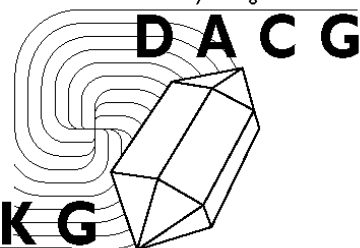


# FACET

dutch association for crystal growth



NIEUWSBRIEF VAN DE NVKG

nederlandse vereniging voor kristalgroei

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## FACET

Nieuwsbrief van  
de NVKG, sectie van  
de KNCV en de NNV

## redactie

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## Omslagfoto/Cover

De figuur toont fractale groei van een ijskristal, opgesloten tussen een grafeenlaag en een mica oppervlak. De afbeelding is gemaakt met behulp van een Atomic Force Microscope (AFM).

De groei van het ijskristal wordt geïnduceerd doordat er warmte aan de dubbele water bilaag wordt onttrokken als de bovenste bilaag verdampt. De onderste bilaag water bevriest in fractale vorm. Fractale groei kan ontstaan als gevolg van Diffusion Limited Aggregation (DLA). In dit geval is echter niet de lokale beschikbaarheid van water de bepalende factor, maar de lokaal vereiste *oriëntatie* van het watermolecule om in het ijskristal te worden ingebouwd.

De fractale vorm, zoals de dikte van de hoofdaders en het aantal vertakkingen wordt bepaald door de dikte van de grafeenlaag en de verdampingssnelheid van de watermoleculen.

De figuur is aangeleverd door Pantelis Bampoulis, Harold Zandvliet, Detlef Lohse en Bene Poelsema van de groepen *Physics of Interfaces and Nanolayers* en *Physics of fluids* van Universiteit Twente.

Voor meer informatie klik [hier](#).

## Electronische verzending FACET

Ten behoeve van de verzending van de FACET is het van belang dat de NVKG beschikt over een geldig emailadres. Indien U deze FACET niet via de reguliere mailing aan de NVKG-leden heeft ontvangen, vragen wij u om aan het [secretariaat](#) een geldig emailadres door te geven.

De FACET verschijnt uiteraard ook nog altijd gelijktijdig met de emailversie op de website van de NVKG. De meest recente FACET kan daar te allen tijde uit het FACETtenarchief gedownload worden.

## Van het bestuur

De Nederlandse Vereniging voor Kristalgroei is springlevend! Dit is, terugblikkend op 2016, welhaast een overbodige mededeling, want in het afgelopen jaar is gebleken dat de belangstelling binnen de kristalgroiegemeenschap in Nederland (en een beetje daarbuiten) om een gezamenlijke bijeenkomst te bezoeken nog steeds groot is. Dit heeft ons als bestuur aangemoedigd om de zaken weer vol energie op te pakken. We streven er naar om de vereniging een platform te laten zijn om kristalgroeiërs uit academia en industrie met elkaar in contact te brengen en ervaringen te laten uitwisselen.

In de afgelopen najaarsvergadering is gebleken dat de behoefte voor een verenigingsorgaan nog groot is. Een nieuwsbrief met promoties, foto's, conferenties en verslagen van activiteiten wordt als waardevol gezien. Deze FACET is het eerste die weer sinds lange tijd verschijnt. We blikken hierin kort terug op de najaarsvergadering en geven geplande data voor activiteiten van 2017 door. Zet ze maar vast in de agenda; in volgende FACET volgt nadere informatie.

In de FACET willen we een breed en interessant overzicht geven van het kristalgroeionderzoek in Nederland en internationale congressen op ons vakgebied. Als bestuur en redactie kunnen wij natuurlijk niet overal vertegenwoordigd zijn om het laatste nieuws op te vangen. Daarom willen wij een **netwerk van correspondenten** opzetten: DACG-leden die voor hun werkgroep de contactpersoon zijn voor de redactie van de Facet en die (ideeën voor) bijdragen kunnen aanleveren. Zo kunnen we elkaar op regelmatige basis op de hoogte houden van wat er leeft binnen de vereniging.

Voor de FACET zijn we op zoek naar artikelen die kristalgroeiërs interesseren:

- Aankondigingen van lezingen, symposia en congressen
- Verslagen van (kristalgroei)-conferenties,
- Artikelen over een opmerkelijke ontdekking
- Advertenties: bijvoorbeeld i.v.m. vacature
- Foto's (met korte toelichting), die in de FACET en op de website worden gepubliceerd

De drempel voor uw bijdragen is *zeer* laag: aanleveren kan per brief, fax, [e-mail](#), of telefoon. Ideeën en correspondenten kunnen zich melden bij de redactie van de FACET ([Arie van Houselt](#))

Namens het bestuur,  
Hans te Nijenhuis, voorzitter

# Algemene ledenvergadering najaar 2016

De Algemene Ledenvergadering werd gehouden in de middagpauze van de najaarsvergadering op 7 oktober op de Technische Universiteit Eindhoven. 18 leden waren aanwezig. Hoewel er enkele jaren geen ALV meer gehouden is, kon toch worden teruggeblikt op een groot aantal activiteiten, georganiseerd door de NVKG zelf, of door (en voor) leden van de NVKG. Hoogtepunt uit het recente verleden is het Co-crystalssymposium op 20 mei 2016 in Nijmegen met 68 deelnemers.

In de vergadering hebben we het bestuur aangevuld en weer op sterkte gebracht. Antoine van der Heijden (TU Delft, tevens werkzaam bij TNO) werd unaniem gekozen tot secretaris; zijn kennis en ervaring op het gebied van kristallisatie zijn een welkome aanvulling op het zittende bestuur. Als voorschot op zijn benoeming had Antoine het jaarverslag over de afgelopen periode al voorbereid. In sportieve termen zou je dat een vliegende start kunnen noemen.

Het bestuur heeft ook een aantal opdrachten meegekregen van de vergadering. Zo bestaat de wens om de FACET weer meer te laten verschijnen. Deze uitgave is een eerste bewijs dat we daar mee aan de slag zijn gegaan. Verder willen we de Kristalgroeprijns weer uit gaan reiken voor de beste dissertatie uit de afgelopen periode. Meer hierover zal in een volgende uitgave van FACET worden gepubliceerd.

We proberen ook de vergaderingen verder van te voren te plannen. **De volgende voorjaarsvergadering kunt u vast in de agenda zetten: 7 april op de Technische Universiteit Delft.** Nadere informatie volgt. Natuurlijk zijn we altijd op zoek naar vergaderlocaties. Wie een goed idee heeft voor een volgende vergadering, kan dat melden bij het bestuur.

Tom Leysens en Rob Geertman schetsten het Belgische kristalgroeilandschap. De Belgische leden zijn in ieder geval van harte welkom op Nederlandse vergaderingen. Mocht er in België een zelfstandige vereniging worden opgericht, dan zullen we zeker relaties aanknopen en bekijken waar het mogelijk is gezamenlijk activiteiten te organiseren.

Terugkijkend naar deze vergadering kunnen we stellen dat er voldoende enthousiasme is om de activiteiten weer op te pakken.

Hans te Nijenhuis



## DACG symposium 'Crystal Growth in Control'

As a follow-up of the co-crystal symposium (20/5) the Dutch Association for Crystal Growth organised its 2016 annual meeting on 7 October. The meeting was held in the Ceres building at the Eindhoven University campus, where Nico Sommerdijk offered to host the event. Part of the annual meeting was, as has become customary, a small symposium, this time with the title 'Crystal Growth in Control'.

There were 6 contributions of invited speakers. Noushine Shahidzadeh (University of Amsterdam), started off with an interesting presentation of her work on the pressure a crystal, growing in confinement, exerts, followed by a contribution of one of the PhD students of Nico Sommerdijk, Giulia Mirabello. Giulia explained us her work on the Bio-inspired crystallization of magnetite, a very special form of iron oxide. Before the for Dutch standards delicious lunch, Tom Leysens (Université Catholique de Louvain, Louvain-La Neuve) gave a tutorial on screening and application of co-crystals. His presentation was initially intended for the Nijmegen co-crystal symposium, but unfortunately he had to cancel for that opportunity, which was made up for with his contribution in Eindhoven. After lunch Hugo Meekes gave a presentation in memoriam of Piet Bennema. Piet was emeritus Professor solid state chemistry at the Radboud University until 1998. He passed away on 25 June 2016 at the age of 83.

Wim Noorduin (Amolf, Amsterdam) presented his latest results in his world of artificial biomineralization, in which he was seeking for a balance between interfacial free energy and local supersaturation. Wim surprised the audience by showing 3D images of his colourful floriferous still lives. The final presentation was a contribution by Burak Eral (Delft University of Technology) on the control of crystal growth through confinement.

An annual meeting cannot do without a lab tour, so the participants were shown around in the laboratories of Nico Sommerdijk, guided by Giulia. During the drinks we could look back at a very interesting meeting, chatting with old and new friends, being confident that the Dutch Association for Crystal growth is still alive and kicking.

Hugo Meekes



*The audience, equipped with stereo-glasses, stares amazed at the wealth of Wim Noorduin's floral arrangements.*



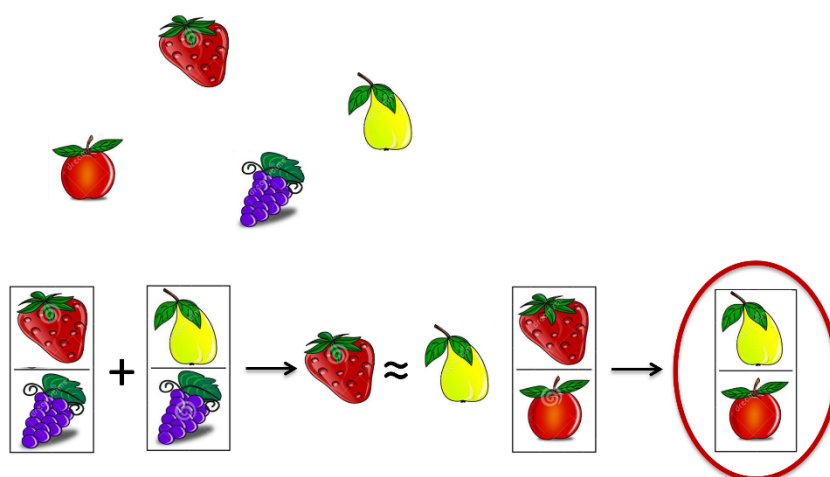
## DACG / NVK symposium 'Co-Crystals'

After a few years of limited activity the Dutch Association for Crystal Growth revitalized its activities by organising a one-day symposium with the title co-crystals, in conjunction with the Dutch Association for Crystallography (NVK). The symposium was held at the Radboud University in Nijmegen on May 20<sup>th</sup>.

Seven presentations on the various aspects of the topic were given by invited speakers both from academia and industry. The symposium was attended by 67 participants, roughly half of them coming from industry. Moreover, there were 8 participants from Germany. This broad interest in the subject of co-crystals stems from the fact that the design of multicomponent crystals provides a means to alter physicochemical properties of crystals without changing the chemical properties of the molecule of interest. This is particularly useful in the case of active pharmaceutical ingredients (APIs), but also in the field of agrochemical products. Although solvates and salts are commonly used in this context, the formation of co-crystals has only more recently been considered, which has significantly increased the solid forms available for formulation.

After an introductory presentation by Joop ter Horst from the University of Strathclyde (Glasgow) on crystal nucleation and deracemization, Elias Vlieg (RU, Nijmegen) presented a paper on the classification of the various types of co-crystals. This topic is not only of fundamental interest but possibly also for a sound legal classification. More general legislation issues were covered in a presentation by Dolores Mendivil (Synthon BV, Nijmegen). Martin Viertelhaus (BASF, Ludwigshafen) presented applications of co-crystals in the agrochemical industry, with a beautiful example of two active components combined into a co-crystal with improved physicochemical properties. René de Gelder (RU, Nijmegen) showed how one can use crystallographic structural databases to find new possible coformers for a given active component, while Ernst van Eck (RU) demonstrated the strength of solid state NMR measurements to understand the local interactions between host and guest molecules in crystals. Finally, Joost van den Ende (RU) showed how such interactions can be studied using molecular modelling techniques.

All together it turned out be an inspiring and fruitful day with a lot of social and scientific interaction, certainly not limited to the drinks afterwards.



Cocystal Prediction via the Domino Approach

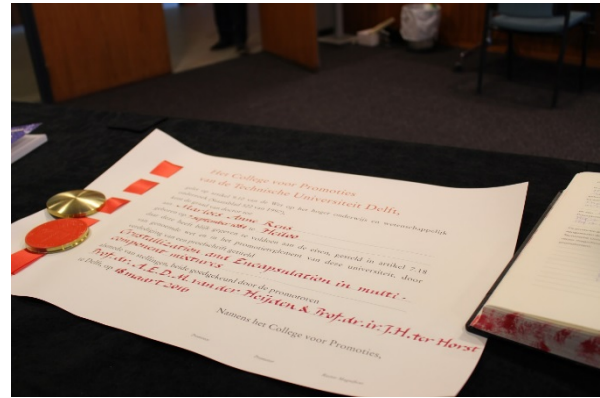
Hugo Meekes

# Recente Proefschriften

## Thesis Marloes Reus

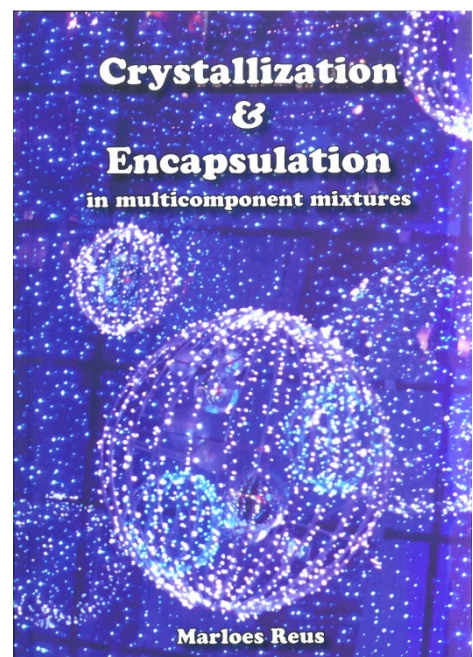


Marloes Anne Reus was born on the 7<sup>th</sup> of September 1984 in Heiloo (the Netherlands). In 2010 she obtained the Master of Science degree in Chemical Engineering from Delft University of Technology and stayed there to pursue her doctoral research at the IRS Group under the supervision of Joop ter Horst and Antoine van der Heijden. The research was done in cooperation with TNO Defence, Safety and Security, where part of the work took place.



Her PhD research focused on using crystallization and microencapsulation processes to produce multicomponent particulate products with different functionalities (improved stability, controlled release, protection from environment, etc.). Many products from chemical industries, such as consumer products, pharmaceuticals, food products and fine chemicals industries constitute particulate products. The functionality of these products depends among others on the properties of its constituents, their interactions and their distribution in the product.

Additionally, she addressed interactions between the components in the processes. In this context, she investigated the crystallization in multicomponent mixtures, such as co-crystallization and anti-solvent crystallization. She employed electrospray crystallization as a technique for producing multicomponent (sub-)micron sized crystals.



Additionally, wheat gluten were encapsulated in a matrix of hydrogel by a dripping method to delay fibrilization in a novel meat analog production process and atomic layer deposition was performed in a fluidized bed on various compounds to protect them from moisture or reactive species in the environment. She used model compounds from various industrial fields (e.g. food, pharmaceutical and energetic material industries) to illustrate the wide applicability

of the tested processes. On 18<sup>th</sup> of March 2016, Marloes successfully defended her PhD thesis and received the last ever handwritten PhD diploma of TU Delft.

An electronic version of the dissertation is available at <http://www.library.tudelft.nl/>

## Thesis Aryan de Jong

Aryan de Jong was born on the 9<sup>th</sup> of January 1983 in Zeddam (the Netherlands). In 2011 he obtained his Master of Science degree in Chemistry from the Radboud University, Nijmegen. Aryan started a PhD research project on X-ray physics and materials science in a collaboration between the ID15 Beamline at the European Synchrotron Radiation Facility in Grenoble, France and the department of Applied Materials Science of the Institute for Molecules and Materials at the Radboud University, Nijmegen, under the supervision of Elias Vlieg. On September 29, 2016 Aryan obtained his PhD degree after defending his thesis 'Ordering at the GaN-Ga solid-liquid interface -an in-situ high-energy X-ray diffraction study-'.

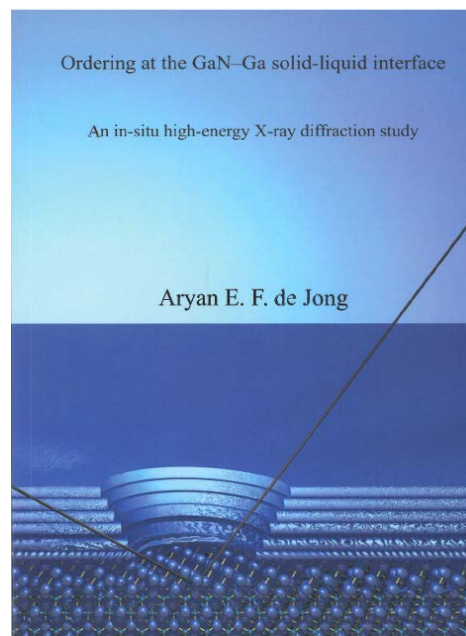
Today Blu-ray disk players, Playstations, flat screen TV's and LED lighting are almost taken for granted. However, all these items would not be possible without the invention of light emitting materials covering the blue part of the visible spectrum. The creation of efficient blue light emitting sources (e.g. LEDs or lasers) was a challenging problem in semiconductor research over many decades. The reports of efficient red and green LEDs made from the combination of elements from group III and V in the periodic table in the early 1960's led to the believe that the III-V combination of nitrogen and gallium would have the right characteristics to form a blue light emitter. Chapter 2 of this thesis introduces the properties and applications of gallium nitride (GaN), the material which solved the blue light problem in the mid-1990's and resulted in the Nobel prize in physics in 2014.

After three decades of research, efficient GaN-based blue light emitting sources became available. However, the yield of the manufacturing methods was low due to the low quality of the grown GaN. To increase the yield, the quality of the GaN had to be improved. Chapter 3 describes several methods which were developed to make GaN crystals of increasingly better quality. These efforts now result in very high quality single crystal GaN wafers which are ideal for device production. Nevertheless, the world's production of GaN-based blue light emitters is still depending on lower quality starting materials since the availability of the high quality GaN wafers is low. In addition, the use of high quality GaN as seed crystal, intended to rapidly increase the stock of high quality GaN, is contractually prohibited. Consequently, the optimization of the crystal quality obtained with currently employed methods is still important.

If one could investigate the crystal growth at the atomic scale in-situ (during growth of new material), optimization of the crystal growth process could be performed much faster than the currently used tedious trial and error investigations. Chapter 4 describes surface X-ray diffraction, the technique to perform such investigations. After decades of GaN growth research the use of surface X-ray diffraction can address the fundamental understanding of the growth which can ultimately result in more efficient growth procedures and better quality GaN crystals in a much faster way than the standard trial and error methods have done so far.

The measurements, in which the atomic geometry of the GaN surface and its growth medium (liquid gallium) are determined, are, however, far from trivial. The measurements require a complicated sample environment able to withstand high pressures and high temperatures to closely follow the growth procedures of GaN from liquid gallium. In addition, the measurements require high energy X-rays since not only the whole sample environment has to be penetrated but also the GaN surface is burried under a column of liquid gallium. In chapter 5 the sample environment developed for the investigations is discussed. A brief introduction on the used synchrotron beamline is given after which the chapter focusses on the sample environment itself. The purposely built furnace is the first high pressure, high temperature device equipped with a carbon fiber X-ray window accessible over a range of 336 degrees that, by using X-ray diffraction, can facilitate in-situ GaN growth investigations at relevant pressures and temperatures. At the same time the use of inconel steel prevents corrosion by hot pressurized ammonia gas and attack by hot liquid gallium. The chapter subsequently describes a test experiment in which GaN is grown from a liquid gallium-sodium mixture in contact with 50 bar of nitrogen gas. This proves that the sample environment is capable of properly performing its job.

The rapid oxidation of liquid gallium causes a thick skin of gallium oxide on top of it. This skin prevents a full contact between solid GaN and liquid gallium. By working in a glovebox and starting all experiments with liquid





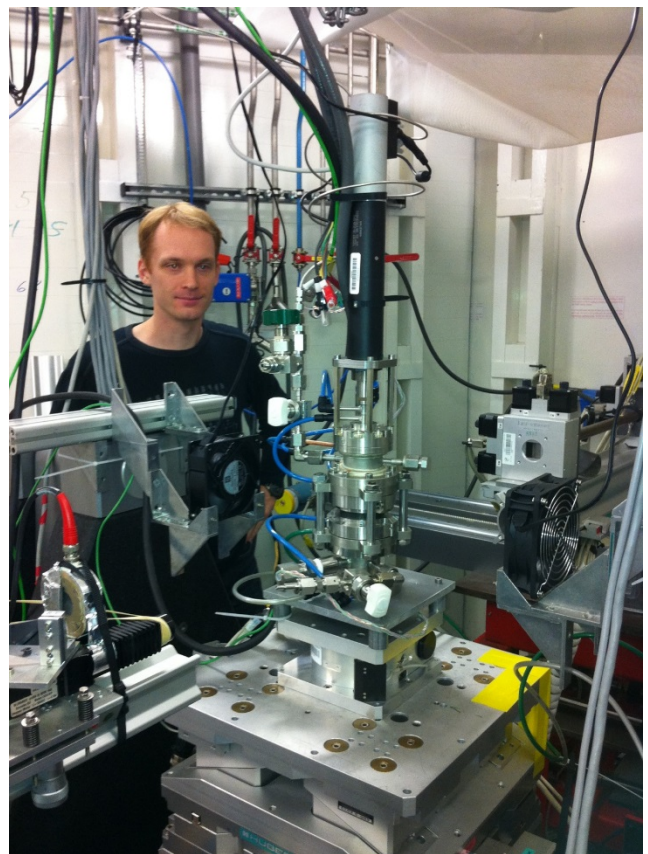
instead of solid gallium the influence of the oxide skin can be minimized, but this is not enough to form a connection between solid and liquid. To create a proper connection the GaN surface has to be heated so high that it partly decomposes. This creates the interface but unfortunately it also creates a rough crystal surface with which surface diffraction experiments become very difficult. By increasing the nitrogen pressure to 10-20 bar and increasing the temperature even more, the crystal's surface roughness reduces rapidly to create a smooth GaN surface in contact with liquid gallium. The whole procedure is described in chapter 6. The same chapter describes the successful measurement of a crystal truncation rod (CTR) with high in-plane momentum transfer. Such a CTR signal is sensitive to only the long range ordered part of the interface. The absence of long range order in a liquid means that such a CTR can be exploited to easily analyze the surface roughness of the solid even in contact with liquid is made.

Varying only the topmost atom's in-plane Debye-Waller factor to account for its thermal motion, the whole CTR is fitted with a surface roughness of  $0 \pm 0.1 \text{ \AA}$ , indicating that the repair successfully resulted in a smooth surface. Furthermore, the width of the CTR diffraction signal parallel to the crystal surface indicates that steps on the surface are present with a spacing of at least  $750 \text{ \AA}$ . Ex-situ analysis shows that numerous crystallites are formed on the GaN surface when the crystal is removed from the liquid. These are most likely caused by a shut-off effect as they were not observed during the in-situ investigation. The in-situ analysis can therefore help to create a suitable interface for continued investigations while ex-situ analysis might obscure this result.

The full interface structure is the subject of chapter 7. When kept in-situ, the interface is suitable for surface X-ray diffraction studies in which parameter changes can be studied to gain detailed atomic scale knowledge of the interface and its change due to the applied ambient. The effects of two parameters have been investigated, pressure and temperature. The effect of the pressure is small, mainly due to the relatively limited pressure range over which it can be changed in the experiment and over which the liquid metal is not expected to change much. However, the variation in temperature shows some surprising results.

So called "layering" of the liquid is observed and up to the highest temperatures investigated 9 layers of liquid gallium are distinguished at preferential distances from the crystal surface. In addition, the 3 layers closest to the crystal also occupy preferential in-plane positions above the crystal surface. In fact, for all investigated temperatures the preferential in and out-of-plane positions support the presence of gallium dimers formed by atoms in the first and third liquid layer. Since also the occupancy of the first and third layer in the liquid is approximately equal, it is concluded that gallium dimers are present in the hollow site of the GaN crystal structure. These results deliver a full 3D atomic scale model of the solid-liquid interface which can be used to explain some of the difficulties encountered in GaN growth from the liquid phase. At the highest temperatures investigated in this thesis GaN growth is slow, but possible, even without the addition of catalysts. The high degree of ordering of the liquid and especially the formation of a gallium dimer close to the solid GaN can hinder incorporation of new material and its decreasing occupancy for increasing temperature facilitates faster growth if the nitrogen pressure can be increased enough to compensate for the changing growth kinetics.

The main conclusion of this work is that the structure of the interface between liquid gallium and solid GaN has been determined. This opens the road for fast optimization of growth parameters of the promising Na-flux growth technique, possibly paving the way for the creation of low cost but high quality, contractually non-limited GaN able to compete with the current GaN used for large scale device fabrication.



*Aryan de Jong at his setup at the ID15 Beamline at the European Synchrotron Radiation Facility in Grenoble, France.*



## Thesis Joost van den Ende

Joost van den Ende was born on the 19<sup>th</sup> of February 1988 in Nijmegen (the Netherlands). In 2011 he obtained his Master degree in Physics and Astronomy from the Radboud University, Nijmegen. Joost started his PhD research project at the department of Theoretical Chemistry of the Institute for Molecules and Materials at the Radboud University, Nijmegen, under the supervision of Herma Cuppen. On September 26, 2016 he obtained his PhD degree after defending his thesis 'Exploring Polymorphism in Molecular Crystals with a Computational Approach'. At present Joost works as a Postdoctoral Fellow at F. Hoffmann-La Roche Ltd. in Basel, Switzerland.

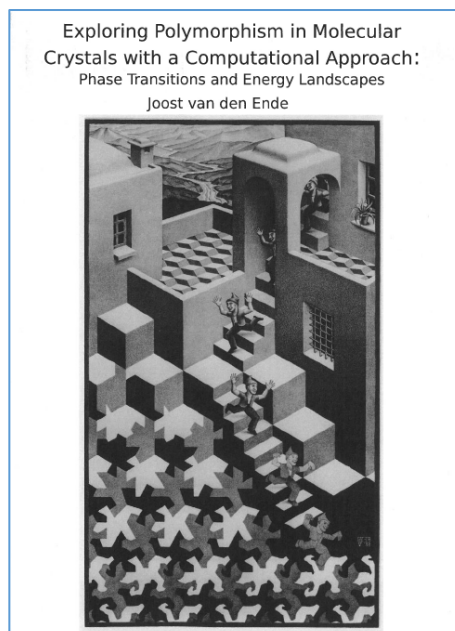
Molecular crystals are widely available in our lives, from ice covered roads to chocolate and from sugar to paracetamol. Some of these compounds have the ability to form multiple crystal structures, this is called polymorphism. Polymorphism in molecular crystals is the subject of study of this thesis. Through a computational approach phase transitions within the solid state between polymorphic forms and energy landscapes considering existing and putative crystal structures are being explored. The background for this study is the relevance of polymorphism in different industries, e.g. the food and pharmaceutical industry.

With different crystal structures come different properties, these might be beneficial or malicious with respect to the desired product properties. Another challenging aspect is occurrence of polymorphic transitions, which means a change from a crystal structure into another crystal structure. In the vast majority of cases, such a transformation starts from a thermodynamically less stable structure and ends in a thermodynamically more stable structure. An effect of such a transition is a decrease of solubility of the molecular compound, which can have a highly deteriorating effect when it comes to the efficacy of a drug and therefore can determine the shelf life of the drug.

The mechanisms behind solid-solid polymorphic transitions within molecular crystals are not yet well understood. A computational study that allows to zoom in at the molecular scale might enhance our knowledge. Within this thesis the amino acid DL-norleucine has been chosen as a model compound to study solid-solid polymorphic transitions. DL-norleucine possesses interesting polymorphic behaviour occurring within its three known polymorphic forms. The forms are enantiotropically related in pairs, which means that all three of them are the thermodynamically stable form in a specific temperature range. The room temperature  $\alpha$  polymorphic form can transform into the high temperature  $\gamma$  polymorphic form or to the low temperature  $\beta$  polymorphic form. Interestingly, the  $\alpha \leftrightarrow \gamma$  transition shows very different behaviour than the  $\beta \leftrightarrow \alpha$  transition.

Chapter 1 forms an introduction to some concepts used in this thesis. Chapter 2 describes briefly some computational aspects of the methods used within this thesis. It starts with a description of the different ways in which energies of systems are calculated, either through classical force fields based on atomic positions or on the density functional theory (DFT) evaluation of the electron density. When this last method is used, it is not trivial to partition the total energy of a crystal over the constituting molecules. A way to do that is the Bader-analysis and this is also described in Chapter 2. The calculated energies can serve as input for different simulation methods. Nudged Elastic Band (NEB) calculations are useful to determine a minimum energy path (MEP) through iteratively optimizing a band of images that connects one minimum and another. The maximum of the MEP is the saddle point. Molecular Dynamics (MD) simulations can be used to study dynamical aspects of a system. The technique iteratively solves Newton's equations of motion and therefore introduces temperature. When the waiting time for an interesting event to occur is too long, it is possible to bias a system through an adapted potential. A way to do this, is by imposing a moving restraint, this technique is called steered MD.

The  $\beta \leftrightarrow \alpha$  transition within DL-norleucine is the topic of Chapters 3, 4 and 5. These polymorphic forms are highly similar since they both consist of 2D hydrogen bonded networks between the amino and the acid groups of the molecules that form bilayers. Moreover, the molecular conformation is the same within the two polymorphic forms. Their difference is within the orientation of the bilayers with respect to each other, shifts over  $a/2$  and  $b/2$  bring the polymorphic forms over to each other. Within Chapter 3 MD simulations are described at stable and metastable temperatures for both polymorphic forms. The results for stable temperatures show



the validity of the chosen force field and other computational settings, because of the agreement with experimental results. The results at metastable temperatures show two interesting aspects. Firstly, the finding that at different temperatures many properties ( $a$ ,  $b$ ,  $c$ ,  $\beta$ ,  $V$ ,  $H$ ) behave identically for the both polymorphic forms. This shows that the difference between the polymorphic forms is indeed only formed by the shift of the bilayers with respect to each other. Secondly, that through the simulations at 350 K of the  $\beta$  polymorphic form, partial phase transitions could be studied with the help of specifically designed 2D distance parameters. These partial transitions have been classified. All partial transitions are shifts along  $b$ . This suggests that a full polymorphic transition might start with a shift along  $b$  and then a shift along  $a$ .

However, the NEB calculations presented in Chapter 4 show that the MEP is actually first sliding along  $a$  and then along  $b$ . The lowest energy barrier starting from  $\beta$  is the slide along  $b$  which would be expected based on the results of Chapter 3, but the rate determining barrier is higher along that route. The MD simulations performed with different simulation cell sizes, together with the higher used sampling rate within one cell size point at a cooperative behaviour instead of a nucleation-and-growth mechanism governing the polymorphic transition. No observation of a forming nucleus has been made. Moreover, in this chapter MD simulations at multiple different metastable conditions are directly confronted with experimental results both from a structural and energetical point of view, the observed agreement results in more confidence about the computational settings. The experiments described in Chapter 4 show that the  $\beta \leftrightarrow \alpha$  transition is highly variable in behaviour.

Chapter 5 focuses further on the mechanism of the polymorphic transition and the scaling of the involved energy barriers with the amount of molecules in the simulation cell. In this chapter, it is shown both by temperatureless NEB calculations and steered MD simulations that the most likely route for the full polymorphic transition is first shifting along  $a$  and then along  $b$ . The NEB calculations are performed at four different simulation cell sizes and show in first approximation a linear and isotropic scaling with the amount of molecules involved in the sliding. This is a strong suggestion for a cooperative mechanism, since a 1D or 2D-zipper mechanism would involve different scaling behaviour. From this linear scaling an estimate, with the help of an Arrhenius law, has been made how large the domains of cooperatively moving molecules can be, this is roughly 180 molecules. In this respect defects within the crystal can help the start of the transition, since it will be a limit to the size of the domains. Another factor that might play a role when temperature is taken into account are the modulations of the aliphatic sidechains of the molecules, these are probably the cause for deviations from the linear scaling of the energy barriers at the larger simulation cell sizes.

The last two chapters of the thesis are not related to solid-solid polymorphic transitions. The focus within these chapters lays on the interactions between molecules in a crystal, which can be used for purposes such as morphology and nucleation rate prediction. Chapter 6 describes q-GRID, a newly developed method to describe intermolecular interaction energies of molecular crystals. Within q-GRID an electron density distribution as directly obtained within the crystal is partitioned over the different molecules through a Bader-analysis. On the basis of the value of the electron density on the grid points and of the nuclear charges, a Coulomb interaction is calculated. This electrostatic interaction is being summed with empirical dispersion and repulsion contributions based on the nuclear positions, to obtain an intermolecular interaction energy. Three test cases for the method are the chemically and crystallographically different molecular compounds: anthracene, isonicotinamide and DL-methionine. For anthracene the ranking of the intermolecular interaction energies of the benchmark isoPAHAP method is best reproduced by q-GRID when compared with two other quantum mechanical methods and a generic force field. For the other two polymorphic test cases q-GRID was able to obtain the correct stability ranking.

This stability ranking is obtained from the summation of the intermolecular interaction energies from a central molecule with all its neighbours till a certain cut-off radius, this is a direct estimate of the lattice energy in which the intra molecular energy of the compound does not have to be evaluated. Within Chapter 7 this lattice energy has been used in order to rank putative structures generated within the context of the sixth blind test on organic crystal-structure prediction methods. This chapter describes the participation of the Radboud University Nijmegen to the blind test. For three of the five possible targets predictions have been made. Within this sixth blind test it was possible to generate two distinct rankings, the primary ranking has been based on the lattice energy as described above and the secondary ranking on nucleation rate predictions. These nucleation rates were calculated with kinetic Monte Carlo simulations on the basis of a crystal graph coming from a classical force field. In this way a new perspective in the field of crystal structure prediction has been introduced. For target XXII, a rigid small molecule, a correct prediction has been made.

The research described in this thesis is a computational study of a specific solid-solid polymorphic transition within the domain of molecular crystals combined with a new perspective on intermolecular interaction energies inside and outside the field of crystal structure prediction. It shows the ability of computational modelling to zoom in at a molecular scale in occurring processes and in understanding crystal structures from an energetic point of view.



*Joost van den Ende finishing one of his athletic performances, participating in the 'Zevenheuvelenloop' in Nijmegen (15 km in 46.21 min. on 20-11-2011).*





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