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Crystallization behavior of poly(L-lactic acid)

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Abstract

This article contains a detailed analysis of the crystallization behavior of poly(L-lactic acid) (PLLA). Crystallization rates of PLLA have been measured in a wide temperature range, using both isothermal and non-isothermal methods. The combined usage of multiple thermal treatments allowed to obtain information on crystallization kinetics of PLLA at temperatures almost ranging from glass transition to melting point. Crystallization rate of PLLA is very high at temperatures between 100 and 118 °C, showing a clear deviation from the usual bell-shaped curve. This discontinuity has been ascribed to a sudden acceleration in spherulite growth, and is not associated to morphological changes in the appearance of PLLA spherulites. Experimental data of spherulite growth rates of PLLA have been analyzed with Hoffman–Lauritzen method. Applicability and limitations of this theoretical treatment have been discussed.

Keywords: Poly(L-lactic acid); Crystallization kinetics; Morphology

1. Introduction

Poly(L-lactic acid) (PLLA) is a biodegradable and biocompatible thermoplastic polyester with high strength and high modulus [1] that can be produced from renewable sources [2]. It can be easily processed to yield articles to be used in either the industrial packaging field [1], or for the biocompatible/bioabsorbable market, for example for dental [3–5] and drug delivery systems [6], and in applications for sutures and surgical implants [4,6,7].

PLLA can be degraded in natural environments by enzymatic or non-enzymatic hydrolysis [8–10]. In both cases, biodegradation rate strongly depends on molecular weight and on crystal structure and morphology [11], which, in turn, are function of the thermal and mechanical history imparted during processing. The large influence on biodegradation, as well as on the other material properties, lead to throughout analysis of the crystallization kinetics and morphology of PLLA along the years.

PLLA crystals can grow in three structural modifications, characterized by different helix conformations and cell symmetries, that develop upon different thermal and/or mechanical treatments. The α form grows upon melt or cold crystallization, and from solution-spinning processes at low drawing temperatures and/or low hot-draw ratios [12]. De Sanctis and Kovacs [13] first determined the chain conformation of α phase to be a left-handed 10_3 helix, that packs into an orthorhombic unit cell with parameters $a = 1.06$ nm, $b = 1.737$ nm, and $c = 2.88$ nm. A few more recent analyses report slightly different parameters for the unit cell of the α form. Extra $00l$ reflections have also been observed, suggesting some deviation from a "pure" 10_3 helix conformation [12].

The β modification, that was first observed by Eling et al. [14], develops upon mechanical stretching of the

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more stable α form, or from solution-spinning processes conducted at high temperatures and/or high hot-draw ratios [12,15]. The crystal structure of β modification has not been solved yet. Hoogsten et al. suggested an orthorhombic unit cell with $a = 1.031$ nm, $b = 1.821$ nm, and $c = 0.900$ nm [12], and a chain conformation with left-handed 3_1 helices. Brizzolara et al., instead, proposed an orthorhombic unit cell with two parallel chains [16]. Very recent studies conducted by Puggiali et al. show that the β phase is indeed a frustrated structure of three three-fold helices in a trigonal unit cell of parameters $a = b = 1.052$ nm, $c = 0.88$ nm, able to accommodate the random up-down orientation of neighbor chains associated with rapid crystallization conditions [15].

A third crystal modification of PLLA, the γ form, has been recently reported to develop upon epitaxial crystallization on hexamethylbenzene substrate, and has two antiparallel helices packed in an orthorhombic unit cell with $a = 0.995$ nm, $b = 0.625$ nm, and $c = 0.88$ nm [17].

Crystallization kinetics from the melt of poly(L-lactide) has also been analyzed by a number of research groups [18–23]. Isothermal bulk crystallization rates were determined in a wide temperature range, from 70 to 165 °C [18,19]. The maximum in crystallization rate was observed around 100 °C, and the most peculiar behavior was a discontinuity in phase change kinetics around 110–120 °C. This discontinuity has been correlated to a transition in regimes II–III growth of spherulites that was observed in the same temperature range [19,23], although other explanations of the unusual crystallization behavior of PLLA have been put forward as well [23,24].

This contribution reports a detailed experimental analysis of the crystallization process from the melt of PLLA, conducted both in isothermal and non-isothermal conditions. The aim is to provide crystallization data in a wide temperature range, which is expected to help clarify the above peculiarities that, at present, have not found a widely accepted explanation.

2. Experimental part

2.1. Material

A poly(L-lactic acid) of molecular mass $M_w = 101{,}000$ Da, produced by Boehringer Ingelheim (Germany) and received in form of small chips, was used without further purification nor thermal treatment.

2.2. Calorimetry

The thermal properties of PLLA were measured with a Mettler DSC-30 differential scanning calorimeter. The apparatus was calibrated with pure indium, lead and zinc standards at various scanning rates. Dry nitrogen gas with a flow rate of $20\,\mathrm{ml\,min^{-1}}$ was purged through the cell during all measurements and thermal treatments. A fresh sample was used for each experimental measurement, in order to minimize thermal degradation. Each measurement was repeated three times to improve accuracy.

To investigate the overall kinetics of isothermal crystallization, PLLA samples (weighting about 10 mg) were heated from 30 to 200 °C at a rate of 20 °C/min, melted at 200 °C for 2 min, then cooled at a rate of 50 °C/min to the desired T_c, and allowed to crystallize. Preliminary investigations showed that the scanning rate used to reach T_c from the melt (50 °C/min) was high enough to prevent crystallization during cooling. The heat evolved during crystallization was recorded as a function of time. The fraction of material crystallized after a period of time t (X_t) was calculated by the ratio of the heat generated at time t and the total heat developed during the phase transformation. Plotting X_t against time, the half-time of crystallization, $\tau_{1/2}$, defined as the time needed for half of the final crystallinity to develop, was obtained.

Crystallization kinetics of PLLA was also analyzed in non-isothermal conditions. The samples were heated from 30 to 200 °C at a scanning rate of 20 °C/min, kept at this temperature for 2 min, then cooled to room temperature at various scanning rates.

2.3. Optical microscopy

Growth rates and morphology of PLLA spherulites were determined by optical microscopy, using a Zeiss polarizing microscope equipped with a Linkam TMHS 600 hot stage. A small piece of PLLA, weighing about 0.3 mg, was squeezed between two microscope slides, then inserted in the hot stage. The thickness of the squeezed sample was lower than 10 μm. The radius of the growing crystals was monitored during solidification by taking photomicrographs at appropriate intervals of time, using a JVC TK-1085E Video Camera. Spherulite radii were measured with the software Image-Pro Plus 3.0. Dry nitrogen gas was purged throughout the hot stage during all measurements and thermal treatments.

The thermal treatments before isothermal and non-isothermal crystallizations were identical to those used in calorimetry. Spherulite growth rates (G) data were obtained in isothermal conditions from the slope of the radius (r) vs. temperature (T) plot [25]. Non-isothermal G measurements were performed at a constant cooling rate following the procedure developed by Di Lorenzo et al. [22,26].

2.4. WAXS analysis

Wide-angle X-ray scattering analysis (WAXS) was carried out on a Philips (PW 1050 model) powder diffractometer (CuNi-filtered radiation) equipped with a rotative sample holder device.

3. Results

The half time of crystallization ($\tau_{1/2}$) of poly(L-lactic acid), measured in isothermal conditions after cooling from the melt, is reported in Fig. 1 as a function of temperature (T_c). As typical for polymers, crystallization of PLLA is slow in the temperature ranges close to the melting point and the glass transition. In addition, the $\tau_{1/2}$ vs. T_c plot presents a broad minimum around 108 °C and a discontinuity around 116–118 °C, evidenced by the arrow in Fig. 1.

Bulk crystallization rate of PLLA was also measured in non-isothermal conditions at various scanning rates. DSC thermograms obtained during cooling from the melt at 5 and 10 °C/min are reported in Fig. 2. As expected, the crystallization curves shift to lower temperatures when high scanning rates are used [27]. When PLLA is cooled at 5 °C/min, the liquid–solid phase transformation begins around 140 °C. As temperature reaches about 118 °C, the exothermic peak suddenly becomes more pronounced, suggesting a rapid increase in crystallization rate. For crystallization analysis conducted at 10 °C/min, the DSC thermogram shows the onset of phase transition to occur at 130 °C. Again, the increase in heat flow rate abruptly becomes much more rapid when a temperature of 118 °C is reached, confirming the discontinuity in crystallization rate of PLLA around 118 °C.

More detailed data on crystallization kinetics of PLLA were gained by determining the rate of spherulite growth (G). Preliminary data of spherulite radial growth rates of PLLA, measured in isothermal and non-isothermal conditions, both from the melt and from the cold state, were presented in Ref. [22]. Crystallization rate data reported in Ref. [22] were obtained in a wide temperature range, which allowed to detect for the first time the complete bell-shaped G vs. T curve for PLLA, but did not include G data from 100 to 125 °C, i.e. in the temperature range where the discontinuity in crystallization rate is observed. The aim of the study reported in Ref. [22] was mainly to show the potentiality of the use of tailored isothermal and non-isothermal procedures to determine crystal growth rates in a wide temperature range. These measurements have been now completed in both isothermal and non-isothermal conditions, and results are illustrated in Fig. 3. Selected data taken from Ref. [22] have also been reported for comparison.

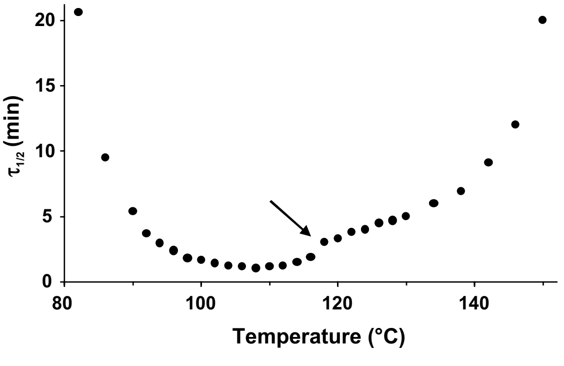

Fig. 1. Half-time of crystallization ($\tau_{1/2}$) of PLLA as a function of the isothermal crystallization temperature.

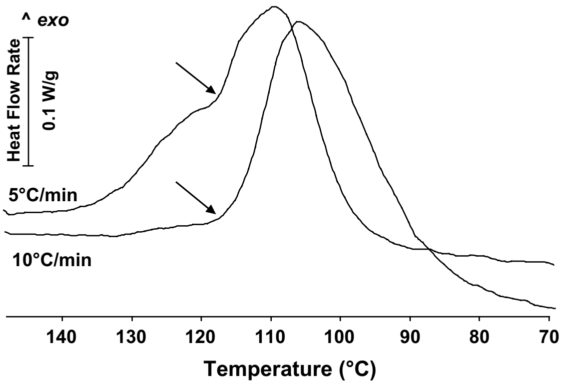

Fig. 2. DSC traces of PLLA measured during cooling from the melt at the indicated rates.

As shown in Fig. 3, the isothermally measured spherulite growth rate curve displays a first broad maximum around 130 °C, and a second, sharper peak at 115 °C, as the G vs. T_c plot diverges from the typical bell-shaped curve below 120 °C, where the rate of spherulite growth becomes much higher. G values measured in non-isothermal conditions during cooling at a constant rate,

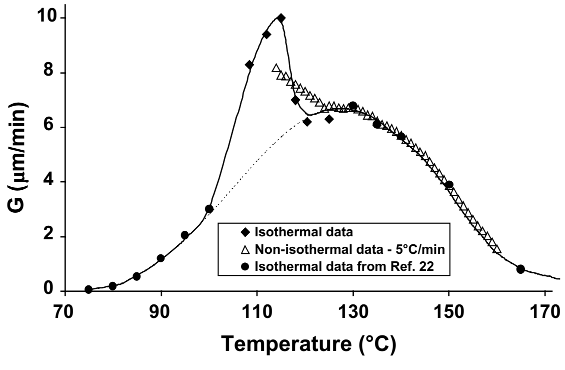

Fig. 3. Spherulite growth rates of PLLA measured in isothermal and non-isothermal conditions. Selected data taken from Ref. [22] have also been reported. The thick line was drawn as a possible interpolation of spherulite growth rates data.

after self-nucleation [22,26], also suddenly deviate from the bell-shaped curve in the same temperature interval. Data measured in non-isothermal conditions were obtained upon cooling from the melt at a rate of 5 °C/min, which allowed to measure *G* at lower temperatures compared to the data reported in Ref. [22], where a cooling rate of 1 °C/min was used.

As shown in Figs. 1–3, below 120 °C crystallization rate of PLLA is very high, due both to the high rate of spherulite growth and to the quite large nucleation density in this temperature range. A high number of simultaneously growing spherulites at a high rate corresponds to a large amount of heat evolved in the unit time. The rapid development of latent heat may cause some local heating and create some thermal gradients within the sample, and the phase transition can occur at temperatures that do not correspond to those detected by the instrumentation. This, in turn, produces an increase in the experimental uncertainty associated with the experimental determination of *G*, both in isothermal and non-isothermal conditions. The error associated to non-isothermal measurements is even higher, since in this type of analysis, temperature is continuously reduced, and the cooling power of the hot stage may not be able to counterbalance the latent heat rapidly developed during crystallization, which may result in a cooling rate lower than expected. This explains the discrepancy below 120 °C in growth rate values obtained during cooling at 5 °C/min with data measured in isothermal conditions.

It is worth noting that *G* data determined during cooling from the melt at 5 °C/min were taken from the same spherulite during its growth at continuously decreasing temperatures. The morphology of the growing spherulite seems not to vary in the whole explored temperature range, even during the very rapid increase of linear growth rate below 120 °C, as shown in Fig. 4. Similarly, spherulites grown isothermally at various temperatures do not show any noteworthy morphological difference, at least for the resolution power of optical microscopy, indicating that the abrupt increase in crystallization rate cannot be ascribed to changes in morphology occurring during growth at different temperatures. Fig. 4 gives also indications on the effects of temperature on nucleation rate of PLLA spherulites. Besides the large spherulite, smaller spherulites start to appear as temperature is decreased. Fig. 4b shows growth of one additional spherulite, in Fig. 4c a few more growing spherulites are evident. They have different sizes, being nucleated at various temperatures during cooling. However, the increase in nucleation density with the decreasing temperature, commonly reported for polymers, is continuous, and does not display a rapid acceleration with temperature. Hence, the discontinuity in crystallization rate of PLLA below 120 °C has to be mainly ascribed to a drastic variation in crystal growth rate, and is not affected by abrupt changes in nucleation behavior.

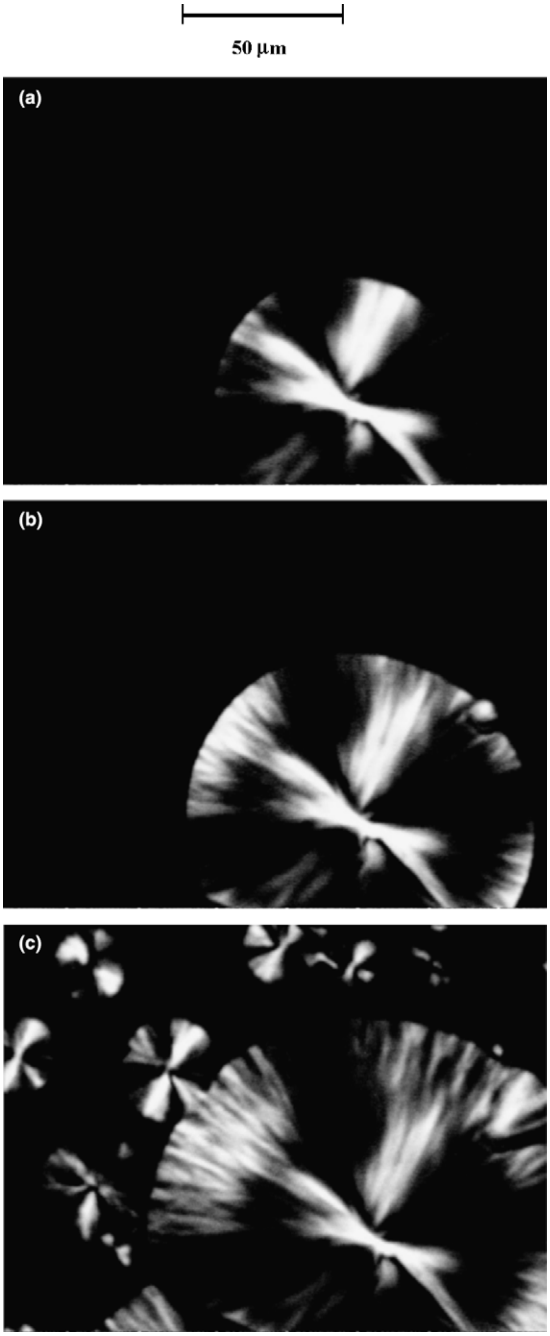

Fig. 4. Optical micrographs of PLLA spherulites grown during cooling from the melt at 5 °C/min: (a) 130 °C; (b) 120 °C; (c) 110 °C.

The sudden change in crystallization rate may be due to growth in a different crystal modification, which might be favored at temperatures below 120 °C. As mentioned in Introduction Section, PLLA is a polymorph material that presents several crystal modifications. Preliminary WAXS analyses conducted after isothermal crystallization at various temperatures indicate that, after the thermal treatments used to follow the crystallization kinetics, only the α modification seems present. However, the powder diffraction patterns of α and β forms are quite similar, which complicates their identification [15]. The two crystal modifications can be easily distinguished only by WAXS fiber patterns, where the α phase gives sharp reflections, and the β phase produces diffuse reflections seen as smeared layer lines in the diffraction patterns [14]. The β form of PLLA is a frustrated crystal modification, that generally develops upon stroking or stretching of the α form. It is a highly disorder structure characterized by a random orientation of chains imposed by rapid crystallization conditions [16], and may, in principle, initially develop at temperatures where crystallization from the melt is very fast, then transform into the more stable α form. Hence, WAXS analyses performed after completion of crystallization are not probing, and more detailed time-resolved WAXS analyses conducted during the progress of crystallization are necessary to completely asses the possible influence of crystal polymorphism on the unusual crystallization behavior of PLLA.

The discontinuity in crystallization rate of PLLA reported above has been sometimes correlated with a transition in crystallization regime, observed in the same temperature range [19,23]. As reported in Ref. [22], Hoffman–Lauritzen analysis of spherulite growth rate of PLLA, measured in the temperature range 75–100 °C, and above 128 °C, allowed to detect a regime II–III transition at 120 °C. Hoffman–Lauritzen analysis has been now completed by including crystallization data between 100 and 120 °C. With the new data reported in Fig. 3, it became possible to apply the method proposed by Hoffman and Laurizten using experimental values of spherulite growth rate that completely cover a wide temperature interval, ranging almost from the glass transition to the melting point. As usual, the following expression was used [28,29]:

$$\ln G + \frac{U^*}{R(T_c - T_\infty)} = \ln G_o - \frac{K_g}{T_c \Delta T f} \quad (1)$$

where G_o is a pre-exponential term; R is the universal gas constant; U^* is the energy required for the transport of macromolecules in the melt; T_c is the crystallization temperature; T_∞ is the temperature where all the motions associated with the viscous flow stop, and is defined as $T_\infty = T_g - C$, where C is a constant that can assume different values; ΔT is the undercooling ($\Delta T = T_m^o - T_c$, where T_m^o is the equilibrium melting temperature); f is a corrective factor that takes into account the variation of the equilibrium melting enthalpy with temperature, defined as $f = 2T_c/(T_c + T_m^o)$; K_g is a term connected with the energy needed for the formation of nuclei of critical size, and is defined as:

$$K_g = \frac{n b_o \sigma \sigma_e T_m^o}{\Delta H_m^o k} \quad (2)$$

where n is a variable that depends on crystallization regime and is equal to 4 for regimes I (high temperatures) and III (low temperatures) and values 2 in regime II (intermediate temperatures), b_o is the thickness of the stem added on the substrate, σ is the lateral surface free energy, σ_e is the free energy of folding, ΔH_m^o is the enthalpy of fusion, and k is the Boltzman constant [29]. For the calculations, literature values of $T_m^o = 207\,°C$ [20] and $T_g = 62.5\,°C$ [19] were used. To fit experimental data, $U^* = 1500$ cal/mol and $C = 30\,°C$ were utilized, as done in previous studies on PLLA [19,20,22,23].

The results of Hoffman–Lauritzen treatment, using the G values presented in Fig. 3, are illustrated in Fig. 5. Their interpretation is not straightforward.

Growth rate data determined in the ranges 75–100 °C and 108–120 °C seem to fall on two distinct straight lines (drawn as dashed trendlines), both intersecting the straight thick line obtained from G data measured at higher temperatures. The slopes of these three linear trendlines, K_g, calculated in the three different temperature ranges are:

(a) For $75\,°C \leqslant T_c \leqslant 100\,°C$: $K_g = 4.38 \times 10^5\,K^2$ (from Ref. [22]).
(b) For $108\,°C \leqslant T_c \leqslant 120\,°C$: $K_g = 5.97 \times 10^5\,K^2$.
(c) For $T_c \geqslant 128\,°C$: $K_g = 1.85 \times 10^5\,K^2$ (from Ref. [22]).

If one considers G data taken between 75 and 100 °C (a), and between 108 and 120 °C (b), as two independent sets of data, and compare them with G values measured

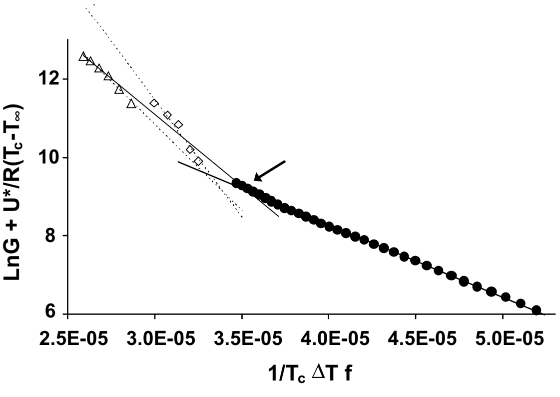

Fig. 5. Hoffman–Lauritzen analysis of spherulite growth rate data of PLLA. $U^* = 1500$ cal/mol and $T_\infty = T_g - 30\,°C$ were used.

at higher temperatures (c), the slope ratio with high temperature data is 2.37 for G values measured between 75 and 100 °C, and 3.23 for G data measured between 108 and 120 °C. In both cases the slope ratio is quite discordant from the value 2 predicted by the theory [28,29], as sometimes reported for PLLA [19]. Hence, Hoffman–Lauritzen analysis independently conducted with either G values measured between 75 and 100 °C (as done in Ref. [22]) or using only the data in the range 108–120 °C (similarly to the studies reported in Ref. [19,20,23]) might give indication of the existence of a regime II–III transition. The temperatures where the this transition occurs are quite similar when either (a) or (b) sets of data are used, being located around 115–120 °C, as commonly reported in the literature for PLLA [19,20,22,23]. It has to be underlined that for no set of data morphological changes in PLLA spherulites are evident, as shown in Fig. 4, which does not help correlate a given regime growth to a specific temperature range. As detailed above, the error associated to the experimental measurement of G between 100 and about 115 °C is not negligible, due to the very high crystallization rate in this temperature range. The experimental data below 120 °C can be all interpolated with a single straight line, as shown by the thin solid line in Fig. 5, considering the deviation from the trendline due to the large experimental error associated to the measurement of G in this temperature range. In this case, K_g determined with G values from 75 to 120 °C results equal to 3.66, and the slope ratio with high temperature data (range c) becomes 1.97. This should point to a regime II–III transition temperature around 130 °C, as indicated by the arrow in Fig. 5.

The above analysis outlines the uncertainty that is sometimes associated with Hoffman–Lauritzen regime growth analysis. It is known that this treatment undergoes serious oversimplifications, and several criticisms to this theoretical approach have been put forward along the years by a number of researchers [25,30–34]. For instance, after analysis of the shapes generated by computer simulation of crystal growth, Binsbergen suggested that it may even be possible that secondary nucleation is a factitious concept [30]. This confirms that large progress still needs to be done in understanding the process of polymer crystallization, as an universally accepted description on the mechanism of crystallization of polymers has not been accomplished yet [25,35].

4. Conclusions

The analysis of the crystallization behavior of poly(L-lactic acid) reported in this contribution has evidenced a series of peculiarities, that can be summarized as follows:

- The crystallization rate of PLLA is unusually high at temperatures between 100 and 118 °C.
- The high crystallization rate of PLLA below 120 °C has to be ascribed to the high rate of radial growth of the spherulites, whose origin has still to be clarified. No particular increase of nucleation rate has been evidenced in this temperature range.
- The discontinuity in crystallization rate seems not associated to morphological changes in PLLA spherulites, as revealable by optical microscopy.
- Hoffman–Lauritzen analysis of spherulite growth rate values of PLLA outlines a probable regime II–III transition, which seems not correlated to the above discontinuity in crystallization rate.

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References

[1] Garlotta DJ. Polym Environ 2001;9:63.
[2] Bogaert JC, Coszac P. Macromol Symp 2000;153:287.
[3] Kulkarni RK, Pani KC, Neuman C, Leonard F. J Biomed Mater Res 1971;5:169.
[4] Leenslag JW, Pennings AJ, Bos RRM, Rozema FR, Boering G. Biomaterials 1987;8:311.
[5] Koyima T, Nakano M, Juni K, Inoue S, Yoshida Y. Chem Pharm Bull 1984;32:2795.
[6] Penning JP, Dijstra H, Pennings AJ. Polymer 1993;34:942.
[7] Vainiopää S, Rokkanen P, Törmälä P. Prog Polym Sci 1989;14:679.
[8] Fisher EW, Sterzel HJ, Wegner G. Kolloid Z Z Polym 1973;251:980.
[9] Iwata T, Doi Y. Macromolecules 1998;31:2461.
[10] Reeve MS, McCarthy SP, Downey MJ, Gross RA. Macromolecules 1994;27:825.
[11] Turner JF, Riga A, O'Connor A, Zhang J, Collins J. J Therm Anal Calor 2004;75:257.
[12] Hoogsteen W, Postema AR, Pennings AJ, Ten Brinke G, Zugenmaier P. Macromolecules 1990;23:634.
[13] De Sanctis P, Kovacs AJ. Biopolymers 1968;6:299.
[14] Eling B, Gogolewski S, Pennings AJ. Polymer 1982;23:1587.
[15] Puiggali J, Ikada Y, Tsuji H, Cartier L, Okihara T, Lotz B. Polymer 2000;41:8921.
[16] Brizzolara D, Cantow HJ, Diedrichs K, Keller E, Domb AJ. Macromolecules 1996;29:191.
[17] Cartier L, Okihara T, Ikada Y, Tsuji H, Puiggali J, Lotz B. Polymer 2000;41:8909.
[18] Marega C, Marigo A, Di Noto V, Zannetti R. Makromol Chem 1992;193:1599.
[19] Iannace S, Nicolais L. J Appl Polym Sci 1997;64:911.
[20] Vasanthakumari R, Pennings AJ. Polymer 1984;24:175.
[21] Myiata T, Masuko T. Polymer 1998;39:22.

[22] Di Lorenzo ML. Polymer 2001;42:9441.
[23] Abe H, Kikkawa Y, Inoue Y, Doi Y. Biomacromolecules 2001;2:1007.
[24] Ohtani Y, Okumura K, Kawaguchi A. J Macromol Sci Part B: Phys 2003;3–4:875.
[25] Wunderlich B. Macromolecular physics, vol. 2: Crystal nucleation, growth, annealing. New York: Academic Press; 1976.
[26] Di Lorenzo ML, Cimmino S, Silvestre C. Macromolecules 2000;33:3828.
[27] Di Lorenzo ML, Silvestre C. Prog Polym Sci 1999;24:917.
[28] Hoffman JD, Davis GT, Lauritzen JI. In: Hannay NB, editor. Treatise on solid state chemistry. New York: Plenum Press; 1976.
[29] Hoffman JD. Polymer 1983;24:3.
[30] Binsbergen FL. Kolloid Z Z Polym 1970;237:289.
[31] Sadler DM. Nature 1987;326:174.
[32] Point JJ, Dosiere M. Polymer 1989;30:2292.
[33] Keller A, Hikosaka M, Rastogi S, Toda A, Barham PJ, Goldbeck-Wood GG. J Mater Sci 1994;29:2579.
[34] Strobl G. Eur Phys J 2000;E3:165.
[35] Di Lorenzo ML. Prog Polym Sci 2003;28:663.