Conundrum of γ glycine nucleation revisited: to stir or not to stir?

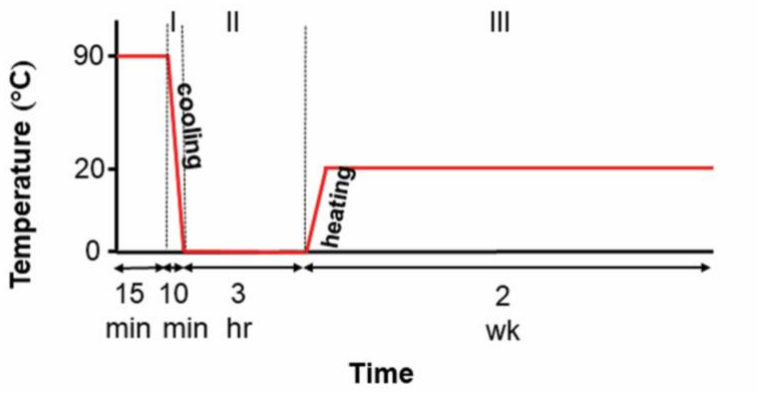
Maria J. Vesga[1], David McKechnie[1,2], Paul A. Mulheran[1], Karen Johnston[1], and Jan Sefcik[1,3]
[1] Department of Chemical and Process Engineering, University of Strathclyde, 75 Montrose Street, Glasgow, G1 1XJ, United Kingdom
[2] Doctoral Training Centre in Continuous Manufacturing and Advanced Crystallisation, University of Strathclyde, Glasgow, G1 1RD, United Kingdom
[3] EPSRC Future Manufacturing Hub in Continuous Manufacturing and Advanced Crystallisation, University of Strathclyde, Glasgow, G1 1RD, United Kingdom

Supplementary Information

In addition to our controlled quiescent experiments at a cooling rate of -1.5°C/min, we also performed experiments with quench cooling and quiescent conditions.

Methodology

The temperature profile for the quiescent quench cooling experiments is shown in SI Figure 1. In this protocol for each concentration, 16 vials were prepared and their crystallisation was monitored over three different periods. After the vials were heated for 15 min at 90°C in Polar Bear, they were swiftly transferred to an ice bath at 0±1°C. Crystallisation was then monitored for 3 hours. After the 3 hours, the vials were left on the bench at room temperature of 20°C (rapid heating) and crystallisation was monitored for two weeks. In order to obtain the quench cooling rate, the decrease of the temperature during cooling was recorded until the final temperature (0°C) was reached. Three vials with solution at 90°C including a thermal probe inside were used. The average cooling and heating rates were found to be 9°C/min and 1.7°C/min, respectively. Crystallisation was monitored visually at the end of each period and if crystals have nucleated they are removed from the vial and dried.

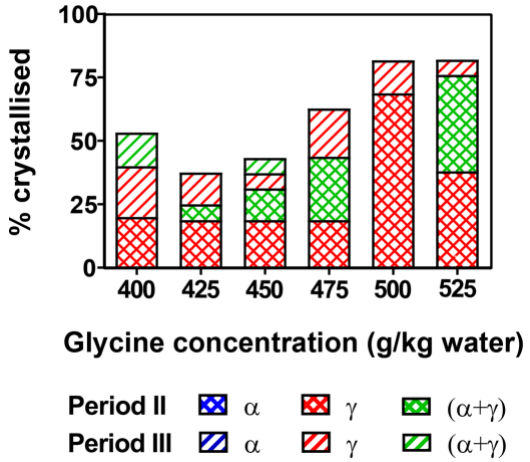


SI Figure 1. *The diagram illustrates the temperature profile used for quiescent conditions and quench cooling (setup 1c).*

Results

The results from setup 1a with controlled cooling at 1.5°C/min to 0°C (Figure 5a,b) can be compared to setup 1c with quench cooling at about 9°C/min to 0°C (SI Figure 2). In both controlled and quench cooling experiments no crystallisation was observed during cooling (period I). However, the percentage of vials crystallised during period II was significantly higher following quench cooling (SI Figure 2) compared with the controlled cooling (Figure 5a) at the same crystallisation temperature. Overall, there was a higher propensity to crystallise

at lower concentrations after quench cooling so the overall percentage of vials crystallised by the end of period III was less dependent on the solution concentration as was the case for the controlled cooling. Similar to the controlled cooling, the crystallisation of the γ form was still predominant for quench cooling, although a higher percentage of α+γ mixtures appeared following quench cooling. Quenched cooling increased the nucleation rate for these lower supersaturations compared to slower cooling.



SI Figure 2. *Crystallisation of glycine solutions under quiescent conditions with quench cooling to 0°C. For each concentration, the percentage was calculated over 16 vials.*

Movement induced nucleation

A total of 14 samples nucleated during transfer from Polar Bear to the stirring plate. All 14 cases are presented in the table below. In Figure 5 in the main manuscript, these cases were included as crystallisation during period I (cooling).

	Concentration (g/kg)	Polymorph
Figure 5a	0	-
Figure 5b	0	-
Figure 5c	500	γ
	525	γ
	525	γ
Figure 5d	0	-
Figure 5e	475	γ
	500	γ
	500	γ
	525	α+γ
	525	α+γ
Figure 5f	525	α+γ
Figure 5g	500	α+γ
	525	α+γ
	525	α+γ
Figure 5h	525	α+γ
	525	α+γ