

# Computer Simulation of the Thermal Epitaxial Nucleation of Crystals

## Previous Track Record

**Dr Richard Sear** is a Senior Lecturer in the Department of Physics, University of Surrey. My expertise lies in theoretical/computational physics and my research is currently split approximately 50:50 between nucleation and biological physics. I have published over 100 peer reviewed papers and invited reviews (since 1993), and have a h-index of 21. This track record will focus on the nucleation work due to its relevance to this proposal.

Over the last 5 years I have published 14 peer-reviewed research papers on nucleation, plus 1 invited review<sup>1</sup>, and 1 Perspective in *Science*<sup>2</sup>. The review has been cited 40 times since its publication in 2007. The research papers are mostly computer simulation studies, but they include two papers with experimental work. Over these 5 years, I have probably published more simulation papers on a broader range of topics in heterogeneous nucleation than anyone else. I am currently writing an invited review on the nucleation of the crystal phase in molecular and ionic systems for *International Materials Reviews*.

Most of the 14 research papers are studies of heterogeneous nucleation, i.e., nucleation of a new phase on a solid surface, although I have also studied the two-step homogeneous nucleation of a crystal<sup>3</sup>. I have not studied thermal epitaxial nucleation, i.e., the nucleation of one crystal phase on a surface that is itself crystalline, and where the two crystal lattices are in registry.

The principal motivation for my work on nucleation to date has been a desire to better understand and hence to predict the crystallisation of proteins. Protein crystals are essential to X-ray crystallography, which is the main way the all-important structure of a protein is determined. I have worked with the leading protein crystalliser Prof Naomi Chayen (Imperial College) to make new materials to induce crystallisation<sup>4</sup>, and to model the behaviour found in experiment<sup>5</sup>. The impact of the work can be judged from the fact that our 2006 *PNAS* paper has already received 45 citations. This work was supported by EPSRC funding (EP/D001439/1).

This experimental work has inspired the work that is most relevant to the proposed research. This is the computer simulation of heterogeneous nucleation in pores and in other non-planar geometries. In 2006, my student and I showed that in a simple model there is an optimal pore size that maximises the nucleation rate<sup>6</sup>. The impact of this work can be judged by the fact that it attracted a News & Views article in *Nature*<sup>7</sup>, and has been cited 33 times. We followed this up by showing that the nucleation rate of the crystalline phase of Lennard-Jones molecules was fastest in a wedge with a particular 'magic angle' where the crystal lattice fitted perfectly into the wedge<sup>8</sup>. This work in particular used both the model and algorithms that will be used in the proposed research. It attracted a ScienceNOW article<sup>9</sup>.

I have also worked on understanding ice nucleation in the Earth's atmosphere, in particular the

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<sup>1</sup>R. P. Sear, Nucleation: Theory and Applications to Protein Solutions and Colloidal Suspensions, *J. Physics: Condensed Matter* 19, 033101 (2007)

<sup>2</sup>F. C. Meldrum and R. P. Sear, Now you see them, *Science* 322, 5909 (2008)

<sup>3</sup>J. A. van Meel, A. J. Page, R. P. Sear and D. Frenkel, Two-step vapour-crystal nucleation close below triple point, *J. Chemical Physics* 129, 164510 (6 pages) (2008).

<sup>4</sup>P. Asanithi, E. Saridakis, L. Govada, I. Jurewicz, E. W. Brunner, R. Ponnusamy, J. A. S. Cleaver, A. B. Dalton, N. E. Chayen and R. P. Sear, Carbon-nanotube based materials for protein crystallisation, *ACS App. Mat. Int.* 1, 1203-1210 (2009).

<sup>5</sup>N. E. Chayen, E. Saridakis and R. P. Sear, Experiment and theory for heterogeneous nucleation of protein crystals in a porous medium, *Proc. Nat. Acad. Sci.* 103, 597 (2006).

<sup>6</sup>A. J. Page and R. P. Sear, Heterogeneous nucleation in and out of pores, *Phys. Rev. Lett.* 97, 065701 (2006).

<sup>7</sup>D. Frenkel, Seeds of phase change, *Nature* 443, 641 (2006).

<sup>8</sup>A. J. Page and R. P. Sear, Crystallisation controlled by the geometry of a surface, *Journal of the American Chemical Society* 131, 17550-17551 (2009).

<sup>9</sup>M. Torres, How Crystals Get Their Groove Back, *ScienceNOW* 2009 (<http://news.sciencemag.org/sciencenow/2009/11/20-02.html>)

observation that in supercooled water droplets on solid particles, ice nucleates along the contact line where the three interfaces (air/water, water/solid, air/solid) meet. Using a simple model I was able to show that rather generally, the nucleation barrier should be low at a contact line<sup>10</sup>. This has been cited 9 times, and used by Shaw (Michigan Technological University) to understand his results on the nucleation of ice on particles, including particles found in the Earth's atmosphere.

I am an active member of the community, serving as Chair of the Committee of the Royal Society of Chemistry's Statistical Mechanics and Thermodynamics Group. In addition, I was a co-organiser of the workshop "Crystallization: from Colloids to Pharmaceuticals" at CECAM at EPFL in Lausanne, Switzerland on 22nd to 24th July 2010, and the 1-day meeting "Liquids at Interfaces: A Conference in Honour of J.R. Henderson" at Imperial College, London on 6th Jan 2011. I am also on the organising committee of "Thermodynamics2011" which will be held in Athens on 1st to 3rd Sept 2011.

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<sup>10</sup>R. P. Sear, Nucleation at contact lines where fluid-fluid interfaces meet solid surfaces, J. Physics: Condensed Matter 19, 466106 (9 pages) (2007).

# Case for Support: Thermal Epitaxial Nucleation of Crystals

## 1 Abstract

The proposed research is the first quantitative computer simulation study of the thermal nucleation of a crystal on a crystalline substrate. It will calculate nucleation rates, and study in detail the microscopic dynamics. Crystallisation is crucial in a number of industries such as chemical processing, pharmaceuticals and the food industry. Understanding the crystallisation of water is also critical to our ability to model the Earth's atmosphere. Crystallisation starts off with nucleation, where a microscopic nucleus of the crystal forms. Nucleation can determine the rate of crystallisation, and can dictate which crystal form (polymorph) is produced. It is well known that nucleation is almost always heterogeneous, i.e. the crystal nucleus forms in contact with a surface. This surface is often crystalline, and then epitaxial nucleation is possible. Epitaxial nucleation is where the lattice of the nucleating crystal is in registry with the lattice of the surface. We will use computer simulation to study thermal nucleation, by which we mean nucleation occurs near equilibrium. Here the nucleus is a rare thermal fluctuation, as it is when a crystal forms from a solution or liquid. This means we will not study far-from-equilibrium situations, such as molecular beam epitaxy. We will study epitaxial nucleation on: 1) perfect planar crystalline substrates, 2) crystalline substrates with steps, and 3) defected crystalline substrates. We hope that the proposed research will enable a more rational approach to controlling the nucleation of crystals, including better polymorph control.

## 2 Context

Crystallisation lies at the heart of many technologically important processes, and of natural phenomena such as snowfall. This research is motivated in particular by a desire to better understand the crystallisation from solution, from liquids and from the vapour, of molecular, ionic and metallic systems. Although control over crystal growth is also important, nucleation defines which polymorphs can form, and can set both the lattice orientation and the size of the crystals produced. Too fast nucleation can produce a shower of small crystals when perhaps a single crystal is desired. However, if nucleation is slower than the experimental timescale then crystallisation will be prevented altogether. In molecular, ionic and metal systems, nucleation occurs on time and lengthscales that are inaccessible to conventional experiments: the nucleus is only briefly at the top of the barrier and is then only a few molecules (and hence nm) across. For this reason, despite its importance nucleation is poorly understood.

Nucleation of a crystalline phase is almost always heterogeneous, i.e., the nucleus forms on a solid surface, and this surface is often crystalline. This raises the question of epitaxy during nucleation, by which we mean the question of whether the lattice of the microscopic crystalline nucleus is in registry with the lattice of the substrate. For molecular and ionic systems this cannot be directly studied in experiment as the nucleus cannot be observed. What can be observed is the final crystal, and in some systems the crystals that form are aligned with the lattice of the substrate, and hence with each other, see Fig. 1(A). Thus the large crystals observable in experiment (the product of nucleation followed by growth) align with the substrate lattice. This is evidence for epitaxy during *crystallisation* but is not direct conclusive evidence of epitaxy during *nucleation*.

It has been known for decades that silver iodide is highly effective at inducing the nucleation of ice. Silver iodide's crystal lattice is an excellent epitaxial match for that of ice, the difference in lattice constants is only 1.5% (1). This observation that a substance with an excellent epitaxial match induces nucleation is also indirect evidence for epitaxial nucleation. However, silver iodide is a rare success. There are few other successes in molecular systems where a substance with a good epitaxial match has proven to be effective at nucleating a crystalline phase. This is despite the

fact that experiments with colloids have clearly shown the expected rapid nucleation on a substrate with a good epitaxial match (2; 3).

The aim of the proposed research is to study the microscopic details of epitaxial nucleation, and hence to develop rules to rationally select surfaces when we want to induce crystallisation, and better understand what heterogeneous substances we need to eliminate if we wish to avoid nucleation and stabilise supersaturated systems. This is highly ambitious.

The substrate in Fig. 1(A) is carefully cleaved mica. This is planar. However, Ward and coworkers (4; 5) cleaved organic crystals to form what they called a ledge, where two crystal planes meet at an obtuse angle along a line. Then they found that crystals formed along these ledges. Apart from being non-planar, crystalline substrates may also have defects in their lattices. Simple model calculations show that these can reduce the epitaxial strain and hence the nucleation barrier, see Fig. 2(A). Thus, in practice nucleation may often be occurring along ledges and at defects. The most adventurous part of the research will be to study these more complex situations, which have received very little attention so far.

I am not aware of even one quantitative calculation of a nucleation rate for nucleation on a crystalline substrate. There have been some qualitative studies, for example van Meel, Sear and Frenkel (6) (as part of a study of nucleation in nanoscale pits) briefly studied crystallisation on crystalline surfaces. As expected, if the epitaxial match was perfect then crystallisation was rapid. However, even small mismatches result in the formation of a strained nucleus, which can arrest the growth and even crack the crystalline nucleus, see Fig. 2(B). Larger mismatches stopped nucleation completely.

## 2.1 Fundamentals of nucleation of a crystal

Fundamentally nucleation is slow because it involves overcoming a barrier and this barrier comes from the free energy cost of creating an interface between the nucleus and its surroundings. Heterogeneous nucleation, i.e., nucleation at a surface, is faster than nucleation in the bulk because

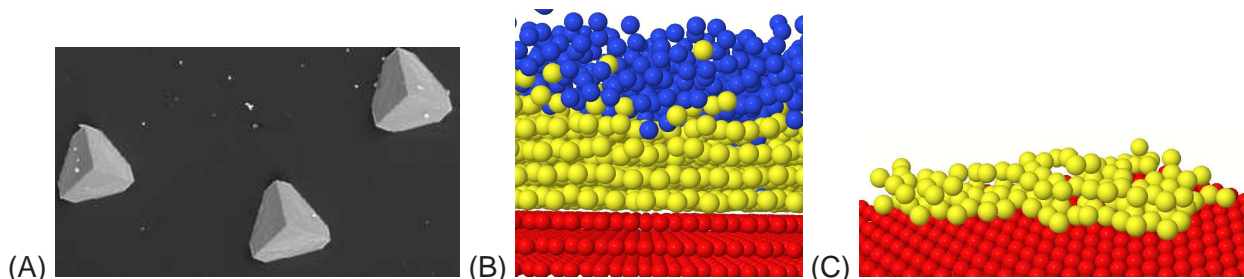


Figure 1: (A) SEM image of crystals of calcite (a polymorph of calcium carbonate) on the surface of the crystalline substrate mica (7). The crystals are of order  $1 \mu\text{m}$  across. Note that the crystals are all oriented the same way. (B) A computer simulation of crystallisation occurring readily on a surface with minimal epitaxial strain. The snapshot shows a crystalline hcp substrate (the red spheres) that exposes a close packed plane to the fluid. Due to the almost perfect epitaxial match, crystallisation is occurring rapidly in the liquid. Molecules in a locally crystalline environment (according to standard order parameters (8; 9)) are shown as yellow and molecules in a liquid environment are shown in blue. Note that all molecules are Lennard-Jones molecules. Colour is used to distinguish between substrate, liquid and crystalline molecules. (C) A crystal nucleus growing on a crystalline (hcp) surface. There is both an epitaxial mismatch and the attractions between the substrate and liquid molecules are only 75% of the strength of the attractions in between the molecules of the liquid. Thus here crystallisation only occurs at a supercooling of 15% of the triple point temperature, this is much larger than in (B). The colour scheme is the same as in (B), however we have removed the liquid molecules so that the nucleus is visible.

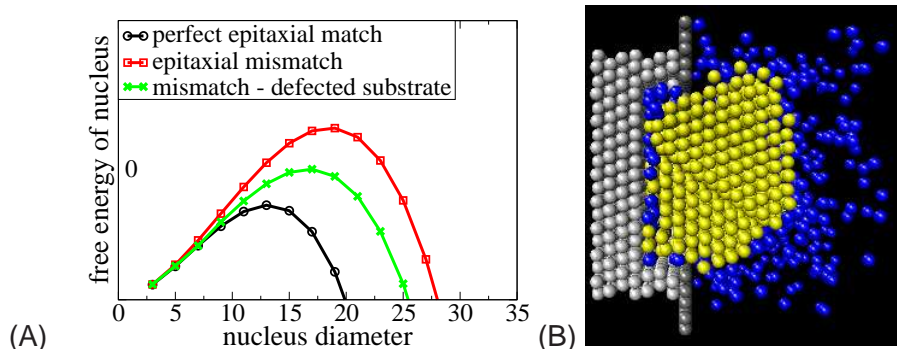


Figure 2: The effect of strain in epitaxial thermal nucleation. (A) Plot of the free energy of formation of (cubic) nuclei, as a function of their size. The black curve is a nucleus on a substrate with a perfect epitaxial match and hence no strain. The red curve is for a nucleus strained due to a lattice mismatch. The green curve is for a nucleus on a substrate with a lattice mismatch but with a dislocation near the surface of the substrate such that the strain in the substrate locally reduces the lattice mismatch and hence the strain in the nucleus. The free energies are obtained from a simple lattice model of strain combined with classical nucleation theory. (B) A cross-section through a computer simulation snapshot (6). A crystal (the yellow particles) has begun nucleating but has cracked diagonally due to strain, and stopped growing. The crack in the nucleus is clearly visible, it forms between two close-packed planes. The particles in the vapour from which the crystal has formed, are shown in blue. The surface is a shallow pit in a crystalline surface. It is composed of light and dark grey particles. The crystalline surface is also fcc. It has a lattice constant 4% smaller than that of the crystal that is nucleating.

at a surface there already is an interface, for which the free energy cost has already been paid. If the surface is crystalline and there is a very good match between the lattice of the surface and that of the nucleus, the lattice of the surface will also aid nucleation by guiding the molecules of the nucleating crystal, into a crystalline lattice.

However, unless the crystal is nucleating on another pre-existing crystal of the same type there will be a mismatch which will create strain. The molecules in the crystal will not be able to both match the pattern of molecules in the surface and be at their equilibrium spacing. Essentially, strain in a nucleus without defects introduces an additional volume term into the nucleus free energy. This inhibits nucleation. However, dislocations can relieve this stress (1). But dislocations cost free energy and they can be difficult to form, i.e., they themselves may have slow kinetics of formation (10).

### 3 Preliminary Data

In this section we will outline some preliminary simulations of crystallisation on crystalline surfaces, as well earlier published results. We will highlight the questions these simulations raise. Some results are shown in Figs. 1(B) and (C). In outline, these results are as expected, crystals nucleate at very low supercooling on substrates with a perfect epitaxial match where the substrate molecules strongly attract the molecules of the liquid. However, nucleation is pushed to higher supercooling if the epitaxial mismatch is increased and/or the attraction of the substrate molecules for the molecules of the liquid is weakened. The proposed research will quantify these results. They will also look at the effects of non-planar geometries and of defects. The work on smooth-walled wedges of Page and Sear (11) found much higher nucleation rates in wedges than on planes, which motivates us to propose research on wedges formed from crystalline surfaces meeting at a point,

as studied experimentally by Ward and coworkers (4; 5).

Simulations of homogeneous nucleation and of nucleation in smooth-walled wedges have found a type of defect called a stacking fault (8; 11), in the nucleus. This is presumably the easiest defect to form. However, it is easy to show that stacking faults cannot relieve epitaxial strain on planar substrates. Dislocations can, however they are not observed in homogeneous or in nucleation on smooth substrates. It is an open question whether they form in the strained nuclei of thermal epitaxial nucleation.

## 4 Programme and Methodology

We propose to use computer simulation to study nucleation on crystalline surfaces. We will study nucleation on both perfect planar surfaces and surfaces with steps/ledges. We will also study systems where the surface lattice is the same symmetry as that of the nucleating phase and where the symmetries are different. Finally, nucleation on substrates with defects will be studied.

Our model will be the simple and well-characterised Lennard-Jones model. Studying activated processes computationally is very demanding on computer time, even with the state-of-the-art computational techniques that we will employ. We need to obtain rates where the nucleation barrier is large, tens of  $kT$ , as it typically is in experiment. Then the nucleation rate is very low, which requires specific computer algorithms and computation-intensive simulations. This rules out studies of models of, for example, water or ionic systems, as they are too computationally demanding.

As we are restricted to studying simple models, we will make generic (i.e., not system specific) predictions. We cannot predict rates in complex and difficult to simulate systems of great interest, such as calcium carbonate. Nobody can do this, it is currently out of reach computationally. However, generic results are very powerful as they apply to the nucleation of all crystals, in this case the nucleation of any crystal where nucleation is occurring on a crystalline substrate. For example, we can calculate how the nucleation rate varies with lattice mismatch. These results will then inform any experiments on a system with a known lattice mismatch.

As supersaturation is decreased, or a nucleation substrate becomes less favourable for nucleation, the nucleation rate drops very rapidly. Thus, we need to calculate low nucleation rates and be able to calculate rates over a large dynamic range. We will do this using the state-of-the-art Forward Flux Sampling (FFS) algorithm of Allen *et al.* (12), plus if required umbrella sampling (US). The PI has prior experience of the use of both techniques for nucleation.

The proposed research will quantitatively calculate nucleation rates for simple substrates. My ambition is to determine what surface features determine the nucleation rate, the microscopic details of how they do this, and where and why is the nucleation rate highest. This will transform our understanding of two important processes. For both processes the crucial data is where is the nucleation rate is highest. The first process is the standard industrial crystallisation setup, where there will be multiple impurities with different imperfect crystalline substrates. Then nucleation will occur where the barrier to nucleation is lowest and the rate fastest. Thus the place where the nucleation rate is fastest is what is determining the experimentally observed behaviour. The second process is the rational selection of substrates to induce the nucleation of a desired crystal at low supersaturations. Again we need to determine what surface features maximise the rate.

### 4.1 Methodology of the Proposed Research: Simulation techniques

We need to calculate nucleation rates over a large dynamic range. We will do this using the state-of-the-art Forward Flux Sampling algorithm of Allen *et al.* (12), plus if required umbrella sampling. FFS is preferred over US for two reasons. The first is that it gives rates directly, thus speeding calculations. The second is that it is less sensitive to the order parameters used to distinguish between liquid and crystalline molecules. US is more laborious than FFS but will be used if free energies are required. There are also indications (from earlier work in my group and the group

of Daan Frenkel) that US can be more efficient for low rates. Thus if we find FFS has difficulty sampling nucleation paths at low rates we will try US.

Both FFS and US require an underlying simulation algorithm. The simulation algorithm we will use is NVT Monte Carlo. This is standard in the field, simple to implement for our geometries and compatible with both FFS and US. Studies of crystallisation require order parameters (OPs) that distinguish fluid from crystalline particles. I have extensive experience with the standard OPs in the field. These are the OPs developed by Frenkel and coworkers (8; 9). We will also use the Common Neighbour Analysis (CNA) of Honeycutt and Andersen (13) to locate defects. Finally, strains and stresses will be calculated in the growing nuclei.

## 4.2 Nucleation on perfect planar substrates

Nucleation will be studied first on defect-free substrates, with varying mismatches,  $\Delta a$ , between the substrate lattice constant and that of the nucleating crystal. For a defect-free nucleus the free energy of the nucleus is increased by a term that scales as  $(\Delta a)^2 v$ , for  $v$  the volume of the nucleus (10). The theoretical expectation is that the rate will then decrease with increasing mismatch as  $\exp[-A/(\Delta\mu - B\Delta a^2)^2]$ , where  $A$  and  $B$  are constants. This expectation has never been tested before. The first quantitative study will be an attempt to determine if this prediction, together with the corresponding prediction for the size of the critical nucleus, is correct or not. We will do this for substrates with surfaces that are close-packed planes (the close-packed planes of an fcc crystal).

For comparison we will also study other planes of fcc and hcp crystals together with one substrate with a symmetry that is neither of the fcc and hcp symmetries favoured by Lennard-Jones molecules. This is relevant not only to heterogeneous nucleation on an impurity but also to the important problem of one polymorph nucleating on another polymorph that is less stable but has nucleated earlier. Understanding this phenomenon is essential to improving our ability to control which polymorph is produced in, for example, new pharmaceutical compounds which have multiple polymorphs.

## 4.3 Nucleation on substrates with steps

The second subdivision of the programme is the study of nucleation on substrates with straight and kinked steps, and on what Ward and coworkers call ledges (4). In all cases the FFS algorithm will be used to calculate nucleation rates quantitatively. We will determine whether the rate is higher at a step/ledge or on a planar surface. Ledges are where a crystal has been cleaved such that two low index planes meet at an obtuse angle to form a wedge. Ward and coworkers (4; 5) found that crystals nucleated preferentially along these ledges and we wish to study the microscopic details that underly this experimental observation.

## 4.4 Nucleation on substrates with defects and with defects in the nucleus

We propose to start this part of the programme by studying the effect of defects in the substrate. Then if time permits we will do the most adventurous part of the research, which is the study of the effect of defects in the nucleus.

A defect, such as a dislocation, in a substrate will deform its lattice. This can reduce the mismatch to the lattice of a nucleating crystal, and hence reduce the strain in this nucleus. This effect is shown in simple model in Fig. 2(A) (compare the red and green curves). Our objective here is to develop an understanding of how a defect such as a dislocation near or at the surface of a substrate will affect nucleation on it. We will calculate nucleation rates on perfect and defected substrates and compare them. The motivation is that in experiment nucleation almost never occurs on a perfect substrate and so we need to know whether the nucleus is likely to form on a locally perfect part of the substrate, or near or at a defect. One possible explanation for the lack of success in rationally picking substrates with a small mismatch is that in fact nucleation occurs near defects, and not on

the perfect lattice currently used to predict which substrate would be best at inducing crystallisation. If time permits we will also consider nucleation near point defects but we will study substrates with edge dislocations first as we believe they will have a larger effect.

The final, and most adventurous, topic of research is the study of the role of defects in the nucleus itself. Virtually nothing is known about the role of defects in nucleation. Crucially, we do not know if there are circumstances where defects can accelerate nucleation. The ambitious aim of this part of the research is to answer this question. There is old work of Turnbull (1; 10) and others showing that dislocations can relieve strain in epitaxial nucleation due to a lattice mismatch. However, they did not consider how dislocations may themselves form. This is not trivial, particularly in view of the fact that in close-packed crystals dislocations presumably have a high free energy cost. Also, dislocations can only readily nucleate near or at surfaces (10). Here we will try and force dislocations to form in nuclei, for example, by nucleating on a substrate with a dislocation and where the geometry is optimised to favour a corresponding dislocation in the nucleus. We will also consider stacking faults, building on our earlier work there (11). We will also make nuclei with dislocations in them and study their stability by watching them melt.

## 5 Academic Impact

The research will impact all those who need to understand crystallisation, and those who need to control crystallisation. This includes scientists from areas of basic inorganic chemistry, the pharmaceutical industry, atmospheric science, and industrial chemical engineering. In all these systems crystallisation starts with heterogeneous nucleation. The impact of the proposed research will of course depend on the findings of the research, but if, for example, we find that epitaxial nucleation is fastest on defects in surfaces this would imply that scientists who wish to induce nucleation should stop trying for substrates with near-perfect epitaxial matches and consider how to make defect-rich crystal substrates. Whatever the findings, we hope to transform the study of crystalline substrates for inducing nucleation. Also, polymorph control is also often hindered by one polymorph nucleating on another. This is a serious problem in the pharmaceutical industry. Our results on the nucleation of one crystal on another will transform our understanding of the microscopic details that control this phenomenon.

The results will be communicated via publication in high impact journals such as *JACS* and via attendance at meetings, in particular the UK's leading crystallisation conference, the annual conference of the British Association for Crystal Growth.

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