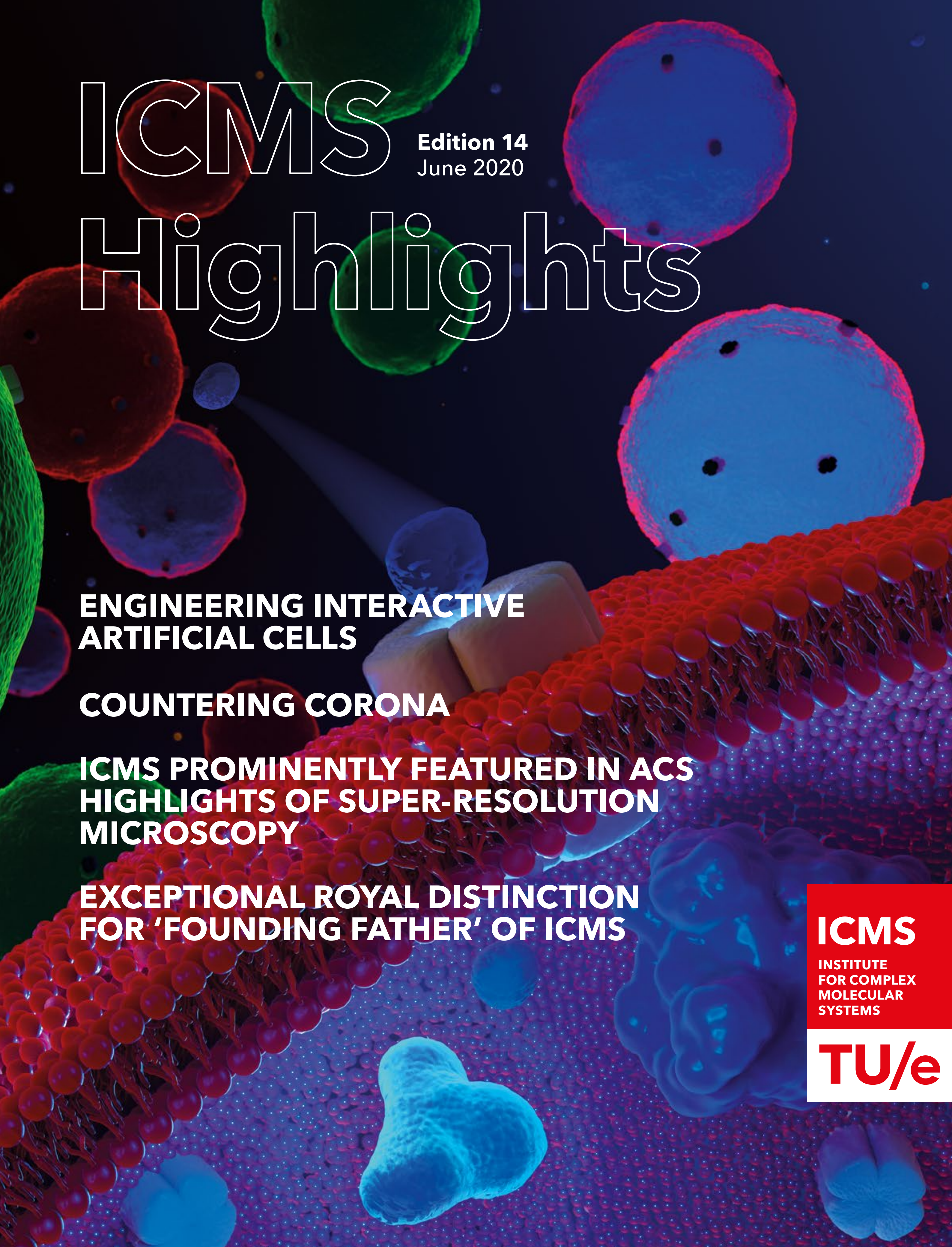


ICMS Highlights

Edition 14
June 2020

ENGINEERING INTERACTIVE ARTIFICIAL CELLS

COUNTERING CORONA

ICMS PROMINENTLY FEATURED IN ACS HIGHLIGHTS OF SUPER-RESOLUTION MICROSCOPY

EXCEPTIONAL ROYAL DISTINCTION FOR 'FOUNDING FATHER' OF ICMS

ICMS
INSTITUTE FOR COMPLEX MOLECULAR SYSTEMS
TU/e

INTRODUCTION

ICMS Highlights

A highly contagious disease, COVID-19, is in our midst and impacts our daily lives. People from all walks of life try to find ways to stay safe while keeping society afloat. It is admirable how we join forces and support one another to cope with this surrealistic situation. Through the eyes of a TU/e scientist, many strategies to tackle COVID-19 can be seen. And indeed, many of these are being pursued. Efforts include accelerating the search for a vaccine, and developing and utilizing predictive models for its transmission. The focus is also on understanding the course of the disease and its effect on the occupancy rates of ICU's.

At ICMS, we are proud to be part of this resourceful community, that takes up these challenges under these difficult circumstances, even on top of regular activities. As one of the TU/e institutes, we are proud to make it possible for researchers to conduct molecular science at the highest level and develop meaningful contributions to combatting the global pandemic.

This edition of the ICMS Highlights outlines a number of TU/e activities to tackle COVID-19. You can also read about interdisciplinary endeavors by ICMS researchers on COVID-19, and about the potential of super-resolution imaging for nanomedicine research. We hope that you enjoy reading it. May we light a spark of hope that together we will overcome this corona-crisis. We see that you go the extra mile both at home and at work, and we are confident that your efforts can make a difference.

Jan van Hest
Scientific director

Monique Bruining
Managing director

Calendar

July 2020
COMPLEX FRIDAY SEMINAR
Lorenzo Albertazzi & Richard Post

STUDIUM GENERALE (SG) AND ICMS LECTURE SERIES ON GRIP OF COMPLEXITY

COMPLEX SYSTEMS AND THE DYNAMICS OF INFECTIOUS DISEASES (LECTURE 1 OF 4)

September 2020
SG INTRODUCTORY LECTURE
BY HANS HEESTERBEEK

October 2020
ICMS COMPLEX FRIDAY: IN-DEPTH LECTURE
BY NELLY LITVAK

CLIMATE AND ENERGY (LECTURE 2 OF 4)

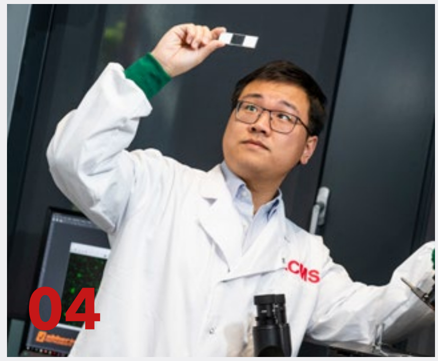
November 2020
SG INTRODUCTORY LECTURE
BY GERT-JAN KRAMER

November 2020
ICMS COMPLEX FRIDAY: IN-DEPTH LECTURE
BY DAVID SMEULDERS

October 2020
NOBELPRIZE EVENING

For more information about our events and exact date and location, please visit our website **www.tue.nl/icms**

Content



COVER The cover shows the communication between two types of vesicles (artificial cells); the conversion of signaling molecules in the green vesicles triggers the production of fluorescent molecules in the red vesicles.

ADVANCED ANALYSIS OF COMPLEX MOLECULAR SYSTEMS

The sharpest view in the world

Yuyang Wang

Yuyang Wang received his MSc in Physical Chemistry from Jilin University (Changchun, China), where he studied molecular physical chemistry and microsphere-based nanolithography. In 2015 he joined ICMS for PhD research into the physical chemistry of nanoparticles. Since October 2019 he is a postdoc at ICMS, working on stimulated emission depletion microscopy (STED).

Yuyang Wang works with a super-resolution microscope, the newest addition to the impressive range of instruments at ICMS. He uses it to zoom in on individual molecules and makes the smallest processes in our body visible. He is pushing the boundaries of this instrument even further by combining it with an electron microscope. This will enable him to study how a drug can attach selectively to cancer cells.

WHY ARE YOU COMBINING DIFFERENT MICROSCOPES?

"I work on microscopy with extremely high resolution. The instrument can resolve individual molecules. Classical microscopes can´t resolve details smaller than half the wavelength of the light used. This means that you won´t see details smaller than 200 or 300 nm. Most molecules are much smaller. Physics doesn´t allow you to zoom in beyond that, unless you use some clever tricks."

"In December last year, we have installed an instrument that circumvents this basic limitation. It´s called a stimulated emission depletion microscope, or STED. It uses lasers to light up molecules in a tiny spot, much smaller than the focal beam of a traditional microscope. This means that you can locate these molecules very well. But you´ll only see fluorescent molecules. That´s the limitation of STED and that's why I started to combine it with electron microscopy. Electrons can detect details as small as 10 nm. But electron microscopes have other disadvantages. You see only details that scatter electrons. And you´ll have to work in a vacuum. I see both tools as complementary. Each has different advantages and disadvantages. That´s why it is so useful to combine them. Right now I'm developing a workflow to correlate both techniques."

WHAT DO YOU EXPECT TO SEE WITH THESE MICROSCOPES?

"I work with inorganic materials. These might be the active substances of a drug. For example, we use the instrument to study how to target such a drug directly to a diseased cell. My interest as a postdoc is the physics of the instrument: I'm investigating how it can be developed and tweaked. I work closely together with Lorenzo Albertazzi and Peter Zijlstra, who study the biophysics of what we see."The idea is to have a drug selectively attach to diseased cells. In this way, you could target cancer cells, for example, while sparing healthy cells. This would minimize the side effects of a therapy. The desired selectivity can perhaps be obtained by transporting the drug with nanoparticles such as proteins. These are recognized by certain cells and attach to them. So the proteins functions as a signal to the cell. The proteins we use to coat the surface of the drug have different shapes, they're not fully spherical. So I will make an assortment of proteins with different shapes and see how that affects their function. We also think that the distribution of the proteins over the surface of the drug influences the signaling. The proteins are usually far from uniformly distributed over the surface. So there may be some spots with more proteins or different proteins might stick in different ways to the surface. This may all affect their selectivity." >>

"This is still a hypothesis which we need to prove. You can´t do that with a traditional microscope. You won´t see those proteins. We use our super-resolution microscope to study this."

HOW DO YOU KNOW WHICH SHAPES ARE BEST?

"We work closely with researchers at the Institute of Bioengineering of Catalonia, IBEC, in Barcelona. They make ´organs on a chip´. This is living tissue, tweaked to function as a part of a human organ, such as a lung or a heart. These organs on a chip are a great way to test a new drug. You can see how a human organ reacts, without having to perform a clinical trial on humans. That's the final step of my project. Once we know how to distribute proteins over the surface of a drug, we want to test how this affects the targeting of the drug. An organ on a chip is a great way to do this. If it has both healthy and cancerous cells, you can test the selectivity of the drug delivery."

TELL US ABOUT THE ICMS INDUSTRIAL CHALLENGE SCIENCE AWARD FOR YOUR PHD WORK.

"I worked on different super-resolution techniques for microscopes. We collaborated with scientists from Sabic, the chemical company at the Chemelot site in Geleen. They wanted to reinforce soft polymers with hard materials. So they needed to know how the constitution of these hard materials affects the mechanical properties of the polymer. We made a plan on how to study this with super-resolution microscopy. That´s how we won the prize. "I did a lot of other work with single-molecule fluorescence microscopy during my PhD. Examples are the characterization of nanoparticles for single-molecule biosensing, and the characterisation of proteins for application in single-molecule spectroscopy. It is great that as a postdoc I am now able to extend this with the new opportunities of STED."

HOW DOES THE COMMUNITY AT ICMS AFFECT YOUR RESEARCH

"ICMS is a great platform for many collaborations. Gradually I'm getting more and more exposed to different scientists with different disciplines. ICMS is a great place to get different perspectives. Scientists just knock on your door to see what's possible with the instruments. For instance, a large group of scientists at ICMS is studying the inner workings of cells. STED can give them new opportunities. With STED you can follow fluorescent molecules on their way through a cell. The idea is to label certain molecules so that they become fluorescent. Then you can resolve the positions of each labelled molecule in the cell."

BUT IN THESE PANDEMIC TIMES, THERE WON´T BE MUCH KNOCKING ON DOORS.

"I have used the lock-down for data-analysis. We studied new algorithms and started to use machine learning techniques. That involves a lot of reading and thinking, which you can do very well at home. Also students could continue their work from home, as a lot of lab data is available online. We set up a lot of video meetings and continued our regular group meetings. Also students could continue to work, as a lot of lab data is available online. But next week we can start working in the lab again, of course with all precautions in place. It will take some time to have everything up and running, but then I will continue working on the correlation of different microscopy techniques. Most of us at ICMS are experimentalists. We are used to getting our hands dirty in the lab."

GENERAL

Exceptional royal distinction for ‘founding father’ of ICMS

Bert Meijer receiving the decoration from the Mayor of his hometown Waalre, Jan Brenninkmeijer.

ICMS founder, Bert Meijer, has been honored with the title Commander of the Order of the Netherlands Lion, an exceptional royal distinction that is only sporadically awarded.

The distinction was awarded to Meijer last February during a special symposium organized by alumni and researchers from his group. The Mayor of his hometown Waalre praised Meijer for being a world-leading top scientist in organic chemistry. He also mentioned Meijer's pioneering research on supramolecular polymers, which are currently being investigated in many international academic and industrial laboratories. Furthermore, the Meijer lab successfully started the company SupraPolix which offers a supramolecular polymer platform for multiple applications, including regenerative heart valves. Meijer has published over 600 peer-reviewed research articles and reviews that have been cited more than 60.000 times. Throughout his career, Meijer has received numerous prominent awards, such as the Gold Medal of the Royal Netherlands Chemical Society (1993), the Spinoza Award of the Netherlands Organisation for Scientific Research (2001) and the honorary membership from the American Academy of Arts and Sciences (2019).

ACHIEVEMENTS WITH SOCIAL IMPACT

According to the official guidelines, the title of Commander in the Order of the Dutch Lion (the Dutch order of chivalry founded by King William I in 1815), is awarded to people that have "demonstrated competence that is considerably greater than society might expect of him or her". This includes "persons with special talents and persons who have realized achievements with social impact, such as groundbreaking (scientific) work". Over the last twenty years, just nine others have received the prestigious royal Dutch distinction. Three of these were also scientists, even Nobel laureates: Ben Feringa, Andre Geim and Konstantin Novoselov. Adding to the honors, the current director of ICMS Prof. Jan van Hest announced that the ICMS Advanced Study Center will be named after Bert Meijer.

"OVER THE LAST TWENTY YEARS, JUST NINE OTHERS HAVE RECEIVED THE PRESTIGIOUS ROYAL DUTCH DISTINCTION"

News, awards & grants

How to find molecular glues to effectively target diseases

Many of the currently available drugs are not specific enough to effectively cure complex diseases such as cancer, neurodegenerative diseases and diabetes. In addition, drug resistance reduces the effectiveness of existing therapies. To address these problems, biomedical engineer Eline Sijbesma designed small molecules that disarm specific disease proteins by gluing them to other proteins. These could lead to more stable and effective drugs and, among other things, might contribute to a new therapy for resistant breast cancer, for which currently no treatment exists. Sijbesma obtained her PhD cum laude on December 2 at TU/e.

Eline Sijbesma, Chemical Biology

Young Academy welcomes two new TU/e researchers

Liesbeth Janssen and Tom de Greef

TU/e researchers Liesbeth Janssen and Tom de Greef are among the ten new members of the Young Academy, who were announced by the KNAW today. Janssen is assistant professor at the department of Applied Physics. De Greef is associate professor at the department of Biomedical Engineering and working at the Institute for Complex Molecular Systems.

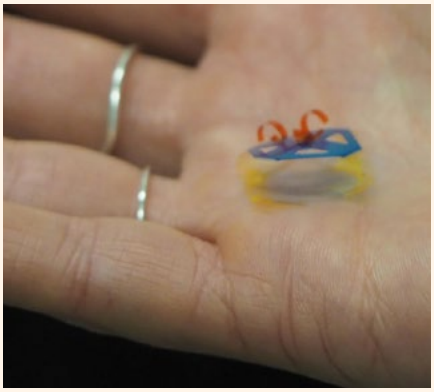
Life-like cells can now communicate over long distances via signal amplification


Jan van Hest (left) and Bastiaan Buddingh (right).

Scientists have big dreams for artificial cells. These replicas of biological cells in the laboratory could help understand how living organisms work. While a lot of progress has been made in how to construct artificial cells, the phenomena behind their communication and their behavior remain largely unexplored. Researchers from TU/e and Radboud University (Nijmegen) have developed communities of artificial cells that communicate with each other with unprecedented power. Their studies advance the development of artificial cells that, by being 'interconnected', could be used — to name a few — to deliver drugs more precisely to their targets, defeat cancer cells, or even improve the accuracy of diagnostic testing. Results are published April 3 in Nature Communications.

Walking plastic delivers packages

Researchers Marina Pilz da Cunha and master's student Bas Ambergen in a collaboration between the research groups of Jaap den Toonder and Albert Schenning at Eindhoven University of Technology have developed the first ever light-controlled 'package delivery robot'. Measuring two centimeters, this plastic mini-robot can 'walk' under the influence of blue light in order to collect and deliver packages. In the future, it should be possible to use the robot to deliver medicines within the human body or to carry out simple repairs to chip machines, for example. The researchers have published their results in the journal Advanced Science.



Peter Zijlstra

Keeping up with the literature is hard. The American Chemical Society (ACS) offers a helping hand by publishing selections of outstanding recent papers linked to a specific theme. This is comparable to a 'Best of...' playlist, but instead of great music, these selections offer great science. In its Virtual Issue on Super-Resolution Far-Field Optical Microscopy published in March, the ACS lists no less than four papers of ICMS researchers: Lorenzo Albertazzi (twice), Ilja Voets and Peter Zijlstra. What are their thoughts on super-resolution microscopy, where are we heading, and what do we need to keep moving forward?

ICMS prominently featured in ACS highlights of super-resolution microscopy

PETER ZIJLSTRA, ASSOCIATE PROFESSOR, MOLECULAR PLASMONICS, DEPARTMENT OF APPLIED PHYSICS

WHAT DO YOU SEE AS A MAJOR CONTRIBUTION OF SUPER-RESOLUTION MICROSCOPY?

"Super-resolution microscopy can provide crucial answers in the quantification of bio-active groups, not only on biological samples but also on synthetic structures such as nanoparticles. These are widely used in applications like biosensing where the particle is functionalized to detect a specific biomarker. The number and the distribution of functional groups on the particle have long remained hidden. Super-resolution microscopy will provide the key to unravel the relationship between the chemical interface and the performance of a particle-based sensor."

HOW DID ICMS ACHIEVE SUCH A PRESENCE IN THIS FIELD?

"We moved beyond the use of super-resolution microscopy as a workhorse technology in a biological setting and applied it to the study of synthetic nanostructures ranging from polymers to nanoparticles and sensor surfaces. This is a topical field that is still in its infancy, but ICMS now has a clear edge over the rest of the world. We operate in a multidisciplinary environment that provides the perfect breeding ground for developing out-of-the-box ideas at the interface of physics, chemistry, and biomedical engineering." >>

"ICMS NOW HAS A CLEAR EDGE OVER THE REST OF THE WORLD"

"IT WOULD BE GREAT TO DEVELOP NEW TOOLS TO CHARACTERIZE THE SURFACE OF LARGE COLLOIDAL PARTICLES — WHICH ARE NOTORIOUSLY DIFFICULT TO CHARACTERIZE"

Ilja Voets

ILJA VOETS, PROFESSOR OF SELF-ORGANIZING SOFT MATTER, DEPARTMENT OF CHEMICAL ENGINEERING AND CHEMISTRY

WHAT DO YOU EXPECT FROM THE SUPER-RESOLUTION FIELD IN THE NEAR FUTURE?

"There are plenty of exciting opportunities ahead. For example, we can move toward 5D approaches that encompass space (x,y,z) but also time and function, for probing spatiotemporal structure evolution in lifelike and living materials. I'm also thinking about experiments on ice crystals, to resolve the working mechanism of antifreeze proteins and to investigate bioinspired materials that protect against freeze damage. And it would be great to develop new tools to characterize the surface of large colloidal particles- which are notoriously difficult to characterize — so that we can improve their use in, for instance, particle-based sensors. And these are just a few of the possibilities I see emerging."

WHAT IS NEEDED TO REALIZE THAT POTENTIAL?

"It all starts with a strong user base. You need an active community of users, frequent discussion sessions, hands-on training and workshops, and support of new users by specialists. This ensures the exchange of ideas and helps us to exploit new methods as they are developed and implemented. The field develops so rapidly and is so multifaceted that the strong interdisciplinary community here at ICMS is ideally positioned to benefit from the new opportunities. But this requires continuous, long-term support of infrastructure and staff to offer training and hands-on assistance to experts as well as to non-specialist users."

LORENZO ALBERTAZZI, ASSOCIATE PROFESSOR, MOLECULAR SENSING FOR DIAGNOSTICS, DEPARTMENT OF BIOMEDICAL ENGINEERING

HOW DO YOU EXPLAIN THE SUCCESS OF ICMS ON THIS TOPIC?

"Super-resolution microscopy has found fertile ground at ICMS. It is a technique that intrinsically requires a multidisciplinary approach, combining knowledge in optics, cell biology and biochemistry, chemical labeling and functionalization, and data analysis.

The ICMS mix of scientists with different backgrounds enabled a special twist to super-resolution research. As a result, we were able to develop new applications in the fields of materials, and new analysis tools based on stochastic modeling. ICMS invested in super-resolution microscopy at the very beginning of the technological development of these methods. The current results show how important it is to invest in infrastructure and to be at the forefront of technological development."

WHAT IS NEEDED FOR THE FUTURE?

"An obvious answer would be to always acquire state-of-the-art infrastructure, but that is only part of the story. Because of the technical challenges that super-resolution poses, just having the microscope is insufficient.

Without skilled scientists who can calibrate the instruments, design smart experiments and procedures, and correctly analyze the output data, we are going nowhere. You need to have the best car, but make sure you also have the right drivers and mechanics."

Lorenzo Albertazzi

"YOU NEED TO HAVE THE BEST CAR, BUT MAKE SURE YOU ALSO HAVE THE RIGHT DRIVERS AND MECHANICS."

Key publications

OCTOBER 2019 – MARCH 2020

01. FUNCTIONAL PEPTIDE PRESENTATION ON DIFFERENT HYDROGEN BONDING BIOMATERIALS USING SUPRAMOLECULAR ADDITIVES
R.C. van Gaal, A.B.C. Buskermolen, B.D. Ippel, P.-P.K.H. Fransen, S. Zaccaria, C.V.C. Bouten, P.Y.W. Dankers
Biomaterials 224, 119466 (2019)

02. INSIGHTS INTO FULLERENE PASSIVATION OF SNO2 ELECTRON TRANSPORT LAYERS IN PEROVSKITE SOLAR CELLS
J. Wang, K. Datta, C.H.L. Weijtens, M.M. Wienk, R.A.J. Janssen
Adv. Funct. Mater. 29, 1905883 (2019)

03. MASS-BALANCE MODELS FOR SCRUTINIZING SUPRAMOLECULAR (CO)POLYMERIZATIONS IN THERMODYNAMIC EQUILIBRIUM
H.M.M. ten Eikelder, A.J. Markvoort
Acc. Chem. Res. 52, 3465–3474 (2019)

04. MULTIVALENT ULTRASENSITIVE INTERFACING OF SUPRAMOLECULAR 1D NANOPLATFORMS
E. Magdalena Estirado, M.A. Aleman Garcia, J. Schill, L. Brunsveld
J. Am. Chem. Soc. 141, 18030–18037 (2019)

05. NONAFFINITY AND FLUID-COUPLED VISCOELASTIC PLATEAU FOR IMMERSED FIBER NETWORKS
D. Head, C. Storm
Phys. Rev. Lett. 123, 238005 (2019)

06. NONCOVALENT SYNTHESIS OF SELF-ASSEMBLED NANOTUBES THROUGH DECOUPLED HIERARCHICAL COOPERATIVE PROCESSES
V. Vazquez-Gonzalez, M.J. Mayoral, R. Chamorro, M.M.R.M. Hendrix, I.K. Voets, D. Gonzalez-Rodriguez
J. Am. Chem. Soc. 141, 16432–16438 (2019)

07. NONEQUILIBRIUM SITE DISTRIBUTION GOVERNS CHARGE-TRANSFER ELECTROLUMINESCENCE AT DISORDERED ORGANIC HETEROINTERFACES
A. Melianas, N. Felekidis, Y. Puttisong, S.C.J. Meskers, O. Inganas, W.M. Chen, M. Kemerink
Proc. Natl. Acad. Sci. U. S. A. 116, 23416–23425 (2019)

08. SMART CANCER NANOMEDICINE
R. van der Meel, E. Sulheim, Y. Shi, F. Kiessling, W.J.M. Mulder, T. Lammers
Nat. Nanotechnol. 14, 1007–1017 (2019)

09. SUPRAMOLECULAR INTERACTIONS BETWEEN CATALYTIC SPECIES ALLOW RATIONAL CONTROL OVER REACTION KINETICS
A.J.P. Teunissen, T.F.E. Paffen, I.A.W. Filot, M.D. Lanting, R.J.C. van der Haas, T.F.A. de Greef, E.W. Meijer
Chem. Sci. 10, 9115–9124 (2019)

10. THE GENOMIC LANDSCAPE OF METASTATIC CASTRATION-RESISTANT PROSTATE CANCERS REVEALS MULTIPLE DISTINCT GENOTYPES WITH POTENTIAL CLINICAL IMPACT
L.F. van Dessel, J. van Riet, M. Smits, Y. Zhu, P. Hamberg, M.S. van der Heijden, A.M. Bergman, I.M. van Oort, R. de Wit, E.E. Voest, N. Steeghs, T.N. Yamaguchi, J. Livingstone, P.C. Boutros, W. Zwart, J.W.M. Martens, S. Sleijfer, E. Cuppen, H.J.G. van de Werken, N. Mehra, M.P. Lolkema
Nat. Commun. 10, 5251 (2019)

11. TRANSPARENT, HIGH-THERMAL-CONDUCTIVITY ULTRADRAWN POLYETHYLENE/GRAPHENE NANOCOMPOSITE FILMS
X. Pan, L. Shen, A.P.H.J. Schenning, C.W.M. Bastiaansen
Adv. Mater. 31, 1904348 (2019)

12. TUNING THE LENGTH OF COOPERATIVE SUPRAMOLECULAR POLYMERS UNDER THERMODYNAMIC CONTROL
G. Vantomme, G.M. ter Huurne, C. Kulkarni, H.M.M. ten Eikelder, A.J. Markvoort, A.R.A. Palmans, E.W. Meijer
J. Am. Chem. Soc. 141, 18278–18285 (2019)

13. ULTRAFAST DYNAMICS OF NONEQUILIBRIUM ORGANIC EXCITON-POLARITON CONDENSATES
M. Ramezani, A. Halpin, S. Wang, M. Berghuis, J.G. Rivas
Nano Lett. 19, 8590–8596 (2019)

14. A SOFT TRANSPORTER ROBOT FUELED BY LIGHT
M. Pilz da Cunha, S. Ambergen, M.G. Debije, E.F.G.A. Homburg, J.M.J. den Toonder, A.P.H.J. Schenning
Adv. Sci. 7, 1902842 (2020)

15. CONTROLLING THE ADAPTION BEHAVIOUR OF NEXT-GENERATION TISSUE-ENGINEERED CARDIO-VASCULAR IMPLANTS VIA COM-PUTATIONAL MODELLING WILL COMPUTATIONAL MODELLING HELP TO EXPEDITE CLINICAL TRANSLATION OF NEXT-GENERATION BIOENGINEERED IMPLANTS?
S. Loerakker, F.P.T. Baaijens, S.P. Hoerstrup, M.Y. Emmert
Eur. Heart J. 41, 1069–1073 (2020)

16. CONTROLLING THE MICROSTRUCTURE OF CONJUGATED POLYMERS IN HIGH-MOBILITY MONOLAYER TRANSISTORS VIA THE DISSOLUTION TEMPERATURE
M. Li, H. Bin, X. Jiao, M.M. Wienk, H. Yan, R.A.J. Janssen
Angew. Chem. Int. Ed. 59, 846–852 (2020)

17. DISTINCT PATHWAYS IN "THERMALLY BISIGNATE SUPRA-MOLECULAR POLYMERIZATION": SPECTROSCOPIC AND COMPUTATIONAL STUDIES
K.V. Rao, M.F.J. Mabesoone, D. Miyajima, A. Nihonyanagi, E.W. Meijer, T. Aida
J. Am. Chem. Soc. 142, 598–605 (2020)

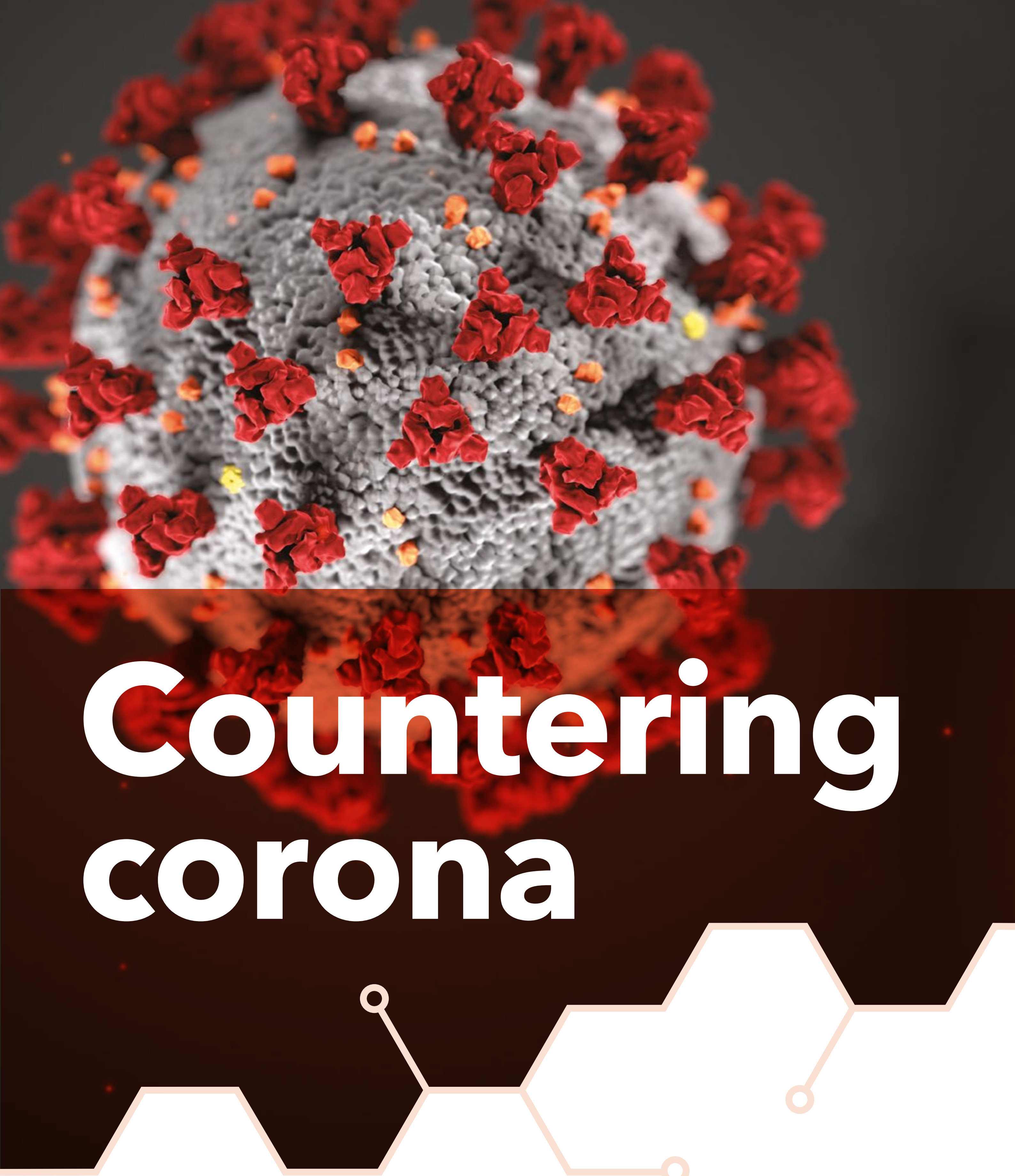
18. ENGINEERING LONG-RANGE ORDER IN SUPRAMOLECULAR ASSEMBLIES ON SURFACES: THE PARAMOUNT ROLE OF INTERNAL DOUBLE BONDS IN DISCRETE LONG-CHAIN NAPHTHALENEDIIMIDES
J.A. Berrocal, G.H. Heideman, B.F.M. de Waal, M. Enache, R.W.A. Havenith, M. Stohr, E.W. Meijer, B.L. Feringa
J. Am. Chem. Soc. 142, 4070–4078 (2020)

19. HIGHLY EFFICIENT AND TUNABLE FILTERING OF ELECTRONS' SPIN BY SUPRAMOLECULAR CHIRALITY OF NANOFIBER-BASED MATERIALS
C. Kulkarni, A.K. Mondal, T.K. Das, G. Grinbom, F. Tassinari, M.F.J. Mabesoone, E.W. Meijer, R. Naaman
Adv. Mater. 32, 1904965 (2020)

20. NANOHYBRID MATERIALS WITH TUNABLE BIREFRINGENCE VIA CATION EXCHANGE IN POLYMER FILMS
B.M. Oosterlaken, Y. Xu, M.M.J. van Rijt, M. Pilz da Cunha, G.H. Timmermans, M.G. Debije, H. Friedrich, A.P.H.J. Schenning, N.A.J.M. Sommerdijk
Adv. Funct. Mater. 30, 1907456 (2020)

21. PROGRAMMABLE BIVALENT PEPTIDE-DNA LOCKS FOR PH-BASED CONTROL OF ANTIBODY ACTIVITY
W. Engelen, K. Zhu, N. Subedi, A. Idili, F. Ricci, J. Tel, M. Merkx
ACS Cent. Sci. 6, 22–31 (2020)

22. PROXIMITY-INDUCED CASPASE-9 ACTIVATION ON A DNA ORIGAMI-BASED SYNTHETIC APOPTOSOME
B.J.H.M. Rosier, A.J. Markvoort, B.G. Audenis, J.A.L. Roodhuizen, A. den Hamer, L. Brunsveld, T.F.A. de Greef
Nat. Catal. 3, 295–306 (2020)



Countering corona

iVAC: Accelerating vaccine development

Willem Mulder on why ICMS is well positioned to focus on vaccines

"With all the expertise and creativity available within ICMS, we strongly believe that developing next-generation vaccines should be an essential activity at the TU/e campus. Together with Maarten Merkx and Tom de Greef, we decided to tackle the general need for flexible vaccine development. The aim of this new ICMS Vaccine Initiative, or iVAC, is to create a modular nanotechnology-based platform that will seriously accelerate the vaccine development track. A group of PhD students and undergraduates with diverse scientific backgrounds is doing the groundwork right now and I am truly impressed with what they have achieved in this short time span. Covering all aspects of the required expertise has already led to real synergy."

Tom de Greef

Willem Mulder

Anna-Maria Makri Pistikou

Glenn Cremers

David Schrijver

Anne de Dreu

A big boost in knowledge

Student team behind iVAC is excited to join forces in a new project.

With labs being closed and experiments put on hold, doing science has become quite a challenge for many PhD students. Unless you shift gears and focus your energy on the questions we are all facing: how to deal with the current pandemic, and how to prepare for future ones? So, when asked to join the ICMS Vaccine Initiative, iVAC, these students were eager to hop on board.

Accelerating vaccine development by creating a modular, plug-and-play nanotechnology platform that allows easy switching of antigens. That is the aim of iVAC, bringing together technology and expertise from three ICMS research groups led by Willem Mulder, Tom de Greef and Maarten Merkx. It also brings together, virtually of course, a group of BSc, MSc and PhD students. They are doing the groundwork of studying the literature, defining the key questions and discussing the experimental approach to get the envisioned vaccine platform off the ground. Let's meet PhD students Glenn Cremers and Anna-Maria Makri Pistikou from De Greef's lab, and David Schrijver and Anne de Dreu from the Mulder lab.

At the heart of the platform is modular nanotechnology developed by the Mulder lab. It enables the flexible generation of targeted vaccines containing critical immune stimulators and a desired antigen — which in the case of SARS-CoV-2 would be (parts of) the spike protein that the virus uses to bind and invade host cells. The platform specifically delivers these antigens to dendritic cells and macrophages, which induces T-cell immunity and will lead to the production of antibodies that can recognize and bind the viral proteins. "That is the general mechanism by which vaccination works", Cremers kicks off. "It can be applied to infectious pathogens, but it can also be used to stimulate an immune response against cancer cells. A major advantage of our nanotechnology approach is that antigens can be introduced using a very generic step, essentially making it a plug-and-play system." The necessary adjuvant technology, to initiate co-stimulatory expansion of B-cells (produce antibodies) and T-cells (destroy invaders), is an inherent part of the platform.

PROTEIN EXPRESSION

One of the obvious ingredients of the whole process are the (recombinant) proteins that serve as antigens. Cremers: "In my PhD research, I work on the design and expression of multiple recombinant proteins. In iVAC, I will focus on the design of constructs for the fusion proteins." His efforts are complemented by those of his group colleague Anna-Maria Makri Pistikou, who has a background in molecular and cell biology. "I use mammalian protein expression in my research, which is focused on in vitro functionalization of cells with synthetic receptors", she explains. "Although that is completely different from the work needed for the vaccine project, the science behind it is universal." The same goes for cell biologist David Schrijver, who contributes his experience in cancer immunology. "My PhD research involves expression of immunomodulatory proteins and studying their functionality in vitro and in vivo. In this project, I will focus on the in vitro screening of antigens and developing assays to investigate the immune response to our vaccine candidates", says Schrijver. Finally, there is Anne de Dreu who was just about to start her PhD work in the Mulder group when the lockdown became effective. Her background in protein engineering comes in handy. De Dreu: "I concentrate on the incorporation of viral antigens, which means selecting the right expression systems and DNA constructs."

So there's lots of expertise and there are lots of plans, but the harsh reality is that everybody is still banned from the lab. How do you develop a vaccine platform from home? "We have lots of discussions and exchange of ideas in regular online meetings", says Cremers, "and there are also three undergraduate students working on this project. There is a lot of interaction. " The group follows an ordered and stepwise approach, according to Makri Pistikou. "We started by defining the general aspects and elaborated those into a more detailed plan. This brought us to various practical issues, such as the need for proteins. How do we make the proteins? Which expression systems work best? For each of these and other questions, we discuss the requirements and needs, divide the tasks and get to work. When we come back again later, we discuss our findings and define the next steps." The added value of working together on such a broad topic is clear, she says. "Each of us has a specific expertise, but there is great synergy between people, which creates a big boost in knowledge when you bring it all together."

SAVE TIME

When asked about the chances of this knowledge boost contributing anything tangible to the search for a vaccine against COVID-19, the group shows a down-to-earth attitude. "It will take a couple of years to firmly establish this new platform and use it for vaccine development", says Schrijver. "But after that it will definitely lead to acceleration of the development track. A major advantage will be that you don't need to test and evaluate the whole platform for every new pathogen. You just need to test the antigen, which will save massive amounts of time." In other words, this really could be a game changer. "We see it as a next-generation vaccine development platform", Makri Pistikou adds. In the meantime, all agree that being able to apply their experience in such a new way is very welcome in the current situation. Cremers: "In a PhD project, you are mostly working on your own, but now we all have this bigger project to work on. It really brings new energy." >>

Changing colors indicate antibody presence

MAARTEN MERKX ON USING PROTEIN ENGINEERING FOR POINT-OF-CARE TESTING

Maarten Merkx

“Conventional methods to detect the presence of antibodies are time-consuming and require specialized equipment and qualified staff. New approaches are needed to enable reliable point-of-care testing. One of the research lines in my group involves the use of fluorescent and bioluminescent proteins as sensors in assays that are faster, easier to use and less costly than the current, classical immunoassays. Since these sensor proteins recognize antibodies, it is immediately interesting to explore their use in a test showing whether someone has been infected with the SARS-CoV-2 virus and has developed immunity against it.”

“Our technology is based on fusing two protein domains to the sensor protein complex: a blue light-emitting luciferase enzyme and a green fluorescent protein. In the absence of the target antibody, these two domains are in close proximity, resulting in the emission of green light. However, upon binding of the antibody to the sensor protein, the two domains become separated and the sensor protein predominantly emits blue light. The change in color from green to blue light not only indicates the presence of an antibody, but the ratio between the two colors can also be used to accurately determine the antibody concentration. The more blue, the higher the antibody levels are. One of the main advantages of our approach is that it can be used directly in solution, which in this case is blood plasma. And we have already shown that our sensor proteins can be combined with a paper strip, which is very convenient for a point-of-care test. For the read-out a simple digital camera can be used, such as the one on your phone, but we are also working on the development of a dedicated reader.”

“Right now, we are developing the assays. The next step is to team up with clinical research groups, to start testing on patient material as the first part of the clinical validation track. It is impossible to foresee whether our efforts will make a difference in the host of initiatives that are popping up around the globe. Of course, everybody is eager to provide a testing solution, but we should be realistic. In science, you can never be sure of the outcome. But if I didn’t believe that our approach could be successful, I would not have started this.”

"Everybody wants to make a contribution"

The pandemic may have turned the otherwise bustling TU/e campus into an oasis of silence, but that doesn't stop a community of inquisitive minds from tackling the problems at hand. Under the banner 'TU/e against COVID-19', a host of initiatives has emerged to deploy the expertise and creativity of staff and students to tackle the pandemic from different angles.

Carmen van Vilsteren, director of Health at TU/e, highlights a few examples. "The Innovation Space has created a platform where student teams are working on questions and ideas from within and outside the university. The variety of topics is immense. For example, a team is working on a chatbot that can be used for interactions with patients, together with the Maxima Medical Center. Another team is evaluating the possibilities for using plasma to clean face masks. And there are also projects that are not directly related to health, but to other consequences of the pandemic, such as the question of preventing fraud during exams conducted from home."

AIR QUALITY

A major part of the work concerns going through the literature and finding out what knowledge is already available and evaluating whether a project is worth pursuing. "Selection is important, it has to be meaningful and feasible for students", says Van Vilsteren. "Some projects are really focused on a short-term solution, but we are also interested in long term projects that student teams can work on and which can be integrated in their course programs." Next to the efforts by students, there is plenty of activity from the staff as well. Van Vilsteren: "Take Edwin van den Heuvel in the department of Mathematics and Computer Science and part of our new Artificial Intelligence institute EAISI. His group is collaborating with several hospitals on predictive models for transmission, disease course and occupancy rates of intensive care units. Marcel Loomans of the department of the Built Environment is leading a project on air quality control in temporary hospitals and building repurposed to house COVID-19 patients. And these are just two of the many examples."

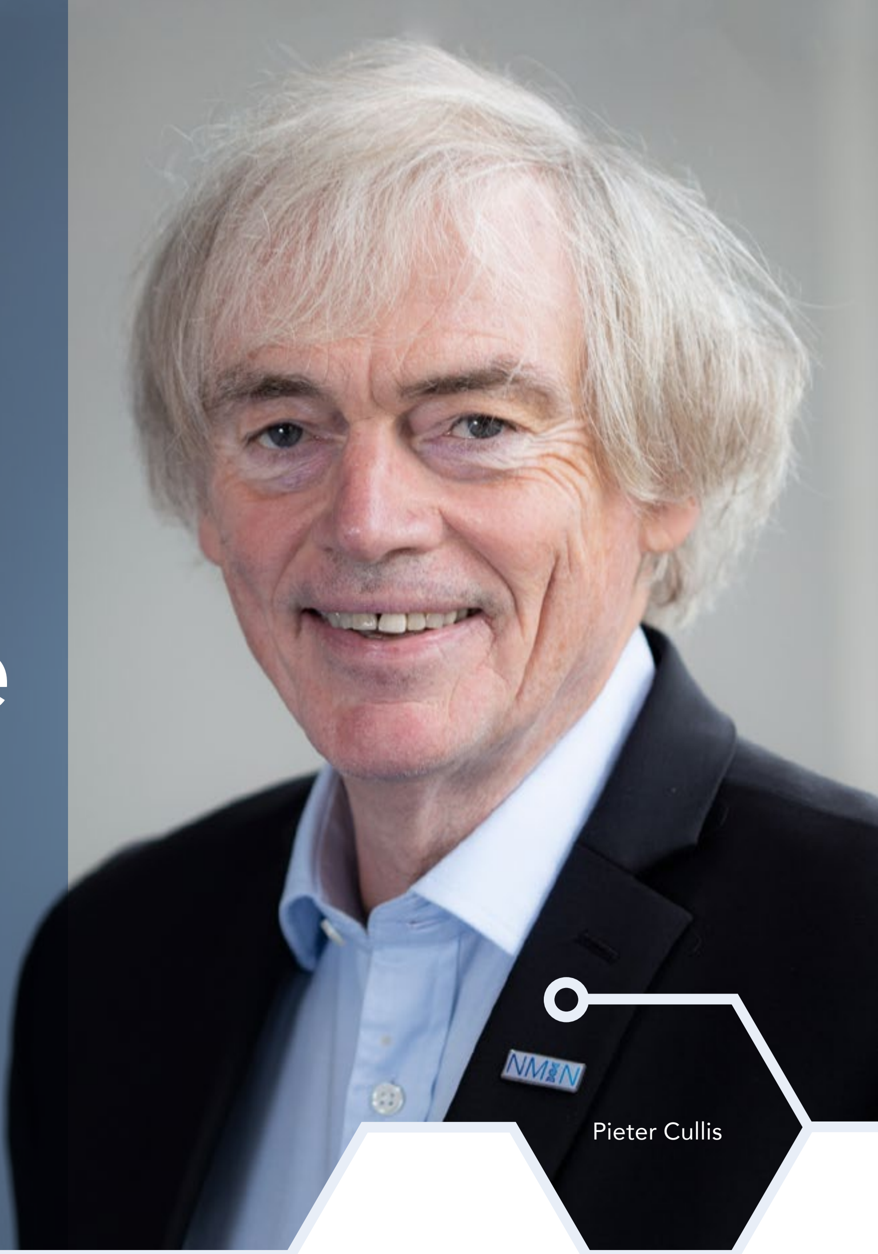
DRIVEN BY PROBLEMS

Browsing the TU/e website immediately reveals the huge number of initiatives that are supported and stimulated by the university. But why is it important to the university? To deliver tangible solutions to real-world problems? Show the value of science? Demonstrate the relevance of the university to society at large? Generate positive publicity? "I think these ingredients all play a role", Van Vilsteren says, "but the primary driver is that scientists are interested in problems. That is what science is about, to identify a problem and, particularly at a technical university, to start working on a solution. This is a perfect opportunity for all our researchers to apply their expertise and tools and techniques and see where it gets them. Of course, it also offers a chance to demonstrate the value of their research. And who knows, it may get them additional funding. But I am convinced that the desire to make a contribution is what really drives our staff and students."

Carmen van Vilsteren

CHEMICAL BIOLOGY

From model membrane to drug delivery vehicle



Pieter Cullis

Will a new generation of lipid nanoparticles (LNP) deliver on the longstanding promise of nanomedicine? LNP pioneer Pieter Cullis is confident that nucleic acid-based therapeutics and vaccines are quickly becoming reality. LNP mRNA systems are already important contenders in the race for Covid-19 vaccines.

"WE ARE NOW FACING A NEW CHALLENGE"

> "THE GROUP OF PROFESSOR LAURENS VAN DEENEN AT UTRECHT UNIVERSITY WAS WORLD-LEADING IN THE AREA"

In 2018, the first — and still only — systemic gene therapy drug, tradename Onpattro, was approved in the United States and Europe. It consists of lipid nanoparticles that encapsulate a short interfering RNA (siRNA), which inhibits the synthesis of a liver protein called transthyretin. It was developed to treat neuropathies caused by haTTR amyloidosis, a very rare hereditary disease. Although the siRNA is the active pharmaceutical ingredient, the packaging of the drug is just as important. That is why the launch of Onpattro is still making waves in the fields of nanomedicine and drug delivery. It is the first demonstration that nucleic acid based drugs can be packaged in lipid nanoparticles (LNP) to generate a safe, yet potent treatment that relies on the delivery of the encapsulated macromolecule to the cytoplasm of target cells.

ANTICANCER DRUGS

The lab of Pieter Cullis, Professor of Biochemistry and Molecular Biology at the University of British Columbia, developed the Onpattro LNP system together with the companies Acuitas Therapeutics and Alnylam Pharmaceuticals. Cullis himself has been involved in LNP research for several decades. "There is an interesting Dutch connection here", he says. "The field started out in the 1960s and the group of professor Laurens van Deenen at Utrecht University was world-leading in the area. At the end of 70s, I went to Utrecht for a postdoc and that is how I got involved. The term LNP wasn't used back then, they were called model membrane systems, or liposomes, and we used them to study the role of lipids in membranes." That changed during the 1980s when it was discovered that anticancer drugs, such as doxorubicin, could be put inside liposomes to enable more specific delivery. "At that point, we got heavily involved in using LNP for drug delivery and developed three different LNP-based anticancer drugs that gained regulatory approval." This success stimulated the search for ways to expand the repertoire with LNP that could be used to deliver much bigger molecules, such as DNA or RNA.

IONIZABLE LIPIDS

"To pack big, negatively charged strands of DNA or RNA into a nanoparticle, you need positively charged packaging material such as cationic lipids", Cullis explains. "Permanently charged cationic lipids were available but were highly toxic. So, we thought about using a cationic lipid that is ionizable and that is positively charged at low pH, but neutral at physiological pH. We were lucky to have one of those in the lab. We found we could encapsulate oligonucleotides at pH 4 and then bring the system to neutral conditions, with the loaded LNP staying intact. Around 2004, our LNP system came to the attention of Alnylam, a Boston-based company that was developing siRNAs as therapeutics. It worked to some extent for liver delivery, but the required dosage was so high that toxic side effects would occur. The lack of potency was a major problem."

By 2012, that problem was solved. "We had developed a new LNP technology that resulted in a huge increase in potency, about a thousandfold. To our surprise, we found that the potency of LNP siRNA systems was extremely sensitive to the particular species of ionizable lipid we employed." These new LNP based on optimized ionizable cationic lipids were used to formulate the siRNA to treat haTTR, leading to the approval of Onpattro in 2018.

VACCINE DEVELOPMENT

But why stop at short loads, like 20-bases siRNA? Cullis says the LNP field is already moving towards much bigger cargo: mRNA strands that can easily contain more than 2000 bases. "Huge companies are now recognizing the potential of LNP to enable mRNA therapeutics and many of them have jumped in already. It is very exciting to see how this technology is now applied in the development of new vaccines. Promising results have been obtained for generating immune responses against zika, influenza and HIV. LNP mRNA systems are also playing a leading role in the race for Covid-19 vaccines.

" When it comes to LNP for drug delivery, Cullis' next goal is expanding the number of target tissues. "Our current systems are very good at transfecting liver cells, but they don't perform well in other tissues. We are now facing a new challenge: how can we design our LNP to stay in circulation long enough to transfect other tissues? But looking how far we have come, I'm sure we will come up with solutions for that."

News, awards & grants

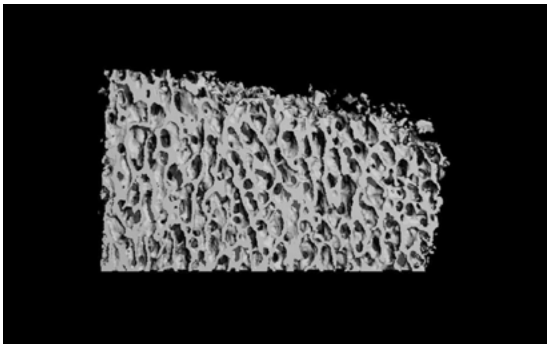
Manufacturing toolbox for porous silica is good news for production of medicine

Researchers Heiner Friedrich and Remco Fijneman

The chemical and pharmaceutical industry relies heavily on porous silica for the purification and conversion of raw materials into products. While silica materials with a range of different pore sizes are commercially available, a toolbox for large scale manufacturing that combines both flexibility and low cost, has thus far been lacking. Researchers from TU/e and Nouryon have developed a scalable strategy to synthesize silica microspheres with precisely tunable porosity and pore size. Their studies advance the understanding of microsphere assembly in emulsions and provide the next generation of tailor-made silica microspheres for use in purification applications and beyond. The results have been published in the leading journal Advanced Functional Materials.

ERC Proof of Concept grant for screening drug effects on bone in 3D

Sandra Hofmann has been awarded a European Research Council (ERC) Proof of Concept grant worth 150,000 euros to develop a platform capable of screening drug effects on bone in 3D. Test results collected with this 3D platform aim to be as accurate as in animal experiments, and will improve drug screening while reducing the number of animal experiments needed.



μCT image of a piece of porcine bone which is cultured ex vivo.

Gold particle shines like a flashlight on proteins

ERC Consolidator Grant for Peter Zijlstra

Peter Zijlstra, researcher in molecular plasmonics at Eindhoven University of Technology, received a Consoli-dator Grant of € 2 million from the European Research Council (ERC). He is using the grant for his research into making protein interactions visible by means of gold particles. In this way he hopes to be able to unravel how the folding of proteins works.

IBEC and ICMS sign a Memo-randum of Understanding on Research Cooperation

ICMS and the institute for Bioengineering of Catalonia (IBEC) have signed the first agreement between the two institutes to foster their collaboration. Both research centres share similarities such as their multidisciplinary approaches, their active missions to connect with industry and clinicians, and strong research in nanomedicine, chemical biology and biomaterials, imaging, Organ on a Chip technology and regenerative medicine and tissue engineering. This institutional alliance will allow to share resources, knowledge and provide mobility programs.

MOLECULAR DEVICES

Illuminating the inner workings of active liquid crystal networks

LASER SPECKLE IMAGING PROVIDES INSIGHT INTO COMPLEX MATERIALS

Hanne van der Kooij

"IT'S JUST FANTASTIC WHAT THEY ARE ABLE TO ACHIEVE"

It was to be a study purely on paint, but now that Wageningen University PhD student Hanne van der Kooij has completed her PhD thesis, it includes striking results on shape-shifting liquid crystal materials. In collaboration with ICMS researchers Danqing Liu and Dick Broer, Van der Kooij and her supervisor Joris Sprakel reveal how in such materials an alternating electric field induces a hierarchical cascade of collective molecular rearrangements. This 'emergent collectivity' brings the nanoscopic movement of the liquid crystals into the macroscopic domain.

Key to Hanne van der Kooij's compelling findings is laser speckle imaging. It is based on the spatially random interference of scattered, diffusive photons, resulting in a so-called speckle pattern that resembles the 'no signal' screen of old-fashioned TV sets. At first sight, the seemingly random flickering image doesn't seem to contain any meaningful information - but nothing could be farther from the truth. "Laser speckle imaging is in fact an extremely sensitive method to detect minute deformations and minimal movements", says Van der Kooij. "By thus observing the dynamic surface of a material with nanoscopic resolution, it is possible to find out what's happening inside." For her PhD research supervised by Joris Sprakel of the Physical Chemistry and Soft Matter research group at Wageningen University and Research, Van der Kooij set out to investigate the drying of paint. "Water-based paints are very complex systems," she says. "They contain dozens of components that interact and evolve during drying, on time scales ranging from a fraction of a second to hours or even days. Also, paint is usually not transparent and extremely heterogeneous. Apart from laser speckle imaging, there is actually no technology that can map all that." Since this research was funded by the Dutch Polymer Institute (DPI), Van der Kooij attended a progress meeting at the institute. There she came into contact with ICMS researcher Dick Broer of the research group Stimuli-Responsive Functional Materials and Devices. Broer quickly saw the potential of laser speckle imaging for research into active liquid crystal networks. Van der Kooij explored this idea together with Danqing Liu from the Broer research group. After a few tests, it became clear that laser speckle imaging indeed held promises for elucidating the inner workings of the new liquid crystal materials on a nanoscopic scale.

ELECTRO-PLASTICITY

Van der Kooij talks with lots of enthusiasm about her research on the "amazing materials" made by Liu and Broer, consisting of hard and rigid polymer networks with liquid crystals embedded. Driven by an oscillating electric field, they can be made to soften locally and become rubbery. The process is reversible: once the field is switched off, they return to their rigid state. Liu and Broer are exploring the use for all kinds of active, self-cleaning and haptic >>

"I REALLY WANT TO TAKE THE TECHNOLOGY TO A HIGHER LEVEL AND STUDY ALL KINDS OF COMPLEX MATERIALS."

devices, for instance in the field of soft robotics. "It's just fantastic what they are able to achieve", Van der Kooij says. "However, it was not clear how these materials exhibit their 'electro-plasticity'. Of course there were ideas, models have been developed and simulations carried out, but experimental confirmation was scarce." This is where laser speckle imaging comes in. It can detect the high-frequency oscillations of the liquid crystals, as well as the much slower deformation of the polymer network. The custom-built setup in Wageningen records dynamic speckle patterns in a (sub-)millimetric frame using two cameras. One records continuous streaming at acquisition rates up to 200 frames per second (fps), the other records shorter sequences at acquisition rates up to 40,000 fps. The setup detects surface displacement at the nanometre scale. After data collection, the speckle patterns are analysed temporally, spatially and spectrally using a short-time fast Fourier transform approach.

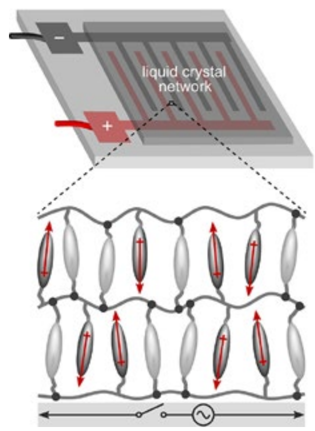
THREE DISTINCT STAGES

Van der Kooij's analysis revealed that the morphing of shape-shifting liquid crystal materials occurs in three distinct stages. At first, the molecular dipoles of the liquid crystals oscillate with the alternating field. This then leads to collective plasticization of the glassy network and ultimately culminates in actuation of the surface topography. These processes all differ in their timescale: the oscillation occurs in 10–100 milliseconds. Plasticization is a process of seconds, while establishing the surface topography typically takes 10–100 seconds. "You could say that the liquid crystals push the boundaries of the polymer material", Van der Kooij explains. "It is clearly their collective vibration which introduces the softening and deformation of the material. It introduces what is called a 'glass transition' in polymer technology. Normally, this requires much higher temperatures of 60–120 °C."

Laser speckle imaging thus provides insight into the operational mechanisms by which artificial shape-shifting occurs in liquid crystal materials. This in itself is a decisive result, but Van der Kooij can't wait to take the next steps. "I'd like to go from this rather fundamental level to a more practical approach. Resulting for instance in design rules to arrive at the best composition of the material and the optimal device architecture. There's a world to be explored with regard to optimizing and amplifying the emergent collectivity and shape-shifting response through tuning the molecular chemistry, the alignment of the liquid crystals and the architecture of the device."

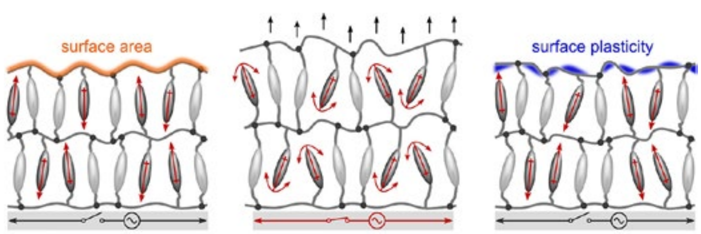
NOVEL INSIGHTS

Van der Kooij is currently continuing her work on laser speckle imaging as a staff researcher at the Physical Chemistry and Soft Matter group of Wageningen University and Research. "Laser speckle imaging is such an incredibly versatile technique, it can be applied to so many different issues! For instance, I expect it can be used to gain novel insights into other systems where the emergence of collectivity is key, for instance living biofilms — thin layers of micro-organisms embedded in a biopolymer matrix. I really want to take the technology to a higher level and study all kinds of complex materials. The possibilities are endless."

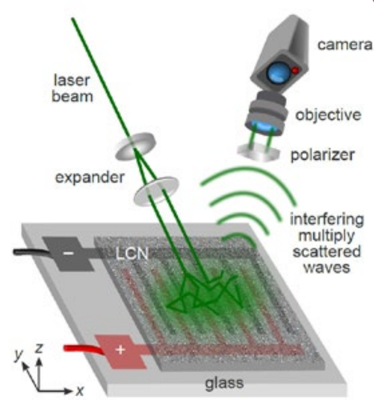


An LCN device (above) consists of a liquid crystal network coating patterned onto a glass support and provided with embedded interdigitated electrodes. Below a schematic zoomed-in cross section is shown of a homeotropically aligned LCN between two electrodes.

Schematic cross sections of a liquid crystal polymer network in the field-off state (a), after switching on a high-frequency AC field (b), and after field switch-off and relaxation (c).



The electric field drives the polar mesogens into oscillation, causing local network plasticization and expansion. After field switch-off, elastic displacements are restored yet plastic deformations (in blue) remain. The dimensions are not to scale.



Laser speckle imaging setup

ICMS and Studium Generale Eindhoven join forces in a series of thought-provoking events on complexity. The series will start in September with meetings about the spread of infectious diseases – especially about intervening in such a complex process.

An intellectual and cultural journey along the front lines of complexity science

Complex systems consist of numerous components with many mutual interactions. Such collective phenomena are found everywhere in nature, society and technology. The ICMS focus area ´Grip on Complexity´ aims to advance the foundations and applications of complexity science. The coming academic year, it will organize a series on complex systems together with Studium Generale Eindhoven. The events are meant to show and discuss how complexity connects scientific activities. They also offer an excellent opportunity to highlight what complexity science has to offer society in times of crises.

FOUR LECTURES, FOUR SEMINARS AND A BOOK

In the series, four leading scientists will come to Eindhoven to deliver a Studium Generale lecture to a non-expert audience, where they will talk about their strides towards getting a grip on complex systems. Each lecture will be followed by a 'Complex Friday seminar' organized within the ICMS Grip on Complexity focus area, facilitating a deepening discussion with experts. On Wednesday 30 September, Hans Heesterbeek (Utrecht University) will speak at Studium Generale about the spread of infectious diseases — and how to stop them. Shortly thereafter Nelly Litvak (TU/e) will examine this subject in a Complex Friday seminar at ICMS with experts from different disciplines. Students from the Honors Academy will be involved in this first lecture and use the input provided to shape their Honors projects within the recently established track "Networked Society". In the continuation of the series in November, the topic of energy and climate will be discussed. The events in February 2021 will turn to the stability of society. The series will close in June with meetings about mimicking life. For each subject, an inspiring paper will be prepared to put the research into a complexity perspective and to give the discussions depth and direction. These papers will be written by science journalist Bram Vermeer and Rutger van Santen, ICMS Fellow and former TU/e Rector. These papers and the discussions they provoke will be the basis of a book on complexity to be published in 2021.

THE RELEVANCE OF COMPLEXITY STUDIES

The ICMS focus area Grip on Complexity explores and exploits the similarities between the diverse scientific fields. Complexity scientists in different disciplines use the same techniques and the same tools. The methods for studying e.g. chemical reactions or networks also prove useful in very different situations — think of studying how fake news spreads through social media. Recently, this complexity analysis has also been applied to the study of the spread of the novel coronavirus in a network of human contacts.

There are other intriguing similarities between complex systems. Disruptive changes occur in many places — be it a tipping point in a chemical reaction or an uprising at the Paris Bastille. This also applies to, for example, evolutionary processes and resilience. Understanding these similarities provides a deeper understanding

"SUCH COLLECTIVE PHENOMENA ARE FOUND EVERYWHERE IN NATURE, SOCIETY AND TECHNOLOGY."

of instability. It also teaches how to achieve stability. It is telling that the eminent biologist Robert May was able to use his thorough knowledge of fragile ecosystems to assess the stability of financial systems. He analyzed the last economic crisis in a seminal paper in Nature, together with the chief economist of the central bank of the United Kingdom.

Ultimately, all complexity scientists face the same question: How can we intervene in collective phenomena? So: How do we stop a virus? Or: How do we push an energy system towards sustainability? How can we use biological processes to produce medicines? Classical, reductionist ideas about the effects of change do not work in such systems. Instead, there are ways of nudging, adaptation and dealing with uncertainty.

The lecture series will highlight how to get a grip on diverse forms of complexity. Together, the meetings form an intellectual and cultural journey along the front lines of complexity science.

In view of the corona pandemic, it is unsure if physical events will be possible. ICMS and Studium Generale are preparing ways to hold the meetings online, partially or completely.

Studium Generale TU/e

Theses

OCTOBER 2020 – MARCH 2020

On the impact of the mechanical environment in vascular tissue engineering: an in vitro study
ELINE VAN HAAFTEN
October 1, 2019
PhD advisors:
prof.dr. C.V.C. Bouten,
dr. N.A. Kurniawan

Dynamic covalent chemistry for UV curable networks
EVELINE MAASSEN
October 2, 2019
PhD advisors:
prof.dr. R.P. Sijbesma,
dr.ir. J.P.A. Heuts

Analysis of high capacity vehicles for Europe: application of performance based standards and improving manoeuvrability
KAREL KURAL
October 3, 2019
PhD advisors:
prof.dr. H. Nijmeijer,
dr.ir. I.J.M. Besselink

UV-cured polymer networks: from processing to properties
ROSARIA ANASTASIO
October 10, 2019
PhD advisors:
prof.dr.ir. G.W.M. Peters,
dr.ir. L.C.A. van Breemen,
dr.ir. R.M. Cardinaels

Influencing the photovoltaic properties and aggregation of diketopyrrolopyrrole based polymers via structural modification
GAËL HEINTGES
October 17, 2019
PhD advisors:
prof.dr.ir. R.A.J. Janssen,
prof.dr. W. Maes

Long-term performance of fibre-reinforced thermoplastics
LEONID PASTUKHOV
October 28, 2019
PhD advisors:
prof.dr.ir. L.E. Govaert,
prof.dr.ir. P.D. Anderson,
dr.ir. T.A.P. Engels

Computational analysis of polymer powder sintering for 3D printing
CAROLINE BALEMANS
October 29, 2019
PhD advisors:
prof.dr.ir. P.D. Anderson,
dr.ir. M.A. Hulsen

Look-ahead tracking controllers for integrated longitudinal and lateral control of vehicle platoons
ANGGERA BAYUWINDRA
October 30, 2019
PhD advisors:
prof.dr. H. Nijmeijer,
dr.ir. J. Ploeg,
dr.ir. A.A.J. Lefeber

Bioactive glass as bone graft substitute: in vitro assessment of the mechanical and biological properties
NICOLE VAN GESTEL
October 31, 2019
PhD advisors:
prof.dr. K. Ito,
dr. S. Hofmann,
prof.dr.ir. J.J.C. Arts

Supramolecular polymer chemistry and the active role of solvents in the molecular assembly
MARCIN ŚLĘCZKOWSKI
October 31, 2019
PhD advisors:
prof.dr. E.W. Meijer,
prof.dr.ir. A.R.A. Palmans

Computer simulations of the structure and dynamics of elongated colloidal particles
MARIANA OSHIMA MENEGON
November 13, 2019
PhD advisors:
prof.dr.ir.
P.P.A.M. van der Schoot,
prof.dr. C. Storm

Stabilization of protein-protein interactions as a drug discovery strategy: fragments as a muse
ELINE SIJBESMA
December 2, 2019
PhD advisors:
prof.dr.ir. L. Brunsveld,
dr.rer.nat. C. Ottmann

Responsive supramolecular self-assembly across length scales
MARIEKE GERTH
December 3, 2019
PhD advisors:
prof.dr.ir. I.K. Voets,
prof.dr.ir. R. Tuinier

Responsive photonic coatings based on semi-interpenetrating polymer networks
STIJN KRAGT
December 4, 2019
PhD advisors:
prof.dr. A.P.H.J. Schenning,
prof.dr. D.J. Broer,
prof.dr. G. Zhou

Particle manipulation with magnetic artificial cilia
SHUAIZHONG ZHANG
December 5, 2019
PhD advisors:
prof.dr.ir. J.M.J. den Toonder,
prof.dr.ir. P.R. Onck

Responsive photonic polymer coatings
ELLEN VAN HEESWIJK
December 10, 2019
PhD advisors:
prof.dr. A.P.H.J. Schenning,
prof.dr. D.J. Broer,
dr. N. Grossiord

DNA origami-based biomolecular organizing platforms
BAS ROSIER
December 12, 2019
PhD advisors:
dr.ir. T.F.A. de Greef,
prof.dr.ir. L. Brunsveld

Combinatorial and dispersion activity coefficient models for molecular solutions
GERARD KROOSHOF
December 17, 2019
PhD advisors:
prof.dr.ir. R. Tuinier,
prof.dr. G. de With

Delay-aware analysis and design of cooperative adaptive cruise controllers
HAITAO XING
December 18, 2019
PhD advisors:
prof.dr. H. Nijmeijer,
dr.ir. J. Ploeg

Fluctuating multicomponent hydrodynamics via the lattice boltzmann models
XIAO XUE
December 18, 2019
PhD advisors:
prof.dr. F. Toschi,
prof.dr. L. Biferale,
prof.dr. M. Sbragaglia

Torque on magnetic particles for biomedical applications
CHRISTIAN MOERLAND
December 19, 2019
PhD advisors:
prof.dr.ir. M.W.J. Prins,
dr. L.J. van IJzendoorn

Transient clusters and networks in isotropic and symmetry-broken dispersions of slender nanoparticles
SHARI FINNER
January 8, 2020
PhD advisors:
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dr. M.A. Miller

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PhD advisors:
prof.dr.ir. L. Brunsveld,
prof.dr.ir. J.C.M. van Hest

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January 15, 2020
PhD advisors:
prof.dr. G.H. Gelinck,
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ROMÀ SURÍS VALLS
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prof.dr.ir. J.C.M. van Hest

Engineering interactive artificial cells
BASTIAAN BUDDINGH
January 20, 2020
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prof.dr.ir. P.P.A.M. van der Schoot,
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February 11, 2020
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FUNCTIONAL SUPRA-
MOLECULAR SYSTEMS

Engineering Interactive Artificial Cells

PHD STUDENT BASTIAAN BUDDINGH CELEBRATES HIS DOCTORATE AND A NATURE COMMUNICATIONS PAPER

Bastiaan Buddingh

Early 2020, Bastiaan Buddingh obtained his doctorate with Jan van Hest on research into cellular interaction and collective behaviour of artificial cells. It has resulted in an appealing publication in Nature Communications showing communication of such cells over long distances. And there's more to come: publication of the thesis is still embargoed since a second high-profile paper
has been submitted for publication.

Buddingh's work is an important step towards the development of artificial cells displaying biologically relevant behaviour. "In life, interaction between cells is crucial," he says. "Organs, tissue, in fact living beings as a whole exist thanks to networks of interacting cells that are continuously monitoring and responding to their environment. So, in the study of artificial cells, at some point you have to pay attention to interaction and communication. That motivated my research: to go from individually functioning artificial cells to a collective of interacting artificial cells."

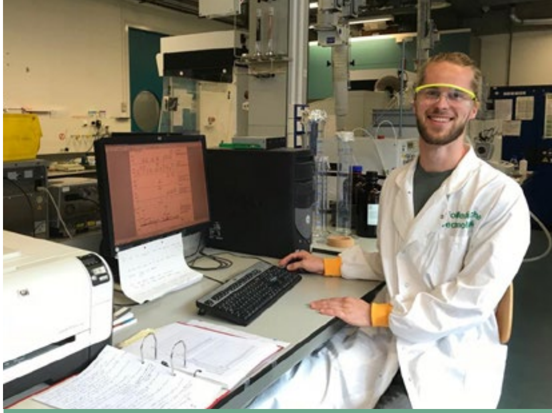
SMALL MOLECULE SIGNALLING

The publication in Nature Communications was based on one of the chapters in Buddingh's thesis where he applied a bottom-up engineering approach starting with a so-called Giant Unilamellar Vesicle (GUV). These are 'water bubbles' contained in a self-assembling phospholipid outer layer. In this layer, he introduced a protein enabling signalling molecules of AMP (adenosine monophosphate) to leave and enter the artificial cell. He then designed two types of cells, senders and receivers, each equipped with a particular enzyme system. The senders are capable of producing the AMP signalling molecules; the receivers process these AMP molecules.
"A special feature of the senders is that they require an external trigger with which we can experimentally start the cellular communication process. The receivers use AMP for the production of fluorescent NADH molecules, enabling us to observe the reception of the signal. Here the special feature is a signal amplification where every AMP molecule yields ten NADH molecules. This resulted in a very sensitive detection mechanism."

In his experiments, Buddingh was able to observe intercellular communication over distances of many cell diameters (see image). "I think we demonstrated the most advanced system of signal exchange between synthetic cells based on a small messenger molecule", he says. "Indeed, this is a very life-like way of cellular communication, adding to already existing artificial systems where larger proteins or DNA fragments are used."

MODESTY ADORNS

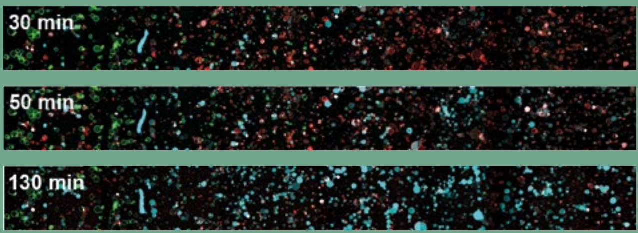
Buddingh underpins that his use of 'real-life' enzymes and signalling molecules yields an artificial cell that can be used to help understand real biological cellular signalling. It can also give rise to biomedical applications, for instance in the field of tissue engineering. However, he notes that it is not imperative to use biological components to produce artificial cells. "Many researchers build functional systems that show cell-like behaviour resulting from purely synthetic building blocks. And then there are materials scientists that are just using cells as an inspiration to work towards completely non-biological complex materials with novel applications.



The research of Bastiaan Buddingh was financed by the research center for Functional Molecular Systems (FMS), a partnership of the organic and macromolecular chemistry teams of the Eindhoven University of Technology, the Radboud University Nijmegen, and the University of Groningen.

So the field is quite divergent." Furthermore, although Buddingh's research is a significant step towards artificial cells that display actual 'biological' interaction, he points out that modesty is in order, particularly here. "We're really just at the earliest onset of building a real-life cell. I always joke to my family that there isn't any risk of my cells escaping from the lab, since they are still far from being 'alive'. It will take huge efforts to combine all what we now know about cellular design into the synthesis of a genuinely life-like artificial cell. I expect the use of artificial intelligence and big data to be instrumental in providing biologists and chemists the clues for building such a cell. But it's all so incredibly complex; there may still be a hundred years of research out there..."

Experimental results of the signalling between cells in a channel (length 5 mm) containing sender cells (green) and receiver cells (red). Upon receiving the AMP signal, the receivers produce NADH that lights up in blue. Signalling is activated at the left side of the channel. Over time, even the most distant cells can be seen to produce NADH.

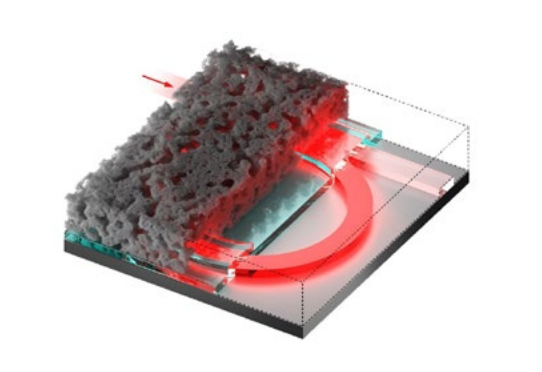


News, awards & grants

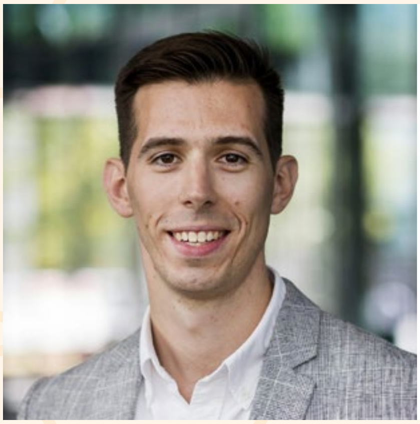
Unique polymer-based fabrication process for low-cost, higher yield reprogrammable photonic integrated circuits

The future looks bright for photonic integrated circuits (PICs) as they look destined for use in quantum computing and deep learning technologies. As PICs carry light signals rather than electrical signals, accurate control of their refractive properties is essential. Traditional techniques for programming photonic devices rely on exposure to light and heat. However, this leads to high power consumption and requires complex control circuits. Researchers from two different departments at Eindhoven University of Technology have developed a new and non-traditional polymer-based approach that significantly reduces the programming time and increases the programming possibilities for PICs. This could radically improve the fabrication yield of programmable PICs. The research has been published in Advanced Optical Materials.

Reprogrammable photonic integrated circuits (PICs) manipulate the path of data-carrying light signals and are made from materials whose refractive index can be changed. To maximize signal control and minimize optical losses, a robust, reliable and rapid method for making PICs is required. With this in mind, researchers from the department of Electrical Engineering (led by Mahir Mohammed and Oded Raz) and from the department of Chemical Engineering and Chemistry (led by Christian Sproncken and Ilja Voets) have developed a novel fabrication method for programmable PICs that involves coating photonic materials with polymers whose optical properties can be widely tuned in a matter of minutes using acidic solutions of varying pH. This is a new and unique approach for making programmable PICs as it involves the use of polymers and acidic solutions, rather than exposing photonic materials to light and then regulating the refractive properties using heat.



TU/e researchers from Electrical Engineering and Chemical Engineering & Chemistry combine their expertise in an innovative manner.



ICMS Fellow-ship for Alex Mason

We are very happy with the appointment of Alex Mason as ICMS Fellow for the focus area Chemical Biology as from December 2019.

TU/e shortlisted for € 35 million award for research on cardiovascular diseases

Carlijn Bouten (left) and Frans van de Vosse (right)

TU/e professors Carlijn Bouten and Frans van de Vosse are shortlisted to receive € 35 million award for two research projects on cardiovascular diseases. The award is the end-result of the Big Beat Challenge, a global competition from the British Heart Foundation. Together with researchers from other universities, Bouten and van de Vosse will work on the development of a soft robotic heart and a wearable technology to monitor heart function, respectively. Both teams will now start work on full applications, with a winner expected to be announced at the end of 2020.

Artificial skin heals wounds and makes robots sweat

Danqing Liu

Imagine a dressing that releases antibiotics on demand and absorbs excessive wound exudate at the same time. Researchers at Eindhoven University of Technology hope to achieve just that, by developing a smart coating that actively releases and absorbs multiple fluids, triggered by a radio signal. This material is not only beneficial for the health care industry, it is also very promising in the field of robotics or even virtual reality.

TU/e-researcher Danqing Liu, the lead author of this paper, and her PhD student Yuanyuan Zhan are inspired by the skins of living creatures. Human skin secretes oil to defend against bacteria and sweats to regulate the body temperature. A fish secretes mucus from its skin to reduce friction from the water to swim faster. Liu now presents an artificial skin: a smart surface that can actively and repeatedly release and reabsorb substances under environmental stimuli, in this case radio waves. And that is special, as in the field of smart materials, most approaches are limited to passive release.

EPL update

Inspired by the brilliant designs of nature

Catarina Esteves

Catarina Esteves works on smart surfaces. Nature inspires her to give materials self-healing and self-cleaning properties. She co-founded a company to develop textiles that extract water from the air. Perhaps a surface with a smart coating could kill viruses.

When we meet via a video call, Catarina Esteves has just given an online lecture to 160 students. The way people communicate has changed, but Esteves has adapted quickly. Researchers under her supervision are now prudently back in the lab to continue their studies of polymer coatings. Esteves follows their efforts closely, albeit from a distance.

One of her research topics concerns polymer coatings with special properties. These look like normal paint, but are not used just for protection or decoration. The coatings provide extra functionality. That´s why they are called functional or smart coatings. Some are easy to clean, or have low friction. They may provide a specific wettability — either superhydrophobic or superhydrophilic. "My interests often converge to how materials interact with water. Water is seemingly the simplest liquid we have. But from a chemical and physical point of view it is the most complex. In the past decades we have learned a lot about its interaction with other materials. Yet we still do not fully understand it."

COLLECTING WATER FROM THE AIR

Esteves also works on materials that can extract water from the air. "The inspiration comes from Nature. In dry regions, many animals and plants have no other source of water but humid air. For instance, the Namibian desert beetle collects water with hydrophilic and hydrophobic areas on its skin. It collects water droplets on the hydrophilic parts and these droplets roll along the hydrophobic parts towards its mouth. A few years ago I started to mimic this using thermal responsive materials that swell and absorb water vapor as it becomes colder in the evenings. They become superhydrophobic as it gets warmer again, and squeeze out the water." A prepared cotton fabric of a square meter could extract more than a liter a day from the air.

Esteves co-founded a company, aptly named Sponsh, to further develop these materials and bring them to the market, with a focus on providing water for reforestation. "Moist air is still largely unexplored as a water source. As the desert beetle shows, it provides a local solution to local water scarcity while other solutions interfere too much with the water cycle. People are pumping water in large volumes over huge distances, which deprives some areas from water and carries too much water to other places. This is energetically very inefficient, costly, and has negative consequences for Nature and for climate. Water is one of the biggest challenges to our society. We as scientists should help in inventing new approaches. We´d better learn a bit from Nature." The challenge is now to make the process more efficient. "We have gels and other materials that absorb a lot of water. But we cannot squeeze the water out completely, or only with a lot of energy. We need also to work on the recycling of these materials. In short, our materials are not efficient enough. To solve that, we are working on new functional groups that will further improve them. That's a challenge because we need to trick Nature and thermodynamics. Water prefers to stay in the vapor state."

SELF-HEALING MATERIALS

Smart surface layers are easily damaged. They are highly reactive and in constant contact with a liquid or with the atmosphere. Think about solar cells, solar panels or food packaging. Even small damages can rapidly reduce the performance of smart surfaces. They become less hydrophobic, less lubricious or less dirt repellent. This often means that the whole device needs to be discarded.

That is why Esteves is working on surfaces that repair themselves. Again, Nature is her inspiration. "If you cut the tail of a gecko, it will regrow. This, of course, is too complex to mimic. But some repair mechanisms of Nature are within reach. Some birds lubricate their feathers by coating them with oils that are segregated from glands. In much the same way, we develop surface layers that are replenished with materials from within. The idea is that small surface damages are immediately replenished by material transported from its interior. As a result, functional surfaces can maintain a high performance for a longer time." One of the difficulties is imparting a certain mobility to materials that otherwise need to be solid and stable. "There are quite a lot of strategies to realize this", Esteves says. "One of the applications we are working on is medical devices, such as pacemakers or inserts. They are in permanent contact with body fluids. Their surface needs to be hydrophilic or have a low friction. Often, they are also anti-fouling, you don´t want organisms to grow on them."

FIGHTING BACTERIA AND VIRUSES

Esteves also dreams about designing smart surfaces that could help fighting bacteria and viruses such as corona. "There are already quite a few anti-bacterial surfaces in the market. It would also be interesting to have an anti-viral surface. It would be very effective if these materials could self-repair once they are damaged. That would make them perfect for door handles, push buttons and toilet seats. That´s ambitious, but eventually ambition is the only way to move forward and fight the virus."

Catarina Esteves studied at the University of Aveiro in Portugal where she obtained her PhD in Nanochemistry. She spent research periods at Carnegie Mellon University (Pittsburgh, USA) and the University of Manchester (UK). Since 2006 she works at TU/e, currently as Associate Professor at the Physical Chemistry Laboratory.

ICMS Industrial Challenge 2019

ICMS fellow Alex Mason joined the ICMS Industrial Challenge (IIC) as a course facilitator in 2019. He reports on its "reboot" as a research-focused course for Master students, that had to finish prematurely due to the corona pandemic. And he looks forward to the 2020 edition

My first contact with the course coincided with the kick-off event in September, where our 3 industrial partners pitched their challenges to a captive audience of enthusiastic students. These industrially relevant problems were legitimately intriguing, and I was already looking forward to seeing what creative solutions the student teams would propose. Originally conceived as an open challenge mainly for PhDs and postdocs, the ICMS Industrial Challenge now has been "rebooted" as a course for Master students, earning them university credits. It takes the form of a group research project where student teams take advantage of the resources provided by both the ICMS and its industrial partners to develop novel, scientifically-sound proposals exploring each industrial challenge. The students, together with academic staff at the ICMS and industrial representatives, met every two weeks to share progress updates and brainstorm new ideas. Each team also had the opportunity to visit the industrial partners' production and research facilities, which provided unique insights into research outside the university setting.

Unfortunately, due to COVID-19, we were not able to hold the final event of the Industrial Challenge. Nevertheless, each team successfully developed a plausible strategy, and in some cases even performed some preliminary "proof-of-concept" experiments! We were genuinely impressed by the research that had been performed, and by the ability of the teams to think outside the box and really flex their creativity.

JOIN THE CHALLENGE
We have big plans for 2020, and are excited to grow the ICMS Industrial Challenge even more! This bilateral transfer of ideas between academia and industry makes the ICMS an exciting place to be, and if you're a Master student or an industrial partner looking to become involved, contact us at icms@tue.nl for more information.

THE ICMS INDUSTRIAL CHALLENGES 2019

DSM – design the next generation of biodegradable food packaging

SABIC – create new applications for cutting-edge polymer processing technology

Stahl – remodel the recycling of automotive leather towards a circular economy

Institute for Complex Molecular Systems (ICMS)

CREATING FUTURE TECHNOLOGIES BY MASTERING COMPLEXITY

Advancing the fundamental understanding of complex molecular systems in materials science, energy, mobility, health, and life is the main driver of the Institute for Complex Molecular Systems. It addresses research challenges and pushes the boundaries of science by unifying basic principles of chemistry, biomedical sciences, engineering, physics and mathematics.

Since 2008, ICMS creates and maintains a versatile and fruitful research environment to:

- Expand and diversify the ICMS expert network;
- Identify the underlying academic research questions;
- Enrich the scientific toolbox and infrastructure;
- Educate talented researchers in an interdisciplinary environment;
- Inspire researchers through industrial research challenges.

The relationship with industry is strengthened via the ICMS Industrial Consortium — where science meets innovation. Furthermore, ICMS hosts the Advanced Study Center that serves as an intellectual home to scientists from all over the world, hosting discussions on the theme of complexity.

The ICMS supports the research of TU/e scientists in seven focus areas:

- Polymer Science and Technology
  We connect the entire chain of knowledge from theoretical calculations to understanding structure-property relationships, to be able to design improved and novel polymers with desired material properties.
- Chemical Biology
  We follow a molecular systems approach to understand and modulate biomolecular networks for the design of new therapies and diagnostics.
- Grip on Complexity
  We push forward the foundations and applications of complexity science in its broadest sense.
- Advanced Analysis of Complex Molecular Systems
  We are building a state of the art characterization centre for the 4D-analysis of complex molecular systems at different length and time scales.
- Molecular Devices
  We adopt an integrative approach for the design and synthesis of hierarchically structured functional and responsive materials for functional electronic and adaptive devices.
- Materials for Regenerative Medicine
  We are aiming to regenerate tissue and organ function with intelligent biocompatible materials, using a materials-driven approach.
- Functional Supramolecular Systems
  We investigate the construction of functional life-like supramolecular systems to push the frontiers of supramolecular chemistry.

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

ICMS in PRESS

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EDITORIAL STAFF
Cindy Plompen (editorial assistant), Harm Ikink

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Bram Vermeer, Esther Thole, Harm Ikink, Valentina Bonito

PHOTOGRAPHY
Leonie Voets Imaging People, Vincent van den Hoogen, Jurgen van Hoof

SECRETARIAL SUPPORT
Wendy Brouwers, Cindy Plompen

CONTACT
Eindhoven University of Technology
Institute for Complex Molecular Systems
P.O. Box 513, 5600 MB Eindhoven
The Netherlands
Telephone: +31 (0)40 247 5074
Email: icms@tue.nl


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