_k] + \sum_1^n[D_k] + \sum_1^n[G_k]) - kde \cdot (i-1) \cdot [R_i] + kde \cdot \sum_{i+1}^{n}[R_j]$................(14)

- $\frac{d[R_T]}{dt} = \sum_0^n \frac{d[R_i]}{dt} = ka1 \cdot [C] \cdot \sum_{i=0}^n [D_i] - ka2 \cdot \sum_{i=0}^n [R_i] \cdot [A] = ka1 \cdot [C] \cdot D_T - ka2 \cdot R_T \cdot [A] \dots\dots\dots\dots\dots..(15)$

- $\frac{d[D_0]}{dt} = -ka1 \cdot [C] \cdot [D_0] + ka2 \cdot [R_0] \cdot [A] + 2 \cdot ks \cdot [R_0] \cdot \sum_1^n [D_j] - 2 \cdot ks \cdot [D_0] \cdot \sum_1^n [R_j] - kte \cdot [D_0] \cdot \sum_1^n [R_j] + kte \cdot \sum_{i+1}^n [D_j] \cdot \sum_0^n [R_k] + kde \cdot \sum_{i+1}^n [D_j] \dots\dots\dots.(16)$

- $\frac{d[D_i]}{dt} = -ka1 \cdot [C] \cdot [D_i] + ka2 \cdot [R_i] \cdot [A] + ks \cdot [R_i] \cdot \sum_1^n [D_j] - ks \cdot [D_i] \cdot \sum_1^n [R_j] - kte \cdot [D_i] \cdot \sum_1^n [R_j] + kte \cdot \sum_{i+1}^n [D_j] \cdot \sum_1^n [R_k] - kde \cdot (i-1) \cdot [D_i] + kde \cdot \sum_{i+1}^n [D_j]$……………..(17)
- $\frac{d[D_T]}{dt} = \sum_0^n \frac{d[D_i]}{dt} = -ka1 \cdot [C] \cdot \sum_{i=0}^n [D_i] + ka2 \cdot \sum_{i=0}^n [R_i] \cdot [A] = -ka1 \cdot [C] \cdot D_T + ka2 \cdot R_T \cdot [A]$…………………(18)

- $\frac{d[G_i]}{dt} = -kte \cdot [G_i] \cdot \sum_1^n [R_j] + kte \cdot \sum_{i+1}^n [G_j] \cdot \sum_1^n [R_k] - kde \cdot (i-1) \cdot [G_i] + kde \cdot \left(\sum_{i+1}^n [R_j] + \sum_{i+1}^n [D_j] + \sum_{i+1}^n [G_j]\right)$……………….(19)

For code details see Appendix-1.3

ODE'S (10-19) were solved using MATLAB – RungeKutta– 4 method.

To calculate the number average molecular weight ($\overline{\mathrm{M_n}}$) (21) and Conversion factor (X) (20) following expressions were defined:

$X = 1 - \frac{[M]}{[M_0]}$ ________________ (20)

$\overline{M_n} = \frac{[M_0.]X}{[R_T]+[D_T]} m_{mon}$ __________ (21)

Where, [M] & $[M_0]$ are the concentration of monomer, $[R_T]$: Summation of all the active chain species ($\sum_0^n \mathrm{R_i}$), $[D_T]$: Summation of all the dormant chain species ($\sum_0^n \mathrm{D_i}$), Mn: The molecular weight of lactide monomer

4.3.3 **Modelling of PLA Reaction Mechanism in Reactive Extrusion**

In order to explain the effect of the flow of material and mixing with several materials(catalyst & cocatalyst) in the extrusion reaction at higher scale, theoretical large scale simulation was performed by Ludovic® software [98]. To investigate the mechanism of ROP of lactide in the compartment flow extruder, in Ludovic®, the whole extruder was divided into several zones. The proper mixing of the materials in the extruder at several zones plays a significant role in obtaining optimum output.

To perform the large scale simulation process through Ludovic®, initial data such as rate kinetics, temperature variation and variation of $\overline{\mathrm{M_n}}$ and X with time were provided by above developed a mathematical model (Heading C) based on batch process and solved with the help of Matlab RungeKutta-4 method. The parameters which are crucial and backbone of Ludovic® software to simulate extrusion reaction are isothermal curves which show variation of $\overline{\mathrm{M_n}}$ vs time (t) and conversion(X) vs time(t) at different temperatures. These details are needed to get the idea of the thermodynamic behaviour of reaction at several stages. The variation provides the trend of change of product as reaction proceeds through the extruder.

4.3.3.1 **Mechanism of Extruder Reaction through Ludovic®**

Ludovic® reproduces the thermo-mechanical behaviour of twin screw extruders [26]. It deals with the parameters, which directly affect the reaction output such as residence time of mixed material, rate constants, viscosity and thermo-mechanical flow.

The geometry of the extruder, which considers the rotation speed of the screw, throughput and melt flow affect the mechanical energy, which will create an impact on the thermal response of the material. Jing et al., Albert et al., Vukomanović et al. and Zhang et al. reported that alternative energy sources (LASER, Ultrasounds, Microwaves) could be a prominent option to facilitate the ROP of Lactide [71], [72], [73], [81], [82]. The implementation of metal-free catalyst and suitable application of alternative energy source in the ROP of lactide may result in the complete replacement of the metal catalysts from the conventional method and production of considerable amount (128–152) kDa of PLA.

4.4 **Results**

4.4.1 **Experimental Data**

Experimental data of average residence time (tR), temperature (T), number average molecular weight ($\overline{\mathrm{M_n}}$) and average molecular weight ($\overline{\mathrm{M_w}}$) obtained using L-lactide as monomer, stannous octoate Sn(Oct)$_2$ as catalyst and tri-phenyl phosphine (PPh)$_3$ as co-catalyst through reactive extrusion process using and not using ultrasounds for initial mixing are provided in Table III. The values of conversion and molecular weight distribution, were characterized by size exclusion chromatography (GPC).

It can be observed that the increase in temperature results in an increase in $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ for the same initial conditions. But also, $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ increase when ultrasound is applied. In addition, for the experiments at 190 °C, the conversion when ultrasounds are applied (80%) is higher than without ultrasound (58%).Therefore, the initial step of mixing monomer and catalyst with ultrasounds boosts/improves the performance of the reactive extrusion.

TABLE III

EXPERIMENTAL DATA

t_R(min)	T(°C)	Ultrasound	$\overline{M_n}$[kDa]	$\overline{M_w}$ [kDa]	PDI
2.30	190	Yes	12.4	15.5	1.25
		No	7.72	10.6	1.37
6.10	200	Yes	14.8	20.2	1.36
		No	13.5	17.6	1.30
7.30	205	Yes	30.1	50.0	1.64
		No	13.7	18.4	1.35

4.4.2 Results of Simulation in Batch Process

Based on experimental parameters and initial conditions, the mathematical simulation was performed for a total reaction time of (0-8) min and temperature range of 190-205 °C. The results are presented in Table IV, including temperature (T), the number average molecular weight ($\overline{\mathrm{M_n}}$) and average molecular weight ($\overline{\mathrm{M_w}}$).

In this case, the increase of the reaction temperature favours the growth of the polymer chain. This is manifested in an increase in $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ and as a result increase in PDI (poly dispersity index). The calculated value of $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ reported slightly higher than the experimental results obtained during reactive extrusion, but the trend is similar. On the other hand, the rates of conversion obtained in the simulated processes are close to the total conversion (around 99.0%) at the very large time and temperature but these results are based on the modelling of a batch process, in which it is assumed a situation of the perfect mixture. It must however be noted that for the same input parameters the output data tends to vary with each experiment. While selecting the input parameters for simulation, a value that leads to output that lies within the output 'cloud' of the experiment was chosen. As a result, there is a slight deviation between the simulation and experimental output. The deviation (delta) will be taken-care of through simulation with Ludovic.

TABLE IV

SIMULATION DATA

t(min)	T(°C)	$\overline{M_n}$ [kDa]	$\overline{M_w}$ [kDa]	PDI
2.30	190	8.5	12.7	1.49
6.10	200	31.1	45.4	1.45
7.30	205	35.0	52.2	1.49

4.5 **Discussion**

The ROP process for PLA production using ultrasound as one of the alternative energy sources in the twin-screw extruder depends on several factors such as temperature influence, throughput influence, screw rotation speed etc. For the polymerization process of Lactide, mixing has proven to be one of the crucial factors. The impact of extruder configuration and design affects the procedure and output of PLA significantly. The design of several mixing chambers within the extruder and the speed of twin screw influence the propagation rate of PLA synthesis [98].

When investigating the rotation speed dependent energy incorporation, interestingly the energy curves for 40, 75 and 150 rpm are nearly equal, while the energy incorporated at 600 and 1000 rpm is nearly equal as well, but much higher as for the lower rotation speeds. The temperature range varies from 160 to 220 °C while in the case of screw rotation speed it varies from (40-600) rpm. In the case of throughput, it varies from 0.5 to 2.5 kg/h. In reactive extrusion process, the configuration of screw and extruders affects the polymerization significantly [98].

The effect of ultrasound source combined with above changes is as follows:

- Ultrasounds enable polymerization at low rotation speed
- Ultrasound seems to improve polymerization at medium rotation speed
- Ultrasound effect on high rotation speed 100 rpm not visible
- Ultrasound accelerates the polymerization of the lactide.
- The heating effect which is a side effect of the sonication treatments seems to influence the polymerization positively

The result mentioned in Table III shows the positive impact of AE source on the reaction mechanism. At the large time and higher temperature in the presence of AE source, the values of $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ are high. A similar effect also reported in Table III, the data calculated through mathematical simulation. Further on to perform the simulation considering reactive extruder condition, the simulation data obtained by the batch process will be used as an input for Ludovic® software which calculates the final result of the continuous reactive extrusion process and compared with experimental result to facilitate reaction parameter details for the production of PLA at the commercial level.

4.6 Conclusion

For the production of safe and effective PLA polymer from lab scale to industrial scale, further investigations will be required, which includes large-scale computational simulation. Research, which involves the experimental and theoretical investigation of PLA synthesis considering metal free catalysts and alternative energy in the reaction, seems to be an effective mechanism to focus on. Theoretical modelling and simulation are useful to provide an estimate of the throughput and help to plan the experimental/industrial production accordingly. The results obtained through theoretical simulation such as information regarding rate kinetics, concentration variation, viscosity change and temperature influence on rate constants are the key parameter for prediction of large scale production of PLA by reactive extrusion process applying Ludovic® simulator [22]. Data created by Ludovic® will help the experimental setup getting more productive and precise output.

The initial experimental tests of ROP of lactide in reactive extrusion process shows that the application of AE can improve the performance of the reaction. It was proven that the application of ultrasounds boosts the growth of polymer chains.

In addition, the simulation of the batch process describes closely the results obtained experimentally. The mathematical model can be implemented in Ludovic® software to simulate and optimize a reactive extrusion process. This can be done by implementing isothermal curves for the conversion and number average molecular weight in Ludovic® software. Currently, this stage is in under development.

Groups such as InnoREX consortium (www.InnoREX.eu) [97] are performing detailed step by step investigations of above defined mechanism to achieve highly precise, controlled and large scale synthesis of PLA by the reactive extrusion process. The group is working on replacing the metal catalysts as well as on the implementation of AE sources in the reaction process. To achieve this target, lab scale experiments and mathematical simulation models to verify the output of the reaction are in progress. To consider the impact of AE sources and to study the production quality/market demands of PLA (Medical, Electronic & Food Packaging), several industrial partners also involved in InnoREX group. For the production of PLA through continuous, highly precise and controlled metal-free polymerization process, not only the InnoREX group but many other experts from industries like Purac [108] and NatureWorks [109] also involved to investigate and develop the innovative method.

5. Mathematical Modelling for Continuous Reactive Extrusion of Poly (lactic acid) formation Using AE sources kinetics -2

5.1. Introduction

[3]The production of large quantities of polymer waste is one of the major challenges of the present era, especially as polymers represent 20%–30% of global waste [1],[2],[16],[23]. As a result, of massive consumption of polymer products, problems such as decomposition and recycling of polymers have emerged. As alternatives, biomass and/or biodegradable polymers such as cellulose acetate (CA), poly-butylene succinate (PBS), poly-lactic acid (PLA), polyurethane (PU) *etc.*, have attracted interest. Among these bio-plastics, poly-lactide or poly lactic acid (PLA) has been the focus of increasing interest, with levels of industrial production becoming much more significant [2–9].

PLA polymer cross-linked with poly vinyl acetate (PVAc) and hexadecanoic acid (HA) exhibits shape memory behaviour. This can be obtained by water driven actuation, thermal effect and electrical effect [105,106] and has a wide range of applications in areas such as aerospace engineering, textiles, automobiles, and medicinal stitches, *etc.*

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[3] All the details of this chapter were taken from the published work
S. Dubey, H. Abhyankar, V. Marchante, J. Brighton, K. Blackburn, C. Temple, B. Bergmann, G. Trinh, and C. David, “Modelling and Validation of Synthesis of Poly Lactic Acid Using an Alternative Energy Source through a Continuous Reactive Extrusion Process,” ***Polymers*****, vol. 8, no. 4, p. 164, Apr. 2016**.

For decades, the conventional commercial method for synthesis of PLA has been ring-opening polymerization (ROP) based on metal (Sn, Al, Zn) catalysis of lactide, using suitable co-catalyst such as dodecanol and solvent [1],[8],[25],[26],[29]. However, PLA production according to conventional methods can still lead to potential toxicity issues, linked to residual metal traces from the catalyst, which can limit the potential scope of applications.

Attempts, were made to substitute tin-based catalysts by organic catalysts that exhibit less toxicity or eco-toxicity. [4],[41],[53]. It was observed through initial experimental trials that alternative energy sources (LASER, Ultrasounds, microwaves) with the combination of a prominent catalyst source, could be an option to facilitate the ROP of lactide monomers [71–86]. It is a well-known fact that the efficiency of the metal catalyst, in general, must be very high in order to perform the polymerization; on the other hand, by replacing a metal catalyst with a metal-free catalyst, it is not easy to obtain similar process efficiency. The implementation of a metal-free catalyst and the suitable application of an alternative energy source in the ROP of the lactide process may result in the replacement of the metal catalysts completely, thus achieving non-toxic PLA production at industrially acceptable rates (30–40) kg/h).

There are several projects underway with research groups trying to optimize the polymerization process of PLA through cleaner, more efficient and safer processes. One such project is InnoREX [97]. InnoREX aims to combine organo-metallic catalysis with reactive extrusion (REX) for ROP of lactide to obtain a high throughput. The project also aims to explore the use of alternative energy sources (microwave, ultrasound) to reduce the total energy consumption and improve eco-friendly design. To the best of the authors' knowledge, there is a dearth of literature in the area of ROP of lactide with ultrasound energy. Jevtić et al. [82] first reported the use of an ultrasound source as a thermal energy source for degradation of the PLA chain. An intense and targeted ultrasound source to separate the PLA chain from poly lactide-*co*-glycolic acid was one of the first attempts to use an AE source for polymer chain separation. This research led to the investigation of an ultrasound as an AE source for the ROP process, as it can provide considerable activation energy to initiate polymerization reaction [82]-[86]].

In this work, the impact of AE on ROP of LA using a metal catalyst has been investigated through extrusion experiments and validated using Ludovic® simulations. For this, the work has been divided into three different stages *Figure 19*: (1) Extrusion—to obtain experimental data of ROP of LA using $Sn(Oct)_2$ as catalyst and the application of ultrasound; (2) Simulation batch process—the model developed in previous work [84] was used to obtain isothermal curves; and (3) implementation of the isothermal curves (output of Step 2) in Ludovic® software [30] to simulate reactive extrusion of ROP of LA. The premise for using an AE source in the metal catalyst process was to reduce the role of the metal catalyst by supporting the AE source by enhancing the efficiency of the process.

Experimental data for reactive extrusion of ROP of Lactide was obtained at the laboratory level. The experiments were conducted using stannous octoate as a catalyst and triphenylphosphine (TPP) as co-catalyst.

In addition, ultrasound source, was applied to facilitate the mixing of monomer and catalyst. The role of the co-catalyst-catalyst ratio is as significant as the monomer to catalyst ratio. In the mathematical model, several range of ratios were tried to quantify the effect of co-catalyst.

On the other hand, the mathematical model to describe the polymerization of PLA in a batch process was presented in a previous work [84]. The reaction mechanism includes three basic stages in ROP reactions (initiation, propagation and termination) and other side reactions (trans-esterification, chain transfer, non-radical chain scission, *etc.*).

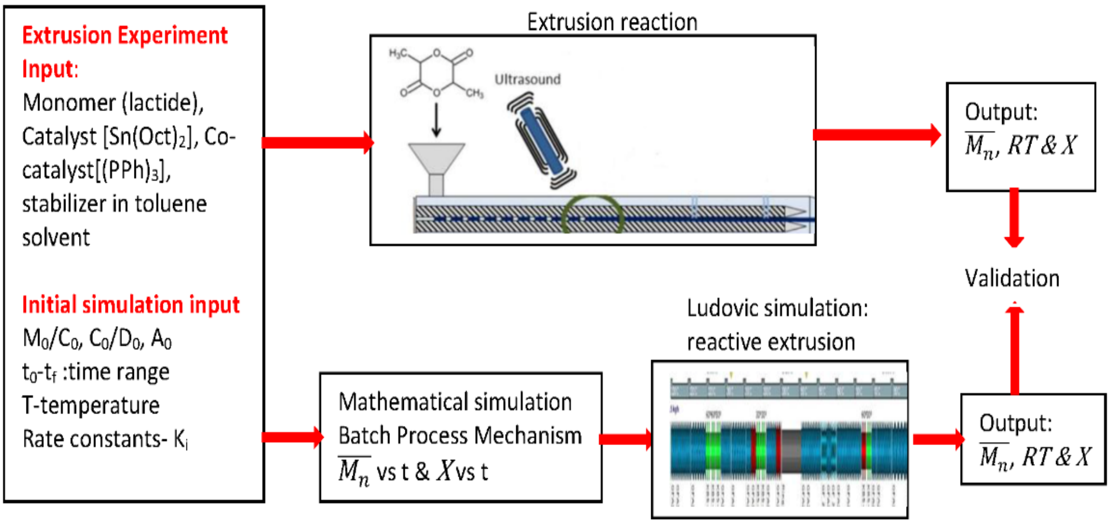

Figure 19. Methodology to explain reaction parameters. M0: Initial concentration of monomer, C0: Initial concentration of catalyst Sn(Oct)2, D0: Initial concentration of OH group source, A0: Initial concentration of phosphine (PPh)3, $(\overline{M_n})$ number average molecular weight, X: conversion, RT: residential time, Ki: rate constants. [103]

This model, was implemented in Ludovic®. This was conducted using isothermal curves, with particular reference to the variation of number average molecular weight ($\overline{M_n}$) and conversion (X) with time. Ludovic® uses the isothermal curves (provided as an input table) to estimate the stage and/or progress of the polymerization during the reactive extrusion.

To the best of the authors' knowledge, this is a significant step forward in the state-of-the-art in this area of research. In addition, the effect of AE has also examined in Ludovic®. Consideration of the AE source in large-scale simulations through Ludovic® software is another innovation in this area.

Finally, analysis and comparison of experimental data and simulated results, were presented in this work. The results obtained through the reactive extrusion experiment, were used to validate the output from the Ludovic® simulation. This work also attempts to explain the discrepancies in the output from the software *vis-à-vis* reactive extrusion.

5.2. Materials and Processes

5.2.1. Materials Details

The monomer used for the reactive extrusion was L-lactide (Sigma-Aldrich, St. Louis, MO, USA), the catalyst, co-catalyst and initiator were stannous octoate [$Sn(Oct)_2$] (Sn-bis-ethyl-2-hexanoate, Sigma-Aldrich), triphenylphosphine (TPP) (Sigma-Aldrich), and 1-dodecanol (Sigma-Aldrich), respectively. Toluene (Sigma-Aldrich) was used as a solvent.

5.2.2. Experimental Process: Reactive Extrusion of PLA

Reactive extrusion experiments, were performed at the Fraunhofer, ICT laboratory [107], using Leistritz 27 HP (Leistritz Extrusionstechnik, Nürnberg, Germany), a co-rotating twin-screw extruder. The configuration of the twin screw extruder used was: barrel dimensions 27 mm diameter and L/D = 52, temperature range (130–220 °C) ultrasound source, as an alternative source of energy applied in this process using a sonotrode "Ultrasound Sonification Device" UIP2000hdT (2000 W) (Hielscher Ultrasonic GmbH, Teltow, Germany) for the time range (3–15) min. The ultrasound power range used for mixing the material in the reaction process is (400–600) Watt. An extruder block was specifically designed to facilitate the application of ultrasound. In this block, the sonotrode was mounted and it was placed at a distance of 25 D from the feed for the reaction, while the monomer and catalysts were pre-mixed under an inert gas atmosphere and fed into the main feed. The initial concentration of the reactants and some initial conditions of the experiments are shown in Table V.

Table V. Extrusion reaction parameters

Symbol	Parameter	Value (Unit)
M_0	Initial concentration of monomer	8.3 mol/L
C_0	Initial concentration of catalyst	0.008 mol/L
D_0	Initial concentration of co-catalyst	0.008 mol/L
T_0	Initial temperature	50 °C
M	Monomer mass flow	1.2–2.5 m/kg
RPM	Rotational speed	75or 600 rpm

5.2.3 *Characterisation Techniques*

Monomer conversion (*X*) and average molecular weight ($\overline{M}_{\mathrm{n}}$) were measured at several temperatures, time and molecular monomer to initiator ratios. Samples, were then taken at different stages of the reaction process to evaluate the polymerization efficiency. Details of the methods and devices used for analysis listed below.

5.2.4. Gel Permeation Chromatography (GPC)

Hexafluoroisopropanol (HFIP), was used as a solvent in GPC for the analysis of PLA polymer. GPC is equipped with a detector and differential refractive index. Depending on the molecular weight of the particular sample, a column technique was used with the calibration standard based on the Poly(methyl methacrylate) (PMMA) system. Details of the GPC configuration are as follows:

- Poly(styrene sulfonate) (PSS) (series 1100, Agilent, Missouri, United States), at 35 °C,
- Columns: [PSS PFG 7 µm × 8 mm × 50 mm (guard column) PSS PFG 7 µm × 8 mm × 300 mm; 100 A PSS PFG 7 µm × 8 mm × 300 mm; 1000 A].
- Flow: 1,0 mL/min, Detector: Refractive Index Detector Agilent 1100.
- Injection volume: 100 µL.

This technique was used to determine the average molecular weight ($\overline{M_{\mathrm{n}}}$) values. The values obtained through GPC are not an absolute measure but at the equilibrium.

5.2.5. Proton Nuclear Magnetic Resonance (^{1}H NMR)

Proton nuclear magnetic resonance analysis was conducted in $CDCl_3$ using a Bruker (250) MHz spectrometer (Coventry, UK) at 30 °C in deuterated chloroform. The solution concentration used was 5 wt/vol %. This technique was applied to determine the monomer concentration and from that the conversion rate (*X)*. This analysis was also applied to the sample extracted from the extruder, which was a mixture of monomer and polymer. Several numbers of scans (100), were performed for each sample until the complete separation of polymer and monomers was achieved.

5.3. Mathematical Modelling of Reactive Extrusion

In general, the ROP of lactide is a complex process, which involves several reaction stages. To assess the impact of the reaction parameters (concentration of monomer, the initial concentration of catalyst, the ratio among reactants, kinetic rate constants, AE source, temperature, *etc.*) on the efficiency of the polymerization (mainly conversion and average molecular weight), it is necessary to formulate a suitable reaction mechanism. Mathematical modelling is a powerful and cost-effective tool to analyze these parameters. It can also help to explain the thermodynamic behaviour of the process and explains how it can be scaled up to commercial levels of production.

Developing a simulation model, which defines the extrusion process (accounting for the polymerization reaction), is complex, due to the interdependencies of the reactions. This process was divided into two parts: firstly, the development of a mathematical model describing the ROP in a batch process and, secondly, integrating this model into Ludovic® software (Saint-Etienne, France). From the ROP model for the batch process, isothermal curves for the evolution of number average molecular weight ($\overline{M_{\mathrm{n}}}$) and conversion ($X$) with time were obtained. These curves, were discretized and integrated into Ludovic®. This way, Ludovic® was able to estimate a degree of conversion and growth of the polymer chains during the simulation of the reactive extrusion process.

Reaction mechanisms can be defined for any ROP reaction (mechanisms will tend to be similar to the one we have defined). However, depending on the monomer, initiator, and catalyst and, indeed, the ratios of the monomer to catalyst and catalyst to the initiator, the reaction parameters will change, and as such they will have to always be validated against experiments. However, once the validation is undertaken, these can be used to model the process based on similar reaction conditions.

5.3.1. Reaction Kinetics Modelling and Mathematical Simulation of ROP of Lactide

In previous related work, Dubey *et al.* [84] covered the details of mathematical modelling of polymerization of PLA based on a five-stage reaction mechanism. The reaction mechanism comprises initiation, propagation, termination, trans-esterification and, probably, non-radical random chain scission. For continuity, the mechanism used was reproduced in Equations (1)–(9).

Activation of catalyst:

$$\mathrm{C} + \mathrm{D}_i \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} \mathrm{R}_i + \mathrm{A} \tag{1}$$

Propagation

$$R_i + M \underset{k_d}{\overset{k_p}{\rightleftarrows}} R_{i+1} \tag{2}$$

Chain Transfer

$$R_i + D_j \underset{k_s}{\overset{k_s}{\rightleftarrows}} R_j + \mathrm{D_i} \tag{3}$$

Trans-Esterification

$$R_j + R_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + R_i \tag{4}$$

$$R_j + D_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + D_i \tag{5}$$

$$R_j + G_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + G_i \tag{6}$$

Non-radical Radom Chain scission

$$R_j \xrightarrow{k_{de}} R_{i-k} + G_k \tag{7}$$

$$D_i \xrightarrow{k_{de}} D_{j-k} + G_k \tag{8}$$

$$G_i \xrightarrow{k_{de}} G_{i-k} + G_k \tag{9}$$

Where, k_{a1}, k_{a2} Activation rate coefficients; k_p, k_d: Propagation rate coefficients; k_s: Chain-transfer rate coefficient; k_{te}: Trans-esterification rate coefficient; k_{de}: Random chain scission reaction rate coefficient; C: catalyst, $Sn(Oct)_2$; A: octanoic acid (OctOH) produced by catalyst; R_i: Active polymer chain with length *i*; D_i: Dormant polymer chain with length *i*; G_i: terminated polymer chain with length *i*, M: monomer.

In the reaction mechanism, Equation (1) represents the activation of catalyst (C), Reaction 2 represents the propagation stage of monomer and Reaction 3 signifies the chain termination part of the reaction. The Equations (4)–(6) are side reactions known as intermolecular trans-esterification. Similarly, Equations (7)–(9) are side reactions called non-radical random chain scission, which mostly occur at high reaction temperatures. [A], in Equation (1), is treated as a concentration of the octanoic acid, which was produced as a bi-product/acid impurity as a result of the reaction of the catalyst and alcohol initiator. The role of AE considered as "natural" acid impurity in the fresh monomer bulk as a result, of the impact of [A] is crucial and consequently must be considered.

The reaction kinetic parameters involved in the reaction mechanism such as reaction rate constants (k values) k_p, k_d and monomer equilibrium concentration ($Me = K_p/K_d$), *etc.* were calculated by the fitting of experimental data using a mathematical formulation. The value of Me was calculated by considering the experimental conversion (X) value with the formula = $M_0 \times (1-X)$ and $X = (1-Me/Mo) \times (1-e^{-Kpt})$. The estimation of Me was calculated through curve fitting of the equation in the form of ($Y = m \times X + C$ or $Y = C + A \times e^{BX}$). In general, Me was formulated as $Me = \text{slope} \times T + \text{intersect}$. Propagation rate constant (k_p) was calculated using the equation of the variation of monomer concentration according to the equation $\frac{d[M]}{dt} \cong -kp \times R_T \times ([M]-[Me]$,where Me is the monomer equilibrium concentration, M_0 is the initial monomer concentration and R_T is the initial concentration of the active catalyst. Other parameters including initial rate constants k_{a1}, k_{a2}, k_{te} and k_{de} were taken directly from the literature [29]. This reference covers mostly the details of research work related to mathematical modelling of the ROP process of lactide over the last decade

5.3.2. Modelling of ROP Reaction Mechanism in Reactive Extrusion

Ludovic® is one of the most widely used software packages for the simulation of extrusion processes [26], [27], [84]. At present, commercial versions of this software are not available with an option to simulate reactive extrusion, *i.e.*, when a reaction happens during the extrusion process (within the extruder barrel). In order to adapt the software for accurate simulation of ROP of LA, it was necessary to introduce the effect of the reaction happening within the extruder barrel to the properties of the system, *i.e.*, variation of the concentrations of initiator, monomer, polymer and their varying percentages as the reaction progresses.

Ludovic® software today has the capacity to simulate the extrusion process (considering all thermal and mechanical degradation processes, *etc.*). It is available commercially and is used by industries to fine-tune their throughputs. Ludovic® software works by breaking down the extrusion process (along the barrel) into small subsections (nodes) and using the (input) isothermal curves (molecular weight *vs.* time, viscosity *vs.* time, shear rate *vs.* time, *etc.*) to predict the outcome of the process of extrusion over each of the subsections. These results during each subsection were integrated over the extrusion barrel. As the reactive extrusion processes (such as that of PLA) take hold in the industry, Ludovic® software will have to be updated to take into account the effect of the continuous reactive extrusion. This means the software will have to be upgraded to take into account the effect of the chemical reaction (batch process modelling) as well as the effect of the extrusion process. Hence, isothermal curves (obtained from the mathematical modelling of the batch process) depicting the ring opening polymerization of PLA process were developed (as in ref [84]) and the Ludovic® software was upgraded to accept these as inputs. Unlike traditional extrusion, the molecular weight undergoes drastic changes (monomer to polymer) during this process and, hence, such attempts at inputting a reactive extrusion model into the Ludovic® software will have to be validated through experiments.

To implement this, isothermal curves for the variation of $\overline{M_{\mathrm{n}}}$ and X with time were generated with the mathematical model based on a batch process reaction mechanism. Some of the properties of the system can be calculated using the degree of polymerization, given by the conversion and average molecular weight, as they represent the percentage of monomer and length of polymer chain at a particular time of reaction. Thus, Ludovic® uses these isothermal curves as initial input. Then, the thermodynamic behaviour of the polymerization reaction at several stages can be calculated. The variation provides the initial start-up and output at various stages, as the reaction proceeds through the extruder. A flowchart describing the development of the whole simulation process is presented in *Figure 20.*

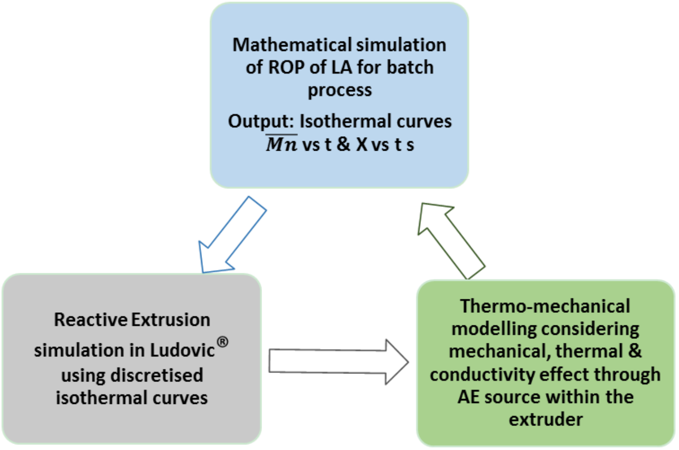

Figure 20. Input and output for continuous extrusion simulation [103]

5.3.3. Mechanism of Extruder Reaction through Ludovic®

Simulation through Ludovic® detailed the thermo-mechanical behaviour of twin-screw extruders [98]. It deals with the parameters, which directly affect the reaction output such as residence time of mixed material, rate constants, viscosity and thermo-mechanical flow. Stationary thermo-mechanical flow is computed on the basis of:

- Geometrical discretization of the channel zone–C chamber of the screw and material flow of the mixture, as shown in *Figure 21*
- Changes in pressure and temperature were computed for discrete volumes. Temperature and pressure both updated from the exit to the upstream part of the screw
- The computation is performed in a regular iterative way

For the sensitivity of temperature effect, Ludovic® provides the temperature at each C-chamber zone. This temperature is the result of mechanical, conduction and alternative energy applied within the extruder. Geometry of the extruder, rotation speed of the screw, throughput and melt influence are factors that affect the mechanical energy from shearing; and this affects the thermal response of the material.

5.3.4. Alternative Energy Implementation in Ludovic® Software

To the best of the authors' knowledge, application of AE source within Ludovic simulator, were not reported in literature. The AE source can be implemented as source of heat or thermal impact on reaction mechanism. Due to its unique application, effect of AE source on reaction is different to those that occur during conventional heating (Heat Furnace). AE source device was attached to the barrel (Grey Zone) in Ludovic® *Figure 21* The two specific requirements are

- Hollow cylinder zone (No metal screw, kneading etc.)
- Fully filled zone

To make the application of AE source effective, full filled zone is to be designed under the alternative energy input section. *Figure 21* [98] shows an example of screw configuration setup with AE source barrel (chamber in grey colour)

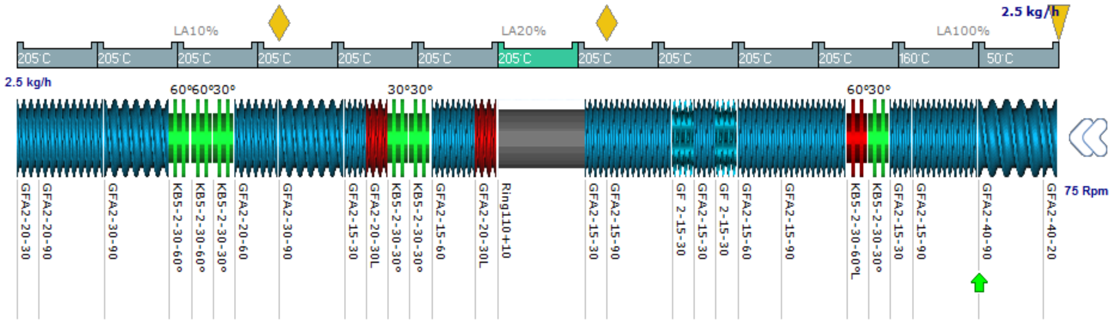

Figure 21: Screw profile with AE source device [103]

5.3.5. Thermo-Mechanical Modelling of Ludovic

Two crucial physical parameters, conductivity and mechanical effect, were considered for the thermal balance equation. This equation includes a third term for the source power of the AE, in the AE source barrel component in the model. The updated heat equation is:

$$\rho * C_P * dT = W_{dissipation} + W_{conduction} + W_{AE} \quad \ldots\ldots\ldots\ldots\ (10)$$

This equation is then computed in each element and Ludovic® provides the variation of temperature due to AE source *Figure 22* with the associated effects of mechanics and conduction. Finally, these three effects are combined in order to finalize the global evolution of temperature within the twin-screw extruder [98].

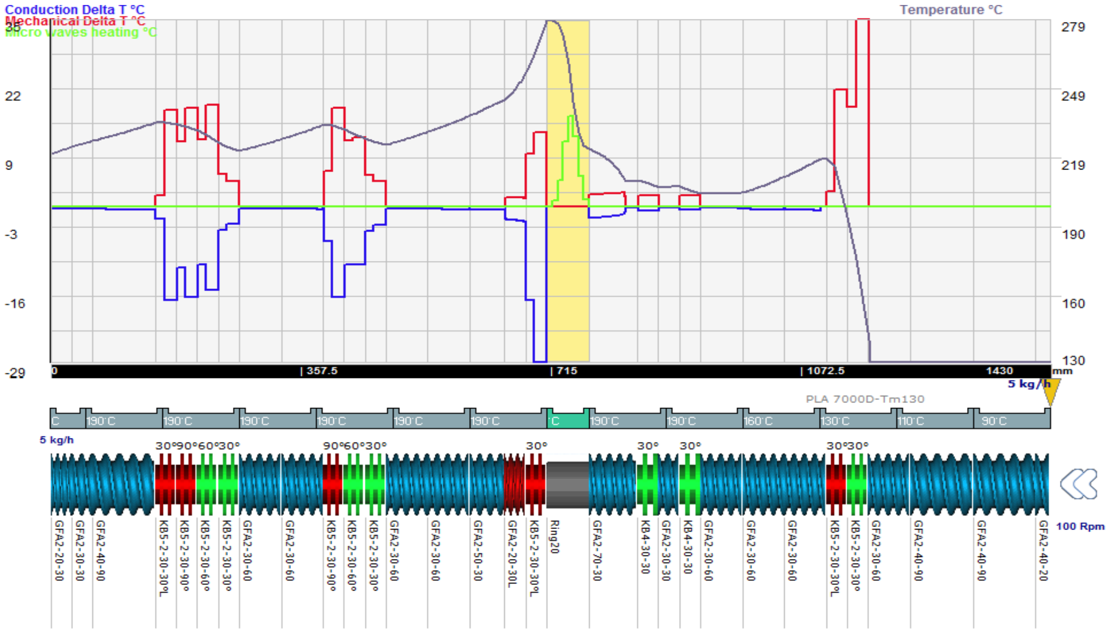

Figure 22: Temperature variation due to conduction (purple), due to mechanical effect (red) and microwave (AE) (100W) (green) effect and result on final temperature (grey). [103]

Figure *22* shows the contribution of three different effects to the variation of temperature. The feeding zone is at the right corner and the mixture flows from right to left side. In fact, in AE source zone, no metallic material (barrel) is mounted. Due to the use of ring (no metal screw), the shear effect is negligible and only AE act as the source of heating. The heating effect of AE source is not higher than dissipation energy (when comparing the magnitude of green curve to red curve) but due to the concentration of energy in a small space and no barrel cooling applied, the increase of temperature is much more significant.

For the implementation of alternative energy in the reaction process, microwave source or Ultrasound Sonification seems to impact the polymerization reaction system [71], [73], [81],[82]. The AE power impact, was taken into account as a third term (in addition to conduction and dissipation power) in thermal balance equation (10).

5.4. Results & Discussion

5.4.1. Experimental Result

Data of average residence time (RT), temperature (T), number average molecular weight ($\overline{\mathrm{M_n}}$), average molecular weight ($\overline{\mathrm{M_w}}$) and conversion (X) from the reactive extrusion experiments using ultrasounds for initial mixing are provided in Table VI It was observed that increase in temperature results in increase in $\overline{\mathrm{M_n}}$, $\overline{\mathrm{M_w}}$ and X for the same initial conditions. Also $\overline{\mathrm{M_n}}$, $\overline{\mathrm{M_w}}$ and X increases when Ultrasound (AE) source applied. In addition, for the experiment at 190°C, the value of conversion was found to be higher when ultrasound was applied (80%) than in the case without ultrasound (58%). Similar trend of increase in conversion (X), were also observed at higher temperature. Therefore, the initial step of mixing monomer and catalyst with ultrasound enhances the performance of the reactive extrusion reaction.

Table VI Reactive extrusion experimental data

RT (min)	T(°C)	Ultrasounds	$\overline{M_n}$ (g/mol)	$\overline{M_w}$(g/mol)	RPM	X (%)
2.30	190	Yes	12396	15500	75	80
		No	7720	10600	75	58
6.10	200	Yes	14800	20200	75	92
		No	13500	17600	75	85
7.3	205	Yes	30100	50000	600	94
		No	13700	18400	600	86

5.4.2. Impact of AE source on Extrusion Experiment:

The ROP process for PLA production using ultrasound as one of the alternative energy sources in the twin-screw extruder depends on several factors such as temperature, throughput, screw rotation speed, etc. For the polymerization of lactide, mixing is one of the crucial factors. The design of several mixing chambers within the extruder and the speed of twin screw influence the propagation rate of PLA synthesis [89]. Several merits of using Ultrasound as AE source apart from controlling the reaction process are following:

- accelerates the polymerization of the lactide

- enables polymerization at low rotation speed observed during trial
- (the heating effect which is a side effect of the sonication treatments (Ultrasounds)) seems to influence the polymerization positively
- The Ultrasound source had a positive impact on polymerization process due to mechanical mixing of lactide and catalyst before the feeding zone

From this set of experiments in Table VI, the most efficient condition for experiment is: 205°C, 600 rpm and using Ultrasound (AE).

The results mentioned in Table VI show positive impact of AE source on reaction mechanism and process output. At high reaction time and temperature, in the presence of AE source, the values of $\overline{\mathrm{M_n}}$ and ($\overline{\mathrm{M_w}}$) are high. At higher temperature, similar effect also reported in Table VI, the data calculated through mathematical simulation. Further on to perform the simulation considering reactive extruder condition, the simulation data obtained by batch process will be used as an input for Ludovic® software which calculates the final result of the reactive extrusion process and compared with experimental result to facilitate reaction parameter details for the production of PLA at commercial level.

5.4.3. Results of Batch Process Simulation

To conduct the mathematical simulation of ROP of LA with the reaction mechanism suggested, initial reaction input details were adopted from the experiments on reactive extrusion. Details are mentioned in Table VII

Table VII Initial reaction parameters for simulation

Symbol	Parameter	Value (unit)
M_0	Initial concentration of monomer	8.326 mol/L
C_0	Initial concentration of catalyst	0.008 mol/L
D_0	Initial concentration of co-catalyst	0.008 mol/L
T_0	Initial temperature	50°C
A_0	Octanoic acid (OctOH)	0.24 mol/L
Me	Monomer equilibrium concentration	0.225 mol/L

Based on experimental parameters and results, mathematical simulation was performed for the reaction times and temperature shown in Table VIII. The results are presented in Table VIII, including temperature (T), number average molecular weight ($\overline{\mathrm{M_n}}$), average molecular weight ($\overline{\mathrm{M_w}}$) and conversion (X). The role of A0 considered as "natural" acid impurity in the fresh monomer bulk because of that, impact of A0 is crucial and needed to be considered.

Table VIII Mathematical simulation results for ROP of LA in batch process

t (min)	T(°C)	$\overline{M_n}$ (g/mol)	$\overline{M_w}$ (g/mol)	**X**(%)
2.30	190	8500	11645	50
6.10	200	31100	40430	74
7.3	205	35000	87500	82

Increase in temperature, supports the propagation stage of the reaction. In general, it favours the higher propagation to support the growth of polymer chain. Growth in chain can be feasible up to certain range of temperature. At very higher temperature beyond 210°C, side reactions (chain scission and trans-esterification) dominate and reduce the $\overline{\mathrm{M_n}}$ which is not suitable for polymerization. The results, mentioned in table VIII shows the increase of $\overline{\mathrm{M_n}}$ and X as temperature increases. This is manifested in an increase in $\overline{\mathrm{M_n}}$, $\overline{\mathrm{M_w}}$ and X. The calculated values of $\overline{\mathrm{M_n}}$ and $\overline{\mathrm{M_w}}$ through batch process simulation founds higher than the experimental values obtained through reactive extrusion, although the trends are similar. On the other hand, the rates of conversion obtained in the simulation processes are close to the total conversion (around 95%) at very high temperature (300°C) but these results were based on the modelling of a batch process reaction set up, in which perfect mixing conditions were assumed.

5.4.4. Isothermal inputs for Large scale extrusion in Ludovic®:

The isothermal curves, conversion(X) and number average molecular weight $\overline{\mathrm{M_n}}$ with time, for total reaction time of 6 min and temperature range of (150-300)°C were developed to facilitate input for Ludovic®. Although, the range of output of simulation at high temperature (up to 300°C), is not valid as the polymer degrades at temperatures above 210°C, the extrapolation of temperature, was made to provide a detailed input to Ludovic to perform extrusion simulation for broader range of temperatures. (The inputs at higher temperatures are unlikely to be used during Ludovic simulations) The duration of the input data was based on the residence time reported by experiments on reactive extrusion of PLA. Details of the input data are shown in *Figure 23* and *Figure 24*.

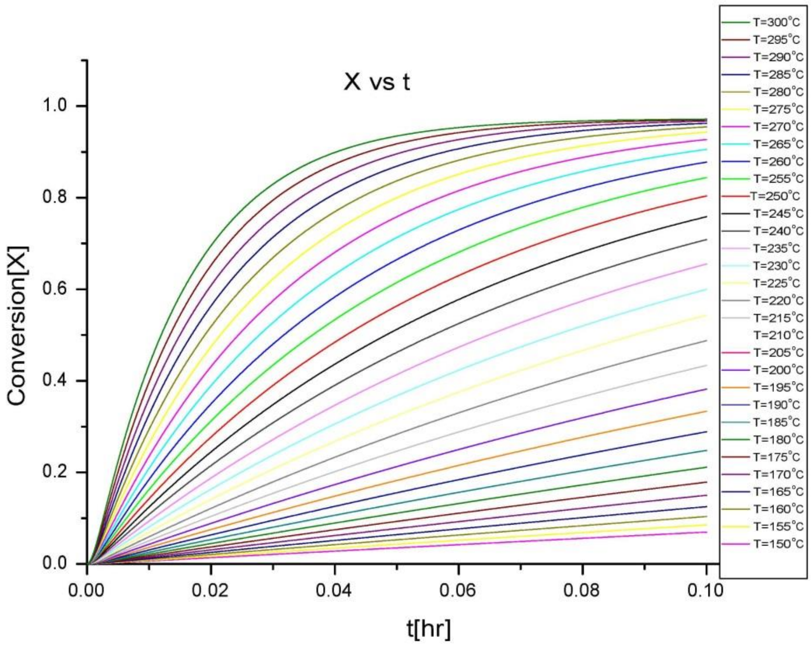

Figure 23: Isothermal curves for conversion (X) vs t [103]

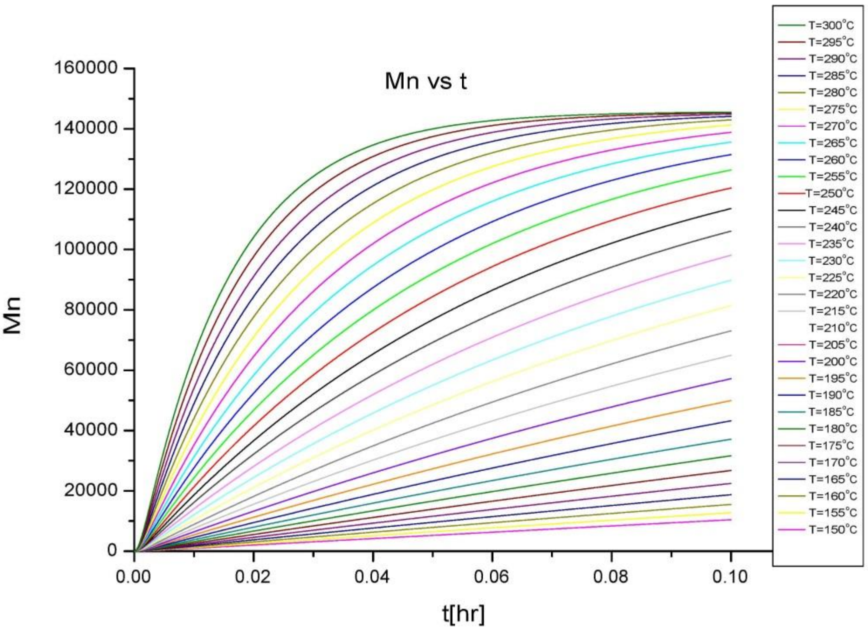

Figure 24: Isothermal curves for average molecular weight ($\overline{M_n}$) vs t [103]

5.4.5. Results of reactive extrusion simulation (Ludovic®)

Figure 25 represents the variation of conversion (X) and number average molecular weight $\overline{\mathrm{M_n}}$ along the length of the screw (which in a continuous process can be correlated with time for the steady state) obtained with Ludovic®, taking into account the effect of the polymerization. These results correspond to the simulation of the experiment with these initial conditions: temperature (50-220°C), AE source (250-600) W, screw speed 300-600rpm. Similar curves were generated for each reactive extrusion experiment.

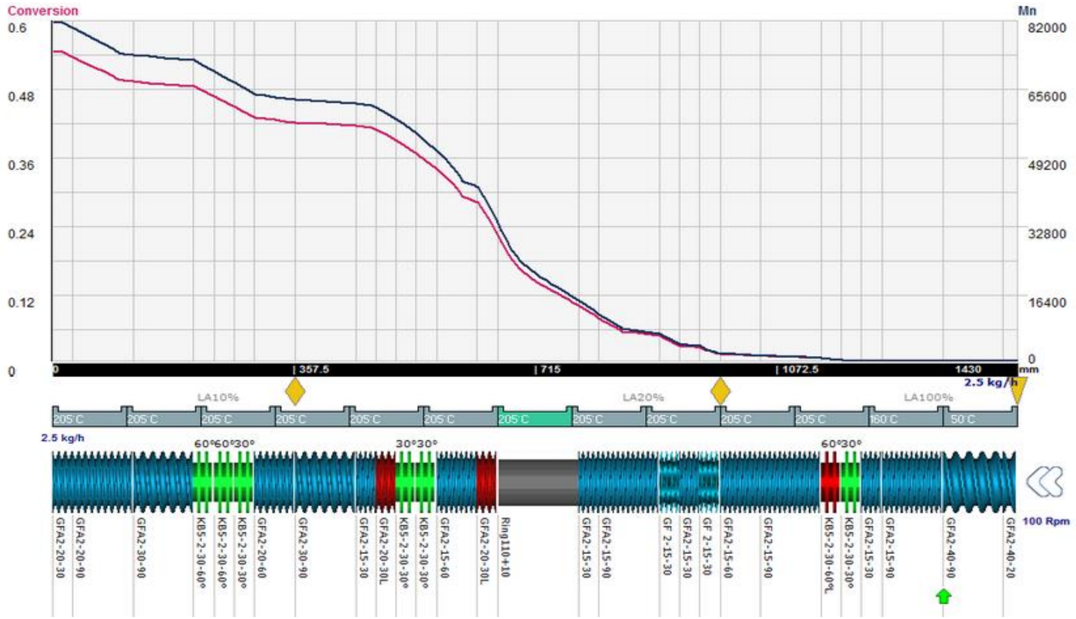

Figure 25: $\overline{M_n}$ *(purple line) vs T & X (red line) vs T obtained with Ludovic® for T (50-220) °C, AE=250 W, 600 rpm. [103]*

5.4.6. Comparison of extrusion experiment and Ludovic® simulation Results:

Validation of reactive extrusion output from Ludovic®:

(a)RTD comparison with throughput and barrel temperature:

The initial trials, were performed to compare local residence time (RT) for extrusion reaction experiments and Ludovic® simulations. The effects of throughput and barrel temperature, were considered in these trials. Significant differences, were found between experimental and simulated results, as *Figure 26* Trial-1 shows. With the implementation of same initial conditions in simulation as used in experiments, the result was expected to be similar but it was not the case.

Trial-1 Measurement considering that reaction starts at the beginning of extruder

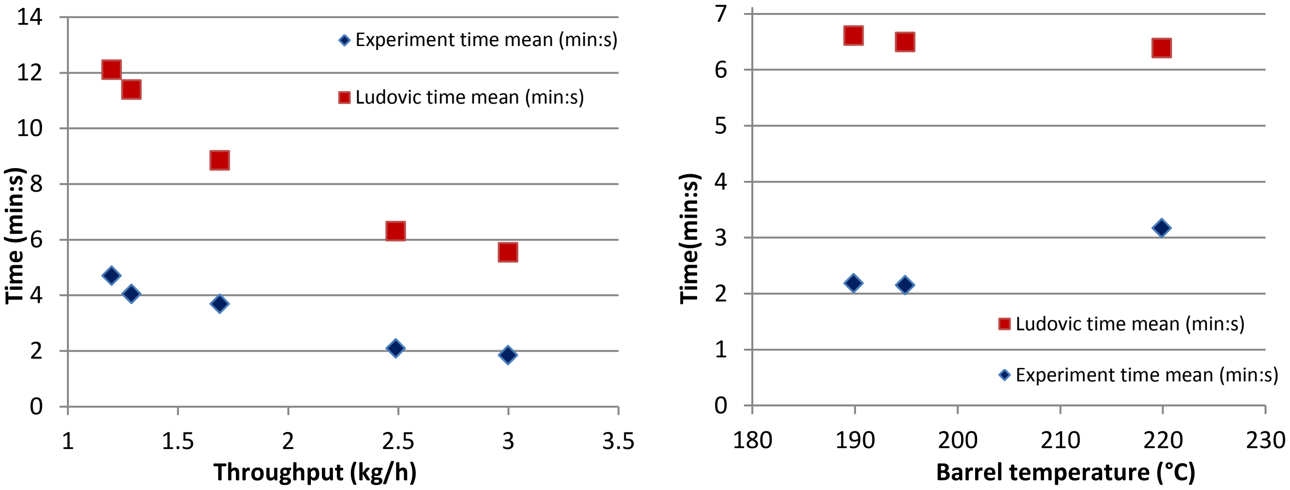

Figure 26: RTD Comparison for Ludovic simulated (red dots) and experimental (blue dots) results for throughput and barrel temperature. [103]

To find out the details why the result (RT values) differs even though same reaction condition was applied, further consideration of reaction mechanism and measurement process was repeated. During reactive extrusion, in the first few seconds, the mixture (catalyst, monomer, initiator, etc.) has low viscosity and flows through the barrel without being sheared/extruded. At this stage, only the effect of temperature influences the mixture and the progress of the reaction. Thus, at this stage (in the barrel) the reaction progress like a batch process until the viscosity increases due to the continuous conversion of the monomer in to higher viscosity polymer. After this point, the mixture undergoes further reactions along with shearing forces and extrusion. This behaviour (reaction starting in the barrel and not at the feeding stage) was observed during the reactive extrusion experimental trials and hence was implemented as an assumption in Ludovic software. Based on this assumption the barrel length available for extrusion simulation was adjusted to half of the barrel length. This assumption leads to simulation outputs that are comparable to the experimental outputs. *Figure 27 and Figure 28*

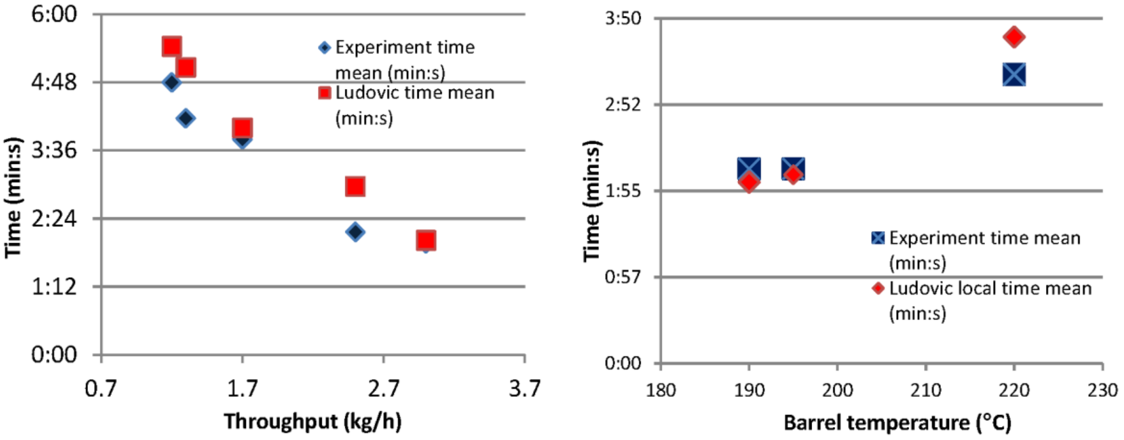

Figure 27: Trial-2 RTD Comparison considering reaction at the later stage of extruder. [103]

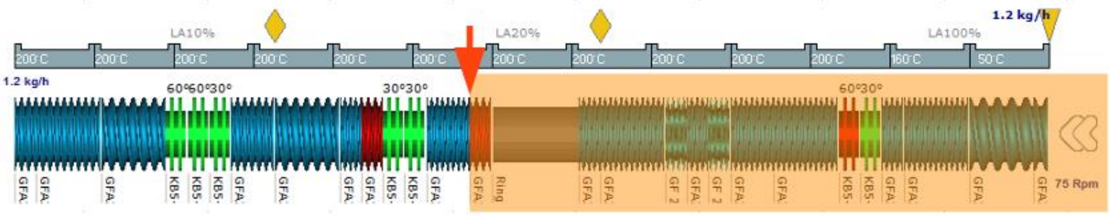

Figure 28: RTD Comparison for Ludovic simulated (red dots) and experimental (blue dots) results for throughput and barrel temperature. [103]

Regarding the throughput, which varied in the range 1–3.5 kg/h, Ludovic® provides results and trends that are similar to the ones from the experiments *(Figure 27)*. Experimental data and simulated results show a similar trend of decrease in RTD while the throughput increases. For the barrel temperature sensitivity (varied in the range 180-220 °C), Ludovic® simulation demonstrates lower effect in comparison to the experiment one.

It has to be stressed that the impact of viscosity of mixture was taken in to consideration at three stages of the extruder barrel. First at the beginning with higher amount of lactide then in the middle with a fewer amounts of lactide monomers and at the very end with polymerized lactide and remaining lactide in the reaction. Theoretically, Ludovic® software can calculate the MW within reactive extrusion and then active the coupling mode in order to link the MW to the viscosity. Implementation of this co-relation will be the subject of a future study.

(b)Average Molecular weight comparison at various temperatures:

Simulation and experimental results for the number average molecular weight ($\overline{\mathrm{M_n}}$) at various temperatures were performed, this comparison shows that at low temperatures $\overline{\mathrm{M_n}}$ value reported through Ludovic® is higher than that for the experiment. This is related to the higher residence time (RT) reported through Ludovic® than the experiment (*Figure 26*). If RT is high, it means the material mixture stays long time in the mix chambers, which facilitate the proper polymerization process and produce high output. Proper mixing of material in the extruder chamber is one of the key features for optimum polymerization. As temperature increases, due to the effect of side reactions, $\overline{\mathrm{M}_\mathrm{n}}$ goes down. At the same time, exact calculation and proper control of $\overline{\mathrm{M}_\mathrm{n}}$ at high temperature in the extrusion experimental setup is not easy.

Applying the hypothesis suggested in the previous section (that only part of the barrel acts as an extruder due to mixing conditions), simulations with Ludovic® was repeated. In this case, the values of $\overline{\mathrm{M}_\mathrm{n}}$ are well predicted by Ludovic®. The results are shown in Table IX.

Table IX Comparison between simulation results ('Ludovic®') and experimental results ('Expt')

S.No	Temp(°C)	$\overline{M_n}$(Expt)g/mol	$\overline{M_n}$(Ludovic®)g/mol
1	190	7700	10000
2	200	14500	16000
3	205	31000	25000

5.5. Conclusion

In this work, reactive extrusion experiments with Ultrasound as an AE source were investigated at ICT (Germany). Reactive extrusion was carried out with and without the application of Ultrasound at different temperatures and it was found that the use of Ultrasound increases the average number molecular weight $\overline{\mathrm{M}_\mathrm{n}}$ of the product in all the cases, with an increase of 46%, 96% and 119.7% for 190°C, 200°C and 205°C, respectively. This demonstrates that the application of AE source aides the polymerization of Lactide and can be used to design a less energy consuming (and more eco-friendly) process. Also, a simulation model that allows the optimization of reactive extrusion was developed by implementing the mathematical model of ROP of lactide in Ludovic® software. This step is critical from an industrial perspective, as it will help in the up-scaling production of PLA and future commercialization. Ludovic® software provides a great detail of information regarding mixing of material and residence time distribution details of mixture in the extruder chambers. However, up to now in literature it was not able to account for reactions inside the extruder barrel. In this work, isothermal curves of conversion (X) and number average molecular weight $\overline{\mathrm{M_n}}$ variation with time (t) were implemented in Ludovic® software. The isothermal curves were obtained by applying the mathematical model developed and validated in a previous work by Dubey et al. [84]. (Cranfield University, UK).

Upgraded Ludovic® software was then used to simulate the reactive extrusion of PLA assisted by AE source. This was performed by SCC (France), the filling ratio profile and residence time of mixture material within extruder were calculated. Initially, significant differences were observed between experimental and simulated results. The predicted values were three times higher than the experimental results in some cases. This led to the assumption that extrusion occurs in the later part of the barrel, and not from the beginning. However, further studies are required to confirm this theory, such as assessing the actual values of viscosity inside the barrel and implement this effect in the calculations.

6. Mathematical Modelling of batch process for the formation of Poly (lactic acid) considering eco-friendly catalyst (Mg-Carbene) kinetics -3

6.1. Introduction

In the last few years, several research communities and groups have investigated the possibility to develop a technique through which the polymerization of PLA becomes possible by using the metal free or organic catalyst. To implement the effect of metal free catalyst in the reaction mechanism, understanding of reaction kinetics is required. It is necessary to develop a theoretical mathematical model to check the suitability of parameters (time, concentration, temperature and rate constants) in reaction mechanism for PLA polymerization. To replace the effect of the metallic catalyst as a catalyst for ROP of LA and its adverse effects on the environment, in 2007 Kamber et al. [4] proposed very detailed review on the state of the art of effectiveness of organic catalyst related ROP reactions mechanism and the importance of organo-catalytic ring-opening polymerization. The work examined several methods for the ROP of polymers such as cationic, anionic, enzymatic, and other organic ring-opening polymerizations. The initial reaction scheme to understand the reaction for ROP of LA is mentioned in *Figure 29*

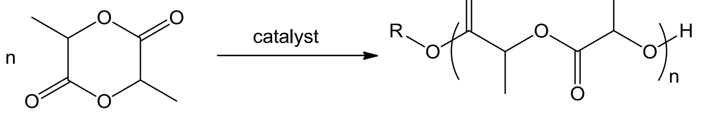

Figure 29 Polymerization of L-LA

6.2. Materials Details

The monomer used for the reactive extrusion was L-lactide (Sigma-Aldrich, St. Louis, MO, USA), the catalyst, catalyst and initiator were carbene-$MgCl_2$ (six membered ring NH) and Pyrene-methanol (Sigma-Aldrich), respectively.

One of the possible chemical structures of Carbene-$MgCl_2$ catalyst used in this work is as follows:

6.2.1. Experimental Process: Reactive Extrusion of PLA

Batch process experiments were performed at the UMONS, laboratory using the initial concentration of the reactants and some initial conditions of the experiments are shown in Table X.

Table X. Batch reaction parameters

Symbol	**Parameter**	**Value (Unit)**
M_0	Initial concentration of monomer	7.84 mol/L
C_0	Initial concentration of catalyst	0.020 mol/L
D_0	Initial concentration of co-catalyst	0.008 mol/L
T_0	Initial temperature	50 °C

6.2.2. Characterisation Techniques

Monomer conversion (X) and average molecular weight ($\overline{M_\mathrm{n}}$) were measured at several temperatures, time and molecular monomer to initiator ratios. Samples were then taken at different stages of the reaction process to evaluate the polymerization efficiency. Details of the methods and devices used for analysis are listed below.

6.2.3. Gel Permeation Chromatography (GPC)

Hexafluoroisopropanol (HFIP) was used as a solvent in GPC for the analysis of PLA polymer. GPC is equipped with a detector and differential refractive index. Depending on the molecular weight of the particular sample, a column technique was used with the calibration standard based on the Poly(methyl methacrylate) (PMMA) system. Details of the GPC configuration are as follows:

- Poly(styrene sulfonate) (PSS) (series 1100, Agilent, Missouri, United States), at 35 °C,
- Columns: [PSS PFG 7 µm × 8 mm × 50 mm (guard column) PSS PFG 7 µm × 8 mm × 300 mm; 100 A PSS PFG 7 µm × 8 mm × 300 mm; 1000 A].
- Flow: 1, 0 mL/min, Detector: Refractive Index Detector Agilent 1100.
- Injection volume: 100 µL.

This technique was used to determine the average molecular weight ($\overline{M_\mathrm{n}}$) values. The values obtained through GPC are not an absolute measure but at the equilibrium.

6.2.4. Proton Nuclear Magnetic Resonance (^{1}H NMR)

Proton nuclear magnetic resonance analysis was conducted in $CDCl_3$ using a Bruker (250) MHz spectrometer (Coventry, UK) at 30 °C in deuterated chloroform. The solution concentration used was 5 wt/vol %. This technique was applied to determine the monomer concentration and from that the conversion rate (*X)*. This analysis was also applied to the sample extracted from the extruder, which was a mixture of monomer and polymer. Several numbers of scans (100) were performed for each sample until the complete separation of polymer and monomers was achieved.

6.3. Mathematical Modelling of batch process mechanism

In general, the ROP of lactide is a complex process, which involves several reaction stages. To assess the impact of the reaction parameters (concentration of monomer, the initial concentration of catalyst, the ratio among reactants, kinetic rate constants, temperature, etc.) on the efficiency of the polymerization (mainly conversion and average molecular weight), it is necessary to formulate a suitable reaction mechanism. Mathematical modelling is a powerful and cost-effective tool to analyse these parameters. It can also help to explain the thermodynamic behaviour of the process and explains how it can be scaled up to commercial levels of production.

Developing a simulation model which defines the batch process (accounting for the polymerization reaction) is complex, due to the interdependencies of the reactions Yu et al. [34]. This process was started with, the development of a mathematical model describing the ROP in a batch process and. From the ROP model for the batch process, isothermal curves for the evolution of number average molecular weight ($\overline{M_{\mathrm{n}}}$) and conversion (X) with time were obtained. These curves then further discretized and integrated into Ludovic®. This way, Ludovic® will able to estimate a degree of conversion and growth of the polymer chains during the simulation.

Reaction mechanisms can be defined for any ROP reaction (mechanisms will tend to be similar to the one we have defined). However, depending on the monomer, initiator, and catalyst and, indeed, the ratios of the monomer to catalyst and catalyst to the initiator, the reaction parameters will change, and as such, they will have to always be validated against experiments. However, once the validation is undertaken, these can be used to model the process based on similar reaction conditions.

6.3.1. Reaction Kinetics Modelling and Mathematical Simulation of ROP of Lactide

In previous related work, Dubey *et al.* [84], [103] covered the details of mathematical modelling of polymerization of PLA based on a five-stage reaction mechanism. The reaction mechanism comprises initiation, propagation, termination, trans-esterification and, probably, non-radical random chain scission. For continuity, the mechanism used is reproduced in Equations (1)–(9).

Activation of catalyst:

$$\mathrm{C} + \mathrm{D}_i \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} \mathrm{R}_i + \mathrm{A}' \tag{1}$$

Propagation:

$$R_i + M \underset{k_d}{\overset{k_p}{\rightleftarrows}} R_{i+1} \tag{2}$$

Chain Transfer:

$$R_i + D_j \underset{k_s}{\overset{k_s}{\rightleftarrows}} R_j + \mathrm{D_i} \tag{3}$$

Trans-Esterification:

$$R_j + R_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + R_i \tag{4}$$

$$R_j + D_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + D_i \tag{5}$$

$$R_j + G_k \underset{k_{te}}{\overset{k_{te}}{\rightleftarrows}} R_{j+k-i} + G_i \tag{6}$$

Non-radical Radom Chain scission:

$$R_j \xrightarrow{k_{de}} R_{i-k} + G_k \tag{7}$$

$$D_i \xrightarrow{k_{de}} D_{j-k} + G_k \tag{8}$$

$$G_i \xrightarrow{k_{de}} G_{i-k} + G_k \tag{9}$$

where k_{a1}, k_{a2}: Activation rate coefficients; k_{p}, k_{d}: Propagation rate coefficients; k_{s}: Chain-transfer rate coefficient; k_{te}: Trans-esterification rate coefficient; k_{de}: Random chain scission reaction rate coefficient; C:

catalyst, $Sn(Oct)_2$; A’: bi-product by catalyst; R_i: Active polymer chain with length *i*; D_i: Dormant polymer chain with length *i*; G_i: terminated polymer chain with length *i*, M: monomer.

In the reaction mechanism, Equation (1) represents the activation of catalyst (C), Reaction (2) represents the propagation stage of monomer and Reaction (3) signifies the chain termination part of the reaction. The Equations (4)–(6) are side reactions known as intermolecular trans-esterification. Similarly, Equations (7)–(9) are side reactions called non-radical random chain scission, which mostly occur at high reaction temperatures. [A], in Equation (1), is treated as a concentration of the bi-product/acid impurity because of the reaction of the catalyst and alcohol initiator.

The reaction kinetic parameters involved in the reaction mechanism such as reaction rate constants (*k* values) k_p, k_d and monomer equilibrium concentration ($Me = K_p/K_d$), *etc.* were calculated by the fitting of experimental data using a mathematical formulation. The value of *M*e was calculated by considering the experimental conversion (*X*) value with the formula = $M_0 \times (1-X)$ and $X = (1-Me/Mo) \times (1-e^{-Kpt})$. The estimation of *M*e was calculated through curve fitting of the equation in the form of ($Y = m \times X + C$ or $Y = C + A \times e^{BX}$). In general, *M*e was formulated as *M*e = slope × *T* + intersect. Propagation rate constant (k_p) was calculated using the equation of the variation of monomer concentration according to the equation $\frac{d[M]}{dt} \cong -kp \times R_T \times ([M]-[Me]$,where Me is the monomer equilibrium concentration, M_0 is the initial monomer concentration and

R_T is the initial concentration of the active catalyst. Other parameters including initial rate constants k_{a1}, k_{a2}, k_{te} and k_{de} were taken directly from the literature [29]. More details of coding and mathematical scripts are available in [Appendix **A1.2**]

6.4. Results & Discussion

6.4.1. Experimental Results

The polymerization performed with different time intervals by maintaining the same molar ratio of catalyst and monomer of each time interval. Data of the number average molecular weight ($\overline{M_n}$), average molecular weight ($\overline{M_w}$) and conversion (X) from the batch reaction experiments using Mg-carbene as an eco-friendly catalyst at a different temperature range, are provided in Table XI.

Tabel XI. Experimental results for ROP of LA in batch process

No.	***t* (min)**	***T* (°C)**	**$\overline{M_n}$ (g/mol)**	***X* (%)**
1	5	150	23000	35
2	30	150	40000	68
3	30	160	40000	82
4	30	170	41000	80
5	30	180	33000	82
6	30	190	24000	90
7	30	210	17000	92

From the above experimental results by comparing the several different temperatures, the average number of molecular weight (Mn) at 150°C increased as the duration increased. On contrary at temperature, 210°C the Mn is quite low due to the possible extensive side reactions.

6.4.2. Results of Batch Process Simulation

To conduct the mathematical simulation of ROP of LA with the reaction mechanism suggested, initial reaction input details were adopted from the experiments on reactive extrusion. Details are outlined in Table XII.

Table XII. Initial reaction parameters for simulation

Symbol	Parameter	Value (Unit)
M_0	Initial concentration of monomer	7.8 mol/L
C_0	Initial concentration of catalyst	0.02 mol/L
D_0	Initial concentration of co-catalyst	0.008 mol/L
T_0	Initial temperature	50 °C
Me	Monomer equilibrium concentration	0.225 mol/L

Table XIII. Mathematical simulation results for ROP of LA in the batch process.

No.	*t* (min)	*T* (°C)	$\overline{M_n}$ (g/mol)	*X* (%)
1	5	150	9000	20
2	30	150	17000	70
3	30	160	22000	80
4	30	170	25000	85
5	30	180	28000	80
6	30	190	26000	92
7	30	210	21000	90

Based on experimental parameters and results, the mathematical simulation was performed for the reaction times and temperature shown in Table XII. The results are presented in Table XIII, including temperature (T), the number average molecular weight ($\overline{M_\mathrm{n}}$), and conversion (X).

6.4.3. Isothermal Inputs for future Large-Scale Extrusion in Ludovic®

The isothermal curves (obtained from the batch process simulation (Figures 30 and 31), conversion (X) and number average molecular weight ($\overline{M_\mathrm{n}}$) with time, for the total reaction time of 1 hour and temperature range of (150–210) °C were developed to facilitate input for Ludovic® to perform further large scale simulation in future. The duration of the input data was based on the residence time reported by experiments on reactive extrusion of the PLA. Details of the input data are shown in *Figures (30* and *31)*.

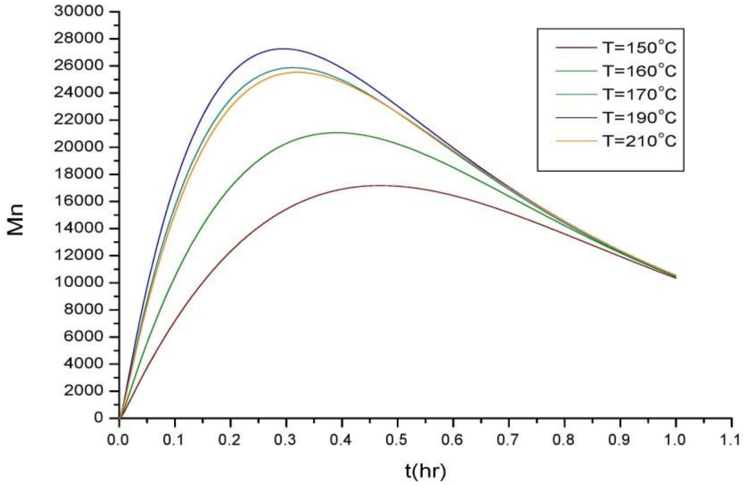

Figure 30 Isothermal curves for average molecular weight ($\overline{M_n}$) vs. t.

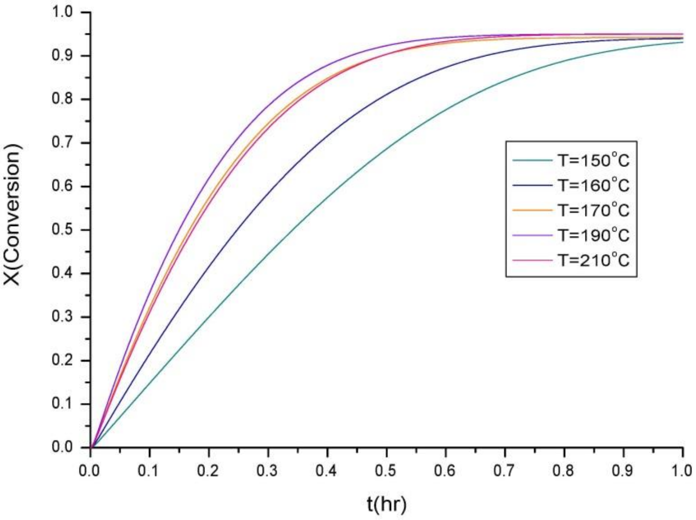

Figure 31 Isothermal curves for conversion (X) vs. t.

6.5. Conclusion

Batch process experimental trials, were performed by implementing eco-friendly catalyst (Mg-Carbene) for the formation of PLA using ROP process. Based on the experimental details and initial condition provided, further mathematical simulation, were conducted. Parameters needed to run the simulation, were calculated by experimental data. For the experimental point of view, several trials, were made at different temperatures and time. From the results that are obtained till now include (150°C-190°C) and 210°C, it is observed that for Mg-NHC catalyst the most favourable temperature lies between 170°C and 190°C. Between these temperatures, we obtained a better $\overline{\mathrm{M_n}}$ and X values. These results show that the magnesium-protected carbene performs well for the ROP of LA. Additionally, the ^{1}H NMR results showed no sign of epimerisation. The simulation of experimental data also shows the similar trends of variation.

Based on the further future planning of experimental trials considering reactive extrusion processes, isothermal curves were created which will implement within Ludovic, to perform large-scale continuous reactive extrusion simulation and validate the result.

7. SENSIVITY ANALYSIS

Sensitivity analysis of any model or system is a method to check the robustness of the model, which consists of several parameters as the building block of the whole model. It also signifies that how small-small changes affect the output of the model created with in the input parameters.

Sensitivity analysis is a method to investigate how the uncertainty scale of output of a mathematical model or method can be influenced by the different source of uncertainty in inputs. It also provides the details of extant of error with in the model and its impact on output.

7.1. Need of sensitivity analysis test

To check the robustness of model

- To investigate the impact of several inputs on reaction process and final output
- Limit the impact of several inputs on model output
- Measuring the extent of error in the model and its scrutiny
- Estimation of relationship between input variable with output of the model
- Reduction of uncertainty in output due to uncertainty in input parameters
- Reduce the complexity of the model and make it more viable
- Enhancing the impact of suitable input parameters and diminishing those which create significant error in the model

7.1.1. Analysis through reaction stages

An attempt to highlight the Influence of several reaction parameters on reaction output, through several sets of the combination are mentioned in Table XIV.

The five stages reaction process for the synthesis of PLA through ROP process is following:

I.

$$\mathrm{C+D_n} \underset{k_{a2}}{\overset{k_{a1}}{\rightleftharpoons}} \mathrm{R_n+A} \qquad \Big| \quad \textbf{Initiation}$$

Initiation reaction which involves the parameters such as monomer, catalyst, and activator etc. is the first stage of ROP process. The parameter, which controls the initiation, is basically reaction rate constant K_{a1} and K_{a2}. The activity of the catalyst and the efficiency of activator to activate the catalyst are derived by K_{a1} parameter. In Table XIV, row 1 & 2, it is clearly noticeable that change in values of K_{a1} and K_{a2}, effects the $\overline{\mathrm{M_n}}$ and X value.

II.

$$\mathrm{R_n+M} \underset{k_{d}}{\overset{k_{p}}{\rightleftharpoons}} \mathrm{R_{n+2}} \qquad \Big| \quad \textbf{Propagation}$$

Propagation reaction, once monomer got activated further addition of monomer to propagate the reaction process consists Kp and Kd as key parameters. In general, Kp plays crucial rule to control the output (higher molecular) value through the process. Calculation of Kp value was made using monomer equilibrium constant (me) and conversion (X) parameter through experimental data and curve fitting. At higher Me value, which means higher Kp value, the $\overline{\mathrm{M_n}}$ and X, shows the significant increase

(Table XIV, row 6). Higher temperature, also influences the propagation of monomer into polymer chain significantly (row 7,8 &9).

III.

$$R_n + D_i \underset{k_s}{\overset{k_s}{\rightleftharpoons}} R_i + D_n$$

Termination

Termination reaction occurs as a reversible chain transfer reaction to deactivate the active chain. K_s is the rate constant for the termination process. After the formation of PLA polymer chain up to certain length, the termination reactions take place by transferring the charge to the active polymer chain and make it un-reactive for further addition of monomers.

IV.

$$R_i + R_j \underset{k_{te}}{\overset{k_{te}}{\rightleftharpoons}} R_{i+j-n} + R_n$$

$$R_i + D_j \underset{k_{te}}{\overset{k_{te}}{\rightleftharpoons}} R_{i+j-n} + D_n$$

$$R_i + G_j \underset{k_{te}}{\overset{k_{te}}{\rightleftharpoons}} R_{i+j-n} + G_n$$

Trans-esterification

$$R_i \xrightarrow{k_{de}} R_{i-k} + G_k$$

$$D_i \xrightarrow{k_{de}} D_{i-k} + G_k$$

$$G_k \xrightarrow{k_{de}} G_{k-j} + G_j$$

Chain-scission

In the ROP process of lactide, the activation and termination reactions were considered as in equilibrium, which means remaining reaction (propagation, transesterification and chain scission) defines the process kinetics. The thermal effect dominates the propagation and side reactions.

An increase in temperature supports the propagation stage of the reaction. In general, it favours the higher propagation to support the growth of polymer chain. Growth in the chain can be feasible up to a certain range of temperatures. At very high temperatures beyond (200-210)°C, side reactions (chain scission and trans-esterification) dominate. Decrease in $\overline{\mathrm{M_n}}$ value can be easily noticed at the higher temperature, Table XII (chapter 6) & Table XIV, (row 8, 9 &10). Because of the activation of side reaction mostly at very high temperatures, the relevance of this state considered as less important than others.

The reaction system involved in the ROP process is relatively complex and involves many parameters, such as reaction rate constants and equilibrium constants. Now to increase the model preciseness, it is required to minimise the number of parameters estimated either by the mathematical fitting of the experimental and through possible estimation. Not all but some of the parameters were taken straight away from the literature. More details regarding initial inputs parameters for the experiment as well theoretical model and their impact are mentioned in chapter 4, 5 &6.

Table: XIV

List of most influential parameters and its impact on simulation:

S.No	t (hr)	T (°C)	$K_{ea}=k_{a1}/k_{a2}$	$Me=k_p/k_d$	k_t	k_d	$\overline{M_n}$	X(%)
1	0.5	160	0.256	0.225	1	1	45001	33
2	**0.5**	**160**	**0.3**	**0.225**	**1**	**1**	**69562**	**48**
3	**0.5**	**160**	**0.256**	**0.3**	**1**	**1**	**72033**	**56**
4	0.5	180	0.3	0.3	1	1	107590	74
5	0.5	180	0.256	0.225	1	1	101030	70
6	**0.5**	**180**	**0.256**	**0.5**	**1**	**1**	**109532**	**80**
7	0.5	190	0.256	0.225	1	1	117760	82
8	**0.5**	**200**	**0.256**	**0.225**	**1**	**1**	**129700**	**90**
9	**0.5**	**220**	**0.256**	**0.225**	**1**	**1**	**119052**	**94**
10	0.5	250	0.256	0.225	1	1	111125	*94*

8. DISCUSSION

The aim of this research thesis work is to fulfil the knowledge gap of PLA production process at the large scale through efficient and safe method, mostly focused on theoretical modelling and simulation of the reaction process. The research work, is very much aligned with the project INNOREX, whose aim is to synthesize PLA through continuous reactive extrusion process by the implementation of AE source and eco-friendly/metal catalyst.

Now to achieve the desired aim, a detailed methodology was designed. Details are mentioned in chapter 3.

8.1 Simulation strategies to model the Ring-Opening polymerization of LA

The initial trials and case study of reaction mechanism was made based on data from the literature. The first trials to develop the code for the batch process reaction mechanism was proposed by Dubois et al. [9] and Mehta et al. [29] and were taken as a benchmark. Later on, several other reaction mechanisms that describe the ROP process of Lactide considering the possible side reaction and impurities, were taken into account.

8.1.1. Experimental reaction modelling and code building

8.1.2. The first trial to model the reaction mechanism

The first trial to understand the three stage viz. initiation, propagation and termination ROP reaction process was based on Mehta et al.'s [29] work.

The reaction mechanism used in the first trial was based on equations (a-c):

$\mathrm{M} + \mathrm{I} \overset{\mathrm{K_0}}{\rightarrow} \mathrm{P_i}$____________________a (Initiation)

$\mathrm{P_j} + \mathrm{M} \overset{\mathrm{K_p}}{\rightarrow} \mathrm{P_{j+1}}$________________ b (Propagation)

$\mathrm{P_j} + \mathrm{M} \overset{\mathrm{K_t}}{\rightarrow} \mathrm{M_j} + \mathrm{P_1}$____________ c (Termination)

Where *M, I* and *Pj* represent the monomer, initiator and polymer chain of length *j* and *Ko, Kp* and *Kt* represent initiation, propagation and termination rate constants.

Mehta et. al. reported that ROP of LA proceeds through “coordination-insertion” mechanism. Kinetics of the Lactide polymerization were investigated at 70°C and the reaction mechanism was expressed as a first order equation [9]. In conclusion, equation (1) represents the rate kinetic law proposed by Mehta et.al.

$$-\frac{d[LA]}{dt} = k_j[LA][Al(OPr)_3] \_\_\_\_\_\_\_\_\_\_\_\_ (1)$$

Where [LA] and [Al(OPr)$_3$] represents the concentration of Lactide monomer and catalyst. K $_j$ stands for rate constant of the reaction.

It must, however, be noted that no consideration was given to side reactions that can significantly affect the output. The mathematical model for reaction kinetics of ROP of LA considered several ordinary differential equations (ODEs). The input file, was coded using ODEs in Matlab by defining each individual parameter with some symbolic expressions. Simultaneously another file, which contains all the required constant values and variation equation, was also created. In total, there were three different files, which were essential for running the designed mathematical model in Matlab software. The mathematical transformation of batch process reaction mechanism using ordinary differential equations (a-c) is following:

$$\frac{d[M]}{dt} = -[M]\{k_0[I] + \sum_{j=1}^{n} k_j[P_j] + \sum_{j=1}^{n} k_{tj}[P_j] \text{\_\_\_\_\_\_\_\_\_\_} \text{i}$$

$$\frac{dy[I]}{dt} = -k_0[I][M] \text{\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_} \text{ii}$$

$$\frac{d[P_1]}{dt} = k_0[I][M] - k_1[P_1][M] + \sum_{j=2}^{n} k_{tj}[P_j][M] \text{\_\_\_\_} \text{iii}$$

$$\frac{d[Pj]}{dt} = [M]\{k_{(j-1)}[P_{j-1}] - kj[P_j] - k_{tj}[P_j]\},\ j > 1 \text{\_\_\_\_\_} \text{iv}$$

$$\frac{d[M]}{dt} = k_{tj}[P_j][M], \qquad j \geq 1 \text{\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_} \text{v}$$

Where: [M], [I] and [Pj] represents the concentration of monomer, initiator and polymer chain of the certain length. K0, Kj and Kt represent the rate constant of initiation, propagation and termination reactions.

The author recreated the Matlab code to solve the equations i-v. The details of the code are in Appendix (A 1.3).

The above simulation model and results, were considered as a state-of-the-art to understand the basic reaction mechanism of ROP of LA. To formulate or validate the actual experimental results, several assumptions were made in Mehta et al. model, such as;

- Estimation of rate constant (K) values at different stages
- Decrease in propagation rate constant as chain length increases
- No impact of bi-products or impurities on reaction output
- Consideration of Termination mechanism as a chain transfer to monomer

ROP of LA experiments was reported in [9] and the output from reaction mechanism stated in equations (i-v) was validated against the data from the experiments. However, it must be noted that several assumptions were made in order to validate the output of code based on the reaction mechanism stated in equation i-v. They are as follows, no impact of bi-product on reaction output, termination as chain transfer and estimation of rate constant values.

Although the investigation and validation of code were also not very straight-forward due to lack of less available work in the field of theoretical investigation of ROP mechanism.

A validation study was performed. The results of developed model and literature model, show comparable trends. The deviation in the result after certain time was due to the approximation of kinetic rate parameter in the model (not reported in literature). Details are mentioned in *Figure 32*

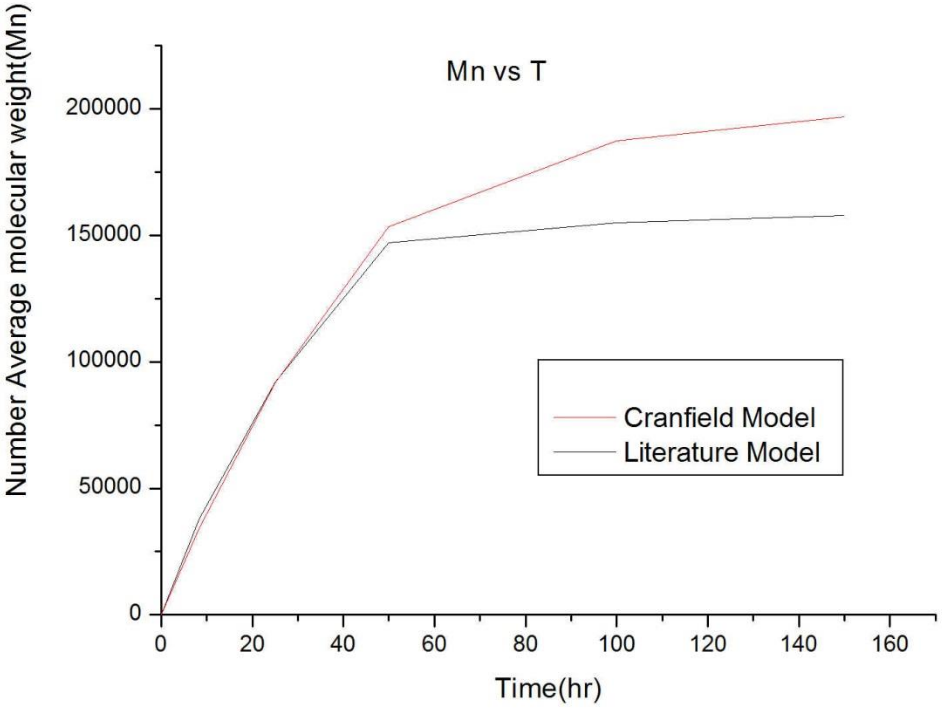

Figure 32 Literature vs developed model validation

8.2. Learning and second trial to model the reaction mechanism

As highlighted in the previous section regarding several assumptions, the details of side reaction and separation of rate constant value “K” should be included and validated. Yu et al. [8], [34], made one such attempt. They proposed a new reaction model, which considered $Sn(Oct)_2$ stannous Octoate as a catalyst and 1-dodecanol as co-catalyst as an initiator to start the ROP of Lactide monomers at 130°C. In this work, different monomer-to-catalyst and cocatalyst-to-catalyst ratio to investigate the proper reaction mechanism of ROP process were also investigated [34]. The more important detail regarding, the significance of “ester interchange” reaction called as trans-esterification and non-radical random chain scission also considered additionally [50].

The details of the new five stages reaction mechanism proposed by Yu et. al. is following:

1.

$$C+D_n \xrightleftharpoons[k_{a2}]{k_{a1}} R_n+A$$

Initiation

2.

$$R_n+M \xrightleftharpoons[k_d]{k_p} R_{n+2}$$

Propagation

3.

$$R_n+D_i \xrightleftharpoons[k_s]{k_s} R_i+D_n$$

Termination

4.

$$R_i+R_j \xrightleftharpoons[k_{te}]{k_{te}} R_{i+j-n}+R_n$$

$$R_i+D_j \xrightleftharpoons[k_{te}]{k_{te}} R_{i+j-n}+D_n$$

Trans-esterification

$$R_i \xrightarrow{k_{de}} R_{i-k}+G_k$$

$$D_i \xrightarrow{k_{de}} D_{i-k}+G_k$$

$$G_k \xrightarrow{k_{de}} G_{k-j}+G_j$$

Chain-scission

Where: *ka_1, ka_2 are the activation rate coefficients, k_p, k_d are the propagation rate coefficients, ks is the chain-transfer rate coefficient, k_{te} is the trans-esterification rate coefficient and k_{de} is the random chain scission reaction rate coefficient;*

C is the catalyst, Sn(Oct)$_2$,
A is octanoic acid (OctOH) produced by the catalyst,
R_i represents the active polymer chains with length "i",
D_i represents the dormant polymer chains with length "i",
G_j represents the terminated polymer chains with length "j" and M the monomer

The introduction of two new additional side reaction steps such as trans-esterification and random chain scission proven to be a suitable step for describing the reaction mechanism of ROP of LA. The consideration of reversibility of initiation, propagation and termination process was also new in the work reported by Yu et al. [8], [34]. As experiments consider several parameters and stages to process, the validation of the same process through mathematical model was not easy.

In any theoretical model, there are always some assumptions, which help to analyse the validation. Similarly, Yu et al. also made the certain assumption regarding the estimation of rate constants (K), the residual amount of catalyst in the reaction and concentration of acidic impurities, generated in the reaction.

Based on the preciseness and detailed reaction mechanism proposed by Yu et al, the second trial was made to model the reaction mechanism. Efforts were made to model the proposed reaction mechanism by using Matlab tool. In context to validation, similar reaction conditions and assumption were adopted.

The validation was found satisfactory. Details are mentioned in *Figure 33*

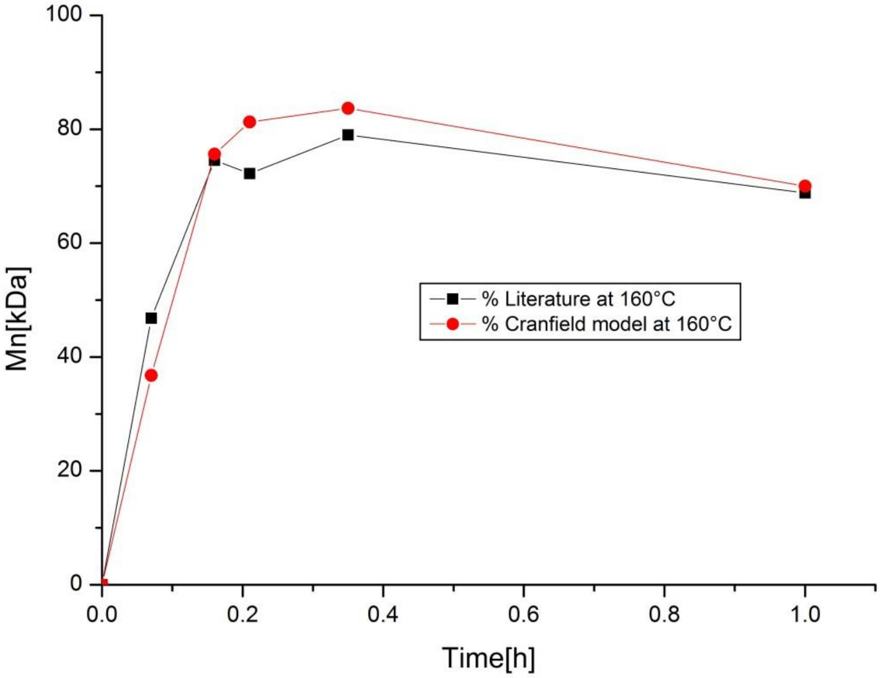

Figure 33 Literature vs developed model validation

Further details regarding the second trial and how to prove the assumptions, made in reaction process as well as their mathematical transformation, are mentioned in detail in chapters 4 & 5.

8.3. Batch process to extrusion process transformation

The reaction mechanism and mathematical model reported by Yu et al. were well defined to consider the ROP of LA through the batch process but as discussed in the beginning of the discussion chapter, the possible gap of how to consider batch process reaction information in reactive extrusion process is still unknown. Now to fulfil this gap, the five-stage reaction mechanism was considered again and details of the reaction parameters which are significant for the reaction output has been re-investigated. Details of this exercise mentioned in chapter 7.

The investigation of reaction mechanism and reaction parameters provides the idea to analyse and implement different reaction parameters such as AE source and thermal effect. Now once the AE and thermal parameter got implemented in the mathematical model, next step was to validate this model through experimental data. This time, the experimental data was not chosen from the literature but through our own actual experiments, performed by research partners (ICT). The experimental trial was based on metal catalyst and AE source (ultrasound) through twin screw extrusion process.

It was believed that the same reaction mechanism of 5 stage will be helpful to validate the model against experimental data but in general it was not the case. The validation provides deviation in the result of theoretical model output and experimental output. The details of the comparison of the result are mentioned in chapter 4.

The primary reason for the output deviation was first because of the process difference. The theoretical model was based on batch process while the experimental result based on extrusion process. Now to overcome this issue, another reaction strategy was developed which was based on the implementation of batch process theoretical model output into continuous reactive extrusion simulation software called (Ludovic). Ludovic in itself is capable of simulating extrusion process by dealing with thermo-mechanical changes occur during the extrusion. The primary requirement for Ludovic to start the simulation process is to collect initial reaction process data in terms of several isothermal curves, which shows the variation of Mn and X with time (t). The data in terms of several isothermal curves generated through mathematical modelling of batch process reaction has been implemented in Ludovic to perform further large-scale extrusion process simulation by considering the similar environment as in experimental process.

Details regarding the mechanism of Ludovic and how the input was used within Ludovic to validate the output calculated through extrusion experiment and simulation of extrusion process are mentioned in chapter 5.

8.4. Consideration of Eco-friendly catalyst

Once the knowledge gap, to utilise the batch process reaction data into extrusion process, based on metal catalyst and AE sources has been achieved, the next target was to investigate the alternative eco-friendly catalyst and implement the reaction data into the mathematical model for validation. A detailed experimental investigation regarding alternative catalyst suitable for ROP of LA was performed at one of our research partner's lab (UMONS) [97]. The investigation highlights the new class of eco-friendly catalyst (Mg-Carbene) as a suitable alternative for ROP process. Now to implement reaction data based on new catalyst system into mathematical model, same 5 stage reaction mechanism with modified parameter was considered. It was expected to be useful for the new catalyst system as well but as the different catalyst has the different efficiency to initiate the reaction, so because of that new set of reaction parameters especially the k values (rate constants) were investigated to obtain the close comparison. Details regarding trials of several k values and validation of batch process theoretical model with the batch process experimental results, were mentioned in chapter 7 and chapter 6.

To check the suitability of the eco-friendly catalyst to perform ROP of LA at higher scale through the extrusion process, isothermal curves were created, which will be further implemented into Ludovic and similarly the new catalyst will be tested on extrusion experiment. The validation will be made once the data through simulation and experiment available. Due to the limited guideline for the research work timeline, these validations will be left as a further recommendation for research.

9. Conclusion

In this research, several aspects of ROP of LA field, were investigated such as:

- Basic understanding of ROP process and the reaction stages involved
- Development of mathematical model based on suitable reaction mechanism by considering metal catalyst and implementation of temperature and AE source within the model and its validation
- The mathematical model developed with the aim to bridge the gap to link the batch process and extrusion process for upscaling the process output at industrial scale by providing suitable input to Ludovic. The validation provides close comparable result as reported through experiment within the range of (5-10) %, variation, mentioned in chapter 4 and 5
- Another area of research which were tried as a novelty in this research and project work was the development of eco-friendly first and then its implementation with in the mathematical model. The validation of both the result provides very comparable result in the range of (10-15) % at several temperature ranges. Details mentioned in chapter 6
- To make the developed mathematical model more precise and viable, detailed sensitivity analysis were performed to analyse the impact of several reaction parameters on reaction output and add new parameters based on desired research demand.

Based on overall effort made to study the desired research area of PLA processing, following significant conclusion may be drawn:

1. The synthesis of PLA using lactide polymerization can be modelled with the suitable 5 stage reaction mechanism which includes, initiation, propagation, termination, chain scission and trans-esterification reactions.
2. The mathematical model has been created by transforming reaction mechanism in the form of ODE'S. The ODE'S were further solved by using RK4-Method implemented through MATLAB tool.
3. The reaction mechanism selected for the simulation model was based on tin-octoate $Sn(Oct)_2$ catalyst and use of AE sources. Use of AE source within the reaction process shows a positive impact on the reaction output in comparison to those without AE source.
4. The impact of AE source has been considered as an effect of the thermo-mechanical parameter, which affects the propagation rate constant as defined by Arrhenius law.
5. One of the most innovative parts of the current research work, which was not reported earlier in the state of the art of PLA polymerization, is to implement AE source in the reaction process and simulate the process. Benefit of using AE source within the reaction mechanism is following:

- Accelerates the polymerization of the lactide

- Enables polymerization at low rotation speed observed during trial
- (the heating effect which is a side effect of the sonication treatments (Ultrasounds) seems to influence the polymerization positively

6. For the industrial production point of view, the most innovative part of this research is to incorporate the result of batch process data as an input with in Ludovic software to make it capable of large scale continuous reactive extrusion process simulation and its validation.
7. Details regarding mixing of reaction materials and there significant within the extruder barrel in terms of resident time and flow has been well defined experimentally as well as theoretically (Ludovic).
8. The research work defines well the details of experimental work as well as theoretical modelling work, which can be used as a background work for further investigation in this field of ROP process by implementing alternative catalyst systems and AE sources.

10. RECOMMENDATIONS FOR FURTHER WORK

The present modelling work needs further improvement and testing to make it more precise and efficient.

- Further investigations will involve the modelling of ROP process for PLA based on future metal-free/organometallic catalysts to replace $Sn(Oct)_2$ and adapting the mathematical model based on new reaction mechanism and new catalyst system.
- Additional data will be collected to test/verify the mathematical model based on several catalyst systems.
- Consideration of AE source in the batch process and validate the experimental data through mathematical simulation.
- Determination of more precise reaction rate kinetics and other parameters will be improved based on the availability of the large set of experimental data.
- In addition, consideration of other AE sources such as microwave and LASER will also be investigated. Data obtained through Ludovic® will help to setup and upscale PLA production facilities.
- More precise mathematical model and simulation is needed to describe the flow of material in the reactive extruder by using Ludovic simulator. The results from these activities will plug the gaps in the literature thus adding to the state-of-the-art in this area of research.

11. REFERENCES

[1] W. Amass, A. Amass, and B. Tighe, “A review of biodegradable polymers: uses, current developments in the synthesis and characterization of biodegradable polyesters, blends of biodegradable polymers and recent advances in biodegradation studies,” Polym. Int., vol. 47, no. 2, pp. 89–144, 1998.

[2] K. Arshak, V. Velusamy, O. Korostynska, K. Oliwa-Stasiak, and C. Adley, “Conducting Polymers and Their Applications to Biosensors: Emphasizing on Foodborne Pathogen Detection,” IEEE Sens. J., vol. 9, no. 12, pp. 1942–1951, Dec. 2009.

[3] P. I. Dalko and L. Moisan, “Enantioselective Organocatalysis,” Angew. Chem. Int. Ed., vol. 40, no. 20, pp. 3726–3748, Oct. 2001.

[4] N. E. Kamber, W. Jeong, R. M. Waymouth, R. C. Pratt, B. G. G. Lohmeijer, and J. L. Hedrick, “Organocatalytic ring-opening polymerization,” Chem. Rev., vol. 107, no. 12, pp. 5813–5840, 2007.

[5] Y. Wang, L. Zhang, X. Guo, R. Zhang, and J. Li, “Characteristics and mechanism of L-lactide polymerization using N-heterocyclic carbene organocatalyst,” J. Polym. Res., vol. 20, no. 3, 2013.

[6] S. Inkinen, M. Hakkarainen, A.-C. Albertsson, and A. Södergård, “From Lactic Acid to Poly(lactic acid) (PLA): Characterization and Analysis of PLA and Its Precursors,” Biomacromolecules, vol. 12, no. 3, pp. 523–532, Mar. 2011.

[7] P. Dubois, C. Jacobs, R. Jerome, and P. Teyssie, “Macromolecular engineering of polylactones and polylactides. 4. Mechanism and kinetics of lactide homopolymerization by aluminum isopropoxide,” Macromolecules, vol. 24, no. 9, pp. 2266–2270, Apr. 1991.

[8] Y. Yu, G. Storti, and M. Morbidelli, “Ring-Opening Polymerization of l,l-Lactide: Kinetic and Modeling Study,” Macromolecules, vol. 42, no. 21, pp. 8187–8197, Nov. 2009.

[9] H. R. Kricheldorf and M. Sumbél, “Polylactones—18. Polymerization of l,l-lactide with Sn(II) and Sn(IV) halogenides,” Eur. Polym. J., vol. 25, no. 6, pp. 585–591, 1989.

[10] H. R. Kricheldorf, M. Berl, and N. Scharnagl, “Poly(lactones). 9. Polymerization mechanism of metal alkoxide initiated polymerizations of lactide and various lactones,” Macromolecules, vol. 21, no. 2, pp. 286–293, Feb. 1988.

[11] G. G. Odian, Principles of polymerization, 4th ed. Hoboken, N.J: Wiley-Interscience, 2004.

[12] Polymers.”,[Online]. Available: https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/polymers.htm.

[13] "59.2 CLASSIFICATION OF POLYMERS | Chemistry Assignment." [Online]. http://www.chemistry-assignment.com/59-2-classification-of-polymers.

[14] "Condensation-Polymerization.",[Online]., Available: http://www.materialsworldmodules.org/resources/polimarization/4-condensation.html.

[15] "ring opening mechanism cyclopropane - Google Search." [Online]. Available: https://www.google.co.uk/search?newwindow=1&biw=1280&bih=528&tbm=isch&sa=1&q=ring+opening+mechanism+cyclopropane&oq=ring+opening+mechanism+cyclopropane&gs_

[16] D. L. Kaplan, "Introduction to Biopolymers from Renewable Resources," in Biopolymers from Renewable Resources, D. D. L. Kaplan, Ed. Springer Berlin Heidelberg, 1998, pp. 1–29.

[17] B. H. Lunelli, R. R. Andrade, D. I. P. Atala, M. R. W. Maciel, F. M. Filho, and R. M. Filho, "Production of Lactic Acid from Sucrose: Strain Selection, Fermentation, and Kinetic Modeling," Appl. Biochem. Biotechnol., vol. 161, no. 1–8, pp. 227–237, May 2010.

[18] C. J. Weber, V. Haugaard, R. Festersen, and G. Bertelsen, "Production and applications of biobased packaging materials for the food industry," Food Addit. Contam., vol. 19, no. sup1, pp. 172–177, 2002.

[19] D. Enders, O. Niemeier, and A. Henseler, "Organocatalysis by N-Heterocyclic Carbenes," Chem. Rev., vol. 107, no. 12, pp. 5606–5655, Dec. 2007.

[20] V. Balasanthiran, M. H. Chisholm, C. B. Durr, and J. C. Gallucci, "Single-site bismuth alkoxide catalysts for the ring-opening polymerization of lactide," Dalton Trans., vol. 42, no. 31, pp. 11234–11241, Jul. 2013.

[21] V. Singh and M. Tiwari, "Structure-Processing-Property Relationship of Poly(Glycolic Acid) for Drug Delivery Systems 1: Synthesis and Catalysis," Int. J. Polym. Sci., vol. 2010, Dec. 2010.

[22] S. Gu, M. Yang, T. Yu, T. Ren, and J. Ren, "Synthesis and characterization of biodegradable lactic acid-based polymers by chain extension," Polym. Int., vol. 57, no. 8, pp. 982–986, Aug. 2008.

[23] S. Jacobsen, H.-G. Fritz, P. Degée, P. Dubois, and R. Jérôme, "Continuous reactive extrusion polymerisation of L-lactide — an engineering view," Macromol. Symp., vol. 153, no. 1, pp. 261–273, 2000.

[24] S. Csihony, D. A. Culkin, A. C. Sentman, A. P. Dove, R. M. Waymouth, and J. L. Hedrick, "Single-Component Catalyst/Initiators for the Organocatalytic Ring-Opening Polymerization of Lactide," J. Am. Chem. Soc., vol. 127, no. 25, pp. 9079–9084, Jun. 2005.

[25] J.-P. Puaux, I. Banu, I. Nagy, and G. Bozga, "A Study of L-Lactide Ring-Opening Polymerization Kinetics," Macromol. Symp., vol. 259, no. 1, pp. 318–326,

2007.

[26] I. Banu, J.-P. Puaux, G. Bozga, and I. Nagy, "Modeling of L-lactide Polymerization by Reactive Extrusion," Macromol. Symp., vol. 289, no. 1, pp. 108–118, 2010.

[27] "twin screw extruder - Google Search." [Online]. Available: https://www.google.co.uk/search?q=twin+screw+extruder&newwindow=1&source=lnms&tbm=isch&sa=X&ei=aQxqU7bwNrPG7AbVz4GICg&ved=0CAgQ_AUoAQ&biw=1280&bih=832. [Accessed: 07-May-2014].

[28] R. A. Auras, B. Harte, S. Selke, and R. Hernandez, "Mechanical, Physical, and Barrier Properties of Poly(Lactide) Films," J. Plast. Film Sheeting, vol. 19, no. 2, pp. 123–135, Apr. 2003.

[29] R. Mehta, V. Kumar, H. Bhunia, and S. N. Upadhyay, "Synthesis of Poly(Lactic Acid): A Review," J. Macromol. Sci. Part C Polym. Rev., vol. 45, no. 4, pp. 325–349, 2005.

[30] K. Okano, T. Tanaka, C. Ogino, H. Fukuda, and A. Kondo, "Biotechnological production of enantiomeric pure lactic acid from renewable resources: recent achievements, perspectives, and limits," Appl. Microbiol. Biotechnol., vol. 85, no. 3, pp. 413–423, Jan. 2010.

[31] D. R. Witzke, R. Narayan, and J. J. Kolstad, "Reversible Kinetics and Thermodynamics of the Homopolymerization of l-Lactide with 2-Ethylhexanoic Acid Tin(II) Salt," Macromolecules, vol. 30, no. 23, pp. 7075–7085, Nov. 1997.

[32] J. L. Robert and K. B. Aubrecht, "Ring-Opening Polymerization of Lactide To Form a Biodegradable Polymer," J. Chem. Educ., vol. 85, no. 2, p. 258, Feb. 2008.

[33] R. Mehta, V. Kumar, and S. N. Upadhyay, "Mathematical Modeling of the Poly(lactic acid) Ring–Opening Polymerization Kinetics," Polym.-Plast. Technol. Eng., vol. 46, no. 3, pp. 257–264, 2007.

[34] Y. Yu, G. Storti, and M. Morbidelli, "Kinetics of Ring-Opening Polymerization of l,l-Lactide," Ind. Eng. Chem. Res., vol. 50, no. 13, pp. 7927–7940, Jul. 2011.

[35] M. Spinu, C. Jackson, M. Y. Keating, and K. H. Gardner, "Material Design in Poly(Lactic Acid) Systems: Block Copolymers, Star Homo- and Copolymers, and Stereocomplexes," J. Macromol. Sci. Part A, vol. 33, no. 10, pp. 1497–1530, 1996.

[36] J. R. Dorgan, H. Lehermeier, and M. Mang, "Thermal and Rheological Properties of Commercial-Grade Poly(Lactic Acid)s," J. Polym. Environ., vol. 8, no. 1, pp. 1–9, Jan. 2000.

[37] O. Coulembier, B. G. G. Lohmeijer, A. P. Dove, R. C. Pratt, L. Mespouille, D. A. Culkin, S. J. Benight, P. Dubois, R. M. Waymouth, and J. L. Hedrick, "Alcohol Adducts of N-Heterocyclic Carbenes: Latent Catalysts for the Thermally-Controlled Living Polymerization of Cyclic Esters," Macromolecules, vol. 39, no. 17, pp. 5617–

5628, Aug. 2006.

[38] S. Kobayashi, “Enzymatic Ring-Opening Polymerization of Lactones by Lipase Catalyst: Mechanistic Aspects,” Macromol. Symp., vol. 240, no. 1, pp. 178–185, Jul. 2006.

[39] L. Gold, “Statistics of Polymer Molecular Size Distribution for an Invariant Number of Propagating Chains,” J. Chem. Phys., vol. 28, no. 1, pp. 91–99, Aug. 2004.

[40] M. Myers, E. F. Connor, T. Glauser, A. Möck, G. Nyce, and J. L. Hedrick, “Phosphines: Nucleophilic organic catalysts for the controlled ring-opening polymerization of lactides,” J. Polym. Sci. Part Polym. Chem., vol. 40, no. 7, pp. 844–851, Apr. 2002.

[41] P. I. Dalko and L. Moisan, “In the Golden Age of Organocatalysis,” Angew. Chem. Int. Ed., vol. 43, no. 39, pp. 5138–5175, Oct. 2004.

[42] R. C. Pratt, B. G. G. Lohmeijer, D. A. Long, R. M. Waymouth, and J. L. Hedrick, “Triazabicyclodecene: A Simple Bifunctional Organocatalyst for Acyl Transfer and Ring-Opening Polymerization of Cyclic Esters,” J. Am. Chem. Soc., vol. 128, no. 14, pp. 4556–4557, Apr. 2006.

[43] U. Ragnarsson and L. Grehn, “Novel Amine Chemistry Based on DMAP-Catalyzed Acylation,” Acc. Chem. Res., vol. 31, no. 8, pp. 494–501, Aug. 1998.

[44] E. Vedejs and S. T. Diver, “Tributylphosphine: a remarkable acylation catalyst,” J. Am. Chem. Soc., vol. 115, no. 8, pp. 3358–3359, Apr. 1993.

[45] H. Tsuji and Y. Ikada, “Properties and morphology of poly(l-lactide) 4. Effects of structural parameters on long-term hydrolysis of poly(l-lactide) in phosphate-buffered solution,” Polym. De grad. Stab., vol. 67, no. 1, pp. 179–189, Jan. 2000.

[46] E. Vedejs and E. Rozners, “Parallel Kinetic Resolution under Catalytic Conditions: A Three-Phase System Allows Selective Reagent Activation Using Two Catalysts,” J. Am. Chem. Soc., vol. 123, no. 10, pp. 2428–2429, Mar. 2001.

[47] R. Breslow, “On the Mechanism of Thiamine Action. IV.1 Evidence from Studies on Model Systems,” J. Am. Chem. Soc., vol. 80, no. 14, pp. 3719–3726, Jul. 1958.

[48] D. Enders and T. Balensiefer, “Nucleophilic Carbenes in Asymmetric Organocatalysis,” Acc. Chem. Res., vol. 37, no. 8, pp. 534–541, Aug. 2004.

[49] J. C. Sheehan and D. H. Hunneman, “Homogeneous Asymmetric Catalysis,” J. Am. Chem. Soc., vol. 88, no. 15, pp. 3666–3667, Aug. 1966.

[50] G. W. Nyce, J. A. Lamboy, E. F. Connor, R. M. Waymouth, and J. L. Hedrick, “Expanding the Catalytic Activity of Nucleophilic N-Heterocyclic Carbenes for Transesterification Reactions,” Org. Lett., vol. 4, no. 21, pp. 3587–3590, Oct. 2002.

[51] R. Auras, B. Harte, and S. Selke, “An Overview of Polylactides as Packaging

Materials," Macromol. Biosci., vol. 4, no. 9, pp. 835–864, Sep. 2004.

[52] M. Movassaghi and M. A. Schmidt, "N-Heterocyclic Carbene-Catalyzed Amidation of Unactivated Esters with Amino Alcohols," Org. Lett., vol. 7, no. 12, pp. 2453–2456, Jun. 2005.

[53] İ. Başaran and A. Oral, "Synthesis and Characterization of Poly(L-Lactic acid)/Clay Nanocomposite via Metal-Free Process," Polym.-Plast. Technol. Eng., vol. 52, no. 12, pp. 1271–1276, 2013.

[54] W. Jeong, J. L. Hedrick, and R. M. Waymouth, "Organic Spirocyclic Initiators for the Ring-Expansion Polymerization of β-Lactones," J. Am. Chem. Soc., vol. 129, no. 27, pp. 8414–8415, Jul. 2007.

[55] M. H. Chisholm, J. Gallucci, and K. Phomphrai, "Lactide polymerization by well-defined calcium coordination complexes: comparisons with related magnesium and zinc chemistry," Chem. Commun., no. 1, pp. 48–49, Jan. 2003.

[56] C. K. Williams, L. E. Breyfogle, S. K. Choi, W. Nam, Victor G. Young, M. A. Hillmyer, and W. B. Tolman, "A Highly Active Zinc Catalyst for the Controlled Polymerization of Lactide," J. Am. Chem. Soc., vol. 125, no. 37, pp. 11350–11359, Sep. 2003.

[57] B. M. Chamberlain, M. Cheng, D. R. Moore, T. M. Ovitt, E. B. Lobkovsky, and G. W. Coates, "Polymerization of Lactide with Zinc and Magnesium β-Diiminate Complexes: Stereocontrol and Mechanism," J. Am. Chem. Soc., vol. 123, no. 14, pp. 3229–3238, Apr. 2001.

[58] H. A. Duong, T. N. Tekavec, A. M. Arif, and J. Louie, "Reversible carboxylation of N-heterocyclic carbenes," Chem. Commun., no. 1, pp. 112–113, Dec. 2004.

[59] N. T. Reynolds, J. Read de Alaniz, and T. Rovis, "Conversion of α-Haloaldehydes into Acylating Agents by an Internal Redox Reaction Catalyzed by Nucleophilic Carbenes," J. Am. Chem. Soc., vol. 126, no. 31, pp. 9518–9519, Aug. 2004.

[60] G. W. Nyce, T. Glauser, E. F. Connor, A. Möck, R. M. Waymouth, and J. L. Hedrick, "In Situ Generation of Carbenes: A General and Versatile Platform for Organocatalytic Living Polymerization," J. Am. Chem. Soc., vol. 125, no. 10, pp. 3046–3056, Mar. 2003.

[61] O. Thillaye du Boullay, E. Marchal, B. Martin-Vaca, F. P. Cossío, and D. Bourissou, "An Activated Equivalent of Lactide toward Organocatalytic Ring-Opening Polymerization," J. Am. Chem. Soc., vol. 128, no. 51, pp. 16442–16443, Dec. 2006.

[62] Fundamentals of Molecular Catalysis. Elsevier, 2003.

[63] M. S. Viciu, G. A. Grasa, and S. P. Nolan, "Catalytic Dehalogenation of Aryl Halides Mediated by a Palladium/Imidazolium Salt System," Organometallics, vol. 20,

no. 16, pp. 3607–3612, Aug. 2001.

[64] C. S. J. Cazin, N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis. Springer, 2010.

[65] M. Ryner, K. Stridsberg, A.-C. Albertsson, H. von Schenck, and M. Svensson, “Mechanism of Ring-Opening Polymerization of 1,5-Dioxepan-2-one and l-Lactide with Stannous 2-Ethylhexanoate. A Theoretical Study,” *Macromolecules*, Jun. 2001, vol. 34, no. 12, pp. 3877–3881,.

[71] Z. Cheng, X. Zhu, N. Zhou, J. Zhu, and Z. Zhang, “Atom transfer radical polymerization of styrene under pulsed microwave irradiation,” *Radiat. Phys. Chem.*, Apr. 2005., vol. 72, no. 6, pp. 695–701,

[72] J. Li, X. Zhu, J. Zhu, and Z. Cheng, “Microwave-assisted nitroxide-mediated radical polymerization of styrene,” *Radiat. Phys. Chem.*, Feb. 2006., vol. 75, no. 2, pp. 253–258,

[73] L. J. Liu, C. Zhang, L. Q. Liao, X. L. Wang, and R. X. Zhuo, “Microwave-assisted Polymerization of D, L-Lactide with Stannous Octanoate as Catalyst,” *Chin. Chem. Lett.*, 2001, vol. 12, no. 8, pp. 663–664,.

[74] F. Wiesbrock, R. Hoogenboom, and U. S. Schubert, “Microwave-Assisted Polymer Synthesis: State-of-the-Art and Future Perspectives,” *Macromol. Rapid Commun.* Oct. 2004., , vol. 25, no. 20, pp. 1739–1764,

[75] “MicroCures, Inc.” [Online]. Available: http://www.microcures.com/.

[76] P. Albert, H. Warth, R. Mülhaupt, and R. Janda, “Comparison of thermal and microwave-activated polymerization of ε-caprolactone with titanium tetrabutylate as catalyst,” *Macromol. Chem. Phys.*, May 1996., vol. 197, no. 5, pp. 1633–1641,

[77] L. Q. Liao, L. J. Liu, C. Zhang, F. He, and R. X. Zhuo, “Heating characteristics and polymerization of ε-caprolactone under microwave irradiation,” *J. Appl. Polym. Sci.*, Dec. 2003, vol. 90, no. 10, pp. 2657–2664,.

[78] B. Koroskenyi and S. P. McCarthy, “Microwave-Assisted Solvent-Free or Aqueous-Based Synthesis of Biodegradable Polymers,” *J. Polym. Environ.*, Jul. 2002. ,vol. 10, no. 3, pp. 93–104,

[79] X. Fang, C. D. Simone, E. Vaccaro, S. J. Huang, and D. A. Scola, “Ring-opening polymerization of ϵ-caprolactam and ϵ-caprolactone via microwave irradiation,” *J. Polym. Sci. Part Polym. Chem.*, Jul. 2002, vol. 40, no. 14, pp. 2264–2275,.

[80] R. M. Paulus, C. R. Becer, R. Hoogenboom, and U. S. Schubert, “Acetyl Halide Initiator Screening for the Cationic Ring-Opening Polymerization of 2-Ethyl-2-Oxazoline,” *Macromol. Chem. Phys.*, Apr. 2008, vol. 209, no. 8, pp. 794–800,.

[81] M. Vukomanovió, M. Mitrió, S. D. Škapin, E. Žagar, J. Plavec, N. Ignjatovió,

and D. Uskokovió, “Influence of ultrasonic processing on the macromolecular properties of poly (d,l-lactide-co-glycolide) alone and in its biocomposite with hydroxyapatite,” Ultrason. Sonochem., vol. 17, no. 5, pp. 902–908, Jun. 2010.

[82] M. Jevtić, A. Radulović, N. Ignjatović, M. Mitrić, and D. Uskoković, “Controlled assembly of poly(d,l-lactide-co-glycolide)/hydroxyapatite core–shell nanospheres under ultrasonic irradiation,” Acta Biomater., vol. 5, no. 1, pp. 208–218, Jan. 2009.

[83] G. J. Price, E. J. Lenz, and C. W. G. Ansell, “The effect of high-intensity ultrasound on the ring-opening polymerisation of cyclic lactones,” Eur. Polym. J., vol. 38, no. 9, pp. 1753–1760, Sep. 2002.

[84] Satya P Dubey, Hrushikesh A Abhyankar, Veronica Marchante, James L Brighton, Björn Bergmann, “Mathematical Modeling for Continuous Reactive Extrusion of Poly Lactic Acid formation by Ring Opening Polymerization Considering Metal/Organic Catalyst and Alternative Energies”,World Academy of Science, Engineering and Technology, International Journal of Chemical, Nuclear, Materials and Metallurgical Engineering Vol:9, No:2, 2015

[85] J. V. Crivello, “UV and electron beam-induced cationic polymerization,” *Nucl. Instrum. Methods Phys. Res. Sect. B Beam Interact. Mater. At.*, May 1999., vol. 151, no. 1–4, pp. 8–21,

[86] J. Deng, L. Wang, L. Liu, and W. Yang, “Developments and new applications of UV-induced surface graft polymerizations,” *Prog. Polym. Sci.*, Feb. 2009., vol. 34, no. 2, pp. 156–193,

[87] G. Oster and O. Shibata, “Graft copolymer of polyacrylamide and natural rubber produced by means of ultraviolet light,” *J. Polym. Sci.*, Nov. 1957., vol. 26, no. 113, pp. 233–234,

[88] T. K. Dash and V. B. Konkimalla, “Polymeric modification and its implication in drug delivery: poly-ε-caprolactone (PCL) as a model polymer,” *Mol. Pharm.*, Sep. 2012, vol. 9, no. 9, pp. 2365–2379,.

[89] H. Kye and J. L. White, “Continuous polymerization of caprolactam in a modular intermeshing corotating twin screw extruder integrated with continuous melt spinning of polyamide 6 fiber: Influence of screw design and process conditions,” *J. Appl. Polym. Sci.*, May 1994., vol. 52, no. 9, pp. 1249–1262,

[90] J.-M. Raquez, P. Degée, Y. Nabar, R. Narayan, and P. Dubois, “Biodegradable materials by reactive extrusion: from catalyzed polymerization to functionalization and blend compatibilization,” *Comptes Rendus Chim.*, Nov. 2006., vol. 9, no. 11–12, pp. 1370–1379,

[91] D. Mecerreyes, R. Jérôme, and P. Dubois, “Novel Macromolecular

Architectures Based on Aliphatic Polyesters: Relevance of the ‘Coordination-Insertion’ Ring-Opening Polymerization,” in *Macromolecular Architectures*, P. J. G. Hilborn, P. Dubois, C. J. Hawker, J. L. Hedrick, J. G. Hilborn, R. Jérôme, J. Kiefer, J. W. Labadie, D. Mecerreyes, and W. Volksen, Eds. Springer Berlin Heidelberg, , pp. 1–59.

[92] “Starcla -Bio-based Bionolle resin.” [Online].

[93] “PlasticsEurope - Plastics – the Facts 2013.” [Online]. Available: http://www.plasticseurope.org/Document/plastics-the-facts-2013.aspx?FolID=2.

[94] R. Datta, S.-P. Tsai, P. Bonsignore, S.-H. Moon, and J. R. Frank, “Technological and economic potential of poly(lactic acid) and lactic acid derivatives,” *FEMS Microbiol. Rev.*, 1999, vol. 16, no. 2–3, pp. 221–231, Feb. 1995.

[95] R. A. Gross and B. Kalra, “Biodegradable Polymers for the Environment,” *Science,* Aug. 2002., vol. 297, no. 5582, pp. 803–807,

[96] K. Tanaka, T. Shichiri, M. Toriumi, and T. Yamabe, “Theoretical study of polymerization of pyrrole,” *Synth. Met.,* Jun. 1989., vol. 30, no. 3, pp. 271–281,

[97] “InnoREX.” [Online]. Available: http://www.innorex.eu/about.php. [Accessed: 04-Oct-2013].

[98] Ludovic.’http://www.kyeonsultants.com/en/ludovic-twin-screw-simulation-software.html

[99] http://pubs.rsc.org/en/Content/ArticleLanding/2007/GC/b608891k#!divAbstract

[100] S.Sinnwell,H.Ritter, Aust.J.Chem.2007,60, 729.

http://dx.doi.org/10.1071/CH07219

[101] K. Madhavan Nampoothiri, N. R. Nair, and R. P. John, “An overview of the recent developments in polylactide (PLA) research,” Bioresour. Technol., vol. 101, no. 22, pp. 8493–8501, Nov. 2010.

[102] “Synthesis and Recycle of Poly(L-lactic acid) using Microwave Irradiation”. Koichi Hirao, Hitomi Ohara, Polymer Reviews, 2011, Volume 51, Issue 1,

[103] S. Dubey, H. Abhyankar, V. Marchante, J. Brighton, K. Blackburn, C. Temple, B. Bergmann, G. Trinh, and C. David, “Modelling and Validation of Synthesis of Poly Lactic Acid Using an Alternative Energy Source through a Continuous Reactive Extrusion Process,” Polymers, vol. 8, no. 4, p. 164, Apr. 2016.

[104] A. Södergård and M. Stolt, “Industrial Production of High Molecular Weight Poly(Lactic Acid),” in Poly(Lactic Acid), R. Auras, L.-T. Lim, S. E. M. Selke, and H. Tsuji, Eds. John Wiley & Sons, Inc., 2010, pp. 27–41.

[105] Jinsong Leng, Haibao Lu, Yanju Liu, Wei Min Huang and Shanyi Du (2009). Shape-Memory Polymers—A Class of Novel Smart Materials. MRS Bulletin, 34, pp 848-855.

[106] K. Inoue, M. Yamashiro, and M. Iji, "Recyclable shape-memory polymer: Poly(lactic acid) crosslinked by a thermo-reversible Diels–Alder reaction," J. Appl. Polym. Sci., vol. 112, no. 2, pp. 876–885, Apr. 2009.

[107] "Compounding and extrusion - Fraunhofer ICT." (Online). Available: http://www.ict.fraunhofer.de/en/comp/pe/ce.html.

[108] "Purac home." (Online). Available: http://www.purac.com/.

[109] "NatureWorks LLC Home Page." (Online).Available:http://www.natureworksllc.com/.

[110] http://www.mapsyn.eu

[111] http://www.alterego-project.eu/CMS/

12. LIST OF EQUATIONS

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$$y_{i,j+1} = y_{i,j} + \frac{\Delta t}{6} \cdot \left[k1_{i,j} + 2 \cdot k2_{i,j} + 2 \cdot k3_{i,j} + k4_{i,j}\right] \text{……….(A)}$$

$$k1_{i,j} = f_i\left(t, y_{1,j}, y_{2,j}, y_{3,j}, \dots, y_{n,j}\right) \text{……………………………………… }(i)$$

$$k2_{i,j} = f_i\left(t + \frac{\Delta t}{2}, y_{1,j} + \frac{\Delta t}{2} \cdot k1_{i,j}, \dots, y_{n,j} + \frac{\Delta t}{2} \cdot k1_{n,j}\right) \text{……… }(ii)$$

$$k3_{i,j} = f_i\left(t + \frac{\Delta t}{2}, y_{1,j} + \frac{\Delta t}{2} \cdot k2_{i,j}, \dots, y_{n,j} + \frac{\Delta t}{2} \cdot k2_{n,j}\right) \text{……… }(iii)$$

$$k4_{i,j} = f_i\left(t + \Delta t, y_{1,j} + \Delta t \cdot k3_{i,j}, \dots, y_{n,j} + \Delta t \cdot k3_{n,j}\right) \text{……… }(iv)$$

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$$-\frac{\boldsymbol{d}[LA]}{\boldsymbol{dt}} = k_j[LA][Al(OPr)_3] \dots\dots\dots\dots\dots\dots\dots.(1)$$

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

$$\frac{dy[I]}{dt} = -k_0[I][M]$$

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

$$\frac{d[Pj]}{dt} = [M]\left\{k_{(j-1)}\left[P_{j-1}\right] - kj\left[P_j\right] - k_{tj}\left[P_j\right]\right\}, \qquad j > 1$$

$$\frac{d[M]}{dt} = k_{tj}\left[P_j\right][M], \qquad j \geq 1$$

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- $\frac{d[C]}{dt} = -ka1 \cdot [C] \cdot \sum_{i=0}^{n}[D_i] + ka2 \cdot \sum_{i=0}^{n}[R_i] \cdot [A] = -ka1 \cdot [C] \cdot D_T + ka2 \cdot R_T \cdot [A]$……………(10)

- $\frac{d[A]}{dt} = ka1 \cdot [C] \cdot \sum_{i=0}^{n}[D_i] - ka2 \cdot \sum_{i=0}^{n}[R_i] \cdot [A] = ka1 \cdot [C] \cdot D_T - ka2 \cdot R_T \cdot [A]$……………(11)

- $\frac{d[M]}{dt} = -kp \cdot [M] \cdot \sum_{i=0}^{n-1}[R_i] + kd \cdot \sum_{i+1}^{n}[R_i]$……..(12)

- $\frac{d[R_0]}{dt} = ka1 \cdot [C] \cdot [D_0] - ka2 \cdot [R_0] \cdot [A] - kp \cdot [M] \cdot [R_0] - ks \cdot [R_0] \cdot \sum_1^n\left[D_j\right] + ks \cdot [D_0] \cdot \sum_1^n\left[R_j\right] - kte \cdot [R_0] \cdot \sum_1^n\left[R_j\right] - kte \cdot [R_0] \cdot \sum_1^n\left[D_j\right] - kte \cdot [R_0] \cdot \sum_1^n\left[G_j\right] + kte \cdot \sum_{i+1}^{n}\left[R_j\right] \cdot \sum_0^n[R_k] + kde \cdot \sum_1^n\left[R_j\right] \ldots\ldots\ldots\ldots..(13)$

- $\frac{d[R_i]}{dt} = ka1 \cdot [C] \cdot [D_i] - ka2 \cdot [R_i] \cdot [A] - kp \cdot [M] \cdot \sum_1^n[R_i] + kd \cdot \sum_{i+1}^{n}[R_i] - ks \cdot [R_i] \cdot \sum_1^n\left[D_j\right] + ks \cdot [D_i] \cdot \sum_1^n\left[R_j\right] - kte \cdot [R_i] \cdot \left(\sum_1^n\left[R_j\right] + \sum_1^n D_j + \sum_1^n G_j\right) + kte \cdot \sum_{i+1}^{n}\left[R_j\right] \cdot (\sum_1^n[R_k] + \sum_1^n[D_k] + \sum_1^n[G_k]) - kde \cdot (i-1) \cdot [R_i] + kde \cdot \sum_{i+1}^{n}\left[R_j\right]$……………(14)

- $\frac{d[R_T]}{dt} = \sum_0^n \frac{d[R_i]}{dt} = ka1 \cdot [C] \cdot \sum_{i=0}^{n}[D_i] - ka2 \cdot \sum_{i=0}^{n}[R_i] \cdot [A] = ka1 \cdot [C] \cdot D_T - ka2 \cdot R_T \cdot [A] \ldots\ldots\ldots\ldots\ldots..(15)$

- $\frac{d[D_0]}{dt} = -ka1 \cdot [C] \cdot [D_0] + ka2 \cdot [R_0] \cdot [A] + 2 \cdot ks \cdot [R_0] \cdot \sum_1^n\left[D_j\right] - 2 \cdot ks \cdot [D_0] \cdot \sum_1^n\left[R_j\right] - kte \cdot [D_0] \cdot \sum_1^n\left[R_j\right] + kte \cdot \sum_{i+1}^{n}\left[D_j\right] \cdot \sum_0^n[R_k] + kde \cdot \sum_{i+1}^{n}\left[D_j\right] \ldots\ldots\ldots.(16)$

- $\frac{d[D_i]}{dt} = -ka1 \cdot [C] \cdot [D_i] + ka2 \cdot [R_i] \cdot [A] + ks \cdot [R_i] \cdot \sum_1^n\left[D_j\right] - ks \cdot [D_i] \cdot \sum_1^n\left[R_j\right] - kte \cdot [D_i] \cdot \sum_1^n\left[R_j\right] + kte \cdot \sum_{i+1}^{n}\left[D_j\right] \cdot \sum_1^n[R_k] - kde \cdot (i-1) \cdot [D_i] + kde \cdot \sum_{i+1}^{n}\left[D_j\right]$……………(17)

- $\frac{d[D_T]}{dt} = \sum_0^n \frac{d[D_i]}{dt} = -ka1 \cdot [C] \cdot \sum_{i=0}^n [D_i] + ka2 \cdot \sum_{i=0}^n [R_i] \cdot [A] = -ka1 \cdot [C] \cdot D_T + ka2 \cdot R_T \cdot [A]$…………………(18)

- $\frac{d[G_i]}{dt} = -kte \cdot [G_i] \cdot \sum_1^n [R_j] + kte \cdot \sum_{i+1}^n [G_j] \cdot \sum_1^n [R_k] - kde \cdot (i-1) \cdot [G_i] + kde \cdot \left(\sum_{i+1}^n [R_j] + \sum_{i+1}^n [D_j] + \sum_{i+1}^n [G_j]\right)$………………..(19)

- $X = 1 - \frac{[M]}{[M_0]}$ (20)
- $\overline{M_n} = \frac{[M_0.]X}{[R_T]+[D_T]} m_{mon}$ (21)

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$\rho * CP * dT = W_{mechanical} + W_{conduction} + W_{AE}$ ………….. (10)

13. APPENDICES

Details of the simulation method and simulation code in terms of mathematical notations is secured due to proprietary code

Appendix A

A.1.1 Simulation code for modelling

```
Proprietary code
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A.1.2 Simulation code for modelling

```
Proprietary code
```

A.1.3 Ordinary differential equations for modelling

```
Proprietary code
```

14. LIST OF PUBLICATIONS:

1. Satya P Dubey[1], Hrushikesh A Abhyankar, Veronica Marchante, James L Brighton, Björn Bergmann, "Mathematical Modeling for Continuous Reactive Extrusion of Poly Lactic Acid formation by Ring Opening Polymerization Considering Metal/Organic Catalyst and Alternative Energies" **International Journal of Chemical, Nuclear, Materials and Metallurgical Engineering-(** Vol:9, No:2, 2015**)**
2. Satya P Dubey[1], Hrushikesh A Abhyankar, Veronica Marchante, James L Brighton, Kim Blackburn, Clive Temple, Björn Bergmann, Giang Trinh, Chantal David, "Modelling and Validation of Synthesis of Poly Lactic Acid using Alternative Energy Source through Continuous Reactive Extrusion Process" **Polymers** (Vol:8, 164; doi:10.3390/polym8040164 (2016))
3. Björn Bergmann[a*], Jan Diemert[a], Jean-Marie Raquez[b], Thomas Hielscher[c], Markus Reichmann[d], Chantal David[e], Satya P Dubey[f], and Carolina Losada Fernández[g], "InnoREX – European Project Reveals Impact of Microwave and Ultrasound Energy on Polymerization of PLA via Reactive Extrusion" **Polymer Processing Society (PPS-32), (2016)**
4. Satya P Dubey[1], Veronica Marchante, James L Brighton, Kim Blackburn, Hrushikesh A Abhyankar, "Chronological Review of The Catalytic Progress Of Polylactic Acid Formation Through Ring Opening Polymerization." (**International Research Journal of Pure and Applied Chemistry**)". 2016 - Volume 12(3): 1-20, DOI: 10.9734/IRJPAC/2016/27469
5. Satya P Dubey[1], Hrushikesh A Abhyankar, Veronica Marchante, James L Brighton, Björn Bergmann, Giang Trinh, Chantal David, "Microwave Energy assisted Synthesis of Poly Lactic Acid via Continuous Reactive Extruder: Reaction kinetics modelling approach" (**European Polymer Journal-in Progress**).

LIST OF CONFERENCES AND WORKSHOPS

1. Matlab Simulink Work-Shop - **Cranfield University, 2014 UK**
2. Fourth International Conference on Multifunctional, Hybrid and Nanomaterials, **Sitges (near Barcelona),2015, Spain.**
3. Oral paper at conference “ICP 2015: XIII International Conference on Polymer, **Paris, France.**
4. Certificate as a speaker @Science for the Green Economy Conference,2016 **Cranfield, UK**
5. Poster and Talk, EU funded Projects-Industrial Workshop,2016 **Brussels, Belgium**

Research is to see what everybody else has seen, and to think what nobody else has thought.

-**Albert Szent-Györgyi**