

Cross-nucleation between concomitantly crystallizing α - and γ -phases in polypivalolactone: secondary nucleation of one polymorph on another

Dario Cavallo,^{1,*} Francesca Galli,¹ Lian Yu,² Giovanni C. Alfonso¹

¹*Department of Chemistry and Industrial Chemistry, University of Genova, Genova, Via
Dodecaneso 31, 16146, Italy*

²*School of Pharmacy and Department of Chemistry, University of Wisconsin-Madison, Madison,
Wisconsin 53705, United States of America*

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ABSTRACT. Cross-nucleation between polymorphs occurs when a new crystal structure nucleates on the surface of a pre-existing crystal of a different modification. The understanding of the phenomenon is still mostly phenomenological and qualitative. Here we report quantitative measurements of cross-nucleation rate of the α phase of polypivalolactone on its γ phase, during melt crystallization over a large temperature range. The cross-nucleation kinetics is well modelled as heterogeneous secondary nucleation of one polymorph on another, in which the

formation of a viable α -phase nucleus on the surface of γ -crystals is the rate-limiting step. According to this analysis, cross-nucleation can occur because the interfacial energy between the two structures is small, and the nucleation free energy barrier is similar to that for secondary nucleation within the same polymorph in crystal growth. Some peculiar aspects of cross-nucleation with respect to conventional heterogeneous nucleation, arising from the continuous growth of the nucleating substrate, are also highlighted.

INTRODUCTION

Many of the physical properties of a material are dictated by the exact way the molecules are arranged in the solid state. As such, the packing of a given substance into different crystallographic structures, *i.e.*, polymorphism, can lead to largely diverse characteristics.¹ For example, polymorphs of a pharmaceutical molecule can exhibit considerable differences in solubility, compromising the bioavailability of some formulations.² The very same semicrystalline polymer can be ductile or fragile at room temperature, depending on the prevailing crystalline structure.^{3,4}

Therefore, being able to control which polymorph will form and dominate the final product is a matter of high technological relevance. Typically, this problem is tackled by acting on the nucleation stage: the crystallizing melt or solution is “seeded” with crystals of the desired polymorph, assuming that this would promote the nucleation of the same form. However, in some cases this rather straightforward strategy can unexpectedly fail, due to the nucleation of a different polymorph on the seed.

The heterogeneous nucleation of one polymorph on a crystalline substrate of the same chemical composition but different structure is known as cross-nucleation.⁵ This phenomenon has been first investigated by Yu et al. in the crystallization of small molecules, such as D-Mannitol^{6,7} or more complex drugs.⁸ In polymers, reports about cross-nucleation are more recent,^{9,10} and include the work of our group on seeded isotactic poly(1-butene).¹¹⁻¹³ However, earlier studies of polymer crystallization recognized the same situation and addressed it as “growth transformation”,^{14,15} the most well-known example being the one of isotactic polypropylene α -on- β -phase.^{14,16,17}

The general features of cross-nucleation are well documented. Experiments on small molecules⁶⁻⁸ and polymers^{11,12,16} and molecular dynamics simulations¹⁸⁻²¹ have shown that the process is governed by kinetics, rather than thermodynamics. In fact, cross nucleation requires that the new polymorph grows faster than the polymorph on which it nucleates.^{8,16} On the other hand, the relative thermodynamic stability of the two structures is not important: both stable-on-metastable and metastable-on-stable cross-nucleation has been observed.^{8,12,16} Despite this progress, a mechanistic understanding of cross-nucleation is still lacking, and several open questions on the topic remain.

For example, the role of epitaxy is unclear: in some small molecules well-defined epitaxial relationships between the two cross-nucleating structures have been established,^{22,23} while in others no evident crystallographic matching exists.⁸ For isotactic polypropylene, epitaxial crystallization of the monoclinic on the trigonal phase has been proposed,¹⁷ but recently called into question.^{24,25} Another intriguing aspect of cross-nucleation is the apparent “selectivity”. The constraint on the relative growth rates of the two polymorphs, with the “daughter” phase growing faster than the “parent”, proves to be a necessary but insufficient condition to observe cross-

nucleation. For the small molecule named ROY⁸, for example, the Y04 structure grows the slowest of all the ten known polymorphs, but only two other phases were observed to nucleate on it. Similarly, in poly(vinylidene fluoride) and isotactic polypropylene the order of the polymorphs' growth rates is reversed with undercooling,^{15,16} however the same does not occur to the “direction” of cross-nucleation, i.e., only α -on- γ and α -on- β nucleation events are reported, respectively.

To make further progress in this area, it is necessary to obtain quantitative cross-nucleation rates and their temperature dependence for different systems. Such data, however, are presently scarce. Yu et al. determined the kinetics of cross-nucleation of α -phase on δ -phase in D-Mannitol, in a temperature range in which the two polymorphs crystallize concomitantly.⁶ Cavallo et al. quantified the kinetics of Form II-on-Form I cross-nucleation in isotactic poly(1-butene) by performing seeded crystallization experiments.¹² For both systems, the rate of cross-nucleation increases with the undercooling, in agreement with existing theories of heterogeneous nucleation.

Here we report the first quantitative measurement of cross-nucleation between polymorph in the system poly(α,α -dimethyl- β -propiolactone), i.e., polypivalolactone (PPVL). For this purpose, the method proposed by Yu for the assessment of cross-nucleation rate between concomitantly crystallizing polymorphs⁶ has been employed. The results are modelled as a process of secondary nucleation of one polymorph on another. By fitting the model to the experimental data, we obtain the values of the free energy barrier for cross-nucleation and of the surface tension between the two crystalline structures. The successful application of a simple nucleation model represents a first step towards quantitative understanding of cross-nucleation.

EXPERIMENTAL SECTION

The polyester under investigation was kindly supplied by Prof. S.V. Meille (Milan Polytechnic) in the powder form, and it was used as received. The material has a weight average molar mass of 616 kg/mol, with a polydispersity index around 3, and its crystallization behaviour has already been characterized in previous studies.²⁶⁻²⁹

Thin films of the polymer were prepared by placing about 15 mg of sample between two glass coverslips on a hot stage at about 240 °C. The material was molten for few seconds and manually compressed to a thickness in the range of 60-90 µm, suitable for optical microscopy observation. The exact thickness, required for data analysis, has been measured by a digital micrometer. The lateral size of the films was about 1-1.5 cm. The sample between the glass coverslips was then quenched in air, prior to the crystallization experiments.

The thermal history for crystallization/cross-nucleation experiments was imposed by means of a Metler Toledo FP82HT hot stage, controlled via a FP90 Central Processor. The sample was molten at 255 °C for 2 minutes in a first hot stage, in order to remove any effect of previous thermo-mechanical history on the subsequent crystallization. The melting conditions were properly chosen to maximize the content of the orthorhombic γ -modification upon re-crystallization,²⁸ while minimizing the risk of thermal degradation. At the end of the melt-annealing step, the polymer was rapidly transferred to a second hot stage, pre-set at the desired crystallization temperature, which ranged between 155 and 175 °C. The lowest temperature value was imposed by the constraint of preventing the crystallization during cooling from the melt. On the other hand, temperatures higher than 175 °C were not explored, since the content of γ -phase becomes negligible at low undercoolings, due to its more difficult nucleation with

respect to α -form.^{13,28,29} The polymer was kept at the isothermal crystallization temperatures for 5 to 15 minutes (depending on the temperature), to allow the completion of phase transition, as judged by in-situ optical microscopy observation.

The morphology of the crystallized PPVL was finally observed with a Polyvar Pol polarized optical microscope, equipped with a 25x objective lens. Digital images were acquired thanks to a Moticam 10 microscope camera connected to a computer. Pictures of the resulting morphologies were taken at different locations in each specimen, and analysed with image processing software (ImageJ) to determine the rate of α -on- γ -phase cross-nucleation at the crystallization temperature.

RESULTS AND DISCUSSION

Polypivalolactone (PPVL) is a highly crystalline polyester which displays three crystalline modifications, α , β , and γ .^{26,27,30} The α - and γ -polymorphs are of interest for this study: both of them share a 2/1 helical conformation which is packed either in a monoclinic (α -crystals) or orthorhombic (γ -crystals) lattice. The monoclinic α -phase is the most stable structure, with a melting point around 230-240 °C, compared to the 210-220 °C of the γ -phase. α - and γ -phases crystallize concomitantly in a wide temperature range, the relative content of the two phases being dependent on both crystallization and melt-annealing conditions.²⁸

A careful analysis of the growth kinetics of α -form spherulites has been performed, including the determination of growth regimes, fold surface free energy and equilibrium melting temperature.^{31,32} On the other hand, γ -phase is the minor component, and γ -spherulites are often

engulfed by the highly nucleated and faster growing α -phase, before attaining dimensions suitable for growth rate evaluation. Therefore, its growth rate can only be indirectly determined, by analyzing the α/γ interspherulitic boundary profile.²⁹ The monoclinic α -phase grows approximately 3 to 6 times faster than the γ -form in the explored crystallization temperature range, thus satisfying the kinetic requirement for the observation of α -on- γ -phase cross-nucleation/growth transformation.

Indeed, α/γ cross-nucleation has actually been reported³³ and it was observed also in the present work. Figure 1 shows some examples, for a PPVL sample crystallized at 160 °C. The two polymorphs are clearly distinguished by optical microscopy, since the γ -phase spherulites display weak birefringence and tight banding, in contrast to the highly birefringent and non-banded morphology of α -spherulites.³⁴



Figure 1. Examples of the morphologies obtained at the end of PPVL crystallization at 160 °C. Cross-nucleation of α -phase can be observed at multiple points of the γ -spherulites periphery.

The morphologies of isothermally crystallized PPVL presented in Figure 1 show relatively small spherulites of the orthorhombic γ -form engulfed by larger spherulites of the monoclinic α -phase, which have cross-nucleated at several points on the front of the slow-growing entities. This crystallization mechanism generates an irregular curvilinear α/γ interspherulitic profile, which indicates a non-negligible growth of the parent γ -structure while cross-nucleation of the α -phase is occurring and which has been previously analyzed to obtain precise quantitative information on the, otherwise inaccessible, growth kinetics of γ -form spherulites.²⁸

The analysis of the cross-nucleated morphology at the end of the crystallization process provides an indirect means to quantify the rate of nucleation of one polymorph by another. The method, proposed by Yu et al. for the cross-nucleation between D-Mannitol polymorphs,⁶ is applicable in the case of concurrent growth of the two different structures. Besides the increase in the number of cross-nuclei in time, the change in the surface area of the parent polymorph during crystallization is also taken into account. Applying this model to the specific case of PPVL, the cross-nucleation rate of α -phase on γ -spherulites ($J_{\alpha/\gamma}$), equal to the number of α -nuclei formed per unit of area of γ -surface (A_γ) in the time dt , is given by:

$$dn = J_{\alpha/\gamma} A_\gamma dt \quad (1)$$

where the area of the γ -polymorph growth front is given by: $A_\gamma = 2 \pi h R_\gamma$, with R_γ being the radius of the γ -phase spherulite and h the thickness of the sample. Expressing the time as a function of the γ -spherulite radius, by dividing it for the growth rate v_γ and integrating, one obtains:

$$n = \frac{J_{\alpha/\gamma} \pi h}{v_\gamma} R_\gamma^2 \quad (2)$$

The value of n represents the average number of cross-nuclei formed within a distance R_γ from the centre of the γ -spherulite or, equivalently, the fraction of α -spherulites nucleated in the range $0-R_\gamma$. To calculate n , the distance from the centre of a parent γ -spherulite to a cross-nucleation site (R_γ) was determined by optical microscopy. For each crystallization experiment, between 20 and 80 cross-nucleation sites were considered. Then, a list with the measured R_γ sorted in ascending order was created. The average number of α -spherulites nucleated within R_γ is finally computed by dividing the ordinal number of a given cross-nucleus in the above mentioned list by the total number of counted nucleation sites.⁶

Equation 2 allows obtaining the cross-nucleation rate from the slope of the plot n vs. R_γ^2 . An example of the raw data and a detailed discussion of the analysis procedure is provided in the Supporting Information.

The results of cross-nucleation experiments performed at different undercoolings are shown in Figure 2. For a meaningful comparison of the data collected on different samples and at different temperatures, the values of R_γ^2 for each experiment are "normalized", taking into account the sample thickness and the temperature-dependent growth rate of the γ -polymorph.²⁹ Accordingly, Figure 2 reports the plot of the average number of cross-nucleated α -spherulites as a function of $(R_\gamma^2 \cdot h)/v_\gamma$, for all the explored crystallization temperatures.

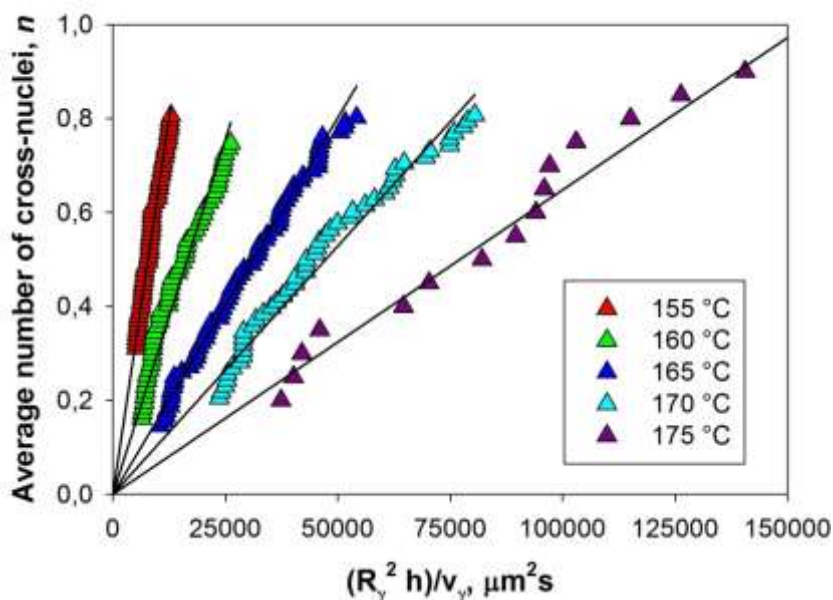


Figure 2. Average number of α -phase cross-nuclei as a function of R_γ^2 multiplied by the thickness of the sample and divided by the growth rate of the parent γ -spherulite. Results for different (indicated) crystallization temperatures are shown. Black lines are best fit of the data, passing through the origin of the axes.

Every crystallization experiment at a given temperature was repeated at least three times, and the curves in Figure 2 are representative data sets at specified temperatures. We note that at 175 °C a relatively small number of data is available, due to the very low content of the parent γ -phase at this high crystallization temperature.^{13,28} The cross-nucleation rates can be directly grasped from Figure 2, since they are proportional to the slope of the lines fitting the data, in agreement with Equation 2. Indeed, the slopes of the regression lines passing through the origin of the axes must be divided by π to determine the actual cross-nucleation rates. The average values of $J_{\alpha/\gamma}$ as a function of crystallization temperature and undercooling are summarized in Table S1 of the Supporting Information.

The cross-nucleation rate becomes approximately one order of magnitude faster with increasing the undercooling of 20 °C. The values of α -on- γ phase cross-nucleation rate in PPVL are comparable with those of D-Mannitol (α -on- δ phase)⁶ Also, they are in line with Form II-on-Form I nucleation rates, measured by direct counting in seeded crystallization of isotactic poly(1-butene).¹² However, while the range of cross-nucleation kinetics is similar in the three cases, the temperature dependence is different for each system, probably reflecting a different magnitude of the free energy barrier for cross-nucleation.

For all the systems for which there are data, the rate of cross-nucleation increases with increasing undercooling. This is a known behaviour of crystal nucleation, be it homogeneous or heterogeneous. The cross-nucleation process is unique in that it is undoubtedly heterogeneous, but the nucleating substrate (the parent phase) is in the process of growing. One path forward is to test whether the existing theory of heterogeneous nucleation³⁵⁻³⁹ can be extended to cross-nucleation between polymorphs. Central to this treatment is the free energy barrier for the creation of a nucleus of one polymorph on the surface of a crystal of the other polymorph. This concept had already been realized by Varga et al., who studied the “growth transformation” between α - and β -phase in isotactic polypropylene.¹⁶ However, due to the lack of quantitative kinetics data, the model proposed by Varga could not be validated.

Following the same approach, cross-nucleation can be described as the secondary nucleation of one polymorph on another, in analogy with the Hoffmann-Lauritzen theory of polymer crystal's growth.⁴⁰⁻⁴² The process is schematically shown in Figure 3, where all the relevant variables and parameters are highlighted.

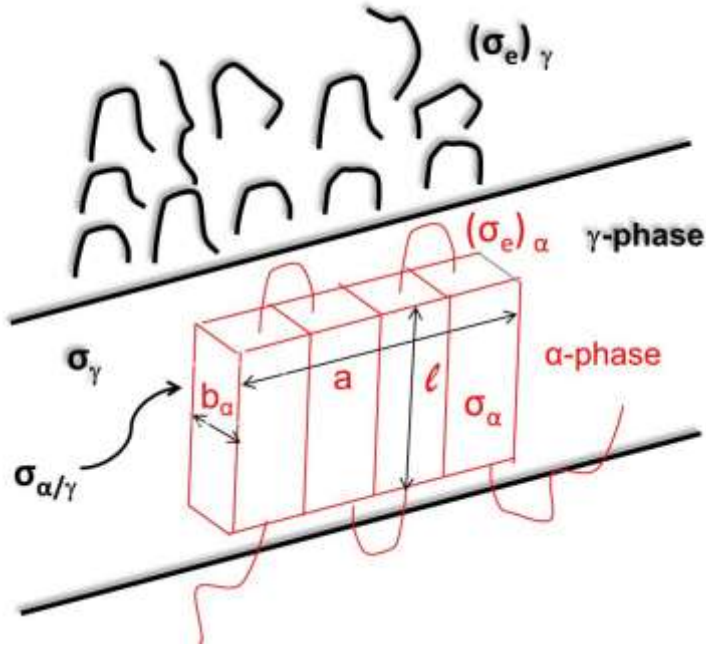


Figure 3. Schematic model for the formation of a α -secondary nucleus on the growth surface of γ -phase lamellar crystal. Adapted from Varga et al.¹⁶

With reference to Figure 3, the change in Gibbs free energy due to the creation of a secondary chain-folded α -nucleus on the surface of a γ -phase crystal can be written as:¹⁶

$$\Delta G_{\alpha/\gamma} = 2 b_{\alpha} l \sigma_{\alpha} + 2 a b_{\alpha} (\sigma_e)_{\alpha} + a l (\sigma_{\alpha/\gamma} + \sigma_{\alpha} - \sigma_{\gamma}) - a b_{\alpha} l \Delta g_{\alpha} \quad (3)$$

The size of the secondary nucleus is defined by its thickness and width, respectively parallel and perpendicular to the growth direction (b_{α} and a), and by the thickness along the chain axis (l). The free energy of the lateral and chain folding surfaces of α - and γ - crystals are indicated as σ_{α} , σ_{γ} and $(\sigma_e)_{\alpha}$, $(\sigma_e)_{\gamma}$, while the interfacial free energy between α - and γ -crystals surfaces is represented by $\sigma_{\alpha/\gamma}$. Finally, the difference in bulk free energy between the crystalline α -phase and the PPVL melt is given by Δg_{α} .

Thus, the free energy barrier for cross-nucleation, associated with the formation of a nucleus of sufficient (critical) size to allow its spontaneous growth, can be obtained by finding the maximum of equation (3):

$$\Delta G_{\alpha/\gamma}^* = \frac{4 b_{\alpha}^2 \sigma_{\alpha} (\sigma_e)_{\alpha} T_{m,\alpha}^0}{b_{\alpha} \Delta H_{m,\alpha} \Delta T_{\alpha} - \Delta \sigma T_{m,\alpha}^0} \quad (4)$$

where: $T_{m,\alpha}^0$ is the equilibrium melting temperature of the α -phase, ΔT_{α} is the undercooling of the α -phase at the cross-nucleation temperature and $\Delta \sigma = (\sigma_{\alpha/\gamma} + \sigma_{\alpha} - \sigma_{\gamma})$ is the difference in surface energy between one α/γ contact surface plus one α -phase/melt interface, and one γ -phase/melt contact surface of the same unit area. Incidentally, this model corresponds to the so-called non-coherent heterogeneous nucleation.^{36,38,43}

With these premises and according to existing theories of polymer heterogeneous nucleation,^{36,38} the rate of α -on- γ -phase cross-nucleation ($J_{\alpha/\gamma}$, number of nuclei per unit of γ -phase area and unit time) can be expressed as:

$$J_{\alpha/\gamma} = J_0 \exp\left(-\frac{U}{R(T-T_{\infty})}\right) \exp\left(-\frac{\Delta G_{\alpha/\gamma}^*}{kT}\right) \quad (5)$$

where J_0 is a temperature-independent frequency term and the first exponential describes the temperature dependence of segmental jump rate across the nucleus-melt interface at large undercoolings. In agreement with Hoffman-Lauritzen secondary nucleation theory of crystals growth,⁴⁰⁻⁴² this latter term can be expressed as in Equation 5, with U being the activation energy for segmental transport, R the gas constant and T_{∞} representing a hypothetical temperature, located around 30 °C below the glass transition temperature, at which all the motions relevant to crystallization cease.

By combining equation (5) and equation (4), and then taking the natural logarithm of both sides, we obtain:

$$\ln(J_{\alpha/\gamma}) + \frac{U}{R(T-T_{\infty})} = \ln(J_0) - \frac{4 b_{\alpha}^2 \sigma_{\alpha} (\sigma_e)_{\alpha} T_{m,\alpha}^0}{kT (b_{\alpha} \Delta H_{m,\alpha} \Delta T_{\alpha} - \Delta \sigma T_{m,\alpha}^0)} \quad (6)$$

The only two unknown parameters in Equation (6) are J_0 and $\Delta \sigma$, which can be obtained by linear regression of an appropriate model on the cross-nucleation kinetics data. The good quality of the regression can be judged from Figure 4.

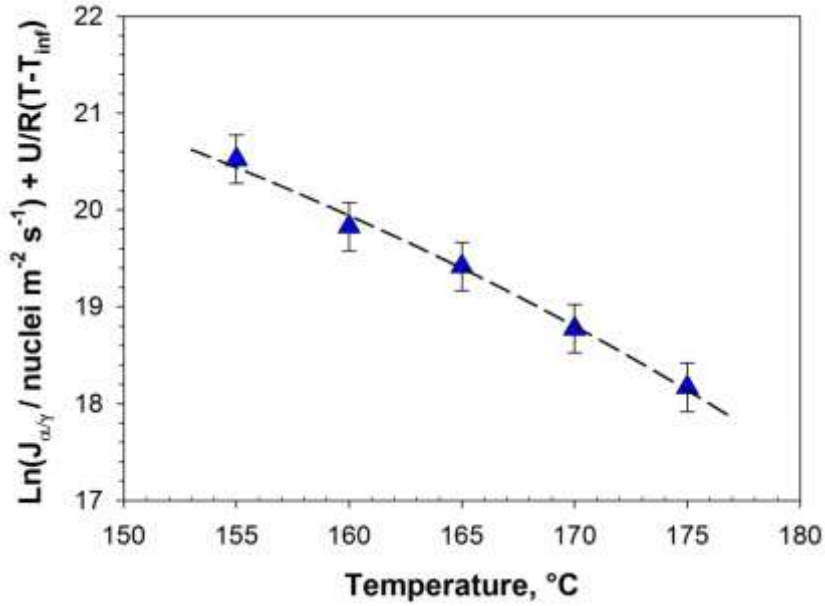


Figure 4. Natural logarithm of the measured cross-nucleation rate corrected for the transport term (see equation 7) as a function of crystallization temperature. Dashed black line represents the fitting of the data with equation 8.

The best-fit values of the searched parameters are: $J_0 = 8,9 \cdot 10^{15} \text{ m}^{-2} \text{ s}^{-1}$ and $\Delta\sigma = -1,7 \text{ mJ m}^{-2}$. Noticeably, the value of the pre-exponential factor is well in line with those obtained by Yu et al. for the α -on- δ phase cross-nucleation in pure D-Mannitol and its blends with polyvinylpyrrolidone, i.e., between $1.6 \cdot 10^{14}$ and $8.0 \cdot 10^{17}$.⁶ A similar value of J_0 between the two systems suggests analogous dynamics of the D-Mannitol molecule with respect to the PPVL repeating unit. The small negative value of $\Delta\sigma$ indicates a slight energy gain associated with the replacement of one γ -crystal/melt interface with one α/γ and one α -phase/melt contact surfaces. This is only possible if we have both a very low surface tension between α - and γ -crystals contact faces ($\sigma_{\alpha/\gamma}$) and a slightly higher value of γ -crystal/melt surface energy (σ_γ), with respect to σ_α . While a low α/γ interfacial energy is expected, it is reasonable to assume that the crystal/melt surface tension should not differ much between the two polymorphs. From the fitting value of $\Delta\sigma$ and the literature value of σ_α ³¹ we can derive that the minimum difference between σ_γ and σ_α required for obtaining a positive value of $\sigma_{\alpha/\gamma}$ is about 7%. Considering a possible σ_γ value 7 to 15% higher than σ_α , the corresponding surface tension between the two crystals is comprised between 0.3 and 3 mJ m^{-2} . Remarkably, this range of values is in agreement with the estimate of Varga et al, based on thermodynamic and morphological considerations, for the analogous case of α -on- β growth transformation in isotactic polypropylene.¹⁶

It is interesting to compare the value of $\Delta\sigma$ for secondary nucleation of α -on- γ phase in PPVL with the ones typically obtained for the heterogeneous nucleation of polymers on diverse substrates. Several examples of polymers nucleating onto the surface of fibres of different materials in composites are available.^{37,44,45} The values of $\Delta\sigma$ observed in these cases roughly span between 0.7 and 10 mJ m^{-2} , the lower the value the higher the heterogeneous nucleation

efficiency. The higher $\Delta\sigma$ values can be attributed to a higher surface tension between substrates and polymer crystal, compared to the extremely low one found for PPVL polymorphs. This comparison corroborates our result, given that a lower interfacial energy is expected between chemically identical substrates, with respect to substrates of unlike chemical nature.

From equation 4, the value of the free energy barrier for cross-nucleation, $\Delta G_{\alpha/\gamma}^*$, can be evaluated. Considering a crystallization temperature of 165 °C, in the middle of the explored range, a $\Delta G_{\alpha/\gamma}^*$ of 63 kJ/mol is obtained. The magnitude of this free energy barrier is perfectly in line with typical values found for secondary nucleation-controlled growth of polymer crystals (30-120 kJ/mol), including that of α -phase PPVL. Unfortunately, the free energy barrier for γ -on- γ PPVL secondary nucleation (i.e, for γ -phase growth) cannot be calculated due to the lack of assessed data. However, the estimated energy barrier for α -on- γ cross-nucleation in PPVL justifies the observed competition between cross-nucleation and homo-polymorphic growth, in terms of probability of the two types of secondary nucleation events.

Despite the proposed model of secondary nucleation between polymorphs yielded reasonable values of the relevant parameters, at this stage it is necessary to underline the approximations that were implicitly made. In deriving Equation 6, we assumed that the measured cross-nucleation rate takes into account all the α -nucleation events occurring at the γ -spherulite growth front. However the situation holding at the lamellar growth surface is certainly more complex, as it can be understood by considering both Hoffman-Lauritzen crystal's growth theory and cross-nucleation. On the surface of the growing γ -crystals four different events can in principle occur. Using the formalism introduced by Hofmann-Lauritzen theory, we can identify the formation of α - and γ -nuclei on the growing surface, at rates i_α and i_γ , and their lateral growth to

cover the crystalline substrate, with a spreading rate g_α and g_γ . Incidentally, we also note that in the explored range of undercooling, the growth of PPVL α -phase (and probably of γ -phase as well), occurs in regime II,³¹ where multiple nucleation events take place on a given crystal's surface to complete a new monolayer.^{40,41}

Given the complex situation outlined above, the competition between homo-polymorphic growth and cross-nucleation is evident. In this situation, the formation of a supercritical nucleus of the α -phase on the γ -phase crystal surface might not lead necessarily to an observed cross-nucleation event. Indeed, as pointed out by Varga,¹⁶ we can hypothesize that the hetero-polymorphic nucleus should grow and cover the whole surface of the lamella, completing one monolayer of the new modification (immediately or after successive attachment of several monolayers). Therefore, only a fraction of the cross-nuclei which form will eventually lead to the observed growth of the new polymorph on the surface of the parent one.

However, we observe that in the specific case of PPVL, as well as in the other investigated cases of cross-nucleation in D-Mannitol and isotactic poly(1-butene),^{6,12} the growth rate of the daughter polymorph is several times higher than the one of the parent phase. As such, the formed cross-nucleus has few chances of getting hampered in its growth by the other polymorph. On the contrary, it is highly probable that it will give rise to a spherulite of the new modification. Therefore, when the ratio of parent to daughter phase growth rates is high enough, the approximation of equation 7 can be considered valid. Of course, the situation could be different when the two polymorphs grow at similar rates, and the two phenomena, i.e., cross-nucleation and homo-polymorphic growth, can effectively hinder each other.

Some indications that cross-nucleation could not be strictly considered a “simple” heterogeneous nucleation process are already present in the literature. Indeed, at the same undercooling, the probability of cross-nucleation of D-Mannitol α -phase on single crystal seed of the β -polymorph is higher for the crystalline face with lower growth rate.⁷ This result indicates either a large effect of lattice matching between the parent and daughter polymorphs, or, as it was suggested, an effect of the seed polymorph’s growth rate on cross-nucleation. However, this possible inverse relationship between the growth rate of the first polymorph and the cross-nucleation rate of another structure on its surfaces is not universal. In fact, for the cases of polypivalolactone and isotactic poly(1-butene)¹² the opposite is true, since the decrease of the parent polymorph’s growth rate with increasing temperature is also accompanied by a substantial decrease of cross-nucleation rate. It can thus be deduced that, at least in these cases, the nucleation energy barrier effect prevails over the hypothetical substrate’s growth rate effect. The other quantitative study, concerning α -on- δ phase cross-nucleation in D-Mannitol,⁶ is not conclusive, since with decreasing the undercooling we encounter both a decrease in the cross-nucleation rate and an increase in the δ -form rate of growth. However, also in this case the observed temperature coefficient of the nucleation rate between the polymorphs is compatible with a simple heterogeneous nucleation mechanism.

Finally, the possible existence of epitaxy between α - and γ -phases of PPVL, leading to the observed cross-nucleation, will be briefly discussed. As outlined in the introduction, epitaxial matching between cross-nucleating polymorphs is not a requisite, although it is sometime observed.^{8,17,22,23,25} Indeed, even for the very same system, cross-nucleation can occur with either lack or presence of preferred lattices orientation between the two polymorphs, depending on the crystallization conditions.²² For the present case of PPVL, unfortunately it is not possible to draw

solid conclusions on the existence of epitaxial matching among the cross-nucleating structures. In fact, the growth plane of the γ -form is not known. However, a hypothesis can be put forward, on the basis of the knowledge of the α -phase fold plane. The growth of α -crystals proceeds by successive addition of chain stems on $(1\bar{2}0)$ planes, resulting in an inter-helical distance of about 0.78 nm at the growth surface.³¹ This inter-chain distance is compatible with the one of the a-axis of the orthorhombic γ -form (0.823 nm²⁷), with a mismatch of only about 5%. Therefore, epitaxy between α -and- γ -phase of PPVL exists, it could possibly occur by matching of the $(020)_\gamma/(1\bar{2}0)_\alpha$ planes. We note that the occurrence of this epitaxial relationship could justify the very low surface tension between the two crystals, found by fitting the cross-nucleation kinetics data with a secondary nucleation model.

CONCLUSIONS

Cross-nucleation, i.e., the heterogeneous nucleation of one crystal polymorph on another, is not a rare phenomenon, as more and more new examples are being reported, both for small and macro-molecules. Despite the increasing number of observations, our understanding of the process is not widening in parallel. This is also due to the scarcity of quantitative studies.

In this work, we investigated the cross-nucleation between concomitantly crystallizing α - and γ - phases of polypivalolactone, determining its kinetics by the analysis of the crystallized morphology. The nucleation rate data are described by a model accounting for the secondary nucleation of one polymorph on another.

In this way, it is shown that the process is favoured by an extremely low surface tension between the two crystals, and by a free energy barrier not significantly different with respect to the one which governs homo-polymorphic growth in the vicinity of the melting temperature.

If the proposed model will be applied to other cross-nucleating systems, it could be possible to understand whether the occurrence of cross-nucleation is controlled by a surface tension criterion. However, it is also recognized that cross-nucleation might be more complicated than classical heterogeneous nucleation on a substrate, since a competition with the growth of the parent polymorph is expected. The present work may serve as a basis for further experimental and simulation studies aimed at gaining a deeper knowledge on the topic.

Supporting Information

Example and discussion of raw data analysis, cross-nucleation kinetics data as a function of temperature and description of the data fitting procedure are supplied as supporting information.

AUTHOR INFORMATION

Corresponding Author

* Dario Cavallo, dario.cavallo@unige.it

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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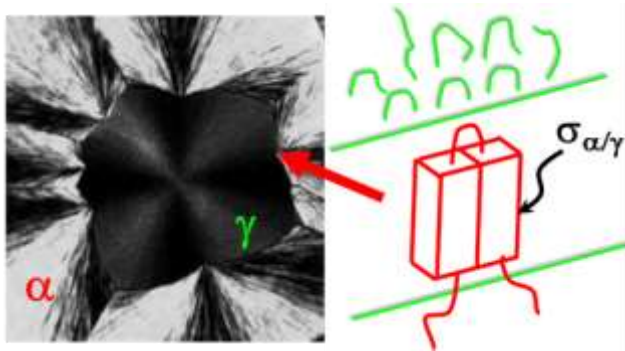
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Cross-nucleation between concomitantly crystallizing α - and γ -phases in polypivalolactone: secondary nucleation of one polymorph on another

Dario Cavallo, Francesca Galli, Lian Yu, Giovanni C. Alfonso



Synopsis: The kinetics of cross-nucleation between two polymorphs of polypivalolactone (α on γ) is measured for the first time as a function of crystallization temperature and successfully explained as heterogeneous secondary nucleation among different crystalline modifications.