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The conference began with two plenary talks, the first delivered by **Michael F. Doherty** of the University of Santa Barbara, California whose topic was "Predicting crystal growth rates and shape evolution for molecules of realistic API complexity". The speaker started by summarising Roger Davey's contribution to the field of crystal growth – In particular he referred to the 1987 Chemical Engineer article written by Davey (Davey, R.J. Looking into crystal-chemistry, Chemical Engineer, 443, 24, 1987) which inspired his own personal interest in the field.

The aim of the presented work was to develop a method of predicting the growth rates of individual crystal phases allowing the prediction of a crystal's final shape from first principles. The steps required to predict the rate of growth of specific crystal faces were outlined:

Step 1 Calculate solid-solid intermolecular interactions – i.e. find all strong periodic bond chains.

Step 2 Calculate critical lengths and kink densities which provide the edge velocity.

Step 3 Calculate crystal steady state shape using the Frank-Chernov condition.

The problems associated with predicting growth rates of crystals composed of non-centrosymmetric molecules were discussed. These challenges are related to the difficulty in determination of the periodic bond chain and the requirement to include kink rates for more than one type of kink. This difficulty in estimating kink rates required the authors to develop an expression for the kink rate for molecules with an arbitrary number of growth units, allowing for a model with predictive capability. The developed model uses a steady state master equation to calculate the probabilities of each possible kink site on the addition or subtraction of a growth unit. Results from the model agree with Chernov for situations with 1 or 2 kink sites and it can accurately predict the crystal shape of paracetamol grown at 5% supersaturation and also the shape of lovastatin needles. The researchers are now designing an application to predict crystal shape.

The second plenary address was given by **Gerard Coquerel** of the University of Rouen on "Crystallisation of Organic Compounds Guided by Solid-Vapour Equilibria". The speaker presented two case studies that demonstrate how crystallisation can be manipulated using the equilibrium between the solid and vapour phases. The first, Rimonabant has 13 different solvated phases when crystallised from different solvents. It has been observed that for the monohydrate form that peaks found during heating by differential scanning calorimetry (DSC) which correspond to the loss of solvent molecules, do not always match the observed mass loss peaks. The crystal structure of the monohydrate is observed from single crystals grown by a slow evaporation of the solvent. In the unit cell there are two conformations of Rimonabant, with a water molecule acting as a bridge between the conformers. This leads to a needle like morphology; the arrangement of conformers and water leads to channels which run along length of the needle.

On fast dehydration by heating to 100°C, the crystal structure collapses as the water leaves. On cooling from this state vitrification is observed at ~76°C, i.e. an amorphous solid rather than a crystalline solid is formed. On visual inspection of monohydrate crystals held at 60°C, lateral cracks can be seen. These cracks are the result of water breaking out of the crystal perpendicular to the length of the needle rather than leaving along the channels which run along the needle. For the

monohydrate, reversible sorption/desorption was observed at 2-4% RH (dehydration) and 14-16% RH (hydration) reproducibly. On slow dehydration at 0% RH over P2O5 the isomorphous phase was observed, which returned to the monohydrate on rehydration. The amorphous solid could not be hydrated to form the crystalline monohydrate.

The second study was based on C-HDMAPP, a drug used to stimulate the immune system. The speaker looked at the crystallisation of the anhydrous and monohydrate forms of the di-sodium salt. The monohydrate is more stable than the anhydrous form - it is stable up to 120 °C and collapse is observed by 150 °C. The anhydrous and monohydrate forms are both stable at high relative humidities – both show limited hygroscopic behaviour. Deliquescence was observed at 90% RH and re-crystallisation at 70% RH. It was found that by slurrying C-HDMAPP using ethanol as an anti-solvent resulted in better purification than recrystallising. Structural determination of single crystals grown in gels showed that the unit cell of monohydrate crystal has organic and inorganic layers. The presence of impurities smaller than C-HDMAPP in the hydrated crystal unit cell allows the incorporations of more solvent molecules into the crystal. A C-ethyl-IPP impurity when incorporated into the unit cell by (substitution for the monohydrate), left space in the structure for two additional water molecules.

Session 1a: Crystal Chemistry in Action: Industrial Crystallisation and Pharmaceuticals

In his keynote presentation “The Thermodynamics of Co-crystal Formation”, **Chris Hunter**, based at the University of Sheffield, discussed how molecular recognition events in both solution and solid states are affected by a large number of different factors. This means that it is difficult to develop a clear thermodynamic understanding of the intermolecular interactions in play. In order to develop an approach to estimate the relative magnitudes of non-covalent interactions in the solid-state, the researchers applied a model they had developed for the solution-state. In the solution-state, approximations were based upon electrostatics. In the talk it was confirmed how and why polarisation, dispersion/repulsion and entropy were all neglected. All functional groups could be assigned a position on the polar scale and, when two scales were plotted against one another, the point of crossing can be analysed. From this position a pair could be picked that would be predicted to have the strongest hydrogen bonds. Good correlation between these theoretical predictions and experimental work was achieved. Extending the ideas to include co-crystals, it was possible to use electrostatic potentials to calculate the difference in energy between the free molecule and the cocrystal. High energy differences appeared, experimentally, to produce co-crystals and consistent results were gained across a number of systems. A number of questions were raised by the audience including ‘Do the most common interactions in the CCD (Cambridge Crystal Database) match your results?’ to which the speaker commented that it had not been specifically investigated, however he felt it was probable. This presentation linked well with other presentations given at this conference with discussions of prediction through theoretical chemistry being confirmed and strengthened by experimental work.

William Jones, based at the University of Cambridge, initiated his presentation by discussing the benefits of forming co-crystals of given APIs. By forming co-crystals solid state properties can be modified and different problems investigated. He went on to discuss how his research group have used the methods of grinding and liquid assisted grinding to explore the range of co-crystals that can be formed for a given API. He stated that grinding and liquid assisted grinding offer an easy method for screening, rather than traditional solution methods. Data were presented showing that by using these methods in the formation of caffeine co-crystals, better results could be gained than from solution. In the case of dry milling caffeine and acetic acid the 1:1 and 2:1 ratio co-crystals were easily formed and also different polymorphs. By changing the milling times, ball size, vessel size and amounts, the different co-crystals and their polymorphs could be selectively formed. Pure

polymorph formation proved difficult until solvent-drop grinding was successfully employed. These results were extended to three other systems theophylline/citric acid, caffeine/citric acid and caffeine/succinic acid. The presentation moved on to the case of artemisinin, a drug used in the treatment of malaria. Due to its poor bioavailability co-crystal formation was attempted to improve this physical property. Finally some general points were made. Prof Jones concluded that the synthon approach does not always provide a correct prediction of whether a co-crystal will form. However, by using the CSD (Cambridge Crystal Database) and identifying molecular descriptors, the results can be ranked, allowing a scale of likely co-crystal formation.

The model pharmaceutical compound caffeine was discussed by **Klaus Rademann**. The compound was studied with respect to its crystal morphology from a range of different surfaces. The speaker gave an interesting history of caffeine, specifically in coffee. Soda lime silicate glasses, silicon and silver surfaces were all investigated for the morphology and structure of the crystal formed. The formation was studied using a range of techniques including optical microscopy, environmental scanning electron microscopy, atomic force microscopy, X-ray diffraction and Raman spectroscopy. The most stable crystal structure of caffeine was determined in 2007 and it grows as long needles, sometimes up to 20 mm in length. In this study, as well as the common needles, hexagons were also grown if the right surface was used. If glass surfaces were used needles were the outcome, however if silver sub-surface ion-exchanged metal operative (SIMO) were used hexagons were observed. The size distribution of the hexagons is limited with an average perimeter of only 10-15 μm . The formation of these hexagons depends upon the interaction of the solvent with the surface, and hence the contact angle. A number of questions were asked of the speaker including 'Is it a new polymorph?' to which the speaker replied that they would much like to know! Another audience member asked whether the porosity of the surface is a factor. The speaker felt that yes, it was important along with the contact angle.

Session 3 Fundamentals of Crystal Growth

Richard Dowling, from the University of Manchester, gave a very interesting and well-attended talk on the acceleration of crystal growth in two systems: glycine and DL-alanine. The solid state properties of the two systems were outlined, and the curious behaviour of glycine was described, where the unstable α polymorph is the solid form typically obtained even in the presence of the stable γ polymorph due to the growth kinetics. He emphasised that both growth and nucleation are important factors in the polymorphic outcome of a given experiment. The growth kinetics of α and γ glycine were plotted against each other as a function of supersaturation, as well as DL-alanine, and the presence of a dead zone in c-directional growth for γ glycine and DL-alanine was clearly shown. Two possible explanations for this behaviour were discussed. The 'Relay' mechanism was first considered, but does not explain the dead zone. The Kubota model, using Cabrera-Vermilyea theory and describing the solvent as an impurity, allows the dead zone to be explained.

Having discussed the pure growth kinetics, the interesting observation of an increase in growth rate of γ glycine and DL-alanine in the presence of CTAB was shown. This is so marked that a change in polymorphic outcome for a crystallisation of glycine may be seen, from α to γ . It was noted that CTAB was likely to bind to the negatively charged (0 0 -1) face, and that it seems to act to lower the critical supersaturation. Two previous studies associating this type of behaviour with desolvation effects or a reduction in interfacial energy were cited.

Studies of nucleation time of DL-alanine in the presence of CTAB were also carried out, and were described using the mononuclear nucleation model. These experiments showed that CTAB increases nucleation by more than an order of magnitude. Additionally, the solution mediated phase transformation from α to γ glycine was shown to be accelerated greatly in the presence of CTAB, with CTAB apparently increasing both γ glycine nucleation and growth. There were a large number of questions which were dealt with well, and the talk was later chosen as the best student presentation of the conference.

Anamaria Soare from the Delft University of Technology gave a clear and enjoyable presentation on the induced nucleation of crystals using a laser technique. The focussed laser creates cavities in the solution which in turn lead to crystal formation. Two model systems were discussed, $(\text{NH}_4)_2\text{SO}_4$ and KMnO_4 . In order for the laser energy to be absorbed, the solution had to be coloured, so red dye was added to the ammonium sulphate solution. Initially, a 2D cavitation bubble set up was studied, with a low (0.2%) supersaturation of ammonium sulphate. A series of images were shown, with crystals seen at the focal point of the bubble ring after 1 second. After the collapse of the bubble, crystals are seen in a ring, suggesting the crystals are formed before the bubble collapses, and it is thought that nucleation actually takes place at the beginning of bubble expansion. The formation and collapse of a bubble was shown from high speed camera pictures. The growth of the bubble is very quick, whereas the collapse is slower. The same experiment was carried out using 7% supersaturated potassium permanganate solution, and also gave similar results, though no ring of crystals was observed. A 3D experiment was also attempted, but crystals were not observed forming. Two possible explanations – that the crystals settle, or that they are thrown away from the focal plane of the camera – were discussed. Currently, the 3D experiment appears too challenging to study.

The theory behind the 2D results was explored in the second part of the talk. The bubble is formed by evaporation, after which a shock wave is sent through the liquid due to the expansion. Supersaturation around the bubble is high, and so nucleation is induced. A model was developed using classical heterogeneous nucleation, and the results from this model appear to match well with the practical observations. A heating period followed by explosion to bubble formation and a consequent drop in temperature was shown. At a supersaturation of 25% in the model, the bubble appears and crystals form. It is predicted that the crystals will grow rapidly after nucleation and then growth will slow. The talk was received with interest, and questions centred around the size of the bubbles.

Yin Yani, from A*STAR in Singapore, gave an engaging talk about her molecular simulation studies on the effect of additives on the habit of salbutamol sulphate crystals. Additives and impurities can act on the surface of crystals to affect growth, which in turn impacts upon the habit of the crystals. Salbutamol sulphate is a compound used for asthma and other breathing disorders, and so must be kept to small particle sizes of around $10\mu\text{m}$. The (2 0 0) and (1 1 0) faces are two of the three dominant faces on a typical crystal, and these were the surfaces studied. Three additives were considered, all of which are pharmaceutically acceptable – PVP, HPMC and lecithin. These additives were allowed to relax onto a fixed crystal surface, using COMPASS or CVFF force fields. Videos of the additives on the crystal surface showed them slowly adsorbing and rearranging. The intermolecular interaction energy with the first layer of the crystal faces shows that the interaction of all of the additives is greater with the (1 1 0) face than the (2 0 0) face. It also demonstrated that PVP was the most effective additive with the strongest binding energy.

A conformational study of the additives was shown, and the position of the oxygen atoms in each additive considered. In PVP, the carbonyl groups are close to the surface of the (1 1 0) face, to a greater extent than in the other additives. Additionally, the number of OH-O contacts that are close to the surface appears to be much higher for the (1 1 0) surface than the (2 0 0), correlating with the binding energy.

The mobility of the additives on each crystal surface was analysed, showing less mobility of the additives on the (1 1 0) face. Mobility was inversely correlated with binding affinity, as expected, for the three additives. Experimental observations of crystal habit showed that the PVP additive produced a significantly shorter crystal along the b axis, and that the other additives had a lesser effect. It was concluded that the work showed clear agreement between the modelling and practical outcomes, suggesting that the model worked well. The questions mainly related to the virtues of the force fields used in the calculations, and how they compared.

The afternoon session began with a very enjoyable **Annual Lecture** delivered by **Professor Michael McBride** of Yale University on “5 lessons I’ve learned by studying the mechanism of Viedma Ripening”. The lecture took the audience on a journey with Professor Mc Bride over the course of his career and highlighted the 5 major lessons he has learnt about crystal growth studying Viedma Ripening. The 5 lessons are summarized below:

Lesson 1: Saturation concentration depends on crystal size. Extended grinding increases solubility by 0.5 to 12%.

Lesson 2: Single crystals grow by cluster aggregation. Ostwald’s ripening mechanism versus Viedma ripening mechanism compared.

Lesson 3: With grinding, starting concentration depends inversely on the amount of solid. Population inversion between solid and solution is essential and occurs with grinding if there is solid.

Lesson 4: Refluxing leads to disequilibrium. At high concentrations invisible sub critical clusters can correlate without grinding

Lesson 5: Computer simulation algorithms can be seriously misleading.

Presentations given in honour of Roger Davey.

Prof. **Marco Mazzotti** of ETH Zurich gave an excellent keynote lecture discussing the precipitation and transformation of the D-mannitol polymorphs. At the beginning of the talk, Prof. Mazzotti discussed initial work with the two forms of L-glutamic acid. IR, Raman and FBRM analysis were carried out to monitor the composition of the solution and detect nucleation. This methodology was carried over to the D-mannitol system, however only Raman spectroscopy was appropriate. They found that particles in solution attached to the IR probe and prevented its use in the D-mannitol analysis.

Investigation into the affect of supersaturation on D-mannitol crystallisation was discussed and results were presented that do not follow Ostwald’s rule of stages. At high supersaturation the least stable α form nucleated first, followed by the transformation to the β and then the most stable γ forms, as per Ostwald’s rule of stages. However, at low supersaturation the γ form of D-mannitol, which is the most stable, was directly formed. A mathematical model has been created which predicts this occurrence and highlights that Ostwald’s rule of stages is indeed only a rule and not a generally applicable law.

An engaging lecture was given by Prof. **Angelo Gavezzotti** of the University of Milano which comprised of three main parts. Initially he spoke about the time he has spend with Roger Davey, and provided us with a number of photos taken from conferences in years gone by. The remainder of the lecture discussed computers and crystals and also the liquid-solid interface. Prof. Gavezzotti talked about the advances in crystal structure prediction and how currently calculations are based on static, perfectly ordered crystal structures, highlighting the future challenges in studying the dynamic aspects of crystallisation.

He also discussed his work on Monte Carlo molecular dynamics simulations with a requirement that an asymmetric index decreased during each move, and this was used as a way to model the crystallisation process. Criticisms were highlighted regarding how realistic a simulation is and how a strong bias drives a simulation too quickly and doesn’t allow for relaxation. The serious nature of these criticisms was addressed in the lecture and Prof. Gavezzotti left us with a memorable quote. “A simulation is neither realistic nor unrealistic; it is useful if it provides new ideas and insights, it is useless if it does not.”

The excitement began to build as Prof **John Garside**, formerly of UMIST took to the floor. Of all the speakers, John was the one who claimed the earliest encounter with Roger Davey, having met him in 1964. John summarised Roger's career, which began with an undergraduate degree in Bristol, and a research project with Bill Dunning examining spiral growth. He went onto join the research group of John Mullin, a founder member of BACG. Roger was already working at the interface of disciplines, being a chemist in a chemical engineering group. This was followed by a post-doctoral position at ETH in Zurich working with John Bourne. In 1977 Roger joined ICI based at the Runcorn site. John explained how working with Roger led him to understand the importance of crystallisation control. When urea is produced on a plant, the crystals are quite chunky in shape, yet when a PhD student grew urea from pure solution, it grew as long needles. Roger identified that a synthesis by-product, biuret acts as a habit modifier.

Roger's work has shown that it is important to have an understanding of molecular structure. As an industrialist, he had academic links being visiting professor at Strathclyde University, home to John Sherwood and Kevin Roberts and was later visiting professor at UMIST. He came onto the BACG committee in the 1980s and returned as chair in the 90s. He always had a strong scientific approach, but was also keen on pragmatic solutions.

After 18 years with ICI and later Zeneca, Roger joined The Chemical Engineering department of UMIST as Professor of Molecular Engineering. At the time there was a movement to re-focus chemical engineering research to build on a molecular foundation, and develop capability for product engineering. Roger chaired a Working Party and has been at the centre of developments in this area. In 2001 he was awarded the prestigious EPSRC Senior fellowship to examine nucleation, and in 2002 the Molecular Materials Centre was founded. John described the range of work, the number of papers and the people Roger has worked with as immense and his contribution wide, covering many areas, but with nucleation as a central theme.

John finished by describing some of Roger's characteristics. Describing Roger as one of the most rewarding and stimulating colleagues he has worked with, he said "Roger is a people person, and it is very easy to collaborate with him. He is an outstanding lecturer: witty, enthusiastic and fun."

As the president and honouree of the British Association of Crystal Growth, Professor **Roger Davey** gave a stimulating and motivating overview on some of his personal favourite research projects he has encountered over the past 40 years in which Roger deservedly displayed his involving effort, passion for discovery, and above all, the art of having fun in the area of crystal engineering.

Terephthalic acid, a much loved favourite which Roger worked with during his ICI years was the focus of the first half of his talk. He focussed on the nature of terephthalic acid including areas of phase characterisation and the morphologies of the polymorphic forms 1 and 2. Preparation of the polymorphs was briefly discussed as well as the crystallography of the structures. The nature of the form 2 to form 1 transition was discussed and it was found that form 2 was the most stable at room temperature and pressure. Roger then went on to acknowledge a publication released 15 years later by Trout et al who proceeded to explore the pathway of transformation of form 1 to form 2 of terephthalic acid which he agreed to be compatible with his own discoveries.

The second half of Roger's talk was concerned with the designing of acid-acid co-crystals where he began working on benzoic acid in the hope of forming a co-crystal. From this work 5 systems were determined and characterised and later published. Finally Roger spoke about the structure property relationship whereby relating molecular to the supramolecular referring to work on a caffeine – maleic acid system where a new polymorph of maleic acid was discovered. Roger closed his talk with a brief conclusion and proceeded to thank many of his collaborators and various researchers in the field who have all, in turn, outlined some significant challenges in crystal engineering.

The Tuesday session was opened by Prof **Simon Black** who gave an interesting, keynote presentation on solubility. He posed the question “Is purity germane to solubility?”, saying that in his group most people would answer “Yes”, but that he would answer “No”. He highlighted the issue of frequently observed differences in solubility measurement and apparent blame on the effect of impurity. In his talk, he gave an example of a current AZ compound where the solubility determination by two different methods (turbidity measurement and UV method) had generated very different solubility profiles. The careful investigation of the solid forms showed that the presence of a metastable polymorph during turbidity measurement resulted in higher measured solubility, as the metastable form crystallises first at higher solubility level. In contrast, the crystallisation of the stable polymorph during equilibration, showed lower solubility when the solution composition was measured by UV.

He also outlined the effect of slight water content and solvate formation on measured solubility. A second case study described a system with two components, one highly soluble in water, one only slightly soluble. Lots of water was required to dissolve the insoluble compound, and the measured solubility of the sample was consequently much lower than that of the major component. Simon concluded his talk by suggesting a number of factors other than impurity which actually affect the solubility and the need to control these factors (different polymorphs, solvate forms, water content etc.) for crystallization process development. His final message was that impurity does not change solubility, but can affect solubility measurement.

The **Young Scientist Award** went to **Joanna S. Stevens** from the University of Manchester. Joanna gave a clear talk about the use of combined ^{15}N SSNMR technique and X Ray Photoelectron Spectroscopy (XPS) in determining whether a product was a co-crystal or a salt. She outlined the principle behind XPS, where a shift similar to SSNMR (due to protonation of amines) occurs owing to differing amounts of energy required to emit an electron.

Joanna showed her work in which she used XPS technique to screen different binary systems (salts and co crystals) of theophylline and various acids. She showed when co crystal formation involving theophylline occurred; there was no change in chemical state of N atoms. However, when salt formation occurred involving theophylline N9 atom, there was strong shift towards higher binding energy indicating a change in chemical environment of N9 due to salt formation ($\text{C}=\text{NH}^+$). SSNMR supported these results. Joanna demonstrated the usefulness of XPS in determining the protonation due to salt formation and it can be used as an alternative and complimentary method to SXRD and SSNMR. Finally she also suggested some difficulties with high vapour pressure samples and radiation damage to samples.

Session 1b Crystal Chemistry in Action: Industrial Crystallisation and Pharmaceuticals

Lian Yu of the University of Wisconsin began his talk with a comparison of amorphous and crystalline materials and their properties, using silicon dioxide as an example, leading to the statement that the same phenomena and properties occur in organic compounds. Amorphous organic compounds, otherwise known as organic glasses, are more soluble, and are often used for drug delivery of poorly soluble drugs. Glasses could be made by cooling the organic liquid to below its value for T_g without crystallisation.

The bulk of the talk was given over to the study of crystallisation within organic glasses. The compound studied for much of this work was nefedipine. It was found that overall, the rate crystallisation of nefedipine in organic glasses was much higher than bulk diffusion techniques – contrary to the statement that diffusion controls crystallisation rate.

Two methods were shown for the crystallisation of nefedipine. The first involved the bulk growth of nefedipine immersed in an organic glass. It was found that if the temperature was dropped to below the glass transition temperature T_g , glass crystal growth was observed, at a rate far higher than diffusion-based bulk crystallisation. Crystal growth was also observed above T_g , in the form of fibres. Further work was carried out using the multi-polymorphic material ROY, where some of its polymorphs also showed glass crystal growth.

The second method involved crystallisation at a surface of an organic glass. The growth rate was found to be much faster at the surface than in the interior of an organic glass, meaning that at the surface of an organic glass, both the rate of nucleation and crystal growth was increased. The crystal layer was shown to be very thin – only a fraction of a micron thick. Crystal growth at the surface could be inhibited by coating the surface with a ~10 nm layer of gold or a polymer. Finally, the thickness of the organic glass was varied, and a new morphology was found when the thickness was less than 400nm. Surface diffusion was found to be far higher than in the bulk, suggesting that the surface of a glass is fluid-like.

Ivan Marziano of Pfizer began with a definition of particle engineering – the manufacture of Active Pharmaceutical Ingredients (API) that perform optimally during drug product manufacture whilst reducing the number of unit operations. The subject of particle diversity was then elucidated. This involves finding the optimal properties of particles before designing a synthesis to make said product. The properties can be found from knowledge of the particles' solid form, morphology predictions and solubility data. All this could be used to control the shape and agglomeration of particles and determine the impact of supersaturation and particle size reduction. An example of this involved studying the effects of solvents upon crystal shape. Rods were seen to be the optimal shape in a certain crystal. Supersaturation increases were found to give the needle-like polymorph. If the crystallisation was carried out in t-amyl alcohol, needles were formed, whereas in a mixture of dimethylsulfoxide (DMSO) and methyl cyanate (MeCN), the rods were formed. It was found that the cyanate was the primary driving force towards the correct shape, by having the highest interaction energy with the [101] face of the crystals. Particle size reduction techniques were also discussed. Two techniques which were used were wet milling and sonocrystallisation. Though wet milling could reduce particle sizes, the crystals stuck to the reaction vessel and clogged up various outlets.

Nick Blagden of the University of Bradford began with an explanation of how nanoparticles can be synthesised. Currently, most methods use a top-down approach, where a drug macroparticle is shrunk to the correct size. Dr Blagden hypothesised that a bottom-up approach works better, using a molecular drug solution to achieve the correct size of particles.

For this work, growth of salicylic acid crystals and steroids were covered. In both cases, the crystallisation was carried out in a custom-built, V-shaped micro channel reactor. Drug solution was funnelled through one of the channels, with anti-solvent entering the other. This can be considered a form of crystallisation in a confined environment. The particles obtained were in the range of 500-600 nm. Videos were shown of the growth of the crystals, showing the growth spiral. Dr Blagden went on to discuss what happened when surface stabilisers were added into the mixture directly. This gave inter-grown crystals, so a new method was demonstrated, where the newly-formed nanoparticles were diverted into a water tank with the surface stabilisers, which was continuously stirred to give a concentrated nanoparticle solution. Future work to be considered includes learning more about the surface texture, specifically about the nano-facets which appear on the nanoparticles when under observation.

Anne Kavanagh of Astra Zeneca spoke on "Crystallisation control in formulation friendly pharmaceuticals. She began by stating that crystal size is of the utmost importance in pharmaceutical chemistry, where size reduction of the crystals is needed even before formulation, ensuring its bioavailability when the drug is in its ingestion form (be it tablet or other oral form). Methods of obtaining particles with controlled particle sizes were then shown. A solution of the

crystalline material was seeded at a low supersaturation (to avoid secondary nucleation), then left to grow and equilibrate. For further growth, the solution was cooled, and the crystals isolated at the final temperature. Characterisation of the crystals was then carried out using microscopy, XRPD and particle size measurers. Seed size and loading were found to determine the final particle size, with more seeds giving smaller particles. Carrying out the crystallisation without seeds gave a wide range of sizes (not favourable). The effects of changing the variables on crystal size were found to be reproducible, but not predictable. In other words, the exact and final size of the crystals could not be predicted simply from the amount of seeding. Many different compounds were tested and similar results were found for each one. With these methods, particle size reduction processes could be rendered obsolete.

The focus now shifted to a drug-type molecule, termed "Compound C", where rod-like crystals were most favourable. In addition to the method previously used, two other ideas were tested. The first entailed the use of additives, which also gave some optimisation. The second method involved temperature cycling – continuous reheating and cooling of the sample, using the solubility curve of the compound to determine what temperature range could be used. This technique gave less thermal degradation of the crystals and also increased the output of rod-type crystals. Anne received a prize for a clear and interesting talk.

Session 4b: Nucleation and Growth of Inorganic Materials

Professor Angelos Michaelides from University College London was keynote speaker in the Nucleation and Growth of Inorganic Materials symposium, giving an interesting talk entitled "Simulating heterogeneous ice nucleation one molecule at a time". Professor Michaelides discussed the application of first principles simulations of the process of ice nucleation on solid surfaces. He showed that ca. one nanometre wide ice chains that nucleate on Cu(110) are not built from hexagons, but instead are built from a face sharing arrangement of water pentagons. The pentagon structure is favoured over others because it maximizes the water-metal bonding whilst at the same time maintaining a strong hydrogen bonding network. It reveals an unanticipated structural adaptability of water-ice films, demonstrating that the presence of the substrate can be sufficient to favour non-hexagonal structural units. Professor Michaelides also discussed the application of the highly sophisticated ab initio path integral molecular dynamics method, which enables the inclusion of quantum nuclear effects in the simulation. Using this method, he was able to discover that the first contact layer of water on transition metal surfaces [Pt(111) and Ru(0001) and Ni(111)] serve to reduce the classical proton transfer barriers within the overlayers and, in analogy to ice under high pressure, to shorten the corresponding intermolecular hydrogen bonds.

Professor Alison Lewis from University of Cape Town, South Africa, presented "Investigation into kinetics and mechanism of selenium precipitation from copper sulphate solution". Selenium removal by precipitation from acidic copper sulphate solution is an important process in hydrometallurgical circuits because selenium affects the quality of copper cathodes. Professor Lewis showed results on the thermodynamic stability of the hydrogen selenate (+6) and selenite (+4) species in the acidic copper sulphate solution. The reduction of these species using sodium sulphate was predicted to go to completion, precipitating copper selenide at an operating temperature range of 85-100° C. Kinetic studies of the reduction of these selenium species also revealed that the reduction of selenite is fast whereas the reduction of selenate is a very slow process.

Another interesting issue regarding the extraction of inorganic material during an industrial process was presented by **Laura O'Shea**, from University of Limerick in Ireland, who gave a talk entitled "Nucleation and growth of sodium aluminosilicate scale on heat exchange surfaces via the Bayer process". The Bayer process is used to extract aluminium oxide from the raw ore bauxite, but the conditions at which it occurs causes the precipitation of sodium aluminosilicate (sodalite) on the heat exchanger surfaces, which reduces heat exchange efficiency and increases downtime.

Alumina is removed from the raw material, bauxite ore, by mixing it with a caustic solution and heating it to 250°C. Not only is the alumina removed but so too are silicate impurities such as kaolin and quartz. The dissolved silica reacts with the alumina to form the sodium aluminosilicate scale. This scale comes in two forms sodalite and cancrinite. Sodalite forms first and over time it transforms to cancrinite. This scale causes a number of problems on the plant, the main one being the requirement for extra energy for heating as sodalite is an extremely good insulator. Laura was able to recreate in laboratory the formation of sodium aluminosilicate during the Bayer process,. To do this a rig was built to allow scale to be formed in the laboratory, and to mimic the conditions found in the heat exchangers on the plant. An in-situ energy dispersive XRD study was undertaken which used synchrotron radiation. A diffractogram was taken every 10 minutes of the scale that was growing in the rig. It was found that sodalite was the first type of scale to form and its rate of formation increased with increasing temperature and dissolved silica concentration. Over time the sodalite transformed to cancrinite and this transformation rate increased with increasing temperature and sodalite concentration. A microscopy study was also undertaken. This showed that the sodalite particles were growing from an aluminosilicate amorphous layer that formed in patches over the metal surface. The sodalite grew in two ways: as single crystals and as clusters of smaller crystals. After a period of time the growth of cancrinite from the sodalite particles was observed. The sodalite continued to be dissolved and replaced with cancrinite crystals until no sodalite remained.

Dr **Devis Di Tommaso** of the University College London discussed his work on the structural properties of phosphate-based bioactive glasses (PBGs) and the hydration properties of the PBGs dissolution products. PBGs are used as implant materials because of their ability to play an active role in the regeneration of the tissue, and their unique property to dissolve completely in aqueous media. Dr Di Tommaso applied *ab initio* molecular dynamics simulations to generate glasses with composition $(\text{P}_2\text{O}_5)_{0.45}(\text{CaO})_x(\text{Na}_2\text{O})_{0.55-x}$ ($x = 0.30, 0.35$ and 0.40) and investigate the effect of the Ca:Na ratio on the structural properties of PBGs. He showed the effect of calcium on the structure of PBGs is that of increase the rigidity of the phosphate tetrahedral network. He then discussed the development of a computational methodology based on the microsolvation-continuum approach to calculate accurate free energies of condensation reaction of phosphate species in water.

Professor **Martin Jansen** from Max-Planck Institute for Solid Research was the second keynote speaker in the Nucleation and Growth of Inorganic Materials symposium, and gave an inspiring talk entitled "The stage of Rational Solid State Synthesis". Professor Jansen started with a review of the work carried out in his group in the development and application of theoretical methods for the prediction of stable crystalline compounds in a chemical system. The methods and approximations used to develop a strategy to explore the energy landscape of a system have been outlined and the application of these methods to binary and ternary materials has been shown. Professor Jansen then moved to discuss recent advancements in the development of finite temperature methods to efficiently calculate free energies.

Pak Yan Moh (University of Manchester) discussed the application of in- and ex-situ AFM to investigate the mechanism of growth of the Zeolitic Imidazolate Framework 8 (ZIF-8). AFM observations suggest two different growth mechanisms: spiral growth and "birth and spread" growth. His work was a good demonstration of the potential of AFM to interrogate the growth of metal organic frameworks.

Another talk on the precipitation of inorganic salts during industrial processes was presented by Dr Eleftheria Mavredaki, from University of Leeds. Dr Mavredaki presented a detailed investigation on the initial stages of barium sulphate formation on a metallic surface in the presence and absence of inhibitors (polyphosphinocarboxylic acid and diethylenetriaminepentaacetic acid). The kinetics of barium sulphate formation was observed using AFM, and her results pointed out that the scale

deposition at surface and the precipitation in the bulk phase should be considered as two different processes.

The last speaker of the symposium was **Jiahui Qi** (University of Sheffield), who gave a talk entitled “Density and kinetics of kinks on calcite (104) face near equilibrium”. In collaboration with Professor Alex Chernov at Lawrence Livermore National Laboratory and Professor James DeYoreo at Lawrence Berkeley National Laboratory, Jiahui investigated the structure and dynamics of kinks on calcite steps using high-resolution AFM near equilibrium. The results have shown that the rate of kink fluctuations and kink density are lower than expected in the rough limit and the kink energy is greater than that required for the Gibbs-Thomson law to apply.

The conference was closed by conference chair Sven Shcroeder and BACG chair Nora de Leeuw with an advertisement for next year’s meeting which will take place at UCL in London, and for the first time will take place in July (10-12th). Details are available on the BACG website <http://www.bacg.org.uk/>