Edition 22 June 2024

ICMS Highlights

IN MEMORIAM
ROELAND NOLTE

ROBOTICS DATA AND AI
WILL RATIONALIZE FORMULATION

COLLABORATING IN PIONEERING RESEARCH ON LIQUID-LIQUID PHASE SEPARATION

ICMS
INSTITUTE FOR COMPLEX MOLECULAR SYSTEMS
TU/e

INTRODUCTION

ICMS Highlights

Our society faces an imminent challenge to change our traditional usage of energy and materials. Although the call for such a transition will have a disruptive impact on established production processes, it will also present many exciting opportunities for scientists in our field of research. It allows us to put our creative minds to work and come up with breakthrough options for both academia and industry. These innovations, whether they involve new molecules, materials, or systems, hold the potential to play pivotal roles in shaping our future society. They can contribute to new value chains and empower industries to meet the demands of these evolving times. With our recently approved grants, Interactive Polymer Materials (Gravitation Program) and Big Chemistry (Growth Fund Program) we have already made a significant step toward developing solutions that fit these challenging times.

In the past six months community members have been successful on various fronts. Join us in congratulating:

- Tom de Greef and Ilja Voets for receiving the prestigious NWO VICI grant.
- Jan van Hest, our scientific director, for receiving the ERC Advanced Grant.
- The Department BME, who celebrates its 25th birthday this year. We appreciate the true partnership.
- Dick Broer who was awarded the title of Doctor Honoris Causa by the Universidad de Zaragoza.
- The PhD Outreach Committee and the ICMS Fellows for organizing successful events.
- The entire ICMS community with a successful Annual Symposium 2024.

Soon we will have a party to celebrate these beautiful accomplishments!

We hope you enjoy reading this edition.

Jan van Hest
Scientific Director

Monique Bruining
Managing Director

Colophon

Please check our website for our upcoming events.
www.tue.nl/icms

EDITORIAL
ICMS Highlights is the half-yearly magazine of ICMS for ICMS members, colleagues, collaboration partners, policy makers and affiliated companies.

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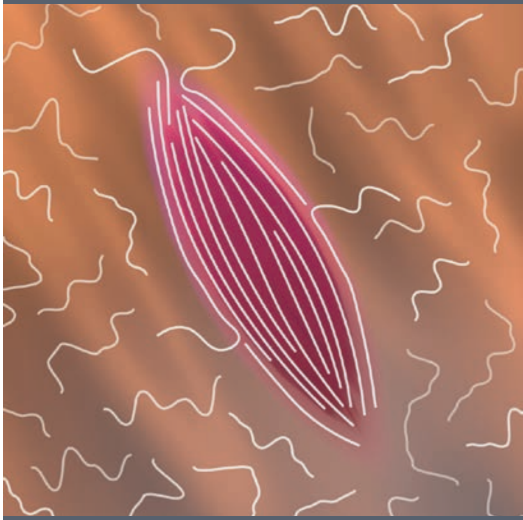

COVER "Tactoid sunset: an artists impression of tactoids in solution"

Content

Roeland Nolte

In Memoriam Roeland Nolte

"Kind, sweet and honest – one of the most talented chemists in the Netherlands"

On February 15, 2024, Roeland Nolte, professor of Molecular Nanotechnology at the Radboud University Nijmegen passed away. With him, the world of chemistry has lost one of the great pioneers of chiral synthetic polymers and a member of "The Golden Quartet of Dutch Supramolecular Chemistry." His merits, however, surpass the field of chemistry. He was above all a fine human being, an epitome of humility, a modest man with the ability to connect people and to make research groups thrive.

"Look there! That is Roeland Nolte, one of the most talented chemists of the Netherlands." Professor Bert Meijer vividly recollects as he alerted his wife upon encountering the scientist, many decades ago, who was shopping with his family in the center of Utrecht. Nolte was a lecturer at the University of Utrecht at the time, excelling in originality at the synthesis of complex molecular systems with an emphasis on stereochemistry. Nolte's research lies at the interface of organic chemistry and polymer chemistry. He published a brilliant thesis in 1973 entitled "Synthesis and isomerization of poly(isocyanides)." "He was the first in the world to make polymers that form a stable helix only turning either left or right. Thus, his name is connected to helical polymers for eternity," Meijer says. Further research topics of his include liquid crystals, catalytic supramolecular systems, self-assembling (macro)molecular systems and viruses, with applications in materials, drugs, information, and catalysis.

CHIRAL SYNTHETIC POLYMERS

Together with the professors Yoshio Okamoto from Nagoya and Mark Green from New York, Nolte first discovered and later developed the field of chiral synthetic polymers; arguably a Nobel Prize worthy accomplishment, although he himself would have been the first to brush that off. Meijer: "Maybe his modesty about his own accomplishments got in the way of this well-deserved recognition."

On that day in Utrecht, during his first sighting of Nolte "in the wild," Meijer was too shy to introduce himself to the man who was ten years his senior. A little later they got acquainted, started collaborating and became friends for life. "It felt as if he was my older brother. He introduced me to many top scientists as we travelled the world together – to the United States, Japan, and India. I remember a trip to Arizona to elaborate on the beautiful piece Roeland had just written for Science. He was stunned, when the editor he had corresponded not turned out to be the elderly woman with a pearl necklace he had imagined, but a very young woman with wild hair in torn jeans. We were even best men at the wedding of two German chemists in Bangalore. We travelled together so often, that many saw us as a duo. On top of that, I learned so much from him," Meijer concludes. Nolte became professor of Organic Chemistry in Nijmegen and Meijer, after a period at Philips and DSM Research, professor of Organic Chemistry at the Eindhoven University of Technology. Later they both also became part-time professors at the university of the other – becoming direct colleagues.

THE CONNECTING ELEMENT

Now let's flash back in time again. Nolte together with David Reinhoudt at the University of Twente had established supramolecular chemistry in the Netherlands. "Together with Ben Feringa in Groningen and myself we were engaged in a sort of friendly competition together, with each successful scientific publication of one pushing the others and their group to ever higher levels of accomplishment," Meijer relates. "This stimulation – not fueled by jealousy, but rather mutual admiration – each from his own specialization, brought the Netherlands to the world top in supramolecular chemistry." Groningen specializes in molecular switches and organic chemistry, Eindhoven in macromolecular and supramolecular polymers and Nijmegen has a position in between both. When the program "Zwaartekracht" (gravity) was launched as a major long term stimulation program for excellent research in the Netherlands, Nolte, Feringa, and Meijer decided to apply together for their own research and that of their colleagues. In the proposal writing and organization, there was a critical role for Jan van Hest, at that time professor in Nijmegen and now the director of our ICMS. Reinhoudt didn't participate as he had already retired at the time. Their application was granted in the first round, safeguarding their position in the field, and prolonging their mutual collaboration.

Meijer: "Without a doubt, Nolte was the connecting element. He was always ready to help and give consultation to others selflessly. More so, he stood for everyone else's interests and gladly gave the podium for others to shine. That is probably the most important thing I learned from him and attempted to replicate in Eindhoven: that is the way to build a team."

AMBASSADOR

After his retirement as professor of Organic Chemistry in 2010 he obtained a special chair in molecular nanotechnology at Radboud University Nijmegen, leading among other things to the publication "Clipping an angel's wings" in Macrocyclic and Supramolecular Chemistry in 2016. Almost until the end, Nolte went to the lab on a daily basis. He will be missed as a scientist and as a fine person. Science has lost one of its finest ambassadors.

LATER THIS YEAR ON OCTOBER 14 AND 15, A COMMEMORATIVE SYMPOSIUM WILL BE ORGANIZED BY WILHELM HUCK, BEN FERINGA, AND BERT MEIJER IN HONOR OF ROELAND'S CONTRIBUTIONS TO SCIENCE.

From left to right: Bert Meijer, Roeland Nolte, Ben Feringa

Silvia Lenaerts

Silvia Lenaerts
"Brainport region and TU/e uniquely positioned to take on the challenges"

The energy transition, the move away from fossil fuels towards sustainable energy sources, is front and centre in the media. The materials transition, however, arguably even harder to realize, has hardly been caught in the spotlight yet. Time for a change, says Rector magnificus Silvia Lenaerts of the Eindhoven University of Technology. "Collaborate with us. TU/e dispenses knowledge and technology to enable transitioning to more sustainable solutions based on advanced materials and complex molecular systems."

"THE FIRST STEP TOWARDS CHANGE IS TO RAISE AWARENESS OF THE OPPORTUNITIES"

She continues: "We should create innovation powerhouses to lead the materials transition by showing how we translate groundbreaking research into innovation in terms of new products, processes, organizations and business models. By coupling academia, research institutes, start-ups, large enterprises and policy makers we can create the future of a circular society in terms of energy and materials. The materials transition is a top priority for us because it strongly steers our geopolitical reliance on less trustworthy partners. Europeans are known to be forward-leaning consumers who prefer circular products and environmentally friendly alternatives. The regulatory environment could also be favorable for advancing the technologies necessary for a faster materials transition."

The urgency of the materials transition is at least as high as the urgency of the energy transition. "We should make the impact of the linear use of materials better visible," says Lenaerts. "For instance the landfills and textile and plastic waste dumps that we as humans have created are immense. The sustainability assessment of these materials should be more explicitly pronounced. As TU/e, with ICMS and EIRES we could demonstrate that we are leading innovators to make this crucial transition. The impact of non-circular materials on humans and the environment is huge and people don't realize this."

FUNDAMENTAL RESEARCH

Some novel materials offer a double whammy: they can at the same time serve the energy transition and the materials transition. Alternative anti-fouling coatings in the maritime sector, for instance, are less harmful to the environment and reduce drag, thus contributing to energy saving. Another example are self-cleaning coatings for use on solar panels. These coatings enhance the yield of sustainable energy systems.

TU/e starts from fundamental research on the foundations of complex molecular systems to enable the discoveries that are necessary. Lenaerts: "We need to understand the fundamental material properties in order to be able to relate them to functional and advanced characteristics. We aim for self-thinking molecular systems and interactive polymer materials and therefore we combine the expertise in design and synthesis, characterization and theory of material science and technology. In the field of engineering life there is also clear need for a more quantitative and engineering approach to better understand and regulate complex biological processes. For applications in sensing, diagnostics and regenerative medicine we are studying very promising concepts. We also have excellent research on functional advanced materials that act by themselves, without the need for external energy."

PERFECT STAGE

Not only are the materials complex, but so is their value chain. The roles of the various players in it are fuzzy. Who should take the lead in the materials transformation? Lenaerts: "I'm happy to provide some clarity in this situation: as TU/e we will actively take up the role of driver of innovation and we are looking forward to collaborate with parties that share our vision on the materials transition. Applications are never about materials as such, the material is used in high tech systems or other applications. We need to connect the different competences to our knowledge and technology."

"Not just the TU/e, but the wider Brainport region also provides a perfect stage for materials transformation projects," says Lenaerts. "This region is perfectly positioned to bring the high-tech elements in the materials transition. For example, the high-tech systems for waste stream separation aimed at dedicated recycling, or the materials design and manufacturing >>

of functional and smart coatings. Furthermore, design-to-recycle and high-tech manufacturing of components and systems needed for the transition are all highly developed here."

MULTIDISCIPLINARY APPROACHES

Lenaerts: "The first step towards change is to raise awareness of the opportunities. Sustainable engineering should be at the start of all development. The deep knowledge of the technical topics we have is also vital to this transition. We are also good at systems research, including Life Cycle Analysis (LCA) and innovation sciences including systemic change and design to inspire alternative concepts. Apart from that, we are uniquely equipped to point out where the bottlenecks for the materials transition are and to provide solutions for them."

The message here is that multidisciplinary approaches, combining chemistry, physics, and mechanical and bio-medical engineering complemented with new LCA and new business and organization models are necessary. Lenaerts: "This should help move away from partial solutions at one point in a supply chain towards systemic solutions for entire supply chains."

WIDE ARRAY OF APPLICATIONS

Having resented the general scope, now it is time for specifics. "Many concepts for a wide array of applications that could support industry in the transition have already been developed," Lenaerts explains. "Such as renewable raw materials for biobased and circular chemistry and of materials that help lowering energy consumption across the board. And then there are alternatives to rare earth materials to stimulate the renewable energy based system, for instance lithium alternative(s) for reduced use of iridium. Or of solar, pressure or movement powered materials."

An NWO Zwaartekracht grant has been awarded to the development of Interactive Polymer Materials. Lenaerts elaborates: "The goal is to move from one material for one purpose to materials with dynamic functions for multiple purposes, dependent on demand. That would allow for a smaller array of polymers in use, which would make polymer recycling much easier as well."
As to recycling, thermosets also still pose headaches. The Polymer Performance Materials group led by Željko Tomović tries to cure those headaches by developing chemically recyclable and upcyclable epoxy resins.

Some solutions are aimed at very specific demands. "Take for instance Yoeri van de Burgt's Neuromorphic Engineering Group, which is busy developing materials as building blocks for next generation low-energy computing and adaptive bio-interfaces, bio-chips, and organic electronics to answer medical challenges. Other medical specializations are materials for regenerative medicine, such as Patricia Dankers' hydrogels with tunable mechanical and dynamic properties and Keita Ito's biomimetic biomaterials which are highly specific and highly important."

"And last but not least we are also doing some tremendous research on PFAS," Lenaerts adds. "Toni Forner Cuenca, Thijs de Groot and colleagues are developing alternatives to PFAS which will be crucial for the development of electrolysers and fuel cells as vital elements in a more electricity based energy system. With these and other developments we are ready to engage in research programs as well as in one-on-one projects with industry and in consortia with other knowledge partners."

Key publications

NOVEMBER 2023 – APRIL 2024

01. A SIMPLE METHOD FOR DEVELOPING LYSINE TARGETED COVALENT PROTEIN REAGENTS
R. Gabizon, B. Tivon, R.N. Reddi, M.C.M. van den Oetelaar, H. Amartely, P.J. Cossar, C. Ottmann, N. London
Nat. Commun. 14, 7933 (2023)
DOI: 10.1038/s41467-023-42632-5

02. HALIDE HOMOGENIZATION FOR LOW ENERGY LOSS IN 2-EV-BANDGAP PEROVSKITES AND INCREASED EFFICIENCY IN ALL-PEROVSKITE TRIPLE-JUNCTION SOLAR CELLS
J. Wang, L. Zeng, D. Zhang, A. Maxwell, H. Chen, K. Datta, A. Caiazzo, W.H.M. Remmerswaal, N.R.M. Schipper, Z. Chen, K. Ho, A. Dasgupta, G. Kusch, R. Ollearo, L. Bellini, S. Hu, Z. Wang, C. Li, S. Teale, L. Grater, B. Chen, M.M. Wienk, R.A. Oliver, H.J. Snaith, R.A.J. Janssen, E.H. Sargent
Nat. Energy 9, 70–80 (2023)
DOI: 10.1038/s41560-023-01406-5

03. (1) MELT-EXTRUDED THERMOPLASTIC LIQUID CRYSTAL ELASTOMER ROTATING FIBER ACTUATORS
S.J.D. Lugger, T.A.P. Engels, R. Cardinaels, T. Bus, D.J. Mulder, A.P.H.J. Schenning
Adv. Funct. Mater. 33, 2306853 (2023)
DOI: 10.1002/adfm.202306853

04. SANDWICH IMMUNOSENSOR BASED ON PARTICLE MOTION: HOW DO REACTANT CONCENTRATIONS AND REACTION PATHWAYS DETERMINE THE TIME-DEPENDENT RESPONSE OF THE SENSOR?
C.M.S. Michielsen, A.D. Buskermolen, A.M. de Jong, M.W.J. Prins
ACS Sens. 8, 4216–4225 (2023)
DOI: 10.1021/acssensors.3c01549

05. SHAPE-MORPHING PHOTORESPONSIVE HYDROGELS REVEAL DYNAMIC TOPOGRAPHICAL CONDITIONING OF FIBROBLASTS
M. Bril, A. Saberi, I. Jorba, M.C. van Turnhout, C.M. Sahlgren, C.V.C. Bouten, A.P.H.J. Schenning, N.A. Kurniawan
Adv. Sci. 10, 2303136 (2023)
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06. TRANSPORT BY CIRCULATING MYELOID CELLS DRIVES LIPOSOMAL ACCUMULATION IN INFLAMED SYNOVIUM
J. Deprez, R. Verbeke, S. Meulewaeter, I. Aernout, H. Dewitte, T. Decruy, J. Coudenys, J. Van Duyse, G. Van Isterdael, D. Peer, R. van der Meel, S.C. De Smedt, P. Jacques, D. Elewaut, I. Lentacker
Nat. Nanotechnol. 18, 1341–1350 (2023)
DOI: 10.1038/s41565-023-01444-w

07. A MODULAR ORGANIC NEUROMORPHIC SPIKING CIRCUIT FOR RETINA-INSPIRED SENSORY CODING AND NEUROTRANSMITTER-MEDIATED NEURAL PATHWAYS
G.M. Matrone, E.R.W. van Doremaele, A. Surendran, Z. Laswick, S. Griggs, G. Ye, I. McCulloch, F. Santoro, J. Rivnay, Y. van de Burgt
Nat. Commun. 15, 2868 (2024)
DOI: 10.1038/s41467-024-47226-3

08. A RETROFIT SENSING STRATEGY FOR SOFT FLUIDIC ROBOTS
S. Zou, S. Picella, J. de Vries, V.G. Kortman, A. Sakes, J.T.B. Overvelde
Nat. Commun. 15, 539 (2024)
DOI: 10.1038/s41467-023-44517-z

09. ARTIFICIAL CELLS WITH VISCOADAPTIVE BEHAVIOR BASED ON HYDROGEL-LOADED GIANT UNILAMELLAR VESICLES
A. Llopis-Lorente, M.J.G. Schotman, H.V. Humeniuk, J.C.M. van Hest, P.Y.W. Dankers, L.K.E.A. Abdelmohsen
Chem. Sci. 15, 629–638 (2024)
DOI: 10.1039/d3sc04687g

10. AXIAL-EQUATORIAL HALIDE ORDERING IN LAYERED HYBRID PEROVSKITES FROM ISOTROPIC-ANISOTROPIC ^{207}PB NMR
M.A. Hope, M. Cordova, A. Mishra, U. Gunes, A. Caiazzo, K. Datta, R.A.J. Janssen, L. Emsley
Angew. Chem. Int. Ed. 63, e202314856 (2024)
DOI: 10.1002/anie.202314856

11. CONTINUOUS MONITORING BIOSENSING MEDIATED BY SINGLE-MOLECULE PLASMON-ENHANCED FLUORESCENCE IN COMPLEX MATRICES
V. Lamberti, M. Dolci, P. Zijlstra
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DOI: 10.1021/acsnano.3c12428

12. EFFECT OF SUB-BANDGAP DEFECTS ON RADIATIVE AND NON-RADIATIVE OPEN-CIRCUIT VOLTAGE LOSSES IN PEROVSKITE SOLAR CELLS
G.J.W. Aalbers, T.P.A. van der Pol, K. Datta, W.H.M. Remmerswaal, M.M. Wienk, R.A.J. Janssen
Nat. Commun. 15, 1276 (2024)
DOI: 10.1038/s41467-024-45512-8

13. ENHANCED EFFICIENCY OF PD(0)-BASED SINGLE CHAIN POLYMERIC NANOPARTICLES FOR IN VITRO PRODRUG ACTIVATION BY MODULATING THE POLYMER'S MICROSTRUCTURE
L. Deng, A. Sathyan, C. Adam, A. Unciti-Broceta, V. Sebastian, A.R.A. Palmans
Nano Lett. 24, 2242–2249 (2024)
DOI: 10.1021/acs.nanolett.3c04466

14. FACILITATING INTERSKIN COMMUNICATION IN ARTIFICIAL POLYMER SYSTEMS THROUGH LIQUID TRANSFER
D. Zhang, D.J. Broer, D. Liu
Adv. Mater. 36, 2312428 (2024)
DOI: 10.1002/adma.202312428

15. MECHANICAL ACTUATION VIA HOMEOMORPHIC TRANSFORMATIONS OF TOPOLOGICAL SOLITONS WITHIN POLYMER COATINGS
J. Peixoto, D. Hall, D.J. Broer, I.I. Smalyukh, D. Liu
Adv. Mater. 36, 2308425 (2024)
DOI: 10.1002/adma.202308425

16. PREDICTING BLOOD GLUCOSE LEVELS WITH ORGANIC NEUROMORPHIC MICRO-NETWORKS
I. Kurt, I. Krauhausen, S. Spolaor, Y. van de Burgt
Adv. Sci. (2024)*
DOI: 10.1002/advs.202308261

17. STIMULI-RESPONSIVE NANOSTRUCTURED VIOLOGEN-SILOXANE MATERIALS FOR CONTROLLABLE CONDUCTIVITY
B.W.L. van den Bersselaar, A.P.A. van de Ven, B.F.M. de Waal, S.C.J. Meskers, F. Eisenreich, G. Vantomme
Adv. Mater. (2024)*
DOI: 10.1002/adma.202312791

18. SUPRAMOLECULAR POLYMERS FORM TACTOIDS THROUGH LIQUID-LIQUID PHASE SEPARATION
H. Fu, J. Huang, J.J.B. van der Tol, L. Su, Y. Wang, S. Dey, P. Zijlstra, G. Fytas, G. Vantomme, P.Y.W. Dankers, E.W. Meijer
Nature 626, 1011–1018 (2024)
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19. SYNTHETIC DNA-BASED SWIMMERS DRIVEN BY ENZYME CATALYSIS
T. Patiño Padial, E. Del Grosso, S. Gentile, L.B. Pellejero, R. Mestre, L.J.M.M. Paffen, S. Sánchez, F. Ricci
J. Am. Chem. Soc. 146, 12664–12671 (2024)
DOI: 10.1021/jacs.4c02094

20. TURNING ANTIBODIES INTO RATIOMETRIC BIOLUMINESCENT SENSORS FOR COMPETITION-BASED HOMOGENEOUS IMMUNOASSAYS
E.A. van Aalen, J.J.J. Lurvink, L. Vermeulen, B. van Gerven, Y. Ni, R. Arts, M. Merkx
ACS Sens. 9, 1401–1409 (2024)
DOI: 10.1021/acssensors.3c02478

21. UREASE-POWERED NANOBOTS FOR RADIONUCLIDE BLADDER CANCER THERAPY
C. Simo, M. Serra-Casablancas, A.C. Hortelao, V. Di Carlo, S. Guallar-Garrido, S. Plaza-Garcia, R.M. Rabanal, P. Ramos-Cabrer, B. Yaguee, L. Aguado, L. Bardia, S. Tosi, V. Gomez-Vallejo, A. Martin, T. Patino, E. Julian, J. Colombelli, J. Llop, S. Sanchez
Nat. Nanotechnol. 19, 554–564 (2024)
DOI: 10.1038/s41565-023-01577-y

* Advanced online publication

Second ERC grant for Jan van Hest

Jan van Hest

Can artificial cells direct the development and function of biological tissue?

ICMS scientific director Jan van Hest, professor of Bio-organic Chemistry, was awarded an ERC Advanced Grant of 2.5 million euros for research into "Protein-regulated artificial cell populations and tissues." With this PRO-ARTIS project, he sets out to use artificial cells for directing and modulating biological processes with unprecedented precision.

The ERC grant adds to Van Hest's impressive record that shows appealing grants and awards, among which the coveted 2020 Dutch Spinoza Prize for outstanding and groundbreaking research. It also includes an earlier ERC Advanced Grant in 2016. The news of this ERC award got to Van Hest when he was in Canada for a work visit. Because of the time difference it reached him at night and despite his "experience" in receiving substantial funding, he could not go back to sleep.

WERE YOU THAT EXCITED ABOUT THE GRANT?

"Well, yes! I'm very happy because it provides significant opportunities to advance our research. And we're talking about a peer-reviewed award here. Surely that does a lot."

WHAT IS THE ERC PROPOSAL ABOUT?

"PRO-ARTIS builds on recent research where we have developed interesting concepts to efficiently move proteins from one artificial cell to another. We are now taking that to the population level, motivated by the fact that in biology many processes are governed not by the action of an individual living cell, but by the interplay between multiple cells. For instance, we hope to mimic the quorum sensing behavior of bacterial populations. When these cellular populations become dense enough, locally produced signaling molecules reach a threshold level that induces a response at the population level. We have developed artificial cells with a capacity for motility, and we are now going to try to make that dependent of the local cell density. We also aim to develop artificial tissue, where different cells each have their own function and interact with each other. That is more complex and requires bringing the artificial cells together in a structured manner."

WAS THIS WHERE YOU WANTED TO GO WHEN YOU GOT YOUR FIRST ERC IN 2016?

"Actually, we are already further along. At the time, the idea was to develop artificial organelles, small synthetic polymeric nanoreactors with which we aimed to add new functions to individual living cells. I had not expected that today we would already be able to create real artificial cells, so we can now move straight to the larger, more complex level of complete tissues. Over the past years, a series of PhD students and postdocs together with our permanent staff have shown how to create artificial cells based on the concept of coacervates: dispersed dense-phase droplets that form spontaneously from aqueous mixtures and provide stable compartmentalization without the need for a membrane. Currently, we are already researching protein-protein interactions in such artificial cells. We are even developing a cytoskeleton, which is crucial for taking the step towards tissue. Part of the work is being done in the major 'Gravity' research program Materials Driven Regeneration. There, for instance, we explore how to make artificial cells interact with living cells in a tissue engineering approach."

HOW WOULD YOU POSITION THE EINDHOVEN RESEARCH WITH RESPECT TO GLOBAL RESEARCH IN ARTIFICIAL CELLS?

"We have seen the field grow tremendously with lots of exploratory research in all sorts of artificial cell concepts. I do see a certain convergence towards nanovesicles and towards coacervates, where our focus is. I think you could say we are ahead resulting from our bottom-up approach where we explore super-molecular assembly to realize a particular function. We are particularly strong where it comes to 'synthetic creativity': we create new molecular concepts. Because we are able to publish these in well-read, leading journals, we see others picking up on that. And of course, this whole field is about mastering complexity, which is at the heart of ICMS. We are combining individual units – artificial cells – into larger systems and trying to design and control the emerging properties. Finally, I think a distinguished expertise of ours is efficiently transporting functional machinery from one cell to another in the form of proteins and enzymes. We are getting closer and closer to nature, where lots of cells also communicate with each other through proteins."

WHAT DO YOU ENVISION WHEN IT COMES TO THE APPLICATION OF YOUR RESEARCH?

"Fully artificial, autonomously functioning tissue could be used for devices that assist biological functions or produce and deliver drugs in situ. But that is really way ahead of us. On a shorter timescale, I think of placing well-prepared artificial cells into biological tissue to assist or enhance its function. In particular, we are aiming to direct tissue engineering using artificial cells. The current approach there is to take cells, possibly seeded into some three-dimensional carrier, add growth factors, and hope the right tissue grows out of all that. We think using artificial cells with the right functionalities can effectively 'instruct' the cellular environment to develop into a certain type of tissue. So, for instance by placing various artificial cells in different places in a cluster of stem cells, you could direct their development into specific tissues – blood vessels, kidney tissue, and so on – with a much higher degree of control. In general, I expect that using artificial 'instructor cells' in conjunction with living cells will enable us to direct and modulate biological processes with unprecedented precision."

An ERC advanced grant allows Keita Ito to set up a research project with revolutionary imaging and tissue analysis aspects. The project intends to finally answer the age-old question, what causes idiopathic adolescent scoliosis (AIS). The answer could open the gateway to improved treatment or even a cure.

Keita Ito

Explaining scoliosis: **Where imaging, orthopedics, computational modeling, biology and biomechanics meet**

For thousands of years now, AIS or "spontaneously arising, unexplained deformation of the spine in adolescents" has haunted about two percent of kids during their rapid growth period and thereafter. For some of the patients, braces help to correct the spinal deformation. In the more severe cases, surgery becomes unavoidable at some point.
"During the last couple of years, my orthopedic surgery colleagues at the University Medical Centre (UMC) Utrecht and I began to realize that the deformity doesn't originate from the vertebrae growing into a wedge, as was long assumed, but that this is preceded by wedging of the intervertebral discs," says Keita Ito, who has been studying intervertebral discs for more than fifteen years now. He is trained as both an orthopedic surgeon and a biomedical engineer and chairs the research group Orthopedic Biomechanics at TU/e / ICMS. His group combines engineering and biology to better understand the biomechanical function of musculoskeletal tissues to develop regenerative treatment strategies. He comments: "Our discovery was a step ahead towards unraveling the unknown cause of the disease."

OVERREACTION

The new finding was the basis for an ERC advanced grant, that thanks to Ito's dual appointment in both Utrecht and Eindhoven, could be split between imaging and clinical research in Utrecht and computational modeling combined with novel experimental approaches at Eindhoven. Ito: "We are working from an observation-based hypothesis. AIS occurs worldwide, during the peak of the adolescent growth spurt, with eighty per cent of it in girls. Significantly those with an early growth spurt. This could lead one to believe that disbalance between increased loading and tissue maturation might play a role. This is also supported by the fact that the incidence of spinal deformation in relatives of a scoliosis patient is thirteen percent as compared to two percent for the general population." This could point at a genetic factor and be related with early occurrence of growth combined with slower tissue strengthening. Ito: "The fact that it's an exclusively human problem also strongly suggests some other factors, for instance our upright posture and unique spinal anatomy. This upright posture necessitates that our spines have double curvatures, which causes some vertebrae to tilt backwards and become unlocked with each other. This might explain the predominance in girls, who generally have a more backwards tilted spine. Next factor is the growth plate, where a lot of biochemical activity is going on during the growth spurt. In other animals, the growth plate is located in the vertebrae, but in humans it sits directly on the disc. Now for the hypothesis: we think that the perfect storm of backwards tilted unstable vertebrae combined with a load that grows faster than the disc tissue can mature, causes micro-damage to stretched fibers in the disc, which – when combined with overstimulation by biochemical factors from the adjacent growth plate – causes the cells to overreact and respond by inappropriately remodeling the fibers into a misshapen form."

TURNING MRI INTO CT

Proving this hypothesis, however, poses some problems, as it requires, among other things, to study healthy kids – before the disease. X-ray and CT-scan imaging cannot be performed in healthy people. "Luckily 'Synthetic CT' can solve this," Ito comments. "It combines MRI with AI so that CT-like images can be derived from it: all the info you need without the radiation. In Utrecht we will apply this in partnership with the spin-off company MRI Guidance."
The clinical study includes two special interest groups, the first consisting of young girls with older siblings and/or parents with scoliosis. They will be followed as early on as possible. Ito: "This enables us to compare those with normal spine growth to those who develop scoliosis." The second group consists of children with DiGeorge Syndrome also known as 22q11 deletion sequence. "This syndrome has a wide variety of presentations, among them a fifty percent occurrence of scoliosis."

NOVEL IMAGING APPROACH

The acquired CT-like images are the starting point for a further process step, enabling to study the biomechanical aspects. To get to that, the images are fed into a computer model of the spine. Ito: "Generic spinal computer modeling is quite common, but in our approach we use the images to make specific models at age 9, 11 and 13 of all the girls included in the study, to closely follow what is happening at the tissue level. This could be key to finding the diseases' origin."
The study will have a huge scale for such a data-heavy approach. "We hope to include sixty healthy girls and also sixty patients with 22q11," Ito says. "During the study four or five scans will be made of each subject. A total of 500 to 600 specific spine models will therefore have to be generated. This is only feasible via an automated and proven accurate AI-driven model making approach."

EARLY

How do the discs'tissue properties change during growth from age 9 to 13? And does the gain in load increase faster than the material of the discs can mature? The answers might reveal the secrets of idiopathic adolescent scoliosis – but, yet again, finding the answers is challenging. Ito explains why: "We need tissue samples from children and of course these are not so easy to obtain. These have to be flown in from biobanks from all over the world. Special attention will go out to the disc and their adjacent growth plates. Does a situation of excessive strain indeed occur and what are the material consequences of that?" "Also, we will need to study the effect of growth plate morphogens on the remodeling discs. This, we will do in the lab but on animal tissues."
The combination of the approaches should be capable of telling the story of what happens in kids during their growth spurt – and what goes wrong when scoliosis develops. "Our approach is quite revolutionary as it spans a wide variety of fields: orthopedic surgery, radiology, biomechanics, computational modelling and biology. Some of the aspects of what we develop can be used in other areas, such as the imaging approach, the automated personalization of computational models and the in vitro platform we use for lab research. The imaging approach has already been adopted by some surgeons. But our hope is of course to attain the ultimate goal: to explain what actually happens during the development of scoliosis as a first step towards better treatment and ultimately a cure."

Big Chemistry in the RobotLab

"Robotics data and AI will rationalize formulation"

The recipe of your favourite shampoo or beer is probably a well-kept company secret. The Dutch Big Chemistry consortium, however, intends to reveal all secrets behind a perfect formulation using artificial intelligence. Soon, two "robot streets" will be up and running at ICMS's Ceres lab performing thousands of high-throughput experiments. "Robotics and AI are the future in chemical research."

"Recipes" for coatings, vaccines, wine or moisturizing cream are often based on decades of research and development, driven by experiments of developers with excellent fingerspitzengefühl. Wilhelm Huck, professor of Physical Organic Chemistry at Radboud University: "Hundred years ago, when new molecules were constantly/rapidly synthesized in large numbers, chemists did try to systematically correlate properties, such as solubility, smell, viscosity, surface tension, toxicity or stability, of mixtures to the ingredients' molecular structures. However, it turned out to be an unsolvable puzzle, because they are the result of many interactions between different components."

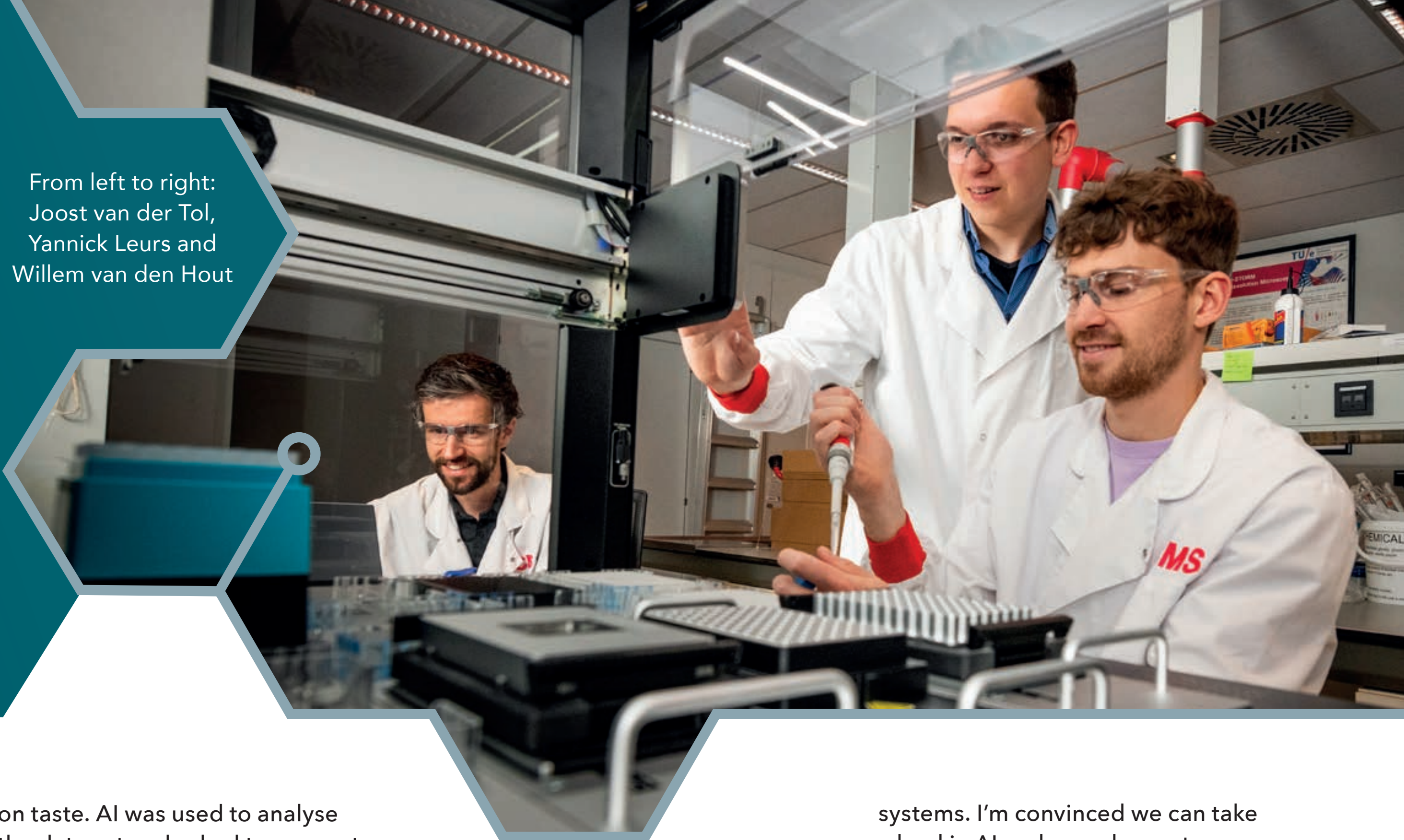
A well-trained, experienced chemist could probably predict correctly if a particular compound is soluble in water or not. Estimating how much of that compound will dissolve is already a game of luck . Even a Nobel prize winner's guess on, for example, the viscosity of a blend of three compounds will not be much better than seeking answers from the wheel of fortune.

That is why formulation never became a data-driven science but a more of an "art". Until now. "Artificial intelligence is a game changer," says Huck, who is the Scientific Director of the Dutch national research consortium Big Chemistry (see box). Big Chemistry is a large research initiative in chemical robotics combined with artificial intelligence (AI). "Autonomous" robots will be preparing and analysing huge numbers of complex molecular systems and use AI to get a grip on formulation's properties.

PREDICTING TASTE, TOXICITY, VISCOSITY, ...

AI has proven to be highly capable of finding correlations in (and "learn" from) in large data sets and use these correlations to make correct predictions. For example, ChatGPT can generate texts after "studying" an immense amount of sentences and the algorithm behind AlphaGo can beat professional go-players after "analyzing" millions of games. Big Chemistry will use AI's strength in finding correlations between complex molecular systems and their composition.

Huck refers to a recently published AI-study on "better beer" from Leuven University as an example of what the result will be. "The group gathered data on 250 different Belgium beers. Data about the almost 200 ingredients and expert reviews



From left to right: Joost van der Tol, Yannick Leurs and Willem van den Hout

on taste. AI was used to analyse the data set and asked to suggest potential improvements. Following the recommendations, the scientists indeed succeeded in improving the taste, according to beer sommeliers. That's exactly how we will proceed, but with a much broader scope. Big Chemistry is about all kinds of complex molecular systems; and not just about taste, but analyses all kind of properties, simultaneously."

High-throughput experiments performed by fast, diligent robots will produce mass data on complex molecular systems. This happens at three different locations, including the Eindhoven ICMS lab. Multiple "robot streets" or platforms prepare thousands of different well-defined formulations and determine their properties. Using AI, a platform can be programmed to work "autonomously" so as to create formulations with desired properties through new experiments. "However, we start from scratch," emphasizes Huck. "We need to generate all necessary data, train AI and figure out how to do that."

A visit to the Eindhoven robotics lab shows the brand new start. Project-leader Joost van der Tol, can only point out the spot where a platform will be placed for studying "paint-like" dispersions and their respective coatings. The equipment has been ordered, and Van der Tol is following an online course to learn the basics of AI. It is a completely new field of expertise for the physical organic and polymer chemist, he admits. "However, that's no problem, I'm eager to learn. Robotics and AI are the future in chemical research. Not only because of their potential to rationalize formulation, but also because of the ever-accelerating discovery of new materials and products."

OUT OF THE COMFORT ZONE

The Big Chemistry consortium is supported by the Dutch National Growth Fund (Groeifonds). Not a typical supporter of academic research, Huck notes. The Growth Fund supports innovations that hold a promise to produce the next "ASML." Is that a realistic prospect for Big Chemistry? Huck: "The Netherlands have not spawned companies such a Google, Microsoft or Alphabet. However, we are a world leader in the chemistry of complex molecular systems. I'm convinced we can take a lead in AI and complex systems, but that requires stepping out of our comfort zone."

Once the robots and analytic equipment is up and running, Van der Tol will start collecting data on coating formulations in a partnership with the Dutch coating industry. Van der Tol: "The chemical industry needs to switch to non-fossil based raw materials before 2050. Usually, it takes a team of developers five to ten years to switch a solvent in a particular paint and achieve the same performance. With AI we may shorten the research and development phase to one or two years. Although the solvent is an important component, it's just one of the many ingredients that often needs to be replaced. Meeting that deadline is a challenge." "Often AI is pictured as a black box technology," continues Van der Tol. "That is correct in the sense that an algorithm doesn't tell you why a change in formulation leads to particular properties. However, AI can guide itself to the 'borders' of the chemical landscape it's working in: the most interesting areas where properties change. Since there are easily as many as ten parameters we can play with in formulations, >>

Wilhelm Huck

we need AI's directions. From its results we can distil new fundamental insights."
Van der Tol intends to start collecting data from well-performing coatings and study what happens when changes are introduced. Which may seem like dedicated studies, but results will be useful for different complex systems, too. "Because we correlate properties to molecular structures," explains Van der Tol. He will be acting as the contact person for all business partners who are interested in the Big Chemistry consortium in Eindhoven.

MEMBRANELESS ORGANELLES

At the Eindhoven robotics lab another platform is being assembled by a couple of PhD candidates – Willem van den Hout and Yannick Leurs. Both hold a master in Biomedical Technology, and their goal is to understand "condensates." In nature, proteins can self-organize through a process called phase separation and form three-dimensional, dynamic, gel-like structures. These are called condensates or "membraneless organelles" and are crucial to the organization of cell chemistry. Leurs: "They are formed in particular circumstances. In stress situations, for example, all non-essential RNA gets stored in a condensate as a survival strategy. It allows the cell to concentrate on producing essential proteins only."

Van den Hout is particularly inspired by a correlation between condensates and health conditions. A common gene variant in people with autism, for example, appears to halt the disassembly of condensates. Van den Hout: "One of the most defining properties of condensates is that they are dynamic. Some are pretty stable, but others are more fleeting. It is fascinating that this process may also play an important role in ailments."

Leurs: "Until now, it is a kind of art to create a condensate. We want to know how to make them and how to tune their size, shape and stability." The PhD students will work with proteins known to form condensates, but also with synthetic polymers, DNA or RNA. "There are numerous options, that's why robotics and AI are so important for these studies." Using trays with 384 tiny wells their robot will study the properties of thousands of mixtures.

What results do they dream of? Van den Hout: "It would be great to make a discovery or create a research tool that can result in a startup company. That's also why this consortium has been established: to stimulate new economic activities." Any particular ideas in mind? "I'm highly interested in possible pharmaceutical applications, but actually the potential range of applications is extremely wide. The dynamic shuttling of biomacromolecules towards and from condensates is related to disease, but poorly understood. Therefore, our research into the principles behind these dynamics may one day result in medicines." Leurs agrees: "Dynamic compartmentalization is a fascinating phenomenon. However, getting a grip on it, is a true challenge. Let's focus on that ambition first, after that we can start dreaming."

big chemistry

BIG CHEMISTRY IN THE ROBOTLAB

The National Growth Fund granted the Dutch research consortium "Big Chemistry" ninety million euros in the coming seven years (2023 - 2030). The research initiative must position the Netherlands as a global leader in chemical robotics combined with artificial intelligence.
Currently, the consortium is starting up an autonomous "RobotLab" at which large numbers of experiments will be carried out, providing huge datasets on the properties of complex molecular systems. On the basis of these data, AI will be able to predict properties of complex molecular systems such as solubility, phase separation, critical micelle concentration, smell, toxicity or viscosity which would be a leap forward in chemistry.
The consortium is formed by research groups from three Dutch universities: Radboud University, Eindhoven University of Technology and Groningen University. It is supported by Fontys University of Applied Science and the physics institute AMOLF. The RobotLab will consist of various platforms that are currently built at three locations. In Eindhoven robot streets are built for studying coatings, condensates and hydrogels.

More information: **www.bigchemistry.nl**.

Designing, understanding, and controlling soft robots

Brandon Caasenbrood

Soft robotics is an upcoming research field. Robots are normally made from rigid and heavy materials, making them vulnerable to collisions and impacts. Soft robots, which are made from less rigid materials, are less vulnerable. And they can move and interact in ways rigid robots cannot. That makes them interesting for applications ranging from healthcare to agriculture. In his PhD research, Brandon Caasenbrood looked at new approaches to design, model, and control soft robots. He received his PhD degree with the distinction cum laude at the Department of Mechanical Engineering this January.

In his public PhD defense presentation Brandon Caasenbrood showed a flexible, rubbery structure that moves like an elephant's trunk, gently grabbing and moving objects. Caasenbrood first learned about soft robots during his master's project in 2015. "Sasha Pogromsky, assistant professor at the Mechanical Engineering Department at TU/e, had an idea for a soft robot with sea urchin-inspired locomotion. It seemed ambitious, yet really interesting." Caasenbroods interest grew in the next years. In 2018 he started his PhD research in soft robotics within the NWO Perspectief program "Wearable Robotics," with supervisors Pogromsky and Henk Nijmeijer – emeritus professor at TU/e.

"Soft robots have some advantages over classic, rigid robotics," says Caasenbrood. "They are less likely to harm themselves or their environment. The production, via casting silicone or 3D printing, is cost effective. And most importantly: they move and interact in ways rigid robots cannot. For example, they can squeeze through narrow spaces like an octopus." As a result, they possess great potential for applications in healthcare, manufacturing, agriculture, and robotic exploration.

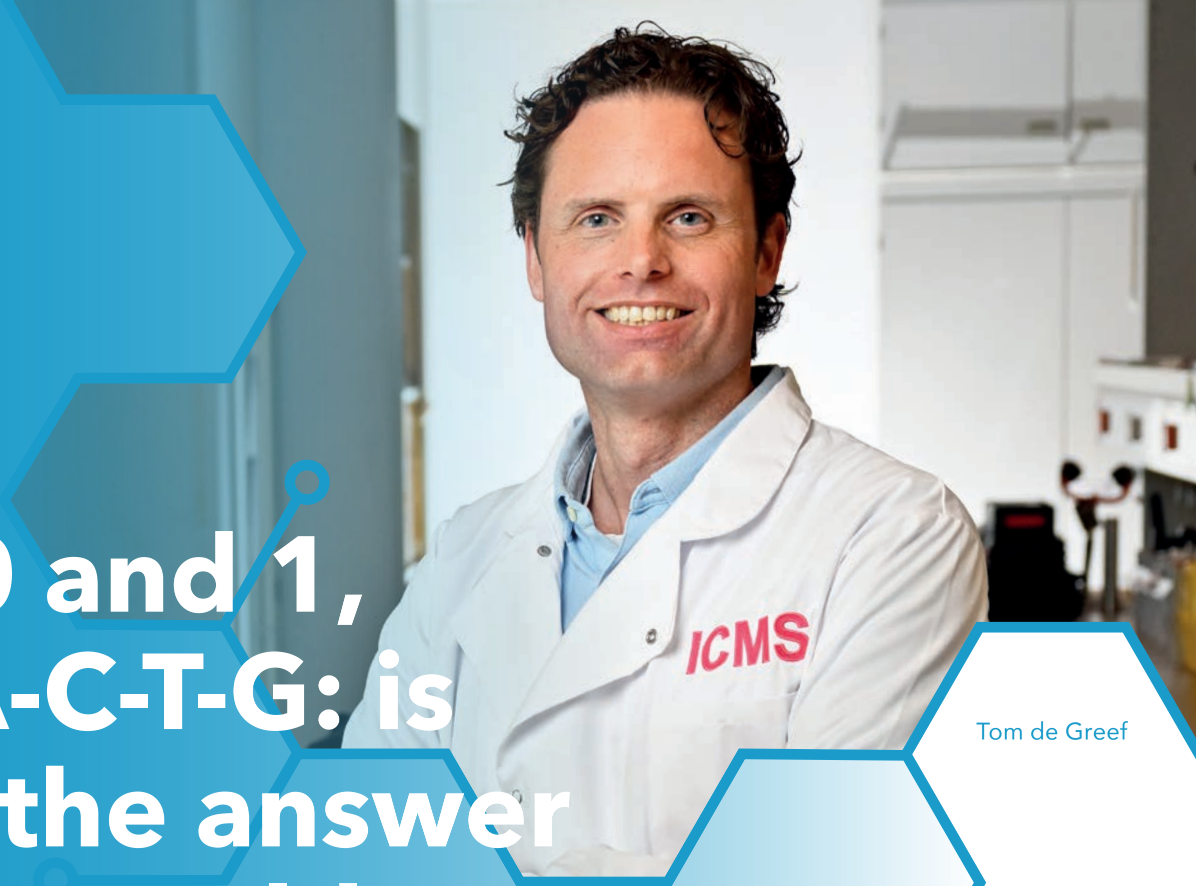
MODELS AND TOOLKIT

Despite these advantages and the first soft (McKibben) actuator being developed as far back as the 1950s, their applications remain limited. Soft robotics lags behind traditional robotics in academic and industrial advancements. "There are challenges for which you need a multidisciplinary approach," says Caasenbrood. "For example, you should take material properties into account when designing the control. Classical controller designs made crude assumptions about materials. That becomes a problem when you work with complex, soft materials."

During his PhD Caasenbrood worked on new approaches to soft robotics. Firstly, he developed algorithms that design soft robotic actuators using numerical optimization. "These algorithms account for material properties. Based on desired motion behavior, like bending or grabbing, they can generate blueprints for soft actuators that can be 3D printed."

Secondly, he developed a computer model that predicts how soft robotic arms deform in response to activation. "It can be used for model-based controllers which can imitate nature. For example, we showed that the interaction between an energy-based controller and the soft structure of a robot can produce complex movements similar to the flexible arms of an octopus."

Finally, Caasenbrood combined the multidisciplinary approaches in a user-friendly software tool called Sorotoki (Soft Robotics Toolkit), which different disciplines can use. "The community seems interested. I currently support researchers from different universities to see how Sorotoki fits their needs. Hopefully Sorotoki will grow over time and become useful for many soft roboticists."



Tom de Greef

Not 0 and 1, but A-C-T-G: is DNA the answer to the world's data storage deficit?

What to do when the world's storage limit is inevitably reached? Perhaps learn from nature, and store information in DNA. Tom de Greef wants to explore the molecule's potential as a data storage device, with plenty of upsides: it is durable and has an exceptional data density. Recently he was awarded a VICI grant to further pursue this trajectory. There are challenges, but also reasons to be optimistic.

The world is facing a data storage problem. Data is being generated at an unprecedented rate, and assuming this trajectory will be continued, there is a risk of running out of storage capacity by 2030.

With this problem in mind, DNA has captured the attention of researchers like ICMS's Synthetic Biology professor Tom de Greef. Like some prebiotic lifeform must have figured out four billion years ago: there may be a future where DNA serves as the ultimate storage medium. Science is just late to the party.

Traditional storage mediums, such as hard drives and magnetic tapes, are becoming too expensive, too big and unsustainable. "The need for data storage surpasses what we can achieve with existing methods," De Greef explains. The world is currently storing an estimated 80 zettabytes – a zettabyte equals 1021 bytes, or a billion terabytes. "We are on the way of reaching 180 zettabytes in 2025. And five years later, it looks like we may not be able to

“DNA OFFERS A DURABLE SOLUTION FOR LONG-TERM DATA PRESERVATION”

store half of our data. We need to explore new avenues for storing data efficiently and securely.”

To further rediscover DNA’s capabilities as a storage “device,” De Greef was recently awarded a prestigious VICI grant – after already having received the VENI and VIDI grants in the past. He was not alone in receiving a VICI: ICMS colleagues Rudie Kunnen and Ilja Voets received one as well.

So why DNA? First and foremost, De Greef points to the exceptional information density of the molecule. “DNA offers the highest data density of any known medium. Compared to traditional storage mediums like hard drives, DNA’s storage density is fifty million times higher. It is even billions of times higher than that of magnetic tape.”

Furthermore, one of the key advantages of DNA storage lies in its longevity. Unlike magnetic tapes and hard drives that degrade over time and need replacement every twenty years, DNA can remain stable for thousands of years when stored properly. “DNA offers a durable solution for long-term data preservation,” de Greef emphasized.

The limitations of the data storage technology on which Big Tech currently relies, have become vastly apparent in the Dutch province Flevoland in recent years. After years of regional and later national political debate, plans to build a large data center near the small town Zeewolde were finally nullified. Opponents pointed to a lack of space in a densely populated country, and estimations of the center requiring twice as much electricity as the city of Amsterdam.

Despite its promise, the widespread adoption of DNA data storage faces significant hurdles, particularly regarding cost. The synthesis of DNA is very expensive, de Greef notes, but there are reasons to be optimistic. “Advancements in DNA synthesis technologies are driving down costs, making DNA data storage increasingly viable. The last ten years, the costs have been decreasing exponentially.”

Within this technology, information is not stored through binary code, consisting of zeros and ones, but by the four nucleotide letters that DNA consists of: A, C, T and G. DNA is stored in little wells, in which mutations are prevented. De Greef’s team has achieved an efficiency in reading DNA data with a precision rate of 99.5 percent. And because of DNA’s stability, hardly any energy is needed to maintain the data. Only writing and reading requires energy. The latter aspect is perhaps the biggest limitation of DNA as a data storage device. Do not expect to use this technology to take a quick glance at your holiday pictures: retrieving data from DNA molecules involves complex sequencing processes that can be time-consuming and impractical for everyday use.

Instead, it’s more suitable for archival storage – or “cold data,” in the words of De Greef. It refers to stored information that must be accessed about once or twice per year, but no one needs to see on a daily basis. “Actually, a lot of data is ‘cold’. After six months, approximately 60 percent of the data we generate is already cold. We do not need it most of the times, but we do need to know it’s lying somewhere.”

De Greef now wants to intensify his work on the writing and reading aspect. A recent Nature Nanotechnology paper focused on “parallel random access,” which would make accessing data much more efficient and less time-consuming. Essentially, it’s about efficiently extracting data sequences from DNA in parallel and simultaneously, significantly reducing retrieval time. This could pave the way for more practical and widespread adoption of DNA as a data storage medium, bridging the gap between the for now theoretical potential and hopefully a real-world applicability.

For De Greef, the appeal of working on DNA storage lies in the intersection between fundamental science and its practical applications. He aims to perform the kind of “inspired basic research” as a quest for fundamental understanding, while also having considerations of its use in mind. “Honestly, you cannot know whether DNA data storage is going to work out. But it’s really about the idea, just like someone in the 60’s may have had an idea for artificial intelligence – while doing purely fundamental research. I love working with fundamental questions, and that is how I view my work as well.”

Unraveling material-ice interactions for better preservation

Ilja Voets

Freezing is not a perfect preservation method. If you ever had a frozen meal, you know some structure and flavor is lost. And researchers who work with cells and tissues see a large portion of it waste away every day because of this storage procedure. Ilja Voets, professor at the Department of Chemical Engineering & Chemistry, will use her NWO Vici grant to study and develop ice-binding materials to minimize freeze-thaw damage in foods, cells and even donor organs.

Voets became interested in ice formation and ice-binding materials when she read a paper about snow fleas that can survive the cold winter months because they have a specialized, ice-binding protein that binds to ice crystals. “Most compounds do not bind to ice. Instead, they are pushed away by a growing ice front when ice forms, so that ice remains predominantly pure,” explains Voets. “That sparked my interest. Why do ice-binding proteins defy those odds and how do they bind to ice?”

KNOWLEDGE GAP

When delving into the literature, Voets discovered that these ice-binding proteins were studied from a cryobiology and ice physics perspective, but a molecular picture of the interaction between ice-binding proteins and ice was missing. “An impressively diverse spectrum of ice-binding proteins had been discovered in animals and plants and their impact on ice growth had been explored with a particular focus on the implications for the survival of their host under extreme circumstances. However, no one had studied how such a small protein can bind to ice and how it impacts or even completely stops ice growth.”

In 2011 Voets decided to fill this knowledge gap together with her new research group at the TU/e. Her background in soft matter science and physical chemistry from Wageningen University & Research and her experience in protein biophysics and advanced in-situ experimentation at the University of Fribourg in Switzerland, made the topic a perfect fit.

Over the past 13 years Voets' research group has become one of the leading teams in the field. New research lines were added to the portfolio which now focuses on structure-activity relations of native ice-binding proteins and on the development of new materials that emulate their functioning. "The goal of the Vici grant is to unravel the mechanisms governing the interactions between synthetic ice-interactive materials and ice," explains Voets. "And to build on this knowledge to design ice-interactive materials that we can tailor to function as we desire and to minimize freeze-thaw damage in diverse settings, such as frozen foods, cell banking, porous materials like concrete, and beyond."

"WITH THIS UNIQUE MOLECULAR LEVEL VIEW, WE CAN NOW UNRAVEL HOW THE ICE-MATERIAL INTERACTION DEPENDS ON MATERIAL STRUCTURE AND COMPOSITION"

PIONEERS

"To develop new ice-interactive materials we need to understand how material properties, like shape, composition and size, impact the material-ice interactions," says Voets. In recent years we learned from experiments, computational studies, and novel theoretical frameworks that the structure and surface chemistry of ice-interactive materials play an important role in the formation and growth of ice crystals. "But what we really needed was missing: a library of materials with sufficiently large variations in the relevant properties and a means to study their interaction with ice at the single molecule level."

Last year, the group achieved one of these grand challenges through the world's first on-ice high-resolution imaging of ice-binders. Using super-resolution microscopy, Roderick Tas and Voets tracked the movements of individual proteins and identified specific ice-binding proteins that appeared completely stuck on ice and others with higher mobility. "With this unique molecular level view, we can now unravel how the ice-material interaction depends on material structure and composition. So far, we have studied ice-binding proteins with super-resolution microscopy, but in this new research program we will develop and study completely new, engineered materials instead. These are inspired by ice-binding proteins, but much larger and composed of entirely different building blocks."

ICE-BINDING COLLOIDS

Why develop new materials that mimic ice-binding proteins when nature provides them for you? "Firstly, these proteins are very sensitive. The three-dimensional fold that is essential for their activity is easily lost, for example due to a modest increase in temperature. Secondly, the proteins are not widely available nor inexpensive," says Voets. "Most importantly, we want to understand how to tune the hallmarks of ice-interactive materials, such as freezing point depression, ice nucleation, and inhibition of ice recrystallization, independently." By designing materials ourselves, we aim to tailor the activities of ice-interactive materials to match application-specific demands.

An example of an application is the preservation of products, like food or tissue, through freezing. This often leads to a loss of quality. "The extent of damage varies greatly. It is dependent on the freeze-thaw protocol, the preservation medium, and it seems related to the subzero temperature at which ice crystals first appear," explains Voets. "Damage may be significantly reduced when ice formation occurs only a few degrees instead of tens below zero degrees Celsius. This is likely due to a reduction in thermal and osmotic gradients, which may induce internal stresses from which food products and patient-derived tissues may not recover."

"In this new research program, we will build colloidal materials that can regulate both ice crystal formation and growth. We hope that these will improve cryopreservation, so that food remains tasty for longer time and banking of complex tissues becomes possible."

INTERDISCIPLINARY

The fascination of thirteen years ago is still very much alive. "One of the things that I enjoy most is the multi-faceted and interdisciplinary nature of this research." Within the Freezing Hearts consortium, an Alliance between Eindhoven University of Technology, Utrecht University, the University Medical Center Utrecht, and Wageningen University, we explore the potential of these materials for regenerative medicine. Together, we are striving to improve cellular, tissue, and organ preservation strategies. I find these collaborations especially fulfilling as they enable us to achieve far more collectively than we could within the boundaries of our individual disciplines."

ICMS Annual Symposium 2024

Bram Bakker

Jules Boesveld

Sofia Artamonova

ICMS Highlights Magazine Science Communication Winners

The ICMS Scientific Skills Course is ran annually for PhD students. Covering a broad range of topics, the purpose is to give the next generation of PhD students skills that they can develop and carry with them throughout the course of their careers. One such skill is scientific communication, where the students submit a competition abstract. A panel of postdocs based within ICMS judge these, and the winners are awarded the opportunity to present at the annual ICMS Symposium.

Having taken place back in March the ICMS Symposium included talks from Sofia Artamonova, Bram Bakker and Jules Boesveld as the winners of the Science Communication: To the point competition. We caught up with all three to get their stories, science, and reflections on both the ICMS Scientific Skills course and the Symposium. >>

Originally having obtained her Bachelor's degree in Biomedical Engineering back home in Russia, **Sofia Artamonova** moved to New York University to pursue her Master's degree. The multi-disciplinary international environment really suited her and with some experience working within a hospital environment as part of her internship, she returned home to pursue further research. However, her experiences in the US led to her looking away from home again for a PhD position and having applied to several, TU/e offered the right mix of translational hot topics to pursue. As part of Carlijn Bouten's Soft Tissue Engineering & Mechanobiology group, Sofia's main aim is not actually the topic she wrote about for the purposes of the competition. Having realised that this was a good opportunity to strengthen a perceived weakness, Sofia used the opportunity to improve her communication skills with the project she is least confident in, building her skillset and gaining more confidence by disseminating the project. The project she presented at the ICMS Symposium concerns macrophage polarisation, or rather how the microenvironment they are in impacts macrophage polarisation. Within the umbrella of tissue engineering at BME, the goal here is to understand and thus better predict the heart valve (HV) mechanics leading to better biomaterial HV tissue engineering.

Inspirational teachers can nurture inquisitive minds and **Bram Bakker** was lucky enough to have a High School Chemistry teacher that instilled and then distilled a curiosity and passion for practical chemistry. Wanting to be a researcher, Bram started his PhD to fulfil this curiosity through research. With both his Bachelor's and Master's degrees in Molecular Chemistry from Nijmegen, with industry experience through his internships, Bram came to TU/e to seek a new challenge to make and test new materials. Under the guidance of Patricia Dankers and Jan van Hest, Bram joined the IPM PhD program in January 2023 with a project aimed at mimicking the communication between cells and the extracellular matrix using synthetic materials. This communication pathway is fundamental in tissue engineering as it can help guide cellular fate. With a basis in tissue engineering, the purpose is it one day leads towards better methods in growing synthetic organs. Worldwide, organ donation has numerous problems, not just organ availability but also regarding matching donors in a timely manner. Synthetic organs could circumvent both these issues and improving methodologies could have a worldwide impact. During his time at TU/e, Bram hopes to develop good foundations for both the cells and his academic career.

Although only starting his PhD in October 2023 **Jules Boesveld**, however, is no stranger to TU/e. Obtaining both his Bachelors and Master's degrees in Biomedical Engineering, Jules's interest in tissue engineering stems from an interest in how the human body works. He is involved with the Research Center for Materials-Driven Regeneration (MDR), a partnership with institutes in both Maastricht and Utrecht, focused on tissue and organ regeneration approaches with use of biomaterials. Also, as part of Carlijn Bouten's Soft Tissue Engineering & Mechanobiology group, Jules is working within the Re-Align team with other PhD students. The goal is to see if function can be restored to hearts that have suffered damage after heart attack, a myocardial infarction (MI). This can hopefully be done by re-aligning the cells within the tissue of the wall of the heart to restore functionality. To do this, the aim is to use a 2D in vitro model system which simulates a post-MI areas, and then look at the response to different environmental stimuli.

Scientific Communications however is not the only session offered as part of the Scientific Skills course. Totalling nine different sessions, they aim to give the students a good grounding across several topics. From all the sessions Sofia found that the scientific communication really helped to re-phrase and re-structure her writing, helping to get the story straight. Managing yourself during your PhD trajectory was also beneficial, but it felt like a great session to end the skills course on, and it was a pity to not be the last session. Bram found the presentation session to be insightful and benefited from the general feedback from all sessions. Jules found all the topics super useful and the general feedback across the board for all of them really helped, with his favourite being the Presentation session and animation studio session, how others see your talk seems to be key take home message Jules has taken to heart.

For Sofia the symposium was her first time presenting to such a large group and she found it to be a wonderful experience, however, she is happy to not have to present again to such a large audience for a while! In keeping with challenging himself, Bram was also happy to be forced out of his comfort zone to give the presentation at the symposium but was grateful it happened. Whilst Jules was also happy to have had the opportunity to put into practice the skills from the course.

For further information regarding the specific courses, please contact Monique Bruining.

IBEC and ICMS: A partnership built on science and personal click

Samuel Sánchez Ordóñez

ICMS and IBEC in Barcelona have a special relationship, which during the last five years has grown on several levels. This is of course thanks to shared research fields, but not in the least the result of excellent interactions on the personal level. Pleasant and beneficial go hand in hand here.

"Our collaboration with ICMS started in 2019," Samuel Sánchez Ordóñez reminisces. He is a research professor for the Catalan Institution for Research and Advanced Studies (ICREA) and both a group leader and deputy director at the Institute for Bioengineering of Catalonia (IBEC). Back to 2019: "As we were looking for international collaboration, the ICMS turned out to be a mirror image of our activities, especially on key words such as bioengineering, tissue engineering, regenerative medicine, supra molecular chemistry and materials science. So we made contact. Communication between ICMS directors Monique Bruining and Jan van Hest together with IBEC director Josep Samitier Martí and me was smooth and clear. They were very supportive of the idea of working together. This really started to fly once group leaders Vito Conte and Lorenzo Albertazzi started part-time working for ICMS while at the same time holding part-time positions in our labs for a while."

CLOSE COLLABORATION

During the last five years, the initial collaboration has evolved into cooperation on several levels. Sánchez: "For starters, we have a student exchange program in which dozens of students participate. On top of that we organize an annual joint workshop, alternating the symposiums between IBEC and ICMS, twice per year. That in itself is a source for further collaboration. And thirdly, we have the research positions project, with a call for three postdocs working at ICMS which ran over the last couple of years, which led to joint papers from IBEC and ICMS scientists. We expect in the upcoming year to have a call for PhD students hired at IBEC but jointly supervised between the two institutions."
Sánchez is happy to announce a new fourth level of cooperation: "It recently came out that Jaap den Toonder, chair of the microsystems research section at ICMS, joined us as a visiting professor during his sabbatical. And the good news just keeps coming, as just this week the excellence accreditation Severo Ochoa came up. This means we can have joint PhD students from now on."

PEOPLE

"You can have lots of common interests and research topics and still get nowhere together," says Sánchez. "Ultimately, the click between people is the gateway to success. We maintain close contacts with for instance Jan van Hest, who visits us often, and Monique Bruining. Tania Patiño Padial was a researcher in my group and she is now an assistant professor of Chemical Engineering and Chemistry at TU/e / ICMS. We build further on bonds like these. We are currently working on a proposal for a European Training Network PhD grant together."
When partners already have so much common ground to work from, they can also benefit from the different emphasis each has. Sánchez: "In general, at IBEC we work more applied. Our instance is in engineering systems for health, with translational approaches, animal models and in vivo research, for instance on microfluids in bioengineering and tissue engineering as well as in 3D-printing and imaging. Eindhoven, on the other hand, puts more emphasis on the molecular and supramolecular level and the advanced imaging capabilities that are required for that. We collaborated also with experts in nanoscopy and some of my students for instance would benefit from training on super-resolution microscopy in Eindhoven. These mutual strengths are interesting starting points for technology transfer. Talent coupled with the right equipment creates optimized conditions to find solutions."

RESULTS

This is no mere slogan, results are already there, Sánchez sums up: "There is the 2021 joint article in Nature Communications authored by Jan van Hest and myself, among others, on 'Engineering transient dynamics of artificial cells by stochastic distribution of enzymes.'
We have the joint publication of Lorenzo Albertazzi and Tania Patiño Padial in 2024 on nanomotors in Nanoscale. In 2023 we had an article by Lorenzo, Peter Zijlstra and myself, among others, on 'Real-Time Optical Tracking of Protein Corona Formation on Single Nanoparticles in Serum.' This all shows we have come a long way together in fields such as intra-cellular communication and the engineering and imaging of nanomotors. We bring in the enzyme propulsion concept for nanomotors and ICMS adds the imaging capabilities to that, amongst other things."

SCIENTIFIC STRONGHOLD

The partnership has actually become such a success that it is very attractive for a third party to join. Sánchez: "We have laid the groundwork for success and are ready to further build on that. Enlarging this community into a triangular connection in European research would be beneficial to a new partner, but also to us as existing partners. A new partner could create even more common ground and some additional specializations. This would create a scientific stronghold with both brilliance and mass on the world level."
IBEC and ICMS are quite advanced on their way to such a tripartite partnership, although it is still too early for an official announcement. It is exactly the kind of consortium the EU Framework Programme for Research and Innovation intends. Sánchez concludes: "To unite talent in this way creates the ultimate win-win situation. I have only nice things to say about our collaboration."

IBEC Institute for Bioengineering of Catalonia — ICMS INSTITUTE FOR COMPLEX MOLECULAR SYSTEMS — TU/e

Chang-lin Wang

Biobased aerogels that are recyclable and more sustainable

The public vote of last year's ICMS PhD publication award went to Chang-lin Wang. Driven by his passion for exploring new territory in organic chemistry he came up with polyimine aerogels that contain reversible chemical bonds that can be cleaved on demand, which leads to full recyclability and reduced environmental impact. Advanced and sustainable super insulating materials are now within reach, he says. "We next hope to further optimize the process and make the aerogels economically feasible. Because the possibilities with these aerogels are endless."

"OUR GOAL WAS TO MAKE CHEMICALLY RECYCLABLE ORGANIC AEROGELS"

INTRIGUING MATERIALS

Isolating our homes has never been so important. You can save approximately 1350 cubic meters of gas by wrapping up an average corner house with insulating material, such as polystyrene or polyurethane foam. "These materials are porous and light-weight," says Chang-lin Wang, PhD researcher in the Polymer Performance Material group at TU/e. "However the pores in these substances are so large that the insulation performance is not yet satisfactory."

Organic aerogels are much better at this, according to Wang. "This material is a kind of polymeric foam but with mesoporous features. Their pores are much smaller than other insulating foams; less than 70 nanometers in diameter. These narrow pores keep the gas molecules colliding with each other; therefore the heat transfer will be hindered and thermal insulation is improved compared to commercial materials."

What makes the aerogels even more special is their high specific surface area: over 100 meters square per gram compared to 10 square per gram of polystyrene. "That is not only interesting for thermal insulation purposes, but could also lead to other interesting applications, like catalytic support or chemical absorption," Wang states.

Unfortunately, the now commercially available organic aerogels pose environmental concerns. "The precursors that are now in use are typically made from fossil-based feedstock," explains Wang. "Also, the recycling back to their original monomers is virtually impossible because they are permanently cross-linked." But now Wang came up with an aerogel that could offer a solution to these problems.

MAKING THE AEROGEL AGAIN

Originally from Taiwan, Wang finished this master's in Chemical Engineering at Delft University of Technology. He first came into contact with aerogels when he applied for the PhD position under the supervision of professor Željko Tomović and Assistant professor Fabian Eisenreich at TU/e. "I was immediately intrigued by these materials, and I like application-focused hands-on experiments. Our goal was to make chemically recyclable organic aerogels." It is safe to say that the goal was met.

Wang used polyimine chemistry that has been proven to be reversible. He used primary amines and cyclophosphazene derivative-aldehydes made from bio-based reagents (vanillin and 4-hydroxybenzaldehyde) to build cross linkers. "These cross linkers make the aerogel both thermally stable and flame retardant," says Wang.

Furthermore, Wang discovered that the polyimine aerogels can easily be degraded into starting monomers under acidic conditions. "The yields and purities it shows allows for us to make the aerogel again and again without loss in quality. This demonstrates that closed-loop recycling of these materials is a realistic possibility. We will now try to develop more and different types of these aerogels. The possibilities are endless. And then hopefully, after further optimization, they can finally be used in the industrial field."

Drugging the undruggable

Proteins are the building blocks of cells, and range in shape from well-defined to spaghetti-like. The malfunction of spaghetti-like proteins causes diseases like neurodegeneration, but there are no treatments. Assistant professor Peter Cossar is searching for new drugs to treat these disease causing proteins.

Peter Cossar

A lack of protein structure is one of the greatest challenges in drug discovery. Medications, such as Ibuprofen, depend on well-defined protein structures to function effectively. However, not all proteins have structured forms; instead, proteins exist along a spectrum from highly structured to completely disordered. Proteins at the disordered end of this spectrum, known as intrinsically disordered proteins (IDPs), do not maintain a stable, three-dimensional shape, making it difficult for drugs to bind to them. This becomes problematic when such proteins malfunction and cause diseases like Alzheimer's and pancreatic cancer, as clinicians have no way of treating patients.

However, proteins do not function in isolation; they often interact with other biomolecules such as DNA, RNA, and other proteins to operate effectively. These interactions provide an exciting entry point to treating diseases driven by IDPs. Peter's research is focused on developing next-generation drugs that capture an IDP within a protein-protein interaction complex. These drugs then leverage the cell's protein recycling machinery to eliminate the malfunctioning protein. His work holds potential for groundbreaking treatments for diseases currently deemed untreatable, including various neurodegenerative disorders and cancers.

NAME:
Peter J. Cossar

POSITION:
Assistant professor, Chemical Biology and Medicinal Chemistry (since January 2023)

PREVIOUSLY:
PhD, University of Newcastle, Australia

MOTIVATION:
Peter is fascinated in understanding how small druglike molecules can be used to modulate how proteins interact in the cell.

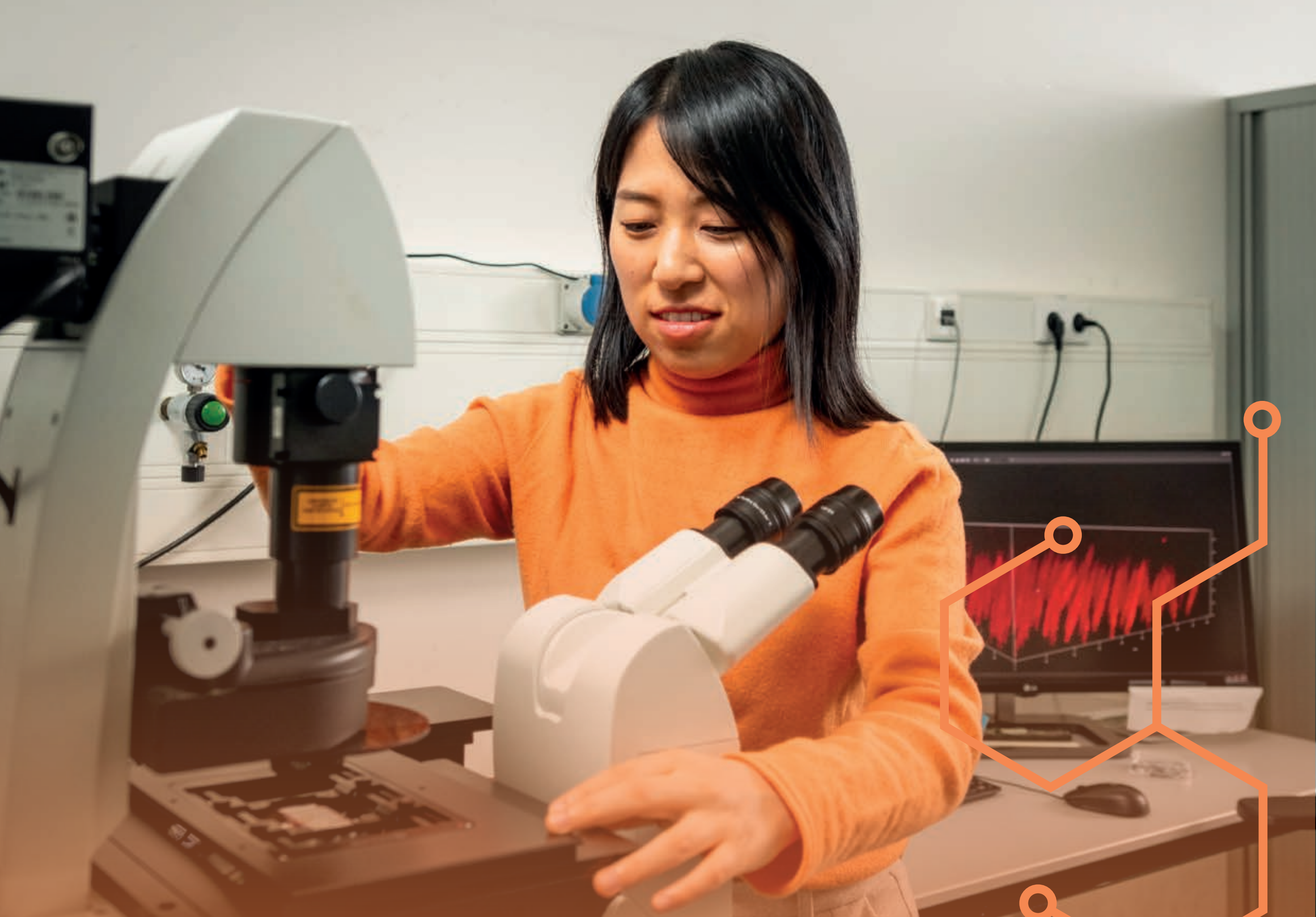
DREAM:
To develop a blueprint for creating drugs that effectively treat diseases driven by IDPs, which are currently untreatable.

SPARE TIME:
In his spare time, Peter is an avid rock climber enjoying weekend trips to the Ardennes and Luxemburg to climb.

Introduction

Collaborating in pioneering research on liquid-liquid phase separation

An exciting discovery that could potentially mark the beginning of a new research field. ICMS researcher Hailin Fu mapped in detail how supramolecular polymer islands – tactoids – form in a liquid environment. The very first description of liquid-liquid phase separation (LLPS) in synthetic polymers was partially made possible because microscopist Yuyang Wang developed a new orientation-resolved microscopic technique in ICMS's Advanced Microscopy Facility. A scientific diptych on rice grains, magic dyes and microscope lenses, successfully ending in a joint Nature paper. >>



Hailin Fu

Connecting two worlds: supramolecular islands in separating liquids

When postdoc Hailin Fu (Macro-Organic Chemistry, Department of Chemical Engineering & Chemistry) leaves a supramolecular polymer solution under the confocal microscope overnight, the next day she sees something unusual from the recorded movie. Her observation eventually leads to a paper in the renowned journal Nature, and the development of a possible new platform that could also give insight into fundamental biological questions.

Excited, Hailin Fu walks into the meeting room in Ceres, holding up a colorful magazine. “Our article is in it, even as a teaser in the Nature News overview.” She is referring to the Nature paper published in late February. That the research described was performed only by ICMS researchers at TU/e is a peculiarity in itself, because usually the list of authors of such papers includes several international collaborations. “We do cutting edge research within ICMS, and take full advantage of its multidisciplinary nature. By looking at a research question from different perspectives, you are more likely to be challenged to think out-of-the-box.”

Fu flips through the Nature journal until she gets to their article which shows colorful rice grain-like structures. In biological systems, liquid-liquid phase separation of biopolymers has been described before, Fu explains. “Biopolymers and supramolecular polymers are similar in many ways, however, LLPS of supramolecular polymers is not reported in literature.”

The elongated rice-like structures Fu finds in her supramolecular polymer solution turn out to be synthetic equivalents – tactoids –, although this is not obvious to her at first. “When I left the UPy solution overnight, the next day I saw under the confocal microscope that the solution was no longer homogeneous. Some areas in the liquid seemed more concentrated than others and some sort of small islands had formed. After we figured out the story and discussed it with others researchers, they mentioned that they had observed similar structures. But couldn’t explain why. It convinced us that LLPS should be a general phenomenon for supramolecular polymers as well. We dived into it and are now the first to describe liquid-liquid phase separation in supramolecular polymers.”

Confocal microscopy helps her study the dynamic tactoid formation. But with the available equipment, she was unable to elucidate the structure in detail. Then she gets in touch with Yuyang Wang, Facility Manager of ICMS’s Advanced Microscopy Facility. In the following pages, he tells how he developed and built a new high-resolution microscopic technique to answer Fu’s research question.

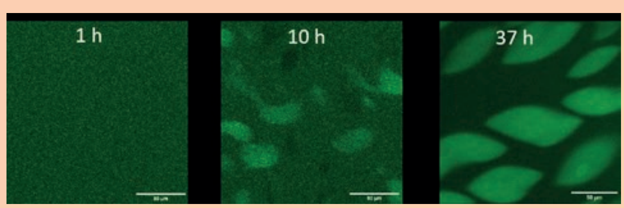
Thanks to Wang’s polarized fluorescence microscopy setting and a “magic dye” created by the research groups of Bert Meijer and Patricia Dankers, Fu can examine the orientation of the polymer fibrils in the tactoids. She sees that they are neatly structured. “That is one of the biggest differences from biological membrane-less organelles; proteins and nucleotides such as RNA are held together in them in a disordered way. Often this also results in a spherical shape of the liquid droplet. Orientation is a very important feature of the elongated structures that we observed. And while studying formation, we could conclude that the length of the fibril is a trigger for segregation. When it starts growing and the fibril reaches a certain length, tactoids are formed.”

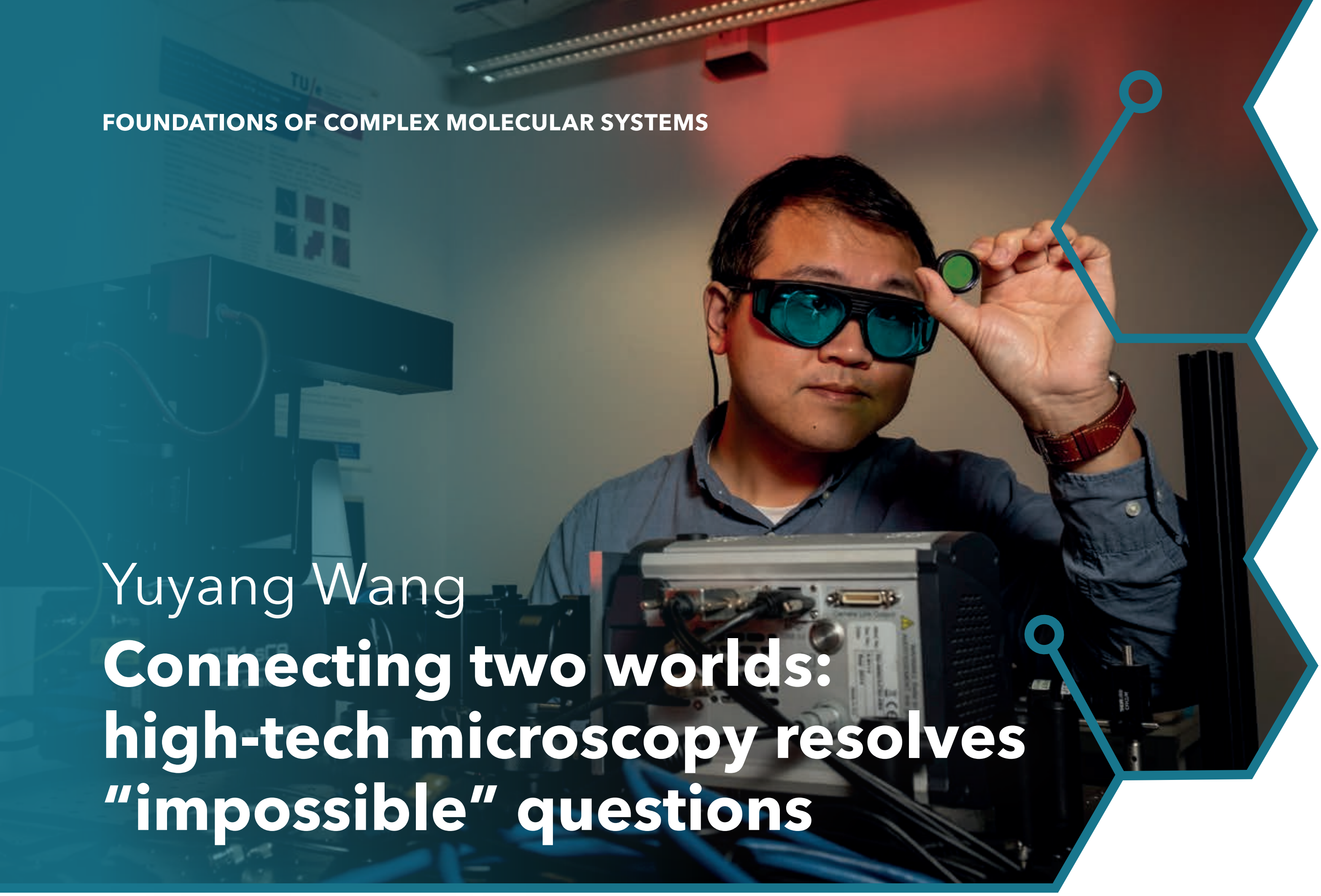
Fu emphasizes that her study is an excellent example of collaborative research taking place within ICMS. “Without the expertise from the different departments we would never have come this far. We might even be able to connect two worlds now. There are already numerous examples of phase separation of solid nanostructures, but the description of liquid structures in supramolecular polymers is much more challenging. We kind of discovered a new phase, that is very exciting for supramolecular polymer scientists.”

“But,” she continues, “these structures could also be developed into a rich and diverse chemistry platform to study and understand biological systems. We could study cellular interactions with these tactoids for future applications in drug delivery or cell manipulation. Many studies link rigidification of membrane-less organelles to diseases like several neurodegenerative disorders. Our research might shine a new light on the dynamics of this misregulation process and could help in understanding pathological conditions. These new insights will help further research in this field.” >>

TACTOIDS IN A UPY SOLUTION

Liquid-liquid phase separation in synthetic supramolecular polymers has never been described before. However, Fu observed in her experiments the transition from a homogeneous solution to a heterogeneous LLPS solution. She used a polymer solution based on ureido-pyrimidinone (UPy) motifs and could demonstrate elongated structures called tactoids, in the UPy solution after an overnight incubation. Using confocal microscopy, she was able to follow the growth of tactoids over time. Spontaneous LLPS of UPy polymers into tactoids could be tuned by the addition of dextran to the solution, which influenced the morphology and density of the formed tactoids.





Yuyang Wang
Connecting two worlds: high-tech microscopy resolves "impossible" questions

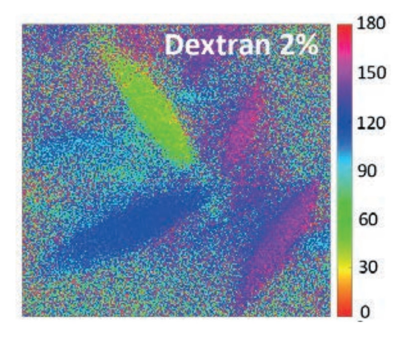
Yuyang Wang's door is always open. As Facility Manager of ICMS's Advanced Microscopy Facility, he is eager to help researchers further their research. When postdoc Hailin Fu is challenged in studying her new structures with the microscope techniques previously available, Wang develops a new microscope setting himself. Thanks to Wang's efforts, they manage to perform orientation-based research with polarization microscopy for the very first time. Their joint research leads to an exciting paper in the renowned journal Nature.

ICMS tries to facilitate its researchers in various ways, for example by clustering expertise. Like at the Advanced Microscopy Facility. Facility manager Yuyang Wang has several state-of-the-art microscopes under his care. "Within ICMS, we do a lot of research at the micro- and nanoscale. Therefore, many microscopes are already present within the various research groups. Researchers try to answer their research questions using the microscopes that are available in their labs. But within the Advanced Microscopy Facility, we look one step ahead. We do not stop when things seem impossible. In those cases, we offer high-level support by developing custom microscopy."

And so is the research question Hailin Fu is struggling with. In a supramolecular polymer solution that she leaves overnight, she discovers that some structures segregate and form small islands. Using various fluorescent labels and microscopic methods, she tries to characterize the structures called tactoids, but fails to make statements about the orientation of fibrils inside. Wang sees it as a challenge. "We like to make the impossible possible. With conventional confocal microscopy, Fu could follow tactoid formation very nicely in the best resolution one can acquire using such microscopy method. But she also wanted to see how the fibrils were oriented inside these structures, at a higher resolution. Polarization microscopy enables such study of orientation." (see box)

TACTOIDS UNDER THE POLYMERIZATION MICROSCOPE

To study the internal order of the tactoids observed by Fu in detail, Wang developed a polarization fluorescence microscopy setting. In this technique, polarized light is used to reveal details in so-called anisotropic specimens by monitoring changes in intensity. For mapping the molecular orientation distribution in the tactoids, Wang and Fu used a simplified orientation fluorescence microscopy method, POLCAM, with a specialized polarization camera. The color bar in the figure represents the linear polarization angle.



But the technique needs to be adjusted for the visualization of the fibrils inside the tactoids, Wang explains. “As a microscopist, I use a lot of organic dyes for the labeling of different things. But these dyes are rigid molecules that emit light in a certain direction. They attach to the desired molecule in a random fashion. In this case, since we would like to investigate the specific orientation of the fibrils, we had to eliminate this randomness.” Therefore, they use a different dye, developed in the research labs of Bert Meijer and Patricia Dankers. Wang quickly draws out the structure on a paper and points to a specific piece. “This is where the magic happens. The short linker within the dye results in less flexibility. In this way, it could indeed reflect the internal geometry of the fibrils inside the tactoids.”

Using the polarization microscopy setting that Wang develops and builds, Fu can finally visualize that the fibrils are highly orderly structured. The start of a whole series of experiments, stresses Wang. “Fu’s results are chemically very exciting. But the microscopic technology we developed for this is also very unique. High-tech microscopy techniques are predominantly developed in the biological field. We are pushing the boundaries of material microscopy, thereby bridging the gap. We are the only material-based super resolution center in the region, giving us a unique position.”

Within the Advanced Microscopy Center, Wang is now busy expanding the microscopic support, he tells enthusiastically. “We want to make it even clearer to researchers that we are here for them, and want to contribute ideas on how (super-resolution) microscopy can help with their research questions. We therefore have new ways to promote our facility. A new logo, a new website (see box) to better communicate our expertise and other possibilities.”

“Fu’s research is a good example on how microscopy can help make the seemingly impossible possible. And the developments do not stop with this paper, because we would also like to visualize tactoid dynamics in even higher detail. Furthermore, TU/e-researchers in several departments are trying to connect live cell imaging and electron microscopy. We are also collaborating with companies such as Thermo Fisher Scientific (Brainport Eindhoven), that designs hardware and software to enable this.”

“Another exciting development is the reorganization of several ICMS labs to create a modular prototyping platform for advanced microscopy. By investing in new infrastructure, new techniques, and high throughput sampling we aim to bring fundamental research from the lab to the industry.” Wang smiles. “Also in this area the interactions are highly dynamic.”

ICMS ADVANCED MICROSCOPY FACILITY

The new website of ICMS Advanced Microscopy Facility is a hub of knowledge, collaboration, and discovery, offering access to a wide range of advanced (high-resolution) microscopy techniques and tools – from STORM to STED, Atomic Force Microscopy, and Correlative Microscopy.

Next to detailed information about the various settings, a new booking system is available. The website is still in progress, but very soon upcoming events such as introductory courses and advanced seminars will be announced, as well as news on the latest advancements in microscopy and opportunities for collaborations.

If you have questions, or if you are looking for support or training, please contact Facility Manager Yuyang Wang, via y.wang8@tue.nl or via the request form at https://superresolution.nl/

News, awards & grants

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to read the full articles

KWF supports metastasized ovarian cancer research with 429,200 euros

IT WAS ANNOUNCED ON DECEMBER 12 THAT THE KWF IS HONORING PATRICIA DANKERS' RESEARCH WITH 429,200 EUROS IN FUNDING.

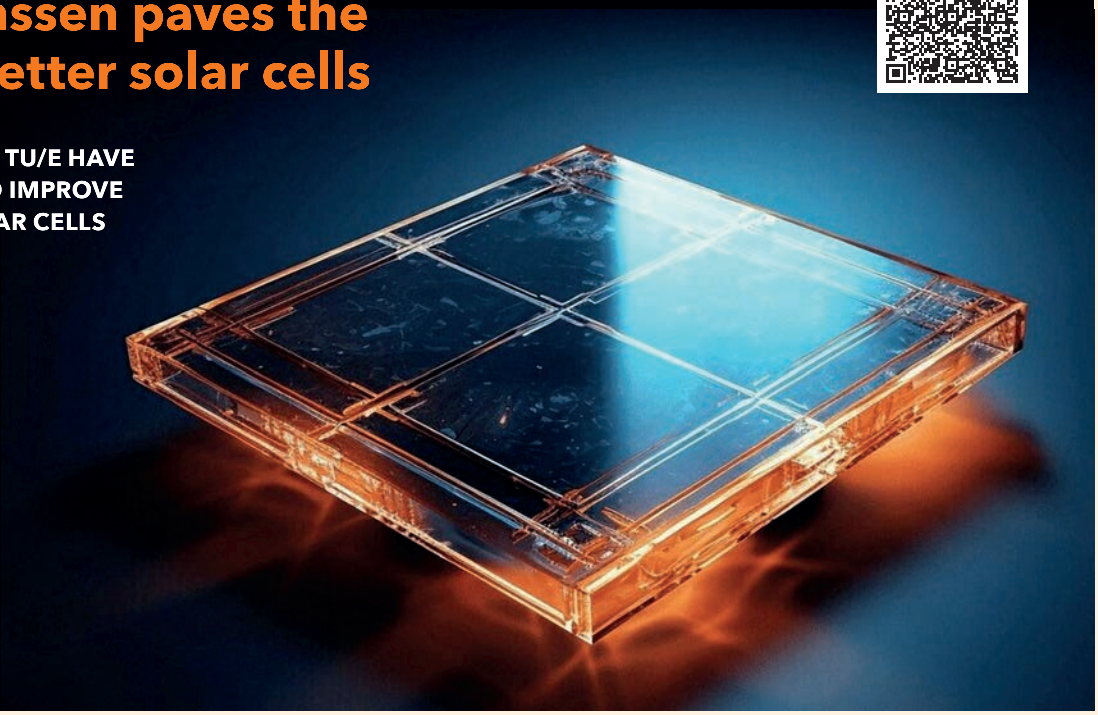
ERC Consolidator Grant of 2 million euros for three TU/e researchers

THE RESEARCHERS ARE ALL INVOLVED IN BUILDING A DIGITAL FUTURE THAT IS BOTH FAST AND ENERGY-EFFICIENT

Scan the QR codes to read the full articles

This is how Professor René Janssen paves the way to better solar cells

RESEARCHERS AT TU/E HAVE FOUND A WAY TO IMPROVE PEROVSKITE SOLAR CELLS



Controlling chaotic turbulence to make "cat-coat" patterns in fluids

RESEARCHERS FROM TU/E AND THE UNIVERSITY OF CHICAGO DISCOVERED HOW TO MANIPULATE TURBULENT FLOWS TO CREATE REGULAR PATTERNS LIKE THOSE SEEN IN THE TABBY COAT PATTERN OF A CAT. THE NEW RESEARCH HAS BEEN PUBLISHED IN NATURE.

Dick Broer

Honorary Doctorate for bridge builder Dick Broer

Emeritus professor of Smart Materials does not have time yet to rest on his laurels

Although Dick Broer, professor of Functional Organic Materials and Devices, has officially been retired to emeritus status in 2015, he can still be found almost daily in his office in ICMS building Ceres. He advises on ongoing lines of research within his old department, is setting up a spin-off in the field of interactive surfaces and travels the world spreading knowledge about the applications of smart materials. As the ultimate crowning glory of his connecting work, he recently received the Honorary Doctorate from the University of Zaragoza.

A motley procession of professors with headgear and capes in all the colors of the rainbow enters the richly decorated university chapel, as choral singing swells in the background. "It gives me goosebumps again," confesses Dick Broer. On his laptop we watch a video of the ceremony of him receiving his Honorary Doctorate, which was conferred to him on February 9 from the Rector Magnificus of the University of Zaragoza. The custom-made bright blue hat he was given during the ceremony – each faculty has its color – was allowed to go home. "And it has found a nice place," Broer smiles.

SCIENTIFIC AND PERSONAL HARMONY

His Honorary Supervisors José Luis Serrano and Luis Teodoro Oriol praise him for his pioneering work in the field of reactive liquid crystals and the way he translates fundamental research from the lab into socially relevant applications. But in addition to his great scientific value, his human qualities shine through, Oriol stresses by email. "He is very approachable, motivating, and interested in you as a person. Whether you are a Nobel laureate or a student. We can look back on thirty years of 'fruitful scientific collaboration' in which beautiful friendships have also developed." "It feels very special that I could be Honorary Supervisor of such an outstanding and internationally recognized expert in polymer and liquid crystal research," also Serrano tells us. "An intense connection between Broer's group and our university has emerged over all these years. His good scientific and personal harmony even took on a very personal twist for me during my daughter's PhD defense, where Broer was one of her supervisors. He has continuously inspired and supported so many researchers."

Those fine words are waved away by Boer, modest as he is. Despite being an introvert he also experienced the academic ceremony as an exciting affair. "You have to like being the center of attention. Nevertheless, I enjoyed it; this crowning achievement feels like an incredible honor." He has changed the world of liquid crystals, as evidenced also by the large number of patents to his name and the highest civilian knighthood Broer was awarded a few years ago "for his exceptional merits to society." We talk to him about his pioneering work at Philips, his love for smart polymers, and the latest advanced applications he wants to commercialize.

FLAT SCREENS

During his time at Philips, where Broer spent most of his career, he was involved in the development of different fields such as data storage, telecommunications, and optics. A big common denominator among them is the use of liquid crystals – they behave like a liquid, but also scatter light and can be influenced by electric fields. The general public is particularly familiar with energy-efficient flat panel displays; Broer had an important part in their design. "We were keen to improve the contrast of traditional computer screens, which was quite dependent on the viewing angle. With a layer of liquid crystals, we made it possible to continue to see the image well even at an oblique angle." The materials that Broer developed at Philips back then can still be found in many displays nowadays.

The first contacts with University Zaragoza also date from that time, Broer explains. "In the early 1990s, we set up a large European project with Philips and two other companies on the application of liquid crystals. For more scientific mass, we were looking for an academic partner, and so my collaboration with José Luis Serrano began. When I switched to TU/e – from 1996 as a part-time professor, from 2010 full-time – those ties were strengthened even more."

FROM MARS ROVER TO SMART PATCH

Gradually, Broer and his colleagues also investigated other properties of liquid crystals with the goal of developing the first smart moving materials – for example a new material that can wavingly move under the influence of UV light. "We developed that further and it marked the beginning of a whole new field of research. On application of electric voltage on a thin coating of liquid crystals, it creates a ribbed surface which can be manipulated, which opens up avenues for numerous applications.. It is useful for developing self-cleaning solar cells – a function which NASA has expressed interest in incorporating into the Mars rover. We are also working on a prosthetic hand with fingers that can feel, and on drug delivery via smart patches and cells that can grow on moving surfaces. With tactile elements, we can connect the virtual and the real world which plays a crucial role in Augmented Reality applications. We can even make surfaces sweat or release a scent molecule already on a small scale," Broer adds.

New lines of research are being rapidly rolled out, often by researchers that Broer trained himself. But also within the TU/e spin-off HaptonTech, of which Broer is one of the founders. He praises the role of ICMS, which has facilitated the merging of many experts within this multidisciplinary research. "It has proven to be very valuable to bring people from different directions together in a living room to brainstorm. In our spin-off, we try to pull all these great ideas out of the lab, that's where my strength still lies. There's still a lot of great stuff in the pipeline."

GENERAL

A quick "glow-in-the-dark" test to diagnose infectious diseases

Harm van der Veer

"OUR FOCUS WAS ON ANTIMICROBIAL RESISTANCE, A GROWING WORLDWIDE ISSUE"

From iGEM-student-project to creating a new bioluminescent sensor that can track minimum amounts of microbial DNA in patient samples – it has been an amazing trip for last years' ICMS PhD publication award winner Harm van der Veer. With the CRISPR-Cas-based platform LUNAS he hopes to help combat infectious diseases all around the world, especially in the developing countries. "All we need is a little black suitcase and a digital camera to diagnose infectious diseases like malaria, for example."

FOCUS ON A WORLDWIDE ISSUE

"I just got the happy news that we received the necessary funding to make the journey to Uganda to evaluate our platform with malaria patients," says Harm van der Veer, PhD student in the group of Maarten Merkx at the Biomedical Engineering department of TU/e. "In the low resource rural areas over there, they do not usually have the capacities, like PCR machines or microscopy expertise, to diagnose the disease properly. With growing resistance to antimalarial drugs, and mutations rendering the malaria parasites invisible to commonly used rapid antigen tests, accurate diagnosis becomes increasingly important and here our LUNAS-test could make a difference."

It all began in 2019, when Van der Veer and his fellow students participated in the International Genetically Engineered Machine (iGEM) competition, where students are challenged to come up with innovative ideas within synthetic biology. "Our focus was on antimicrobial resistance, a growing worldwide issue," Van der Veer tells. "We thought of bacteriophages, viruses that selectively infect bacteria. Our thought was that we could use the same principle for diagnostics."

From there Van der Veer and colleagues arrived at DNA sensing, which eventually lead to the Luminescent Nucleic Acid Sensor, or LUNAS. "It is based on the CRISPR-Cas9 protein, a protein that we can program to specifically bind to a certain sequence of DNA that is a hallmark of a particular pathogen. The microbial concentration in sample fluid of an infected person is usually very low, thus we combine the CRISPR-based sensor with the DNA amplification method RPA, and we do this in a single reaction mixture that yields a result within 30 minutes."

GLOWING BLUE LIGHT

Another essential component of the platform is a split luciferase, consisting of two fragments fused to two CRISPR-Cas9 proteins. The luciferase enzyme produces light when the Cas9 proteins bind to the target DNA, bringing the two fragments back together. "This bioluminescence effect is the most exciting part of our system," states Van der Veer. "There are detection methods that use a fluorescent reporter, but you need to excite those with an external source of light and that brings along background effects. Our platform only needs a digital camera to spot the glowing blue light, that indicates a positive result."

According to Van der Veer the sensor system is very suited to be an excellent, simple and portable point-of-care-test. It can be deployed wherever it is needed to diagnose various infectious diseases. A colleague of his, Yosta de Stigter, is now working with Fontys along with other partner institutes to bring the platform to the general practitioners' office so as to quickly diagnose sexually transmitted diseases, like chlamydia. And early next year Van der Veer will be travelling to Sub-Saharan Africa to assess the method there. "All together we managed to combine a lot of components from nature and build a beautiful new technique which we believe can make an actual impact in the world."

Theses

NOVEMBER 2023 – APRIL 2024

Ex vivo bone explant cultures for evaluation of remodeling and bone substitutes
ESTHER CRAMER
November 1, 2023
PhD advisors:
S. Hofmann
K. Ito

Continuous monitoring of health markers: a study on BPM immunoassays and microdialysis
LAURA VAN SMEDEN
November 7, 2023
PhD advisors:
M.W.J. Prins
A.M. de Jong

Structure, dynamics, and aging of active glasses
GIULIA JANZEN
November 9, 2023
PhD advisors:
L.M.C. Janssen
C. Storm

Design rules to dynamically control supramolecular hydrogel-cell interactions
LAURA RIJNS
November 10, 2023
PhD advisors:
P.Y.W. Dankers
E.W. Meijer

Geometric TSP and related problems in (almost) low-dimensional spaces
HENK ALKEMA
November 21, 2023
PhD advisors:
M.T. de Berg
R.W. van der Hofstad

Cell-free characterisation of novel genetic networks
ARDJAN VAN DER LINDEN
November 22, 2023
PhD advisors:
T.F.A. de Greef
P.A.J. Hilbers

Electronic structure calculations and machine Learning: from theory to multiscale applications
ONUR ÇAYLAK
December 5, 2023
PhD advisors:
B. Baumeier
O. Anatole von Lilienfeld

Notochordal cell-derived therapeutic approaches for intervertebral disc regeneration
TARA SCHMITZ
December 6, 2023
PhD advisors:
K. Ito
M.A. Tryfonidou

Supramolecular polymeric materials: the interplay between macromolecules and supramolecular polymers
JOOST VAN DER TOL
December 7, 2023
PhD advisors:
E.W. Meijer
G.M.E. Vantomme

Electronic excitations in complex molecular environments: a computational investigation via many-body perturbation theory
GIANLUCA TIRIMBO
December 8, 2023
PhD advisors:
B. Baumeier
R. Coehoorn

Real-time analysis of particle motion for continuous biosensing with single-molecule resolution
MAX BERGKAMP
December 13, 2023
PhD advisors:
M.W.J. Prins
L.J. van IJzendoorn

Experimental study of the interplay between electrokinetic effects for electronic paper displays
MOHAMMAD KHORSAND AHMADI
December 20, 2023
PhD advisors:
H.M. Wyss
J.M.J. den Toonder
A. Henzen

The ultracold electron source: from experiment to instrument
TIM DE RAADT
January 9, 2024
PhD advisors:
O.J. Luiten
J.G.H. Franssen

Design, modeling, and control strategies for soft robots
BRANDON CAASENBROOD
January 10, 2024
PhD advisors:
H. Nijmeijer
A.Y. Pogromskiy

Development of nervous system-on-chip technology
RAHMAN SABAHI KAVIANI
January 17, 2024
PhD advisors:
R. Lüttge
J.M.J. den Toonder

Lung cancer protein tumor markers: development, validation and clinical use of quantitative serum tumor marker assays
SYLVIA ROOVERS-GENET
February 1, 2024
PhD advisors:
V. Scharnhorst
L. Brunsveld
D.H. van de Kerkhof

Accurate and fast modeling of opto-electronic processes in organic light-emitting diodes: from master equation to multiverse kinetic Monte Carlo modeling
MAHYAR TAHERPOUR
February 8, 2024
PhD advisors:
P.A. Bobbert
R. Coehoorn

Polymers in extension: from crystallization to filament breakup
JESSICA PEPE
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PhD advisors:
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R.M. Cardinaels
G.W.M. Peters

Spins for energy: local probing of structure, magnetism and conductivity of chiral molecules and complex oxide perovskites
MICHAEL VERHAGE
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R.A.J. Janssen

Exploring compartmentalization for DNA nanotechnology
BAS BÖGELS
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M. Merkx

Engineering time and length scales into supramolecular hydrogels
MARTIN RUTTEN
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P.H.J. Kouwer

Excitons in polymer-fullerene morphologies: multiscale modeling, implementation and application
VIVEK SUNDARAM
February 27, 2024
PhD advisors:
B. Baumeier
A. Lyulin

Towards developing a hemocompatible inner lining at the blood-biomaterial interface of artificial hearts
DINA IBRAHIM
March 5, 2024
PhD advisors:
C.V.C. Bouten
A.I.P.M. Smits

Engineering function into biomaterials using supramolecular interactions: turning static functions into dynamic reciprocity
JOYCE BROUNS
March 6, 2024
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R.P. Sijbesma

Discretised microfluidics for noninvasive health monitoring
EMMA MOONEN
March 7, 2024
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J.C. Heikenfeld

Low-order dynamic modeling for electroactive surfaces
ANAHITA AMIRI
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N. van de Wouw
D.J. Broer

Metachronal motion of magnetic artificial cilia
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Mixed-halide wide-bandgap perovskite semiconductors for photovoltaics
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Towards understanding the mechanisms behind structural organization of the human myocardium using human in vitro models
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Ultracold electron source development and X-band acceleration for a compact ICS-based x-ray source
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P.H.A. Mutsaers

Chiral supramolecular materials: from fundamentals to application
MARCO PREUSS
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G.M.E. Vantomme

Characterizing estrogen receptor differences between breast cancer patients
STACEY JOOSTEN
March 26, 2024
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Modeling the formation and mechanics of hybrid hydrogels
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A golden key to microseconds: plasmon-enhanced single-molecule fluorescence for ultrafast biomolecular dynamics
SJOERD NOOTEBOOM
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PhD advisors:
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Organic neuromorphic electronics for smart sensing and processing
IMKE KRAUHAUSEN
April 10, 2024
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