ICMS Highlights

Edition 7
October 2016

Creating visible nanostructures

INTERVIEW
/ Yao Lin

STRONG, LIGHT AND INCREDIBLY SMART

INTERVIEW
/ The ICMS alumni

& more...

Institute for Complex Molecular Systems

TU/e Technische Universiteit Eindhoven University of Technology

Where innovation starts

ICMS Highlights

Dear reader,

2016 will be remembered not only as the year in which our university celebrated its 60th anniversary with great pride but also as the year in which the ICMS had to continue without the daily support of Sagitta Peters. She was with us from the start, and many of our activities and instruments have been initiated by Sagitta. CERES will be her building as long as CERES is the home of the ICMS. We would like to thank Sagitta for all of her input, inspiration, and hard work, and we wish her all the best in the years to come.

2016 will also be remembered as the year that our friend and colleague Ben Feringa was awarded with the highest distinction in science: the Nobel Prize. We would like to congratulate Ben and his group with this well-deserved recognition for their outstanding science and thank Ben for our long-standing collaboration and friendship.

Our university is growing with a continuous increase in the number of students, which is great for strengthening the Dutch high-tech industry. But as a result, education is demanding more input and time from all of our staff members. Since there can be no more hours in a day or days in a week, we must become as effective as possible in performing our science. Synergy through collaboration is a key aspect of the ICMS, and we will continuously strive for excellence by supporting our members in their interdisciplinary research. We can only then achieve the targets set to educate our graduate students and post-docs with the best possible research that is aimed to solve long-term societal challenges. Some of our people, ideas and research are highlighted here.

We hope you enjoy reading,

Bert Meijer
Scientific director

Calendar

October 18, 2016, 12.00 hr
PhD course on Out-of-equilibrium
Location: Ceres

October 21, 2016, 15.00 hr
ICMS Discussion meeting Jessica Clough
Location: Ceres

November 4, 2016, 15.00 hr
ICMS Discussion meeting Maarten Biesheuvel
Location: Ceres

November 11, 2016, 15.00 hr
ICMS Discussion meeting Paul Dalton
Location: Ceres

December 9, 2016, 15.00 hr
ICMS Discussion meeting Albert Schenning
Location: Ceres

January 19 & 20, 2017
ICMS Outreach Symposium
Location: Zwarte Doos

February 13-17, 2017
ICMS Winterschool
Location: Ceres

The complete calendar can be found on our website.

Content

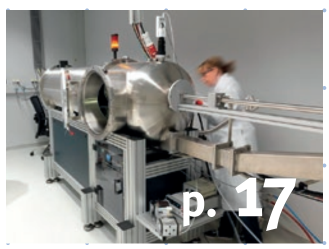
Edition 7
October 2016

Ideas need to flow
Figuring out how to make ‘living’ materials that are both self sustainable and adaptable is a very intriguing problem.

Strong, light and incredibly smart
Our central question is how can we stimulate the regenerative potential of bone.

Creating visible nanostructures

The ICMS alumni



Caught in the act

SensUs 2016

p. 2 **Calendar**

p. 12 **EPL Update**

p. 18 - 21 **Outreach**

p. 21 **Top publications**

p. 23 & 28 **News, awards & grants**

p. 26 & 27 **Technique**

p. 29 **Thesis**

p. 31 **Corporate information & ICMS in press**

Cover
Artist impression of bone resorbing cells on a piece of trabecular bone, inspired by the work of Keita Ito and Sandra Hofmann

> FIGURING OUT HOW TO MAKE 'LIVING' MATERIALS THAT ARE BOTH SELF-SUSTAINABLE AND ADAPTABLE IS A VERY INTRIGUING PROBLEM.

/ Yao Lin

Ideas need to *flow*

In 2015, Yao Lin, Associate Professor in the Chemistry Department and the Institute of Material Sciences of the University of Connecticut, spent a five month-sabbatical at the ICMS. Now, almost a year on, Lin is back in Eindhoven for a quick visit and we look back on his ICMS-days. "It is a very organic working environment where ideas really flow and are formed by different people."

Did you already collaborate with the ICMS before coming here?
"No, but I had already been following the work of Bert Meijer and his group for a considerable time, even before I first met Bert at a Gordon Conference where he approached me during the poster presentations. I became interested in supramolecular chemistry during my PhD research and afterwards I chose a postdoc in molecular biology engineering. Nature is just so intriguing."

What is it that got you hooked on biological systems?
"Well, mainly the fact that they are alive. We can make structures that are very much like biological structures, but we cannot make life. Figuring out how to make 'living' materials that are both self-sustainable and adaptable is a very intriguing problem."

Intriguing indeed, but also mind-boggling in complexity. Where do you start?
"I'd like to know the level of complexity we needed for a biological system to initiate self-organization. We know a lot of the individual reactions, but we don't know yet how to connect them all to reach the tipping point at which the system starts acting on its own."

Can you tell us a bit about your research at the University of Connecticut?
"When you consider a protein, the linear structure is fairly simple, but the complexity is in the amount of different building blocks, the amino acids. Controlling the buildup of an amino acid sequence is therefore difficult. My idea was to focus on using complexity in macromolecular architecture instead of in the sequence, to create functional structures. As a kind of protein mimic. Nature has evolved around linear structures, but why not use branched ones as a source of complexity in structures? So we started out with a type of synthetic polypeptides with brush-like or comb-like architectures. Their repeating units can be either natural or synthetic amino acids."

How did that work out?
"After five years, we had some moderate success. We figured out how these polypeptides may fold in the solution and how they can be assembled into large supramolecular structures. It was enough to get me tenure, but our structures were not nearly as sophisticated as proteins. And at that point I found myself running out of ideas. Luckily, I was granted a National Science Foundation Career Award, a program that helps young research staff establish their own independent research program. This program stimulates interaction with European Research Council awardees. I started browsing the list and saw Bert Meijer among the awardees. I decided to take a shot and ask him if I could spend some time at his lab. To my pleasant surprise, I got a positive response almost immediately and in March 2015 I arrived here in Eindhoven."

Did you have a research plan for your stay?
"By then I was able to use artificial building blocks to create supramolecular fibers and I wanted to introduce dynamic behavior. I also wanted to learn how to analyze the complex kinetic processes that exist within multiple pathways. That was my research plan, but I also wanted to use the sabbatical to experience a new working environment and see how people here approach science in this leading institute."

And did it all live up to your expectations?
"Oh yes, I had a very inspiring and stimulating time here. It is a very dynamic team and there is an organic way of working. All the techniques are in place and you can quickly assemble a dedicated team if you have a plan. Ideas really flow around and are formed by different people working in diverse fields. The combination of openness and intellectual flow makes ICMS a great place for science. I took home a lot of inspiration for my research as well as new ideas for organizing the way we work. Technically, I have gained very useful insights in the kinetic analysis of cooperative behaviors. This knowledge facilitated a real breakthrough in a collaborative project with professor Cheng at the University of Illinois at Urbana-Champaign this year."

I guess you would recommend a sabbatical to fellow researchers?
"Yes, I encourage everyone to arrange a stay in an exciting lab such as Bert's, even though it might be difficult to organize. Leaving my family behind was very hard, but it was worth it. My time at ICMS gave me so many new ideas and I feel refreshed in my work."

/ Albert Schenning

Creating visible nanostructures

Prof.dr. Albert Schenning is organically an organic chemist. He engineers at a molecular scale, but can see the results of his work with his own eyes. His research group, Functional Organic Materials and Devices, is working towards for example the development of smart windows. These will reflect infrared light and keep you cool during the summer.

"We develop smart films and coatings, which can change their shape, color or porosity when they are exposed to some form of stimulus, for example light or temperature. I often compare those materials to the human skin. When your skin gets in touch with sunlight, it changes color. When you're cold, you get goose bumps. We want to create materials that work like that."

Smart windows

One of the applications for these smart materials is a smart window. When you run an electric current through it, it changes from an infrared reflecting state to a transparent state. "Infrared light is what heats up buildings and cars," explains Schenning. "When you are able to block infrared light, you need less energy to cool your building in the summer. In the winter, you do want all the infrared light inside, because it saves you energy heating up your building. We're busy making the best window possible."
Schenning: "The TU/e-spin-off Peer+, who now is part of Merck, is also developing smart windows and just made a giant investment. I expect it to be on the market in 5 years or so, because otherwise Merck would not have invested that kind of money." Meanwhile, Schenning and his colleagues are working on the next step in the field of smart windows: developing a coating that can convert a regular window into a smart one.

The materials used in those smart windows is the same as used in LCD screens: liquid crystals. Schenning: "They are our favorite material to work with, because you can play with the order and orientation and hence influence the properties of the material. Then we can make these LC materials to reflect infrared light. Another technology is to be able to make glass opaque, so you can switch between a clear window and a milky window."

Possibilities

"We can also make nanoporous materials to purify water using liquid crystals. Or we can make smart textile, that keeps water out but allows moisture vapor to go out, which is very useful in rainwear. Or clothing that can generate electricity when you move, which can be used to charge your mobile phone," explains Schenning.

"You could combine these ideas with a material we've developed recently," says Schenning. If you put this material in sunlight, it starts to wiggle. It is not clear yet how this exactly works. Schenning: "There are at least 3 parameters that are changing continuously when we put this material in sunlight. It is very hard to make a model of this movement that matches our data. We are working on this with mathematicians from ICMS, because by understanding its behavior we like to improve the performance and apply it as a smart coating."

Visible

That Schenning is able to see his work, that is one of the things he loves about it. "I'm engineering at a molecular scale, but I see the result with my own eyes. I see the shape change, I see it happening right before my own eyes." The fact that the changes are visible to the human eye makes another application of liquid crystals a possibility. "If we can make a strip that changes color when it gets in contact with chemicals that rotting food produces, that strip can be used as an indicator for the freshness of the food," Schenning explains. "Currently, we use a date to determine if the food is fresh or not, but that date is just an average. When we can use such a strip to indicate the freshness, less food will be thrown out because we know for sure if it is still fresh or not."

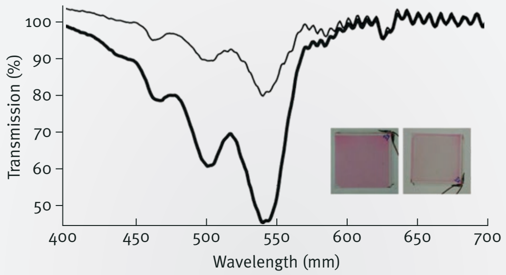
Devices

"To be able to make devices, we need people with different backgrounds. That's why we are at ICMS," explains Schenning. "But our research group itself is very interdisciplinary as well. We have a liquid crystal expert, mechanical engineer, a physicist and we have people from the industry connected to our research group. And here at the ICMS we have even more expertise within reach, like the mathematicians we're collaborating with for the model of the flappy material. You need all those people to make the ideas to come to life."

More about this research

M.G. Debije, A.P.H.J. Schenning, Materials Science and Materials Engineering, 1-9 (2016)

K. Kumar, C. Knie, D. Bléger, M.A. Peletier, H. Friedrich, S. Hecht, S.D.J. Broer, M.G. Debije, A.P.H.J. Schenning, Nature Communications, 7, 11975 (2016)



FACTS

The German multinational Merck invested 15 million euro's in a TU/e-spin-off to develop

smart windows.

According to the European Commission, around

88 million tons of food are wasted annually,

with costs of around 143 billion euros.

Many proteins and cell membranes are

liquid crystals.

The ICMS alumni

Established in 2008, the Institute for Complex Molecular Systems (ICMS) of the Eindhoven University of Technology (TU/e) brings together mathematics, physics, biology, chemistry and engineering to stimulate education and research in this emerging field of science. Since then, ICMS has provided an ideal training environment for several young students and scientists. In this ICMS highlights magazine edition, four excellent ICMS alumni will talk about about their experience at ICMS, and how the Institute helped prepare them for their future career in science and industry.

The Friday afternoon meetings

Thomas Hermans: “When the ICMS institute was created, in 2008, I was a PhD researcher in the group of Bert Meijer. It all started with the Friday afternoon meetings. The first months, only a few people joined the meetings. After a while, the meetings became a regular appointment for a number of PhD students, researchers and professors from different departments”. English is generally considered to be the lingua franca of the scientific community. A rock-solid guarantee to understand, yet not always truly comprehend each other. Martin Wolffs: “Initially, we all struggled a bit because of the different scientific backgrounds of those at the meetings. However, eventually, we started to understand how to deal with it, and, ultimately, how to benefit from it”. Maartje Bastings: “When re-phrasing our research for that multidisciplinary audience, we were indirectly pushed to look at our own research from a different perspective. Looking back now, those meetings offered excellent training for the future and my actual career. ”

The ICMS experience as excellent training for the future

After successfully completing her PhD at TU/e, Maartje Bastings moved to the Wyss Institute for Biologically Inspired Engineering, at the Harvard Medical School, Boston (US). Working side by side at the Wyss facilities are scientific luminaries and graduate students, biologists and engineers, corporate executives and academics. Such an extended community encompasses a wide range of disciplines, perspectives, career stages and backgrounds. As a postdoctoral fellow, Maartje Bastings is exploring synthetic biology approaches for the development of self-assembling DNA-origami nanoparticles for biomedical applications. Maartje Bastings: “What I love the most about the Wyss institute is the easiness of network expansion. My research is constantly exposed to new inputs and new audiences. The absence of rigid structural barriers strongly encourages open exchange of ideas, unexpected connections and, ultimately, unprecedented breakthroughs. These are also all characteristics of the ICMS institute.”
Thomas Hermans: “Being part of such the ICMS multidisciplinary institute slowly shaped my way of thinking and solving problems. The flexibility my research acquired over the years is for sure mirrored in the ICMS experience. For my master thesis, I investigated supramolecular polymers and modular approaches towards developing bioactive materials. With my PhD research, I further strengthened my knowledge on that particular field, looking at non-covalent pathways to supramolecular systems such as meta-stable dendrimer-based patchy particles, supramolecular hydrogels, multivalent guest-host interactions, and the possibility of controlling these systems via microfluidics. With my postdoctoral research at Northwestern University I then moved far away from supramolecular chemistry, focusing much more on the cell motility of cancer cells”. Thomas Hermans would have put together tiny and different pieces of a bigger puzzle when he moved to the Institut de Science et d’Ingénierie Supramoléculaires (ISIS) of Strasbourg, and founding his own lab, the Hermans Lab. Thomas Hermans: “When choosing the research directions of my own lab, I decided to go back to supramolecular chemistry, but with a new twist.” Hermans Lab focuses on supramolecular assemblies out of equilibrium and the possibility of creating highly organized non-equilibrium structures.

> “The ICMS institute: *source of* opportunities and model of inspiration”

Creative collaborations across the globe are one of the hallmarks of the ICMS institute, with seed grant programs, annual prizes, symposia and educational outreach with internationally renowned speakers, leading to unique opportunities for the ICMS members. Maartje Bastings: “During my PhD, the Director of the Wyss Institute was invited to Philips Natlab to give a lecture, as advertised by ICMS. On that occasion, I had the chance to speak with the Director, and in doing so, make the first steps towards my current research position at the Wyss Institute." Thomas Hermans: "I have always considered the ICMS symposia as perfect initiatives for the promotion of excellence, a model the Hermans Lab is now taking inspiration from."

The ICMS Animation Studio

"A picture is worth a thousand words" is the motto of the ICMS Animation Studio, the spearhead of the ICMS institute. The ICMS Animation Studio aims to create animations and illustrations for presentations and publications that allow researchers to convey their ideas to fellow researchers, and to get the research of the institute noticed in the vast amount of scientific work presented each year. In the case of Thomas Hermans, the Animation Studio produced a video on the self-assembly of soft nanoparticles with tunable patchiness. Thomas Hermans: "That movie was one of the first to be done by the Animation Studio, and it showed in an exceptional way how supramolecular chemistry can be used to assemble nanoparticles with small hydrophobic patches. I remember people being amazed when showing the video at international conferences. The research described was published in 2009 in Nature Nanotechnology."

Joep Evers: "I am grateful to the Animation Studio members for the video they made to visualize some of the simulation of my PhD results. The animation perfectly reflects the outcome of my simulations on the dynamics of crowds in an appealing way. The scenario is a so-called counterflow: two groups of people moving in opposite directions in a corridor. The key point is that the number of people determines whether or not the flow self-organizes." The animation on the dynamics of crowds was just the first step of a prolonged collaboration with the ICMS Animation Studio. Joep Evers: "In 2013-2014, together with the team leader of the Animation Studio, dr. Koen Pieterse, I supervised a group of four students in the TU/e Honors Horizon Program. The project revolved around the real-time visualization of multi-agent simulation results. As interesting as it was ambitious. The students had to develop pedestrian models and run simulations, which strengthened their programming skills. At the same time, the students had to think about real time visualization tools that might make the simulations' output more appealing for a broader scientific audience."

The ICMS and industry

One of the main strengths of the ICMS institute is the close collaboration with industry. Mutual benefits are being sought by combining industrial research and development with more fundamental sciences via a consortium established between ICMS and five industrial members of the Netherlands and some neighboring countries. One of them is Royal DSM, a global science-based company active in health, nutrition and materials. Martin Wolffs, ICMS alumnus, now project leader at the research and development department of DSM: "I am working with a multidisciplinary team on developing engineering plastics for smaller objects such as components of mobile phones, or for applications in the automotive industry. My work team is comprised of mechanical engineers, chemists and material scientists. There is no need for me to be an expert in each of these fields; however, adaptiveness and flexibility are required." These are qualities that Martin Wolffs developed during his stay at ICMS, and further strengthened at MRL in Santa Barbara and DSM. Martin Wolffs: "When I started at the TU/e, I was extremely convinced that I wanted to be a chemical engineer. After a couple of years, I moved towards applied organic chemistry and its use for the development of innovative classes of materials. With a solid background in organic chemistry and supramolecular materials acquired during my PhD in the group of prof.dr. Bert Meijer, and further exploration in polymer chemistry in Santa Barbara, I was finally ready for the next step, the translation of the technology and the research language developed within ICMS to industry."

Martin Wolffs

Thomas Hermans

Maartje Bastings

Joep Evers

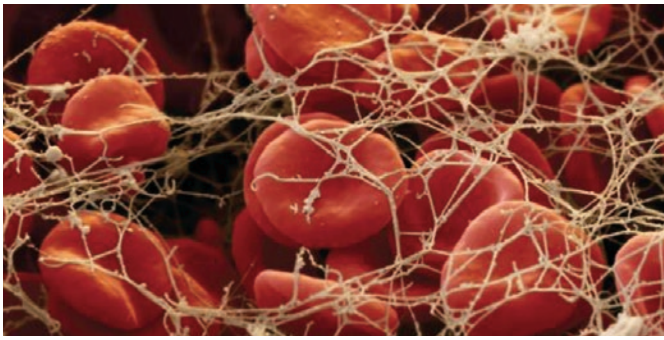
Martin Wolffs, PhD MSc
Martin Wolffs started Chemical Engineering & Chemistry at the Eindhoven University of Technology (TU/e) in 2000. In 2003, he obtained his bachelor degree cum laude and continued his masters in Molecular Engineering, which he finished cum laude in 2005. Starting from 2005, he performed his PhD research in the group of prof.dr. E.W. Meijer and dr. A.P.H.J. Schenning on the self-assembly of pi-conjugated systems. In 2009, he was awarded the Rubicon Fellowship for a postdoctoral study in the group of prof.dr. C.J. Hawker at the University of California, Santa Barbara. Currently, he is the R&D program manager at Royal DSM (Geleen, The Netherlands).

Thomas Hermans, PhD MSc
Thomas Hermans obtained his master degree in Chemical Engineering & Chemistry (Molecular Engineering) at the Eindhoven University of Technology (TU/e) in 2005. His thesis was based on supramolecular polymers and modular approaches towards developing bioactive materials. He carried out the research at the laboratory of prof.dr. E.W. Meijer. In 2006, he started a PhD in Biomedical Engineering in the same group, with a project on multi-step non-covalent pathways to supramolecular systems. From 2010 to 2013 he joined the group of prof.dr. Bartosz A. Grzybowski at Northwestern University (USA) as a HFSP postdoctoral researcher. Since 2013 he is the Director of the “Laboratoire des systèmes complexes hors équilibre” (Laboratory of non-equilibrium complex systems) and Assistant Professor at the Institut de Science et d’Ingénierie Supramoléculaires (ISIS), at the University of Strasbourg (France).

Maartje Bastings, PhD MSc
Maartje Bastings studied Biomedical Engineering at the Eindhoven University of Technology (TU/e). Her graduation project on protein interactions in supramolecular architectures was completed under the supervision of prof.dr. E.W. Meijer and prof.dr. M. Merkx. In September 2008, after the award of a NWO (Dutch Science Foundation) Toptalent fellowship, she started a PhD at TU/e. Her project focused on the design and interaction mechanisms of polymer supramolecular building blocks for bio-inspired technology in medicine. Since 2012 she has worked as a postdoctoral fellow at the Wyss Institute for Biologically Inspired Engineering, Harvard Medical School, Boston (US). Recently, she was appointed Assistant Professor at the Biomaterials division of the Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland.

Joep Evers, PhD MSc
Joep Evers studied Industrial and Applied Mathematics at the Eindhoven University of Technology (TU/e), with a minor in Applied Physics. From 2011, he was a PhD researcher in the Department of Mathematics and Computer Science of Eindhoven University of Technology, under the supervision of dr. Adrian Muntean and prof.dr. Mark Peletier. He obtained his PhD degree cum laude in 2015. Afterwards, he became a postdoctoral fellow in Burnaby, BC, Canada, and is employed by both Simon Fraser University (Burnaby) and Dalhousie University (Halifax, NS, Canada). He recently moved to Halifax to continue his postdoctoral position there. His research interests are collective behaviour in systems of socially interacting individuals, measure-valued evolution equations, interacting particle systems and discrete-to-continuum limits.

EPL Update



Natura Artis Magistra

Bio-inspired concepts for new polymer materials

Eindhoven Polymer Laboratories; EPL-affiliated Theory of Polymers and Soft Matter (TPS) research group is developing next-generation polymer materials using design strategies borrowed from Nature.

Bio-inspiration

The materials that our bodies are made of are remarkable. They are 100% bio-based, autonomously assembled, renewable, strong, and self-healing. We literally trust these materials with our lives. To develop the next generation of consumer polymeric materials requires innovative, nontraditional use of biological and bio-inspired materials, and their application in high-tech materials. A key strategy to address this challenge is to borrow design concepts from natural materials to enhance the performance of synthetics. Given the vast space of possible material motifs, trial-and-error formulation is not a viable option. Within the department of Applied Physics, the TPS group is building a research team that uses state-of-the-art computational approaches to uncover the physical principles responsible for superior performance in natural materials, and to determine from them optimized design strategies for synthetics.

Plastics between two worlds

A striking feature, shared among many naturally occurring polymer materials (such as the cell cytoskeleton, the extracellular matrix, cartilage and even bone) is that their molecular structure is not fixed. Rather, crosslink connections between the molecules are able to break and reform repeatedly. This contrasts starkly with the plastics that we are surrounded by day to day, in which the polymers are either not linked at all but connected only through entanglements (thermoplasts) or, at the other extreme, are permanently chemically linked (the thermosets). Thermoplasts melt at elevated temperature, which facilitates their recycling, but they sacrifice mechanical performance for this advantage. Thermosets exhibit superior strength, and may be employed in highly demanding settings but are, generally, extremely difficult to recycle or reshape.

The reversible nature of their bonds permits biomaterials the structural plasticity to adapt to loading, without sacrificing strength and toughness. The principle of reversible crosslinking, where much like in the natural materials the crosslinks are strong but still able to unbind and rebind, points the way to an inbetween world of polymeric materials. It has been applied, with striking success, in gels and plastics and there is currently something of an explosion of new synthetic designs that derive superior mechanical performance from reversible bonds. Vitrimers and general exchange-bond soft materials are prime examples, but the addition of reversible bonds to otherwise permanently linked soft materials has been shown – in sacrificial bond materials and double networks – to boost the toughness (the amount of energy required to break a material) without adverse effects on the linear response. What is unclear, however, is which molecular and mesoscopic processes are responsible for the improved mechanical response. Because these underlying principles are unknown, the question of how to design and target these properties, and how to optimize them, is one that we currently cannot address.

In a series of connected projects, TPS is establishing this physical underpinning of reversible, bio-inspired materials.

Team and projects:

The reversible materials project involves TPS staff members: Wouter Ellenbroek, Alexey Lyulin, Paul van der Schoot and Kees Storm. The staff is joined, in April 2017, by Liesbeth Janssen who brings her expertise in modeling glassy systems to these and other projects.

Chiara Raffaelli (Ph.D. student since September 2016) works in a FOM-funded project that aims to develop highly responsive materials using reversible crosslinkers whose activity can be tuned using external physical or chemical queues such as pH or light.
Nick Tito (Postdoc since September 2016) is part of the 4TU High Tech Materials research programme (“New Horizons”) and works on understanding and optimizing the toughening obtained in materials that contain both permanent and reversible crosslinks.

Simone Ciarella (Ph.D. student since October 2016) is funded through the Eindhoven Polymer Laboratories and will develop new models for the structural dynamics of vitrimers.

Cyril Vrusch (Ph.D. student since April 2014) works on dynamically structured polymer networks and aims to capture the real-life behavior of collagen in the extracellular matrix.

Undergraduate students are also actively involved: ICMS student Stijn van Leuken is currently performing his thesis research at Harvard in the group of Vinothan Manoharan, exploring ways to use DNA to make reversible interactions in soft materials that are specific and even programmable.

This line of research relies upon and aims to strengthen collaboration within ICMS and EPL and with partners outside Eindhoven. The projects mentioned above all involve such collaborations, including the group of Carlijn Bouten in Biomedical Engineering and those of Rint Sijbesma, Dick Broer, and Albert Schenning in Chemistry and Chemical Engineering. The 4TU project is performed in close collaboration with Costantino Creton from ESPCI, who will spend several months at TU/e as visiting professor.

With this research programme, TU/e is a frontline participant in an exciting field of research where insights from fundamental physics serve to enhance the development of novel, sustainable, high-performance polymer materials. We are eager, particularly at this stage, to embed these projects in further public-private collaborations and warmly invite interested parties to discuss the possibilities.

/ Sandra Hofmann and Keita Ito have a bone to pick with our body's support structure

Strong, *light* and incredibly smart

Most of us see bone as an essential, but rather dull and static material. Two people who certainly think otherwise are dr. Sandra Hofmann and prof.dr. Keita Ito. To them, bone is one of the most fascinating materials in science, and that fascination is easily transferred. Talking to them will turn anyone into a true bone aficionado.

"When you look at bone from an engineering perspective it is simply the framework that gives our body its form and allows it to function. From that viewpoint, it is comparable to inanimate, heavy materials like steel or concrete", says Keita Ito, professor of Orthopedic Biomechanics. "What makes bone so special is that it is very strong and very light." To prove his point, Ito walks to a cabinet and comes back with a bone. A real, human thigh bone! This is the biggest bone we have in our body, yet it feels surprisingly light.

To understand why bone can be both strong and lightweight, we have to look at the inner structure of bone. Sandra Hofmann, assistant professor of Bone Tissue Engineering in the Orthopaedic Biomechanics Group, points to a picture on her laptop. It shows a cross-section of a thigh bone, which looks like a miniature maze. "It may look random at first sight, but this structure is highly organized", she explains. The alignment of the lines of the maze and the width between them varies according to the loads and pressures that bone has to withstand. "Bone can adapt its structure according to changing mechanical needs, without gaining weight. It really is a smart material", Ito adds. This adaptive, 'smart' nature of bone originates from its cellular composition. There is not just one type of bone cell. In fact there are three different types. The osteoblasts are the bone forming cells that build the extracellular protein matrix where mineralization of calcium phosphate takes place. The osteoclasts do exactly the opposite: they melt away the crystalized minerals and

Protruding fingers

It goes without saying that strict regulation of these two opposing functions is essential for overall bone health. This brings us nicely to the subject of the third and most elusive bone cell: osteocytes. "These are intriguing characters", says Ito. "They start out as osteoblasts, but while building the extracellular matrix, they become locked in. At that point, they transform into sensing cells that are able to pick up, send out and transmit signals to neighboring cells. We don't yet fully understand how they do this, but we know that they develop long 'fingers' that can protrude through the matrix and touch other cells. All the special features of bone are derived from interactions between these three different cell types." It is this complex communication network that Ito and Hofmann wish to unravel.

Hofmann: "Our central question is how can we stimulate the regenerative potential of bone. We know that bone is one of the few tissues in the body that can completely renew itself, so the potential is there. We also know that new bone grows best alongside existing bone, but we don't know why." To this end, Hofmann is growing what she calls mini-bones in the lab. Not in 2D cell cultures, but in 3D scaffolds made of silk fibroin protein where bone can grow in an almost real-life setting. Sounds straightforward, but it is extremely complex, according to Ito. "Sandra will probably not mention this herself, but she is one of the very few people in the world who can grow bone in the lab in a 3D architecture and keep it alive outside the body. That is a really special skill."

Pulling at the surface

The mini-bones are subsequently exposed to different external stimuli, particularly mechanical loading. Hofmann: "That way, we can study how the cells interact with the scaffold and how they respond to changes. We know osteoblasts can sense elasticity. They exhibit pulling behavior when attached to a surface to test its stiffness. The stiffer the surface, the better they grow and attach to the surface. They are also capable of aligning themselves. When you grow osteoblasts in 2D on a randomly patterned surface, no structure will emerge. But when the surface has a well-defined pattern, say lines, then the cells will follow that pattern and align themselves accordingly. Clearly, osteoblasts can sense their immediate environment and react to that, but we don't know how they do that." And there is more. "Osteoblasts also have a clear sense of orientation", Ito adds. "They attach themselves to a surface and then start forming bone underneath, so they push themselves upwards. But because there are many osteoblasts operating simultaneously from different directions, most of them are eventually surrounded by bone. Locked in their newly formed matrix, the osteoblasts turn into osteocytes."

This process is well mimicked in the laboratory. The osteoblasts attach themselves to the sponge-like scaffold and start forming the extracellular matrix in 3D, which leads to mini-bones that strongly resemble natural bone in terms of structure. Hofmann has designed several experimental set-ups in which mechanical forces can be applied to the mini-bones. "We have different types of bioreactors. One example is our flow perfusion bioreactor. Here, fluids are pumped through the center of the scaffold, creating shear forces on the cells. The cells are being pulled off so to speak, which allows us to study their response. So far, we have seen that the flow rate influences cell differentiation. At low flow velocity, the cells focus on growth and start dividing. But when the flow velocity increases, they start mineralizing."

Personal bone

Despite the impressive lab-grown bones, clinical applications, especially for the regeneration of large bone fractures, still seem very far away judging by the size of the mini-bones and the difficult, labor-intensive production process and missing vascularization. Are these primarily research tools or is there a clinical application down the line? Hofmann sees potential for personalized medicine. "When we work from a patient's own bone cells, we can also get personal mini-bones that may be used to study the effect of medication so we can determine the best treatment option for that particular patient. I think this will be the first real application for tissue engineered bone."

FACTS ABOUT BONE

We are born with around

300 bones

but end up with

just 206.

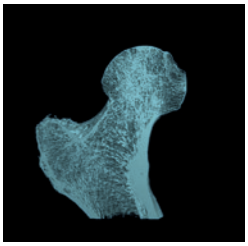
The 54 bones

in your hand, fingers and wrists allow you to write, use a smartphone and play a piano.

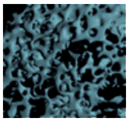
The bones are also constantly worn down and re-made, to the point where every

7 years

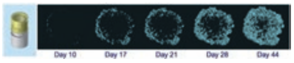
we essentially have a new bone.



Micro-computed tomography image of the top of a healthy human femur, showing the porous structure of the bone and the specific orientation of the trabeculi along the stress lines (Image courtesy of dr. Bert van Rietbergen).



Tissue-engineered mineralized extracellular matrix produced by the cells, mimicking trabecular bone structure (Hofmann et al., Eur J Pharm Biopharm, 2013).



In-house designed bioreactor showing the development of mineralized tissue produced by osteoblasts over time with micro-computed tomography (adapted from Hagenmüller et al., Ann Biomed Eng 2007).

/ Ilja Voets

Caught in the act

Soft matter constitutes a broad class of materials including the fabric of life, cells and tissues, as well as a plethora of everyday products and materials that we now take for granted, such as foods, paints, cosmetics, detergents, healthcare, organic displays, etc.

Knowledge-based design of functional soft matter requires insight into the interrelations between dynamics, structure, processing, and properties. Clearly, this is a major tour-de-force when the full hierarchy of length- and timescales becomes relevant. The challenge is truly multiscale in the sense that it spans orders of magnitude from the ultrafast, such as femtosecond dynamics of molecular reorientations and covalent bonds of a few angstroms, to the ultraslow aging of (colloidal) glasses and macroscopic deformations under shear and extensional flow. But, this is not all that makes in-depth characterization of soft materials difficult. This 'stuff that dreams are made of' is something in between simple liquids and simple solids, and composed of vastly different classes of building blocks (colloids, (bio)polymers, liquid crystals, etc.), heterogeneous and dynamic by nature, responsive to its environment, and – more often than not – perturbed by the very probes used to understand the matter.

The grand challenge

Clearly, this cross-disciplinary domain between chemistry, physics, biology and engineering is where forefront research and technological developments go hand in hand. It is this synergy that motivates and inspires a range of collaborative activities at the ICMS including discussion meetings and dedicated workshops to further support and strengthen the experimental facilities of the institute, which include super-resolution microscopy, small angle X-ray scattering, stopped-flow spectroscopy, and liquid phase electron microscopy. Each of these has given unprecedented insight into the molecular make-up and evolution of complex soft materials. Examples of these include the exchange dynamics of supramolecular fibers, the flexibility of bacterial adhesins, bundling in thermo-responsive hydrogels, and the growth of crystals from solution. And still, there is much more to be discovered.

So what can't we do yet?

Presently, we can visualize fast motion of big colloids, probe slow dynamics of plastics, quantify fast motion of single molecules, measure the mechanics of stressed cells, watch crystals form in solution. However, we cannot monitor all of the relevant length- and timescales simultaneously. Without doubt, the grand challenge is simultaneous, non-invasive, multiscale characterization of the structure and dynamics of complex, multicomponent soft materials both in and out-of-equilibrium on the ensemble and single-molecule (or particle) level without compromising statistics. Exciting developments are on the horizon: time-resolved X-ray scattering under flow in a microfluidic chip on a table-top synchrotron, femtosecond-pulsed electron diffraction on thin films, fast single-molecule detection of ligand-receptor interactions in blood, and single-shot imaging with nanometer and nanosecond resolution by dynamic electron microscopy of liquid specimens. So join us and stay tuned.

Multidisciplinarity, Curiosity, *Innovation*

Multidisciplinarity, curiosity, and innovation; all fingerprints of the concerted research performed at TU/e in departments, research institutes, and centres of excellence. The Institute of Complex Molecular Systems (ICMS), the High Tech Systems Center (HTSC), the Institute for Photonics Integration (IPI) and the Data Science Center (DSC/e) are selected by the Board of the University to foster interdisciplinary activities and to excel in the four areas of science and engineering. "In the last decade, the Eindhoven University of Technology has taken giant steps forwards in the national and international scene via top quality education and internationally prominent research" says Bert Meijer, "turning into a real magnet for smart people". Talented students, and professors with solid scientific basis and a penetrative entrepreneurial attitude. Bert Meijer: "In this scenario, we will join forces, where possible, between scientific institutes and the industry-oriented centres, and activate new channels of communication, to increase awareness and, ultimately, explore new possibilities in terms of collaborative research." In this ICMS highlights magazine, an interesting conversation with the directors of the other three strategic institutes and data centres of TU/e: Maarten Steinbuch (HTSC), Ton Backx (IPI), Wil van der Aalst (DSC/e).

High Tech Systems Center (HTSC)

There has been growing attention for better integrated components and correct system architectures for high tech machines. Superior mechatronic systems and manufacturing technologies and infrastructures, which are critical for final performance and manufacturability, are achieved across all application sectors. "The HTSC's research integrates technology for a broad range of market segments, such as robotics, healthcare, semiconductor manufacturing, printing, solar energy and instrumentation, agrifood, into a multidisciplinary, industry-driven science approach" says Maarten Steinbuch. One of the mission statements of HTSC is to be the primary driver and network centre of the Dutch Mechatronics Ecosystem, expanding internationally. HTSC actively supports and initiates long-term strategic partnerships with industry consisting of larger, mutually defined, multidisciplinary research programs.

The University as a dynamic, open innovation space

Maarten Steinbuch: "The divergence between the pace of university research and technology development is undeniable. Technology is growing exponentially, while doing high quality research requires time and dedication. To speed up innovation and entirely benefit from the capabilities of universities, one solution might be to define a next generation of university:

a dynamic open innovation space, with open channels to industrial, entrepreneurial, societal engaged individuals." A system promoting worldwide games for societal challenges, where bachelor, master, PDEng and PhD students set up inter-disciplinary teams competing in pressure cookers session, like hackathons. "The university is in urgent need of *disruptive thinkers*" says Maarten Steinbuch, "the same applies for companies in urgency of innovation.

HTSC and the strategic institutes

"With the impressive acceleration of technology development, as University, we need strong collaborations within departments for wide-ranging research" says Maarten Steinbuch. "With the compartmentalized structure of the University, communication is not always that easy. The strategic institutes and datacenters should promote regular exchange of ideas via meetings, shared Master, PDEng and PhD students, symposia, and special events. That is what we need." Maarten Steinbuch, foreseeing directions for possible collaborations: "Main goal of the ICMS institute is to understand complexity of molecular structures at different levels. The HTSC institute has in mechatronics its key pillar, and in robotic surgery one of is successful application, and we are going into a world of molecular engineering and manufacturing". According to many scientists, in a not-to-distant future, the human brain could be enhanced by tiny robotic implants that connect the brain to cloud-based computer networks. "Prerequisite for that, and for the design of the next generation nanorobots, is a thorough knowledge of the molecular structures of the brain, or, in other words, of its complexity. For this to be realised at industrial scale, we need manufacturing and high tech machines and equipment, and this calls for cross-contamination of different expertises: biology, chemistry but also material science, systems and control, software, electrical engineering and mechanics." Maarten Steinbuch envisions room for proliferative collaborations with IPI and DSC/e too: "Within few years, photonics technology will extend the capabilities of traditional electronic chips. Mechatronics might give a big hand and we definitely can explore the crosslinks between the HTSC and the Data Science Center."

Maarten Steinbuch, HTSC

Maarten Steinbuch is Distinguished University Professor and Professor in Systems and Control at the TU/e. His research interests are design and control of motion systems, robotics, automotive powertrains, and of fusion plasmas. In 2016, Prof. Steinbuch was awarded with the Simon Stevin Meester title.

Institute for Photonics Integration (IPI)

"By 2022, all the electrical power we generate nowadays will be necessary to handle the data traffic only" says Ton Backx, former dean of the TU/e Department of Electrical Engineering: "Until very recently, microchips were exclusively micro-electronic chips using electrical signals and electrons as carriers of information. Due to their charge, electrons are sensitive to electromagnetic fields. This makes that electrical signals require signal repetition at relatively short distances, due to significant power losses. Photonic microchips instead have the advantage of being faster and simultaneously far more energy efficient that makes them an appealing alternative to process massive data streams at reduced power consumptions."
In the last two decades, TU/e has achieved a world leading position in integrated photonics, optical materials and optical communication systems. TU/e has developed standards for the design and manufacturing of the so-called PICs, Photonic Integrated Circuits, based on indium phosphide, which allows for the integration of various optically active and passive functions on the same chip. *EffectPhotonics*, a TU/e spinoff, recently succeeded in marketing its first photonic chip based transceiver systems for medium distance communication. Ton Backx: "In this scenario, the Institute for Photonic Integration

aims at maintaining this top level research, and, at the same time, apply this technology on a large scale in the years to come." The Institute for Photonic Integration is the natural extension of the highly reputable *COBRA* research institute. "The *COBRA* institute is the fruit of a long lasting cooperation between Philips and TU/e. With its in-house infrastructures, the facility belongs to the most advanced in the world of Photonic Integration for materials research, processing of photonic materials, R&D on photonic devices, lithography and ultrafast broadband optical communication."

Photon Delta

TU/e and the Institute for Photonic Integration, with a research section including more than 300 scientists already, have recently joined the forces with several stakeholders of the Brainport Area, Twente, Delft, and Memphis partners to create a new ecosystem in the field of photonics, Photon Delta. Ton Backx: "The global market for Photonic Integrated Circuits was €2 billion in 2015 (exclusive equipment). It is growing exponentially with a factor of approximately 1.5/year. In 2020 it will already exceed €20 billion and in 2030 exceed €1000 billion. The strength of the Institute for Photonic Integration lies in its interdisciplinary nature, and the tremendous opportunities it opens.

Ton Backx, IPI

Ton Backx is Professor in Electric Engineering at TU/e. In 2016, he founded the Institute for Photonic Integration (IPI), a research institute for integrated Photonics and Photonic Systems at TU/e. His interests, besides the new developments in the field of Photonic Integration, include process identification, model based process control and model reduction and its applications to a wide range of processes in hydrocarbons processing, chemical processing, glass manufacturing and steel production.

Data Science Center (DSC/e)

"The trend of *big data growth* presents enormous challenges, but it also presents incredible business and research opportunities. Therefore, data science is growing in importance and becoming an integral part of different types of engineering and scientific research" says Wil van der Aalst. The Data Science Center Eindhoven (DSC/e) is TU/e's response to the growing volume and importance of data. The DSC/e combines both scientific and technological depth with multi-disciplinary width. Nevertheless the center of gravity is hard-core data analytics grounded in computer science and mathematics, with strong involvement of the enabling technologies and application domains (health, logistics, maintenance, lifestyle, marketing, social media, etc.). This includes competences ranging from the data driven business development up to knowledge in the domains of law, ethics and privacy.

It is the process and the data stupid

Wil van der Aalst: "Organizations that are unable to use (big) data in a smart way will not survive." However, it is not sufficient to focus on data storage and data analysis. The data scientist also needs to relate data to process analysis. Process mining is the missing link between model-based process analysis such as simulation and business process management techniques, and data-centric analysis techniques like machine learning and data mining. Wil van der Aalst: "process mining seeks the confrontation between event data and process models, extracting information about processes from transaction logs". Through easy to use software, data science can be applied directly to analyse and improve processes in a variety of domains. Wil van der Aalst:

"15 years ago researchers from TU/e started developing ProM, an extensible framework supporting several process mining techniques in the form of more than 1500 plug-ins. ProM has been implemented in Java and can be downloaded free of charge. The flexibility of the framework allows users for easy create and reuse of the code during the implementation of new process mining ideas. Many commercial vendors have adopted ideas from ProM (Disco, ProcessGold, Celonis, Minit, QPR, myInvenio, etc.). Seldom one can witness university research contributing directly to the creation of an entirely new breed of software tools."

Wil van der Aalst, DSC/e
Wil van der Aalst is Distinguished University Professor and Professor of Information Systems at the TU/e. His interests include workflow management, process mining, Petri nets, business process management, process modelling, and simulation. With more than 600 journal papers and refereed conference/workshop publications, and several influential books, Prof. van der Aalst is one of the most cited computer scientists in the world.

ICMS TOP PUBLICATIONS

April 2016 – September 2016

1. *A. Aloi, A. Vargas Jentzsch, N. Vilanova, L. Albertazzi, I.K. Voets*
Imaging nanostructures by single-molecule localization microscopy in organic solvents
J. Am. Chem. Soc. 138, 2953-2956 (2016)

2. *N.J. van Zee, M.J. Sanford, G.W. Coates*
Electronic effects of aluminium complexes in the copolymerization of propylene oxide with tricyclic anhydrides: access to well-defined, functionalizable aliphatic polyesters
J. Am. Chem. Soc. 138, 2755-2761 (2016)

3. *B. van Genabeek, B.F.M. de Waal, M.M.J. Gosens, L.M. Pitet, A.R.A. Palmans, E.W. Meijer*
Synthesis and self-assembly of discrete dimethylsiloxane lactic acid diblock co-oligomers: The dononacontamer and its shorter homologues
J. Am. Chem. Soc. 138, 4210-4218 (2016)

4. *R.M.P. da Silva, D. van der Zwaag, L. Albertazzi, S.S. Lee, E.W. Meijer, S.I. Stupp*
Super-resolution microscopy reveals structural diversity in molecular exchange among peptide amphiphile nanofibers
Nat. Commun. 7, 11561 (2016)

5. *L.H. Beun, L. Albertazzi, D. van der Zwaag, R. de Vries, M.A.C. Stuart*
Unidirectional living growth of self assembled protein nanofibrils revealed by super-resolution microscopy
ACS Nano 10, 4973-4980 (2016)

6. *J.J. De Yoreo, N.A.J.M. Sommerdijk*
Investigating materials and formation with liquid-phase and cryogenic TEM
Nature Reviews Materials 1, 16035 (2016)

7. *R.H. Zha, B.F.M. de Waal, M. Lutz, A.J.P. Teunissen, E.W. Meijer*
End groups of functionalized siloxane oligomers direct block-copolymeric or liquid-crystalline self-assembly behavior
J. Am. Chem. Soc. 138, 5693-5698 (2016)

8. *M. Garcia-Iglesias, B.F.M. de Waal, A.V. Gorbunov, A.R.A. Palmans, M. Kemerink, E.W. Meijer*
A versatile method for the preparation of ferroelectric supramolecular materials via radical end-functionalization of vinylidene fluoride oligomers
J. Am. Chem. Soc. 138, 6217-6223 (2016)

9. *P. Pourhossein, R.K. Vijayaraghavan, S.C.J. Meskers, R.C. Chiechi*
Optical modulation of nano-gap tunneling junctions comprising self-assembled monolayers of hemicyanine dyes
Nat.Commun. 7, 11749 (2016)

10. *J.A. Berrocal, C. Biagini, L. Mandolini, S. Di Stefano*
Coupling of the decarboxylation of 2-cyano-2phenylpropanoic acid to large-amplitude motions: a convenient fuel for an acid-base-operated molecular switch
Angew. Chem., Int. Ed. 55, 6997-7001 (2016)

11. *A.J.P. Teunissen, T.F.E. Paffen, G. Ercolani, T.F.A. de Greef, E.W. Meijer*
Regulating competing supramolecular interactions using ligand concentration
J. Am. Chem. Soc. 138, 6852-6860 (2016)

12. *Z. Li, X. Xu, W. Zhang, X. Meng, W. Ma, A. Yartsev, O. Inganäs, M.R. Andersson, R.A.J. Janssen, E. Wang*
High performance all-polymer solar cells by synergistic effects of fine-tuned crystallinity and solvent annealing
J. Am. Chem. Soc. 138, 10935-10944 (2016)

13. *R.P.G. Bosmans, J.M. Briels, L.-G. Milroy, T.F.A. de Greef, M. Merkx, L. Brunsveld*
Supramolecular control over split-luciferase complementation
Angew. Chem. Int. Ed. 128, 9045-9049 (2016)

14. *J.M. Clough, C. Creton, S.L. Craig, R.P. Sijbesma*
Covalent bond scission in the Mullins effect of a filled elastomer: real-time visualization with mechanoluminescence
Adv. Funct. Mater. published on line (2016)

15. *A.H. Gelebart, M. Mc Bride, A.P.H.J. Schenning, C.N. Bowman, D.J. Broer*
Photoresponsive fiber array: toward mimicking the collective motion of cilia for transport applications
Adv. Funct. Mater., 26, 5322-5327 (2016)

16. *K.H. Hendriks, A.S.G. Wijpkema, J.J. van Franeker, M.M. Wienk, R.A.J. Janssen*
Dichotomous role of exciting the donor or the acceptor on charge generation in organic solar cells
J. Am. Chem. Soc. 138, 10026-10031 (2016)

17. *K. Kumar, C. Knie, D. Bléger, M.A. Peletier, H. Friedrich, S. Hecht, D.J. Broer, M.G. Debije, A.P.H.J. Schenning*
A chaotic self-oscillating sunlight-driven polymer actuator
Nat. Commun. 7, 11975 (2016)

18. *J.F. Lutz, J.M. Lehn, E.W. Meijer, K. Matyjaszewski*
From precision polymers to complex materials and systems
Nature Review Materials 1, 16024 (2016)

19. *C. Duan, K. Gao, J.J. van Franeker, F. Liu, M.M. Wienk, R.A. Janssen*
Toward practical useful polymers for highly efficient solar cells via a random copolymer approach
J. Am. Chem. Soc. 138, 10782-10785 (2016)

This overview lists publications in high end journals with ICMS as affiliation.

NEWS, AWARDS & GRANTS

Netherlands Scholar Award for

DR. RAFAL KLAJN

On September 21st 2016, Associate professor Rafal Klajn (Weizmann Institute of Science, Israel) was awarded with the Netherlands Scholar Award for Supramolecular Chemistry by the Research Center for Functional Molecular Systems during a colloquium at The Royal Netherlands Academy of Arts and Sciences in Amsterdam. This prize is in recognition for his outstanding contribution to the field of supramolecular chemistry and responsive materials in the early stage of his career.

PATRICIA DANKERS

starts pre-clinical research hydrogel in cancer treatment

The recently received ERC Proof of Concept Grant (PoC) provides Patricia Dankers PhD PhD, in collaboration with Geert van Almen PhD, with the means to start pre-clinical research on the application of a new hydrogel drug combination for the treatment of tumors in the peritoneum. The concept of combining this hydrogel with medication was developed in the research group 'Supramolecular Biomaterials for Translational Biomedical Science' led by Dankers. This concept is a potential game changer in the delivery of drugs in the human body.

NWO ECHO grant for

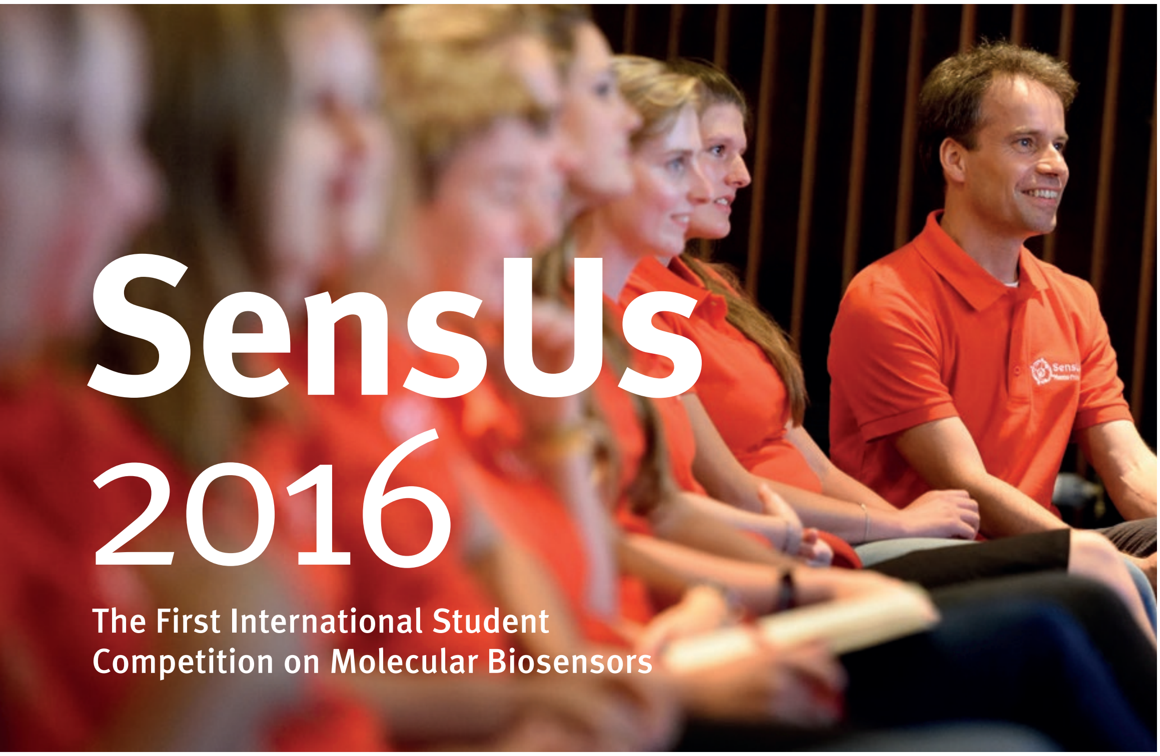
DR. ILJA VOETS

Dr. Ilja Voets (TU/e) has received an NWO ECHO Grant of € 260,000 from The Netherlands Organization for Scientific Research (NWO). This is for her planned research on ice-binding protein-polymers for control over ice growth in soft materials (POLICE).

Veni Award for

DANQING LIU

Researcher dr. Danqing Liu has received a Veni grant. The Netherlands Organisation for Scientific Research (NWO) has awarded a Veni grant, which amounts to € 250,000 in funding, to 158 researchers who have recently received their doctorate. Dr. Liu will develop 'communicating polymers' to channel communication between humans and machineries. Using an external trigger, the 'smart' surfaces deform locally and impart tactile perception to the human fingers, thus enabling devices to 'talk' to humans. Reversibly, the surfaces can receive touch commands from humans that are dependent on touch location and associated force.



SensUs 2016

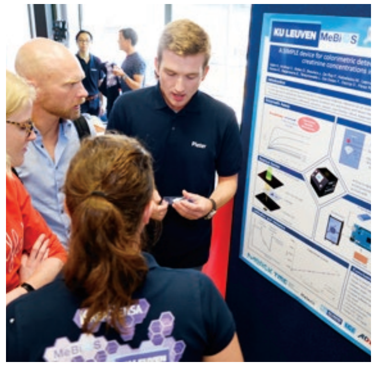
The First International Student Competition on Molecular Biosensors

On 9-10 September the first edition of SensUs – the international student competition on Molecular Biosensors for Healthcare Applications – has taken place at the Eindhoven University of Technology. SensUs was founded by prof. Menno Prins, core member of ICMS, and is organized for students, by students.

Menno Prins: "We all know the power and pleasure of international contests such as the RoboCup, the World Solar Challenge, and iGEM. Teams of students from different universities design, build and demonstrate demo's and strive for the best possible performance. Such a contest is a perfect way to stimulate students toward creative, multidisciplinary, function-oriented teamwork, and to accelerate the development of novel technologies in an international context".

"The vision of SensUs is that rapid molecular sensing devices will change healthcare in the 21st century, for the best possible monitoring, coaching, and treatment of people. Healthcare is developing toward highly personalized solutions, attuned to the needs of patients, and based on real time, precise and reliable data. Important enablers are miniaturized and easy-to-use sensing devices. This includes devices for near-patient testing (point-of-care) as well as sensors that are worn on or in the body (in-vivo sensors). For this to become reality, novel sensing principles, molecular materials, and device concepts need to be investigated and developed.

"My intention with SensUs is that it catalyses new ideas and forges cooperation. It creates a strong international community, with universities, companies, patient organizations, and healthcare professionals. SensUs will become an engine for multi-year technology development in the field of molecular health sensing: smaller, faster, more precise, more integrated, more specific, more sensitive, etc."



This year, the specific goal was to detect creatinine in blood plasma

Over a period of 9 months teams of students in 5 countries (Belgium, United Kingdom, Sweden, Denmark, Belgium, and the Netherlands) have been designing and building biosensor prototypes, and they have all demonstrated their prototypes at the contest in Eindhoven on 9-10 September. The teams consisted of up to 15 BSc and MSc students, from a variety of backgrounds such as biotechnology, chemistry, physics, mechanical and electrical engineering, software science, and medical and innovation sciences.

“This year, the specific goal was to detect creatinine in blood plasma. Creatinine is a waste product of muscle metabolism that is excreted by the kidneys. A rise of creatinine in blood is a sensitive and reliable marker for kidney failure. Millions of people suffer from or are at risk of kidney failure, and the related applications demand for the development of novel compact and cost-effective biosensor technologies”.

During the Testing Event on 9 September, the biosensor prototypes were tested with real biological samples. It was a very lively contest, with excitement as data gradually appeared on central screens. On 10 September Awards were given for Analytical Performance, Creativity, Translation Potential, and Public Inspiration.

Next year SensUs will grow from 5 to 10 universities. New countries are Switzerland, Germany, Egypt, and the United States of America. The target molecule will be B-type Natriuretic Peptide, which is an important biomarker for heart failure.

“I am very proud of the student teams and of the students with whom I organize the competition. It is amazing to see how they perform and how much they learn in a short timespan. Organizing the competition is a lot of work, but it is rewarding to see how it stimulates education, research and innovation in the field of molecular biosensing”.

For more information, please visit **www.SensUs.org**

SensUs

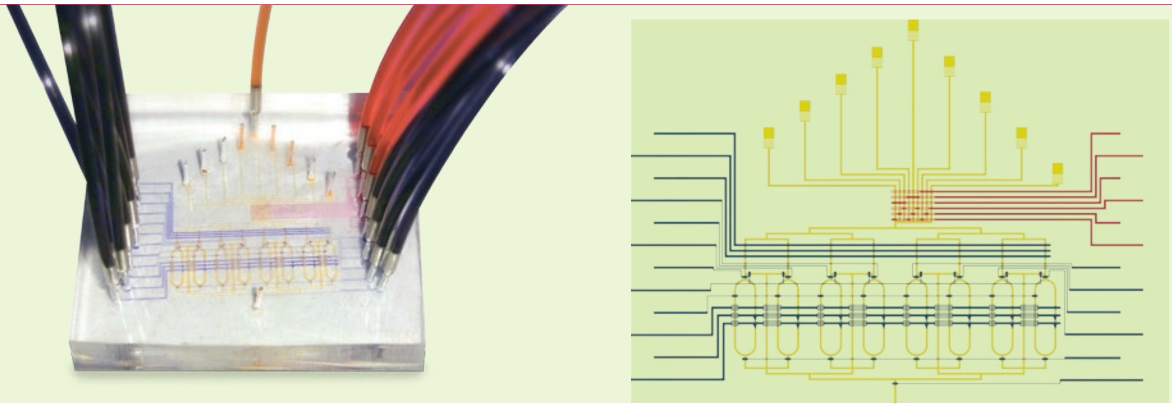


Figure 1: CAD drawing of a collection of eight, 50 nL microfluidic flow reactors. The red and blue channels represent control layers while the yellow channels are flow layers trough which fluid can flow (left). Multilayer PDMS-based chip connected to the pressure valves and input flow (right).

/ Tom de Greef

The cell as a living computer

Akin to an electronic computer, cells have evolved to process enormous amounts of information. However, while computers only rely on digital information processing and make decisions under relatively simple conditions, cells have to use a mixture of analog and digital information processing and have to cope with a noisy environment. How cells are able to handle such large amounts of biochemical information in such a challenging environment is currently poorly understood.

We are interested in exploring how biomolecular systems are 1) able to sense and process molecular information and 2) use feedback to control their regulatory behavior. Such insights would, for example, make it possible to engineer novel cells with enhanced sensing capabilities or would allow the construction of powerful in-vitro diagnostics. To answer such questions, we use a bottom-up approach in which in-vitro biomolecular networks are constructed de novo using a design-build-test cycle that has become the cornerstone of synthetic biology. In order to prototype these molecular networks under out-of-equilibrium conditions, pneumatically controlled, microfluidic flow reactors are used (Figure 1). By combining measurements with detailed mathematical models we are able to unravel how molecular networks are able to interpret and process molecular information. Currently, we are designing and testing biomolecular circuits that display bistability, are able to filter noise or are capable of performing transient logic tasks.

Given the importance of molecular networks and chemical out-of-equilibrium behavior within the FMS program, we have a number of collaborations with other groups in the area of systems chemistry and bottom-up synthetic biology. During the FMS course in Eindhoven, I will discuss how relatively small biochemical networks are able to process biochemical information. Questions that will be answered are: 1) how do molecular networks generate digital responses? 2) how do enzymatic systems amplify an input? and 3) how do biochemical pathways prevent disruptive cross-talk? I will also give an overview of several key regulatory network motifs which are able to generate out-of-equilibrium behaviors such as bistability, oscillations and adaptation. To answer these questions, I will make use of simple kinetic models that are implemented in Matlab® and available to all the participants. Understanding the basic principles behind molecular information processing will help the participants in designing and analyzing life-like molecular networks with applications in material science and biology.

Personal data

Name: Dr.ir. Tom de Greef
Current Position: Associate professor Synthetic Biology
Academic background:

- 1998-2004: Bsc and Msc (cum laude) Biomedical Engineering (TU/e),
- 2004-2009: PhD in Chemistry with prof. dr. E.W. Meijer & prof. dr. R. Sijbesma (Tu/e) working on the synthesis and characterization of hydrogen-bonded polymers,
- 2008-2010: Post-doc with prof. P.A.J. Hilbers focusing on the development of computational methods to understand 1D self-assembly.
- 2003: Visiting scholar with prof. dr. D. Weitz (Harvard) working on droplet microfluidics for library screening.

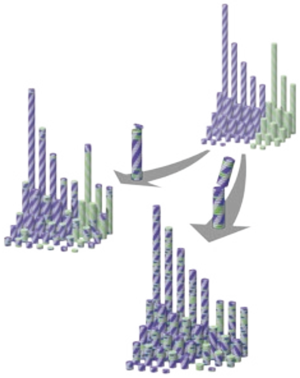


Figure 1: Atomistic MD simulation of a DNA origami, coarse grained MD simulation of dendrimer host-guest interactions, and stochastic simulation of 1D supramolecular polymerizations.

/ Bart Markvoort

Modeling molecular self-assembly and self-organization

Self-assembly and self-organization

Arrangement of molecular building blocks into ordered patterns or structures is ubiquitous in nature. These arrangements can be either spontaneous (self-assembly), i.e. driven by the tendency of systems to minimize their free energy in accordance with the second law of thermodynamics, or driven by a constant input of energy (self-organization). Deepening our understanding of these processes, which lie at the interface between molecular biology, chemistry, polymer science, materials science and engineering, will not only provide us with new opportunities to study complex and previously intractable biological phenomena, but also serve as a basis for designing new classes of materials and molecular systems at the nanoscale.

Molecular modeling

Our interest lies in deepening the understanding of molecular self-assembly and self-organization processes using theoretical models. The first technique used is based on molecular dynamics (MD) simulations, where one integrates the Newtonian equations of motion of individual atoms (atomistic) or groups of atoms (coarse grained). Functioning as a computational microscope, such simulations allow for highly detailed study of for instance the behavior of proteins, self-assembled DNA origami (Figure A), highly dynamic aggregates as lipid membranes, or the role of multivalency in dendrimer host-guest interactions (Figure B). Because many phenomena span larger time and length scales than can be reached using such simulations, we also employed mass-balance and ODE models as well as stochastic simulations at the molecular level. A nice illustration of how this allows to study equilibrium as well as kinetic distributions of molecular complexes and aggregates is provided by the study of 1D supramolecular (co-) polymerizations (Figure C).

Collaborations

The past years have shown numerous successful collaborations with other groups within the ICMS and the FMS program, where our modeling approach guided and deepened the understanding of experimental studies. We continue to be open for new collaborations. To further illustrate the importance of modeling, I will discuss kinetic models of one-dimensional supramolecular polymerizations based on ODEs as well as stochastic simulations during the FMS course in Eindhoven. Starting from the first kinetic models developed in the early 1960s that describe one-dimensional (protein) aggregation as a series of monomer additions, we will increase complexity via kinetic models describing self-assembly into a single aggregate state by homogeneous nucleation, fragmentation and recombination, or secondary nucleation. It will be shown how the presence of multiple aggregation pathways can strongly affect the self-assembly kinetics and that complex self-assembly mechanisms can only be fully understood by kinetic analysis, requiring investigation of the time-dependent behavior through a combination of experiments and models.

Personal data

Name: Dr.ir. A.J. Markvoort

Current Position: Assistant professor Molecular Modeling, within the Computational Biology group

Academic background:

- 1991-1997: Student applied physics (TU/e)
- 1997-2001: PhD-student in Computer Science (TU/e), within the Parallel Systems group.
- 2001-current: Computational Biology group within the Biomedical Engineering department
- 2013-2014: Program for Evolutionary Dynamics (Harvard University)

NEWS, AWARDS & GRANTS

PROF.DR. BERT MEIJER

awardee for the MAINZ Visiting Professorship in 2016

Prof. Bert Meijer has been awarded the MAINZ Visiting Professorship in 2016. The MAINZ Visiting Professorship will allow him to finance travel as well as prolonged research and teaching visits to the Graduate School MAINZ at Johannes Gutenberg University over the course of a two-year period (2016-2018). An award ceremony will take place on December 12th 2016 at Johannes Gutenberg University in Mainz, Germany.

PATRICIA DANKERS

in board The Young Academy

Since June 2016, Patricia Dankers PhD PhD is a member of the board of The Young Academy of the KNAW, a platform for 50 top young scientists in The Netherlands. The board supports their members with guidance in relation to their ideas and activities. Dankers is responsible for one of the Young Academy's themes, i.e. 'Content and Interdisciplinarity in Science'.

Prof.dr. Albert Schenning

Prof.dr. Nico Sommerdijk

1.75 MILLION GRANT FOR NEW MATERIALS WITH SPECIAL PROPERTIES

NWO Chemical Sciences has awarded TU/e professors Albert Schenning and Nico Sommerdijk a TOP-PUNT grant. The researchers will receive 1.75 million euros funding for their research proposal 'Bi-Hy'. Four additional PhD-students and two postdocs will be recruited to work on this research over the next five years and there will be invested in research equipment for electron microscopy.

THESES ICMS

April 2016 – September 2016

1 **Integrated evaporation driven microfluidic device for continuous sweat monitoring**
Chuan Nie

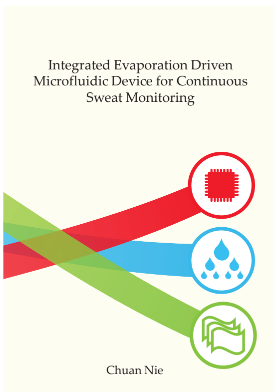
April 5, 2016
PhD advisors:
prof.dr.ir. J.M.J. den Toonder, dr.ir. A.J.H. Frijns

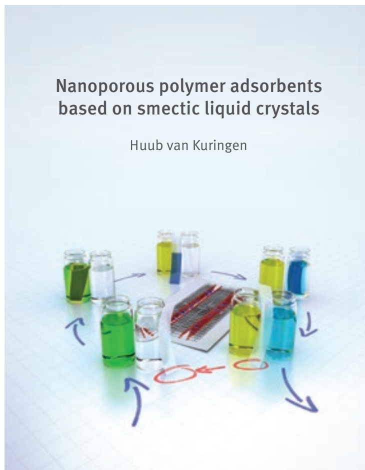
2 **Nanoporous polymer adsorbents based on smectic liquid crystals**
Huub van Kuringen

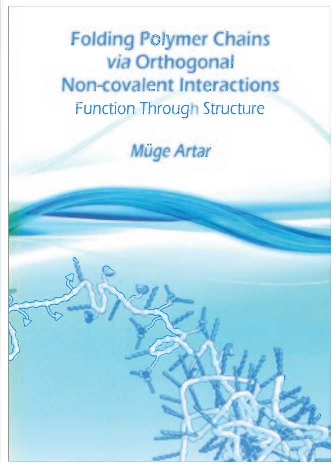
April 19, 2016
PhD advisors:
prof.dr. A.P.H.J. Schenning, prof.dr. D.J. Broer

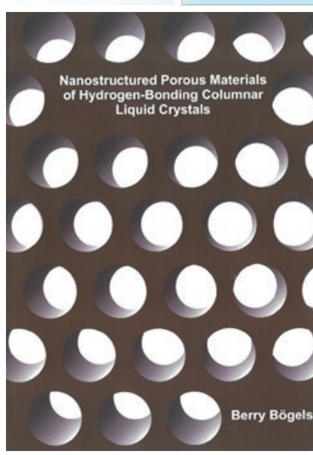
3 **Folding polymer chains via orthogonal non-covalent interactions – Function through structure**
Müge Artar

April 28, 2016
PhD advisors:
prof.dr. E.W. Meijer, dr.ir. A.R.A. Palmans









4 **Towards predicting chondroprotective capabilites of meniscus prostheses**
Juan Parraga Quiroga

May 31, 2016
PhD advisors:
prof.dr. K. Ito, dr. C.C. van Donkelaar

5 **Nanostructured porous materials of hydrogen-bonding columnar liquid crystals**
Berry Bögels

June 13, 2016
PhD advisors:
prof.dr. R.P. Sijbesma, prof.dr. D.J. Broer

6 Notochordal cells and tissue explants for intervertebral disc regeneration

Irene Akesteijn

June 28, 2016
PhD advisors:
prof.dr. K. Ito,
dr. M.A. Tryfonidou

7 Molecular modulation of nuclear receptor conformational states

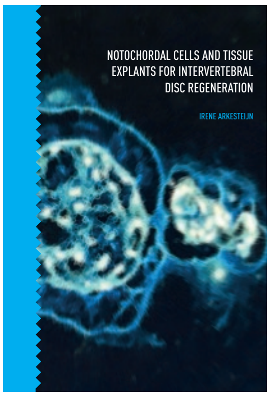
Marcel Scheepstra

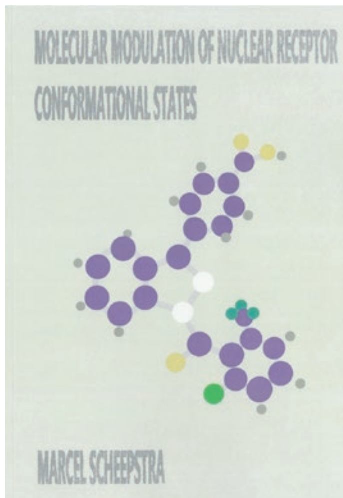
September 7, 2016
PhD advisors:
prof.dr.ir. L. Brunsveld,
dr. L.-G. Milroy

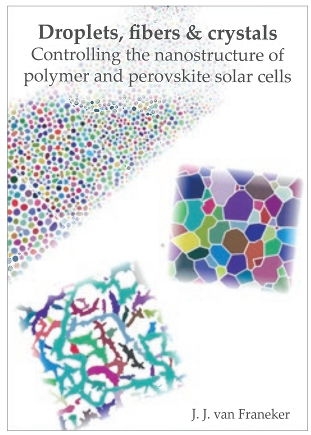
8 Droplets, fibers & crystals: controlling the nanostructure of polymer and perovskite solar cells

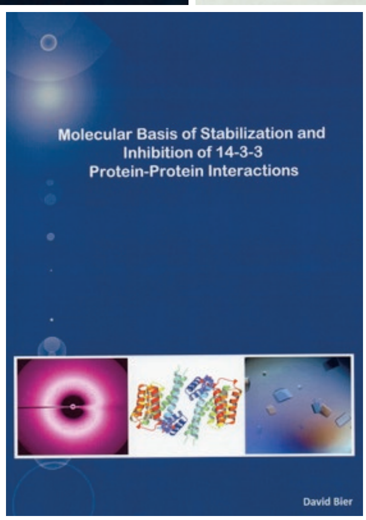
Hans van Franeker

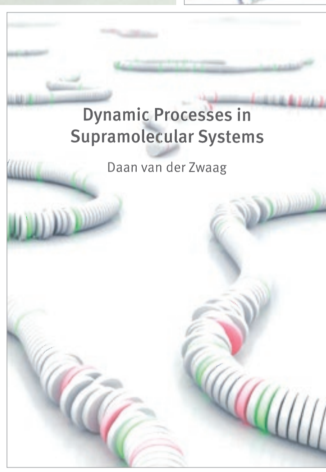
September 8, 2016
PhD advisors:
prof.dr.ir. R.A.J. Janssen,
dr.ir. M.M. Wienk











9 Molecular basis of stabilization and inhibition of 14-3-3 protein – protein interaction

David Bier

September 14, 2016
prof.dr.ir. L. Brunsveld,
dr. C. Ottmann

10 Dynamic processes in supramolecular systems

Daan van der Zwaag

September 19, 2016
PhD advisors:
prof.dr.E.W. Meijer,
dr.ir. T.F.A. de Greef

Institute for Complex Molecular Systems

New technologies by mastering complexity

Mastering complexity requires a deep understanding on how matter – both natural and artificial – self-organizes into functional molecular systems. The Institute for Complex Molecular Systems, established in 2008, brings together mathematics, physics, biology, chemistry and engineering to stimulate education and research in this emerging field of science. Interdisciplinarity is the core of ICMS; with the input from leading specialists in different branches, new avenues are explored.

Our mission is to be a leading institute for research and education in the engineering of complex molecular systems. We do this via:

- Performing top research
- Training of talented young scientists
- Being the hotspot for interdisciplinary science activities of TU/e
- Foundation and housing of the Advanced Study Center

The scientific agenda consists of three lines of research:

1. Functional molecular systems (program leader prof.dr. Bert Meijer)
2. Bio-inspired engineering (program leaders prof.dr.ir. Menno Prins and dr.dr. Patricia Dankers)
3. Complexity Hub (program leaders prof.dr. Rutger van Santen and prof.dr. Mark Peletier)

ICMS hosts the *Advanced Study Center*. This serves as an intellectual home to scientists from all over the world, hosting discussions on the theme of complexity. It is the home of *Eindhoven Multiscale Institute* (EMI) and *Eindhoven Polymer Laboratories* (EPL).

We aim at offering an ideal training environment for young students and scientists to prepare themselves for a career in science and engineering in a world of increased complexity. Therefore, master and PhD students can participate in *certificate programs*, in addition to their departmental programs. The relationship with industry is strengthened via the *Industrial Consortium* – where science meets innovation.

More information can be found via **www.tue.nl/icms**. Please contact us with specific questions or remarks via icms@tue.nl or +31 (0)40 247 5074.

ICMS IN PRESS

Editorial
ICMS Highlights is the half-yearly magazine of ICMS for ICMS members, colleagues, collaboration partners, policy makers and affiliated companies. ICMS Highlights is published twice a year.

Editorial staff
Carla Bouwman
(editorial assistant)

Design and print
ECHT marketingcommunicatie

Illustrations and cover
ICMS Animation Studio

Article contributions
Valentina Bonito, Odette Knappers, Esther Thole

Photography
Rien Meulman, Bart van Overbeeke Fotografie, Elodie Burrillon, Charlotte Grips, Hans Dirksen

Contact
Eindhoven University of Technology
Institute for Complex Molecular Systems
P.O. Box 513, 5600 MB Eindhoven
The Netherlands
Telephone: +31 (0)40 247 2482
Email: icms@tue.nl

ICMStue - 40 videos

Subscribe 494

618 7

Please visit the ICMS Animation Studio
www.youtube.com/user/icmstue