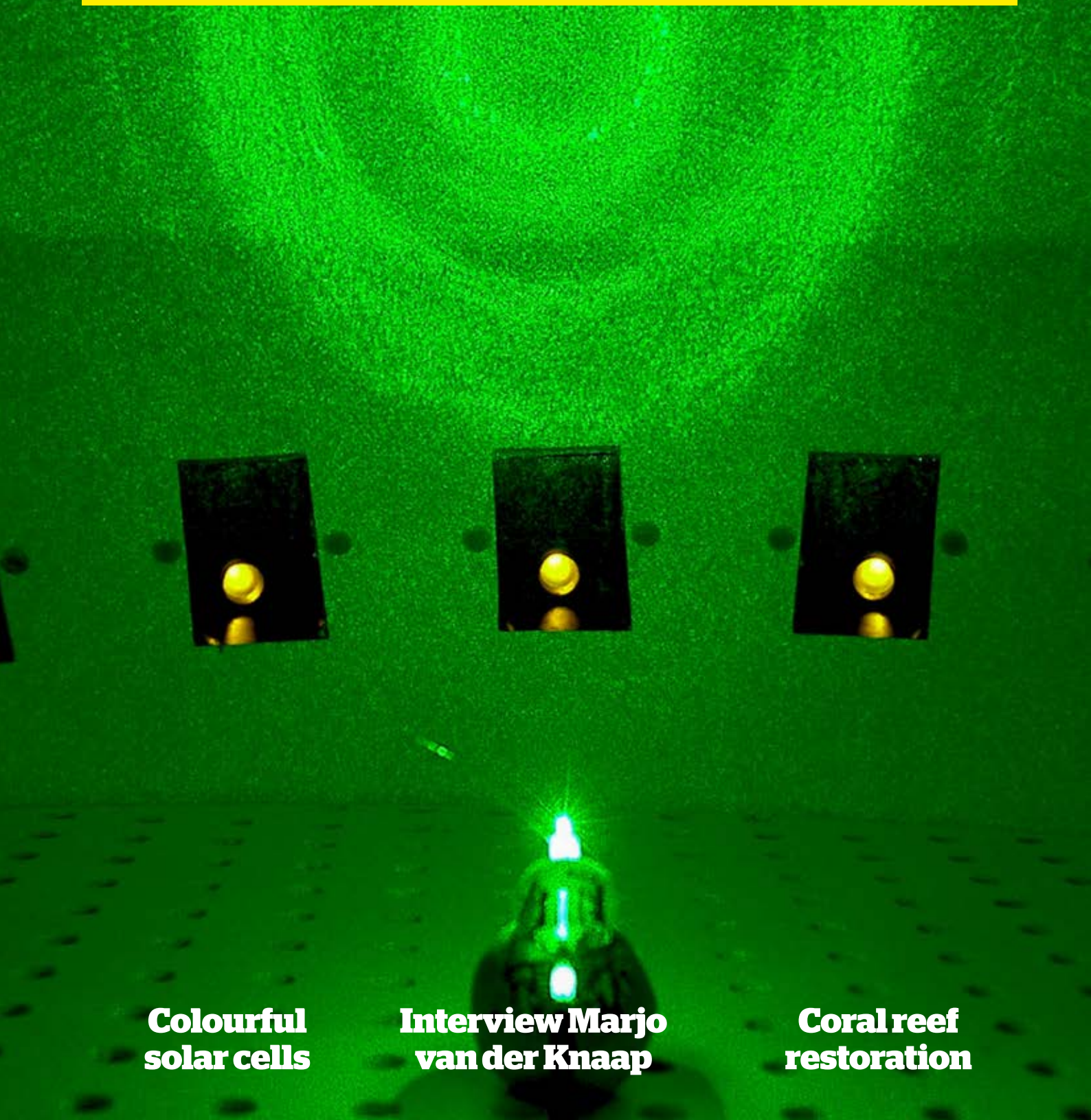
Issue #07 May 2018

Amsterdam Science



Colourful solar cells

Interview Marjo van der Knaap

Coral reef restoration

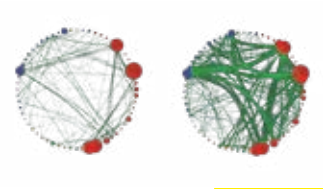
Dear reader,

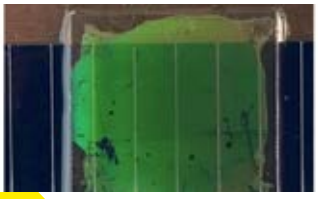
The 2018 spring edition of Amsterdam Science magazine is out!
An issue with many different highlights and interesting scientific findings from the Amsterdam Science community. This time, there is an emphasis on neuroscience, with four contributions from VU research groups inside the magazine and an intriguing image on the cover. This image is of a behavioural testing box for studying attention and impulsivity of rodents. The box allows projection of brain activity during behavioural task. A psychedelic image indeed!
Inside this issue you'll find contributions on the importance of the extracellular matrix of brain cells, on how caffeine keeps brain cells from becoming tired and on the genetics of complex diseases like schizophrenia. Marja van der Knaap, head of the Department of Paediatric Neurology of the VU Medical Centre, tell us about her research on white matter in the brain using MRI and the application of this knowledge in rare diseases that affect young children.
And there is more: two contributions from the Amsterdam Water Science consortium: one on the use of social media in global flood detection, and one on how we can sow corals for reef restoration; both important for the future of our world. Viral ecologist Corina Brussaard is starring in the Q&A section. This issue also highlights the shared interest we have in evolution. You'll read about the evolution of soil life during nature restoration, the evolution of the genetic code and the colourful evolution of solar cells. In his column, Albert Polman presents his commitment to solar energy as a means to reduce global warming and battle climate change. Plant scientists present their work on the diagnosis of plant diseases and the discovery of a hub that helps plants find a balance between growth and increased immunity. Cell biologists present their latest finding on the specialisation of immune cells and contributed a colourful back cover highlighting the internal structures of cell with fluorescent biosensors. A female moth stars on the centrefold and in the cartoon: love is in the air!
With the publication of this seventh issue, Amsterdam Science is proud to present a new event: Amsterdam Science Now. In collaboration with SPUI25, an academic-cultural centre in the heart of Amsterdam, we have organised a science lectures event on Thursday 31 May. Three contributors to this issue will give you a flavour of what they have been working on and why it makes them tick. This first Amsterdam Science Now edition is about sexual selection in moths (p.22), the physical behaviour of hydrogel balls in a hot pan (p.13), and how coffee affects your brain (p.20). To know more about the event, go to http://www.spui25.nl/en/shared-content/events/events/2018/05/amsterdam-science-now.html
This issue is different from all previous issues because two founding Editors in Chief, Hamideh Afsarmanesh and Mark Golden, decided to step down because of their busy schedules. I would like to thank both of them for their inspiring contributions and their support in getting this magazine started. It has been a pleasure working with you! In addition, Mustafa, Joshua, Renske and Sarah also left the editorial board: thanks for your help and enthusiasm. New on the board are Evangelos, Adriaan, Huub, Laura and Mohit: great to have you on board!
Enjoy the seventh issue and don't forget to visit our website (amsterdamscience.org) to submit your own Amsterdam Science contribution!

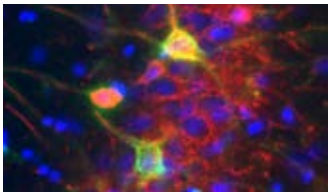
On behalf of the Editors in Chief,
Michel Haring

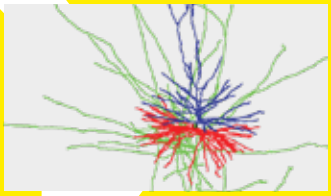
ABOUT THE COVER IMAGE:
This behavioural testing box for rodents contains five cue holes that are illuminated. When the rodent makes a response in one of them, it earns a consummatory reward. This test measures both attention and impulsivity. The green light that illuminates the wall of this box is derived from a so-called microdrive. This system allows to record activity from neurons in the brain during the behavioural task, and at the same time allows to manipulate activity from neurons, and hence behaviour.

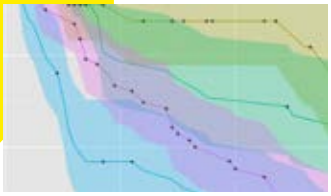
HUUB TERRA and BASTIAAN BRUINSMA are PhD students at the Center for Neurogenomics and Cognitive Research (CNCR), VU / Amsterdam Neuroscience, and MARCEL VAN DER ROEST is research analyst at the Dept. of Anatomy & Neurosciences, VUmc / Amsterdam Neuroscience.











& more

colophon

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Is "biological water" really different from normal water?

MARTIJN TROS performed this research while a MSc student Chemistry at UvA. Currently, he is a PhD student at the Faculty of Science, Department of Physics and Astronomy, VU.

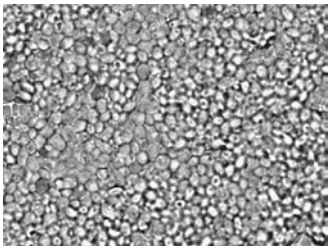
→ For decades, the very controversial theory of "biological water" in cells has persisted in the field of cell biology. Although the majority of scientists is convinced the water molecules in cells don't behave different from normal tap-water in any way, the theory has never been confirmed or disproven. We gathered experimental evidence showing biological water indeed does **not** exist.

The idea of biological water arises from the extremely crowded environment of the cell cytoplasm, containing very high concentrations of different biomolecules (e.g. proteins). The high viscosity of the cytoplasm (~10^6 times higher than that of bulk water) is found for even the smallest probe molecules, leading some to believe that water molecules in cells behave differently from bulk water molecules.

Using two techniques, time-resolved vibrational spectroscopy and dielectric relaxation spectroscopy, both the individual and collective orientational motion of the water molecules can be monitored in real-time on an ultrafast timescale of picoseconds (10^{-12} s). With these tools we investigated the water molecules in cells of three different organisms: *E. coli* (a very common bacterium that lives in our intestines), *S. cerevisiae* (baker's yeast), and dried spores of *B. subtilis* (bacterial spores). In all three organisms, the majority of the water molecules behave the same as those in bulk water. Only a small fraction of the water moves on a slower timescale. Experiments on concentrated solutions of proteins and ions (cytosol mimics) mimicking the cell cytoplasm indicate that the fraction "*slow water*" molecules are in fact bound to the dry mass of the cell, thereby affecting their dynamics.

These results are finally putting an end to this long-persisting theory about the existence of biological water and indicate that in experiments any observed changes in the biological processes of a cell cannot be attributed to water behaving differently. Ω

↓ Figure
Microscope image of the investigated samples of *Saccharomyces cerevisiae* cells (yeast). The extracellular space is filled with water. Scale bar represents 10 µm.



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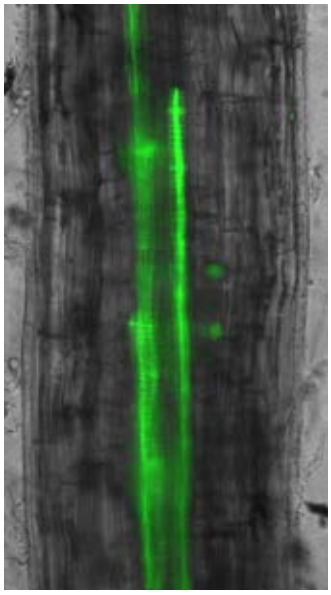
M. Tros *et al.*, Picosecond orientational dynamics of water in living cells, *Nature Communications* ***8***, 904 (2017). https://www.nature.com/articles/s41467-017-00858-0

A plant goes to the doctor: diagnostics of plant disease

PETER VAN DAM carried out his PhD thesis research at the Swammerdam Institute for Life Sciences (SILS), UvA. He is currently working at Genetwister Technologies N.V.

→ Plants are challenged by many pathogens, including the fungus *Fusarium oxysporum*. This pathogen will infect many plant species, including melon, tomato and banana, causing them to wilt or rot. Currently, there are no effective curative treatments for *Fusarium* disease, meaning that accurate and quick diagnostics would an incredibly useful tool for plant growers and breeders alike. In the case of *Fusarium*, however, identifying which plant species can be infected by a newly encountered fungal strain is very difficult, because a strain infecting for example melon can genetically be more related to a strain infecting only tomato than two melon-infecting strains. Looking for differences in conserved genes or ribosomal DNA sequences, which is often used for species identification, is not useful in this setting. The explanation for the fact that melon-infecting fungal strains do not group together as a single cluster in a species tree is hypothesised to be caused by exchange of pathogenicity chromosomes. This process is known as "horizontal chromosome transfer" and the transferred chromosomes contain genes that will allow the fungus to colonise a plant species. We decided to use these genes as a target for diagnostic marker design, as we noticed that they (in contrast to classically used genes) were often identical between strains affecting the same plant species. In our recent paper we describe diagnostic DNA markers that allow quick and reliable detection of the seven host-specific forms of *Fusarium* that affect cucumber, melon, watermelon and other cucurbit species. With these markers we are now able to specifically detect and quantify the pathogen in small tissue or soil samples. The concept presented in our article can be extended to other strains of this pathogen as a tool for researchers and plant "doctors". Ω

↓ Figure
Fusarium oxysporum (in green) growing inside a cucumber root.



→ Reference
P. van Dam *et al.* Comparative genomics-based markers: discrimination of host-specificity in *Fusarium oxysporum*. *Applied and environmental microbiology* ***84*** (2017), http://aem.asm.org/content/early/2017/10/09/AEM.01868-17

Under the magnifying glass: soil life

ELLY MORRIËN is postdoctoral researcher in soil ecology at the Department of Ecosystem and Landscape Ecology (ELD) of the Institute for Biodiversity and Ecosystem Dynamics (IBED), UvA.

→ Earthworms, spiders, springtails, mites, nematodes and microbes such as fungi, bacteria and protists: soil is booming with life! Together, all soil life forms a giant society. But how is this society structured? And what happens during nature restoration, which is the process by which grasslands formerly used as agricultural fields are slowly returned to natural ecosystem functioning? When trying to restore nature on abandoned grasslands, we saw that the evolution of soil life is commonly overlooked.

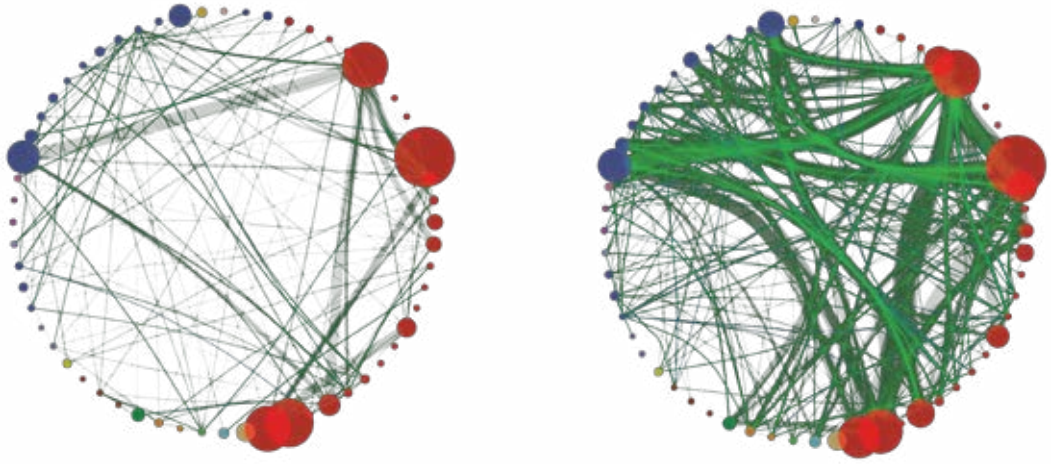
To understand how the full soil network changes during restoration, we examined and compared 20-cm deep soil cores collected from semi-natural grasslands in The Netherlands that were abandoned recently (5 years) and longer ago (30 years).

By labelling the carbon atoms, we were able to follow the food flow throughout the whole soil ecosystem. In the lab, we fed the plants in the soil cores CO_2 with labelled carbon atoms in an air-tight chamber. During photosynthesis, plants turn this CO_2 into labelled sugars, exuding them from their roots into the soil. Here, they can then be taken up by microbes such as bacteria and fungi that live in, on or around the roots. Microbes are the primary consumers of these plant products. As the microbes, in turn, get eaten by secondary consumers such as springtails and mites, and those again by predators such as predatory mites and spiders, the carbon trickles up the food web. Tracing the amounts of labelled carbon in all species allowed us to see where plant-generated sugars went in the belowground soil network. Sugars are the fuel of the system, but plants need more than only sugars to grow. They need nitrogen and phosphorous as well, just as microbes do. Therefore, in natural systems, there is a constant competition for sugars and nutrients in the soil, leading to dense networks among the players. By applying fertilisers in agricultural systems, crop plants no longer depend on the interaction with soil life. During nature restoration, slow-growing successional plants need to re-establish the connections with the soil biota; this network tightening takes time.

Fungi turn out to play a very important role in nature restoration, as they appear to drive the development of denser networks in the soil. In agricultural soils, the fungal hyphae are severely reduced for example by ploughing, and therefore, in the undamaged soil bacteria have an advantage and rule there. With time, there is a strong increase in the role of fungi (see Figure). We discovered that already at an early stage (5 years) in succession, half the amount of carbon that flows from plants into soil is taken up by the soil fungi. After 30 years, that share has risen to three quarters of the plant-derived carbon stored in the soil by fungi. This is an enormous achievement by the fungi, as they only make up about 10% of the total microbial biomass in most grasslands. We discovered that if fungi are stimulated to become active in an early stage of secondary succession, a denser soil network can be stimulated that locks in most of the available nutrients, which allows successional plant species to establish sooner. Thereby, it is possible to speed up nature restoration considerably in the future. Understanding the role of fungi in sequestering carbon in grasslands will be a very useful tool in understanding how carbon enters the soil on steppes, tundras, prairies and savannahs.

Our results provide an intriguing glimpse of how tightening of belowground networks and compositional shifts in soil species might be related to enhanced efficiency of carbon uptake during nature restoration. Ω

→ Reference
Elly Morriën et al., Soil networks become more connected and take up more carbon as nature restoration progresses, *Nature Communications* **8**, 14349 (2017). https://www.nature.com/articles/ncomms14349



→ Figure
Comparison of the interaction strength between the species subgroups in semi-natural grasslands on recently (left) and long-term (right) abandoned agricultural fields. Between each combination of species we calculated the Spearman's rank correlation, which is a measure of how their relative abundances are correlated. Line colour and transparency are proportional to the interaction strength. Size of the circles is proportional to the number of species/taxa in that subgroup. Red-filled circles are bacterial groups, blue-filled circles are fungal groups.

The evolution of the genetic code

PETER VAN DER GULIK is PhD student at the Algorithms and Complexity group, CWI.

→ In 1968, Marshall Nirenberg won the Nobel Prize in Physiology or Medicine for his seminal work on deciphering the genetic code. What is this code? DNA strings consist of four different kinds of "letters": T, C, A and G. This four-letter code has to be translated into proteins, which are essential for the processes of life. The set of translation rules from the DNA string to the protein string is called the genetic code.

First, parts of the DNA, the genes, are transcribed into RNA, in which the letter T from the DNA code is replaced by a U. This messenger RNA carries the code for an entire protein. Next, the translation of the RNA into a protein takes place on ribosomes in the cell with the help of small tRNAs. These tRNAs have two important properties: they are chemically linked to one specific amino acid and they carry a three-letter RNA code that fits the genetic code of the messenger RNA. In this way, the tRNAs specify which sequence from the genetic code corresponds to which amino acid.

The translation of the RNA is based on a genetic code that consists of triplets of A, C, G or U, called codons. The complementary triplets of the tRNAs are called anticodons. There is a universal start of translation, the "start codon" AUG. This codon fits the tRNA that carries the amino acid methionine. Each of the next triplets on the RNA codes for a specific amino acid. Which triplet codes for which amino acid is summarised in the universal codon table (Figure 1). In this way, the RNA is translated into a chain of amino acids, a protein. The process is terminated when one of three different "stop codons" ("Ter" in the table) is encountered. You probably calculated that a triplet combination of the four letters A, C, G or U results in 64 possibilities. However, only 20 amino acids are known to exist in living organisms. This means that several different triplets will code for the same amino acid.

The basics of the genetic code were discovered fifty years ago. In recent years, more genomes of microbes (archeabacteria and modern species) and higher organisms have become available, shedding more light on the evolutionary history of the genetic code. Researchers from the CWI have pointed at a strict regularity in the genetic code, which is not generally known in the field.

As indicated in Figure 1, CWI researchers discern four colour groups: red, blue, green and yellow. The blue group concerns codons of which the first two nucleotides are both either U or A. These blue codon boxes are all split into two different translations. This splitting of boxes into translations also occurs in the green group. When the first two letters in a codon box are both either G or C, the translation is identical for all codons in the box; this is the red colour group. The yellow group consist of the remaining four boxes, each with an identical translation for all codons involved. The basic structure of the genetic code is thus strictly regular, posing the question: why is this the case and how did it evolve?

To understand this regular structure of the genetic code, we have to introduce an additional phenomenon. This is called "wobble": in specific cases, a tRNA molecule is able to recognise more than just one codon. For instance, the anticodon GAA is able to recognise not only codon UUC but also codon UUU. In the red and yellow codon boxes, originally a single tRNA was present with a U-starting anticodon that could "wobble" to U, C and G. In the green and blue codon boxes, this "wobble" was not possible, and two separate tRNAs were present: one with a G-starting anticodon "wobbling" to U, and another with a C-starting anticodon which did not "wobble". As a consequence, 23 tRNAs would be sufficient to cover all 20 amino acids in a primitive cell. These cells would have a relatively "slow" translation system because the "wobbles" do not fit perfectly.

UUU Phe	UCU Ser	UAU Tyr	UGU Cys
UUC	UCC	UAC	UGC
UUA Leu	UCA	UAA Ter	UGA Ter
UUG	UCG	UAG	UGG Trp
CUU Leu	CCU Pro	CAU His	CGU Arg
CUC	CCC	CAC	CGC
CUA	CCA	CAA Gln	CGA
CUG	CCG	CAG	CGG
AUU Ile	ACU Thr	AAU Asn	AGU Ser
AUC	ACC	AAC	AGC
AUA	ACA	AAA Lys	AGA Arg
AUG Met	ACG	AAG	AGG
GUU Val	GCU Ala	GAU Asp	GGU Gly
GUC	GCC	GAC	GGC
GUA	GCA	GAA Glu	GGA
GUG	GCG	GAG	GGG

↑Figure 1.
Four colour groups in the universal genetic code. Triplets such as "GUG" are the RNA codons; amino acids encoded by the triplet(s) are abbreviated. For example, "Arg" stands for arginine.

"tRNA-modifying enzymes are key players in the evolution of the genetic code."

During evolution, primitive cells became more sophisticated and evolved to contain a larger amount of DNA. As a consequence, more tRNA genes could be afforded to make translation more efficient, and four-fold degenerate codon boxes could have a tRNA with a G-starting anticodon next to the one with a U-starting anticodon. With two tRNAs for the red and yellow boxes, the total number of tRNA genes would rise to 32 (for the careful reader: the number of tRNAs in the AUN codon box becomes three as there are two tRNAs for methionine

("Met"), one of which is dedicated to a "start" function; the number of tRNAs in the UAN codon box is just one as there are two "stop codons" in this box).

The next step in evolution was improvement of the "wobble" by introducing enzymes that modify tRNAs in such a way that translation proceeds faster. A major change was the introduction of inosine, a modified A that fits to U, C and A. Nowadays, this system is present in bacteria and in eukaryotes (fungi, humans, plants and animals), but absent in archaea (archaic microbes that are fundamentally different from bacteria and eukaryotes). By looking at the similarities and differences in anticodon modifications between bacteria and archaea, we can try to formulate the codon usage system of the Last Universal Common Ancestor (LUCA) of all life on earth (see Figure 2). For this we have to include the use of both tRNAs with U-starting anticodons and tRNAs with C-starting anticodons in all codon boxes. In this way, the number of tRNA genes goes up to 32 + 13 = 45, while several modification enzymes are necessary to reach this state. We propose that the most parsimonious explanation is that the LUCA did not have inosine, that archaea never acquired inosine and that bacteria evolved inosine. All other organisms inherited the inosine system from bacteria.

Our story shows that tRNA-modifying enzymes are key players in the evolution of the genetic code. Understandingly, mutations in these enzymes are often deleterious and have been associated with certain forms of cancer. Understanding the evolution of the genetic code will thus remain an important quest for scientists. In the computational biology theme of CWI's Algorithms and Complexity group, we work on this topic with enthusiasm! Ω

UUU UUC tF	UCU UCC tS3	UAU UAC tY	UGU UGC tC
UUA tL5	UCA tS2		
UUG tL3	UCG tS4		UGG tW
CUU CUC tL2	CCU CCC tP2	CAU CAC tH	CGU CGC tR3
CUA tL1	CCA tP1	CAA tQ2	CGA tR2
CUG tL4	CCG tP3	CAG tQ1	CGG tR4
AUU AUC tI	ACU ACC tT2	AAU AAC tN	AGU AGC tS1
	ACA tT1	AAA tK2	AGA tR5
tMi tMe	ACG tT3	AAG tK1	AGG tR1
GUU GUC tV2	GCU GCC tA2	GAU GAC tD	GGU GGC tG2
GUA tV1	GCA tA1	GAA tE2	GGA tG1
GUG tV3	GCG tA3	GAG tE1	GGG tG3

↑ Figure 2.
Colour-coded explanation of the 45-tRNA set of the Last Universal Common Ancestor (LUCA). Colours are chosen such that no fields bordering each other have the same colour, in order to provide maximum contrast. Codons are followed by the principal tRNA decoding them; for instance, "tS2" stands for "second serine tRNA". Standard one-letter abbreviations of amino acids are used (for instance, "K" stands for "lysine"). For the methionine tRNAs, "e" stands for "elongator" and "I" stands for "initiator".

Acknowledgements
Jop Briët and Jeroen Zuiddam produced the figures.

VALENTIN HAMMOUDI carried out his PhD thesis research at the Swammerdam Institute for Life Sciences (SILS), UvA. He is currently working as a postdoc at the Freie Universität Berlin, Germany.

Growth or defence: how plants regulate this choice

→ Plants have to decide whether they spend their energy on growth or on defending themselves against microbes or herbivores that are attacking them. A plant that spends most of its energy on growth will impair its immune system, while a plant with a constant activation of its defences will grow slower. Plants must therefore be able to keep a right balance between growth and immunity. In particular, environmental conditions such as temperature tend to deregulate this balance. For instance, a mild increase in temperature will prioritise growth over defence. With the current trend of increasing temperatures on Earth, we need to understand how plants maintain a healthy balance. This knowledge could open new ways to breed crops that can maintain this balance, leading to higher and healthier crop yields.
Within cells, the growth/defence balance is maintained by labelling the key proteins that control this process with a small chemical modification (called "post-translational modifications"). An advantage of such a strategy is that this protein-labelling is a reversible process: detaching the small chemical modification from the key protein will revert the protein to its initial status. We investigated an important protein modification called "Small Ubiquitin-like Modifier" (SUMO).
We made transgenic plants that were unable to use these SUMO molecules for labelling their proteins and discovered that these became dwarfs, which is the term used when plants are significantly smaller than standard members of their species. Therefore, our hypothesis was that these plants spend most of their energy in defence instead of growth. This means that SUMO molecules act as a handbrake for plant defence: losing this handbrake by removing SUMO molecules results in hyper-defensive plants, explaining the dwarfism. Remarkably, even when we promoted growth by mildly increasing the temperature, the SUMO-deficient plants remained dwarfs. We figured out that the dwarfism of these plants is in fact the result of a combination of effects. SUMO modification appears to have a dual function: it represses plant immunity at different levels and, at the same time, promotes plant growth by affecting hormones involved in elongation and development of plant tissues. SUMO molecules are then crucial actors in the control of the trade-off between plant immunity and growth. Affecting the attachment of SUMO molecules to specific proteins might therefore be a way to favour either growth or defence, and consequently to modulate crop yield. Ω

→ Figure
The two plants on the left show normal growth and development. In contrast, the two plants on the right have a hyper-activation of their immune system: their energy is mostly spent on defence processes instead of growth, which explains their severe dwarfism.

→ Reference
V. Hammoudi *et al.* The Arabidopsis SUMO E3 ligase SIZ1 mediates the temperature dependent trade-off between plant immunity and growth. *PLOS Genetics* (2018). doi:10.1371/journal.pgen.1007157

Caught in the net: The role of the extracellular matrix in chronic depression

DANAI RIGA is postdoctoral researcher at the Department of Molecular and Cellular Neurobiology, Center for Neurogenomics and Cognitive Research (CNCR), VU.

SABINE SPIJKER is Professor of Molecular mechanisms of cognition, Center for Neurogenomics and Cognitive Research (CNCR), VU.

→ Depression is a chronic mental disorder affecting more than 300 million people worldwide. In 2017, depression was declared the global leading cause of disability, with its financial burden due to loss of productivity reaching 1 trillion dollars per annum (World Health Organization). The disorder is traditionally linked to a negative mood, overwhelming sadness and a loss of interest in pleasurable activities. Less acknowledged but equally debilitating are its cognitive symptoms, which include distractibility and impaired memory. These persist after treatment with common antidepressants. At present, there are no specialised treatments of cognitive deficits caused by depression. Consequently, these deficits contribute considerably to disease burden, prolonging the depressive state, and hindering full recovery of patients.

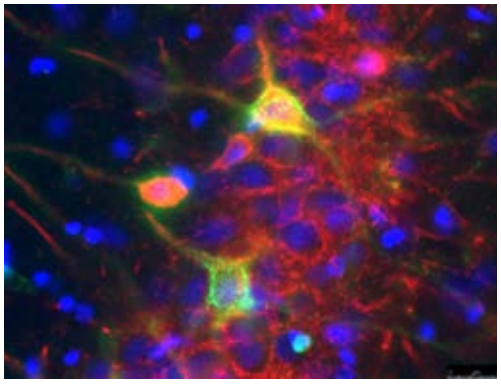
In order to devise novel treatments that target cognitive symptoms in depression, we need to understand their neurobiological principles. Our research aimed to address this question, by providing evidence on the molecular and cellular processes that underlie impaired memory in an animal model for chronic depression, the so-called social defeat-induced persistent stress (SDPS) rat model. Animals undergoing SDPS are forced to submission to a large, dominant rat. This is combined with prolonged subthreshold emotional stress induced by social isolation. Exposure to these stressors results in a chronic (up to 6-months long) depressive-like state in rats that is characterised by reduced sociability and dysregulated pleasure-seeking, as commonly seen in depressed human patients.

SDPS is also known to induce severe and persistent cognitive deficits such as impaired spatial memory. As it is well-established that spatial memories depend on the proper functioning of the hippocampus, a brain region that shows both structural and functional changes in depressed individuals, we investigated the effects of SDPS on the rat hippocampus. First, we found that hippocampal long-term potentiation (LTP), a process that is considered the cellular correlate of learning, was decreased in depressed rats. Interestingly, this deficit could be normalised by treatment with the antidepressant imipramine. Next, we aimed to unravel the particular molecular changes underlying impaired spatial memory and reduced hippocampal LTP seen in depressed rats.

For this, we zoomed in to the contact sites between neuronal cells, so-called synapses, and looked at their protein composition. Proteins are the building blocks of many biological processes, including neuron function and communication. We identified a family of proteins, the chondroitin sulphate proteoclycans (CSPGs) that considerably increased after SDPS and returned to normal levels after imipramine treatment. Together, CSPGs make up the extracellular matrix, a lattice-like network of molecules occupying the extracellular space. In the hippocampus, this matrix envelops inhibitory neurons and contributes to synapse formation and maturation, neuron-to-neuron communication, and neuronal plasticity.

Next, we visualised the extracellular matrix in the hippocampus and we found that in depressed rats, a larger number of inhibitory neurons were surrounded by it. This resulted in inhibitory neurons having trouble communicating with other brain cells, which in turn contributed to a reduction in hippocampal inhibitory neurotransmission. We wondered whether the 'thickened' extracellular matrix was mediating the debilitating effects of SDPS on hippocampal plasticity and on spatial memory. To answer this question, we used an enzyme that breaks down the matrix, thereby freeing the extracellular space and allowing for new synaptic contacts and increased neuronal communication. Intracranial (that is, in the brain fluid) administration of this enzyme not only normalised the number of matrix-enveloped inhibitory neurons of the hippocampus, but it also restored both inhibitory neurotransmission and hippocampal LTP. Most importantly, after a single treatment with this enzyme, depressed rats showed normal spatial memory.

In short, we identified a novel neurobiological substrate involved in memory deficits during depression. Our data suggest that the extracellular matrix contributes to a "rigid" molecular and cellular state, where new information is not properly communicated and memories cannot be stored or retrieved. Reduction of the surrounding matrix increases neuroplasticity and counteracts these effects. This has great promise for future therapeutic strategies against cognitive symptoms of depression. Ω



↑ Figure
Chronic depression increases the number of hippocampal neurons that are enveloped by extracellular matrix (ECM).

→ Reference
D. Riga et al., Hippocampal extracellular matrix alterations contribute to cognitive impairment associated with a chronic depressive-like state in rats. *Science Translational Medicine* **9** (2017). http://stm.sciencemag.org/content/9/421/eaai8753

"Rigid neurons impair cognitive performance after depression."

An interview with Marjo van der Knaap, head of Paediatric Neurology of the AMC & VUmc, and Professor of Translational Neurosciences at the VU. She dedicated her life defining white matter disorders, analysing children suffering from them and searching for therapies.

Brain white matter disorders

BIO MARJO VAN DER KNAAP

Born
1958, Delft, the Netherlands

Study
Propaedeutic exam Classical languages, Leiden University
1984 Medicine, Erasmus University Rotterdam
1984-1991 Residency Neurology and fellowship Paediatric Neurology, University Medical Center Utrecht
1991 PhD thesis "Myelination and myelin disorders, a magnetic resonance study in infants, children and young adults", Utrecht University.

Job
1991 Paediatric neurologist
1999 Professor of Paediatric Neurology
2007 Head of Paediatric Neurology, VUmc
2009 Professor of Translational Neurosciences, Faculty of Earth and Life Sciences, VU
2017 Head of Paediatric Neurology, AMC & VUmc

Selected awards and honours
1999 Gold Medal, International Society of Magnetic Resonance in Medicine
2007 Michael J. Bresnan visiting professor of Neurology, Harvard Medical School, Boston, USA
2008 Spinoza Prize, Netherlands Organisation of Scientific Research (NWO)
2010 Member of the Royal Netherlands Academy for Arts and Sciences (KNAW)

We meet Marjo van der Knaap in her office at the VUmc after going through corridors decorated with cheerful bunnies and waiting rooms full of toys. "Children are often scared of yet another white-coated doctor," she says, "but I have my ways to get them into my game", while showing us her miniature doctor's suitcase packed with playful equipment...

What is the white matter of the brain, and what do the associated diseases mean for the affected child?
"The brain is composed of neurons, the grey matter, which is studied by most neuroscientists. White matter refers to the fibres that connect the neurons both within and between brain areas and with the rest of the body. The diseases I study are called leukodystrophies; they form a group of disorders specifically affecting the white matter of the central nervous system (CNS). In addition, they have in common that they are genetically determined. The symptoms and age of onset of leukodystrophies are variable, but many children show progressive neurological dysfunction and die (sometimes much) earlier than normal."

What attracted you to study child neurology and these devastating paediatric diseases?
"Most people think I have carefully planned my career, but it has been far from a straight line. I have always loved languages and linguistics. I also liked physics, mathematics and chemistry in high school. When choosing my undergraduate studies, I thought of doing either psychology, classical languages or mathematics. In the end I chose classical languages. I soon realised I would be either a teacher or end up in a museum, neither of them was ideal for me. So, I decided to switch to medicine. Initially, I didn't like the study very much. I started to really like it when I was training in neurology. Every patient had an individual problem and I enjoyed the process of observing, teasing out and making a diagnosis that fits."

So, starting from adult neurology, how did you end up in the field of MRI and leukodystrophies, which are mainly seen in children?
"At the time I was resident in Neurology, two things happened. First, I fell for paediatric neurology. I liked to work on the complex neurological disorders seen in children and I was deeply impressed by the courage and resilience of affected children. Second, MRI was a huge development in medicine. For the first time we could see details in patients' brains. I decided to specialise in MRI, and chose an internship in Neuroradiology, here at the VUmc. I prepared my-

self very well, so I knew all about the physics of MRI. The professor in Neuroradiology, Jaap Valk, was impressed and on the third day he offered me a PhD position. I turned that down as I was doing a PhD in Utrecht. On the fifth day he said "Shall we write a book together on white matter disorders?" That sounded like fun, so I dived into this, and in the end, I devoted my whole career to it! The book is still seen as a hallmark in the field of leukodystrophies. I changed the topic of my PhD in Utrecht, namely into the application of MRI to children with white matter disorders. MRI is phenomenal for this type of diseases. It has a fantastic sensitivity and very high diagnostic specificity, keeping the different (genetic) subtypes apart. For other neurological disorders, like Alzheimer's or Parkinson's disease, an MRI scan can visualise volume changes but not at an early stage. The beauty of MRI of leukodystrophies is that the brain's white matter structures as well as substructures have different selective vulnerability for the different genetic defects. The different patterns of selectively affected structures in the brain can easily be visualised by MRI."

What attracted you in these relatively rare diseases? Most students want to solve big diseases that affect a lot of people.
"I have never been somebody with a heroic perspective. If you want heroism then you work in the emergency room or you become a surgeon. I never had such aspirations. I enjoy the complexity of things and like to sort out puzzles. Adding to the knowledge of how these diseases occur, what their mechanism is and how they can be solved makes my daily life meaningful. Everything I do, whether it is seeing patients or talking about scientific results related to these diseases, matters. Another thing is that I am drawn to subjects that are avoided by most colleagues. Some leukodystrophies, like Vanishing White Matter, are devastating and patients cannot be cured. But if nobody would work on these diseases, that would be terrible. Imagine the parents of an affected child. In fact, I also felt drawn towards elderly and demented people, as for a long time there was not much attention going in that direction. Fortunately, that has changed a lot.
Neurology fits me well. One of my slogans is 'Neurology is a slow profession'. In the ER you have to make decisions on a time scale of seconds, and that is too fast for me. In Neurology, we typically have time to think about a diagnosis and a treatment plan. We view and analyse decisions from many angles before we do something. I like this careful decision making."

↑ One of the other toys from Marjo's miniature doctor's suit-case (left) is a mouse.

"Neurology is a slow profession; we view and analyse big decisions from many angles before we actually do something."

What are your expectations for a treatment?
"It will take a bit, but we will for sure achieve a cure at some point. Since leukodystrophies are caused by a single mutated gene, we know the cause. I am a person who likes to have concrete results within my life time. That is why I prefer to work on these monogenic diseases over diseases like Alzheimer's disease, in which the cause is multifactorial and in part unclear. Still, there will not be a single magic pill for a leukodystrophy. Even although leukodystrophies are 'simple' monogenic diseases, in the end, treatment will need to target multiple facets. On one hand, I therefore invested in the development of stem cell and gene therapy for the disease Vanishing White Matter, with Dr. Vivi Heine. On the other hand, we also work on drug therapy with Dr. Truus Abbink, thus targeting the disease from different angles. The development will be step-by-step and we will have to learn as we go. For most patients, Vanishing White Matter is a disease of the CNS only, but for cases with early infantile onset, which are the most serious cases, it is a multi-organ disease. If we successfully treat 'milder' patients with a CNS-only disease and they live longer, we may be confronted at a later stage with multi-organ involvement, for instance in the form of liver failure or bone marrow failure. At this moment we never reach such a stage as patients die earlier due to the CNS disease. When we see such complications, we will decide what we need to do. So, in the end, I am totally optimistic about finding a cure for leukodystrophies, but there is long way to go. We will get there step by step, using all tools and means we can think of."

One of the diseases you discovered is also called "Van der Knaap disease". Do parents of patients suffering from this disease have higher expectations of you?
"I do not like diseases being called after a person. To want a disease with one's name is vanity. I wrote a letter to the editor saying "Forget about Van der Knaap disease", and I proposed a different name, namely 'MLC', which describes what the disease looks like, namely Megalencephalic Leukodystrophy with subcortical Cysts. Also, when we discovered the mutated gene, I called it MLC1. So, there is no way around the name.

So you do see patients? And how does that work with children?
"As head of paediatric neurology at VUmc and AMC I do the weekly clinical paediatric neurology grand rounds for both institutes. Additionally, colleagues pass by to ask me clinical questions. We often discuss life decisions, such as when to start and when to stop treatment. Typically, no one makes such decisions alone. I personally see patients as well. Dealing with children is a specialty on its own, because of course children are scared of doctors. But I have a trick for that; I seduce them into interaction with this...."

At this point in the interview, Marjo pulls open a drawer to show us her doctor's miniature suitcase. It contains all kinds of funny items, a few of which are visible on the photographs we took. She pulls out a colourful stick and a yellow puppet with its hands raised upwards.

"When I show them these things, reservation goes away. For example, I have this wonderful stick, which contains stars that can move; I ask children whether they want to hold it. When they grab it or handle it, I can see how they move and how their fine motor coordination is. The same goes for my puppet with the glowing head, when I ask them to greet him and shake his hand. I collected these items over the years, wherever I could find them."

Triggered by another toy, namely the mouse, we get into the subject of van der Knaap being a medical doctor by training who runs a biology lab.

So how did you find yourself suddenly studying mouse models and doing stem cell research?
"I am very much interested in the disease process, the biology of diseases. I have a 'research brain' that is focused on the understanding of →

how the disease works. Although I'm very interested in my patients in terms of caring, I also view them as experiments of nature. I can be deeply puzzled by features I consistently see and then I cannot help myself from making hypotheses on how and where these symptoms could originate from. If I would have been a researcher only, I probably would have been extremely fanatic. Medicine keeps me grounded. The suffering of these children and their families is a deep motivation for me; I want to work for them. It is my responsibility to move the field of leukodystrophies forward. I realised that if I really wanted to make a difference, I would have to work on basic disease causes and mechanisms. I needed lab space to study the genetic basis of leukodystrophies. I collaborated with geneticists like Jan Pronk and Peter Heutink. We were extremely successful in gene finding. But now this period is over and we have to make the next step in understanding gene functionality and disease mechanisms. I needed mouse models, so we created them. So basically, we had to move from genes to proteins to cellular work, even looking at the whole mouse and its physiology and behaviour.
It is not that I had pre-formed concepts of all of this in my mind. Each time I achieved one step, it meant that I needed to take the next step as well, which I did. This went from doing genetics to making a mouse to making induced pleuripotent stem cells, each time gathering the right people and raising money for it."

So, although your choice of studies wasn't clear at the beginning, the topic for your PhD was. After that, was your career plan clear?
"No, after finishing my PhD and being in my first permanent position I had something like a midlife crisis. I did my PhD cum laude and had a great job, all beautiful of course, but what should I do next? It took me a couple of years before I decided to work on unclassified white matter disorders, and started to 'collect' and study them. The path from there to here took several years. But I'm satisfied with all we have accomplished and the progress we have made now, as we're heading more towards understanding gene function and therapy."

↑ This little boy has a motor coordination problem, but there is nothing wrong with his attention (published with parental permission).

"It is important to focus, make a decision on your topic of interest and then stick to it."

What would be your advice to young PhD students and early-career scientists?
"Go for what crosses your path and what suits you. You should not be driven by money or by your ego. Go for what you think is challenging, tickling your mind. I liked neurology as it is a profession in which you have to know a lot. After my decision to go for neurology I came into contact with paediatric neurology and thought "this is it!". The same for MRI. But even if I would not have chosen MRI, I would have ended up being okay somewhere, as I'm a driven person. Along that line, one should not be scared to go into the unknown. I was never hindered by pre-set borders. Some people might feel "Why do you work with MRI, you are not a radiologist?" Or "Why do you work on genetics, as you are not a geneticist?" You should go for what you like, because then you mostly do what you are good at. On the other hand, it is also good to focus and to stick to that. There are so many interesting things I ran into, like muscle disorders for example, really fascinating. Yet, when you meander too much, you get nowhere."

The AMC and VUmc are merged nowadays, what do you see as challenges?
"Patient care is very much the same in both hospitals, and we have great people in Paediatric Neurology at both the AMC and VUmc. The thing that is troublesome is that each hospital is very focussed on quality issues. This means there are lots of forms to be filled in, lots of bureaucracy - and that on both sides. Now, a more interesting topic is education, as that is still separate for the two medical centres. So, I'm curious to see how that is going to work out in the future. Paediatric neurology is a small subject in the medical curriculum. Yet if students need to make a decision about their specialisation studies and the direction they want to take, they need to be aware of what is out there; they need to know paediatric neurology is also an option."

With your busy life, do you take time off from work? What is the ideal me-time for you?
"I read a lot; that has never changed. There is no good day and certainly no good week without reading a book. To be physically busy I like gardening. My garden of 1200 m2 keeps me busy from March to November. If I would have lived in the city in an apartment, I probably would have worked 7 days a week, and have had no means of liberating myself from my daily-work worries. My garden really needs me and I need my garden!"

You have achieved so much already! What do you view as a next step in your career?
"I came from the unclassified and unknown leukodystrophies, we have defined new leukodystrophies that nobody knew about, we have set the diagnostic criteria and identified the genes involved. We have a better understanding of how some leukodystrophies work. Now, we are thinking about the first clinical trials for e.g. Vanishing White Matter, as there are drugs that look promising. If I could complete a first clinical trial and see whether I could alter the course of the disease, it would mean a lot to me. Not that I expect patients to be cured in one go. No, just being able to alter the disease progression. As soon as that happens, it means the beginning of the end of the disease. So, I'm now working with the EMA [European Medicines Agency] on protocols, orphan drug designation and all that. I learn a bunch of new words that I never heard of. If we can make a clinical trial happen and make a difference for patients, then I can round off my career in a very satisfactory way." Ω

Pancake science: How a hot griddle puts a perpetual bounce in hydrogel spheres

SCOTT WAITUKAITUS is a post-doc working in the Mechanical Metamaterials group at AMOLF, shared with Leiden University.

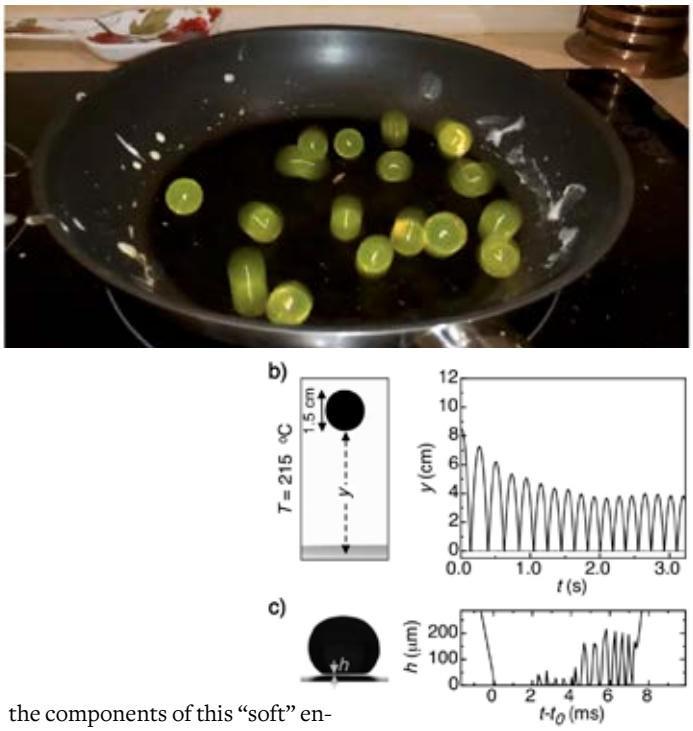
→ Reference
S.R. Waitukaitis, A. Zuiderwijk, A. Souslov, C. Coulais, M. van Hecke, Coupling the Leidenfrost effect and elastic deformations to power sustained bouncing. *Nature Physics* **13**, 1095–1099 (2017). https://www.nature.com/articles/nphys4194

→ The basic recipe for pancake batter should be well-known to anyone living in the Netherlands: flour, milk, eggs, a bit of sugar and a pinch of salt. Beyond these essential ingredients, one can add ham and mushrooms for a savoury dish or strawberries and whipped cream for something sweet. Recently, however, a Ukrainian man posted a YouTube video where he threw a rather unusual ingredient onto a hot pancake griddle: hydrogel spheres (see figure, panel a). Measuring about 1.5 cm in diameter and consisting of more than 99% water, these synthetic polymer-based objects can hardly be expected to make a tasty pancake, but as it turns out they do exhibit some fascinating physics. When cast onto a hot pan they spring to life, vigorously jumping around and producing shrill screeching sounds.

Inspired by this YouTuber's curiosity, and with zero mention of such an effect in the scientific literature, my research efforts of late have been dedicated to discovering the physics behind this phenomenon. Panel b of the figure shows what happens when a single hydrogel sphere is dropped from an initial height of 8 cm onto a hot (215°C) surface. Using a high-speed camera to observe the motion, we see that the sphere loses a little energy at first, but soon comes to an equilibrium bounce height of about 4 cm. Surprisingly, a sphere dropped from below this height climbs *higher* with every bounce, ultimately arriving at the same height. This equilibrium bouncing typically endures for 2-3 minutes, although we sometimes observe lifetimes as long as 10 minutes. In order to keep jumping, the spheres must be gaining energy each time they strike the surface. How does this energy injection occur?

As it turns out, the spheres' screams give us a clue. Zooming in on a single impact with a much higher frame rate and image magnification (panel c), one observes a tiny (~0.1 mm) gap that rapidly opens and closes below the sphere. It does so with a frequency of 2-3 kHz, producing the high-pitched screeching sound we hear. These oscillations arise because the sphere consists of so much water – each time it strikes the surface, a tiny bit of water is converted into steam, which causes a burst of pressure as it expands. This pressure does mechanical work on the sphere, deforming it elastically to produce both the sound and add a little bit of momentum. Once the pressure is sufficiently reduced after a burst, the sphere bottom elastically recoils back toward the surface, thus initiating a new cycle. Quite literally, this pressure-burst cycling mechanism is analogous to a steam engine. What's remarkable, however, is that virtually all the components of this "soft" engine are embedded in a single object made from a single material.

"When cast onto a hot pan the hydrogel spheres spring to life."



↑ Figure
a) Hydrogel spheres bouncing on a hot pancake griddle. b) The spheres reach a steady bounce height of around 4 cm, which typically persists for several minutes. c) Zooming in on the moment when a sphere interacts with the hot surface, we see that vapour pressure build-up coupled with elastic deformations of the sphere lead to a small fluctuating gap between the sphere and the surface.

By pure chance, this new effect is related to an older one that is also involved in the cooking of pancakes. As any seasoned chef knows, the temperature of a pan can be roughly determined by splashing a bit of water on it. On a moderately hot pan, the water will quickly sizzle and boil away, but at higher temperatures, the water will bead up into small droplets that glide around the surface and the pan is ready to cook on. This counterintuitive temperature dependence is due to the *Leidenfrost effect* (named after the 18th century German academic Johann Gottlob Leidenfrost), and it occurs because at sufficiently hot temperatures enough vapour forms below the water for it to float like a hovercraft – thus insulating it from contact and prolonging its life. The new phenomenon, which we have named the *elastic Leidenfrost effect*, is similar, but with the important new aspect we have laid out. Namely, it is the soft, elastic nature of the gel that allows the vapour pressure to couple synergistically with the sphere's deformations and hence lead to bouncing instead of hovering. Far beyond a curiosity, this discovery gives us a relatively powerful way to inject mechanical energy into gels, which could lead to applications in fields like active matter or soft robotics. There is a fair amount of work to be done before we understand the effect well enough to be able to do such engineering, but it's safe to say that this discovery will be a hot topic of research for years to come.Ω

Love at first... smell

Moths are ideal animals to study the evolution of sexual attraction. This is because female moths attract males through a well-defined sex pheromone -- essentially an odour. With around 130,000 species, they are also one of the most diverse groups of animals on Earth. Pictured here is a female *Heliothis virescens* moth, the study of which has given us important insight into why variation in attractiveness can persist in populations.

More information, on page 22 in the article by Astrid Groot and Michel van Wijk (IBED, UvA).

Photo by Laila Kee.

Global flood detection and monitoring using social media

JENS DE BRUIJN is PhD researcher at the Institute for Environmental Studies (IVM), VU.

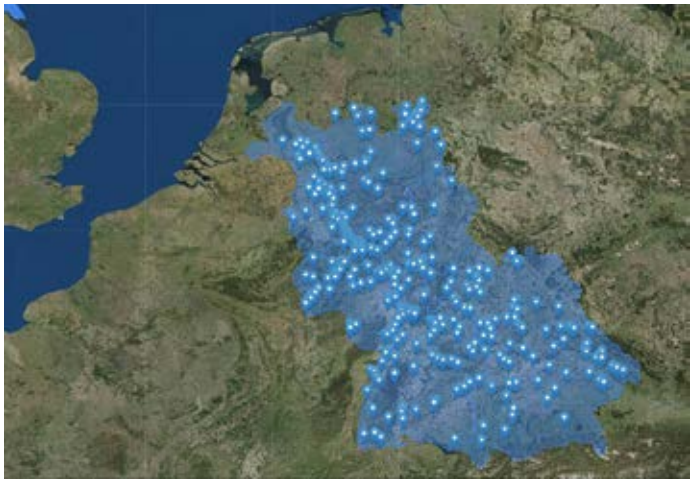
→ Reference
J. de Bruijn et al., TAGGS: Grouping Tweets to Improve Global Geotagging for Disaster Response. *Journal of Geovisualization and Spatial Analysis* **2**, 2 (2018). https://link.springer.com/article/10.1007/s41651-017-0010-6

→ Over the last 10 years, floods have caused almost 60,000 casualties and 400 billion euros in damage. Research shows that rapid response efforts are often hampered by a lack of timely and useful information. Usually, floods are detected and monitored using hydrological models or satellite imagery. However, many flood events remain unreported and the average time-lapse between the start of a flood and its detection by response organisations is long. More recently, people and organisations have started using information from online media to monitor flood events. Using a series of flood-related keywords in 12 major languages, roughly 75,000 flood-related tweets can be collected each day. Naturally, the number of tweets highly varies depending on the characteristics of currently ongoing flood events. For example, when Hurricane Harvey made landfall in the USA, upwards of 600,000 tweets were collected within 24 hours.

Researchers at the Institute for Environmental Studies (IVM, VU/Amsterdam Water Science) and the Dutch social enterprise FloodTags developed a new tool, the Global Flood Monitor (GFM, www.globalfloodmonitor.org) that detects and monitors flood events using this data. To do so, tweets need to be located first. Unfortunately, only ~2% of tweets have a GPS location of the user at the time of posting available. Another option is to use location mentions in tweets. However, linking individual tweets with confidence to a particular location is not as straightforward as it sounds as many locations have multiple occurrences worldwide (e.g., Amsterdam is the name of the capital of the Netherlands as well as of several towns in the USA). Therefore, we created a special algorithm called Toponym-based Algorithm for Grouped Geoparsing of Social media (TAGGS). The algorithm first splits a tweet's text into individual words (unigram) as well as sequencing individual words up to a length of 3 (bigrams and trigrams). These n-grams are then matched to the near-comprehensive set of geographical locations (a so-called gazetteer) extracted from an online repository of place names. Often, multiple candidate locations are found for a specific word. The algorithm then disambiguates these candidate locations based on the tweet's metadata, such as the user's home town and time zone. Additionally, all tweets that mention the same location within a 24-hour time frame are analysed together to increase the amount of available metadata for localisation.

In this way, the algorithm finds, in real-time, regions with enhanced flood-related Twitter activity and classifies them as flood events. Finally, a world map is generated visualising these events and their relevant tweets. As an example, the figure shows the located tweets (light blue) in the floods in western Germany (dark blue) in January 2018. By far the largest number of tweets were located along the Rhine river.

The GFM reveals the prevalence of floods in the world and their impact on communities. The tweets, often sent by affected people, show that almost daily, people need to be evacuated, losing their homes and even losing their lives due to floods. Even though many people work towards reducing flood risk and mitigating their impact when a flood hits, further efforts to reduce the impact of flood events on people's lives are required.



↑ Figure
TAGGS map of floods in Germany in January 2018.

Disaster relief organisations increasingly use online media to improve their situation awareness. As an example, FloodTags used, after careful validation within a specific region, parts of the GFM in their dashboard. These located tweets are enriched with other information based on natural language processing and hydrological information (e.g., rainfall measurements, river discharge data), to create a tool that is currently being used at the Philippine and Tanzanian Red Cross.

"Disaster relief organisations increasingly use online media to improve their situation awareness."

Although social media cannot provide an extensive overview of all flood events, many events that are not available in other disaster databases are detected. The platform also provides access to these historic events going back to July 2014. These historic events can be used, for example, as a reference for validation of various flood risk models and historic flood mapping.

Finally, when satellites observe the earth, their cameras can be pointed towards areas of interest. When a flood event is detected using, for example, social media, these satellites can be tasked to investigate the impacted area and thus provide more information about the event. Ω

Sowing corals for reef restoration

VALÉRIE CHAMBERLAND and MARK VERMEIJ are researchers at the Institute for Biodiversity and Ecosystem Dynamics (IBED), UvA, and part of an international team of researchers (www.secore.org).

→ The troubling loss of coral reefs worldwide has prompted scientists and conservationists to assist the reefs' recovery through active restoration approaches. A new innovation to sow coral larvae onto degraded reefs has potential for effective large-scale reef restoration, minimising costly and time-consuming approaches.

The aim of transplanting corals on degraded reefs is to increase coral cover and promote structural habitats. Until now, actual restoration has been done manually by divers who had to attach each coral, whether a fragment or a coral recruit settled on a substrate, individually. This is a costly and time-consuming approach. For instance, transplanting 10,000 individual corals on one hectare using common methods has until now required several hundred to a few thousand man-hours, whereas reef degradation occurs at a scale of hundreds and thousands of square kilometres.

We devised a new sowing approach, in which coral larvae are settled on specifically designed substrates that are self-stabilised and attach to the reef via natural processes. The design of the substrates not only promotes the attachment on the reef, but is also intended to enhance the survival of the coral settlers. After a few weeks to months these so-called 'Seeding Units' (i.e., substrates together with initial coral polyps) are sown on the reef by simply wedging them in crevices rather than requiring manual attachment. This method is 10 times more time-efficient than previous methods.

In the Seeding Units we made use of sexually propagated corals. This helps maintaining genetic diversity. Different gene combinations, so-called genotypes, arise within the population by recombination—the reshuffling of the genetic characteristics of parents among their offspring. New genetic combinations may therefore equip some coral offspring with better capabilities than their struggling parents to cope with future conditions.

We are now working on improving the sowing approach. The substrate design (see Figure) is being optimised to further increase coral settler survival and growth and to be able cover a wider range of reef habitats. Ω

→ Reference

V.F. Chamberland et al., New Seeding Approach Reduces Costs and Time to Outplant Sexually Propagated Corals for Reef Restoration. *Scientific Reports* **7**, 18076 (2017). https://www.nature.com/articles/s41598-017-17555-z

"Our approach to transplant corals on degraded reefs is 10 times more time-efficient."

→ Figure

Settlement tiles covered with tiny settlers of the boulder brain coral are marked (with red ties) and lined-up to be outplanted by the research team at CARMABI Marine Research Station, Curaçao. Photo: SECORE International / Kelly Latijnhouwers.

Amsterdam Water Science (AWS) is a research consortium between Vrije Universiteit Amsterdam and the University of Amsterdam combining expertise from both the natural and the social sciences. The consortium stimulates collaboration between knowledge institutes and the private and public sectors in the Netherlands, integrating science and education at all levels. AWS collaborates with leading universities and other knowledge institutes on a national and international level.

The key research topics are: Freshwater & marine ecology; Water quality & microbiology; Water & climate; Hydrology; Water governance; Environmental economics. http://www.amsterdam-water-science.nl

Solar energy can do it!

ALBERT POLMAN heads the programme on solar energy at AMOLF. He is professor of solar energy at UvA.

We all know global warming poses a serious threat to our society. With the Paris climate agreement in place, we are all committed to solve this problem. But how are we really going to do this? It turns out a fully renewable energy supply for our society will only materialise if scientists, engineers, industry, government and financial investors work together in a way they have never done before.

To avoid catastrophic climate change we need to install, at a very large scale, four sources of renewable energy: solar energy, wind energy and, for countries that are lucky to have it, hydroelectric and geothermal power. Together, these four technologies can fully replace the generation of energy from fossil fuels. The goal is that solar energy will take a 30% share of the energy we must generate. What do we need to do to make this happen?

First, the costs of solar energy (solar panels, energy storage, rebuilding the energy grid) should be further reduced by improving the technology. If we manage to reduce the costs of solar energy by a factor 4, we are done: solar energy will beat fossil fuels! In fact, solar electricity already is the cheapest source of energy in countries that are much sunnier than the Netherlands; it is offered at a cost below € 0.04/kWh. Over the past 30 years, the price of solar panels has dropped by a factor 20 as a result of improvements in efficiency and reductions in manufacturing costs. So now the challenge is to gain another factor 4!

Second, we must roll out solar energy at an extremely large scale. We need 400 solar fields of 30x30 km2, distributed across the globe to catch the energy from the Sun. We can invisibly integrate solar panels in our landscape and make them float at sea. And we can also turn solar panels into building materials so they are seamlessly integrated into our buildings. Moreover, we need to build the chemical factories to generate fuel from solar electricity. All this requires new technology and a new industry at a scale that has never been demonstrated before. We must really think big! We should develop revolutionary ultrafast large-scale manufacturing technologies in order to print solar panels as fast as we print newspapers today.

Unfortunately, all of this will likely not happen using the scientific and engineering knowledge that we have today: we do not know yet how to reduce the costs by a factor 4 and we do not have the technology to roll it out on an ultra-large scale. Therefore, as scientists and engineers we must use all our creativity to solve this. As soon as possible, we must invent new materials that make solar panels more efficient and cheaper to fabricate, discover new catalyst materials so we can create solar fuels, and improve battery materials so they store more energy. In particular, finding the new materials that can make this all happen is one of the most difficult scientific problems today. It requires an understanding of matter at the atomic level, and control over light and electricity at the nanometre scale. Creating major breakthroughs requires a man-to-the-moon-type approach in which tens of thousands of scientists worldwide work together. That means a multi-billion-euro investment in research.

But all of this is not enough. While we improve the technology and make it cheaper, it is essential that a solar industry develops in order to turn all these new ideas into practical systems at a very large scale. This requires enormous capital investments. Such investments will be triggered by innovations generated by scientific research. Therefore, scientists, engineers, industry and financial investors must work intimately together to make this happen.

In this process, the government can help by regulating the way energy is generated and used, for example by closing coal-fired power plants and taxing highly polluting cars. However, that will not automatically and rapidly create the breakthrough innovations that are essential in the near future. Therefore, the Ministry of Education, Culture and Science and the Ministry of Economic Affairs and Climate must team up to make a plan. We need a national man-to-the-moon-type solar-energy research and technology programme. We already have the scientists that can do it: over 400 experts at academic and technology institutes in our country -many of which in Amsterdam- are ready to get started, in close collaboration with their partners from all over the world. And we need to integrate this plan with a major industrial investment plan. If we do it right, we can solve the energy problem and at the same time have great economic benefits for our country.

If we succeed, global warming comes to a halt, air quality will strongly improve, we will have cleaner water in developing countries, and many geopolitical conflicts come to an end. We will have a more peaceful and wealthy society, and the resources to focus on all the other problems that we're facing. Let's do it now! Ω

Q&A

CORINA BRUSSAARD is leading scientist for Antarctic viral ecology working for the Royal Institute of Sea Research (NIOZ), and professor by special appointment of viral ecology at the University of Amsterdam. She is part of the national multidisciplinary expedition Netherlands Initiative Changing Oceans (NICO), a seven-month expedition to study the changing oceans in various locations, aiming to get a better grasp of opportunities and threats.

1. The first experiment I ever did was..,

... Actually, I cannot remember. I do know I often asked my parents and later on myself questions that started with "why" and "what": Why is the grass green? Why are not all peanuts looking the same? Why do birds fly away in winter? What makes that we do not fall over as the Earth moves? What is intelligence? These questions for me form the base for scientific experiments and discussion.

2. My constant source of inspiration is...

... a constant wonder about all kinds of things, in combination with wanting to know how it works. Add to this my paradoxical fascination for the small stuff & the larger concept and you get an oceanographer whose research focuses on the bad & the good of marine viruses.

3. One book that I recommend to all young scientists is..

... There are actually three I would like to recommend. *Brave New World* by Aldous Huxley and *1984* by George Orwell, as both books are dated and topical at the same time. And *This thing of darkness* by Harry Thompson. This book deals with "The Origin of Species" by Darwin but also described how it was to be on an expedition. It explains all kinds of scientific disciplines and the unbelief that is also related to science.

4. If I headed the Ministry of Science the first thing I would change is...

... aiming for the use of one terminology for primary and secondary school subjects (activities) related to science. At least clarify better to the young generation (from toddler to high-school student) that school classes and our own lives are full of happenings that comprise scientific approaches and concepts. Clear use of a consistent term (e.g. "science project") will improve recognition and understanding by the society (general public) for the need of fundamental science.

5. If I had to switch roles with a famous person for one day, I would choose to be...

... somebody with a lot of societal influence so I could push for improving animal living conditions (particularly factory farming) and environmental awareness. It would be good if this famous person were rich so I could donate lots of money at the same time.

6. I am most creative when...

... brainstorming. Approaching an issue from all different sides during an active brainstorming discussion with colleagues gives me a lot of energy that makes my brain go faster in creative thinking. I also brainstorm alone. Either way, subsequent causal thinking supports many nice ideas and initiatives.

7. If I could choose my field of study and university once again I would choose...

... probably the same. Retrospectively, the study of biology is so interesting, so diverse and always challenging. In particular, marine microbiology is fascinating and timely. Thinking about it, I am glad to be part of those trying to decipher and increase awareness of the immense value microbes in the oceans have for the planet.

8. When I am not being a scientist I am mostly...

... a person with science as one of my hobbies, as my husband says.

AMBER KERKHOFS carried out her PhD research at the Center for Neurogenomics and Cognitive Research (CNCR), VU. She is currently working for NWO and ScientistWanted.

Helping tired neurons with caffeine

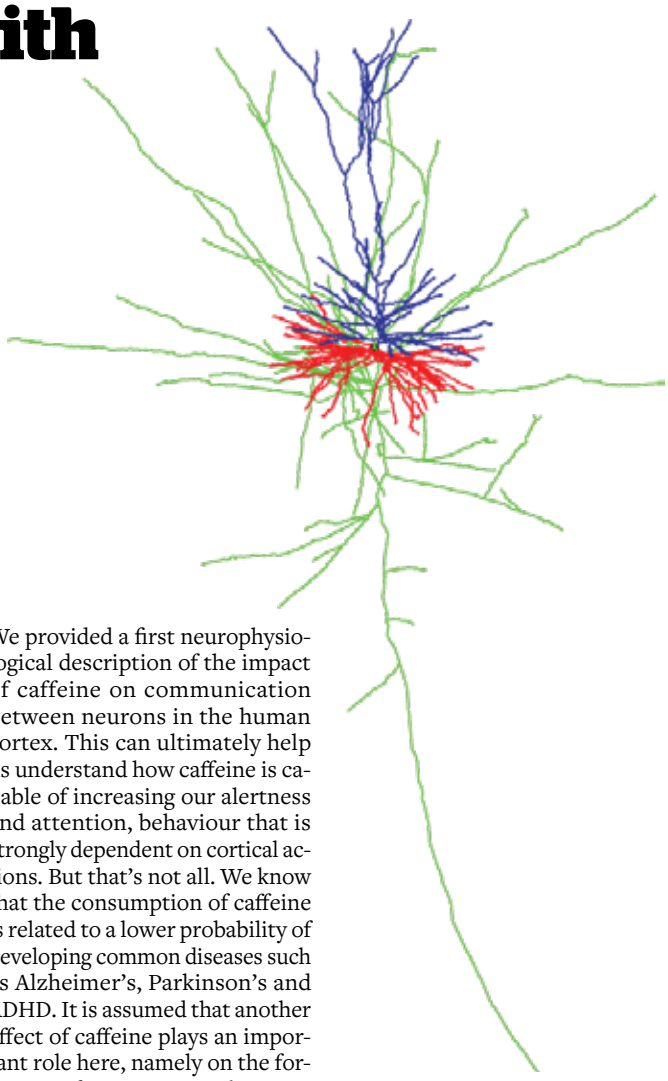
→ As scientists, we all know what caffeine does: it helps us make it through long working days, stay focused during long experiments or while reading papers. Surprisingly, the mechanisms of how caffeine affects our human brain are poorly understood. In our most recent article [1] we investigated how brain cells, called neurons, are affected by caffeine. We show that caffeine is helping tired neurons to communicate again.

Caffeine is consumed all over the world and as such it sits together with alcohol and nicotine at the top of the most widely consumed psycho-active drugs. This is not surprising, as caffeine has a positive effect on cognitive behaviour such as attention and alertness. However, very little is known about the effect of caffeine on human cortical signalling, especially in the case when it is applied in dose of moderate consumption: 50 µM of caffeine, which is equivalent to about one cup of coffee. The amount is important, as caffeine is only a psychostimulant with neuroprotective actions at moderate doses, but is a depressant with harmful effects at higher doses. At moderate doses, the only known biochemical action of caffeine in rodents is to block adenosine receptors, which are responsible for inhibiting cortical signalling. Whether and how caffeine affects human cortical signalling was not yet known.

By recording the electrical properties of single neurons of the human cortex (see figure), we found that caffeine strengthens synaptic transmission, which is the communication between neurons. Moreover, it has an effect on the probability that neurons become active after receiving a signal from another neuron, effects that were only present in neurons that were bathed in adenosine. In adenosine, neurons become 'tired' and communicate less often with each other. When they receive information, they pass this information on with a lower probability. Interestingly, when caffeine is present these effects are reversed. This indicates that caffeine in the human cortex has restorative capacities. While this is in line with common beliefs in the field, some of our results are also in conflict. Namely, in rodents it is assumed that caffeine mainly affects cortical signalling at the presynaptic level – the part of the cell that is sending the signal – while we showed that in the human cortex caffeine mainly affects postsynaptic signalling, the receiving end of the cell. The human cortex thus seems to respond differently to caffeine than the cortex of rodents. Thus, although the human and rodent brain rely mainly on similar mechanisms, small differences can have a large impact on the overall effect, stressing the importance of doing translational research on tissue from the human cortex.

"Caffeine strengthens synaptic transmission, which is the communication between neurons."

We provided a first neurophysiological description of the impact of caffeine on communication between neurons in the human cortex. This can ultimately help us understand how caffeine is capable of increasing our alertness and attention, behaviour that is strongly dependent on cortical actions. But that's not all. We know that the consumption of caffeine is related to a lower probability of developing common diseases such as Alzheimer's, Parkinson's and ADHD. It is assumed that another effect of caffeine plays an important role here, namely on the formation of contact points between neurons, called synapses. Normally, neurons that receive a lot of input from other cells increase the number of synapses, ensuring stronger communication between each other. Caffeine and other adenosine blockers can prevent the build-up of synaptic contacts. Studying whether this process is indeed taking place in the cortex can help us to better understand the effects of caffeine on cognition-related diseases. The results of our study of this process have also been published recently [2]. In conclusion, studying the effect of caffeine on neuronal communication can thus help us better understand human cognitive behaviour in terms of both short-term processes, such as those increasing alertness and attention, and long-term processes such as the prevention of diseases. Ω



↑ Figure
A reconstruction of a brain cell (neuron) from the human cortex after recording its electrical properties, with the information-receiving part of the neuron (dendrites, blue and red) and the sending part (axon, green).

→ Reference

1. A. Kerkhofs et al., Caffeine Controls Glutamatergic Synaptic Transmission and Pyramidal Neuron Excitability in Human Neocortex. *Front. Pharmacol.* **8**, 899 (2018). https://www.frontiersin.org/articles/10.3389/fphar.2017.00899/full

2. A. Kerkhofs et al., Adenosine A2A receptors control glutamatergic synaptic plasticity in fast spiking interneurons of the prefrontal cortex. *Front. Pharmacol.* **9**, 133 (2018). https://www.frontiersin.org/articles/10.3389/fphar.2018.00133/full

Nanoparticles bring colour to solar cells

VERENA NEDER is PhD student in the Photonic Materials group, AMOLF

→ Solar cells play a crucial role in the worldwide transition to renewable energy production, which is needed in the near future in order to reduce carbon emissions and mitigate their impact on our climate. Highly efficient solar cells are optimised to absorb as much light as possible and therefore have a black or dark blue surface. However, their salient appearance makes their application often limited to concealed places like rooftops or fields next to traffic routes. If they could be colourful, solar cells could also be applied in townscapes, integrated into house walls or exposed as part of architectural design. However, a colourful appearance means reflection of light and thus a lower solar cell efficiency. Therefore, a balance between losing light and creating colour must be found. We created a reflection layer for solar cells employing nanoparticles, which interact with one colour of light only, thus producing a colourful perception without causing additional loss of energy.

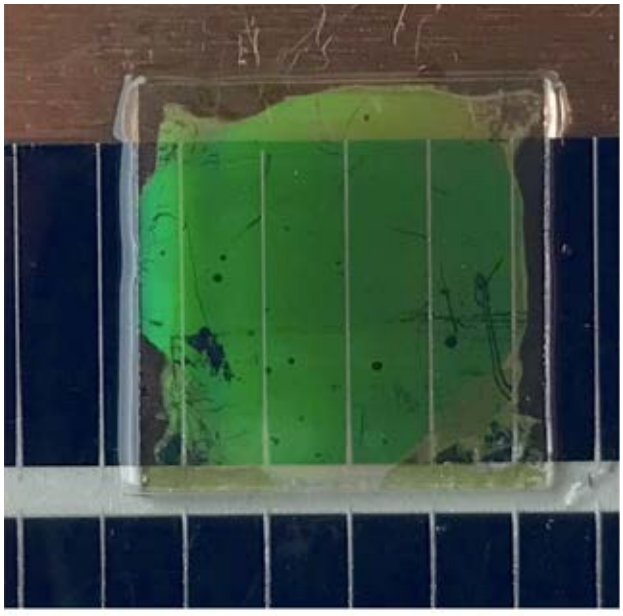
When light is shone on nanoparticles, particular strong interactions arise, which are different from those expected for conventional flat surfaces. One such interaction is the so-called Mie resonance, which takes place at a specific narrow range of wavelengths, i.e., one colour. Hence, the nanoparticles are invisible for the rest of the wavelengths. As this interaction is a linear effect, the wavelength, and therefore the colour, at which the resonance occurs can be modified by tuning the size of the nanoparticles. Moreover, the density of these particles allows for tuning the strength and the wavelength of the resonance, given that there is interaction of the electrical fields of particles that are placed close to each other. The effect of Mie resonances has been used before in solar cell designs for light trapping purposes and anti-reflection layers, but here we used it for the first time to create colourful solar cells [1].

To fabricate such solar cells, we used nanoimprint lithographic techniques to create an array of nanocylinders, made from silicon, on top of a transparent sapphire slide. The size of the nanocylinders was chosen to support a strong interaction with green light (Mie resonance around 540 nm). The nanoimprinted layer served as module glass to a silicon solar cell of 26% efficiency from our collaborators at ECN (Energy Institute of the Netherlands). Every solar cell has such a transparent layer as protection against environmental conditions. The rest of the light (the other colours) transmits unaffected through the layer of nanoparticles towards the solar cell and can be converted to electricity there. This combination of nanoimprinted sapphire slide and solar cell resulted in a green-coloured solar cell mini-module with a colourful appearance.

The green reflection from the nanostructured layer was fully visible at angles of incidence between 0° and 70°, so almost for any angle of observation. This is advantageous compared to other methods of colouration of solar cells. Due to the reflection and the absorption of green light by the nanoparticles, the performance of the solar cell was slightly reduced. In this particular case, the efficiency dropped from the initial 26% of the dark mini-module to 21% for the bright green cell containing nanoparticles. In a follow-up project [2], we created other colours and combined arrays of different nanoparticles to create any colour including white, in a similar way as done for example in LED screens [2].

The possibility to give them a colourful appearance adds a novel way for solar cells to be integrated into the landscape, and to use urban areas for energy generation. The effect of Mie resonances in dielectric nanoparticles delivers a strong scattering of the selected colour but avoids losses for all other colours. Moreover, the fabrication method of nanoimprint lithography is scalable and could pave the way for industrial application. Ω

"The possibility to make solar cells colourful opens a new way to apply them in townscapes."



← Figure
Photograph of a silicon solar cell partially covered by a nanopatterned module slide specifically designed to achieve a bright green appearance. https://aip.scitation.org/doi/abs/10.1063/1.4986796

→ References

1. V. Neder, S. Luxembourg, A. Polman, Efficient colored silicon solar modules using integrated resonant dielectric nanoscatterers, Applied Physics Letters 111, 7 (2017). doi:10.1063/1.4986796
2. V. Neder, S. Luxembourg, A. Polman, Colored Solar Modules Using Integrated Pixelated Resonant Dielectric Nanoscatterer Arrays, Proceedings of the 33rd European Photovoltaic Solar Energy Conference (2017).

Get a little closer: Female moths use scent proximity to attract mates

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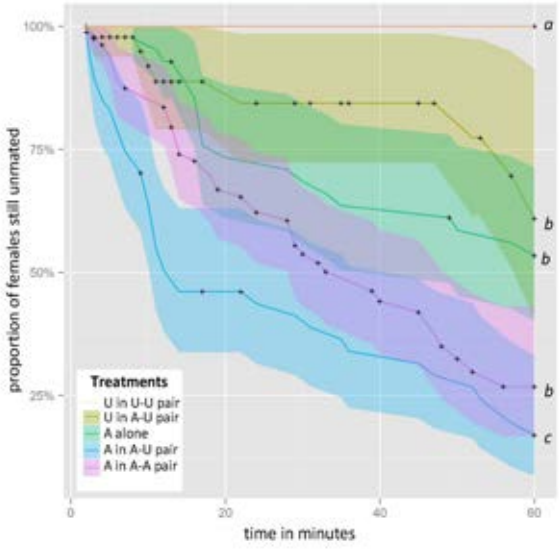
ASTRID GROOT is Professor of Population and Evolutionary Biology at the Institute for Biodiversity and Ecosystem Dynamics (IBED), UvA



← Figure
The fraction of unmated females for moths in various conditions (A = attractive female, U = unattractive female). The shaded regions indicate a 95% confidence interval. Curves with the same letter (a,b,c) show no statistically significant difference in mating rate.

→ References
M. van Wijk, J. Heath, R. Lievers, C. Schal, A.T. Groot, Proximity of signallers can maintain sexual signal variation under stabilizing selection. *Scientific Reports* **7**, 18101 (2017). https://www.nature.com/articles/s41598-017-17327-9

→ Who has the best mating chance? Most of the time we assume that these are the most attractive individuals in a population. If this were always true, then we should see an ever-increasing attractiveness of individuals and a reduction of variation in attractiveness. However, in most species – be it in birds, fish or mammals like ourselves – we find a wide variety of more and less attractive individuals.

For moths, the attraction is in the odour: females emit a sex pheromone through which males are attracted from distances up to several kilometres. It is generally assumed that the sex pheromone of a species is not variable, because each species has its species-specific sex pheromone. Closely related species produce similar sex pheromones that only differ in the combination of pheromone components and/or the relative amount in which these components occur in the blend. Hence, pheromone variations within species may result in an overlap with the sex pheromone of another species, which intuitively would not be beneficial for either species.

However, in the noctuid moth Heliothis virescens (*see Figure centerfold page x*), females can vary significantly in their sex pheromone blend, even within populations. When measuring the sex pheromone of hundreds of females over several years and multiple locations, we always found some females to have a blend with ratios so different from the known attractive blend that we suspected them to be unattractive females. In the lab it was possible to select for these unattractive blends, such that attractive and unattractive selection lines could be produced in which the attractive and unattractive sex pheromones were fixed. These selection lines enabled us to do field experiments with the assumed attractive and unattractive females to determine whether and how quickly males would find and mate with these females.
By placing two immobilised females on a plant leaf, and observing these females closely, we could determine not only which females attracted a male, but also the time it took before a female was mated. We placed three different combinations of females on a leaf, either two females from the unattractive selection line, two females from the attractive selection line, or one female of each line together. As expected, the two females from the unattractive selection line never attracted any male and remained unmated, while the pair of attractive females readily attracted males and most mated within the hour that all females were tested. Interestingly, the unattractive females in a mixed pair were as successful at being mated as single attractive females. Tests in the wind tunnel at the University of Amsterdam showed that males approached unattractive females only when these females were situated less than 30 cm from an attractive source.

"Assessment of mate quality is a complicated process that partially relies on relative measures."

Even more surprisingly, attractive females paired with unattractive females were mated faster than when sitting next to an attractive female. The increase in apparent attractiveness of the attractive females in a mixed pair is also seen in humans: it has been shown that we tend to rate the attractiveness of a face higher if it is presented next to a less desirable face, an idea popularised in the 2015 movie 'The DUFF'. However, it is not known if in our case the less desirable friends also benefit from the presence of a more attractive friend, as is the case in moths.

These findings indicate that, as in humans, assessment of mate quality is a complicated process that partially relies on relative measures. The observation that both the unattractive and the attractive females in the moth experiments benefitted from each other's company is important in an evolutionary context because it may explain why variation in the female sex pheromone composition persists in the population. The results thus demonstrate the importance of the social environment in mate choice experiments and provide a novel explanation of how variation in attractiveness can remain in a population. Ω

Genetically informed patient selection to reduce cellular heterogeneity

STEPHANIE HOEKSTRA is PhD researcher at the Department of Complex Trait Genetics, Center for Neurogenomics and Cognitive Research (CNCR), VU

→ To date, mutations in the DNA that have been associated with psychiatric diseases are induced in mice in an attempt to create in vivo models of such diseases. However, several psychiatric diseases, including schizophrenia, major depression, autism and bipolar disorder, have been shown to be polygenic. This means that several mutations together with many small variations scattered throughout the genome only slightly increase the risk of developing such diseases and only when combined, these mutations and variations can have a significant increase in vulnerability. Such a complex genetic architecture is hard to model using gene editing techniques in animals. The recent development of induced pluripotent stem cells (iPSCs) allows us to generate otherwise inaccessible human tissue such as neurons and culture them in the lab. In this regard, when derived from patients carrying such diseases, iPSCs can be used to study genetically complex diseases since they are genetically identical to their donor.

However, there is a problem with genetically complex diseases: heterogeneity. If patients are selected solely based on diagnosis, a small sample size typical for iPSC research might result in in the selection of patients carrying different genetic variants. If genetic heterogeneity is correlated to cellular heterogeneity, this will even further reduce the statistical power of the biological readout. Larger sample sizes are required to obtain the same power when heterogeneity increases, although that is not always feasible with labour-intensive samples like iPSCs.

There are several ways of reducing heterogeneity in iPSC samples. A well-known method is to study families in which several members are affected with the disease of interest. A limitation of this approach is that most often these families carry rare copy number variants (CNVs) with a large effect. Copy number variation is a phenomenon in which sections of the genome are repeated. CNVs are often also associated with other diseases and are sometimes present in unaffected individuals, which is also the case for the cellular phenotype associated to the CNV. This means that such CNVs are not fully reliable, and that other genetic risk variants can be involved in the disorders, which complicates the interpretation of the results obtained in such studies. To claim causality, studies into specific CNVs associated with a psychiatric disease should include healthy controls carrying the same CNV (see figure). If the same iPSC phenotype is present in the controls, it is apparently not directly causing the disease.

Furthermore, the selection of specific genetic variants is sensitive to bias. Psychiatric diseases are often considered to be diseases of the synapse, which leads to researchers selecting CNVs affecting known synaptic genes. However, there is a growing body of evidence that other cell types can also be involved in such disorders, such as glia in schizophrenia.

Another way of decreasing heterogeneity is by selecting subjects based on common variants with small effects (see figure). In this case, researchers should select patients carrying many of such variants, which we call cases with a high polygenic risk score (PRS). This way, subjects will be selected without a potential bias towards genes involved in specific biological pathways and if controls with a low PRS are selected, the two extremes of the distribution will be chosen. This will lead to a smaller heterogeneity and potentially a larger effect size, which will result in more statistical power. But just as mentioned above, researchers should also include cases with low PRS and controls with high PRS to confirm the causal effects of the iPSC phenotype found.

Decreasing heterogeneity will aid iPSC research into genetically complex diseases by reducing the number of nonspecific phenotypes found within a study and between studies, increasing the comparison and replications between studies. This will increase the chance of finding the causal biological pathways in psychiatric diseases. Ω

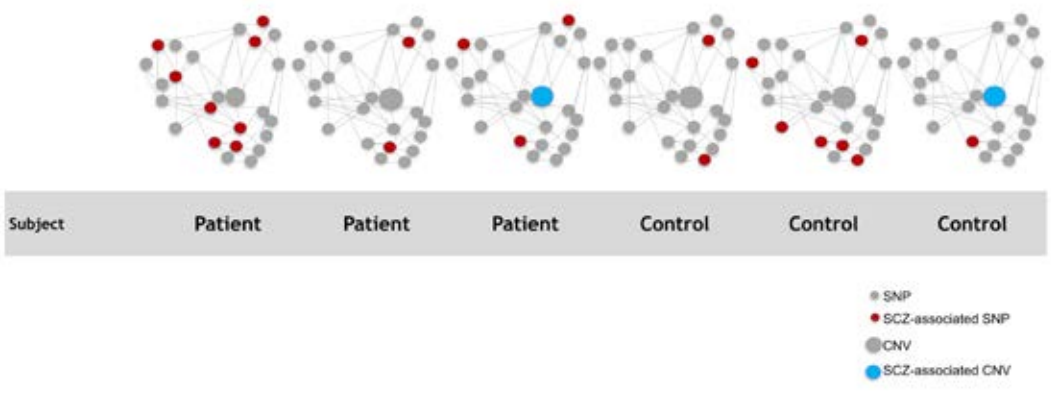
→ Reference

S.D. Hoekstra et al., Genetically-Informed Patient Selection for iPSC Studies of Complex Diseases May Aid in Reducing Cellular Heterogeneity, Front. Cell. Neurosci. (2017). doi:10.3389/fncel.2017.00164

"Causality is difficult to claim in complex trait diseases."

↓ Figure

Types of subjects (patients and controls) with different types of variants in schizophrenia (SCZ), namely single nucleotide polymorphisms (SNP) or copy number variants (CNV).



Macrophage therapeutic targeting: changing Pacman into Handyman

JAN VAN DEN BOSSCHE is Principal Investigator at the Department of Molecular Cell Biology and Immunology, VUmc.

→ Macrophages, named after the Greek word for 'big eater' (makrós = large; phagein = to eat), are specialised white blood cells. Depending on the stimuli they encounter, macrophages can acquire distinct activation states, which are broadly classified as M1 and M2. They could be regarded as the Pacman (M1) and Handyman (M2) of our immune system, respectively. Pacman macrophages engulf and digest foreign substances, microbes and even cancer cells. The resulting inflammatory immune response of the so-called M1 macrophages keeps us healthy. However, if this activation persists too long, it can cause chronic inflammatory diseases like atherosclerosis and rheumatoid arthritis. That is where anti-inflammatory Handyman macrophages come into play. They fulfil crucial roles during development, tissue repair, healing and resolution of inflammation. As a drawback, the M2-associated 'handyman'-like properties can also promote tumour growth.

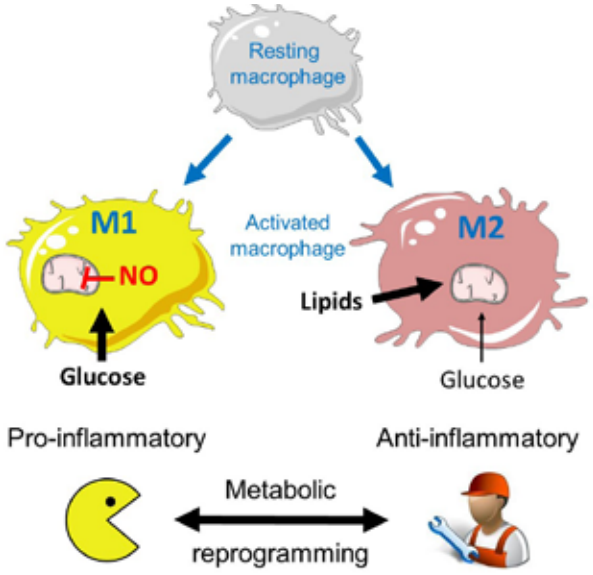
It is clear that macrophage responses need be precisely controlled and failing to do so can result in disease. The aim of my research group at the VU University Medical Center is to develop new therapies for cancer and cardiovascular diseases by understanding and adapting the metabolism of macrophages. Our work surfs the immune-metabolism wave; a booming research field that describes the metabolic pathways in immune cells that control their energy production and also directly determine their activation status.

During my work at the Academic Medical Center in Amsterdam, we discovered that M1 macrophages fail to convert into M2 cells [1]. We identified the disturbed energy metabolism of M1 macrophages as the factor responsible for preventing the M1-to-M2 conversion. One could compare these macrophages with different types of runners. M1 macrophages are fast, but short-lived, sprinters that burn sugar through glycolysis for their energy supply. M2 macrophages are the marathoners and can also burn lipids (FAO; Fatty Acid Oxidation) for long-term energy production. While you can force a marathoner to do a last sprint at the end of his marathon, a sprinter will never finish a marathon after an all-out 100-meter sprint. Accordingly, M2 macrophages can be converted to M1 macrophages, but the reverse appears more difficult.

Nitric oxide (NO) is a highly reactive molecule that enables microbial killing in the macrophage, but at the same time obstructs energy production in the mitochondria. By inhibition of NO production, we relaxed the M1 macrophage's energy status and thereby converted them into handyman-like M2 cells. Therapeutically restoring the macrophage's energy metabolism might be useful to improve the reprogramming of inflammatory M1 macrophages into anti-inflammatory M2 cells to control diseases such as atherosclerosis and rheumatoid arthritis. Vice versa, reprogramming M2-like macrophages that support tumour growth into M1-like tumour killers could be valuable for cancer therapy.

The field of immune-metabolism now enters an exciting period in which key open questions will be addressed [2]. For instance, while the metabolic characteristics and requirements of M1 and M2 macrophages are quite well-described in mice, how can these findings be translated to the human system? What are the metabolic characteristics and requirements of macrophages that are present in tumours and atherosclerotic plaques? What are the underlying mechanisms that translate altered metabolism to macrophage function?

By unravelling these questions, the *Translational Macrophage* Immunometabolism group will help develop new therapies. Supported by Netherlands Heart Foundation (Hartstichting), we aim to target particular immunometabolic circuits in atherosclerotic plaque macrophages to improve their function and disease outcome. Ω



↑ Figure
The fraction of unmated females for moths in various conditions (A = attractive female, U = unattractive female). The shaded regions indicate a 95% confidence interval. Curves with the same letter (a,b,c) show no statistically significant difference in mating rate.

"Macrophage metabolism as a key to new therapies."

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2. J. Van den Bossche, L.A. O'Neill and D. Menon, Macrophage Immunometabolism: Where are we (going)? *Trends in Immunology* **38**, 395 (2017). http://www.cell.com/trends/immunology/fulltext/S1471-4906(17)30042-X

Alumni @Work

Where do the alumni of the Amsterdam science community end up in the worldwide job market? This item zooms in on the experiences of two alumni.

Jordi Cabanas-Danés

Application Scientist at LUMICKS, a company developing ready-to-use instruments for single-molecule research. Former postdoc in single-molecule biophysics at the VU.

→"I have always thought of scientific research as a tool for understanding the world and contributing to society through new advances and solutions to long-lasting issues. Throughout my PhD and postdoc, I felt, however, that my efforts and time were directed more towards delivering an end result within a definite period of time (either my PhD thesis or publications), rather than truly generating any impact on the world with my findings. I also came to the realisation that I was being pushed into a very specific scientific niche, while I felt that my scientific interests were much broader.

Close to the end of my postdoc, I shared this struggle with the PI of my lab. A couple of seconds later, he talked to me about the role of Application Scientists at LUMICKS. Although I had heard of such positions within corporate companies and I knew LUMICKS' technologies very well, I did not know what that would imply in the context of a fast-growing start-up company. After some hesitation, I decided to learn more about this position and I finally joined the company about one and a half year ago.

What I like best about my job is the large variety of projects and tasks in which I am involved, while working in an extremely open and creative environment. I feel that here, there is room for everyone to bring in fresh, new ideas and take the initiative to push them forward. Also, I love the level of interaction and team work with both the different departments within the company and with researchers working on different topics in different environments. One day I can be generating content for marketing material with product designers, the next I can be brainstorming ideas for the development of a new software platform with software developers, or even be in a conference talking to scientists about their latest results." Ω

→ Insider's advice:
"I know many academic scientists who see the option of working in a company as a 'second best'. In my experience, I have learned that one can contribute to the scientific community not only by being a part of it, but also by developing and providing new tools and assays to enable scientists to make breakthrough discoveries."

Anne Marieke Eveleens

Co-founder of The Great Bubble Barrier and business consultant for Atos. Graduate of the Master's programme in Neurobiology at the UvA.

→ "When I started studying Psychobiology, I never expected to end up combining science, corporate business and social entrepreneurship at the same time! In 2012, after my BSc in Psychobiology at the UvA, I enrolled in the Research Master's in Neurobiology, where I started to appreciate critical thinking. This was followed by the Tesla minor, which applies science directly into society. Here, I really experienced how to use my scientific skill set in interdisciplinary projects. The UvA brought me the skills to search and analyse solutions for big challenges. After graduation, I started working as a business consultant for Atos, analysing strategic decisions. Especially sustainability projects had my interest, as a lot of different disciplines come together in this field. It was this passion that created the amazing opportunity to become Corporate Responsibility & Sustainability manager in the Benelux region, Nordics, Poland and Russia. With this position, Atos gives me the freedom to follow my personal interest, develop my career and focus on sustainable projects at the same time.

While working at Atos, two of my friends and I started our own start-up. What initially started as brainstorming about fixing world problems, ended up with trying to solve the question: How can we prevent plastic pollution in the water? This is a major environmental problem nowadays. We thought of the idea to clear plastic waste from the rivers without interfering with the natural environment, simply said, a barrier that you can swim through. This resulted in starting a company called The Great Bubble Barrier, which I now work for in evenings and weekends next to my job at Atos.
Our company designed a bubble barrier, which removes plastic soup from rivers before it reaches the ocean. My scientific background in neuroscience and business experience at Atos allows me to lead our scientific research and develop our business strategy. In 2017 we were able to successfully pilot our first barrier. We placed a 200-metre pilot in the IJssel river for three weeks together with Rijkswaterstaat, Deltares and BAM/VandenHerik, where we caught 80% of our test material. Now we are ready to expand this to many other places and leave it in for at least ten years. To reach this goal, we are running a crowdfunding campaign and are trying to find sponsors. I'm so grateful to be able to work with dedicated people and spend all my time on what I like best: finding the right solutions for sustainable challenges we face."Ω

→ Insider's advice:
"Hang on and don't expect to find your dream job at once. Also, take time to drink coffee with as many people with appealing jobs as you can. This helps to get an idea of what a job entails and whether you'd like it."

puzzle

These words can all have a letter added and then be rearranged to make a new 5-letter word, e.g. NOUN + I = UNION.

The 8 added letters are an anagram of an 8-letter word.

What is the 8-letter word, and what are the new words?

THIN	+	☐	=	☐	SWAT	+	☐	=	☐
RIND	+	☐	=	☐	MAIL	+	☐	=	☐
SITE	+	☐	=	☐	CITY	+	☐	=	☐
TOGA	+	☐	=	☐	DENY	+	☐	=	☐

☐☐☐☐☐☐☐☐

answer puzzle issue 6

The solution to the puzzle in issue #6 of Amsterdam Science magazine was:

3	+	2	●	4	−	1	●	5	= 12
+		+		●		●		●	
5	●	3	−	1	●	2	+	4	= 45
−		●		+		●		+	
1	●	5	●	2	−	4	●	3	= 109
−		−		●		−		●	
4	●	1	●	3	−	5	+	2	= 410
−		●		−		+		●	
2	●	4	+	5	●	3	●	1	= 555
=		=		=		=		=	
1		23		59		122		375	

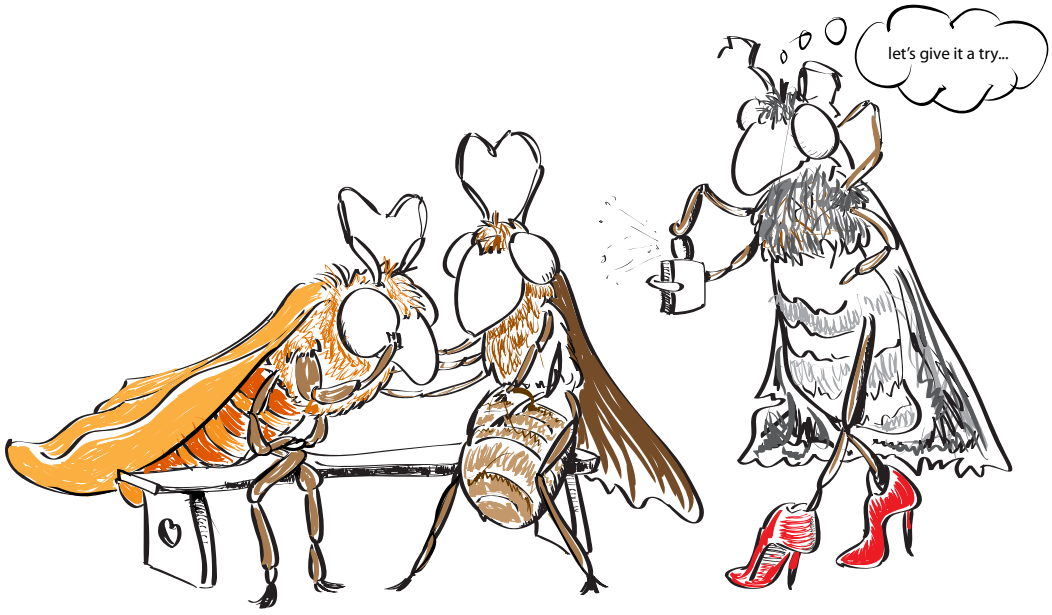
Congratulations to Xanthe, Zazo and Sophie, who sent the correct answer and won an Amsterdam Science t-shirt.

mail the answer to
amsterdamscience@gmail.com

before 1st July 2018

win
the first ten correct answers will win an Amsterdam Science T-shirt

cartoon



Short information about the magazine

→ Amsterdam Science gives Master's students, PhD and postdoc researchers as well as staff a platform for communicating their latest and most interesting findings to a broad audience. This is an opportunity to show each other and the rest of the world the enormous creativity, quality, diversity and enthusiasm that characterises the Amsterdam science community. Amsterdam Science covers all research areas being pursued in Amsterdam: mathematics, chemistry, astronomy, physics, biological and biomedical sciences, health and neuroscience, ecology, earth and environmental sciences, forensic science, computer science, logic and cognitive sciences.

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Have a look at www.amsterdamscience.org for the remit of the magazine and upload your contribution for consideration for a future issue of Amsterdam Science.

One of the editors will contact you, primed to hear about your exciting story or striking image, and to discuss with you how it could reach a broad audience via publication in the magazine.

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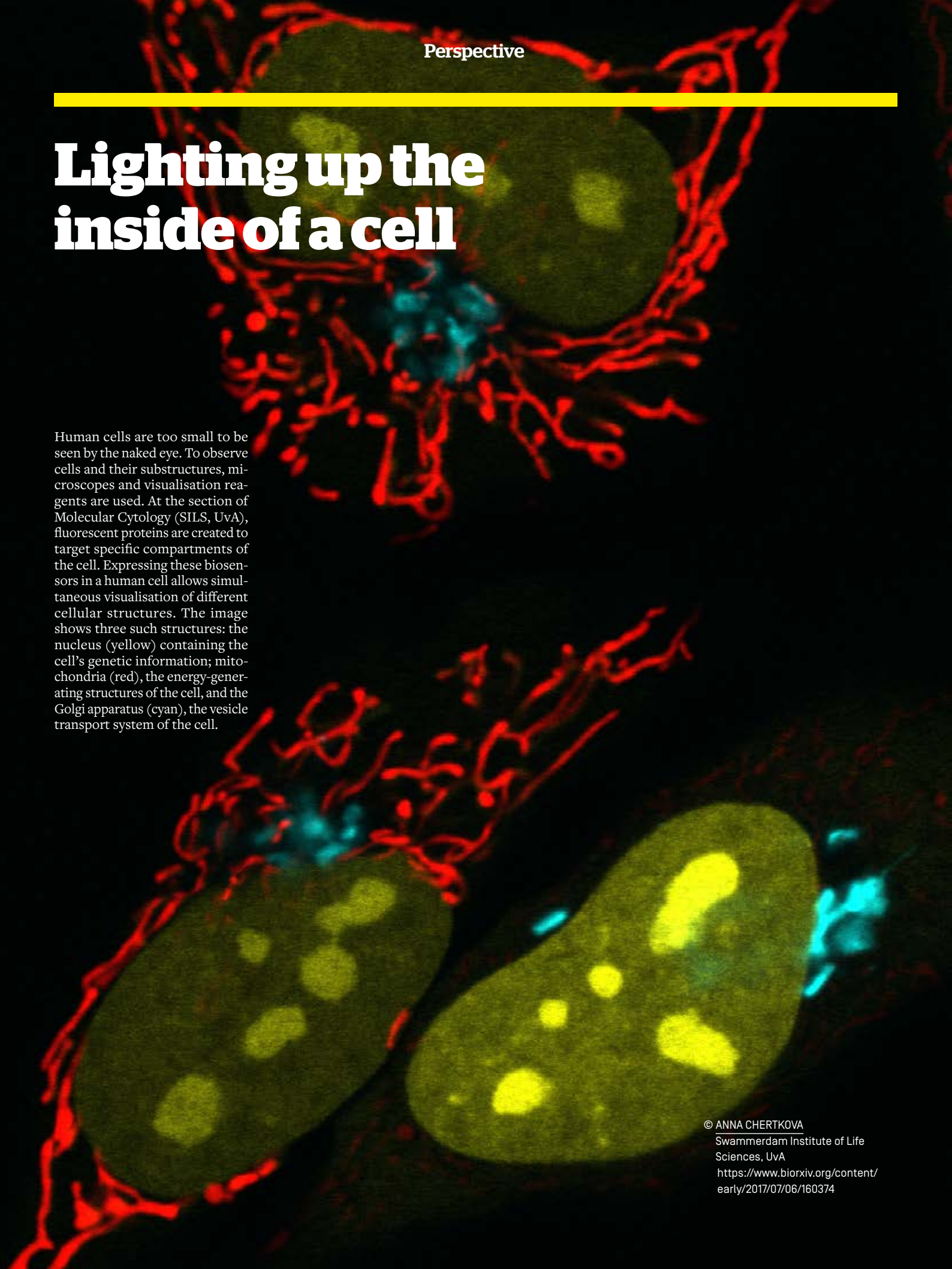
Lighting up the inside of a cell

Human cells are too small to be seen by the naked eye. To observe cells and their substructures, microscopes and visualisation reagents are used. At the section of Molecular Cytology (SILS, UvA), fluorescent proteins are created to target specific compartments of the cell. Expressing these biosensors in a human cell allows simultaneous visualisation of different cellular structures. The image shows three such structures: the nucleus (yellow) containing the cell's genetic information; mitochondria (red), the energy-generating structures of the cell, and the Golgi apparatus (cyan), the vesicle transport system of the cell.



Swammerdam Institute of Life Sciences, UvA
https://www.biorxiv.org/content/early/2017/07/06/160374