

## Diffusionless Crystal Growth from Glass Has Precursor in Equilibrium Liquid

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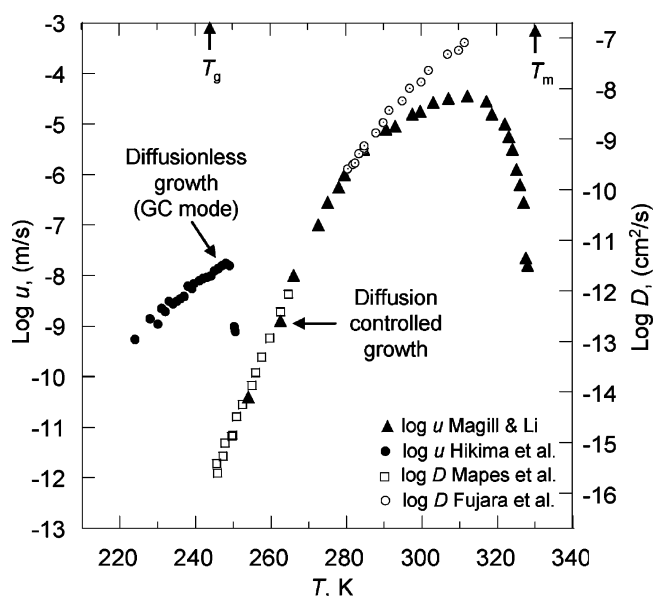
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A remarkable property of certain glass-forming liquids is that a fast mode of crystal growth is suddenly activated near the glass transition temperature,  $T_g$ , and continues in the glassy state. This mode of growth, termed GC (glass-crystal), is so fast that it is not limited by molecular diffusion in the bulk liquid. We have studied the GC growth by growing multiple crystal polymorphs from the liquid of ROY, currently the top system for the number of coexisting polymorphs of known structures. We observed a new feature of GC growth that conflicts with its current description in the literature. We found that the GC mode is not truly a new growth mode suddenly appearing near  $T_g$  but one already existing in the equilibrium liquid up to approximately  $1.15 T_g$ , in the form of fast-growing fibers. This finding is relevant to testing different explanations for GC growth and favors the view that GC growth is enabled by molecular motions that are native to the glass but still persist in the viscous liquid.

The rate of crystal growth from a one-component liquid typically increases and then decreases with supercooling. This kinetic pattern is shown in Figure 1 (triangles) for *o*-terphenyl.<sup>1</sup> This pattern exists because, at small supercooling, the growth rate is limited by the thermodynamic driving force for crystallization and, at larger supercooling, the growth rate is limited by molecular mobility in the liquid. It has been argued that diffusion is the molecular motion in the liquid that defines the kinetic barrier for crystal growth.<sup>2–6</sup> For *o*-terphenyl, the diffusion control of crystal growth is evident from the proportionality of the growth rate to the self-diffusion coefficient (open symbols)<sup>5,7</sup> when supercooling is sufficiently large. This proportionality exists over a temperature range in which  $u$  changes by 5 orders of magnitude.

Diffusion-controlled crystal growth serves as a reference point for a new mode of crystal growth that is activated near the glass transition temperature,  $T_g$ . If the liquid of *o*-terphenyl is cooled to 249 K ( $T_g + 6$  K) or lower, the rate of crystal growth abruptly increases (Figure 1, solid circles).<sup>8,9</sup> The new growth mode is observable deep in the glassy state, and for convenience, we shall refer to it as the glass-crystal or GC mode. The growth rate of the GC mode is orders of magnitude faster than expected for diffusion-controlled growth. Because the onset of GC growth is not accompanied by a similar increase in diffusion coefficient (Figure 1, open squares),<sup>5</sup> the GC mode is appropriately called “diffusionless”, in contrast to diffusion-controlled growth. The GC mode is important for understanding the stability of glassy (amorphous) materials and especially the stability of amorphous drugs, which are typically stored and used near  $T_g$ .

Current explanations differ for the GC growth process. Oguni and co-workers describe it as the coalescence of homogeneous



**Figure 1.** Crystal growth rate,  $u$ , and self-diffusion coefficient,  $D$ , of supercooled *o*-terphenyl liquid.

nuclei onto the surface of existing crystals (“homogeneous-nucleation-based crystallization”).<sup>8</sup> They attribute its fast rate to enhanced nucleation near  $T_g$  and the control of the process by a secondary relaxation (the  $\beta$  process), rather than the structural relaxation of the liquid (the  $\alpha$  process). Tanaka views the fast GC growth as a result of the extensional stress around a crystal growing in a glass due to the crystal’s higher density.<sup>10</sup> He suggests that this stress “should provide the free volume to the particles surrounding the crystal, increase their mobility, and help further crystallization”.

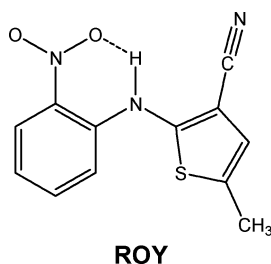
We have studied GC growth by growing different crystal polymorphs from the same liquid to learn how crystal structure

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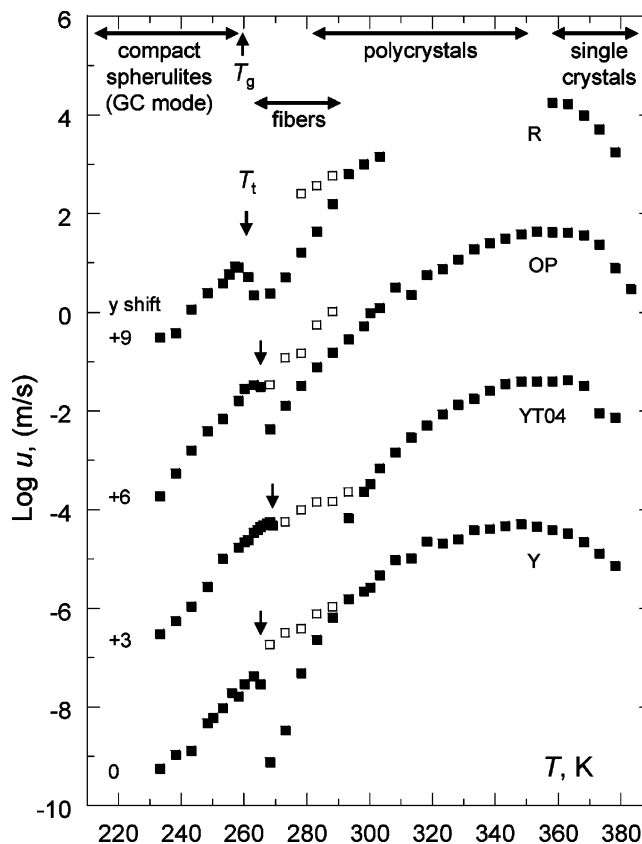
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influences growth kinetics. For this study, we used the polymorphs of 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile, named ROY for its numerous red, orange, and yellow polymorphs.<sup>11–14</sup> ROY is currently the top system for the number of coexisting polymorphs of known structures (seven)<sup>13</sup> in the Cambridge Structural Database.<sup>15</sup> In the course of this study, we observed a new feature of GC growth that conflicts with its current description in the literature. In particular, the previous work has described GC growth as suddenly emerging at some temperature on cooling and being completely turned off at the same temperature on heating.<sup>8,16</sup> We observed, however, that the growth mode already exists in the equilibrium liquid in the form of fast-growing fibers up to approximately  $1.15 T_g$ . This feature was observed for the four ROY polymorphs showing GC growth. This finding is relevant to testing different explanations for GC growth and favors the view that GC growth is enabled by molecular motions that are native to the glass but still persist in the viscous liquid.



To crystallize different polymorphs from the ROY liquid, we relied on spontaneous nucleation, cross-nucleation between polymorphs,<sup>13,14</sup> and seeding. In all, nine polymorphs were crystallized: R (red),<sup>11</sup> R05 (second red form discovered in 2005),<sup>14</sup> ORP (orange-red plate),<sup>11</sup> ON (orange needle),<sup>11</sup> OP (orange plate),<sup>11</sup> Y (yellow),<sup>11</sup> YN (yellow needle),<sup>11</sup> Y04 (second yellow form discovered in 2004),<sup>13</sup> and YT04 (Y04 transformed).<sup>13</sup> The growth of various polymorphs was initiated as follows: (1) spontaneous crystallization at room temperature yielded Y04 (most often), YN, and ON (least often); (2) spontaneous crystallization at room temperature following nucleation at 258 K yielded ORP in addition to the list in (1); (3) cross-nucleation between polymorphs yielded R (on Y04),<sup>13</sup> R05 (on Y04),<sup>14</sup> and YN (on R) near room temperature<sup>13,14</sup> and yielded YT04 (on Y04) and R (on ORP) at 258 K; (4) seeded crystallization yielded Y (at any temperature) and OP and YT04 (above 358 K). Seeding was performed by introducing seed crystals to liquids or by partially melting existing crystals and allowing remaining crystals to serve as seeds for subsequent crystallization. The polymorphs could be identified on sight from their colors, morphologies, and crystal optics, but their identity was confirmed with Raman microscopy (Renishaw System 1000 Micro-Raman spectrometer with a HeNe laser and peltier-cooled CCD detector), X-ray diffraction (Bruker D8 Advance diffractometer with Cu K $\alpha$  radiation), and melting-point determination (Linkam THMS 600 hot/cold stage).

Crystal growth rates were measured with the aid of a light microscope (Nikon Optiphot Pol) and the hot/cold stage. ROY crystals (ca. 3 mg) were melted between two 15 mm cover glasses at 403 K for 5 min and cooled at 20 K/min to temperatures of crystallization. The thickness of the liquid sample was 10–15  $\mu\text{m}$  and confirmed (by varying thickness from 5 to 150  $\mu\text{m}$ ) not to affect the growth rates. We changed the silicate cover glass to aluminum foil or Kapton (polyimide) film and observed no effect of the container material on the growth rates. The crystal growth rate was measured from the

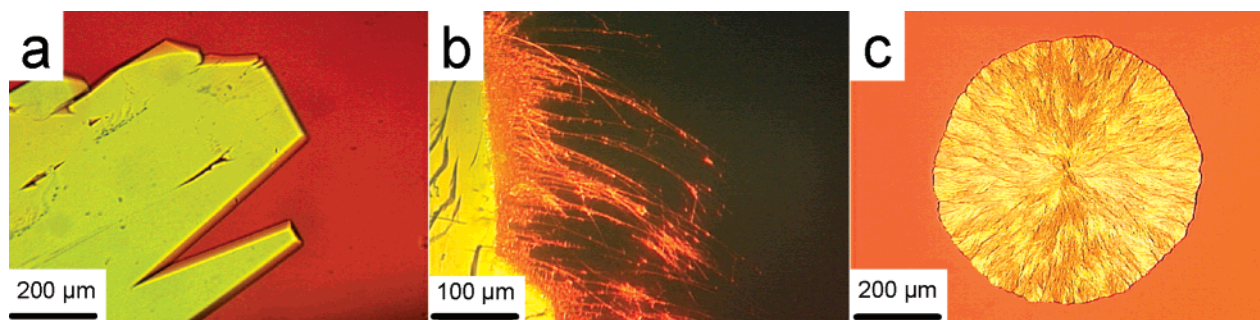


**Figure 2.** Growth kinetics of ROY polymorphs that show GC mode. For clarity, growth rates are offset as shown.  $T_t$  (down arrow) is the onset temperature for GC growth. Approximate temperatures are indicated for various growth morphologies: single crystals, polycrystals, isolated fibers, and compact spherulites of GC growth. Open symbols are the growth rates of isolated fibers. All polymorphs show an abrupt change in volume growth rate at  $T_t$  but no apparent discontinuity in linear growth rate if the GC growth is compared to the fast fiber growth above  $T_t$ . The growth of R could not be measured between 303 and 358 K because YN crystallized on it. The fibers of R could not be tracked between 263 and 273 K because they were dense and curved.

advance speed of the crystal front into the melt at a constant temperature and was found to be independent of time. To increase experimental output, crystal growth rates were sometimes measured from growth rings developed at different temperatures.<sup>17</sup> For this experiment, one or more samples were placed in a DSC cell (TA Instruments Q1000) and the temperature and duration of crystallization were programmed via the DSC control. On complete crystallization, the samples were removed from the DSC cell and the growth rings developed at different temperatures were measured through the microscope. Each crystal growth rate reported was the average of three to six measurements.

Some ROY polymorphs did not show the GC mode, while others did. Those not showing the GC mode consistently grew as spherulites, and their growth rates smoothly declined with falling temperature. Those showing the GC mode, in contrast, changed growth morphologies with temperature. This paper concerns the second group of polymorphs; a subsequent paper will discuss the difference between the two groups of polymorphs.

The ROY polymorphs showing GC growth were YT04, Y, OP, and R. Figure 2 shows their growth kinetics. Near their melting points,  $T_m$ , these polymorphs grew as faceted single crystals (see Figure 3a for an example). With falling temperature, the growth became polycrystalline with decreasing grain size.



**Figure 3.** Change of growth morphology of ROY polymorphs with temperature illustrated with polymorph YO4. (a) Faceted single crystal observed near the melting point (380.0 K). (b) Fibers growing at 278 K from a single crystal previously formed near  $T_m$ . Crossed polarizers were used to reveal the fibers; they were otherwise difficult to see. (c) A spherulite growing at 267 K in the GC mode.

**TABLE 1: Kinetic Parameters for the GC Growth Mode<sup>a</sup>**

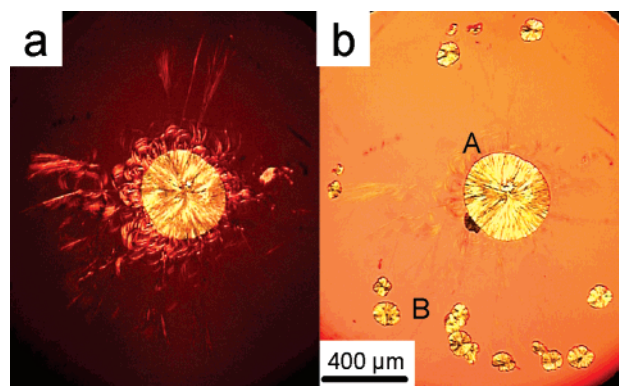
transformation	$T_i$ , K	$\log(u, \text{m/s})$ at $T_g$	$n_\alpha = u\tau_\alpha/a$ at $T_g$	$E_a,^b$ kJ/mol	ref
ROY, $T_g = 260$ K, $a = 7.5$ Å					
L/G $\rightarrow$ YT04	269	-7.7	2700	$83 \pm 2$	this work
L/G $\rightarrow$ Y	265	-7.5	4200	$76 \pm 4$	
L/G $\rightarrow$ OP	265	-7.5	4200	$88 \pm 3$	
L/G $\rightarrow$ R	261	-8.0	1400	$71 \pm 4$	
<i>o</i> -terphenyl, $T_g = 243$ K, $a = 7.7$ Å					
L/G $\rightarrow$ C	249	-8.1	1100	65	8
salol, $T_g = 215$ K, $a = 7.2$ Å					
L/G $\rightarrow$ C	226	-7.7	2800	57	19
toluene, $T_g = 117$ K, $a = 5.9$ Å					
L/G $\rightarrow$ C	116	-8.2 <sup>c</sup>	1100	50	20

<sup>a</sup> L/G  $\rightarrow$  X: crystalline phase X growing from liquid and glass.

<sup>b</sup> Error given is one standard deviation. <sup>c</sup> Extrapolated value.

Down to ca. 303 K, the growth morphology remained compact (space-filling) with sharp interfaces with the liquid. Below ca. 303 K, these polymorphs began growing fiberlike crystals that did not fill space. The fiber growth could be observed simultaneously with the compact growth over a small range of temperature, with the fibers growing ahead of the compact crystalline layer. Below ca. 293 K, the new growth was composed of fine fibers (Figure 3b). Some fibers were observed to extend deep into the liquid, while many others trailed behind, slowly filling space. For this morphology, we report two growth rates (Figure 2): the faster rate (open symbols) for the growth of far-reaching individual fibers and the slower rate (solid symbols) for the expansion of maximally thickened layers of fibers into the liquid (rates of the fibers filling space). For polymorph YT04, the maximally thickened fiber layer was slow to form and difficult to follow; the growth rates reported are mainly those of individual fibers.

Below a transition temperature,  $T_i$  (Table 1), each polymorph showing GC mode grew as compact, space-filling spherulites with sharp interfaces with the liquid (Figure 3c) and without thin fibers protruding into the liquid. Observation by light microscopy showed that the spherulites were composed of fine fibers whose sizes were comparable to the isolated fibers observed at higher temperatures. In all cases,  $T_i$  was near and slightly above  $T_g$  and the GC mode could be observed deep into the glassy state. The transition between fiberlike growth above  $T_i$  and the GC growth was sharp; a temperature change of several degrees K (3 K for YT04) was sufficient to switch between the two morphologies. Table 1 shows the kinetic parameters of the GC growth of ROY, which are similar to those reported for other GC systems.<sup>8,16,19,20</sup> The growth kinetics were Arrhenius, and the corresponding energies of activation are given. Table 1 also shows the number,  $n_\alpha$ , of molecular layers



**Figure 4.** (a) Fibers of YT04 emerging at 270 K in 250 min from a spherulite previously grown at 267 K. Crossed polarizers were used to reveal the fibers and resulted in a dark background. (b) Same as part a but after returning to 267 K for 30 min, allowing GC growth to occur. One polarizer was used, resulting in a bright background and low visibility of the fibers seen in part a.

being added to the crystalline phase during GC growth in one structural relaxation time,  $\tau_\alpha$ , of the liquid. The number  $n_\alpha$  is given by  $u\tau_\alpha/a$ , where  $a$  is the molecular diameter<sup>18</sup> and  $\tau_\alpha \approx 100$  s at  $T_g$ .  $n_\alpha$  is 1700–4200 for the GC growth of ROY, and similarly large for other GC systems. These values contrast with the relation  $n_\alpha < 1$  found for diffusion-controlled growth.<sup>6</sup> For a GC system, no substantial  $\alpha$  relaxation of the liquid occurs during the time one layer of molecules is added to the crystalline phase, whereas this is feasible for diffusion-controlled growth. This difference justifies the description of GC growth as diffusionless.

Despite their different morphologies, the compact GC growth below  $T_i$  and the fiber growth above  $T_i$  were found to be related. One piece of evidence is that the linear growth rates of the two modes fall on a smooth curve (Figure 2), showing no discontinuity at  $T_i$ . A second piece of evidence came from temperature-cycling experiments. To be specific, we describe the finding with polymorph YT04 ( $T_i = 269$  K); the other polymorphs behaved similarly. Upon warming to 270 K, a spherulite previously growing at 267 K apparently ceased to grow. Careful observations, however, revealed thin fibers emerging from the spherulite (Figure 4a). The fibers were difficult to discern initially because they were thin and sparse but over time became denser and more apparent, especially if viewed between crossed polarizers. These fibers resembled those in Figure 3b, which grew from a single crystal cooled to lower temperature. Real-time observation showed that the fibers could continue to grow, branch (nucleate new fibers), or stop growing. Over time, the combination of these three processes led to some fibers (the “survivors”) reaching deep into the liquid while most fibers trailed behind. This situation is illustrated in Figure 4a for a

holding time of 250 min at 270 K. At this time, both actively growing and “dead” fibers existed in the liquid and the farthest-reaching ones were still actively growing. The growth rate calculated from the farthest-reaching fibers was approximately the same as that of the GC growth at 267 K; that is, no discontinuity existed in the linear growth rate. A discontinuity, however, existed in the volume growth rate at  $T_i$  because the compact GC growth filled space and the fibers did not.

If the sample in Figure 4a was returned to 267 K, the GC growth resumed but not from all crystal/liquid interfaces (Figure 4b). The GC growth resumed predominantly from the ends of the farthest-reaching fibers (B), not the original growth front (A) or the fibers in between. This result indicates that the ends of *actively growing* fibers are the preferred sites for initiating new GC growth.

Oguni and co-workers describe GC growth as suddenly emerging at some temperature,  $T_i$ , on cooling and being completely turned off at  $T_i$  on heating.<sup>8,16</sup> This description implies a sharp discontinuity in the linear growth rate at  $T_i$ . We report here, however, that the growth mode already exists in the equilibrium liquid in the form of fast-growing fibers up to approximately  $1.15 T_g$ . We found no evidence of discontinuity in the linear growth rate at  $T_i$ . This feature was observed for all four ROY polymorphs showing GC growth.

In their study of crystal growth from the liquid of *o*-terphenyl, Scherer et al. observed fast-growing “protuberances ahead of flat interface” below  $1.16 T_g$ .<sup>21</sup> The growth rates of the “protuberances” approximately match the GC rates of Oguni and co-workers<sup>8</sup> extrapolated to higher temperatures. The fast-growing protuberances of *o*-terphenyl appear to correspond to the fast-growing fibers of ROY reported here.

The results presented here are relevant to the theory of GC growth. Oguni and co-workers used the rate of homogeneous nucleation to explain the rate of GC growth.<sup>8</sup> One difficulty this model faces is to explain the sharp onset and termination of GC growth at  $T_i$ ; it would require sharp changes in the homogeneous nucleation rate with a small temperature change. Our study identifies another difficulty: to explain the resumption of GC growth at some but not all crystal/liquid interfaces after heating the system (Figure 4), this model would require a spatially heterogeneous reactivation of homogeneous nucleation.

In Tanaka's explanation of GC growth,<sup>10</sup> the extensional stress caused by a denser crystal growing in a less dense glass is assumed to “provide the free volume to the particles surrounding the crystal, increase their mobility, and help further crystallization”. This process would be possible only at temperatures so low that liquid flow cannot relieve the stress on the time scale of crystal growth. This model can explain why the GC mode differs from ordinary crystal growth at low temperature but in some manner disappears at higher temperature. Because tension builds with the progress of crystal growth, this model has difficulty explaining why the GC growth rate is independent of time. Another difficulty this model faces is to explain the persistence of GC growth as fast-growing fibers well above  $T_g$ ; at these temperatures, the liquid relaxes so rapidly that tension should be easily dissipated.

The existence of diffusionless crystal growth from glass is consistent with, though not proof of, the view that certain crystal structures can grow through local, oscillatory motions that are

native to the glass, requiring no bulk structural relaxation (the  $\alpha$  process). This view would explain the persistence of GC growth well above  $T_g$  by the persistence of local molecular motions characteristic of the glass in the viscous liquid.<sup>22</sup> An example of such motions is the  $\beta$  relaxation, which is observed in both glasses and viscous liquids and which merges with the  $\alpha$  relaxation at approximately  $1.2 T_g$ . It is noteworthy that  $1.2 T_g$  approximately matches the temperature below which fast-growing fibers are observed for ROY (Figure 2) and the temperature at which fast-growing crystals (protuberances) are observed for *o*-terphenyl.<sup>21</sup>

In summary, we observed a new feature of the diffusionless crystal growth from glass (the GC mode) while studying the growth of ROY polymorphs from its liquid near  $T_g$ . The GC mode is not truly a new growth mode suddenly emerging near  $T_g$  but one already existing above  $T_g$  in the form of fast-growing fibers. This finding is inconsistent with the current explanations of the phenomenon. A subsequent paper will examine the difference between ROY polymorphs that do and do not show GC growth in order to understand the role of crystal structure in this process.

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