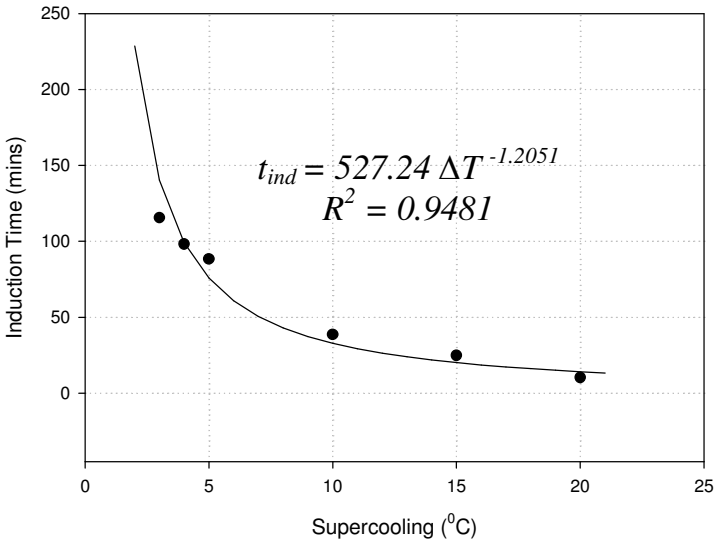
Project 7: ***Crystal Transformations and Crystallisation Methodologies*** Date: **23/8/2010**	Author: **Niall Mitchell** Strand: **Particle Engineering** Institute: University of Limerick

Title: Numerical Modelling of the Cooling Crystallisation of Paracetamol and Ethanol Solutions.

Principal Focus: The main aim of the project is to develop a numerical model capable of describing a batch cooling crystallisation process. The model utilises the method of moments, the population balance and solute mass balance equations to describe the evolution of the particle size distribution (PSD) throughout a batch process. The model employs experimentally determined kinetics to account for the competing processes of particle nucleation and crystal growth, the main factors affecting the quality of the final product.



Induction time Experiments:

Induction time experiments were conducted using in order to evaluate the nucleation kinetics of the solution system [1], shown in figure 1. The induction time is defined as the time required for 'first nucleation events' to be detected in a solution kept at a constant level of supersaturation. From the theory of Kubota the induction time, t_{ind} is given as a function of supercooling, ΔT, as follows:

$$t_{ind} = \left(\frac{N_m}{k_n V}\right)(\Delta T)^{-n}$$

The experiments were performed using a 500mL scale LabMax reactor from Mettler-Toledo, with a FBRM® probe employed to detect the point of nucleation.

Figure 1: Induction times versus degree of supercooling, measured using FBRM® probe.

Model Validation - Process Runs:

In order to validate to numerical model for the system a series of process type runs are utilised. Solution of initial concentration of 0.296kg/kg prepared on 500mL scale. Held above solubility for 30 minutes to ensure complete dissolution. Solution then cooled from 60^{0}C at 1^{0}C/min to 10^{0}C and solution concentration monitored using ATR-FTIR probe, shown in figure 2. Solution held at 10^{0}C for 1 hour to allow completion of crystallisation. Final PSD measured by sieve analysis.

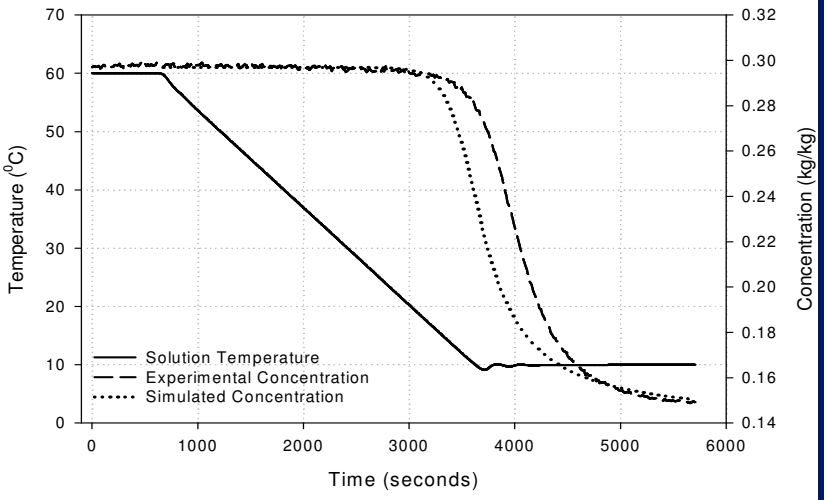


Figure 2: Solution temperature, experimental and simulated solution concentration for 1^{0}C/min process runs.

Discussion: Three key experimental variables are measured, namely solution concentration, crystal yield and final product PSD's. The simulated concentration is found to exhibit a similar trend to the experimental data. The model is found to provide a very accurate indication of crystal yield, with experimental and simulated yields of 46.7% and 49.3%, respectively. Final experimental PSD, found to exhibit smaller mean of size of 250µm, than simulated PSD, with a mean size of 300µm [2].

Future Work: The growth kinetics of the solution system will be estimated in isolation from seeded batch crystallisation experiments, which should improve the predictive ability of the numerical model. The polymorphic transformation from Form II to I of paracetamol in seeded batch crystallisations will be examined and a numerical model will be developed to describe the process.

References: [1] N.A. Mitchell, P.J. Frawley, J. Crystal Growth (2010), doi:10.1016/j.jcrysgro.2010.05.043
[2] N.A. Mitchell, P.J. Frawley, K. Hutton, 'Numerical Modelling of the cooling crystallisation of paracetamol-ethanol solutions', 4th IC-SCCE, Athens, Greece, 7-10 July, 2010.