

**Integrated Master in Chemical Engineering**

***Study of lactic acid polycondensation and  
lactide production***

**Master Thesis**

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## Abstract

Poly(lactic acid) is a biodegradable polyester which, due to its physical and chemical properties is the best candidate to replace on the market petroleum-based polymers. The most interesting route to produce PLA involves three steps, the polycondensation of lactic acid until low molecular weight, depolymerisation of the prepolymer into the cyclic dimer of lactic acid, lactide, and ring opening polymerization of lactide to achieve high molecular weight. In the literature there are several papers concerning the polycondensation of lactic acid and the ring opening polymerization of lactide but the same does not happens with the production of lactide. Moreover, discrepancies exist in the published literature. In order to fully characterize the two first steps of this process, reactions at different temperatures, pressures, with or without catalyst were carried out in a semi-batch reactor. Special efforts have been devoted to achieve full characterization of both polymer melt and gas phases. Different analytical techniques have been adopted, and comparatively used, in order to evaluate polymer average properties. On the base of these detailed experimental data, which were not accessible so far in the literature, a more comprehensive description of the system has been obtained. At the same time, a comprehensive model accounting for both PC reaction and LT formation is developed.

**Key Words:** Poly(lactic acid), Lactide, Polycondensation, Depolymerization

## Index

|   |    |
|---|----|
| Abstract .....  | ii |
| 1 Introduction.....                                       | 1  |
| 1.1 PLA Production .....                                  | 2  |
| 1.1.1 Polycondensation of Lactic acid .....               | 2  |
| 1.1.2 Production of HMW PLA.....                          | 4  |
| 1.2 PLA properties, degradation and recycling .....       | 6  |
| 1.3 Lactide properties and production .....               | 9  |
| 1.4 Aim of the work .....                                 | 13 |
| References .....  | 14 |
| 2 Experimental Work.....                                  | 16 |
| 2.1 Experimental plan.....                                | 16 |
| 2.2 Reaction setup .....                                  | 17 |
| 2.3 Characterization Techniques .....                     | 19 |
| 2.3.1 High performance liquid chromatography (HPLC) ..... | 19 |
| 2.3.2 Size Exclusion Chromatography .....                 | 22 |
| 2.3.3 Gas Chromatography .....                            | 23 |
| 2.3.4 Karl Fischer .....                                  | 24 |
| References .....  | 26 |
| 3 Lactic Acid Polycondensation.....                       | 27 |
| 3.1 Experimental results.....                             | 27 |
| 3.1.1 Bulk Phase.....                                     | 27 |
| 3.1.2 Gas Phase.....                                      | 32 |
| 4 Lactide Production .....                                | 34 |
| 4.1 Experimental results.....                             | 34 |

|       |  |                                     |
|-------|--|-------------------------------------|
| 4.1.1 | Temperature effect .....                 | 34                                  |
| 4.1.2 | Pressure effect.....                     | 39                                  |
| 4.1.3 | Industrial Conditions .....              | 44                                  |
|       | References .....                         | 50                                  |
| 5     | Model development.....                   | <b>Erro! Marcador não definido.</b> |
| 5.1   | General background .....                 | <b>Erro! Marcador não definido.</b> |
| 5.2   | Model assumptions and equations .....    | <b>Erro! Marcador não definido.</b> |
| 5.2.1 | Vacuum stream flow rate evaluation ..... | <b>Erro! Marcador não definido.</b> |
| 5.2.2 | Mass transport evaluation .....          | <b>Erro! Marcador não definido.</b> |
|       | References .....                         | <b>Erro! Marcador não definido.</b> |
| 6     | Conclusions.....                         | 63                                  |

## Index of Figures

|  |    |
|--|----|
| Figure 1.1 - Lactic acid isomers [5].....  | 1  |
| Figure 1.2 - Lactic acid polycondensation scheme [9].....  | 3  |
| Figure 1.3- Synthesis methods for high - molecular - weight PLA. (Adapted from Garlotta et al.[1]).....                                    | 6  |
| Figure 1.4 - Fossil energy used for preparation of different petroleum based polymers and PLA produced from ROP of lactide [17].....       | 8  |
| Figure 1.5 - Contributions to global climate change for petrol based polymers and PLA [17].....  | 8  |
| Figure 1.6 - The three possible forms of lactide [1]. ....   | 9  |
| Figure 1.7 - Detail of the back-biting reaction of the -OH group in a general chain of poly(lactic acid) [19]. ....                        | 10 |
| Figure 1.8 - Two points where the ester bond can break: alkyl-oxygen bond (a) and carbonyl-oxygen bond (b) [10]. ....                      | 11 |
| Figure 2.1 - Reaction set up. (TI-temperature indicator; TCI-temperature controller and indicator).....                                    | 18 |
| Figure 2.2 - Chromatogram of a LMW-PLA. The separation is well succeeded in HPLC. ....   | 21 |
| Figure 2.3 - Chromatogram of an HMW-PLA sample. For higher oligomers the separation is not well succeeded in HPLC. ....                    | 21 |
| Figure 2.4 - Molecular weight as a function of reaction time determined by: □ HPLC and ◇ GPC. ....   | 23 |
| Figure 3.1 - Bulk volume as a function of reaction time:* 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C. ....                                       | 27 |
| Figure 3.2 - Water concentration in bulk phase as a function of time:* 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C. ....                          | 28 |
| Figure 3.3 - Polymer molecular weight as a function of time for different reaction conditions:* 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C. .... | 29 |
| Figure 3.4 - PDI as a function of the extent of reaction for all the reactions:* 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C. ....                | 30 |

|  |    |
|--|----|
| Figure 3.5 - Oligomers mole fraction as a function of time, bulk phase: * 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C.....                | 31 |
| Figure 3.6 - Lactide concentration in bulk as a function of reaction time: * 130 °C; □ 150 °C; ◇ 170 °C; o 190 °C.....             | 32 |
| Figure 3.7 - Cumulative mass of the condenser species as a function of reaction time: □ 150 °C; ◇ 170 °C; o 190 °C. ....           | 33 |
| Figure 4.1 - Bulk volume as a function of reaction time: □ 190 °C; ◇ 200 °C; o 210 °C. ....  | 35 |
| Figure 4.2 - Polymer molecular weight as a function of time for different reaction temperatures:□ 190 °C; ◇ 200 °C; o 210 °C. .... | 36 |
| 4.4 - Oligomers weight fraction as a function of time, bulk phase: □ 190 °C; ◇ 200 °C; o 210 °C.....                               | 37 |
| Figure 4.5 - Lactide mass fraction as a function of time: □ 190 °C; ◇ 200 °C; o 210 °C. ....                                       | 38 |
| Figure 4.6 - Cumulative mass of water, monomer, dimer and lactide in condensed gas phase: □ 190 °C; ◇ 200 °C; o 210 °C.....        | 39 |
| Figure 4.7 - Change in bulk volume for reactions at different pressures: □ 25 mmHg; ◇ 10 mmHg. ....                                | 40 |
| Figure 4.9 - Water concentration in the bulk as a function of time: □ 25 mmHg; ◇ 10 mmHg. ....                                     | 41 |
| Figure 4.10 - Oligomers weight fraction versus reaction time: □ 25 mmHg; ◇ 10 mmHg. ....   | 42 |
| Figure 4.11 - Lactide weight fraction over time for the reaction performed at 25 mmHg (□) and 10 mmHg (◇).....                     | 43 |
| Figure 4.12 - Cumulative mass of water, monomer, dimer and lactide in condensed gas phase: □ 25 mmHg; ◇ 10 mmHg.....               | 44 |
| Figure 4.13 - Volume change for the reaction performed at industrial conditions. ...   | 45 |
| Figure 4.14 - Number average molecular weight over time for the reaction performed at industrial conditions. ....                  | 45 |
| Figure 4.15 - Water concentration in bulk as a function of reaction time for the last reaction performed. ....                     | 46 |

|  |    |
|--|----|
| Figure 4.16 - Oligomers weight fraction as a function of reaction time for the reaction performed at industrial conditions. .... | 47 |
| Figure 4.17 - Lactide weight fraction over reaction time for the reaction performed at industrial conditions. ....               | 48 |
| Figure 4.18 - Cumulative mass in the condenser for the reaction performed at “extreme” conditions. ....                          | 49 |
| Figure 5.1 - $W_x$ distribution as a function of $p$ ( $p=0.25$ —, $p=0.45$ - -, $p=0.75$ ···, $p=0.9$ ---). ....                | 52 |
| Figure 5.2 - $P_x$ distribution as a function of $p$ ( $p=0.25$ —, $p=0.45$ - -, $p=0.75$ ···, $p=0.9$ ---). ....                | 52 |
| Figure 5.3 - Concentration based equilibrium constants. ....   | 55 |
| Figure 5.4 - Interchange reactions occurring in PC (from Kotliar[14]). ....  | 55 |
| Figure 5.5 - Interface concentration profile. ....   | 59 |

## Index of Tables

|   |                                     |
|---|-------------------------------------|
| Table 1.1- Physical Properties of Lactic Acid [6].....                          | 2                                   |
| Table 1.2 – Polycondensation literature review. ....                            | 4                                   |
| Table 2.1 - Experimental conditions used in the first set of experiments. ....  | 16                                  |
| Table 2.2 - Experimental conditions used in the depolymerization reactions..... | 17                                  |
| Table 2.3 - Analytical techniques used. ....                                    | 19                                  |
| Table 2.4 - HPLC parameters. ....   | 20                                  |
| Table 2.5 - GPC parameters. ....  | 22                                  |
| Table 5.1 - Antoine’s parameters. ....  | <b>Erro! Marcador não definido.</b> |



# 1 Introduction

Poly(lactic acid) (PLA) is a biodegradable aliphatic polyester produced from renewable sources which, due to its excellent physical-chemical properties and environment compatibility, is considered the best candidate to replace on the market petroleum-based plastics. It has a wide range of applications ranging from medical devices, such as suture threads and scaffolds, to commodity products like bottles and films for food packaging [1-3].

The monomer, lactic acid (LA), is the smallest optical active organic compound present in nature. Due to the presence of a chiral carbon, LA exists in the two optical isomers, L (+) and D (-) (Figure 1). It was first isolated in 1780 from sour milk and first commercially produced around 1880. It can be obtained by petrochemical synthesis or fermentation process. Nowadays, due to the improvements in bacterial fermentation of D-glucose, optically preferentially pure lactic acid is produced through the batch fermentation process of corn and other carbohydrates [4] which involve key steps as cell mass and protein removal and, LA recovery, purification and concentration [3]. In the United States, LA is largely used in food applications such as acidic flavouring agent or buffering agent [1]. Some of its physical properties are shown in Table 1.1.

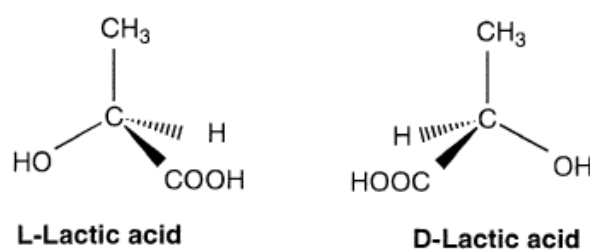


Figure 1.1 - Lactic acid isomers [5].

Table 1.1- Physical Properties of Lactic Acid [6]

| Properties                         | Value                                    |
|------------------------------------|--|
| Molecular Weight (Da)              | 90.098                                   |
| Melting Point (D(-) or L(+))       | 52.8 – 54 °C                             |
| (DL)                               | 16.8 – 33 °C                             |
| Boiling Point DL (0.5 mmHg)        | 82 °C                                    |
| (14 mmHg)                          | 122 °C                                   |
| Dissociation constant (Ka at 25°C) | $1.37 \times 10^{-4}$                    |
| Heat of combustion ( Hc)           | 1361 KJ.mol <sup>-1</sup>                |
| Specific heat (Cp at 20 °C)        | 190 J.mol <sup>-1</sup> °C <sup>-1</sup> |

In next part of the chapter, a brief review on PLA properties and production processes is summarized as long as the main contributions reported in the literature regarding LA polycondensation and lactide production.

## 1.1 PLA Production

The production of PLA with low molecular weight (LMW) is known since 1932 [7]. It is characterized by substandard properties and is useless for the majority of PLA applications. Due to this, new techniques were developed to produce a high molecular weight (HMW) polymer, of larger industrial and commercial interest. In the next sections a description of the main routes used to produce PLA is reported.

### 1.1.1 Polycondensation of Lactic acid

Polycondensation of lactic acid is the simple process used to produce PLA. LA is a bifunctional monomer that undergoes self-esterification through a reversible step-growth mechanism in which polymer chains react together leading to longer chains with the production of water [8]. The reaction scheme is represented in Figure 1.2.

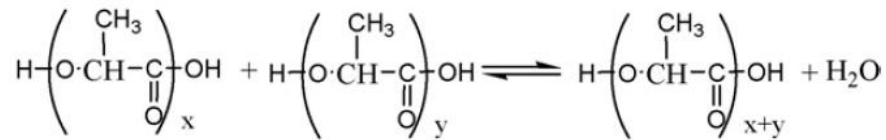


Figure 1.2 - Lactic acid polycondensation scheme [9].

Water can be considered as the side product of the reaction and has to be removed from the reacting mixture in order to shift the chemical equilibrium to the right side and enhance the polycondensation reaction. Water removal is a key aspect which limits the extent of reaction and thus the polymer molecular weight. Due to increase in viscosity during polymerization, water removal efficiency decreases and only LMW polymer can be produced by PC [9].

The polycondensation of LA is studied in several papers, many from a qualitative point of view, and discrepancies are reported. A summary of the major works in polycondensation is listed in Table 1.2. Moreover, a systematic study of the parameters affecting the process is missing. Many aspects have to be taken into account such as: reaction temperature and pressure, nature, concentration and addition of catalyst and role of water mass transport. A wide variety of metal based catalyst such as Tin and Zn compounds were found to be effective in enhancing the polycondensation of lactic acid [10]. An additional aspect regards the possible discoloration of the final polymer. During the polycondensation PLA undergoes side reactions leading to colour changes from yellow to brown and finally to black. These side reactions occur mainly at high reaction temperature and time but are still not well known [3]. The addition of co-catalysts, as *p*-toluenesulfonic acid (TSA) is reported to be more effective than single metal catalysts, in terms of molecular weight achieved and in the effective prevention of the polymer discoloration [9, 11].

Table 1.2 - Polycondensation literature review.

| Ref.                          | P (bar) | T (°C) | Mn (Da) | t <sub>r</sub> (h) |
|-------------------------------|---------|--------|---------|--------------------|
| <b>Ajioca et al. (1995)</b>   | 1.013   | 130    | 115,000 | 24                 |
| <b>Miyoshi et al. (1996)</b>  | 0.013   | 230    | 75,000  | 24                 |
| <b>Moon et al. (2000)</b>     | 0.013   | 180    | 22,000  | 5                  |
| <b>Moon et al. (2001)</b>     | 0.00066 | 150    | 335,000 | 37                 |
| <b>Quain et al. (2003)</b>    | 0.013   | 150    | 100,000 | 73                 |
| <b>Yoda et al. (2004)</b>     | 240     | 80     | 13,500  | 24                 |
| <b>Zhao et al. (2004)</b>     | 0.0007  | 180    | 2,000   | 10                 |
| <b>Chen et al. (2006)</b>     | 0.0013  | 170    | 65,000  | 13                 |
| <b>Nagahata et al. (2007)</b> | 0.04    | 200    | 8,000   | 0.5                |
| <b>Lei et al. (2007)</b>      | 0.15    | 180    | 25,000  | 16                 |

Another concern in polycondensation of lactic acid is the occurrence of cyclization and transesterification side reactions which are detailed in section 1.3. Impact of ring formation and intermolecular transesterification for PC reactions has been extensively studied in the literature [12-15]. Out of all the possible reaction, as fully addressed in chapter 3, describing the model assumptions, only depolymerization reactions leading to small ring is reported. It is worth to mention that, as reported by Kotliar (1981) [12], among the possible transesterification reactions, alcoholysis is the most favourable. Anyway, due to the small extent of reactions investigated, it was not considered.

### 1.1.2 Production of HMW PLA

HMW PLA can be produced mainly by three different processes, schematically reported in Figure 1.3. The less attractive process is based on azeotropic dehydrative condensation of LA in the presence of organic solvents, such as toluene, xylene and diphenyl ether [1]. This method was first patented in collaboration with the Japanese company Mitsui Toatsu Chemicals in 1994 [12]. Due to the use of those environmentally non-friendly solvents, even if the process leads to HMW PLA, it does not present large attention from the industrial point of view. The other two processes

are based on chain coupling agent (CCA) and ring opening polymerization (ROP) reactions and pass through a common initial step of LA polycondensation [1]. In the CCA process, chain coupling agents are added to the mixture in order to link different chains producing HMW polymer. The drawback of the process is that the use of those linkers leads to a lower polymer purity in terms of chemical composition. Depending on the nature of the coupling agents used, PLA based polymers with different structures and properties are produced [1].

The ROP process is the most attractive route to obtain HMW PLA with high degree of crystallinity [1]. Instead of adding linkers, as it is done in the CCA process, the strategy is to produce by pre-polymer degradation an intermediate product, cyclic dimer of LA called lactide (LT), which then reacts by ROP leading to HMW PLA. The process consists mainly of three steps: LA polycondensation, lactide (LT) production by degradation of the LMW PLA, and ring-opening polymerization (ROP) of LT which leads to HMW PLA [1]. ROP reaction is not revised since it is not part of the present work. For some information and general aspect regarding ROP of LT the reader is referred for example to(2009) that made a review about this topic [13].

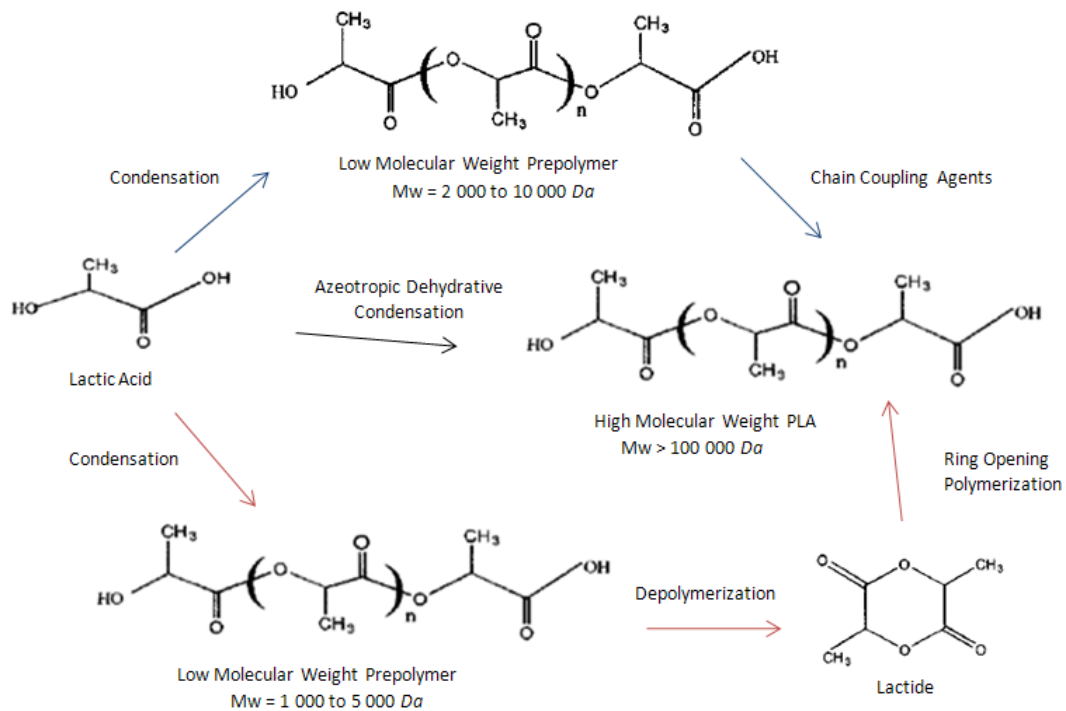


Figure 1.3- Synthesis methods for high - molecular - weight PLA. (Adapted from Garlotta et al.[1])

## 1.2 PLA properties, degradation and recycling

PLA has attracted large attention due to its biodegradability and mechanical properties similar to the ones of polyethylene terephthalate (PET), polypropylene (PP) and other common petrol-based plastics [3]. It is a thermoplastic polymer with high mechanical strength and flexural modulus higher than the one of polystyrene (PS) [14]. It can be stress crystallized, thermally crystallized, copolymerized, and processed in a variety of existing processing equipment. It has also good organoleptic characteristics [3], resistance to fatty foods and dairy products and presents excellent flavour and aroma barrier [14]. Due to these features, it is one of the polymers with the wider range of applications on the market [3]. As introduced previously, PLA can be produced with different enantiomeric compositions, depending upon the L and D content in the polymer chains also referred as polymer optical purity. Due to this aspect, PLA shows properties varying in a range of values as a function of the enantiomeric composition. Depending upon the application, polymers ranging from fully amorphous (50 % D

content) to high crystalline (> 99% L content) behaviour can be selected. PLA glass transition temperature ( $T_g$ ) ranging from 50°C to 80°C and melt temperature ( $T_m$ ) ranging from 130°C to 180°C are reported in the literature [15].

In general, regarding PLA degradation and recycling, polymers undergo different types of degradation such as chemical, thermal, photo and mechanical degradation [16]. Since biopolymers contain hydrolysable bonds, the most important degradation mechanism is chemical degradation via hydrolysis. It is reported that LMW PLA can be totally degraded by microorganism in aerobic or anaerobic environments in a time range from two to five years, and early chain fragmentation can be obtained at higher humidity and temperature in composting facilities in fifteen days. On the other hand microbial degradation occurs only with LMW PLA, which represents an advantage of PLA use in food related applications [15]. Thermal degradation of PLA is reported to occur only at high temperatures (temperatures larger than 200 °C). It occurs by specific scission (after called biting) and random scissions (radical pyrolytic elimination that occurs at higher temperatures and produces a chain with a vinyl end group) [17].

In the frame of sustainability and sustainable development, PLA shows, once more, advantages compared to other synthetic polymers. As introduced previously, PLA is produced from renewable sources, such as starch and other carbohydrates. Besides that it uses less energy to be produced, in comparison with petroleum based plastics. In Figure 1.4 it is represented the amount of fossil energy required to produce one Kg of different petroleum based polymers and of PLA produced by ROP of lactide. The crossed lines represent the fossil energy used as a chemical feedstock while the black part represents the fossil energy used for fuels and operations supplies during the process. “PLA 1” is the polymer produced nowadays and as it is possible to see it takes less 25 to 55 % of energy to be produced than petroleum based polymers such as polypropylene (PP) and (PET). “PLA Bio/WP” represents the PLA produced by an improved process that is being developed by the company Cargill Dow, using biomass and wind power. This future PLA can reduce the use of fossil energy in more than 90% [17].

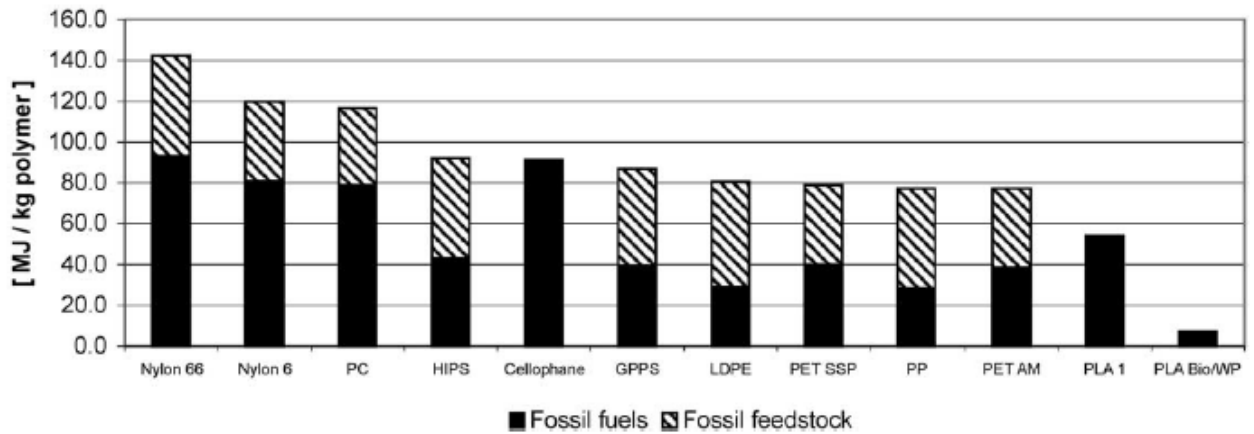


Figure 1.4 - Fossil energy used for preparation of different petroleum based polymers and PLA produced from ROP of lactide [17].

After use, PLA can be recycled or degraded into soil and humus, basic nutrients for plants growth<sup>[26]</sup>. Moreover, in contrast with the volatile organic compounds (VOC) and CO<sub>2</sub> generated during the incineration of petrol-based polymers, the CO<sub>2</sub> generated during the biodegradation of PLA is balanced with CO<sub>2</sub> from the atmosphere consumed during the growth of plant feedstocks. In addition, in a long term consideration, PLA could be used as CO<sub>2</sub> sink and contribute the reduction of the greenhouse gases<sup>[12]</sup>. This consideration is clearly explained by Figure 1.5 where for different polymers it is reported the amount of equivalent CO<sub>2</sub> produced per Kg of polymer. Among all polymers PLA1 present the smallest impact and PLA Bio/WP has even a favourable balance [17].

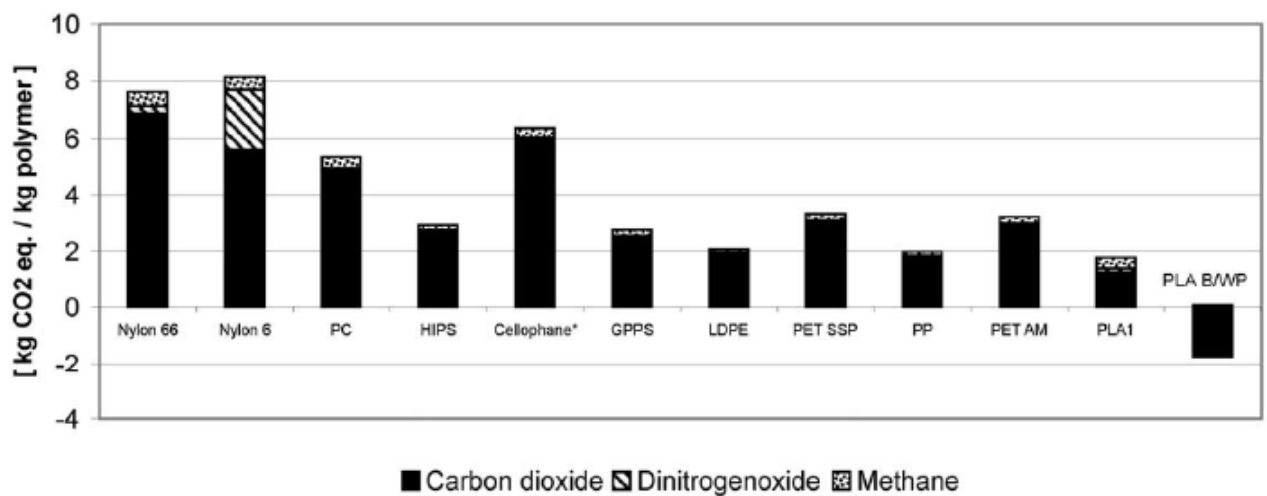


Figure 1.5 - Contributions to global climate change for petrol based polymers and PLA [17].



### 1.3 Lactide properties and production

Lactide is the cyclic dimer of lactic acid and, as previously introduced, it is the monomer in the ROP reaction leading to HMW PLA. Due to the stereo-isomeric nature of lactic acid, lactide exists in three different forms, L-lactide, D-lactide and meso-lactide, which are depicted in Figure 1.6. D- and L-Lactide have a melting point of 97°C whereas meso-lactide has a melting point of 52°C [1]. Depending on the composition of the lactide mixture, PLA with different D unit content is obtained. In particular pure L-lactide and pure D-lactide will produce high crystalline PLA whereas meso-lactide will give mainly an amorphous polymer [3]. Lactide purity is function of the reaction conditions in the lactide production step and of the prepolymer composition obtained in the polycondensation step. Thus both steps have to be taken into account in optimizing the reaction conditions.

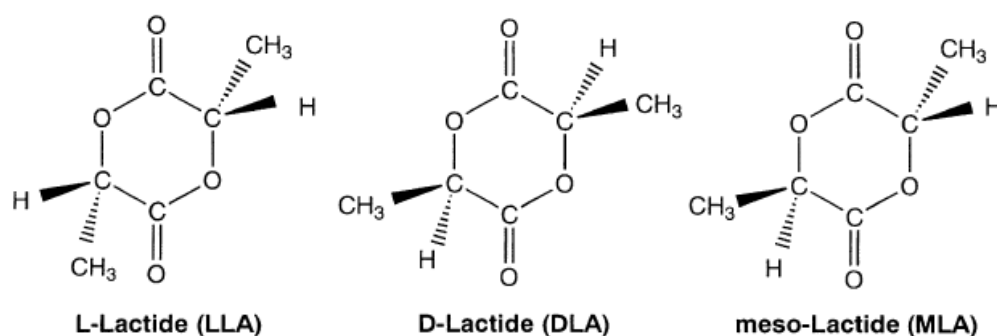


Figure 1.6 - The three possible forms of lactide [1].

Lactide is produced through the depolymerization of oligomeric PLA in which back-biting and end-biting reactions are involved [1, 18-19]. In particular back-biting reaction refers to the formation of cyclic compounds through intra-molecular reactions between the carboxylic end group of the chain and the ester bond of the chain backbone (Figure 1.7) [18]. These reactions are equilibrium reactions which depend upon temperature and ring size mainly, as described in section 3.2. Instead, end-biting refers to the ring closure reaction of a linear chain. The main difference between back-biting and ring-closure is that end-biting reaction produces a cyclic compound and water whereas back-biting produces a cyclic and a linear compound.

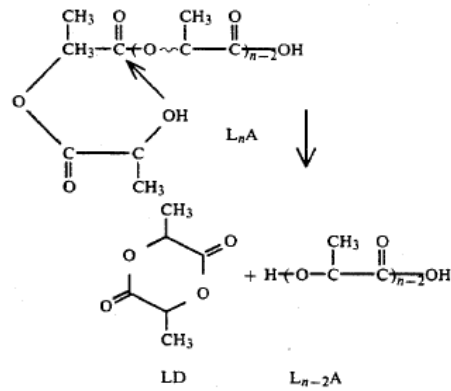


Figure 1.7 - Detail of the back-biting reaction of the  $-OH$  group in a general chain of poly(lactic acid) [19].

Regarding LT production, no many works are reported in the literature. Moreover, lactide purification is a crucial step which can increase the price of PLA products, turning PLA into a specialty chemical and thus preventing its introduction in the market of commodity plastics [3]. Regarding LT purity, PLA racemisation is one of the major problems in PLA production and it is reported that it occurs mainly in both the LT production step and PC step. Thus, it is necessary to understand the influence of the operating parameters on the process in order to optimize the lactide production and minimize side reactions leading to racemisation.

In this frame the production of lactide with high purity is a key step of the entire process.

Hiltunen et al. (1996) [10] studied the effect of different catalysts and polymerization conditions on the preparation of low molecular weight PLA focusing on final molecular weight achieved, amount of lactide produced and degree of crystallinity. Reactions were carried out at different temperatures in the range of 180 to 220 °C. For all the catalysts studied (apart of sulphuric acid), as long as for the non catalyzed system, it was found that the higher the reaction temperature, the higher the racemisation. In particular, it was found that sulphuric acid was the best catalyst, leading to the highest molecular weight (30 kDa) and crystallinity (over 50%), whereas Sn(II)oct produced amorphous HMW PLA (26 kDa). The authors stated that during PC, ester interchange reactions are causing racemisation. These reactions occur through

the cleavage of an ester group which can take place in two points, as depicted in Figure 1.8, the carbonyl-oxygen bond and the alkyl-oxygen bond. Only the breakage of an alkyl-oxygen bond, enhanced at high temperature, leads to racemisation. In particular, it was found that Lewis acid catalysts catalyze the breakage of the alkyl-oxygen bond while strong proton acids, like sulphuric acid, catalyze the carbonyl-oxygen bond.

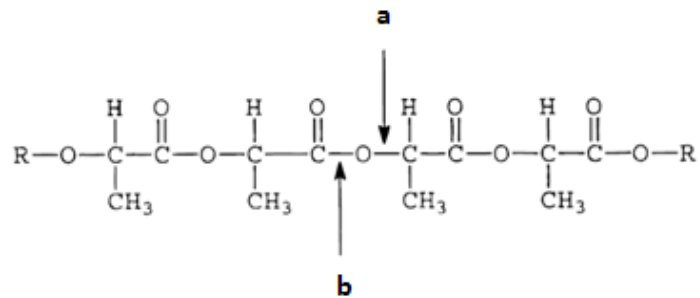


Figure 1.8 - Two points where the ester bond can break: alkyl-oxygen bond (a) and carbonyl-oxygen bond (b) [10].

Achmad et al. (2009) [20] studied the synthesis of PLA by direct polycondensation under vacuum with no use of catalysts, solvents and initiators, in an effort to reduce the PLA production cost. The reaction temperatures were in the range of 150-250 °C. The maximum molecular weight achieved in their experiments was of 90 kDa at 200 °C and 10 mmHg, during 89 h. They detected degradation of PLA above 200 °C under reduced pressure and, from their results, they claim that it just occurred by specific scission (biting reaction) and did not yield vinyl compounds.

Noda and Okuyama (1999) [21] studied the effects of different metal catalysts in the thermal catalytic depolymerization of Poly(L-Lactic Acid) oligomers into L-lactide. The depolymerization was performed in temperatures between 190 and 245°C under 4 to 5 mmHg vacuum, for a maximum distillation time of 3h. The molecular weight of the prepolymer was of about 1170 Da for all the experiments. The catalysts studied were Al, Ti, Zn, Zr based, in comparison to the conventional used Sn(II)oct. These catalysts were chosen for their less toxicity compared to the one of Sn based. In their results, Ti and Al based catalysts gave the lowest yields with maximums between 40 to 50% of lactide produced in 2h, with purities ranging from 80 to 90%. Zn and Zr compounds provided higher yields of lactide, in the range of 70 to 90% with high L-

lactide purities, between 90 and 97%. They concluded that aluminium compounds are the least reactive catalysts in intra-molecular transesterification. Ti based catalysts produced lactide with a low catalyst concentration (0.2 mol %), but an acceleration of the polymerization reaction occurred. Zinc and zirconium catalysts provided good yields. With the same catalyst concentration (1 mol %), Zn compounds produced slightly higher quantities of lactide and smaller racemisation was obtained. However, neither of these catalyst achieved the yield of lactide obtained by the use of 0.2 mol % of Sn(II)oct. This catalyst yielded 89% of lactide, 98% pure, in only 1 h. The authors concluded that the optical and chemical yields of the lactide are dependent on the coordination activity of the catalysts. In the specific case of intra-molecular transesterification, the best catalyst was tin octoate, followed by zinc and zirconium based compounds.

Yoo et al. (2006) [18] studied the effects of temperature, pressure and different Sn based catalysts (SnO, Sn(II)oct and SnCl<sub>2</sub>) on the lactide synthesis starting from oligomeric PLA. Reactions were carried out at temperatures ranging from 200 to 240 °C, and pressure between 10 and 100 Torr. It was observed that at higher reaction temperature and pressure, LT with lower yield and higher purity was produced. No large differences were found for the different catalysts tested. Moreover, for SnO catalyst, it was found that the conversion of PLA into lactide was maximized for a molecular weight of 1380 Da and it is independent upon catalyst concentration for SnO concentration above 0.1 % w/w.

Sinclair et al. (1993) [19] patented an innovative method to produce lactide from LMW lactic acid. They found that a maximum of lactide is obtained during the polycondensation of lactic acid for a degree of polymerization equal to 2. They claimed that LT is formed by ring-closure reaction of linear dimer and they suggested recovering LT directly from the LMW PLA mixture bypassing the step where back-biting reaction are involved (discussed in the literature work previously reported). They also state that higher temperatures are needed to distill LT as the molecular weight and melt viscosity increases. Obviously, if their findings are verified, this process represents a breakthrough in the lactide production since ring-closure reactions occur at lower temperature than back-biting reactions and LT racemisation is minimized.

## 1.4 Aim of the work

Following the literature works introduced previously, it can be concluded that LT production and LA polycondensation are reactions strictly linked. PC reaction temperature and pressure, as well as catalyst addition and prepolymer degree of polymerization, represent key parameters in the LT production process. Those parameters have to be optimized in order to achieve high LT conversion minimizing racemization.

In this frame, in the present work, two main goals have been identified:

- i) detailed investigation of LA polycondensation
- ii) study of LT production reactions

In particular, reactions in semi-batch have been carried out in two steps, a prepolymerization step, in which a LMW prepolymer is produced under nitrogen flow and low temperature (130-190°C) in order to limit possible side reactions, and a LT formation step, in which by increasing temperature (190-210°C) and decreasing pressure (5-25 mbar), conditions suitable for LT production were accessed. In the last step, the use of Sn(Oct)<sub>2</sub> as catalyst has been investigated.

Special efforts have been devoted to achieve full characterization of both polymer melt and gas phases. Different analytical techniques have been adopted, and comparatively used, in order to evaluate polymer average properties as well as chain length distribution. On the base of these detailed experimental data, which were not accessible so far in the literature, a more comprehensive description of the system has been obtained.

At the same time, a comprehensive model accounting for both PC reaction and LT formation is developed to simulate the polymerization process. In a future work the model will be applied for parameters evaluation.

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## 2 Experimental Work

In this chapter, reaction setup and procedures, as well as analytical techniques used, are described.

### 2.1 Experimental plan

As introduced previously in chapter 1, the production of lactide involves mainly two reactions, the LA polycondensation reaction, leading to a prepolymer and the prepolymer depolymerization, which leads to the production of LT. In this frame, the experimental work was differentiated into two main classes of experiments focused on lactic acid polycondensation and lactide production. Both experiments were performed by means of the same reaction setup, under different reaction conditions.

PC experiments were performed without catalyst at different temperatures, in the range of 130 to 190 °C, as reported in Table 2.1. For all runs, a pretreatment step was performed for 2h at 120°C, in order to reduce the amount of water without enhancing too strongly the polycondensation reaction.

A constant nitrogen flow was applied in order to favour the removal of water from the reaction mixture. Stirring speed of 400 rpm and nitrogen flow rate of 200 ml.min<sup>-1</sup> were applied. These conditions were proved to limit diffusion limitation phenomena and ensure kinetic controlled regime.

*Table 2.1 - Experimental conditions used in the first set of experiments.*

| Reaction | Temperature<br>(°C) | Nitrogen Flow<br>rate (ml.min <sup>-1</sup> ) | Catalyst |
|----------|---------------------|---|----------|
| A        | 130                 | 200   | no       |
| B        | 150                 | 200   | no       |
| C        | 170                 | 200   | no       |
| D        | 190                 | 200   | no       |



LT production reactions were carried out at different temperatures, from 190 to 210°C, and pressures from 25 to 5 mmHg, with and without catalyst. The stirring rate applied was the same as in the PC reactions. The prepolymer of about 600 Da was prepared during the night for 15h, at a temperature of 140°C. The experimental conditions used in the different reactions performed are listed in Table 2.2.

*Table 2.2 - Experimental conditions used in the depolymerization reactions.*

| Reaction | Temperature<br>(°C) | Pressure<br>(mmHg) | Catalyst               |
|----------|---------------------|--------------------|------------------------|
| E        | 190                 | 25                 | no                     |
| F        | 200                 | 25                 | no                     |
| G        | 210                 | 25                 | no                     |
| H        | 190                 | 10                 | no                     |
| I        | 200                 | 5                  | 0.25 % (w/w) Sn(II)oct |

## 2.2 Reaction setup

A simple draw of the reaction setup is reported in Figure 2.1. All reactions were carried out in a 250 ml stirred glass reactor (Buchi, Switzerland) heated by an external oil bath (Polystat CC3, Huber, Germany) and equipped with liquid and gas temperature indicators (TI). Since PC reactions are carried out under nitrogen and LT production reactions under vacuum conditions, the reactor is connected to a nitrogen line and to a vacuum pump. The nitrogen line is intercepted by a needle valve. In LT production reactions, the nitrogen line is used to reestablish atmospheric pressure and collect the samples. The vacuum is regulated by a digital vacuum controller (DVR-300-MR, K-JEM Scientific Inc, USA). All lines are electrically heated by heating tapes controlled by temperature controllers.

Between the vacuum controller and the reactor, a vertical condenser was installed.

Depending on the reaction performed, different condenser temperature conditions were set. For PC reactions the condenser temperature was regulated by means of an aqueous solution of ethyleneglycol (0.3 % w/w) circulating in a cryostat system (RK20 Lauda). Since some volatile compounds accumulate in the condenser, the system is equipped with an opening cap placed at the top of the condenser. During the sampling, acetonitrile is flushed through the condenser in order to wash out all the condensed products.

For LT production reactions, due to the large amount of LT produced, in order to avoid clogging of the condenser, the cryostatic bath was substituted with an heating bath and the temperature in the condenser was set at 90°C. In these conditions, LT in gas phase is liquefy and collected. In both cases, in order to ensure that all volatiles are collected in the condenser, a cold trap was placed at the condenser outlet. For all run, no condensate was found in the trap.

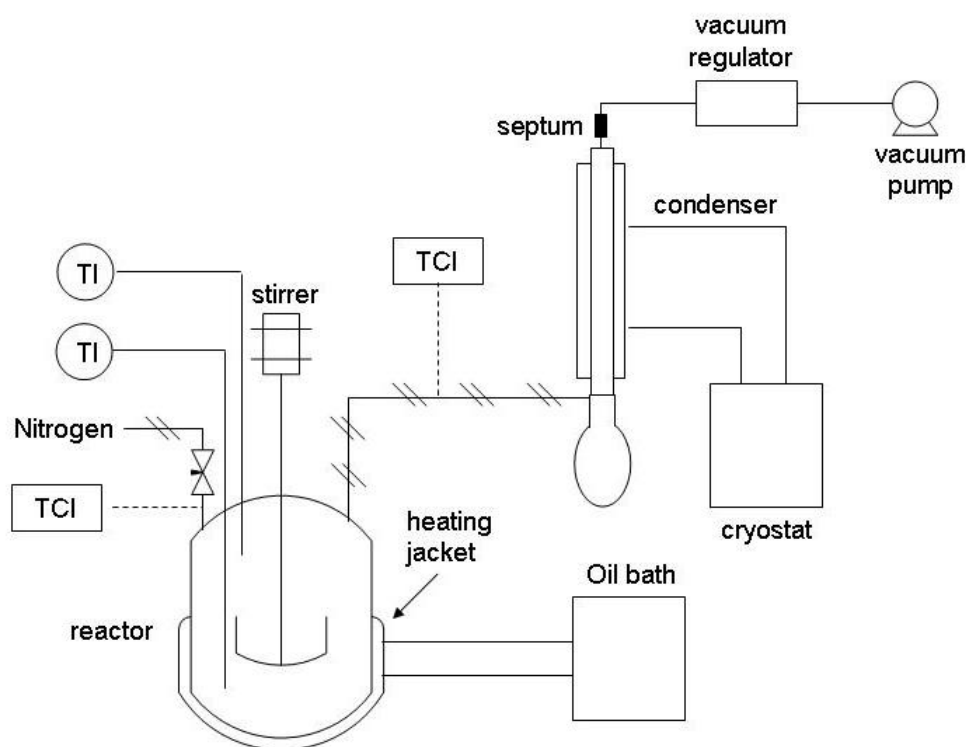


Figure 2.1 - Reaction set up. (TI-temperature indicator; TCI-temperature controller and indicator).

## 2.3 Characterization Techniques

Different analyses were carried out in order to obtain a good characterization of both polymer melt and condensed phases. The different techniques and the corresponding measured polymer properties are reported in Table 2.3 and will be detailed in this section.

*Table 2.3 - Analytical techniques used.*

| Techniques                    | Characterizations   |
|-------------------------------|---|
| Reversed Phase Chromatography | Mn, Mw, PDI;<br>Oligomers distribution in melt and condensed phase;<br>Lactide content in melt and condensed phase; |
| Gel Permeation Chromatography | Mn, Mw, PDI   |
| Gas Chromatography            | Condensed phase water content   |
| Karl Fischer                  | Polymer water content   |

Additionally, during the reaction the liquid volume change was evaluated by visual inspection.

### 2.3.1 High performance liquid chromatography (HPLC)

HPLC is a type of column chromatography that can be used either for analytical or preparative purposes.

The separation in HPLC is performed by means of the different interactions between the solutes and the stationary phase. In the specific case of reverse phase HPLC, the mobile phase is significantly more polar than the stationary phase and the analyte adsorbs to the stationary phase through the hydrophobic effect [1-2].

Being the area of the peak proportional to the number of moles of a single component, through a constant named calibration factor, a calibration has to be performed in order to obtain quantitative information of the system composition [3].

During the analysis, the composition of the mobile phase can be either constant or changed in a specific gradient. The gradient elution is a way of improving the separations and obtaining best resolutions in complex solute mixtures, without affecting the calibration factors [3].

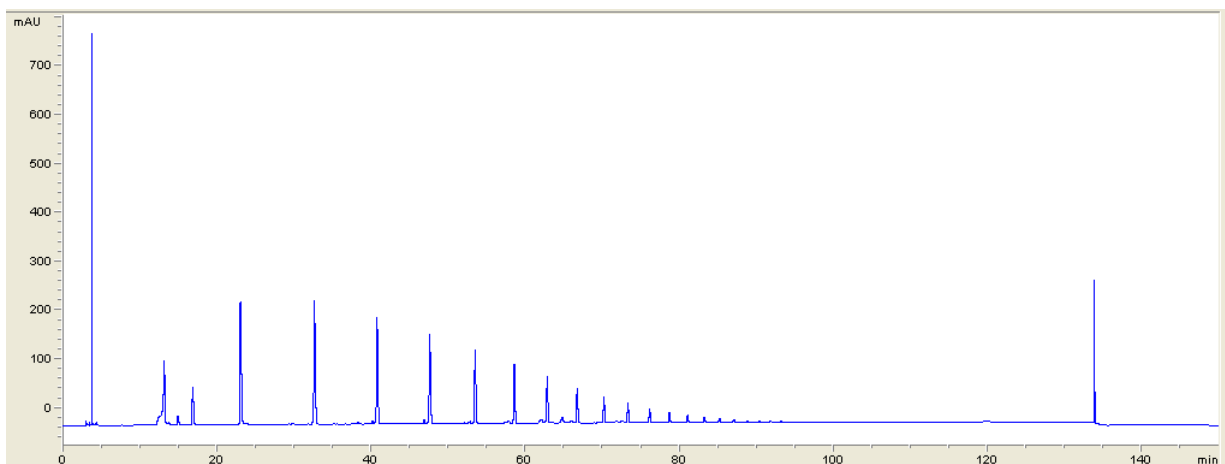
In the frame of this work, reverse HPLC was used to determine both oligomers composition and polymer molecular weight. Two Agilent Eclips XDB C18 columns were used, with an Agilent 1200 series apparatus (Agilent, USA). The mobile phase was a water/acetonitrile (Acros Organics) mixture in gradient concentration, both acidified with phosphoric acid 0.1 vol.-% (Merck). This acid pH was chosen in order to preserve the efficiency of the column. The following gradient profile was selected: starting with a mobile phase of 98 vol.-% water, after 2 minutes the acetonitrile concentration was ramped linearly to 100 vol.-% in 120 min, maintained constant at 100 vol.-% for 30 min and finally returned back to 98 vol.-% water. The main parameters used are listed in Table 2.4.

*Table 2.4 - HPLC parameters.*

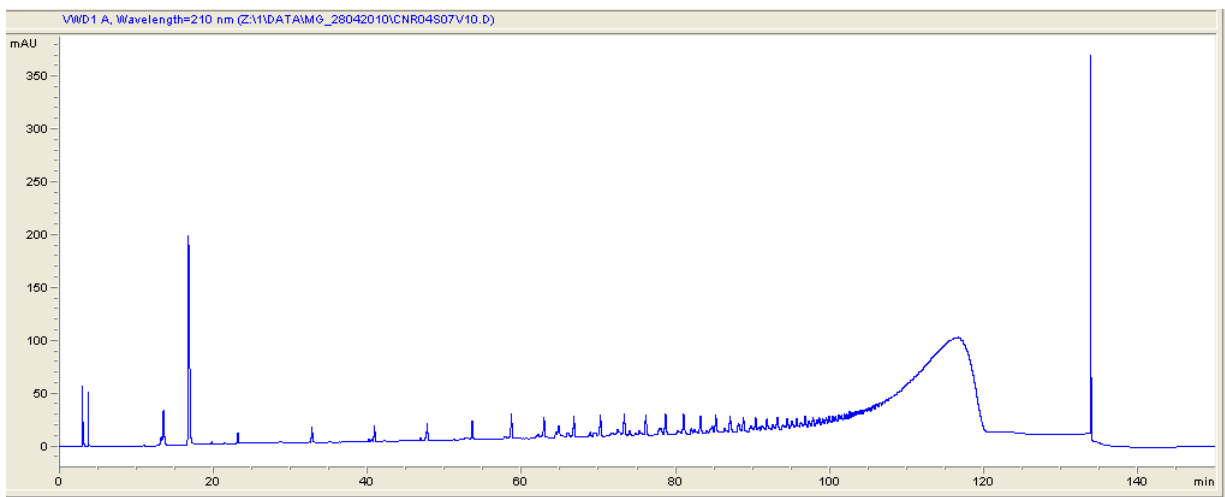
| Parameter        | Value                             |
|------------------|-----------------------------------|
| Particle Size    | 5 $\mu\text{m}$                   |
| Column Area      | 4.6 x 150 $\text{mm}^2$           |
| Temperature      | 40 $^{\circ}\text{C}$             |
| Flow rate        | 1 $\text{ml}\cdot\text{min}^{-1}$ |
| UV wavelength    | 240 nm                            |
| Injection Volume | 10 $\mu\text{l}$                  |

In Figure 2.2 a typical chromatogram of a LMW-PLA sample is represented. All oligomers are well separated and from the measurement of the area of the peaks a quantitative determination of the polymer composition is obtained.

However, as it is possible to see in Figure 2.3, for larger MW, a good separation was not achieved for higher oligomers. For this reason samples with HMW cannot be fully characterized by HPLC being its limit of quantitative evaluation of about 800 Da. For those samples Gel Permeation Chromatography (GPC) was applied.



*Figure 2.2 - Chromatogram of a LMW-PLA. The separation is well succeeded in HPLC.*



*Figure 2.3 - Chromatogram of an HMW-PLA sample. For higher oligomers the separation is not well succeeded in HPLC.*

### 2.3.2 Size Exclusion Chromatography

Size Exclusion chromatography (SEC), also known as Gel Permeation Chromatography (GPC), is the most used method for determining the average molecular weight and the molecular weight distribution of polymers. The main difference compared to HPLC is that the separation is based on the hydrodynamic volume of the sample rather than by its interactions with the stationary phase. Big molecules will not diffuse into the pores and will be eluted first, whereas small molecules will penetrate into the pores, eluting at longer elution time. Since SEC is a relative method, a chromatogram calibration is needed. The calibration is performed by analysing a series of samples with a known molecular weight and then relating the sample MW with the retention time determined.

The polymer is dissolved in a solvent (for example chloroform in the case of PLA), and injected into a column with fairly defined pore size. The mobile phase is usually the same as the solvent used to dissolve the sample [4-5].

The detection in GPC can be done by several kinds of detectors such as refractive index (RI), viscometer and ultraviolet (UV) detectors [5]. In this special case it was performed by means of an RI detector.

The GPC conditions used in this work are listed in Table 2.5.

*Table 2.5 - GPC parameters.*

| Parameter            | Value                  |
|----------------------|------------------------|
| Temperature          | 30 °C                  |
| Flow rate            | 1 ml.min <sup>-1</sup> |
| UV wavelength        | 240 nm                 |
| Injection Volume     | 25 µl                  |
| Max elution time     | 45 min                 |
| Sample concentration | 5 mg.l <sup>-1</sup>   |

In Figure 2.3, the time evolution of the molecular weight for a LT production reaction performed at 200 °C and under a 25 mmHg is shown and the blue and the green markers represent the MW as determined by HPLC and GPC respectively. A significant difference between the two measurements is observed. Moreover, the profiles are different. Through HPLC analysis the molecular weight seems to reach a plateau or even decrease while by GPC the molecular weight is always increasing.

These significant differences have strong influence in the data analysis, and wrong values can lead to wrong interpretations of components behaviour during the reaction. In the specific case of the depolymerisation of low molecular weight PLA to lactide, the results obtained through HPLC may lead one to think that the rate of depolymerisation was higher than the one of polymerization, while by the results of GPC, the reverse conclusion is obtained.

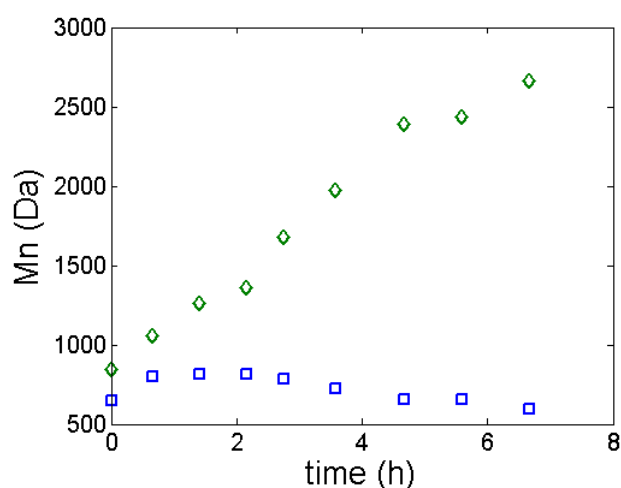


Figure 2.4 - Molecular weight as a function of reaction time determined by: □ HPLC and ◇ GPC.

### 2.3.3 Gas Chromatography

Gas Chromatography is, together with HPLC, the most used technique in analytical chemistry. It is very accurate and precise. It differs from liquid chromatography for the nature of the mobile phase which is a carrier gas [6].

After injection the sample is vaporized and transported through the column. The separation is performed by means of the different affinities between the compounds of a sample and the stationary phase. Depending upon these interactions and column

temperature, the solute will split between the mobile and the stationary phase. The longer the components spend in the stationary phase the more likely it is to be separated from components of similar volatility. In gas chromatography, the retention factor can be altered by changing the stationary phase or the temperature of the column. When the solutes enter the gas phase, they are swept to the detector by the carrier gas [7].

Therefore, the flow of the carrier gas has strong influence in the retention times of the samples components, with the retention time decreasing in the same rate as the flow of the gas increases [7].

One concern is that the gases used in GC must be of very high purity and all traces of moisture, oxygen and hydrocarbons must be removed before the gas enters the instrument [7]

In this work Gas Chromatography was used to determine the water content of the condensed samples, as well as the one of acetonitrile used to wash the condenser before each sampling. The equipment used was a GC system HP 6890 using helium as a carrier gas. In Table 2.3 are listed the main parameters of the method used.

*Table 2.3 - Parameters of GC.*

| Parameter            | Value  |
|----------------------|--------|
| Oven Temperature     | 60 °C  |
| Inlet Temperature    | 250 °C |
| Inlet Pressure       | 11 Bar |
| Detector Temperature | 250 °C |
| Injection Volume     | 0.5 µl |

#### 2.3.4 Karl Fischer

Karl Fischer is a quick and simple method designed to determine small contents of water in substances, up to an extent which depends upon the equipment specifications. It is based in the quantitative reaction of water with iodine and sulphur dioxide as depicted in



eq(1). Pyridine is added to the system in order to shift the reaction to the formation of the strong acid and an alcohol is used to dissolve all the before referred compounds [8].



There are two types of titration: coulometric or volumetric. The main difference between the two is that with the volumetric method, the titrant is added directly to the sample while in the coulometric method, the titrant is generated electrochemically in the titration cell. The coulometric method measures water levels much lower than the volumetric method [9-10]. In the frame of this master work, coulometric titration was performed to analyse the water content of the polymer samples, using an 831 KF Coulometer (Metrohm, Switzerland). The PLA samples were dissolved in acetonitrile (water content < 10 ppm; Acros Organics), and analysed in the liquid phase. Since acetonitrile is hygroscopic, its initial water content was accounted when treating the data.

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## 3 Lactic Acid Polycondensation

As anticipated in Chapter 2, semi-batch reactions at 130 – 190 °C under nitrogen flow and without catalyst were performed to fully characterize the polycondensation of LA. For each reaction, bulk and condenser samples were collected at different reaction times and analysed using the techniques previously described.

In the next sections, experimental results are reported in a qualitative point of view.

### 3.1 Experimental results

#### 3.1.1 Bulk Phase

The evolution in time of the liquid volume for the four reactions performed is presented in Figure 3.1. In all cases a decrease in volume around 15% was observed. This suggests that the variation of reaction volume has to be accounted for when modeling the system.

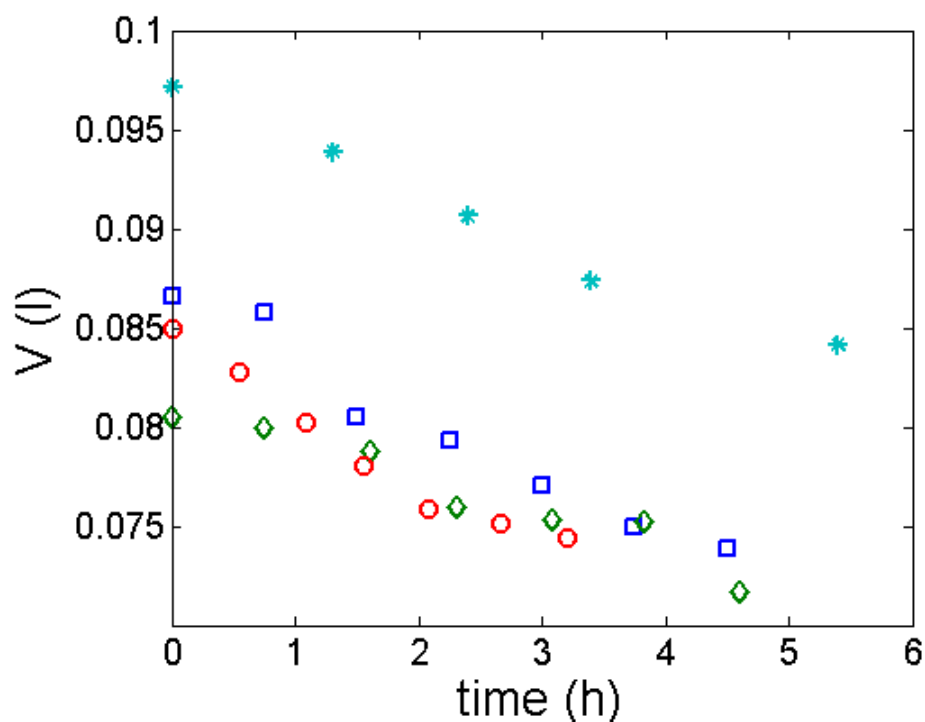


Figure 3.1 - Bulk volume as a function of reaction time: \* 130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

The concentration of water in the bulk phase for all the reactions is reported in Figure 3.2; all profiles show similar time evolutions. The water content decreases in the beginning of the reaction and approaches a plateau at longer reaction times. For the reactions at lower temperature (130 and 150 °C), the plateau value was not established during the reaction time since the decreasing of the water concentration is slower compared to the reactions carried out at higher temperature. It is possible to observe that the decreasing of the water concentration is faster the higher the reaction temperature. Moreover, for the reactions carried out at 170 and 190 °C, the same final plateau value of water concentration is reached.

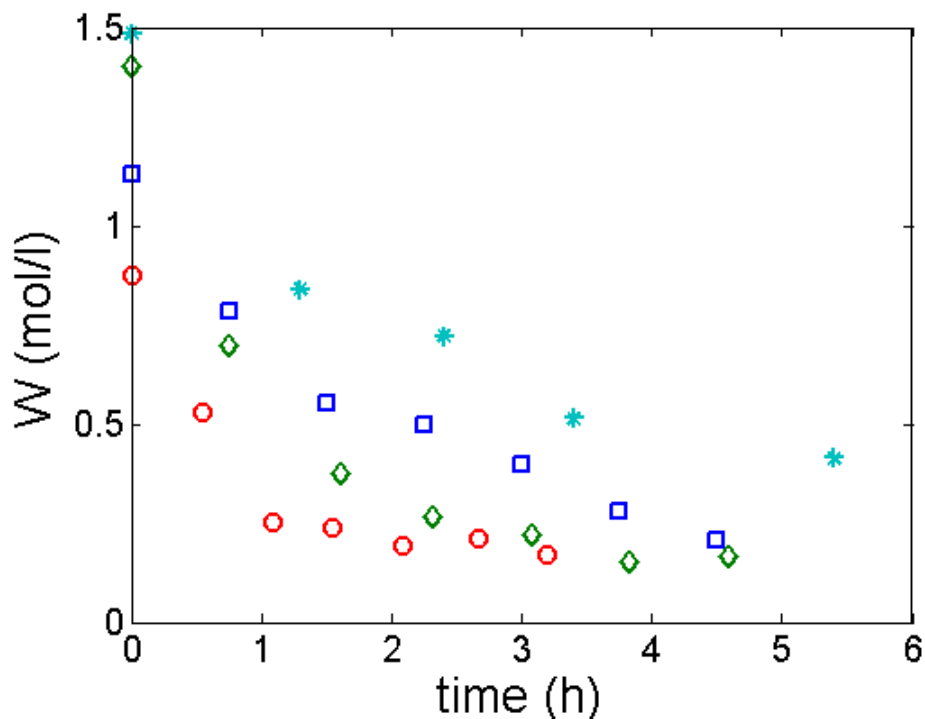


Figure 3.2 - Water concentration in bulk phase as a function of time: \* 130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

For all reactions, the number average molecular weight as a function of reaction time is reported in Figure 3.3. The linearity of these profiles confirms that chemical regime conditions are achieved. As expected [1], the higher the reaction temperature, the faster the molecular weight growth is.

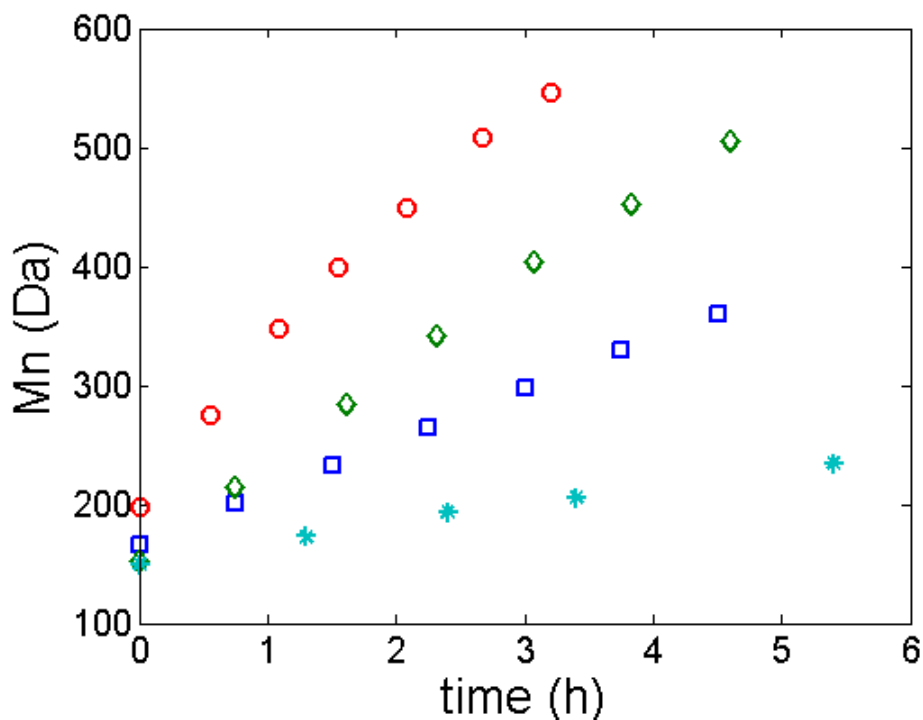


Figure 3.3 - Polymer molecular weight as a function of time for different reaction conditions: \*

130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

Polydispersity index (PDI) is a parameter representing the broadness of the molecular mass distribution of a polymer. According to Flory, the maximum value of PDI is 2 for step-growth polymerization, achieved at 100% conversion ( $p$  equal to 1 in Equation 8 – Chapter 5). In our reactions the maximum value of PDI was around 1.7, as depicted in Figure 3.4; PDI increases during the reaction reaching a plateau at long reaction times. Moreover, it was observed that for a given reaction time, the higher the temperature, the larger the polymer PDI. However, the higher the temperature the larger the degree of polymerization obtained; therefore, for a fair data analysis, the PDI values have to be plotted at same extent of reaction, as shown in Figure 3.4. For all reactions, a unique PDI vs.  $p$  curve was found: therefore, it can be concluded that temperature is not affecting the polymer PDI.

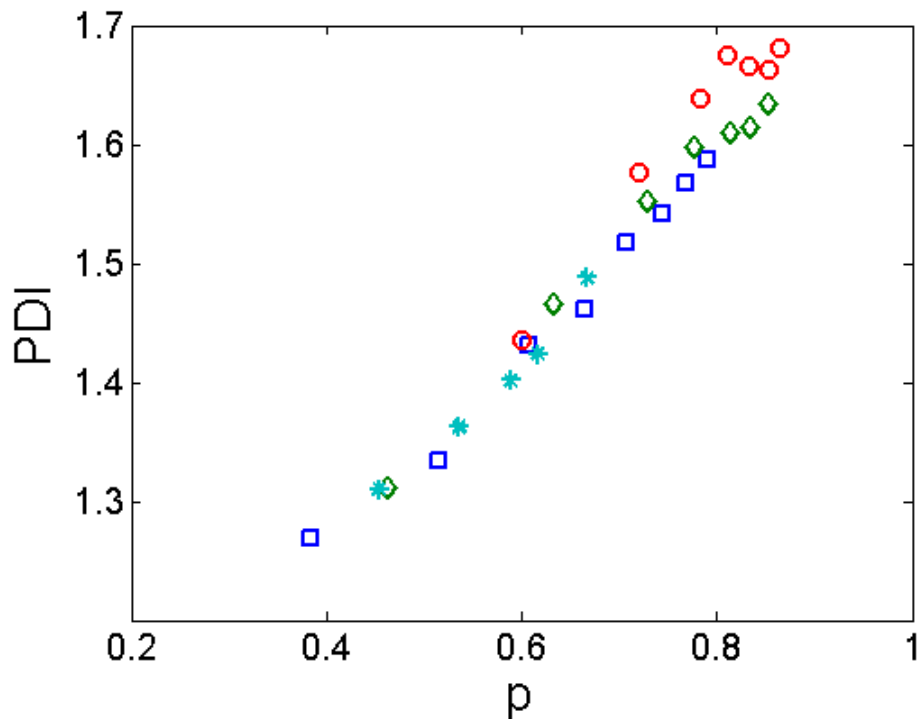


Figure 3.4 - PDI as a function of the extent of reaction for all the reactions: \* 130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

Figure 3.5 shows the oligomer mole fraction profiles for all the reactions. Such profiles are fully consistent with the step growth mechanism of the polycondensation in which shorter chains react together to produce longer ones. For all reactions, the mole fractions of monomer ( $x_1$ ) and dimer ( $x_2$ ) decrease at increasing reaction time, since they are consumed by the reaction to produce higher oligomers. Different trends are observed at the different temperatures for trimer ( $x_3$ ) and tetramer ( $x_4$ ), in agreement with the step-growth polymerization mechanism. Oligomers profiles up to chain length 60 were detected for long reaction times.

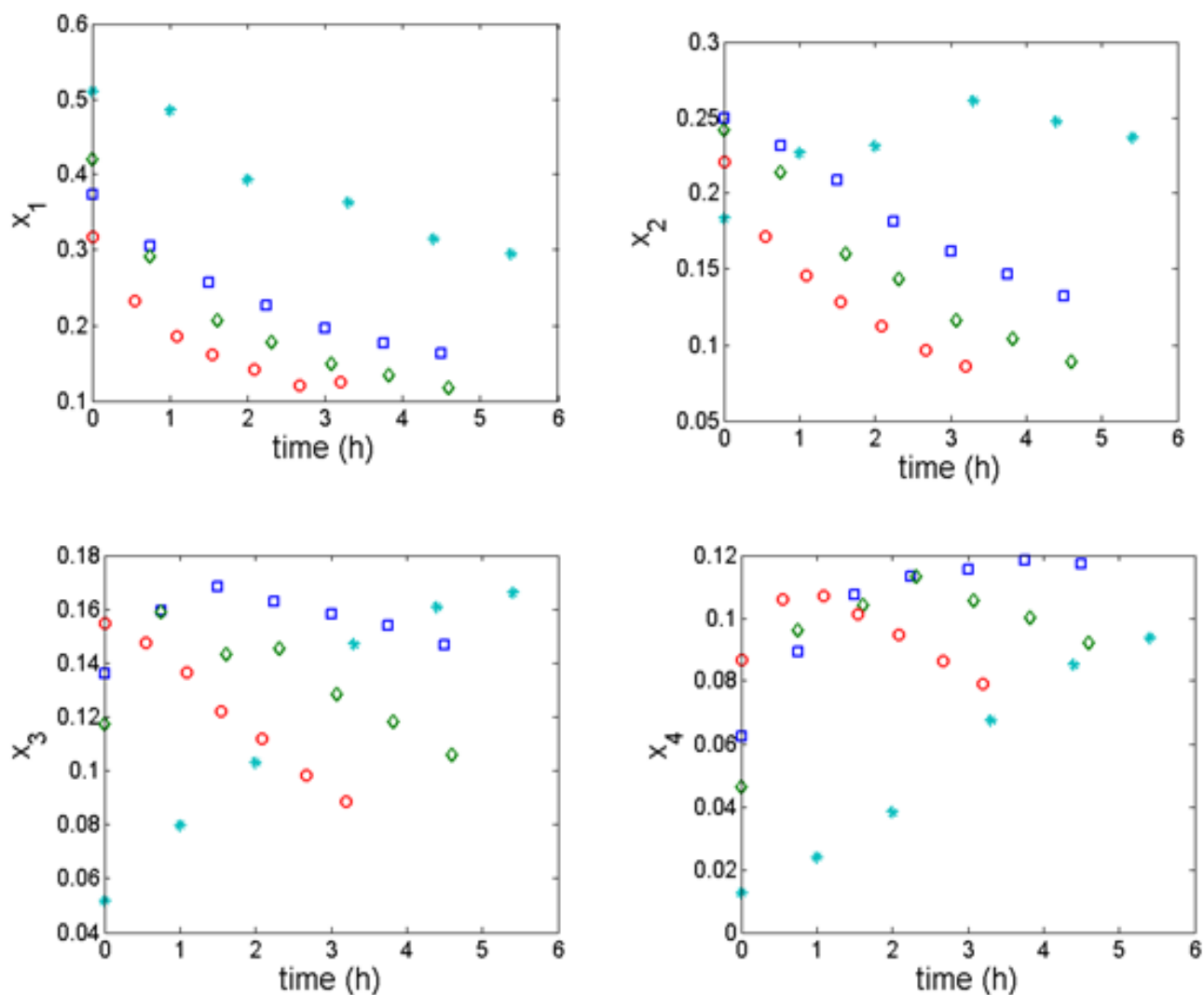


Figure 3.5 - Oligomers mole fraction as a function of time, bulk phase: \* 130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

For all studied temperatures, lactide concentration is reported in Figure 3.6. For all the reactions, lactide concentration increases in the first hour achieving a plateau value for larger reaction times. This suggests that lactide is being formed in the beginning achieving an equilibrium stage for long reaction times.

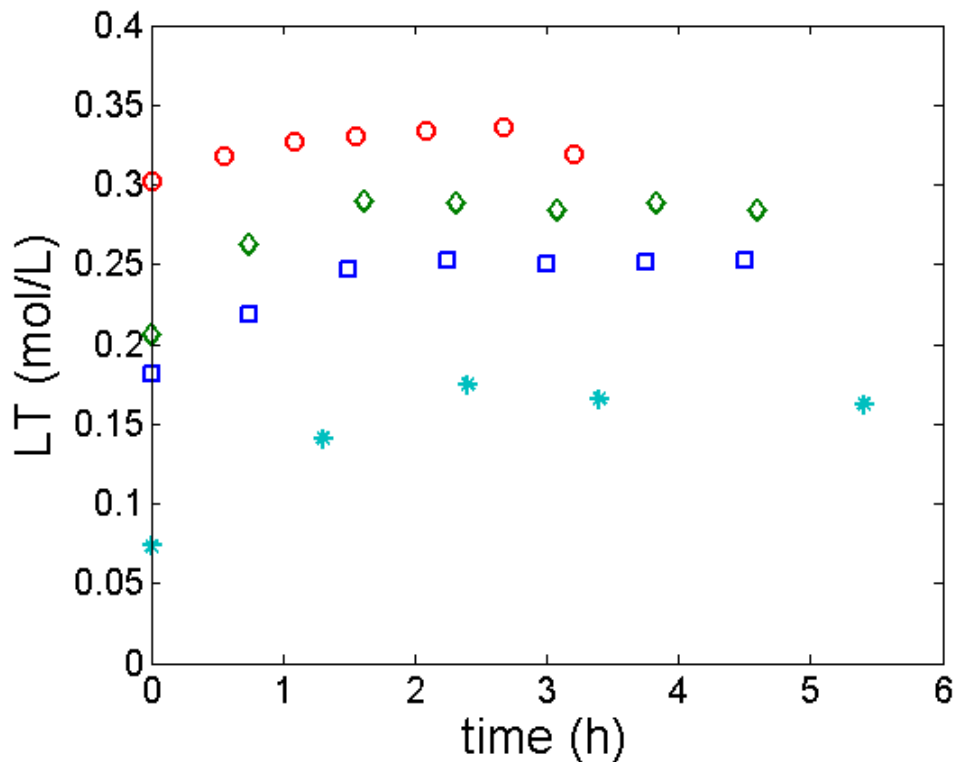


Figure 3.6 - Lactide concentration in bulk as a function of reaction time: \* 130 °C; □ 150 °C; ◇ 170 °C; ○ 190 °C.

### 3.1.2 Gas Phase

The cumulative masses of the species in the condensed gas phase are plotted in Figure 3.7. For the reaction performed at the lowest temperature this data is not available. Only water, monomer, dimer and lactide were detected and, as expected, the main component was water, being monomer, dimer and lactide present only in small traces. These findings prove that, under these operating conditions, apart from water, the volatilization of other species can be neglected in the development of a model for polycondensation.



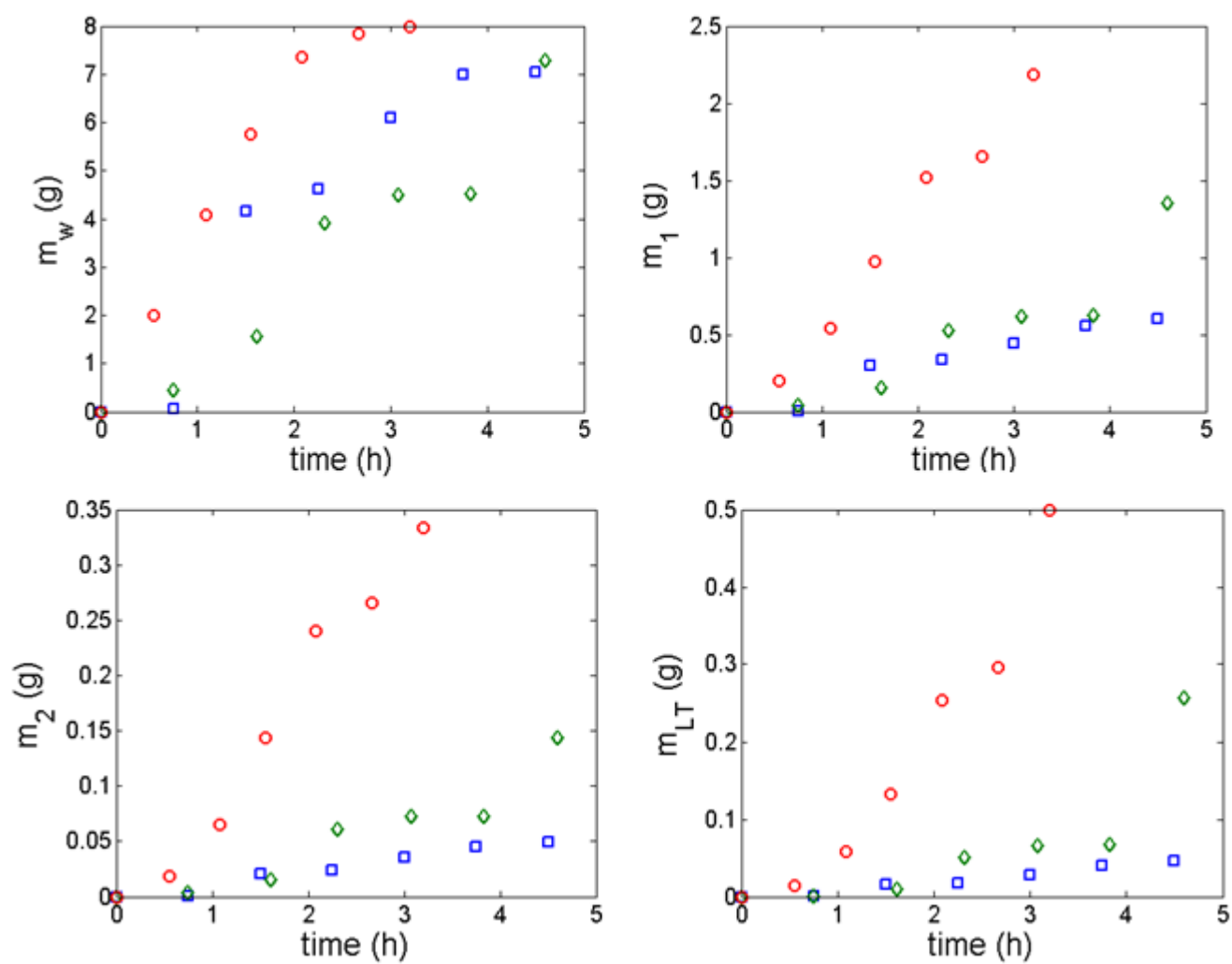


Figure 3.7 - Cumulative mass of the condenser species as a function of reaction time:  $\square$  150 °C;  $\diamond$  170 °C;  $\circ$  190 °C.

## 4 Lactide Production

In this chapter, the results concerning lactide production reactions are reported. As previously discussed (Chapter 2), these reactions involve two steps, a lactic acid polycondensation step performed at 130 °C over the night (15 h) under nitrogen flow, and a second step aimed to lactide production carried out at higher temperatures (190 – 210 °C) and low pressures (25 – 5 mmHg), with and without catalyst. Due to the difficulties in obtaining complete oligomer separation by HPLC, GPC was used to determine the molecular weight of the polymer samples and, moreover, components mass fractions are used instead of mole fraction. In the next sections, the effect of temperature, pressure and catalyst addition on the lactide production step is discussed from a qualitative point of view.

### 4.1 Experimental results

#### 4.1.1 Temperature effect

Three reactions at different temperatures (190, 200 and 210 °C, at 25 mmHg without catalyst), were performed in order to evaluate the effect of temperature on lactide production.

The time evolutions of the liquid volume are shown in Figure 4.1; as expected, higher temperatures lead to larger volume change.

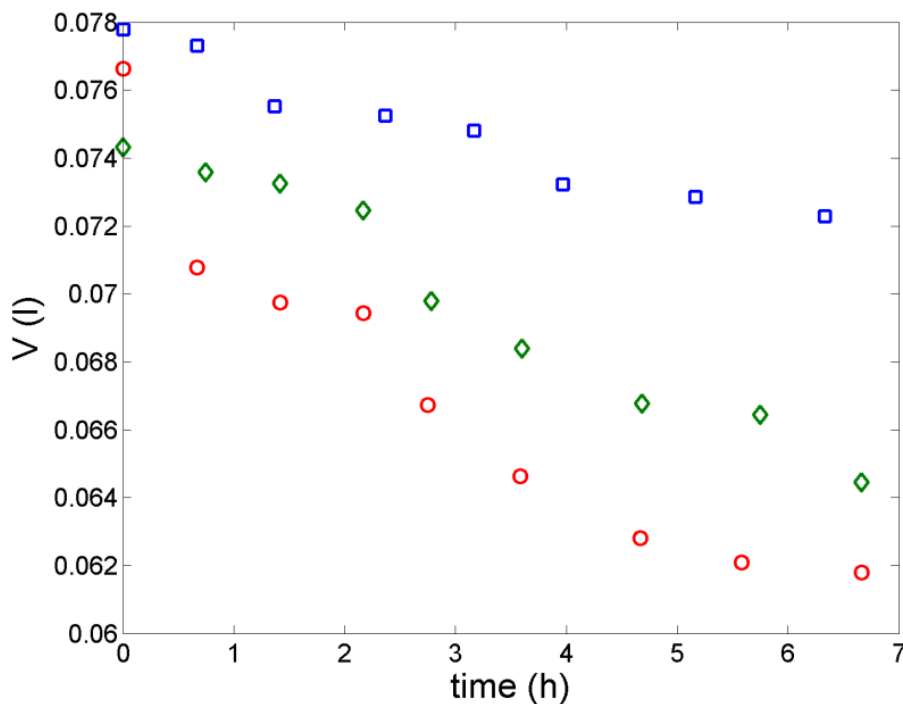


Figure 4.1 - Bulk volume as a function of reaction time:  $\square$  190 °C;  $\diamond$  200 °C;  $\circ$  210 °C.

The molecular weight as a function of time is shown in Figure 4.2. For all the reactions, molecular weight increases at increasing reaction time. As detailed in Chapter 1, lactic acid polycondensation and lactide formation are parallel reactions. In this frame, from the experimental data it can be concluded that even with conditions reported to be favourable to lactide production, polycondensation reaction is still the main reaction occurring. For the reactions carried out at 200 and 210 °C, no significant difference in reactivity was noticed during the first 4 hours of reaction. At larger reaction times,  $M_n$  attained plateau values of 2300 and 2700 Da for the two reactions, respectively.

The water concentration as a function of time is depicted in Figure 4.3. Such overall concentrations are lower compared to those of the reactions discussed in Chapter 3. Again, the reactions carried out at 200 and 210 °C showed similar water profile; on the other hand, no conclusions can be drawn for the reaction carried out at 190 °C due to data scattering.

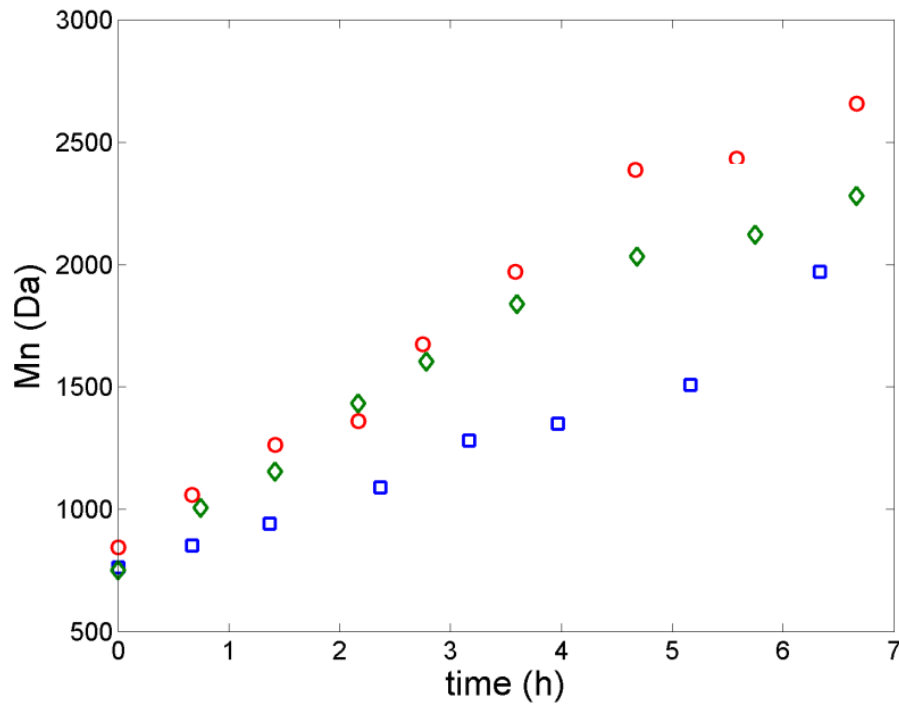


Figure 4.2 - Polymer molecular weight as a function of time for different reaction temperatures:  $\square$  190 °C;  $\diamond$  200 °C;  $\circ$  210 °C.

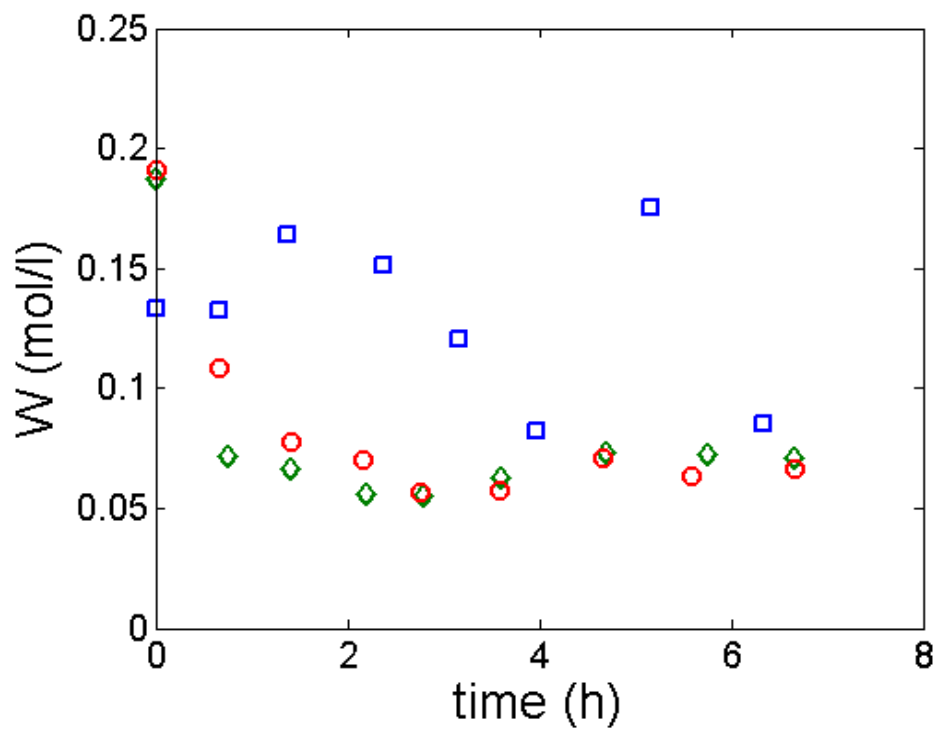
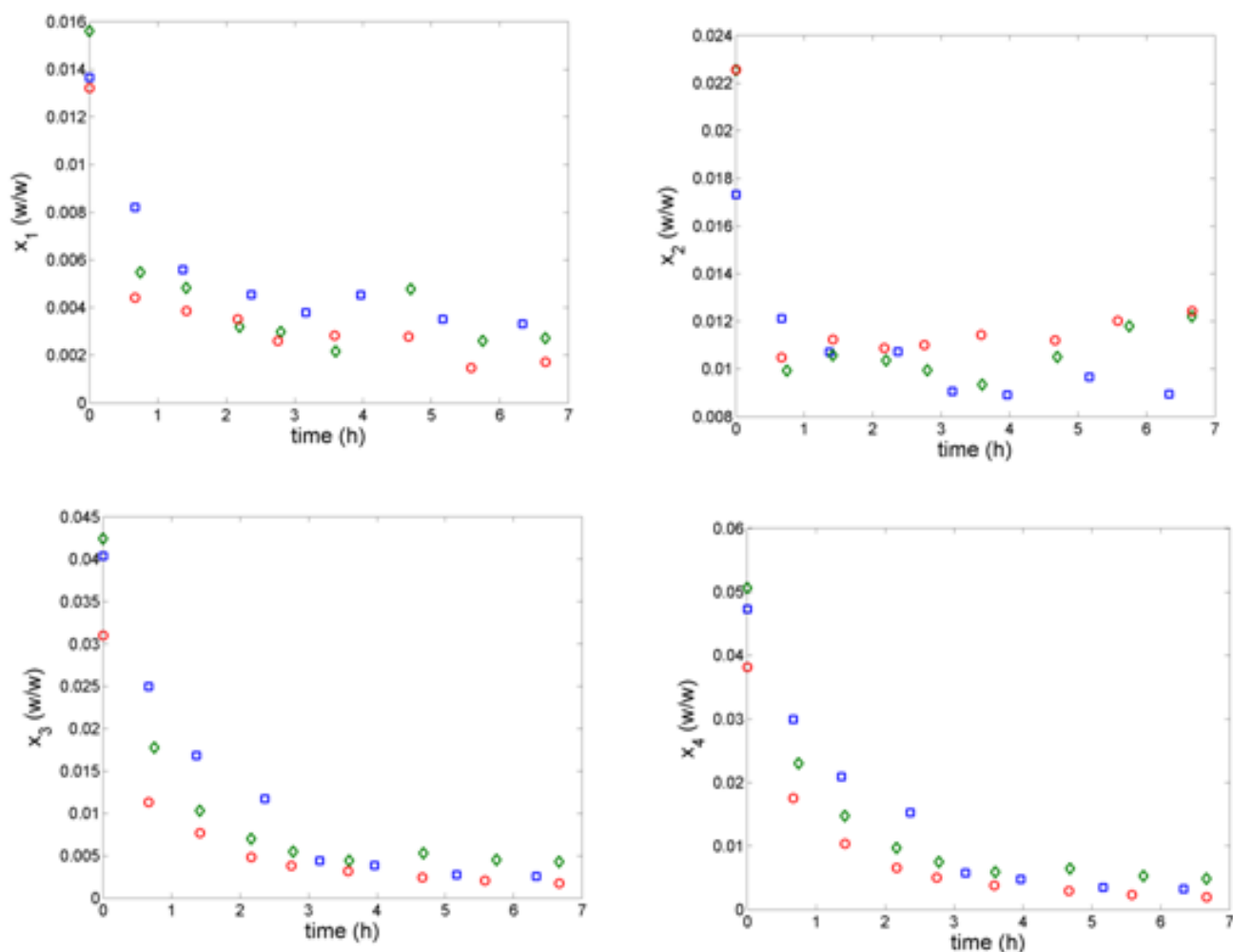


Figure 4.3 - Water concentration in bulk phase as a function of time:  $\square$  150 °C;  $\diamond$  170 °C;  $\circ$  190 °C.

The concentration profiles for monomer, dimer, trimer and tetramer are shown in Figure 4.4 for all the temperatures and all the components. In all cases, very similar behaviours are exhibited, with weight fraction decreasing during all the reaction and achieving plateau values at long reaction times. Compared to the reactions in Chapter 3, the major difference is that all the short oligomers are “consumed” to produce longer chains, thus producing higher molecular weight polymer.



4.4 - Oligomers weight fraction as a function of time, bulk phase:  $\square$  190 °C;  $\diamond$  200 °C;  $\circ$  210 °C.

The lactide mass fraction for the different reaction temperatures is shown in Figure 4.5. Surprisingly, the weight fraction of lactide is constant at all studied temperatures, with values ranging from 0.04 to 0.055 % (w/w). However, compared to the reactions in Chapter

3, lactide was found in the condenser in much large amount. The cumulative weight of water, monomer, dimer and lactide collected in the condenser is plotted in Figure 4.6: the most abundant component in the collected mixture is lactide. The plateaus of liquid phase composition and accumulation in the condenser for lactide suggest that the reactions leading to lactide production exhibit fast kinetics and equilibrium conditions are quickly established. Thus, lactide removal is the limiting step of the process.

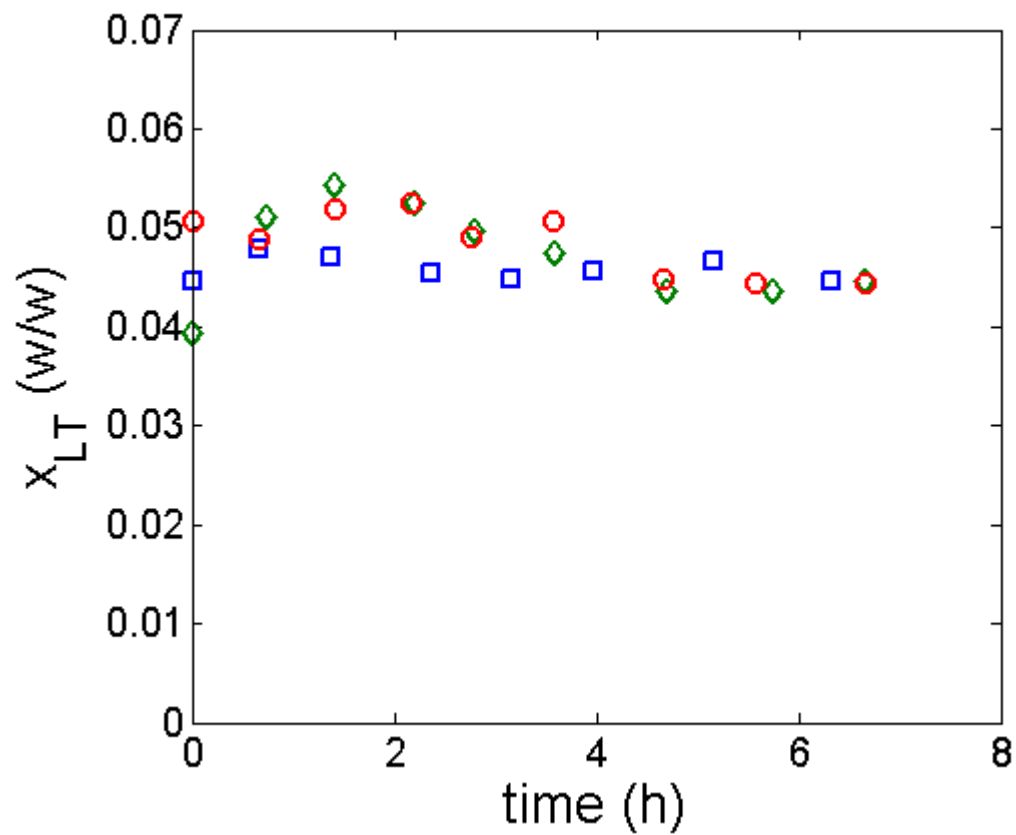


Figure 4.5 - Lactide mass fraction as a function of time:  $\square$  190 °C;  $\diamond$  200 °C;  $\circ$  210 °C.

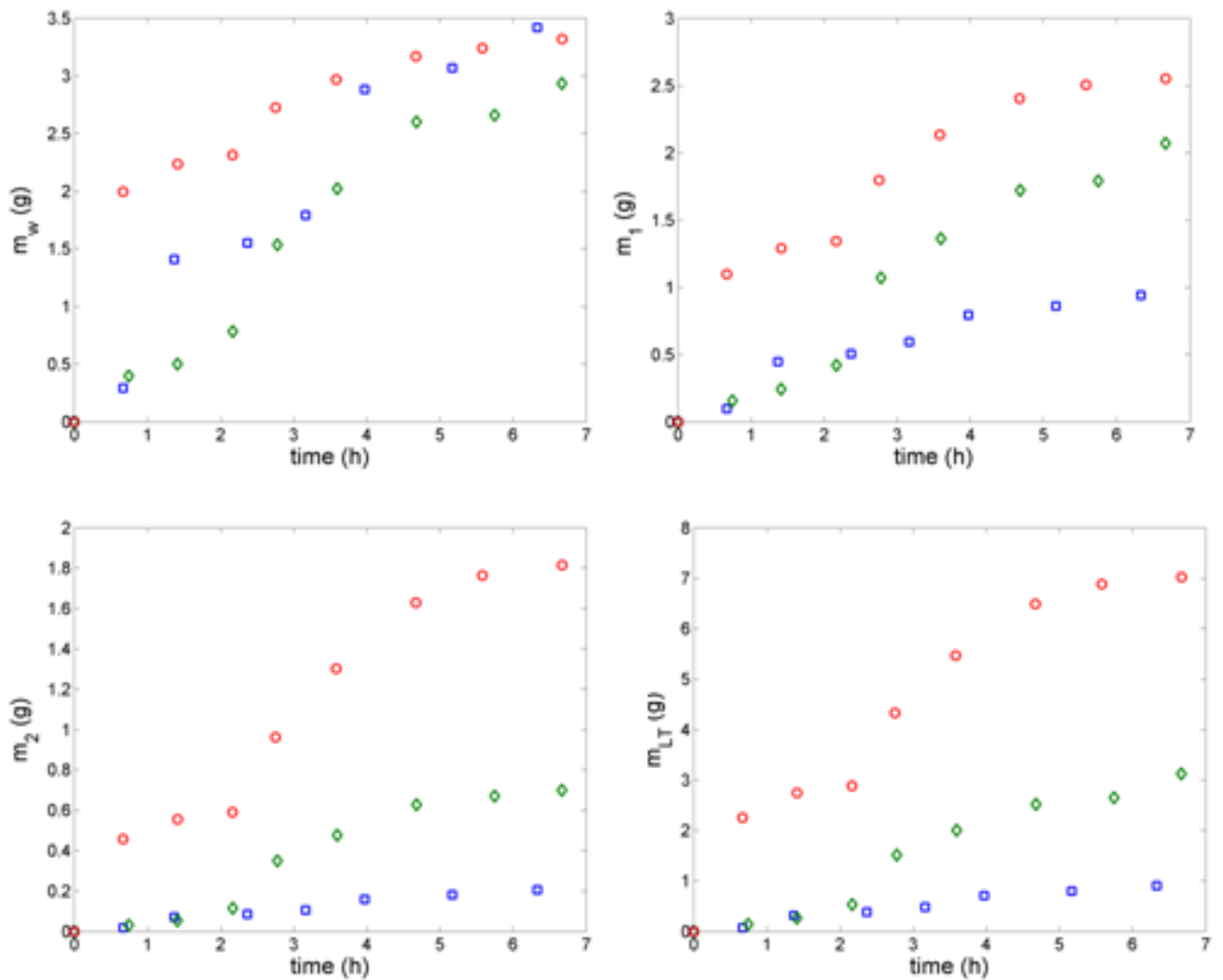


Figure 4.6 - Cumulative mass of water, monomer, dimer and lactide in condensed gas phase:  $\square$  190 °C;  $\diamond$  200 °C;  $\circ$  210 °C.

#### 4.1.2 Pressure effect

In order to evaluate the effect of pressure, two reactions were performed at 190° C without catalyst, at 25 mmHg and 10 mmHg.

The time evolution of the bulk volume is shown in Figure 4.7, while  $M_n$  is reported in Figure 4.8. As expected, the change in volume was higher for the reaction at lower pressure. For the reaction carried out at 25 mmHg, a linear

increase of  $M_n$  vs time was experienced, while  $M_n$  increased faster and attained a plateau value of circa 2500 Da for the reaction carried out at 10 mmHg.

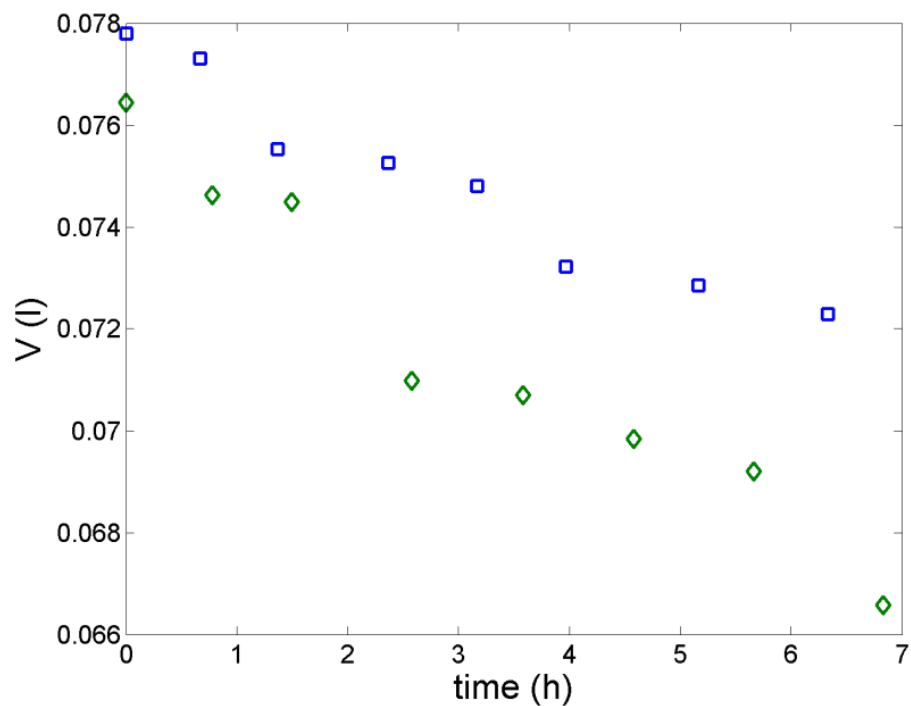


Figure 4.7 - Change in bulk volume for reactions at different pressures:  $\square$  25 mmHg;  $\diamond$  10 mmHg.

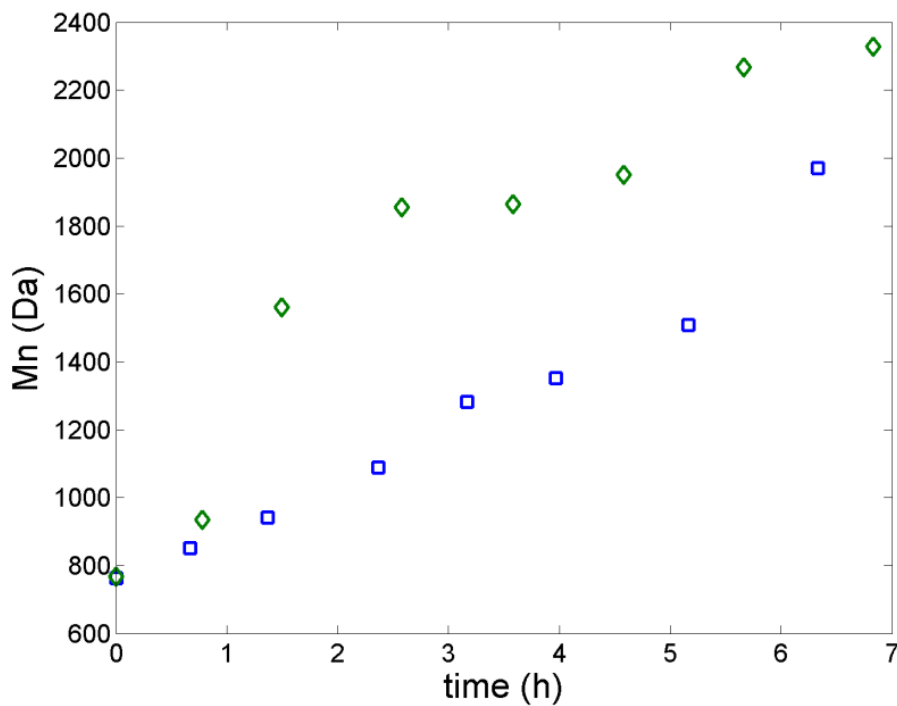


Figure 4.8 - Molecular weight as a function of reaction time:  $\square$  25 mmHg;  $\diamond$  10 mmHg.



The water concentration is shown in Figure 4.9; a lower concentration of water is found in the reaction performed at lower pressure. Moreover, both reactions show quite constant water concentration profiles but with a significant data scattering.

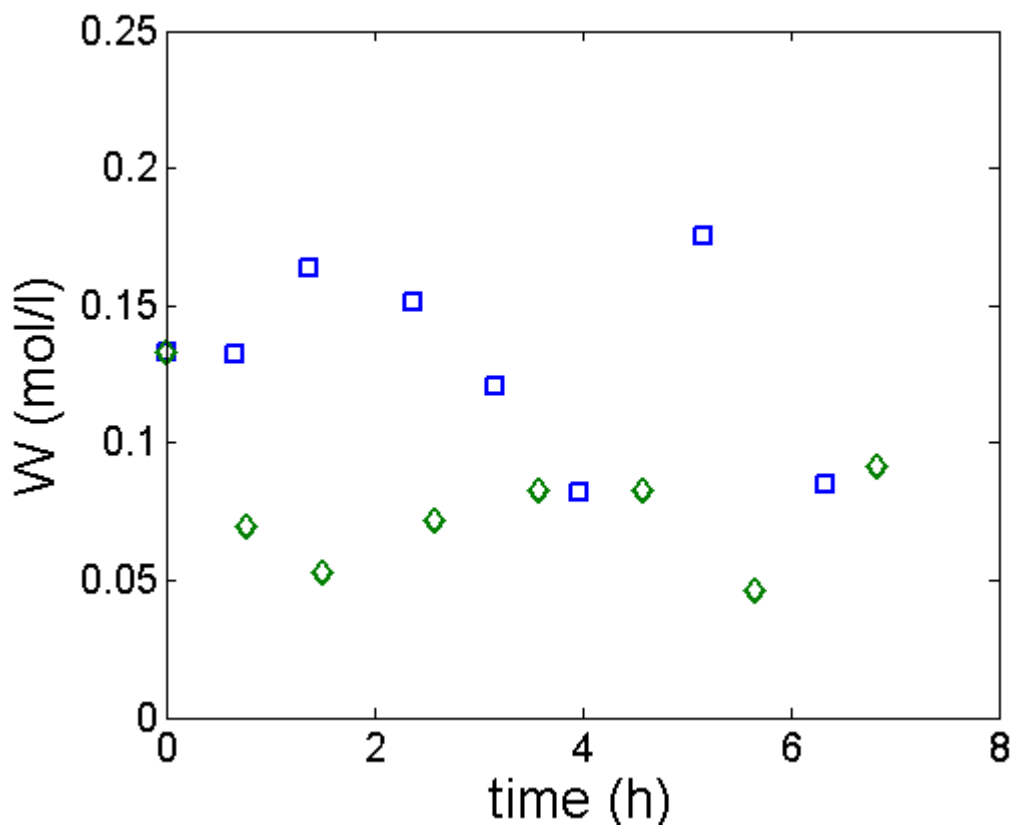


Figure 4.9 - Water concentration in the bulk as a function of time:  $\square$  25 mmHg;  $\diamond$  10 mmHg.

The oligomers weight fractions are shown in Figure 4.10. Monomer and dimer weight fractions decrease much faster in time for the reaction performed at 10 mmHg. On the other hand, larger oligomers do not present large differences. This is in agreement with the assumption reported in Chapter 3 about the ranking of volatilities, being monomer and dimer much more volatile than longer chains.

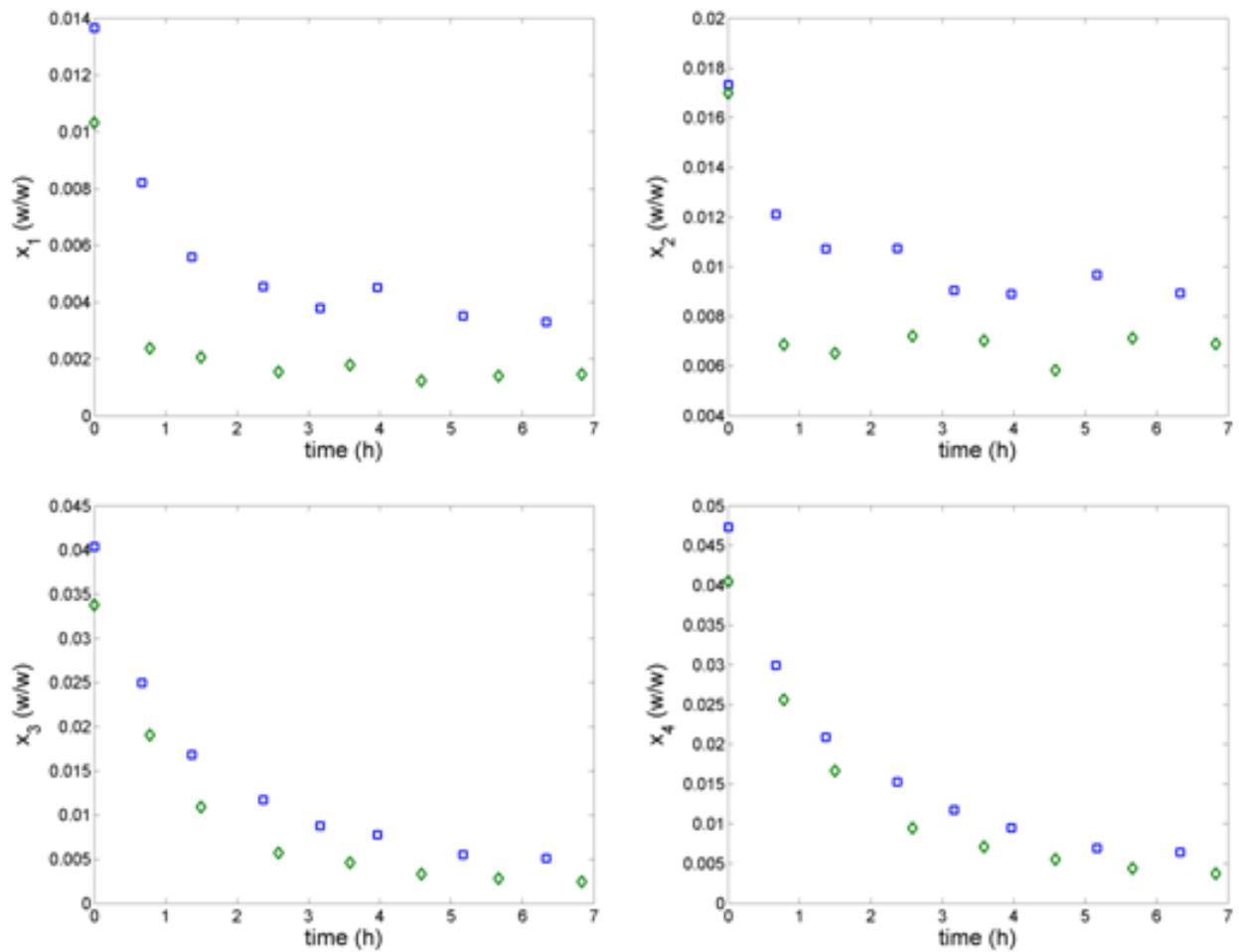


Figure 4.10 - Oligomers weight fraction versus reaction time:  $\square$  25 mmHg;  $\diamond$  10 mmHg.

About the lactide weight fraction, again a plateau value is found. This value is shown in Figure 4.11. In particular it can be noticed that lactide weight fractions of 0.035 and 0.045 % (w/w) were obtained for the reaction carried out at 25 mmHg and 10 mmHg, respectively. This is apparently not in agreement with what proposed previously regarding the fast kinetic of lactide reactions and attendance of equilibrium conditions, since pressure should not affect the equilibrium constants. On the other hand the lower the pressure the larger the volatility of lactide.

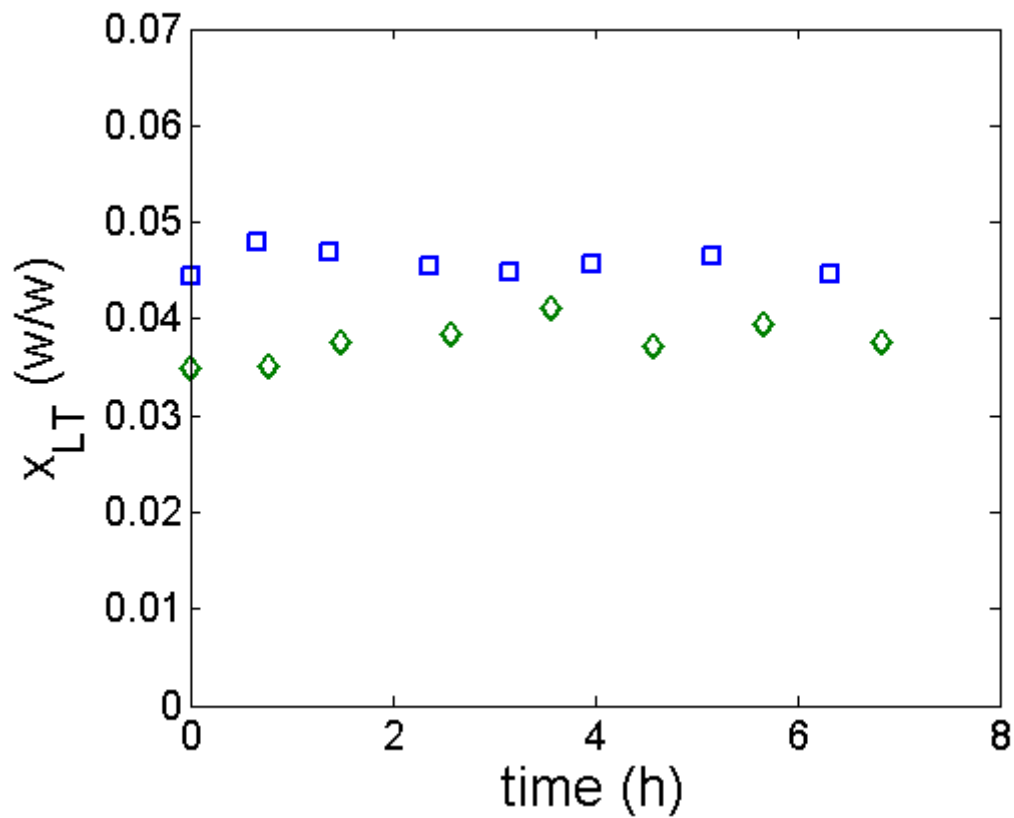


Figure 4.11 - Lactide weight fraction over time for the reaction performed at 25 mmHg ( $\square$ ) and 10 mmHg ( $\diamond$ )

Finally, the cumulative mass of lactide and lower oligomers collected in the condenser is shown in Figure 4.12. The amount of collected species was much higher compared to the reaction performed at higher pressure, as expected from the analysis of the change in bulk volume (Figure 4.7).

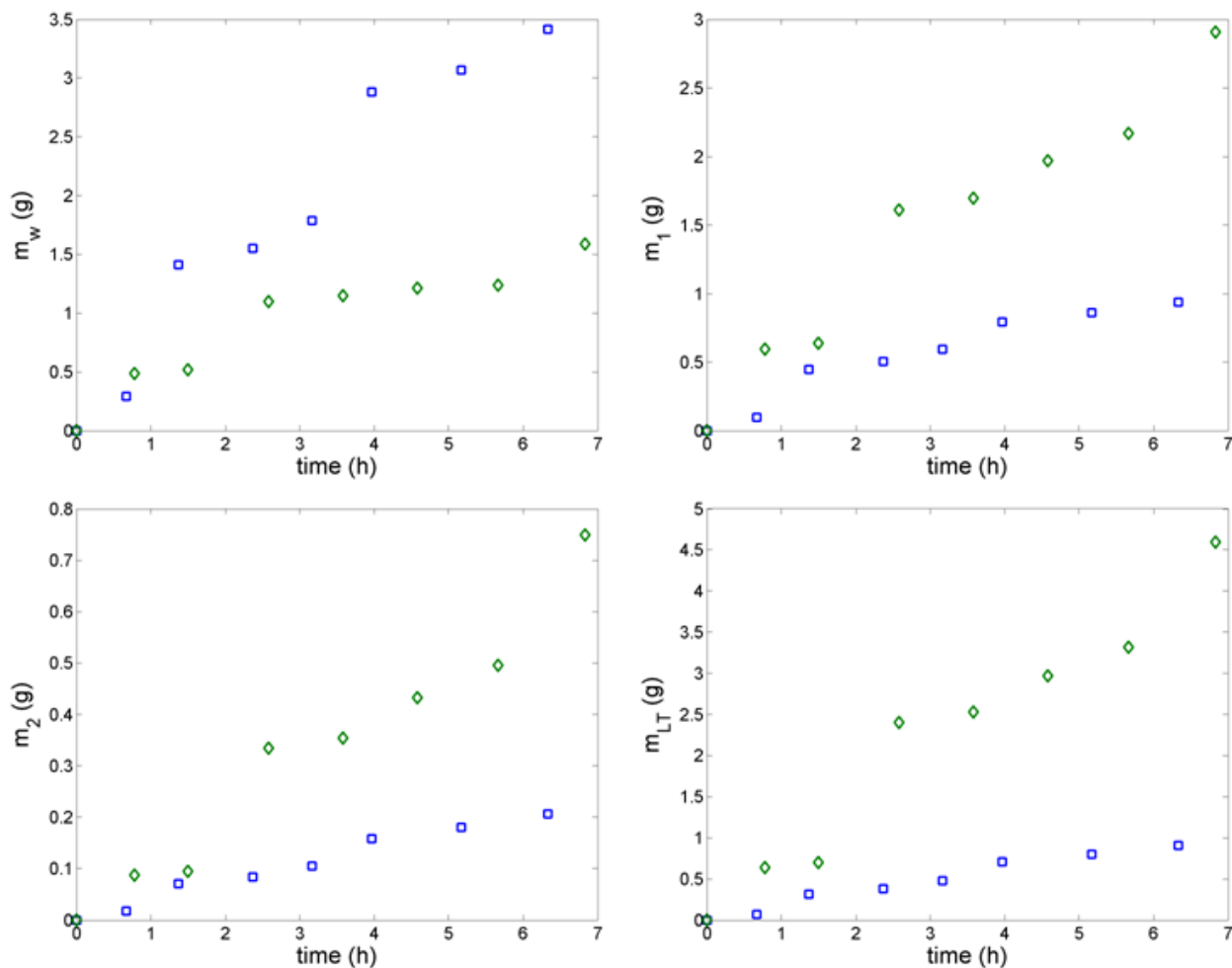


Figure 4.12 - Cumulative mass of water, monomer, dimer and lactide in condensed gas phase:  $\square$  25 mmHg;  $\diamond$  10 mmHg.

### 4.1.3 Industrial Conditions

In order to enhance the volatility of lactide, a reaction was performed at 200 °C, 5 mmHg and 0.25 % (w/w) of Sn(II)oct catalyst. These conditions are the ones used in industry and moreover, tin octoate is also reported in literature to enhance the lactide production [1]. The results for the bulk samples are reported bellow. In the end of the 3 hours of reaction, 40 grams of crude lactide were collected. Crude lactide is the lactide collected which is not pure and contains traces of monomer, water and linear dimer.

The change in the bulk volume (Figure 4.13) was more than the double compared to the previous reactions, and in half the reaction time.

The molecular weight over time for this reaction is reported in Figure 4.14. The maximum value of all the reactions performed in this thesis was achieved in this reaction, in only 3 h. This fact proves once again that polycondensation and lactide formation are parallel reactions and the selectivity of the lactide reaction over the polycondensation is difficult to achieve.

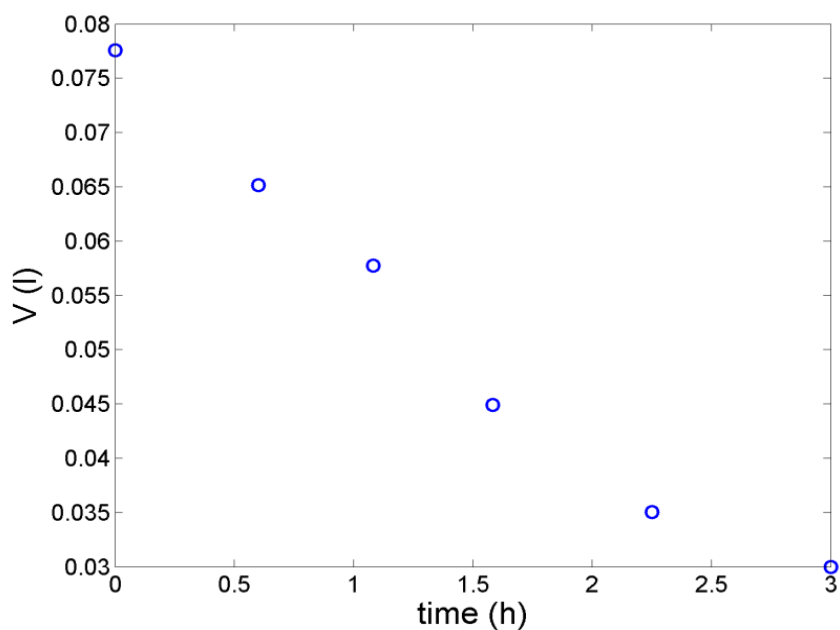


Figure 4.13 - Volume change for the reaction performed at industrial conditions.

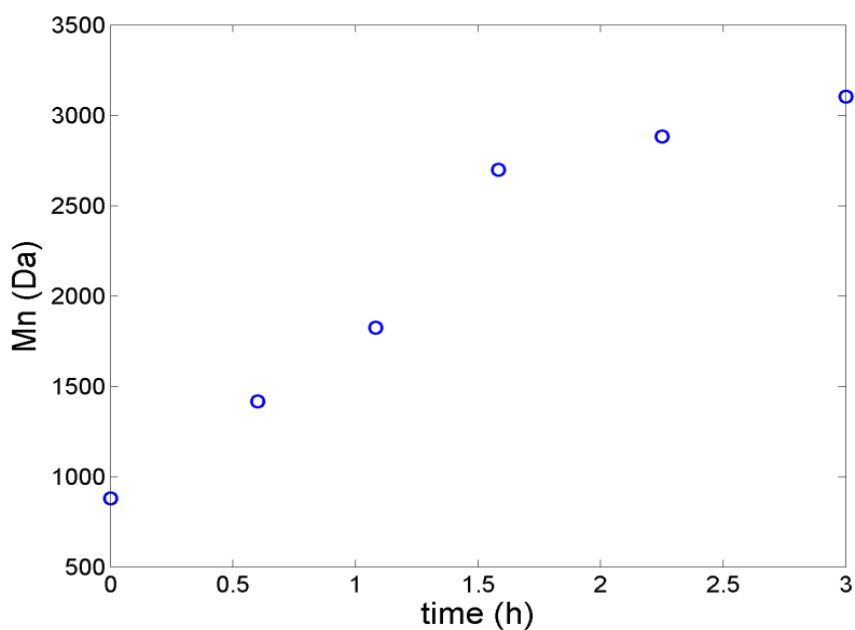
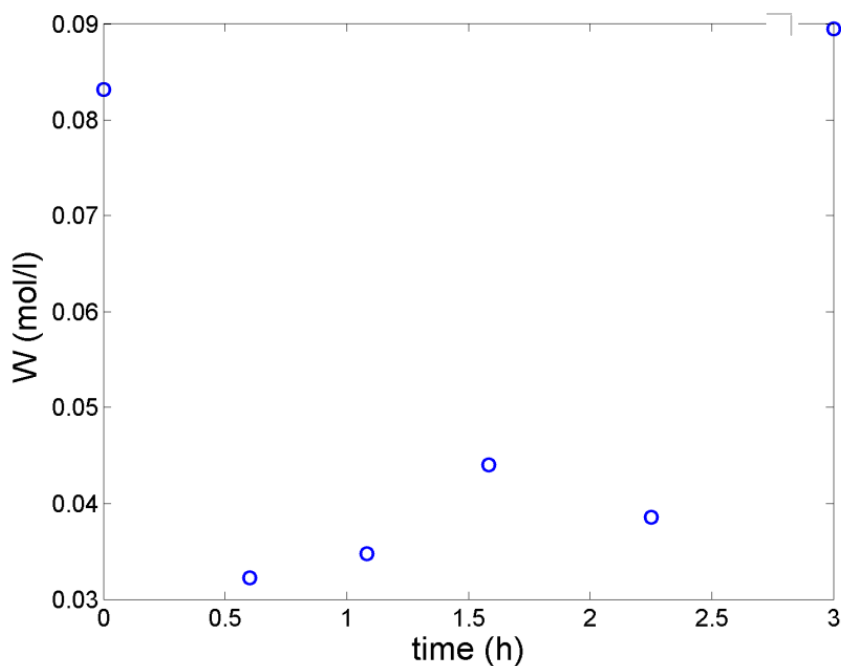


Figure 4.14 - Number average molecular weight over time for the reaction performed at industrial conditions.

The water concentration values for the last reaction, plotted in Figure 4.15, were also the lowest among all the reactions performed. Moreover the plateau value for the water concentration was achieved faster than for all other reactions.



*Figure 4.15 - Water concentration in bulk as a function of reaction time for the last reaction performed.*

Monomer, dimer, trimer and tetramer weight fractions are plotted in Figure 4.16.

In concern to lactide, again a weight fraction plateau was achieved. Moreover, this plateau value was the same as for the other reaction performed, without catalyst. These results are depicted in Figure 4.17. Since that even at these experimental conditions lactide is still in equilibrium in the system, it can be concluded that the catalyst does not have effect in the lactide production but just affects the polycondensation rate.

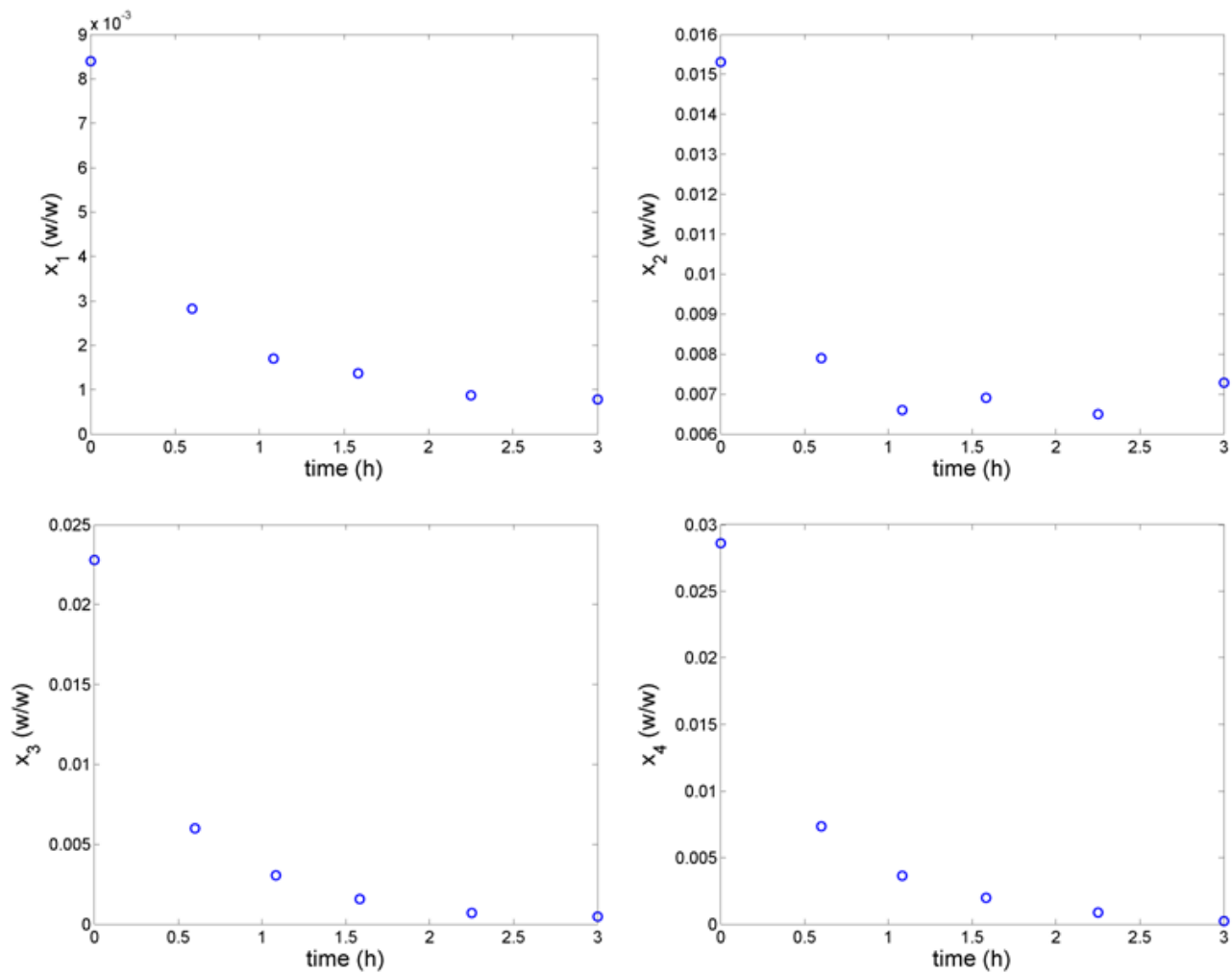


Figure 4.16 - Oligomers weight fraction as a function of reaction time for the reaction performed at industrial conditions.

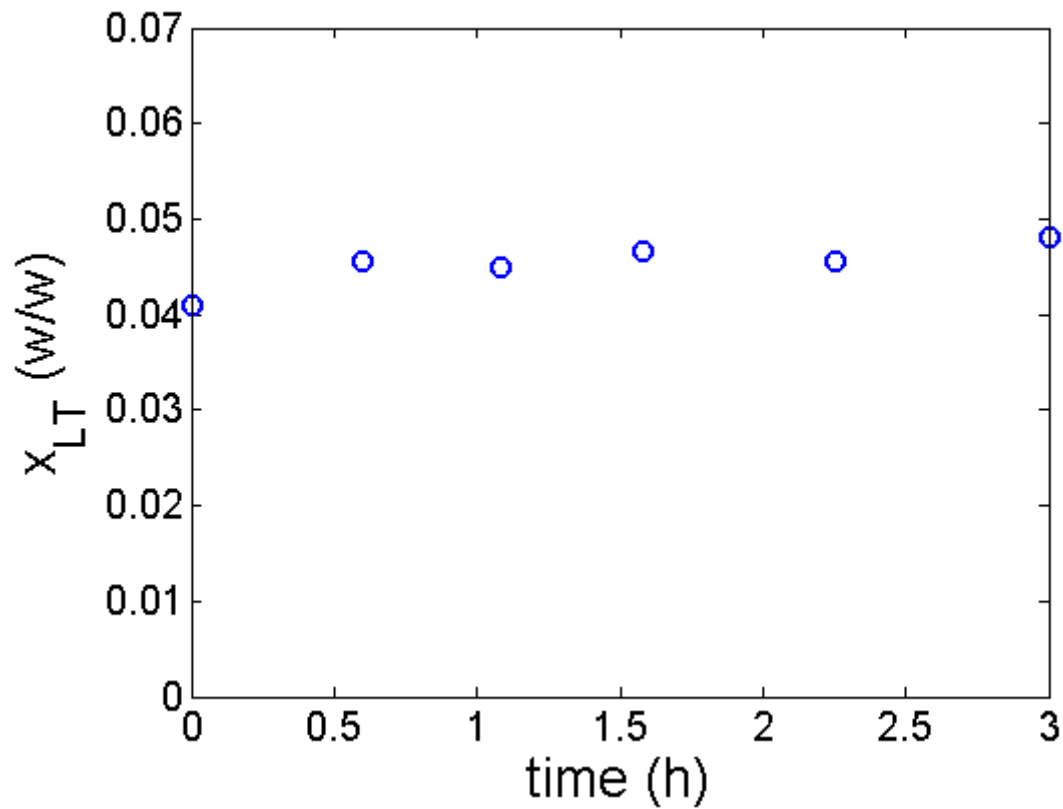


Figure 4.17 - Lactide weight fraction over reaction time for the reaction performed at industrial conditions.

The cumulative mass collected in the condenser for this reaction is shown in Figure 4.18. An amount of 35 grams of pure lactide were collected, which is a much higher value compared to the previous reactions performed. With these results it is clear that lactide reactions are in equilibrium in the system.



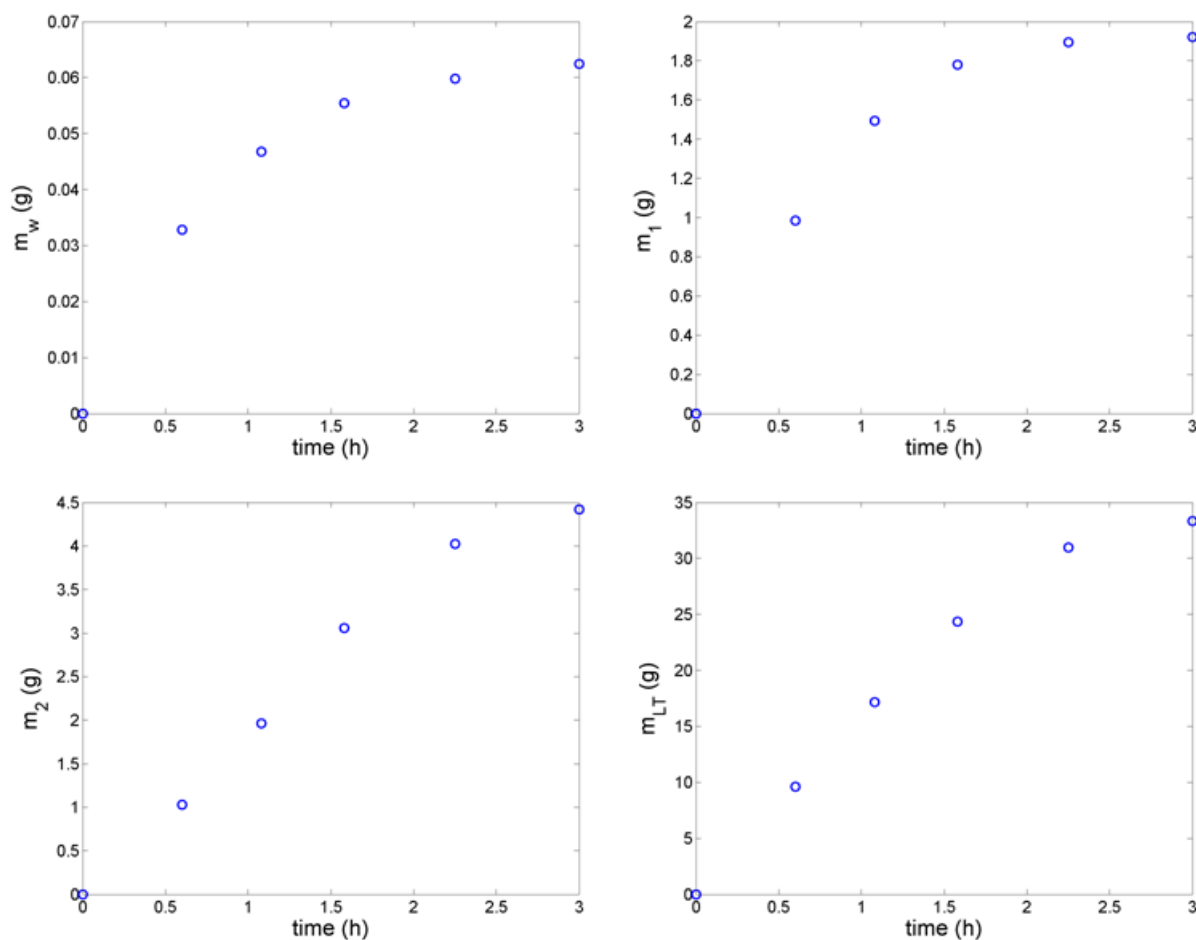


Figure 4.18 - Cumulative mass in the condenser for the reaction performed at "extreme" conditions.

## References

1. Yoo, D.K., D. Kim, and D.S. Lee, *Synthesis of lactide from oligomeric PLA: Effects of temperature, pressure, and catalyst*. *Macromolecular Research*, 2006. 14(5): p. 510-516.

## 5 Model development

In this chapter the developed model accounting for both lactic acid polycondensation and lactide production is reported. As a future work the model will be used to evaluate the parameters involved in the process.

### 5.1 General background

As already mentioned in Chapter 1, polycondensation (PC) is a reversible polymerization reaction which follows a step growth mechanism. It involves a carboxylic acid (*COOH*) and an alcoholic (*OH*) group of two polymer chains of length *n* and *m*, respectively, which react together to produce a polymer chain of length *n+m* with the formation of an ester bond (*E*) and the release of water (*W*). The produced water may react with polymer, thus introducing reversibility in the system. PC is described by the general scheme:



It is worth to mention that, due to the lack of experimental data, PC systems are often modelled focusing on functional groups rather than on all the species at different chain lengths [1-2]. In this frame, the previous scheme reduces to:



In the present work, due to the highly detailed experimental data obtained (see Chapter 2), PC is modelled distinguishing all the different chain lengths.

Two main approaches were used in the literature to model PC reaction, the probabilistic approach, based on the randomness feature of the stepwise mechanism, and the deterministic approach, based on kinetic rate equations.

Fundamental studies of PC were carried out mainly by Carothers[3] and Flory[4]. In particular, using the probabilistic approach, Flory described the molar and weight mole fraction distributions,  $P_x$  and  $W_x$  respectively, as well as the polymer average properties, such as number average molecular weight ( $M_n$ ), weight average molecular weight ( $M_w$ ) and polydispersity index (*PDI*), as a function of the extent of reaction, *p*, as:

$$p = \frac{N_0 - N}{N} \quad (3)$$

$$W_x = xp^{x-1}(1-p)^2 \quad (4)$$

$$P_x = p^{x-1}(1-p) \quad (5)$$

$$M_n = M_0 \frac{1}{1-p} \quad (6)$$

$$M_w = M_0 \frac{1+p}{1-p} \quad (7)$$

$$PDI = 1 + p \quad (8)$$

where  $N$  and  $N_0$  represent the total number of non reacted repeating units at the generic reaction time and the initial number of repeating units, respectively. The previous equations were obtained under the following assumptions:

- a) equal reactivity of functional groups independently upon polymer chain length;
- b) equal reactivity of all linkages (degradation kinetic independent upon ester groups);
- c) negligible side reactions, such as cyclization and transesterification.

In Figures 5.1 and 5.2, weight and mole fraction distributions, as described in Formulas 4 and 5, are plotted as a function of the extent of reaction. About  $W_x$ , it is worth to notice that the monomer is the most abundant specie at reaction extents smaller than 0.5, while at larger  $p$  a maximum in the distribution is found and increases at increasing  $p$ . On the other hand, the mole fraction distribution does not present a maximum for any  $p$  and the monomer is always the component present in larger amount. Moreover, from equation 6, the maximum theoretical  $PDI$  which can be obtained is 2 for  $p$  equal to unity.

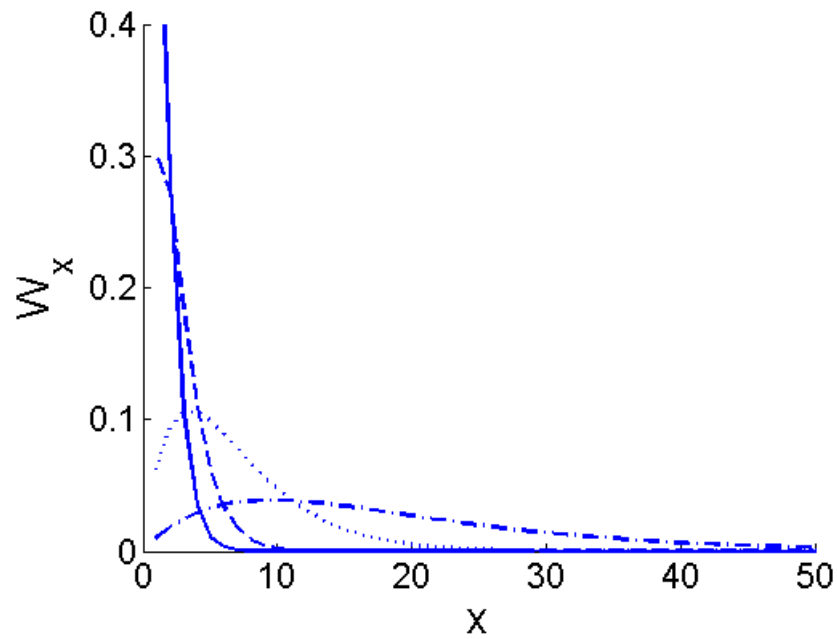


Figure 5.1 -  $W_x$  distribution as a function of  $p$  ( $p=0.25$  —,  $p=0.45$  - -,  $p=0.75$  ···,  $p=0.9$  -·-·).

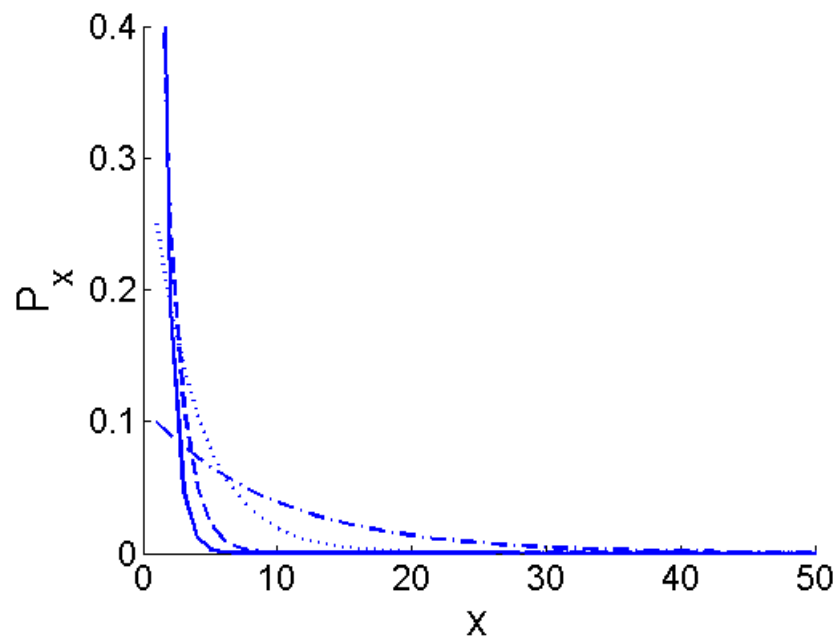


Figure 5.2 -  $P_x$  distribution as a function of  $p$  ( $p=0.25$  —,  $p=0.45$  - -,  $p=0.75$  ···,  $p=0.9$  -·-·).

The previously discussed statistical approach represents the basis of the PC reaction modelling. It is based on strong assumptions which were found to be valid for certain

polymers and conditions, such as large extent of reaction and no influence of diffusion limitations [5].

More recently, a kinetic approach was adopted and various models, differing mainly in terms of model assumptions and kinetic scheme, were proposed. A comprehensive description of the basic equations involved, as long as the different solution methods applied, has been reported by Dotson et al. [6]. In particular, moment discrete method and direct sequential solution are commonly used. By means of the first method, the polymer molecular weight distribution (MWD) is described through the definition of specific moments and the average polymer properties ( $M_n$ ,  $M_w$  and PDI) can be readily evaluated. Using the second method, the mass balance equations (MBEs) of all the species and involving all the reactions, are solved leading to a more complex and computationally demanding solution but with the major advantage of the direct evaluation of the entire MWD.

In the present work, kinetic approach and direct sequential solution of population balance equations (PBE) and MBEs have been adopted. In the next section, kinetic scheme as well as model assumptions and equations, are reported.

## 5.2 Model assumptions and equations

In order to define a comprehensive kinetic scheme, accounting for both PC and LT formation reactions, the model assumptions already discussed are revised and extended including all observations and information found in the literature.

The following assumptions are introduced:

- *monomer has different reactivity than larger oligomers*

From chemical equilibrium studies (performed in this research group but not yet published [7]) it was noticed that LA presents different reactivity compared to larger oligomers. This finding is in agreement with literature data on both PLA [8] and other polycondensation systems [5]. On the other hand, it was shown that the assumption of reactivity independent upon chain length is reasonable and does not introduce large errors in the modelling of lactic acid polycondensation [7, 9]. In this frame, the model equations

are derived accounting for the different reactivity of LA and this assumption will be further discussed in the next chapters.

- *ideal system behavior*

It is reported in the literature that PC processes, such as Nylon 6,6 [2, 10-11] and PET [1] productions, exhibit non ideal behaviour. In particular, it was reported that kinetic and equilibrium constants, defined in terms of concentrations, show composition dependence especially at high degree of polymerization. Since non ideal behaviour affects both kinetic and transport phenomena, the assumption of ideal system can lead to large error in the model prediction. However, while Nylon and PET are polymers produced by PC until high molecular weight (HMW), LA polycondensation is applied only up to low conversion and low degree of polymerization: under such conditions, the extent of non-ideality is limited and the assumption of ideal system is considered reasonable.

- *negligible formation of large cyclic compounds by intramolecular reactions*

It is reported in the literature that the formation of cyclic species is a function of the reaction temperature and the size of the ring formed. Cycles formation and equilibrium between linear and cyclic chains can be described by the Jacobson-Stockmayer theory [12]. In their original study, the authors have investigated the equilibrium molecular size distribution of different polycondensation systems. For cycles larger than 15 units, short range steric effects do not play any role and thus the probability of ring closure can be expressed as a function of ring size. At such conditions, the formation of cycles with size larger than 4 was found negligible. In the frame of this work, it is assumed that LT is the only cyclic compound formed at a significant extent.

For PLA, Kèki et al. [13] have recently investigated the formation of cycles occurring in PLA polycondensation through MALDI-TOF investigations. The monomer used was D,L lactic acid and cycles were formed at large extent only for reaction temperature larger than 180°C. Moreover, the ring-chain equilibrium constants have been reported for different temperature and different chain length (data are shown in Figure 5.3).

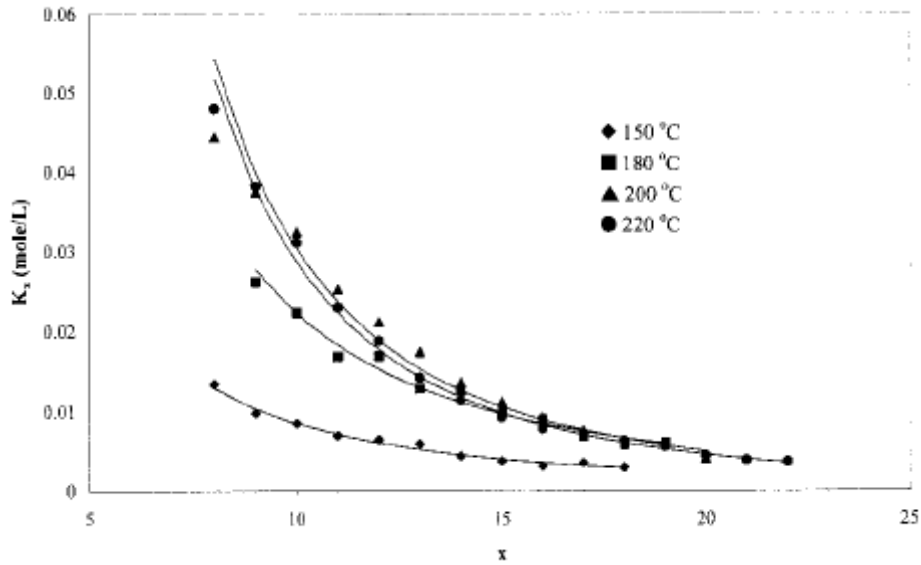
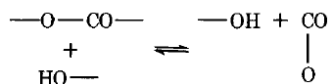


Figure 5.3 - Concentration based equilibrium constants.

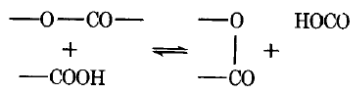
- Interchange reactions are negligible

Kotliar reported the different kind of interchange reactions occurring in polyesters and their mechanisms [14]. Mainly three reactions are distinguished and are intermolecular alcoholysis, intermolecular acidolysis and transesterification (see Figure 3.4).

Intermolecular alcoholysis:



Intermolecular acidolysis:



Transesterification:

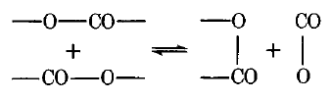


Figure 5.4 - Interchange reactions occurring in PC (from Kotliar[14]).

Out of all the reactions involved, alcoholysis is the most favorable in PC of lactic acid. It consists in the attack of a hydroxyl group to an ester group of a different polymer chain which results in a size reduction of the attacked chain and size elongation of the chain

inducing the reaction. Many works reported in the literature for polycondensation systems are focused on the estimation of the interchange reaction kinetic parameters but large discrepancies in the values are present. For this reason and since no evidence was previously reported about the occurrence of interchange reactions in the PLA case, such reactions are not considered in the present work.

- *molecular diffusion does not affect the reaction kinetic*

In general, the kinetic of polymerization can be influenced by the diffusion of macromolecular chains in the reaction mixture [15-16]. However, due to the limited extent of reaction achieved in the present work, it is reasonable to assume that the diffusion of the oligomers is fast enough to have a negligible effect, or no effect at all, on the reaction kinetics.

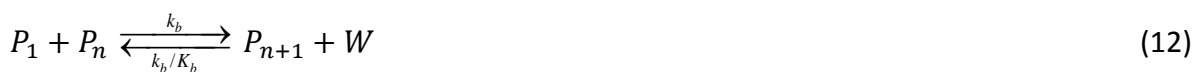
- *water, LA and LT only are considered volatile*

In a recent publication by Achmad et al. [17], it is reported that under vacuum condition (10 mmHg) mainly water, LA and LT are detected in gas phase. This is reasonable since larger oligomers exhibit smaller vapour pressures and thus scarce volatilities. Moreover, this assumption is in agreement with the data detailed in Chapters 3 and 4 concerning the condensed species collected.

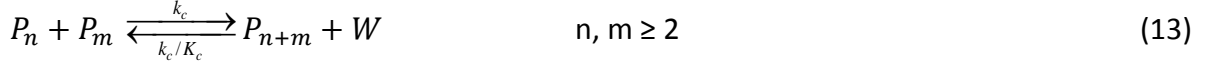
- *completely mixed system*

The system is mechanically stirred and does not present concentration and temperature gradients.

From the first assumption, three main polycondensation reactions have to be distinguished:







As already discussed in Chapter 1, in parallel to the polycondensation main steps detailed above, the reactions forming LT have to be considered. LT can be formed by two reactions named end-biting (or ring-closure) and back-biting respectively:



In the previous equations,  $P_i$  represents a polymer chain with chain length  $i$ ,  $W$  water,  $LT$  lactide and  $k_i$  and  $K_i$  are the kinetic direct constant and the equilibrium thermodynamic constant of reaction  $i$ , respectively.

According to the introduced reaction scheme (Equations 11-15) and assumptions, the balance equations are written as:

$$\begin{aligned} \frac{dP_1}{dt} = & -2k_a P_1^2 + 2\frac{k_a}{K_a} P_2 W - 2k_b P_1 (\lambda_0 + P_1) + 2\frac{k_b}{K_b} W \sum_{m=3}^{\infty} P_m + k_e P_3 + \\ & -\frac{k_e}{K_e} LTP_1 - \frac{P_1}{V} \frac{dV}{dt} - R_{v,1} \end{aligned} \quad (16)$$

$$\begin{aligned} \frac{dP_2}{dt} = & k_a P_1^2 - \frac{k_a}{K_a} P_2 W - 2k_b P_2 P_1 + 2\frac{k_b}{K_b} W P_3 - 2k_c P_2 (\lambda_0 - P_1) + \\ & + 2\frac{k_c}{K_c} W \sum_{m=4}^{\infty} P_m - k_d P_2 + \frac{k_d}{K_d} LTP_2 + k_e P_4 - \frac{k_e}{K_e} LTP_2 - \frac{P_2}{V} \frac{dV}{dt} - R_{v,2} \end{aligned} \quad (17)$$

$$\begin{aligned} \frac{dP_n}{dt} = & -2k_b P_1 P_n + 2k_b P_1 P_{n-1} - 2\frac{k_b}{K_b} W P_n + 2\frac{k_b}{K_b} W P_{n+1} - 2k_c P_n (\lambda_0 - P_1) + \\ & + \sum_{m=2}^{n-2} P_m P_{n-m} - \frac{k_c}{K_c} W (n-3) P_n + 2\frac{k_c}{K_c} W \sum_{m=4}^{\infty} P_m - k_e P_{n+2} + \\ & -\frac{k_e}{K_e} LTP_n - \frac{P_n}{V} \frac{dV}{dt} - R_{v,n} \quad \text{valid for } n \geq 3 \end{aligned} \quad (18)$$

$$\begin{aligned} \frac{dW}{dt} = & k_a P_1^2 - \frac{k_a}{K_a} P_2 W + 2k_b P_1 \sum_{m=2}^{\infty} P_m - 2 \frac{k_b}{K_b} W \sum_{m=3}^{\infty} P_m + k_c (\lambda_0 - P_1)^2 + \\ & - \frac{k_c}{K_c} W \sum_{m=4}^{\infty} (m-3) P_m + k_d P_2 - \frac{k_d}{K_d} W L T - \frac{W}{V} \frac{dV}{dt} - R_{v,W} \end{aligned} \quad (19)$$

$$\frac{dLT}{dt} = k_d P_2 - \frac{k_d}{K_d} L T W + k_e \sum_{n=3}^{\infty} P_n - \frac{k_e}{K_e} L T \sum_{n=3}^{\infty} P_{n-2} - \frac{L T}{V} \frac{dV}{dt} - R_{v,LT} \quad (20)$$

$$\frac{dG_i}{dt} = R_{v,i} \frac{V}{V_g} - \frac{Q_g}{V_g} y_i - \frac{G_i}{V_g} \frac{dV_g}{dt} \quad (21)$$

where  $P_i$ ,  $W$  and  $LT$  represent the mole concentration of polymer chains of length  $i$ , water and lactide in the melt liquid phase,  $G_i$  the concentration of component  $i$  in gas phase,  $Q_g$  the total flow rate removed by the vacuum pump,  $V$  and  $V_g$  the volumes of the liquid and gas phases and  $R_{v,i}$  the transport terms due to vaporization. The expression for  $R_{v,i}$  and  $Q_g$ , as well as the involved assumptions, are reported in the next section.

All previous equations account for volume changes. Defining as  $V_{tot}$  the total reaction volume,  $V_g$  is given by:

$$V_g = V_{tot} - V \quad (22)$$

and the gas volume change is expressed as

$$\frac{dV_g}{dt} = - \frac{dV}{dt} \quad (23)$$

The volume change has been calculated taking advantage of the volume additivity rule:

$$V = \sum_{i=1}^{NC} V_i = \sum_{i=1}^{NC} \rho_i M W_i C_i \quad (24)$$

Taking the differential form of equation 24, the following equation is obtained:

$$\frac{dV}{dt} = \sum_{i=1}^{NC} \rho_i M W_i \frac{dC_i}{dt} \quad (25)$$

Plugging in equations 16-20, a direct expression for  $dV/dt$  could be obtained; however, in order to simplify the model, the volume change was not predicted but directly given as a known functional by fitting the volume change experimental data by a suitable polynomial function. In other terms,  $V$  and  $dV/dt$  are considered as input variables.

### 5.2.1 Vacuum stream flow rate evaluation

For reactions carried out in vacuum, the flow rate of the stream removed by the vacuum pump is evaluated by imposing constant pressure to the system. In particular, the total moles of volatiles in gas phase are equal to:

$$n_g = V_g \sum_{i=1}^{NC} G_i \quad (26)$$

Introducing equation 21:

$$\frac{dn_g}{dt} = V \sum_{i=1}^{NC} R_{v,i} - Q_g \quad (27)$$

Expressing  $n_g$  through the ideal gas law,  $Q_g$  is finally obtained as:

$$Q_g = V \sum_{i=1}^{NC} R_{v,i} + \frac{P}{RT} \frac{dV}{dt} \quad (28)$$

### 5.2.2 Mass transport evaluation

In agreement with the classical theory of the two films[18], transfer resistances occur in a thin layer at the phase interface for each low molecular weight, volatile species, as clearly sketched in Figure 5.5.

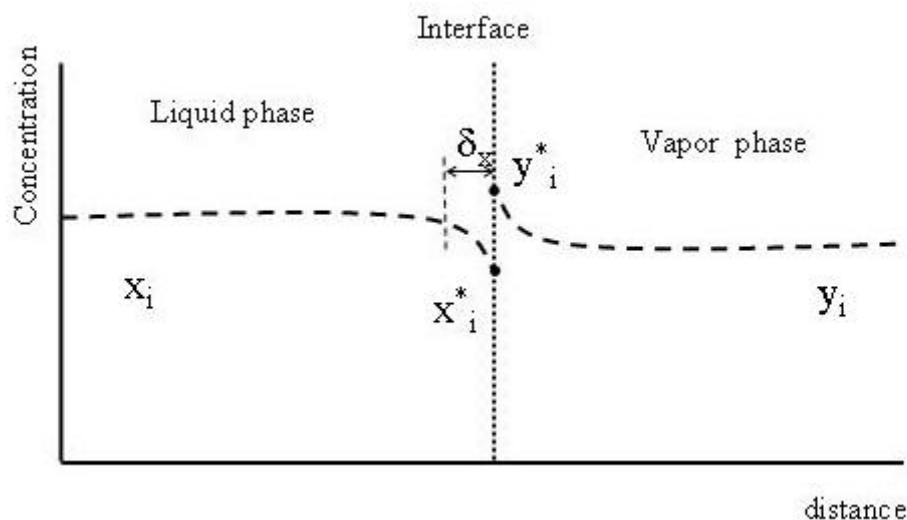


Figure 5.5 - Interface concentration profile.

For each volatile component  $i$ , assuming steady state conditions, the removal rate can be defined as:

$$Rv_i = k_i^x a \rho (x_i - x_i^*) = k_i^y a \rho (y_i^* - y_i) \quad (29)$$

where  $k_i^x$  and  $k_i^y$  are defined as the mass transport coefficients of the liquid and gas phase, respectively,  $x_i^*$  and  $y_i^*$  the mole fractions in equilibrium with the bulk concentration in liquid and gas phase,  $a$  is the specific area of transport and  $\rho$  the density of the system. The specific area is defined per unit of liquid volume as:

$$a = \frac{A}{V} \quad (30)$$

where  $A$  represent the total interfacial area. When the evaluation of the interfacial area is especially difficult, for example for boiling mixtures, a modified mass transport coefficient, lumping together area and transport coefficient,  $k_i' = Ak_i^x$ , is often used.

- *reactions carried out in vacuum*

For reactions carried out in vacuum, the partial pressure of the volatile components in the gas phase is very low and the resistances, and therefore the concentration gradients, in gas phase can be neglected. Thus,

$$Rv_i = k_i^x a \rho (x_i - x_i^*) \quad (32)$$

Assuming VLE conditions at the interface, the modified Raoult's law can be applied in order to evaluate the liquid mole fraction of the volatile component at the interface. The final expression for  $R_{vi}$  is:

$$Rv_i = k_i^x a \rho \left( x_i - \frac{y_i^* P}{P_i^0} \right) \quad (33)$$

where  $P$  is the total pressure of the system and  $P_i^0$  the vapor pressure of  $i$  at the reaction temperature. For each volatile component  $i$ , the vapor pressure can be evaluated, given the interfacial temperature, by means of the Antoine's equation:

$$P_i^0 = \exp \left( A - \frac{B}{T+C} \right) \quad (34)$$

The Antoine parameters for all volatile species are listed in Table 5.1.

Table 5.1 - Antoine's parameters.

|                | A       | B        | C       | T range (K)     |
|----------------|---------|----------|---------|-----------------|
| water          | 7.0436  | 1636.909 | -48.23  | 373.15 - 23.15  |
| LA             | 7.51107 | 1965.7   | -91.021 | 273.15 - 500.15 |
| L <sub>2</sub> | 7.534   | 2289.99  | -136.0  | 300.15 - 600.15 |
| LT             | 5.798   | 1605.4   | -122.68 | 398.15 - 463.15 |

- reactions carried out under nitrogen flow

For reactions carried out under nitrogen flow, assuming that the flow is large enough to ensure negligible partial pressure of the volatile components, the mole fraction of  $i$  at the liquid interface can be neglected and equation (27) reduces to:

$$Rv_i = k_i^x a \rho x_i \quad (39)$$

In this case, the evaluation of  $\gamma_i$  and  $P_i^0$  is not required.

Finally, it is worth to observe that the mass transport coefficient is considered constant all over the reaction. In the literature, studies on polycondensation systems proposed that the mass transport coefficients are function of several variables, such as molecular weight of the polymer, density of the mixture and stirring rate. However, due to the low extent of reaction examined in all experiments, the mass transport coefficients were considered constant in this work.

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## 6 Conclusions

It is known from literature that lactide production and lactic acid polycondensation are reactions strictly linked. In this frame, in the present work, two main goals were identified:

- i) detailed investigation of LA polycondensation
- ii) study of LT production reactions

Two sets of semi-batch reactions were carried out. A first set was performed under nitrogen flow at different temperatures (130-190<sup>o</sup>C) aiming to study the influence of this parameter in lactide polycondensation, at the same time limiting possible side reactions. The second set of reactions was performed at higher temperatures (190-210<sup>o</sup>C) and low pressures (5-25 mbar), conditions suitable for LT production. In this last step, the use of Sn(Oct)<sub>2</sub> as catalyst was investigated.

Detailed data for both liquid and gas phases was obtained applying different analytical techniques such as reverse phase high performance chromatography (HPLC), size exclusion chromatography (SEC) and Karl Fischer water titration. The complete distribution of species during time is something there is not reported in the literature so far.

Regarding the polycondensation of lactic acid, it was found that the polymerization is enhanced with temperature, and that within the studied experimental conditions water can be considered the only volatile specie. Lactide was detected even at 130 °C and for all the reactions it achieved equilibrium conditions for long reaction times.

In concern to the reactions aiming lactide production it was found that temperature and pressure play important roles in the process, since that the larger amount of lactide collected in the gas phase was obtained at the higher temperature and lower pressure studied. In fact, in these conditions lactide was the main component in the gas phase. Moreover the lactide content in the liquid phase was always constant for all the studied reactions which means that lactide reaches equilibrium conditions very quickly.

Finally a general mathematical model accounting for both lactic acid polycondensation and lactide formation was developed. Due to time limitations, the comparison between the experimental data and the model was not performed. As a future work the model developed will be used to estimate the parameters involved in the process.