POSTER 51

CMAC FUTURE MANUFACTURING RESEARCH HUB

Nucleation and Crystal Growth of α-glycine: Classification of Crystallisation Behaviour

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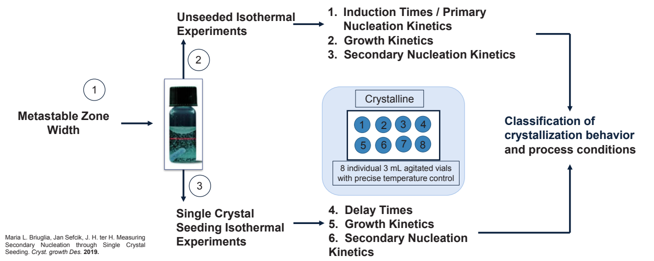
Introduction

- Assessing nucleation and growth kinetics at small, laboratory scale can rapidly and economically enable the optimization of crystallization processes by providing the tools to make more informed decisions early in process development.
- With a good understanding of the nucleation and growth kinetics, crystal size distribution and solid form can be controlled.

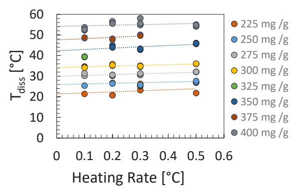
Workflow

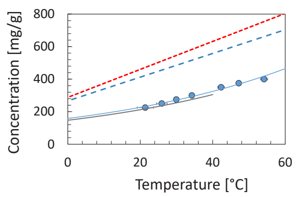


Maria L. Briuglia, Jan Sefcik, J. H. ter H. Measuring Secondary Nucleation through Single Crystal Seeding. Cryst. growth Des. 2019.

Solubility and Metastable Limit

1

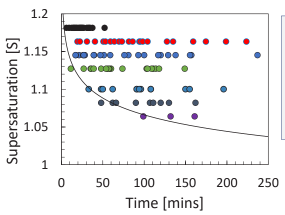




- Solubility recorded using the Crystal 16 at different heating rates. There is a clear dependence of solubility on the heating rate and as a result extrapolation to 0°C/min enables determination of true equilibrium solubility.
- Equilibrium solubility was then compared with metastable limit at 0.1 and 0.5°C/min to determine the metastable zone width.
- S (= C/C*) at 25°C calculated using α-glycine solubility concentration C* = 249.5 mg/g - best estimate from literature (Rowland, *J. Phys. Chem. Ref. Data* 2018, 47, 023104) (black line).

Induction Time and Primary Nucleation

2

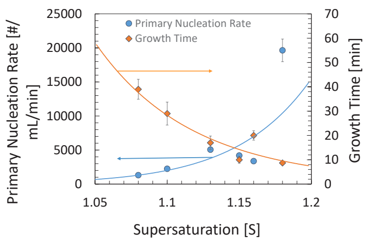


Induction time probability measurements recorded under isothermal conditions. With an increase in supersaturation the probability of nucleation taking place within a given time also increases.

The black curve indicates the estimated induction time.

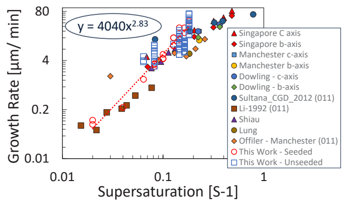
Induction time data was plotted as probability distributions (*P(t)*) and the primary nucleation rate (*J*) and growth time (t_g) were estimated.

S. Xiang, J.H. ter Horst, Crystal Growth Design 11, 2011 256-261



Growth Kinetics

3



Growth rates estimated using an image analysis algorithm. The data was compared with literature values and are seen to be in good agreement.

Data is plotted on a log scale to highlight the absence of a 'dead zone'. Instead, it may be better to think of this as an insignificant growth region.

L_{min} and Secondary Nucleation Kinetics

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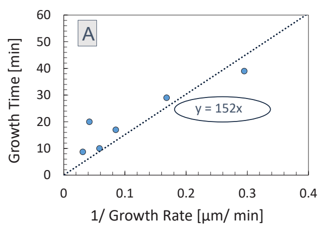
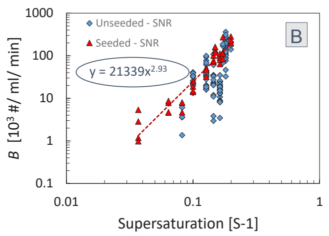
(A) The inverse of growth rate is shown against t_g at the same supersaturation. It was then possible to estimate the minimum crystal size required to initiate secondary nucleation (L_{min}). This value was estimated to be **152 μm.**





(B) Secondary nucleation rates from seeded and unseeded experiments. Secondary nucleation rates from unseeded experiments compared well with those from seeded experiments. Their similarity provides support for the single nucleus mechanism.

1. Briuglia, Sefcik and ter Horst. *Cryst. Growth Des.* 2019, 421, 423–4.
2. Brown et al, *Mol. Syst. Des. Eng.* 2018, 3, 518-548.

Classification of Crystallization Behaviour

5

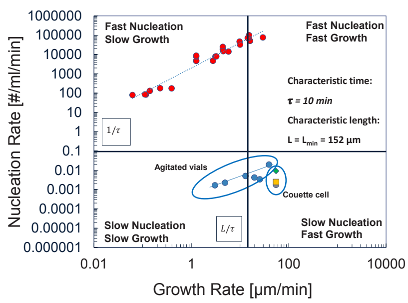
Nucleation rate: fast/slow vs 1/τ

Crystal growth rate: fast/slow vs L/τ

Characteristic time: τ
(e.g., crystallizer residence time)

Characteristic length: **L**
(e.g., target particle size)

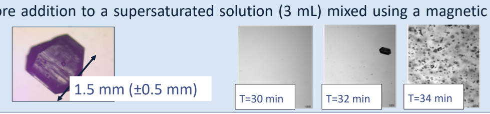
Secondary nucleation many orders of magnitude faster than primary nucleation at all supersaturations



Forsyth, C.; Mulheran, P. A.; Forsyth, C.; Haw, M. D.; Burns, I. S.; Sefcik, J. Influence of Controlled Fluid Shear on Nucleation Rates in Glycine Aqueous Solutions. Cryst. Growth Des. 2015.

Seeding Procedure

Single seeds were grown, characterised (optical microscopy and Raman spectroscopy) and washed before addition to a supersaturated solution (3 mL) mixed using a magnetic stirrer (700 RPM).



Conclusions

- A rapid small-scale workflow enabling the assessment of secondary nucleation and crystal growth kinetics has been developed.
- Absence of crystal growth dead zone and secondary nucleation threshold.
- Classification system has been developed for nucleation and growth kinetics.
- Glycine classified with primary nucleation slow and secondary nucleation fast with moderate growth rates up to S = 1.2.

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