ICMS Highlights

Edition 2
March 2014

The foundations of complexity

INTERVIEW
/ Menno Prins

MICROFLUIDICS

INTERVIEW
/ Bert Meijer

& more...

Institute for Complex Molecular Systems

TU/e Technische Universiteit **Eindhoven** University of Technology

Where innovation starts

ICMS Highlights

Dear reader,

“By mixing talent and ideas we can work faster, better and with more joy”

This quote of visiting professor Takuzo Aida nicely reflects one of the main thoughts behind the ICMS. We are convinced that breakthroughs in science can only be realized when talented people work together on relevant and challenging ideas and problems. More than ever, tackling these challenges necessitates interdisciplinary collaborations, providing essential solutions for emerging societal issues.
Therefore, the ICMS is focused on bringing scientists together and facilitating the exchange of knowledge, ideas, concepts and dreams. This will promote synergy among goals and approaches. Additionally, the ICMS serves as a 'scientific home', in which inspiration and excellence are naturally fostered.
The Friday Afternoon Discussion series has been organized from the inception of the institute, and these will continue with increasing fervor, as new and exciting ideas and topics are continuously generated from the broad expertise of the members. The discussions consistently give rise to new collaborations and research directions. Ceres is also the site of many seminars and lectures from renowned visitors across the globe. You're welcome to join and find your own inspiration!
It is our great pleasure to present the second edition of ICMS Highlights.
Our hope is that this magazine will provide an outline of the areas that are important to us and help make ICMS special. An overview of recent publications and news is provided. Most importantly, however, the personal views of our members are presented to highlight what is needed for building a strong future.

We hope you enjoy reading,

Sagitta Peters
Managing director

Bert Meijer
Scientific director

Calendar

April 4, 2014, 11.30 hr
NRSCC-DIFFER
Solar Fuels Workshop
Location: Ceres 0.31

May 9, 2014, 15.00 hr
Discussion meeting with
prof.dr.ir. Menno Prins
Location: Ceres 1.26

May 23, 2014, 15.00 hr
Discussion meeting with
prof.dr. Rutger van Santen
Location: Ceres 1.26

June 6, 2014, 15.00 hr
Discussion meeting with
dr. Patricia Dankers
Location: Ceres 1.26

October 9 & 10, 2014
NextGenChem@NL 2014
Location: Ceres

October 16, 2014, 17.00 hr
Nobel Prize meeting
Location: Zwarte Doos

January 22 & 23, 2015
ICMS Outreach Symposium
Location: Zwarte Doos

The complete calendar can be found on our website.

Content

Edition 2
March 2014

/ Menno Prins

Biology becomes DIGITAL

"Biology becomes digital," says prof.dr.ir. Menno Prins, part-time professor at TU/e and Research Fellow at Philips. It is a statement derived from his work in the field of biosensing. His aim is to create technologies to measure the presence and behaviour of molecules within complex biological environments. Methods and instruments are being developed that will enable 'on-the-spot decision making' in medical diagnostics. The new devices will have to be fast, affordable, reliable and easy to use, by professional caregivers and later also by patients themselves. Prins: "This requires the development of novel principles and novel architectures, focused on integration rather than separation".

In health care we see a clear tendency towards decentralisation. This development has arisen because care in hospitals is extremely expensive. Prins: “Every bit of care that doesn’t require the high education level of medical specialists should no longer take place in the hospital.” Technology is an important enabler in this field. A large part of the input for diagnoses is gathered by *in vitro* analysis of blood, cell or tissue samples. The analysis of such samples is mostly carried out by specialised laboratories using advanced robotic equipment.

With the trend of decentralisation, an era is arriving where testing should become widely available, providing caregivers with relevant information for making on-the-spot decisions in a single patient interaction. Prins: “A good example is the monitoring of patients taking anti-coagulants. The first tests could only be done in a hospital with a well-equipped lab. For a number of years, there are devices available for use outside hospitals and even at home. These devices improve the lives of patients and cut costs on the side of professional care.”

The biosensor roadmap

However, developing *in vitro* diagnostic equipment for use further down the chain involves exploring new principles and developing new architectures. Traditional testing in centralized labs is based on series of separate fluid handling steps suited for automation by robotic equipment. Different concepts are needed for small, fast, reliable and affordable handheld devices.

Prins: “We work on measurement methods to detect the presence of molecules within complex environments, such as blood. The challenge is to detect few specific molecules in an environment with many other molecules that are present at high concentrations. To be able to crack this problem we use micro- or nanoparticles that can bind the targeted molecules thus making them visible for our optical sensing systems. We use biofunctionalized magnetic particles that can be actuated by magnetic fields, and we also study plasmonic particles that exhibit optical resonances. We cannot directly see the targeted molecules, but we can detect and monitor the particles and thereby detect and study the targeted molecules.”

A concrete application based on magnetic nanoparticles is Minicare, a handheld testing platform for near-patient testing, e.g. to determine whether a patient is suffering from acute myocardial infarction, which

"It is IMPORTANT to have a theme in mind, a *CROSS-SECTIONAL FOCUS* that makes sure that different learnings can *enhance* each other."

is currently being developed at Philips. Prins: "A point-of-care device like this can help a physician to come to a proper diagnosis in minutes instead of one hour. That can be life-saving."

Unravel the human body

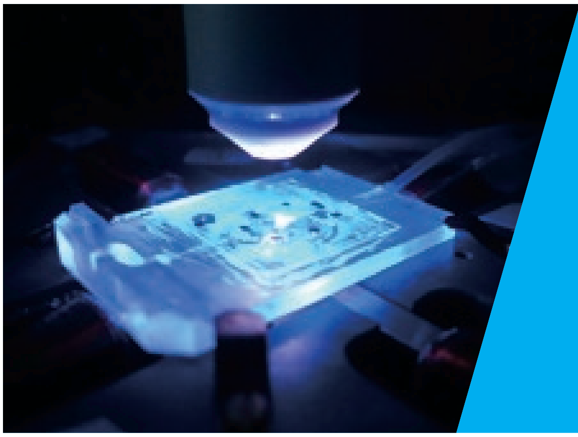
Prins: "In the bigger picture, our research is part of the quest to quantify biological processes, unravel biological principles, and understand how the human body works. In our research work at TU/e, we aim for concepts that have single molecule resolution. Biology is digital: it consists of digital units: molecules. Therefore, biological analysis methods are also becoming digital, based on counting and following single molecules, in real time, directly within complex biological environments.

We divide the research problem into smaller pieces in order to make it manageable. You cannot ask a student to try to investigate three new aspects at the same time. You make sure just one of the aspects is brand new and that the rest is available from experts in the environment.

For example, one can investigate new measurement methodologies using existing biomaterials, or new biomaterials with existing measurement methods. Such research can flourish when students have access to high-level scientific knowledge from multiple disciplines, in an atmosphere of open communication. That is the power of the ICMS."

It is all about function

Prins: "I like to combine science with engineering. I think science is great, trying to really understand the principles behind phenomena.



BIOLOGY IS DIGITAL: IT CONSISTS OF DIGITAL UNITS: MOLECULES.

But for me it becomes even more interesting if what you discover can help to make something with a function. Something that can propagate into society, something that other people can use. Deep down I am more like an applied scientist. This resonates well with my work at TU/e and Philips. Both environments are working toward functionality. And the fun part is, as soon as you start talking about function, you invariably have to involve different scientific disciplines. This multidisciplinary approach to science is very challenging and very motivating. Every week I learn new things. Since I started in physics and worked through chemistry toward biology, I have experienced that diving into new disciplines is very rewarding. It is important to have a theme in mind, a cross-sectional focus that makes sure that different learnings can enhance each other, and that brings people together from different backgrounds. Crossing disciplines is difficult and it is critically looked at from the traditional scientific angles. However in industrial environments it is encouraged enormously.

I think that with a solid scientific background one should not be afraid to advance into new directions. Keep on learning, develop a vision, collaborate around this vision, and the chance that you will discover and leverage new things and really contribute to society is much larger."

NEWS, AWARDS & GRANTS

2.5 M Euros for

FAST ELECTRON MICROSCOPY

The Foundation for Fundamental Research on Matter (FOM) has granted the Industrial Partnership Program 'The Foundations for Faster Electron Microscopy'. The Eindhoven research group Coherence & Quantum Technology of prof.dr.ir. O.J. (Jom) Luiten will carry out this project together with FEI Company and the group of Pieter Kruit of TU Delft. The total size of the program is 2.5 M Euros, paid by FOM and FEI together.

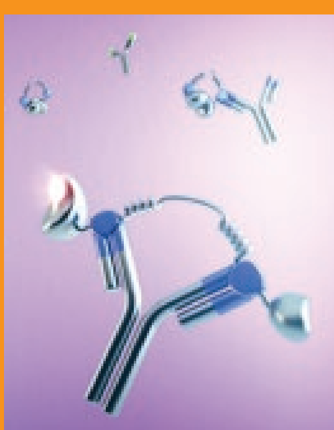
Cum Laude PhD defense

PETER KOREVAAR

Dr.ir. Peter Korevaar successfully defended his PhD thesis on January 24, 2014. Because of his excellent scientific work he obtained the degree cum laude. His thesis describes pathway complexity in pi-conjugated materials.

MAARTEN MERKX

receives ERC Proof of Concept



Dr. Maarten Merkx received an ERC Proof of Concept grant for a new way of antibody diagnostics. The grant of 150,000 Euros is meant to help this new strategy, developed by Merkx, towards commercial application.

With antibody diagnostics you can find for example infectious diseases, auto immune diseases or allergies by proving the presence of antibodies in the blood. Current technologies however need much time and complex equipment. The new technology that Merkx developed can take over several steps, like immobilizing the virus, getting in contact with the blood, washing, binding of antibodies and detecting the signal, with just one protein. This makes the test simple and cheap. Besides, the test can be more convenient to use. At this moment the enzyme is made that can prove the presence of antibodies with a simple color change. The enzyme is tested on antibodies that are present with HIV, part of the flu virus and dengue.

STUDENT TEAM
in iGEM finals

The MRiGEM project of the Eindhoven student team made it via the European pre-finals to the world championships at MIT in Boston in November 2013. iGEM is an international competition for synthetic biology in which student teams create biological building blocks and inject those into living cells.

The Eindhoven team, under supervision of dr.ir. Tom de Greef and dr. Maarten Merkx (both of the Department of Biomedical Engineering and the Institute for Complex Molecular Systems), developed bacteria that can be used to visualize tumors in an MRI scanner. The students injected a piece of DNA they developed themselves into an E. coli bacterium. As a result, in a hypoxic environment – which often occurs around tumors – the micro-organism produces a protein that's contrasting on MRI images.

From left to right: Zandra Felix, Stijn Aper, Ardjan van der Linden, Pascal Pieters, Sander de la Rambelje, Nick van der Zon, Jacques Ernes and Yicong Chen

2014 Jan Rajchman Prize for

DICK BROER

Prof.dr. Dick Broer has been awarded the 2014 Jan Rajchman Prize of the Society for Information Display (SID). Dick Broer receives this recognition for his pioneering discovery and development of UV-polymerizable liquid-crystalline polymers and his outstanding contributions to their applications in flat panel displays. The award will be presented in a ceremony to be held on June 2, 2014 in San Diego, CA.

European awards for

BERT MEIJER

Prof.dr. Bert Meijer has received two prestigious European awards. With an inaugural lecture in Brussels, he has received the 2013-2014 international Solvay chair for chemistry. The Solvay Institutes were established in 1912 by Ernest Solvay and are renowned for the stimulus of the sciences. Bert Meijer will visit Belgium for several weeks during the year 2013-2014 to deliver lectures and present the work of his group.

The ETH Zürich has awarded Bert Meijer the 2014 Prelog Medal. With this medal, named after Nobel laureate Vladimir Prelog, the work of chemists with extraordinary achievements is honored. In November 2014 Bert Meijer will receive the medal in Zürich.

Outreach Symposium 2014

The third ICMS Outreach Symposium was held on January 23 - 24, 2014. This symposium highlights the ongoing research conducted across multiple disciplines within ICMS. Additionally, several international visiting scientists presented their findings to the TU/e community.

Willem de Vos (Wageningen University)

Visited by more than

150

scientists from
ICMS, Dutch academia
and industry

The symposium was visited by more than one hundred and fifty scientists from ICMS, Dutch academia and industry. With that, the trend of growing interest has continued. Bio-inspired engineering was the theme of the first day. With lectures from among others Nico Sommerdijk, Carl Figdor (Radboud University Nijmegen), Willem de Vos (Wageningen University), Lorenzo Albertazzi, and Sandra Hofmann Boss, the different aspects of the theme were highlighted. A still of the animation about antifreeze proteins as shown by Ilja Voets is disclosed on the cover of this magazine.

Our friends from industry, Carel Fitié (DSM) and Jacques Tacx (SABIC), disclosed their challenges in two inspiring lectures. This also gave ICMS' master and PhD students and postdocs the opportunity to learn about these companies and meet their researchers. Together with speakers as Frank Würthner (Universität Würzburg), Dick Broer, Daan Frenkel (Cambridge University), Albert van den Berg (University of Twente) and Remco van de Hofstad the second line of the ICMS scientific agenda, functional molecular systems, was covered.

The combination of lectures, a poster presentation and moments for informal discussion enabled the exchange of knowledge and ideas. Several discussions already got a follow-up and the new research plans are very promising.
The next Outreach Symposium is January 22 and 23, 2015. We are looking forward to your attendance.

NEXT OUTREACH SYMPOSIUM

JANUARY 22 & 23
2015

Industrial consortium

With the establishment of an industrial consortium ICMS reaches out. Mutual benefits are being sought by combining industrial research and development with more fundamental sciences. While the industrial members stay up to date with the most recent developments, ICMS scientists get inspiration for their research. As part of the membership company coworkers can visit lectures and workshops, use the Advanced Study Center, participate in courses and access ICMS' state of the art infrastructure. To further promote knowledge exchange, ICMS organizes the yearly Outreach Symposium.

Interested to join the consortium? Please contact us.

/ Bert Meijer

We have to face multi-step non-covalent synthesis

> “CAN WE MAKE ARTIFICIAL LIFE?

This question is probably among the most intriguing scientific questions. Being able to create life in a laboratory may provide adequate solutions to food, environment, energy and health issues that future generations will have to face. It may take over a century of scientific exploration before humans are able to recreate a simple form of life. Nonetheless, the ICMS takes on the challenge of leading part of its research. The group of Bert Meijer, scientific director of ICMS, is convinced that important answers are to be found in an enormously challenging and unorthodox route: multi-step non-covalent synthesis of functional molecular systems.

Today it is possible to make nearly every imaginable molecule in a laboratory. That in itself is a major achievement. However, we are still far from turning these molecules into a system that resembles a living organism. If we look at a single cell – as a fundamental building block of life – we are not able to reproduce it artificially. We simply lack knowledge and understanding of how to assemble these complex structures, let alone being able to build a system with billions of different molecules in continuous interaction. We are able to reveal the necessary molecules and their ratios, but if we put them together in a flask and shake it, you can be pretty sure that the chance of them turning into a living structure is negligible. This leads to the conclusion that the route of self-assembly or self-organization is unsatisfactory.

Interactive bonds

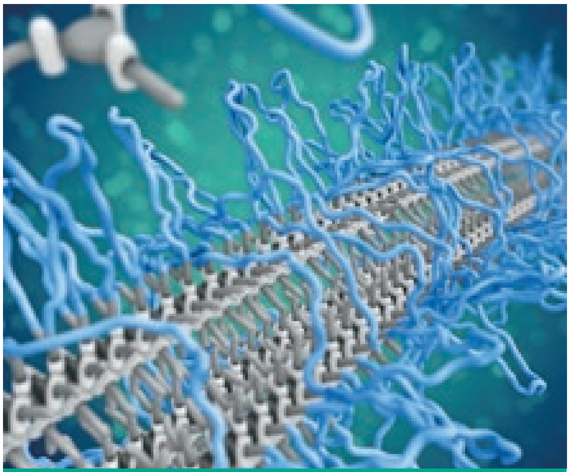
To delve deeper into this problem, we have to distinguish covalent and non-covalent bonding of molecules. Our knowledge of covalent bonding goes back a long way. The field uses the links in which the atoms of molecules share their electrons, thus establishing a firm covalent bond. From trial-and-error experiments some 150 years ago, covalent bonding has evolved into multi-step (and often complex) organic synthesis by using specific reagents, catalysts, procedures, protocols, et cetera. Nowadays covalent bond formation is done on targets (i.e. modify DNA) and the methodology and physics behind it are carefully studied and mapped. Non-covalent bonding is all about interactions *between* molecules. Interactions can be found at the intramolecular as well as the intermolecular level, and the huge differences in length scale and time scale (i.e. dynamics) of the systems made out of the various molecules are adding even more to the complexity.

Taking control

It is not surprising that contemporary chemistry is focussing largely on the self-assembly of molecules to create systems and structures. It is the easiest route. But is it the only route? And does this route deliver results when more advanced molecular systems are required? In October 2013, Professor and international chair of ICMS, Takuzo Aida, gave an inspiring lecture at ICMS on his nanotube Chaperonin (see in this issue of ICMS Highlights) which performs an open-close motion when encountering the high energy concentrate ATP (found in cancer cells). Aida is actually making a first step in increasing complexity and taking control over a molecular system. This and other experiments lead to the conviction that in order to develop more advanced systems, we have to manage the interactions at the next level. With Nature as a source of inspiration and using the retrosynthetic approaches from covalent synthesis, Meijer's group is now exploring the concept of multi-step non-covalent synthesis.

Start

But where do we start? The most promising strategy towards multi-step non-covalent synthesis seems retrosynthesis. Like car manufacturers do when optimising an engine. They take a complete engine apart, and analyse and improve every



ASSEMBLY OF DYNAMIC SUPRAMOLECULAR STACKS

part. The trick in non-covalent synthesis is to identify the chronological path by which a certain molecular system is built and can be rebuilt. This requires profound knowledge of the interactions and we can learn from the approach in covalent synthesis: target, methodology and physics. Meijer's research group is making fast progress in this new line of molecular engineering: adaptive systems, new supramolecular materials, supramolecular buffering, dilution-induced self-assembly, non-linear recruitment of guests, autoregulation in catalysis, folding of novel single-chain polymer nano-particles, and detailed studies of the mechanism behind non-covalent synthetic steps are just a few of the topics under investigation. During the long and winding road to artificial life, the research group will master molecular complexity with major impacts in areas like material science and bio-inspired engineering.

Micro fluidics

In microfluidic devices, precise control over liquid micro-environments is possible. This enables micro-scale analysis, lab-on-a-chip systems, and research tools for chemistry, tissue engineering and biological and biomedical research. In the Microfab Lab, microfabrication technology is developed and applied to create these microfluidics applications.

FACTS

In microfluidics, the Reynolds number

$$Re = \frac{UL}{\nu}$$

is smaller than one, so that the flow is always laminar

Typical sizes of microfluidic channels are

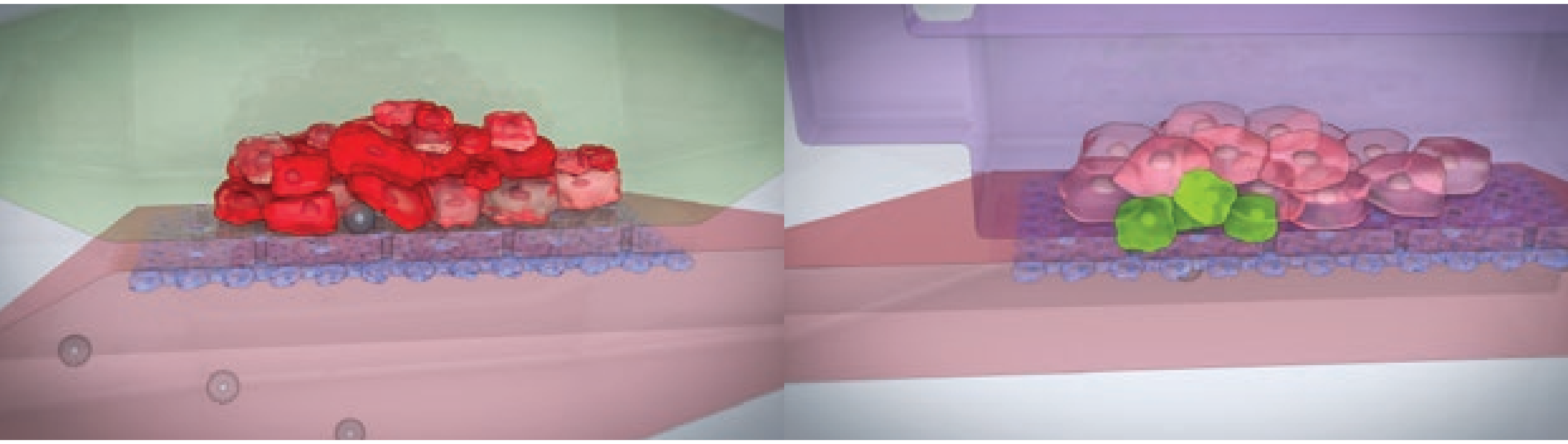
1 to 100 µm

Most microfluidic devices for research are made of

Polydimethylsiloxane (PDMS)

What is microfluidics?

Microfluidics is the science and technology of manipulating, processing and analyzing small volumes of fluids, using channels with dimensions of tens to hundreds of micrometers. The development of the field started in the beginning of the 1990's, with early applications in chemical analysis. It enabled the introduction of micro-scale analytical methods – gas-phase and liquid chromatography, capillary electrophoresis – which, in microfluidic format, revolutionized chemical analysis. In the past decade, the number of applications in which microfluidics plays a role has been growing: usually negligible at macroscopic scales become prominent: electrical effects, magnetic effects, optical effects, temperature, surface tension, and so forth, all may play an important role, and may all be used to control microfluidic flow.



in medical diagnostics for example, where microfluidics enables miniaturization and integration of diagnostics processes ultimately resulting in the 'lab-on-a-chip'; another example is its use as a research tool to study biological systems and processes, and develop understanding about health and disease. The size of microfluidic channels is perfectly compatible with cells and tissues, and therefore single cell analysis studies, as well as research into the behavior of biological tissues and organs at a small scale ('organs-on-a-chip') are made possible by microfluidics.

Control of micro-environment

An important characteristic of microfluidic flow is that it is always laminar. This offers the possibility of precise control over the micro-environment within microfluidic devices: for example fluid flow, concentrations of molecules in space and time, temperature, geometrical features and mechanical cues like stress and strain can be accurately controlled. Moreover microfluidic devices are compatible with microscopy so that processes can be observed in real time. Also, interestingly, at the small scales of microfluidics, physical phenomena that are

Microfluidic technology and ICMS

Microfluidic devices typically are cm-sized chips containing networks of channels and chambers with dimensions of 1 to 100 micrometers. Active elements like electrostatic, magnetic, and pneumatic micro-actuators can be integrated to achieve fluid pumps, mixers, valves, or mechanical actuators. The initial technologies used for the fabrication of microfluidic devices originated from silicon microelectronics and microelectromechanical systems (MEMS). However now, especially in exploratory research, polymers such as PDMS (polydimethylsiloxane) and thermoplastic polymers like polycarbonate are primarily being used, together with associated fabrication processes like soft lithography, (injection) molding, printing and laser machining. Within ICMS, these technologies are available in the Microfab Lab of the Department of Mechanical Engineering for rapid, flexible, out-of-cleanroom manufacture of microfluidic devices. Spin coaters, UV illumination sources, a sputter coater, several surface treatment systems (ozone plasma, UV ozone, corona treater), etching facilities, a laser cutter, an excimer laser, femtosecond lasers, micromechanical tools, a 3D printer, a Dimatix printer are all available. In this lab new fabrication approaches, materials, and components for microfluidics are being continually studied and developed, and made accessible for all ICMS researchers. A complete renovation, extension, and improvement of the Microfab Lab are planned for 2014, to realize a state-of-the-art microfabrication facility.

/ Prof.dr. Takuzo Aida

The surprising and promising field of biomachines

“IN ORDER TO RELEASE THE DRUG IN THE RIGHT PLACE WE UTILISE AN EXISTING BIOLOGICAL PROCESS

Prof.dr. Takuzo Aida (Riken Advanced Science Institute and University of Tokyo) has been awarded the first international ICMS Chair in Chemistry for his major achievements in the field of supramolecular chemistry. Over the past years, he and his team have developed an interesting and relevant 'molecular toolbox' containing components such as graphite nanotubes, stretchable electronic circuits, advanced hydrogels and biomachines. His current work and granted chair was motive to visit the ICMS last October.

Motions

Aida: "In our body we have many biological processes that use - what I call - biomachines. These are little systems of molecules that are programmed to undergo certain actions when triggered. For example, motions like open-close, stretch-shrink, move from one side to the other. These biomachines can detect a signal (often a concentration of certain proteins or enzymes in the body) and perform their action. We decided to utilise this interesting principle."

Really targeted drug delivery

As laid out in his 'Aan de Dommel' lecture called Stimuli Responsive Soft Matter with Noncovalent Interactions, Aida's team has been working on a biodevice that could evolve in an effective cancer treatment. Aida: "We are currently using a biomachine that performs an open-close motion for which we developed a nanotube of the protein Chaperonin as a carrier. What happens is this. We encapsulate a drug inside the protein. Normally if you get a drug injected, your body will immediately send in a load of enzymes to break down the 'intruder'. However, by placing the drug inside a carrier it is invisible for the body. In order to release the drug in the right place we utilise an existing biological process. When Chaperonin circles through your vessels, nothing happens. However if it detects ATP – a high-energy compound which can be found in high concentrations in cancer cells – it opens and releases the drug."

Current research on targeted drug delivery for cancer cells has primarily focused on differences in PH-values of the tissue or cells. But the differences are very small and thus hard to detect. Aida's research shows a promising alternative and may result in a very effective and highly accurate way of targeted drug delivery.

Scientific climate

The research Aida conducted shows that what used to be two different scientific disciplines, biology and chemistry, are now rapidly evolving into one new field. Biochemistry is a broad and complex area with a lot of terra incognita. However, it is also a field with the potential to produce effective health and energy applications in the future.

Aida: "The complexity is ever-increasing and this adds to the required knowledge and skills of students. Biochemistry students cannot lean back and just sponge off information, they really have to develop themselves. We need great ideas on what direction to turn to. But great ideas and their emergence cannot be planned and forced. It is unpredictable, but nonetheless fun! We must merely open our eyes to the enormous possibilities. It is hard to say where we will stand in 10 years."

Stimulate

"To be able to progress, we need to build a climate for our students in which they experience freedom of thinking. In which serendipity can thrive and be a part of the process. And that's what I think makes ICMS and Riken such great institutes. By working freely from multidisciplinary approaches, we give great power to idea generation. It is fun and promising to combine even more knowledge, know-how and visions into new concepts and eventually applications. This is also how I see my role as international ICMS Chair: to stimulate interaction between our groups. By mixing talent and ideas we can work faster, better and with more joy. And the applications we produce, such as biomachines, will hopefully inspire other scientists to develop new things."

NEWS, AWARDS & GRANTS

Marie Curie Integration grant for

CECILIA SAHLGREN

Dr. Cecilia Sahlgren received a Marie Curie Integration grant for the project StressFate. The proposed research combines molecular stem cell biology and biomaterial engineering. The specific focus is to understand the crosstalk between the mechanical properties of the microenvironment and signaling mechanisms regulating cell fate in cardiac progenitor cells (CPCs). The ultimate goal is to generate scaffolds for cardiac regeneration by combining the necessary biological and mechanical cues.

Valorisation Grant for

INTERVERTEBRAL DISC PROSTHESIS

Prof.dr. Keita Ito received a Valorisation Grant of STW. The Valorisation Grant helps academic entrepreneurs with their startup companies to make the step from idea to product.

The grant knows two types of awardings; Phase-1 and Phase-2. Phase-1 is for a feasibility study while Phase-2 is for the valorization phase, in which the first steps are taken on the valorization trajectory. Ito received a Phase-1 awarding in the amount of 25,000 Euros for an intervertebral disk prosthesis.

LUC BRUNSVELD

wins Liebig Lectureship

Prof.dr.ir. Luc Brunsveld became Liebig Lecturer 2013. For this, he made a scientific journey through Germany in the autumn of 2013. He visited six universities in cities like Berlin, Jenna and Frankfurt, where he delivered his lecture with the theme ‘(Supra)molecular modulation of protein-protein interaction’.

CHRISTIAN OTTMANN

receives Young Chemical Biologist award

Dr. Christian Ottmann received the Young Chemical Biologist award of the International Chemical Biology Society. Ottmann receives this award for his contribution to small molecule modulations of protein-protein interactions. During a three-day conference held in October 2013 in Kyoto, Ottmann received the award during the special session 'Global Rising Stars of Chemical Biology'.

DIFFER

@ Ceres

Since January 2014 the DIFFER@TU/e group has its home in Ceres. Both office and lab activities will be started. Because of the moving of the DIFFER institute from Nieuwegein to Eindhoven and the ongoing realization of their building at the TU/e campus, a temporary home was sought for these new activities. Their presence in Ceres will be the start of a long-term collaboration between ICMS and DIFFER.

University professors deliver

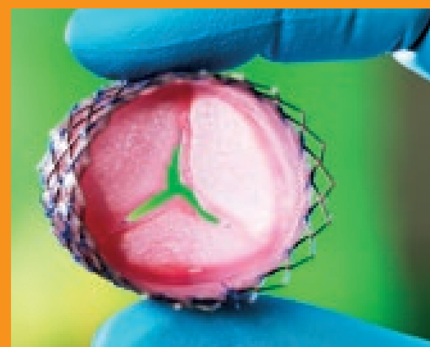
'AAN DE DOMMEL' LECTURES

In March 2013 the Executive Board of TU/e appointed four new university professors. Prof.dr.ir. Maarten Steinbuch, prof.dr.ir. Wil van der Aalst, prof.dr.ir. Anthonie Meijers and prof.dr.ir. René Janssen are regarded as ambassadors of the university and follow in the footsteps of prof.dr. Bert Meijer, who was appointed university professor as early as in 2004.

To allow the university staff and students to get acquainted with the university professors' scientific work, ICMS organized a special series 'Aan de Dommel' lectures. Wil van der Aalst kicked off in September in the Zwarte Doos. His lecture entitled 'Mine your own business – Using process mining to turn big data into process models' discussed how process mining can help to chart the way in which people use a system, where the bottlenecks are and how organizations can structure their process better. In early October René Janssen talked about organic solar cells and explained how new organic semiconductors with extensive optical absorption can lead to better results. In November it was Maarten Steinbuch's turn. In his lecture entitled 'Caring Cars and Curing Robots' he shed light on the developments in the area of 'high tech motion systems'. Anthonie Meijers concluded the series in January with a lecture about changing behavior through technology. His specialization is in the area of the philosophy and ethics of technology.

CVON Grant for

ONE VALVE FOR LIFE (1VALVE)



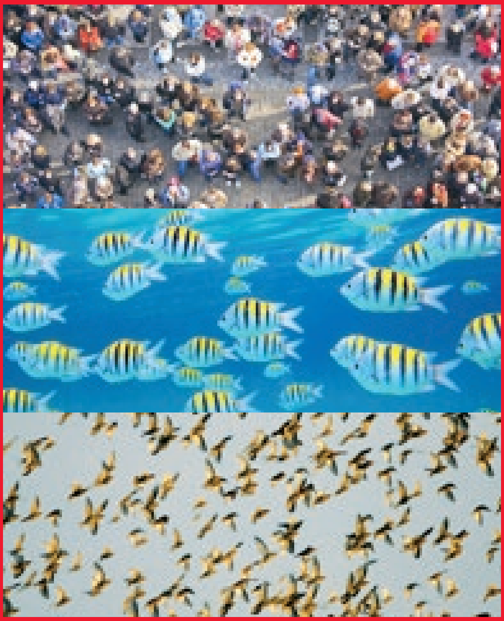
CVON, a Dutch public-private initiative for cardiovascular research, has granted the One Valve for life (1Valve) project. Researchers from TU/e, UMCU, Erasmus MC and University Hospital Zurich will collaborate with prof.dr.ir. Frank Baaijens as research leader.

Recently, in-situ tissue engineering using endogenous cells recruited from the bloodstream or using on-the-fly harvestable cells has emerged as a promising alternative to create living heart valves having the potential to grow, repair and last a life-time: one valve for life. Compared to classical tissue engineered heart valves, this new exciting technology has off-the-shelf availability at substantially reduced cost. This program aims to deepen the mechanistic understanding of the in-situ tissue engineering of heart valves, and to translate this exciting technology to clinical application. The research started early 2014.

/ Mark Peletier / Rutger van Santen

The foundations of complexity

Much research within ICMS focuses on complex chemistry. The study of functional molecular systems and bio-inspired engineering are the cornerstones of the institute. But scientists need to reach out to really understand complexity. That's why the 'Complexity Hub' was started.



Many scientists study an aspect of complexity. By studying cross-connections between different subject, common grounds of complexity science may be identified.

Complexity science is much broader than complex chemistry. One scientist who knows is the chemist Rutger van Santen. He now runs a research program 'crossing borders' sponsored by the Royal Netherlands Academy of Arts and Sciences (KNAW). "When studying the complex interactions between particles, don't think only about systems of atoms and molecules, consider anything that connects and interacts. And that includes animals, mobile phones and humans." Exploring these cross-connections will be a new pillar for research at ICMS, Van Santen explained. That's why he took the initiative to start a working group on the fundamentals of complexity, together with Mark Peletier, professor of mathematics. Both are board member of ICMS. Peletier observed that there are many scientists in Eindhoven who study an aspect of complexity. Complexity science is a strongly developing area and it can be applied to a wide range of fields. "But these are scattered initiatives, without much contact between the different groups. We think that we can learn from each other. By studying the cross-connections, we can identify the common grounds of complexity science." That's why the two coined their initiative 'Complexity Hub'.

Peletier, who is also on the board of the Eindhoven Multiscale Institute, mentions the study of dissipation in computer science. "It is now widely accepted that precision and speed of calculations comes at a cost of energy. And we begin to understand how we can calculate the minimal required energy." ICMS now explores these concepts in a biological context. The biological information processing in DNA likewise requires a theoretical minimum amount of energy. Also, it may be the key to understanding why our brains require so much energy. "Exploring these cross-connections lays a structure bare, which may help us get grip on its complexity", according to Peletier.

Van Santen thinks of the study of crowd management. Scientists at Eindhoven use computer simulations to mimic how people interact in dense crowds. This gives important clues as to how best to evacuate people in emergencies, for example. There are striking parallels with swarming birds or schools of fish. More importantly, these swarming phenomena appear to match chemical experiments with colloidal charged particles in an electric field. Van Santen explained: "One can probably use the same mathematics. Many swarming models do not use any assumptions of energy or momentum conservation, as we commonly do in hydrodynamic models. However, the phenomena appear to be related through complexity models that are similar. By seeing how we can capture such diverse phenomena in similar models, we can hope to uncover a more general understanding of complex systems. It may also give us insight in essential differences – if any – between complex behavior of physical, biological and social systems, a most important question."

Technologies we are good at

The 'Complexity Hub' brings together scientists who study non-linear systems, which have feedback and particular network structures. These systems may behave in turbulent, self-organizing, and self-assembling ways. "The research at the Santa Fe Institute is a great source of inspiration", Van Santen added, "but as we are embedded in a technology university, we will stay closer to our origin. Economics and biology are central to Santa Fe. These areas are important for the challenges of our time, but we will start with biochemistry and chemical engineering, robotics, related engineering and network models of the brain and possibly logistics – the technologies we are good at." Peletier adds that "it is like a network organization, we hope it will be crowded. We don't have a fixed roadmap, as we hope that others will adopt this idea as enthusiastically as we are. That will also determine our direction."

"It's a challenge to bring these different fields together," Van Santen admits. "You need to learn to understand each other's language. You need to understand the kinds of problems that others are working on. But bridging different disciplines helps to establish the type of interdisciplinary research in which technological and social issues are central."

The first event organized by the 'Complexity Hub' will be a summer school for PhD students. Around eight top scientists from Eindhoven will teach complexity science as integrated courses. Since the teachers need to present their courses in a coherent body, the two originators hope that a lasting cooperation between them will be forged. "The emphasis will be on the methodology, as this will reveal the common ground between the disciplines", Van Santen states. "The courses will show the new contours of complexity paradigms with interesting new methodological developments."

MARK PELETIER AND RUTGER VAN SANTEN ARE LOOKING FOR SYNERGY AND MUTUAL INSPIRATION BETWEEN RESEARCH GROUPS

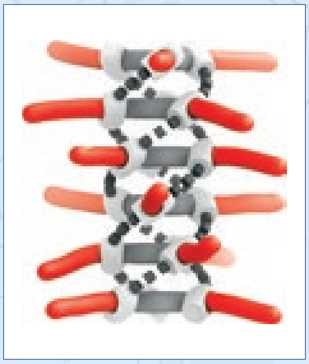
"Eventually, we will touch some very fundamental questions", Van Santen added. "Can we really bring methods from different fields together in a common framework, or are there basic differences? Is the physics of life different from the physics of non-life? Can we really model a pedestrian and an ion with the same mathematical toolkit? We think we can, but we are not sure. This is a basic question, which also drove people like Pasteur."

"We don't have a ***fixed roadmap***, as we hope that others will adopt this idea as **ENTHUSIASTICALLY** as we are."

ICMS TOP PUBLICATIONS

September 2013 – February 2014

1.



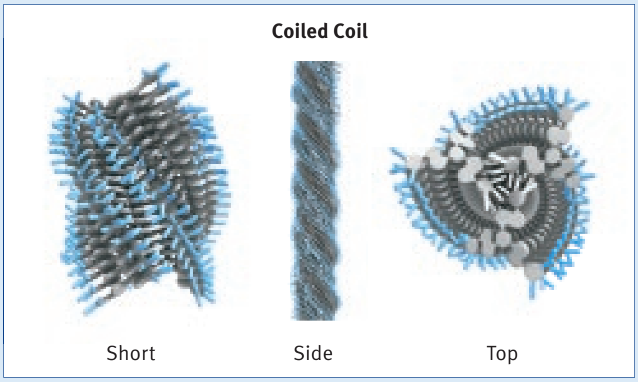
Y. Nakano, A.J. Markvoort, S. Cantekin, I.A.W. Filot, H.M.M. ten Eikelder, E.W. Meijer and A.R.A. Palmans
Conformational analysis of chiral supramolecular aggregates: modeling the subtle difference between hydrogen and deuterium
J. Am. Chem. Soc. 135, 16497-16506 (2013)

2. *P.A. Korevaar, C. Grenier, A.J. Markvoort, A.P.H.J. Schenning, T.F.A. de Greef and E.W. Meijer*
Model-driven optimization of multicomponent self-assembly processes
Proc. Nat. Ac. Sci. U.S.A. 110, 17205-17210 (2013)

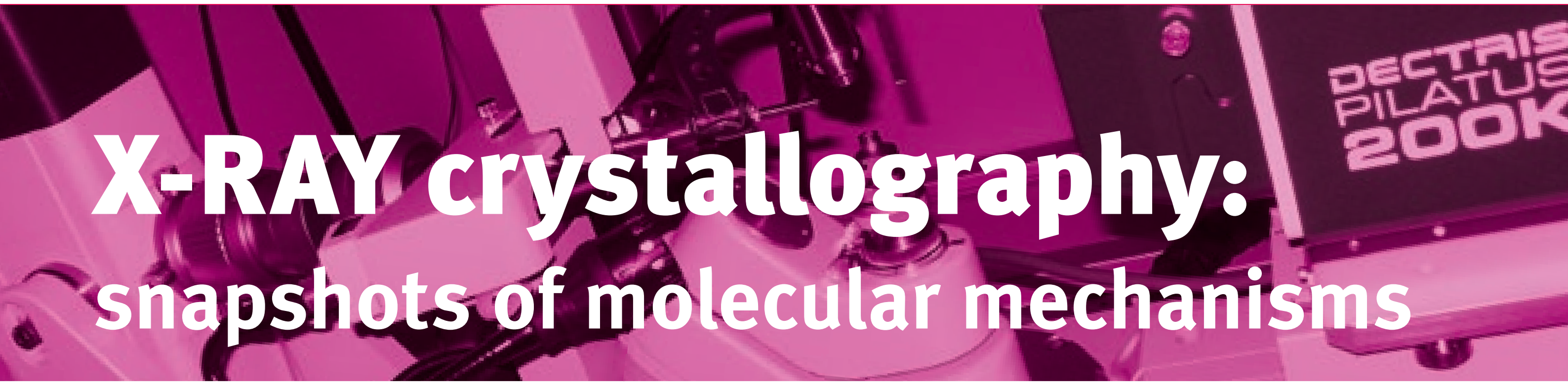
3. *M. Dennison, M. Sheinman, C. Storm and F.C. MacKintosh*
Fluctuation-stabilized marginal networks and anomalous entropic elasticity
Phys. Rev. Lett. 111 (2013)

4. *Z. Guo, I. de Cat, B. van Averbeke, E. Ghijsens, J. Lin, H. Xu, G. Wang, F.J.M. Hoeben, Z. Tomovic, R. Lazzaroni, D. Beljonne, E.W. Meijer, A.P.H.J. Schenning and S. de Feyter*
Surface-induced diastereomeric complex formation of a nucleoside at the liquid/solid interface: Stereoselective recognition and preferential adsorption
J. Am. Chem. Soc. 135, 9811-9819 (2013)

5. *M.A.J. Gillissen, M.M.E. Koenigs, J.J.H. Spiering, J.A.J.M. Vekemans, A.R.A. Palmans, I.K. Voets, E.W. Meijer*
Triple helix formation in amphiphilic discotics: demystifying solvent effects in supramolecular self-assembly
J. Am. Chem. Soc. 136, 336-343 (2014)

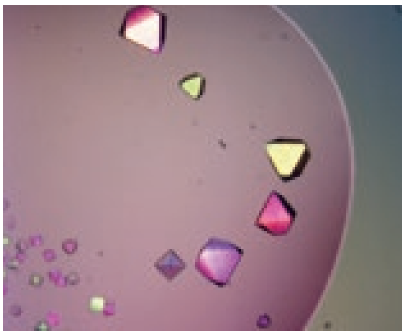


This overview lists publications in high end journals with ICMS as affiliation.



X-RAY crystallography: snapshots of molecular mechanisms

For fully understanding (bio)chemistry at the deepest level, a clear picture of the processes at atomic resolution is very useful. Especially the details of the interactions of proteins with each other or with small-molecule ligands help to understand for example the basis of diseases and the regulation of physiological processes. Hence, protein X-ray crystallography is also an essential part of the drug development process.



Crystals of the proteinase SBT3

FACT

Bragg's Law

$$n\lambda = 2d\sin\theta$$

is used to interpret the diffraction patterns of crystals

A. Glas, D. Bier, G. Hahne, C. Rademacher, C. Ottmann, T.N. Grossmann (2014). Angewandte Chemie, DOI: 10.1002/anie.201310082

Nowadays every pharmaceutical company disposes over considerable structural biology divisions with X-ray crystallography being the predominant technique employed. In addition, the number of universities and public research institutes that perform X-ray crystallography is constantly increasing and since a few weeks the ICMS can be counted among this group.

Workhorse of structural biology

The importance of protein crystallography is also reflected by the number of solved crystal structures per year. Whereas until the mid-nineties elucidation of a protein structure was a major undertaking with only about 750 structures reported worldwide each year, considerable technological advancements helped to raise this value to almost 9000 in 2013. Of the 97,000 protein structures deposited in the Protein Data Bank (PDB) 86,000 have been elucidated by X-ray crystallography.

Wanted: crystals!

As the name implies, a prerequisite for protein X-ray crystallography is the necessity to grow a crystal from the protein that is to be analyzed. Despite significant progress in protein production and screening for suitable conditions crystal growth remains clearly the bottleneck. However, once a suitable crystal is obtained, modern X-ray home sources like the one now operating in the ICMS lab can collect a suitable dataset for structure elucidation within a few hours. Here, a focused X-ray beam is shot at the crystal and the internal crystal lattice scatters this beam producing a specific diffraction pattern that can be used to calculate the electron density map. The nature of these diffraction patterns were first explained by William Lawrence Bragg and William Henry Bragg in 1913 in the description of Bragg´s law. Both were awarded the Nobel prize for this achievement making them the only father-son pair and William Lawrence Bragg the youngest (25 years) Nobel laureate in history.

THESES ICMS

September 2013 – February 2014

1 **Seeing structure in supramolecular systems**
Martijn A.J. Gillissen

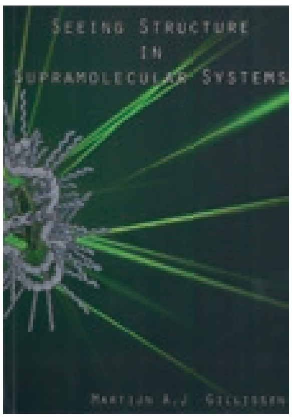
September 12, 2013
PhD advisor:
prof.dr. E.W. Meijer

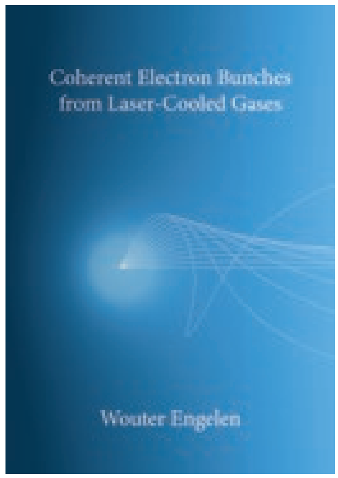
2 **Coherent electron bunches from laser-cooled gases**
Wouter J. Engelen

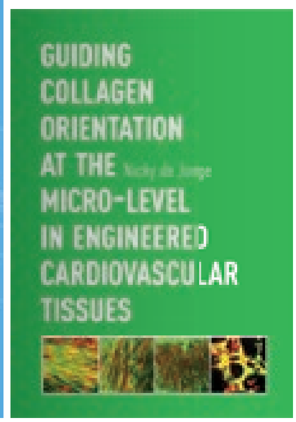
September 23, 2013
PhD advisor:
prof.dr.ir. O.J. Luiten

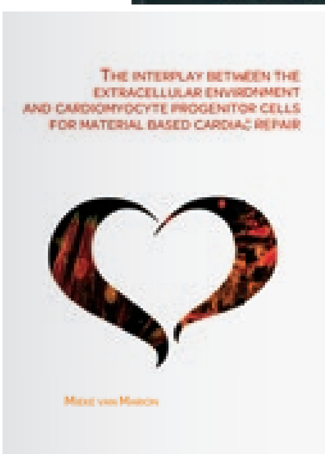
3 **Guiding collagen orientation at the micro-level in engineered cardiovascular tissues**
Nicky de Jonge

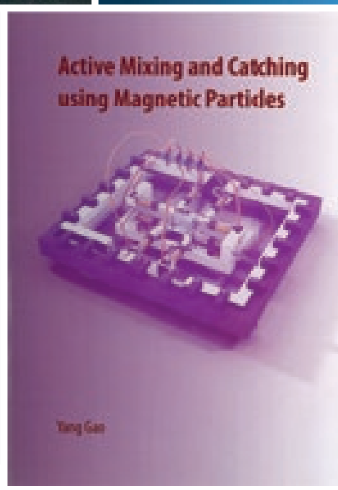
October 8, 2013
PhD advisors:
prof.dr. C.V.C. Bouten,
prof.dr.ir. F.P.T. Baaijens

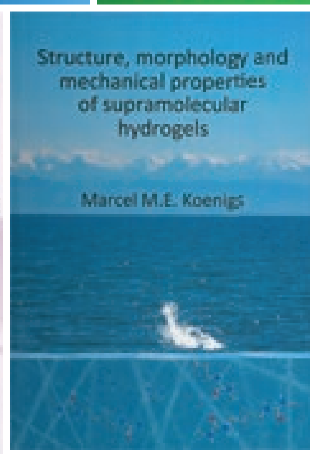












4 **The interplay between extracellular environment and cardiomyocyte progenitor cells for material based cardiac repair**
Mieke H. van Marion

October 10, 2013
PhD advisor:
prof.dr. C.V.C. Bouten

5 **Active mixing and catching using magnetic particles**
Yang Gao

October 24, 2013
PhD advisor:
prof.dr. J.M.J. den Toonder

6 **Structure, morphology and mechanical properties of supramolecular hydrogels**
Marcel M.E. Koenigs

November 18, 2013
PhD advisor:
prof.dr. R.P. Sijbesma

7 **Competitive interactions in supramolecular polymer systems**
Marko M.L. Nieuwenhuizen

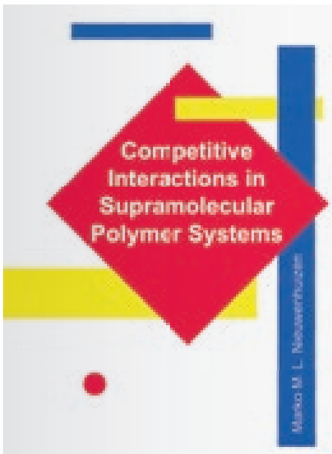
December 2, 2013
PhD advisors:
prof.dr. E.W. Meijer,
prof.dr. R.P. Sijbesma

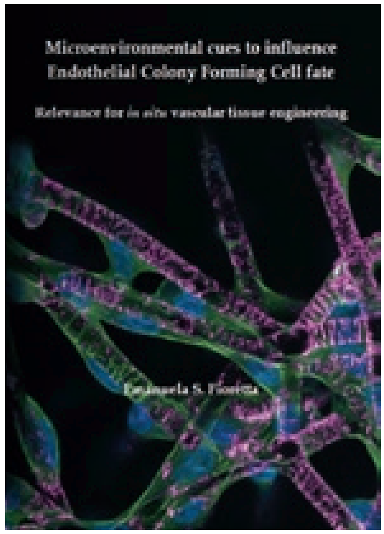
8 **Microenvironmental cues to influence endothelial colony forming cell fate**
Emanuela S. Fioretta

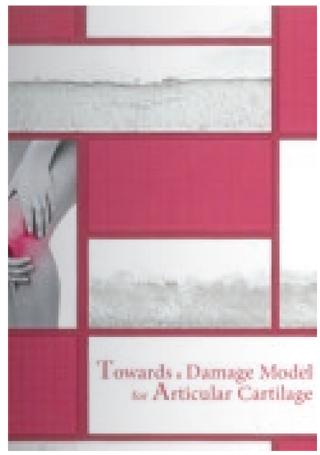
January 14, 2014
PhD advisors:
prof.dr. C.V.C. Bouten,
prof.dr.ir. F.P.T. Baaijens

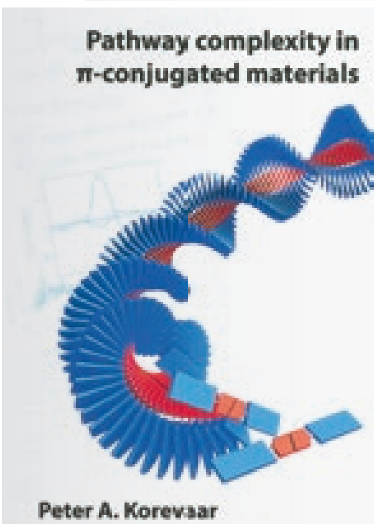
9 **Towards a damage model for articular cartilage**
Sayyed Mohsen Hosseini

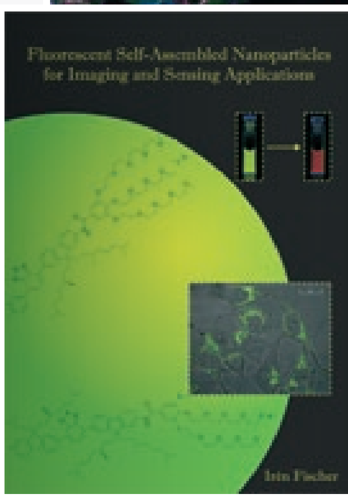
January 14, 2014
PhD advisors:
prof.dr. K. Ito,
dr. C.C. van Donkelaar

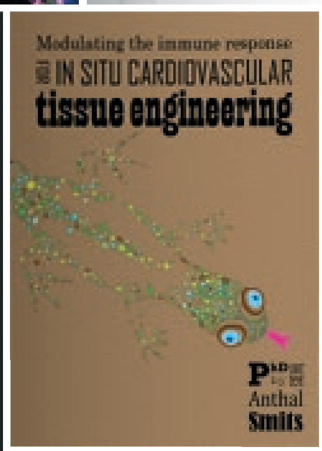












10 **Pathway complexity in π-conjugated materials**
Peter A. Korevaar

January 24, 2014
PhD advisors:
prof.dr. E.W. Meijer,
dr.ir. T.F.A. de Greef

11 **Fluorescent self-assembled nanoparticles for imaging and sensing applications**
Irén Fischer

February 6, 2014
PhD advisors:
prof.dr. D.J. Broer,
prof.dr. A.P.H.J. Schenning

12 **Modulating the immune response for in situ cardiovascular tissue engineering**
Anthal I.P.M. Smits

February 25, 2014
PhD advisors:
prof.dr.ir. F.P.T. Baaijens,
prof.dr. C.V.C. Bouten

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 (ICMS) of the Eindhoven University of Technology (TU/e) was established in 2008 and 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 specialized input from leading specialists in different branches of science and engineering, new avenues are explored, where mastering complexity is the leading theme.

The scientific agenda of ICMS consists of two lines of research:

1. Functional molecular systems
   (program leader prof.dr. E.W. Meijer)
2. Bio inspired engineering
   (program leader prof.dr.ir. F.P.T. Baaijens)

ICMS hosts the Advanced Study Center, a breeding ground for new interdisciplinary research. It serves as an intellectual home to scientist from all over the world, hosting discussions on the theme of complexity. It is also the home of the Eindhoven Multiscale Institute (EMI) and the Eindhoven Polymer Laboratories (EPL).

ICMS aims at offering an ideal training environment for all young students and scientists to prepare themselves for a future career in science and engineering in a world of increased complexity. Therefore, we offer the Graduate Program in Complex Molecular Systems (MSc and PhD).

The relationship with industry is strengthened via the Industrial Consortium – where science meets innovation.

More information can be found via our website www.tue.nl/icms. Please contact us via email icms@tue.nl or telephone +31 40 247 2482 with specific questions or remarks.

ICMS IN PRESS

Editorial
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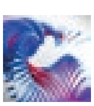

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