# mRNA


YEAR 2 // ISSUE 3 // JUNE 2017

STAN BROUNS // THE MOZART EFFECT // HYUN YOUK'S TALKING CELLS // SABINE'S COLLECTION THREATENED // RICK AND MORTY REVIEWED // LETTER FROM DENMARK

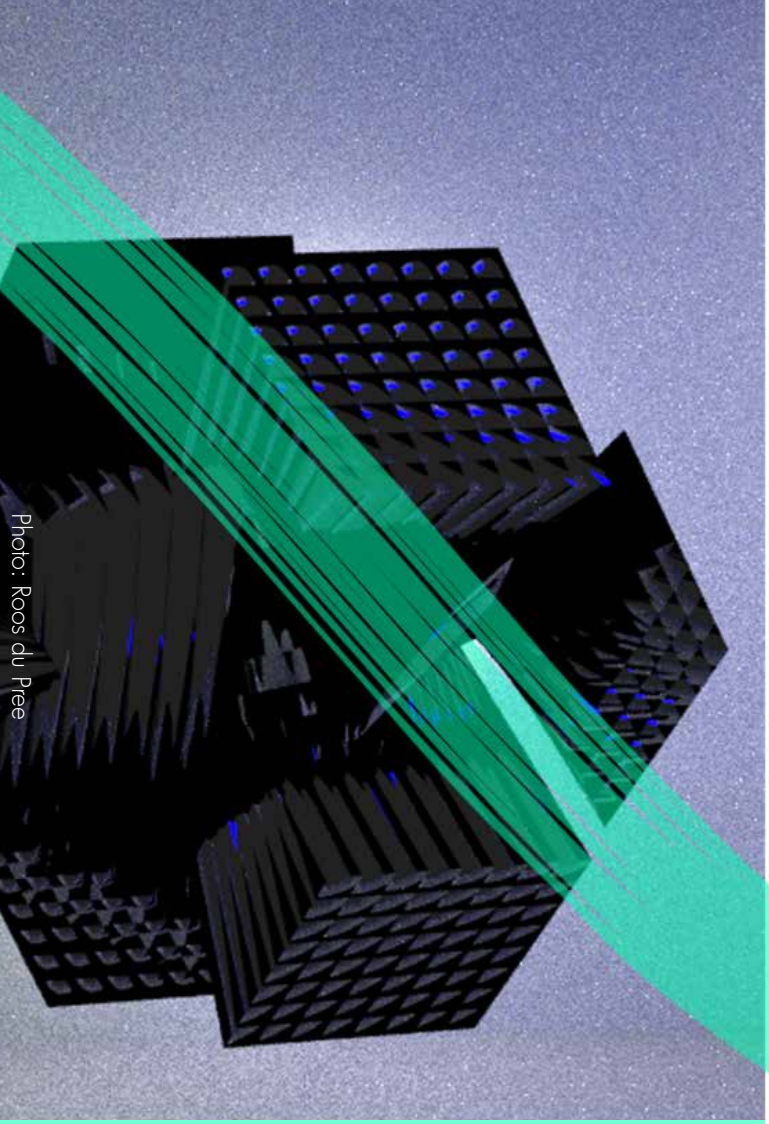

Photo: Roos du Pree

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## COLOPHON


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## DEAR READERS,

In my previous editorial, I mentioned the great improvements the mRNA has made this year: a fully English version that is delivered to every single member of our association! Of course, it costs some money to let everyone receive a copy. Within the last issue we took a risk, because we did not have the necessary amount of money yet. For this edition, we have spent two mornings calling driving schools, food suppliers and other sorts of companies to acquire some acquisition. Without many results, unfortunately. Luckily we still have our commissioner of external affairs, Rachel Los. She has contacted Applikon and Delft Health Initiative, and this edition of the mRNA has been made possible by them.

Still, it was not useless for us to have called all these companies, since we learned from it. Some of us did not like the idea of calling 'strangers' at first, but once they did, they realised it was not that scary. That is what it is all about in life: trying new things, failing, learning from it, trying again, and eventually succeeding.

When I started this year as editor-in-chief, I did not really see myself as a leader. Nonetheless, I gave it a shot and I learned a lot from it. Even though I did not feel completely comfortable in my role in the beginning, I became more confident when I noticed things worked out.

And yet, this is already my last editorial. I would like to wish our successors the best of luck and I am truly looking forward to the upcoming issues of this magazine. My advice to them and all of you is to get out of your comfort zone and try something new next year. But first, good luck with the final exams and enjoy your well-earned summer holiday! :-)

Tom Aarts
Editor-in-chief of mRNA 2

## FROM THE BOARD

Dear members,

We have arrived at the end of our board year and it feels a little bit weird to look back at things rather than having a lot of events ahead. Until a couple of months ago, we were all looking forward to a lot of big and exciting activities, but now most of them already passed by. The whole year, I have been speaking and writing about the Multi-Day Excursion (MDE), the symposium and the gala, for example, which have all taken place last month. Board two also had their share in Hooke's agenda while we were on holiday. We greatly appreciate their effort to look after all of you and organise fun activities! We have heard great stories about the hitchhiking contest and the bowling, which we unfortunately could not attend because we were laying on the beach in Málaga; drinking sangria and eating tapas… In spite of a slight tension during the last weeks, I am happy that it all went well. We visited cool companies during the MDE, had very inspiring speakers at the symposium and we all looked splendid at the gala.

As the association grows older, we accumulate activities that keep coming back each year. However, as we are growing, we also find lots of possibilities to change and add things before we get stuck in old habits. For example, recently the very first ASconnect event took place, a career event for students of the faculty of Applied Sciences. It is very exciting to add these kind of new and big events to our agenda and hopefully to the agendas of upcoming years. Speaking of next year, you can all be sure that there will be even more room for initiatives, as we are granted financial support on the basis of Graduation Support Scheme (RAS) for a full time board! Our successors will not have to worry about studying and can completely focus on taking Hooke to the next level. Speaking of the next level, as I am writing this, a lot of first years are studying super hard for their retakes to gather those critical ECs for their BSA. Of course hoping that they can continue to the next level of Nanobiology, I wish them all good luck with these tough retakes! I also wish you all good luck with the tempting weather outside; studying does get a lot harder when the sun is shining bright and all you want to do is lay down in the grass without thinking of exams or deadlines. But, it is very important to take a break from studying every now and then and move a little. And for that we have a small soccer ball and a volleyball at our office, come by for a break and we might join you for a little game outside!

I have spoken,

Amanda van der Sijs
President of S.V.N.B. Hooke

# A TWO-FRONT WAR AGAINST CANCER JOINING THE FORCES OF TWO DRUGS

**In the field of fighting cancer using nanobiology, one way of eliminating tumour growth is by blocking the function of certain proteins. This can be done in multiple ways, but in the case of chronic myeloid leukaemia (CML), a form of leukemia characterised by excessive production of white blood cells, this is done by binding a specific inhibitor called imatinib to ABL1 kinase's ATP binding site.**

Although imatinib therapy is successful up to 90%, there is still a high number of unsuccessful treatments. This is due to a single point mutation in the code for ABL1 kinase, which turns a threonine into an isoleucine, causing the kinase to be unsusceptible for the imatinib, making the patient insensitive to their treatment.

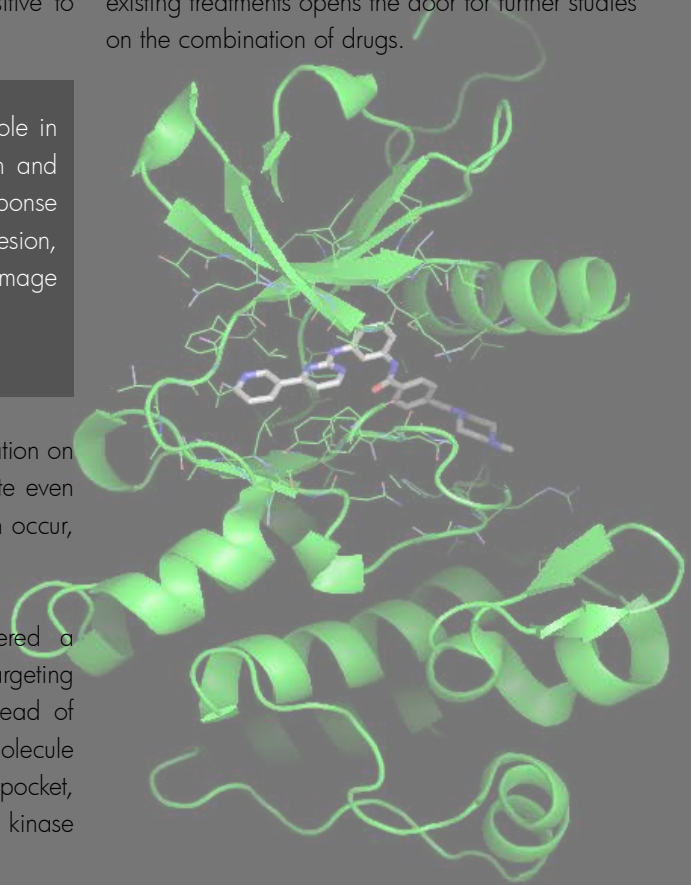
ABL1 kinase is an enzyme that plays a role in many key processes linked to cell growth and survival, like cytoskeleton remodeling in response to extracellular stimuli, cell motility and adhesion, receptor endocytosis, autophagy, DNA damage response and apoptosis.
(UNIPROT; www.uniprot.org/uniprot/P00519)

This problem was solved by creating a variation on imatinib, called ponatinib, which fits the site even with the mutation, but again a mutation can occur, making the patient insensitive.

However, scientists have recently discovered a new way of fighting CML: by effectively targeting a different binding site of the kinase. Instead of targeting the ATP binding site, their new molecule called ABL001 targets the Myristate binding pocket, which, instead of blocking ATP, inhibits the kinase independent of ATP concentration.

When tested in mice, resistance to ABL001 still occurred over time due to point mutations. However, they found out that mutations causing resistance to nilotinib, a variation on imatinib, and mutations causing ABL001 resistance did not overlap. More importantly, they found out that when a mouse was treated with both nilotinib and ABL001 simultaneously, the tumour volume not only went down, but stayed down. This is because the chance that two specific point mutations happen at once is extremely small.

The discovery of an ABL1 kinase inhibitor with a resistance profile that does not overlap with other, existing treatments opens the door for further studies on the combination of drugs.



## A NEW FACE ON CRISPR RESEARCH

## BROUNS MOVED FROM WAGENINGEN TO DELFT

Last year, Dr Stan Brouns moved his entire research lab from Wageningen to Delft. The focus of his lab lies on CRISPR, something which we as Nanobiology students are all very excited about, naturally. We were wondering what his background is and what he thinks of the new research area here at the south of the campus, so we asked him for an interview.

**What did you study in Wageningen?**

Today, it is called Molecular Life Sciences, but when I started in 1996, it was called Molecular Sciences. It is somewhat the integration of Biology, Chemistry and Physics.

**What was the biggest achievement of your student career?**

I did a thesis in Wageningen in microbiology and I got the Junior level Research Prize. So, that went extremely well, and I really liked doing research. The thesis was about combining enzymes of two different organisms by a genetic approach, called gene shuffling. It basically entails fragmenting genes; in this case an enzyme for degrading sugar polymers. After recombining those genes into one, I screened for improved properties. When I started doing this, nobody expected it to work, but it worked surprisingly well.

**How did you end up doing research on CRISPR?**

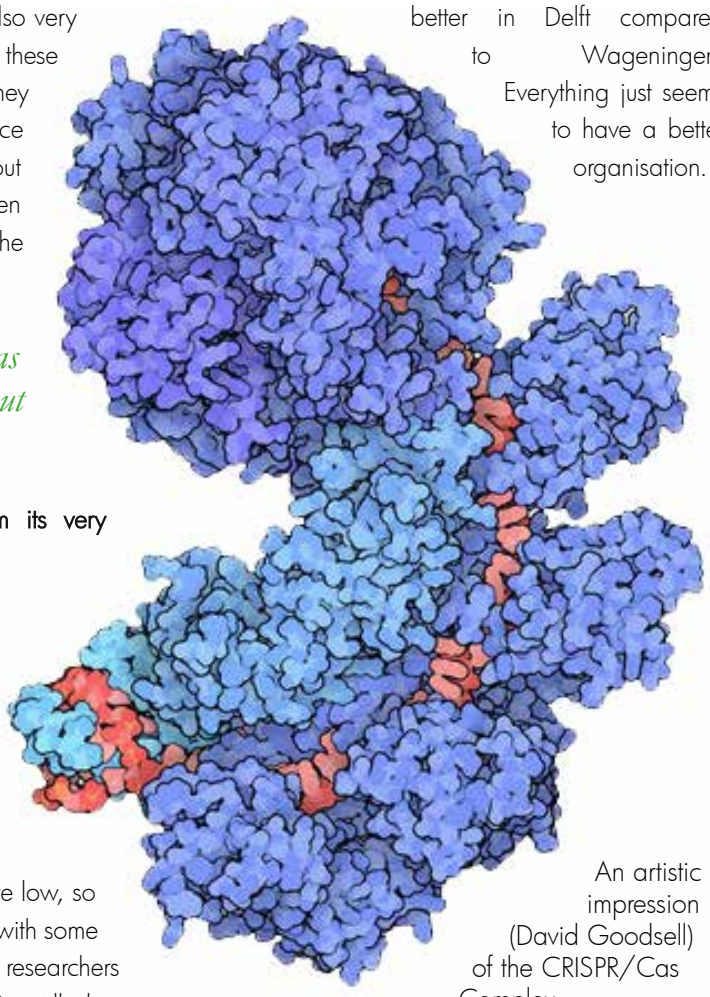
That was a big jump: I did my PhD in microbiology and that was on a completely different topic. It was on enzymes from thermophilic archaea: microbes living in volcanic areas, hot acidic pools of 80 °C and with a pH of 3. We explored what kind of metabolic pathways they had and what was different compared to organisms that lived at lower temperatures. After we had completed this, we were visited by a professor in bioinformatics who predicts gene functions. He ran into large sets of genes that he predicted to encode for the immune system or an RNA interference system in bacteria and archaea.

At the time, there was hardly any information about this. There were some articles, but nothing really described what these genes were doing. My boss at the time, John van der Oost, had the flexibility to redirect grant money. So, together with him I started to work on CRISPR, and pretty soon we were joined by a PhD student. During my PhD, I worked on archaea, but for this project we chose something as simple as possible: *E. coli*, which also has a CRISPR system and is very easy to modify. Doing experiments with *E. coli* is also very quick. We tried to figure out what these CRISPR systems are, and what they do, whether they provide resistance to phages, and so on. It turned out to be a really fun experience, given what we now know about it and the possibilities.

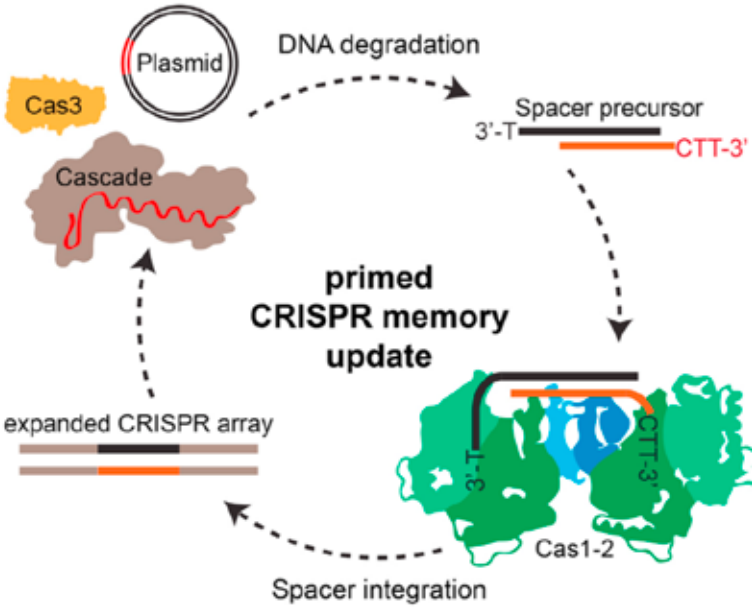
*"At the time, there was hardly any information about this."*

**So, you worked on CRISPR from its very beginning?**
From the very beginning, yes.

**You moved from Wageningen to Delft with your research group? Do you like it here?**
Yeah, I like it here. I like that there are so many different group leaders, either small or big groups. Furthermore, the general age is quite low, so the group leaders are quite young, with some exceptions to more experienced researchers like Marileen, Cees and Nynke. But still, there is a large group of young scientist that are in for new things and collaborations and that is what I like. There is also a lot of independence. This also means that you have to make sure that there is enough money to do research. However, when you know that you are completely independent, you feel much more responsible. You have to make sure that there are enough resources to continue the research. I also think that the technical support here is much better. They can help you with all sort of techniques, like the electron microscopy and mass spectrometry facilities. We even have sequencers here. We did not have that in Wageningen. Furthermore, the other types of support, for instance financially and administratively, are arranged better in Delft compared to Wageningen. Everything just seems to have a better organisation.



An artistic impression (David Goodsell) of the CRISPR/Cas Complex.




Künne, Tim, et al. "Cas3-Derived target DNA degradation fragments fuel primed CRISPR adaptation." Molecular Cell 63.5 (2016): 852-864. Image from a paper published by Brouns's lab.

*"It is unbelievable that we have such a good solution, but that it is not used."*

**How can Nanobiology students help you in the lab?**

We have had a number of different projects. The project Marre Niessen worked on was really new and somewhat exploratory. This means that the PhD supervisor was working on something different, so she set up the initial experiments. It looked so incredibly promising that we now have more people working on the same topic. This shows that as a student, you can really make a difference. You can start something up that is not yet running in the lab, or help a PhD or postdoc to do something critical to speed up, or explore a different area the group leader cannot do because he does not have enough hands. Student projects are really helpful. They also provide a good atmosphere in addition to the technicians and the postdocs, and we also have some fun. They genuinely are part of the team.

**What do you hope to discover in your lab?**

In terms of phages, I hope that we can start helping some patients by collaborating with doctors, because phage therapy is really overlooked. It has been used somewhat 80 years ago, but then antibiotics came up. It is unbelievable that we have such a good solution, but that it is not used. It is not allowed, because there is legislation against everything unknown for medical purposes. To legalise these purposes, there are procedures that take a lot of time and are very expensive. I hope that my research can merge with some therapy in the future.

Another goal is to look beyond CRISPR. I am sure that nature is full of methods against phages, that might have the same impact as CRISPR, so I am also looking for new things.

**What is your favourite cell organelle?**

Bacteria do not have organelles but if I have to choose, I think that I would go for mitochondria. Partly because they emerged from bacteria, I think it is a very nice that the merge of different life forms gave rise to the eukaryotic life forms we see today.

**Do you have a last message for the reader?**

If you are interested in the above questions on CRISPR, let me know. Do not hesitate to contact me via stanbrouns@gmail.com.

## OVERVIEW OF THE SYMPOSIUM

## A TRIPTYCH IN THE NANOFIELD

**On 17 May, SOX3 hosted the annual symposium of S.V.N.B. Hooke. They invited three very interesting speakers to discuss the $10^{-9}$.**

The first speaker of the afternoon was Dr Wiro Niessen, an expert on image analysis, pictured below. In his talk, he focused on the rising influence of technology. He speculated that soon anything in healthcare that is repetitive will be automated. According to Dr Niessen, this overtake of artificial intelligence is necessary, because patients need to be informed and treated better, and algorithms will be able to do this.

After Dr Niessen's fascinating talk, Dr Christie Mummery took over. Dr Mummery is active in the field of developmental biology. Her talk focused on how future medicine will allow people to age healthy. She mainly discussed the different ways in which induced pluripotent stem cells could be used to treat certain medical conditions or as a model for pharmaceutical drug testing, for example using organs on a chip instead of mice.

Finally Professor Sir Vincent Icke closed the symposium with an interesting talk on how even the largest processes he, as an astrophysicist, encounters depend on processes on the nanoscale. His talk was mainly focused on speculating about what future technologies might bring, like personalised medicine that can read DNA, but he also shared some interesting findings about how cosmic dust can act as a catalyst to help molecules form. According to Professor Icke, life is simple. Proteins, DNA and RNA are all composed out of chains. The real difficulty lies in the immaterial things, like language, thinking or intelligence.

*"I wouldn't dream of studying psychology; I'd stick to something simple, like the universe."*

With three interesting speakers the annual symposium was once again a great success.

Photo: Variscopic

## DUTCH RESEARCHERS JOIN FORCES

## BUILDING SYNTHETIC CELLS

The Dutch research consortium BaSyC is taking on the challenge of building a synthetic biological cell. To that end, it has received a grant of almost €19 million from the Gravitation programme of the Netherlands Organisation for Scientific Research (NWO). The research partners themselves will fund the remaining six million of the more than €25 million that the research programme will cost in total. TU Delft coordinates the consortium, which is made up of researchers from five universities and AMOLF, one of the NWO research institutes. "A fundamental understanding of life within a cell will bring huge intellectual, scientific and technological rewards."

### BOTTOM-UP

"We intend to build this synthetic cell from the bottom up, which is the most fundamental strategy for learning to understand a cell", continues Dogterom. "A fundamental understanding of life within a cell will bring huge intellectual, scientific and technological rewards. At the same time, it will raise philosophical and ethical questions about how society should deal with this new understanding and potential."

"We plan to derive the molecular building blocks and mechanisms for our synthetic cell from various existing rudimentary organisms. This means that the end product will function based on the principles of life as we know it, without mimicking any specific existing species."

### LIFE

The cell is the basis of all organisms. Building a synthetic biological cell is one of science's greatest challenges of the 21st century. We already have extensive knowledge of the molecular building blocks that form the basis of life, but we do not yet understand how they work together to make life possible. "The BaSyC consortium therefore aims to combine biomolecular building blocks to construct an autonomous, self-reproducing cell: one that can sustain itself, grow and reproduce", says coordinating scientist Prof Dr Marileen Dogterom, head of TU Delft's Department of Bionanoscience.

### OPPORTUNITIES

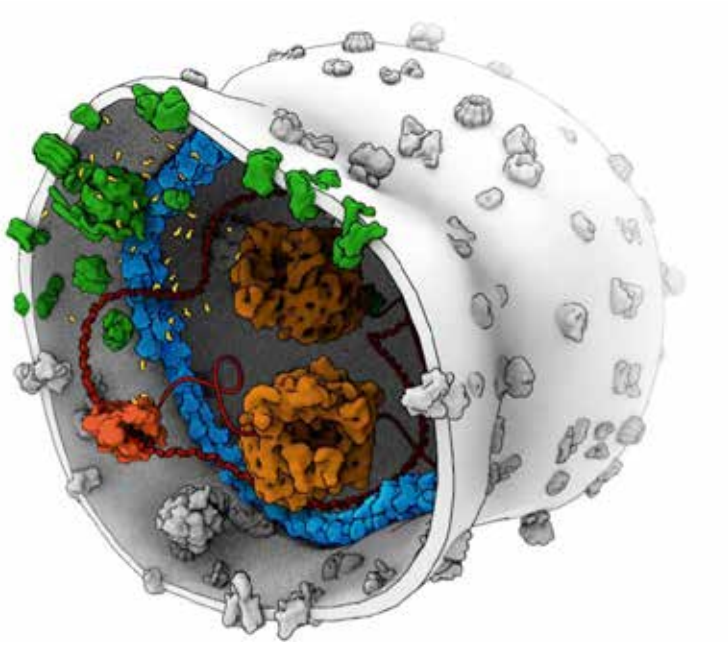
Knowledge of the processes of life opens up unprecedented opportunities for a healthy and sustainable world in many areas, such as healthcare, agriculture, materials and energy. According to Dogterom, a better understanding of the molecular basis for cellular behaviour can contribute to the future development of targeted medication and personalised treatments for chronic diseases, such as cancer.

"Potential applications include new screening methods for antibiotics and medicines, biosensors and solutions to antimicrobial resistance." Designing synthetic cellular systems will also enable humankind to produce new, smart and environmentally friendly materials for high-tech industry, new biofuels and biodegradable polymers. It will also help facilitate the sustainable production of safe and healthy food.

## CONSORTIUM

"A major challenge of this kind cannot be tackled by a single research group or even a single scientific discipline", says Dogterom. "It calls for the concerted efforts of scientists who excel in various fields of research. This is why we are taking on the challenge of building a synthetic cell with a group of leading Dutch scientists with complementary knowledge of chemistry, physics and biology. For the first time, the consortium brings together a truly interdisciplinary team of experts to construct the first synthetic cell from the bottom up."

BaSyC (Building a Synthetic Cell) is a joint project involving TU Delft, University of Groningen, VU Amsterdam, Wageningen University & Research, Radboud University Nijmegen and AMOLF. With the NWO Gravitation programme, the government encourages outstanding research in the Netherlands. It is intended for scientific consortia that have the potential to rank among the world's best.



Artist's impression (Graham Johnson) of a synthetic cell, representing the three basic processes taking place in a living cell: cell fuelling (green), DNA processing (orange/red), and cell division (blue). In the BaSyC programme, we take on the challenge to bring the essential components of a cell together, controlling the complex interactions among them and constructing a synthetic cell with the basic functionalities of a living cell: self-sustained growth, transmission of information, and division.

TU Delft | Health Initiative

## CONTACT

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# DRONES AS A REPLACEMENT FOR BEES

## MERGING TECHNO AND NATURE

Bee deaths are a big problem. As bees are the main pollinators using massive amounts of insecticides destroy the natural mechanism of crop reproduction. Already a few years, farmers in China have been pollinating their crops by hand, and now the next step has been made in agricultural pollination.

Researchers from Japan are developing drones that might once replace the bees. They stick horse hair on the drones and put a for this purpose developed glue on it. This glue is just strong enough to grab the pollen grains, but weak enough to also drop some grains when the drone hits a flower. The only step in bringing this device to the field is the development of the right software that will fly the drone autonomously in the field.

It is an interesting idea to tackle a complex problem, but if you imagine the scale the drones must operate on - a single fruit tree can already have ten to a hundred thousand flowers - it would very fast be economically unfeasible. Let alone that almost all flower plants rely on bees for their pollination.

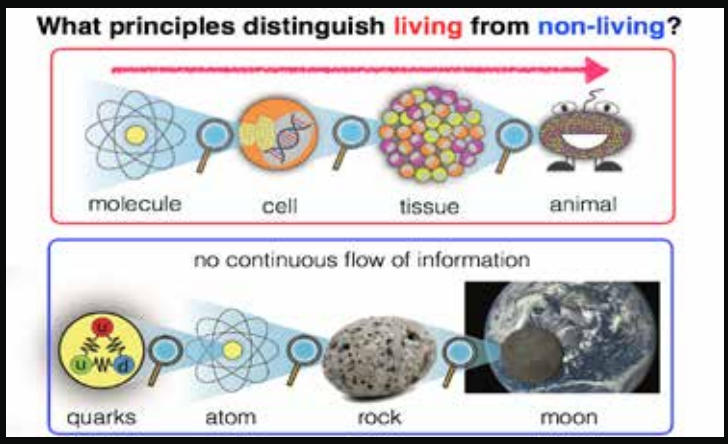
Technology has become a very important aspect of our lives. We cannot even speak about the effect of technology on our lives; our lives and technology have already intertwined so much. If drones will replace the bees, not only humans will intertwine with technology, but nature itself will also be intertwined with it, and thereby even dependent.

It is doubtful whether drones will ever replace bees, but it will probably not surprise you that other researchers are trying to create a genetically modified bee species that can withstand insecticides. Cultivating nature for our own needs is something very old, but we are close to bringing the enhancement of nature to a whole new level.

# TALKING CELLS IN YOUK'S LAB
## SIGNAL TRANSDUCTION FROM SMALL TO LARGE

Image: Roos du Pree

One of the most remarkable features of living systems is that some small event, perhaps occurring at the nanoscale, can influence how life works at the very large scale that we experience in our daily lives. For example, a change of just three sequences in a gene can cause a chain of events that lead to a person developing cystic fibrosis - a debilitating disease without a cure and with symptoms that include the inability to gain weight, accumulation of thick mucus, and shortness of breath. Let's stop and think about how profound this is. The spacing between two adjacent bases in a DNA is about 0.3 nm. Three bases that are next to each other, take up about half of a nanometer. Yet changes at such a tiny scale lead to symptoms that last a person's lifetime and at the human-level scale. This is just one of many examples in which events at the very small scale can influence life at the very large scale. Many living systems possess such an uncanny ability to transmit information from the smallest to macroscopic scales. Deep reasons behind this remain a mystery. Finding principles that enable this unique ability of living systems, which I believe can be posed in quantitative terms, is my laboratory's overarching goal.



So what is the big deal? Consider non-living systems around you such as your desk, a piece of rock, your bicycle, or the kroket that you had for lunch. Almost all non-living systems in our world cannot transmit information from the smallest to the largest scale. If they could transmit effects from the smallest to the largest scale, it would be like saying that Newton, for deducing how the moon orbits the Earth, had to know not only about every single rock that made up the moon but also he had to know about the quantum mechanics that govern the atoms that made up each of those rocks as well as the quantum chromodynamics that govern the nuclei of all those atoms. This would be ridiculous and thankfully it was not true! In fact, the reason for the stunning advancement of physics in the past centuries and for Newton's discovery of the famous laws of classical mechanics that now bear his name is precisely that physicists did not need to know about atoms, nuclei, electrons, or anything that was much smaller than the non-living systems that they were studying to understand how their systems functioned. For example, classical mechanics that you learn in Physics 1A do not require any knowledge of quantum mechanics. Quantum mechanics of atoms does not require us knowing anything about theories that describe structures much smaller than atoms as string theories. But the same logic does not seem to work for understanding why a person gets cystic fibrosis or why an *E. coli* is able to find its food by randomly tumbling around and swimming towards the food. It is no wonder that quantitative sciences like physics have been so successful in describing non-living objects while it had comparatively limited successes in describing living organisms. The motivation behind all the projects in my laboratory is finding what causes this distinction between the living and the non-living systems.

A hypothesis that my students and I have is that multicellular systems can transmit information from the small to the large-scale due to communications between cells. To test this hypothesis, my group performs experiments on baker's yeasts and mouse embryonic stem cells in which we can precisely tune and quantify the amount and type of cell-cell communications. Our main idea is that, just as a group of people can exchange information with each other to coordinate their actions, as in rowing together in a canal in Delft, cells can also coordinate which genes to turn on or off and when and who should do this in a population by exchanging signals with each other. Such multicellular systems are incredibly complicated. Just as you cannot see sound coming out of someone's mouth, you cannot see molecules coming out of one cell and going into another cell in real-time. Thus, my group invents experiments in which we can deduce, without seeing, whether cells "talk" to each other and if so, who is talking to whom to do what. In the case of mouse embryonic stem cells, Hirad Daneshpour (a PhD student in my group) recently discovered that these cells in a culture dish can "quorum sense" - they exchange signalling molecules with each other in a way that depends on the cell-population density. If the cells detect that they are living in a population of a low density, then all the cells die! By using quantitative methods, we can determine a "threshold" population density at which this occurs. We are now investigating what exactly

happens near this "extinction threshold" and what that means for differentiation of the stem cells. Here, an intriguing possibility that we are exploring is whether having one more cell above the threshold makes all the difference between the population becoming extinct or surviving - an example of how a small change can have a huge impact at the macroscopic scale. In budding yeasts, Diego Gomez-Alvarez (a PhD student in my group) is engineering genetic circuits that allow the entire cell population to remember a past event that occurred hundreds of years ago. For example, is it possible that a group of yeast cells can remember that they had seen a special type of sugar hundreds, or even thousands of years ago? Engineering genetic circuits that enable the yeasts to pass on the information about their past seems to enable such permanent, long-term memory - an example of some small event in time (i.e., short in duration) having a lasting impact at a large-scale.

Of course, these projects will not unlock all "secrets of life", whatever they may be. But I believe that when we look at results from a collection of such projects from my laboratory, we will learn deep principles that make you and I different from the piece of paper or the computer screen on which you are reading this sentence. That is what drives me and my current group of wonderful nanobiology students (Max Betjes, Tim Allertz, and Raymond Padmos) and PhD students (Mehran Mohebbi, Diego Gomez-Alvarez, Yiteng Dang, Yuliia Didan, and Hirad Daneshpour). If you have any questions, feel free to drop by!

## WHO IS HYUN YOUK?

As the new teacher of our Bachelor's course Physics 1A, some of our students have already met Hyun Youk in the lecture hall. Here he mainly talks about forces working on bricks and ropes: classical mechanicals. In his lab, Youk tries to answer a number of broad question about life, which involves much more complicated physics. His main passion is seeking mathematical and physical principles that govern dynamics of biological systems. These principles might give deep insights into what it actually means for a networks of molecules to be 'alive', and Youk believes that we should ultimately be able to discover and use mathematical rules and principles to explain any behaviour of any living system.

Source: www.youklab.org/hyun.html

Photo: Roos du Pree

## MEMBER OF ALL STUDY ASSOCIATIONS

## OWNER OF A UNIQUE BUT THREATENED COLLECTION

It all started back in 2007, when the Association Collector saw a flag of the student association Virgiel which she thought was beautiful. She started taking pictures of it. A little later she discovered an annuarium of Virgiel with the same symbol on it as the flag, which meant the start of her collection. Two OWee posters and OWee shirts followed, and when she went to Leiden for the first time, in 2011, it all went very fast. After Leiden, Utrecht, Amsterdam and Rotterdam followed. Now, Sabine van Holsteijn, which is the name of the Association Collector, owns 400 almanacs, 70 ties, 8 chokers and about 100 T-shirts from associations across the whole country. However, her collection is being threatened by little creatures called *Psocoptera*, or booklice. We could not imagine how horrible this must be for someone with such a great passion, so we decided to go ask her for an interview.


**What threatens your collection?**

The booklice have been a huge problem for over a year now. These little creatures entered the collection through a leakage in the shower, which is next to my room. People advise to ventilate and dry to get rid of them, but this did not work. However, with a little luck, I discovered that the creatures do not have adhesion with slippery surfaces, so I covered all my books with foil. Furthermore, the room is full of silverfish traps, because they eliminate booklice too.

**Are you afraid to lose your collection? Would you consider another hobby or start another sort of collection?**

I am so careful and strict on my collection that I do not expect that this would happen easily. So no, I am not really afraid, but cautious. I do not think that I would consider to look for something new. There are only a few hobbies that combine special items, adventurous trips and nice people! If I would lose my collection through a fire or something, I would start all over.

**Are you a member of an association yourself?**

No, but it almost happened in Leiden back in 2013. However, due to doubts on my study, I decided to wait a year. After two months, I stopped with the study. Right now, I am a little bit member of every association! (I like to say so)


**Which association has the most beautiful magazine?**
That varies each year. I hand out prizes for 'favourite association magazine' each year. Last year the mRNA got one of the prizes!

**What is your favourite association?**
Like the association magazine, it varies hugely each year. An association is like a limousine. The appearance does not change so fast, but the driver lets you decide whether you want to take a ride or not. The senate or board forms the association.

**What do you think of the student culture, why do you think it is so special?**
It is beautiful because it is like the real world, but then smaller. Next to your study, you can get so much life experience with for example making a book (almanac), learning how to finance (a FiCo), working together on sunny and rainy days (with your year club) and maintaining a culture (in a board). When you go to a traditional 'zaalavond', you go way back in time. An association is like an accessible history book. Not strange that student life will become intangible cultural heritage soon!

**What did you have to put aside for your collection?**
The most I put aside for my collection is money. Money to travel, money for my own house with a beautiful collection room. All the money, money is the word. (From *The Morning* of The Weeknd)

**What is your favourite cell organelle?**
I choose the cell membrane. This separates the internal from the external environment of a cell. However, it has the ability to let particular things through, which is also applicable to my role in the student life!

Did you know that the flags and medals of Virgiel are all different? You have to look a little longer before you see it (just like when you watch cells through a microscope), but this lets you discover a lot of things!

And… Did you know that "Gezelschap Leeghwater" is not only the oldest association of Delft, but of the whole Netherlands? That is why they chose an elephant as a mascot, because they can become very old, too.

## MULTI-DAY EXCURSION
## TO HEIDELBERG AND FRANKFURT

**In the first weekend of May, 29 Nanobiology students (both Bachelor's and Master's) went on a trip to Germany to visit interesting institutes. Cohecie organised the whole trip, including the drive, dinners and parties. It was a fun weekend in which we learned a lot.**

On Friday 5 May, after a six hour drive in small vans, we arrived at the European Molecular Biology Laboratory (EMBL). EMBL is located in the mountains, so it was challenging to get there. We entered the big, round main building where a congress was held simultaneously. At EMBL, we got an introduction about what they do and our possibilities as Nanobiologists in the field of molecular biology. After this, two PhD students told us about their research, which was even coupled with a research group at the TU Delft: the group of Bernd Rieger, whom we know from our beloved Systems and Signals! Finally, we got a tour through the building. It had a nice architectural design, where we could reach the different floors by walking all the way up on the spiral stairs in the form of a double helix. At the roof, the view of Heidelberg was beautiful and we could easily understand why someone would build a research institute right at that place.

After having visited EMBL, we drove our buses back into Heidelberg and went to our hostel. From there, we walked to the restaurant, which gave us a satisfying look of the little city we were in. The dinner was amazing, with big steaks and schnitzels. The ice cream afterwards was also delicious, accompanied by the view of Heidelberg's castle. Later in the evening, the people who were not that tired went bowling. The day was ended with a party nextdoor.


Photo: HITS

The next morning, everyone woke up early. We ate some breakfast, packed our stuff and went to the buses. Time to go to the next institute! This institute was once again located in the mountains, which gave us a panoramic view on Heidelberg. The Heidelberg Institute for Theoretical Studies (HITS) was an interesting combination of a futuristic building with glass walls, and an old country house. HITS was prepared well and provided us with a lot of promotional material from their institute. We got talks from multiple groups, which showed how diverse this institute is. Hereafter, these groups showed their posters so that we could walk around and ask questions. The visit was concluded by making a group picture in front of the building.

In the afternoon, we went to the Zentrum für Molekulaire Biologie Heidelberg (ZMBH). This is a research centre attached to the University of Heidelberg. The tour gave us a look into how other universities arrange their labs. For example, they have their computers inside their labs instead of in seperate offices. Afterwards, some of the group leaders told us about their researches.

After the visit to the last institute, we drove to Frankfurt. The difference between Frankfurt and Heidelberg was big; Frankfurt can be called a metropolis compared to the little student-city Heidelberg. That evening, we went out for dinner with the whole group and partied at different places. Most of us had a hard time waking up the morning after, but it was all worth it since we went to the zoo! This was a fun conclusion of our trip.

See you next year!

Ilse de Bruin

## MY YEAR IN DENMARK

## DANISH 'HYGGE' AND STEM CELLS

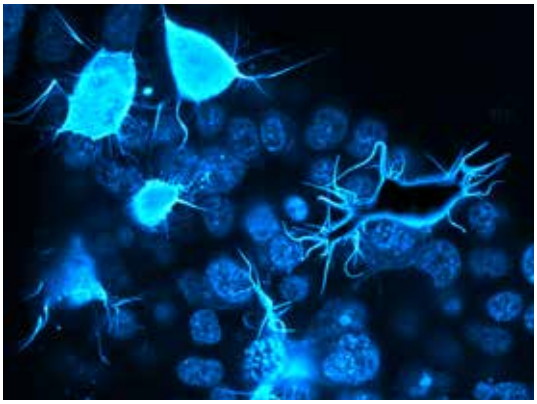
It was not Donald J. Trump's obsession with the country (search for Donald Trump + Denmark on YouTube) that influenced my move to Denmark. I had studied abroad before, and since that had been a pleasant experience, I decided to apply for another round. In my quest to find an interesting place, I was guided by my interest in stem cell biology and mechano-regulation. A special centre for research relating physics with stem cell biology had started up the year before and thus seemed to be an obvious place. After a skype interview with one of the principal investigators of the centre, it was settled. Copenhagen would be my destination: the place where I would write my Master's thesis.

Denmark is not that different from the Netherlands. It is flat and windy and people speak a funny tongue. Like the Dutch, the Danes like to cycle (the entire city is equipped with bike paths) and, although the price is rather high, to drink beer (Danes are the most unrestrained alcohol users of Europe). Surprisingly, the Danes share our traditions to eat "pepernoten" (peppernødder) in December and to consume "oliebollen" around the end of the year. Additionally, the Danish language is equipped with a word for "gezellig", termed "hygge". Differences can be observed in the daily schedules; people usually work here from 9.00 to 16.00, which may explain the relaxed atmosphere around town.

Being the capital of the Nordic, Copenhagen is a great city to live in. Multiple events are arranged each weekend and there is always something going on. Striking is the difference between summer and the relatively long winter. During summer, we share the streets with a crowd of tourists and during wintertime, we find ourselves wandering around the city centre with locals only. Copenhagen University, which has the largest population of international students in Scandinavia, and the presence of multiple multinationals give the city an international feeling.

The last nine months, I have been involved in a project that tries to unravel the role of mechanical perturbations on the expression of lineage specific markers in early mouse embryonic stem cells. Although the influences of soluble factors have been studied in great detail (think about the discovery of the four Yamanaka factors), only little is known about the role of mechanical forces on early stem cell priming. During my time here, I have applied optical tweezers and multiple reporter cell lines expressing fusion-products of several lineage specific markers, to unravel a potential relationship. Some more months and the work is done, and I will not only end my time in Denmark but also my time as a Nanobiology student.

To conclude this story, I would like to give some advice to those of you that also have the ambition to study abroad. Choose wisely and start planning



on time. Ask local scientists for recommendations, since they know where to find good groups. Do not let yourself be guided by the choice of a city (in the end you will find your place anyhow). But most of all, trust on your background, you are a pioneer in nanobiology, that is something to be proud of!
For more information about the group check stemphys.nbi.ku.dk.

Bram Verhagen

**Visiting Copenhagen?** In case you will be visiting Copenhagen this summer, here are some suggestions to make your stay a bit more pleasant.
**Cheap beer:** Check out Studenterhuset. Beers are sold for 1/3 of the price in a regular bar (You have to befriend a Dane or international student to get it for you as a University of Copenhagen-card is required). Peder Oxes: This restaurant has a small bar in the basement, on Wednesdays the bar sells two beers for the price of one. Friday bars: The student bars of Copenhagen University often organise Friday bars with beers from 9 DKK (€1.30) a bottle.
**Music Venues:** Copenhagen is the Jazz-city of Europe. Many cafés offer multiple performances per week. During summer, every Sunday evening, free concerts will be given at free-town, or hippy-Walhalla, Christiania and Pumpehuset (starting at 18.00 and 20.00, check out the site for the correct schedule).
**Cultural centres:** Two cultural centres that I think are worth a visit are Huset-KBH or Absalon. These centres offer a variety of events and venues, ranging from a board-game café to movie screenings and live music. There is always something going on!


Bram (in the white T-shirt) standing in front of the Niels Bohr Institute

# THE CRAZY ADVENTURES OF IGEM
## REACHING BEYOND THE LIMITS

**It all started right before Christmas. We received the email announcing our selection for this year's iGEM TU Delft team. Then, shortly after the holidays, the team sessions commenced: we would meet all our excited teammates and brainstorm for hours in the company of our supervisors.**

We did our best to gather as many crazy ideas as possible. The sky was the limit: bacteria that made self-healing materials, produced rocket fuel or powered bio-batteries... We even thought of bacteria that could actually detect and quantify radiation!

However, our team came across the issue of antibiotic resistance and how it, besides being a worldwide problem, currently poses one of the biggest challenges to the agricultural sector of the Netherlands. We felt that it was a topic in which we could really make a difference and accomplish a social impact. Accordingly, we agreed on developing a diagnostic tool so simple and user-friendly that it could be utilised on the spot by farmers: a disposable microfluidics paper containing Cas13a that would activate upon presence of antibiotic resistance genes in the sample and subsequently cleave all kinds of surrounding RNA, triggering an optical readout. This way, farmers could know which antibiotics will have an effect and thus employ them more specifically.

That being said, detailed research is not the only thing we do at iGEM. We need to ensure that companies and the general public are familiar with our project. For this reason, we participated in the NBC-17, Museum Night in Leiden and even TEDxDelft.

Furthermore, we are organising a European iGEM meetup this summer in which teams from all over the continent will come to Delft to share their projects and arrange collaborations. So far, more than 150 attendants have been confirmed!

The best is yet to come. Stay tuned via:
Facebook: TU Delft iGEM
Instagram: igemtudelft
Twitter: @TUDelft_iGEM
Website: igemtudelft.nl
You can always drop by at our office E0.120.

TUDelft iGEM 2017
CASE 13A

## OLD COUSINS

### PRIMITIVE HUMANS LIVED ALONGSIDE MODERN HUMANS

A group of international researchers discovered that around 300 thousand years ago, a primitive human called *Homo naledi* lived alongside modern Humans in the southern part of Africa. The age of the found fossils was determined by researching the age of the ground layers in which they were found, but also by measuring the amount of uranium decay in the teeth of the primitive humans. The peculiarity is that this creature, which was about one and a half meter long and had a brain around the size of an orange, lived an extremely short while ago in terms of human development. There is also evidence that they buried each other in caves, which might be a first sign of cultivation.

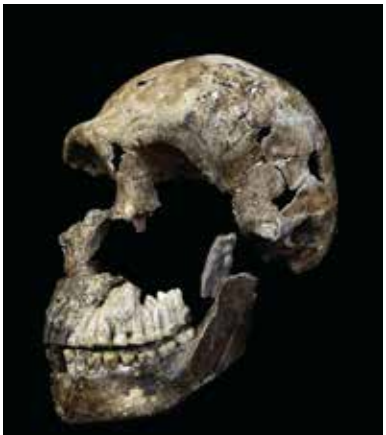


Photo: Wits University/ John Hawks

## TRANSHUMANISM

### TECHNOLOGY TAKING OVER OUR BRAINS

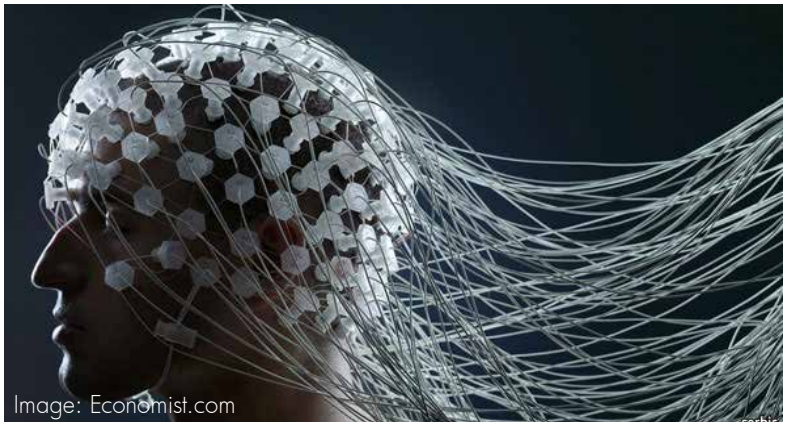


Image: Economist.com

After the smartphone revolution of the last decade, there are plans in Silicon Valley to change our lives completely once more. This time, they want to go let our brains communicate with our devices and with each other. A mysterious research group within Facebook, Building 8, wants to develop a technique that could 'catch' brain signals through the skull. People would be able to type 100 words a minute with this technique, only by thinking about these words. Elon Musk, founder of SpaceX and Tesla, presented his new company Neuralink last March. In the short-term, its goals are to develop treatments for serious brain diseases, but in the long-term, it also wants to work on human enhancement. Musk wants to implant the technique under the skull into the brain, in such a way that the brain can also be simulated and people could communicate with each other purely with their thoughts. A lot of obstacles still have to be overcome, of course, and not everyone is as optimistic as the researchers in Silicon Valley. Several neuroscientists say that we know way too little about the brain at this moment and that Facebook should be happy if they could read one word a minute in ten years.

## THE MOZART EFFECT AT ERASMUS MC
## EVIDENCE-BASED POWER OF MUSIC

**A delightful sonata resonates across the hall of Erasmus MC. For a moment, doctors forget their next patient and let Beethoven ease their minds. Next, an impromptu from Chopin alleviates the thoughts of a worried mother, who waits her turn at the pharmacy. Subsequently, a tragic suite from Prokofiev reminds the Nanobiology students of their re-exam for Systems and Signals.**

Since March 2016, a white grand piano shines in the passage of the Erasmus MC. The idea came from Prof Dr Myriam Hunink (Clinical Epidemiology and Radiology). Everyone can demonstrate their piano skills to the passers-by, which is not always equally appreciated. Nevertheless, the piano adds a cosy ambiance to the hall of the hospital.

In Ancient Greece, medicine was often integrated with culture and arts. For instance, the sanctuary in Epidauros did not only involve a medicinal temple sacred to the god Asclepius. It included a Hellenistic theatre with an auditorium, orchestra and staging building. Before the healing process, which happened overnight in the abaton underneath the temple, patients first experienced an ancient tragedy. The catastrophe in the protagonist's life would cleanse the watchers' emotional clutter – a process called catharsis. This was believed to be healing for mind and body.

*After ten minutes of a Mozart sonata, participants scored significantly higher.*

Today, the Ancients' belief in catharsis seems not so far from scientific truth. The effects of music on the body and mind have been researched for years. In 1993, the so-called "Mozart effect" was first investigated and confirmed by Frances H. Rauscher in Nature. A short-term effect on spatial reasoning IQ has been demonstrated. After ten minutes of Mozart's sonata for two pianos in D major, participants scored significantly higher (8-9 IQ points) compared with listening to a relaxation tape or nothing. (Nature 1993; 365:611)

Nevertheless, a popular claim that music makes you intelligent is still unfounded. The enhancing effect does not extend beyond 10-15 minutes. Rauscher writes: "Our results on the effects of listening to Mozart […] have generated much interest but several misconceptions, many of which are reflected in attempts to replicate the research, [like] that listening to Mozart enhances intelligence. We made no such

claim. The effect is limited to spatial–temporal tasks involving mental imagery and temporal ordering." (Nature 1999; 400:827)

*"It is not just a matter of listening to your own favourite music, Heavy metal does not work."*

At Erasmus MC, the effect of perioperative music in children surgery has been studied by Marianne van der Heijden and colleagues. In their review, they found a significant positive effect on postoperative pain, anxiety and distress. They suggest that music therapy may be considered for clinical use and emphasise the advantage of non-invasive therapies. (PLoS One 2015; 10:8)

It is not just a matter of listening to your own favourite music, says Hans Jeekel in de Volkskrant. He is emeritus professor in surgery at Erasmus MC. "From many studies can be concluded that heavy metal does not work." In research, classical music with tempi around the heartbeat is mostly used.

The sonata finishes with a point d'orgue. For a second, the hall is filled with the feeling of slight amazement and onward progression to the daily business. The fallboard is closed and the pianist disappears in the crowd.

## INTERVIEW WITH PIANO PLAYER HAYATI KART

"I still have to get used to the small smiles on the faces of passers-by; little experience with playing in public as I have. But I often play during work time to meet new people. Patients in particular. Currently, I work on the implementation of a new electronic patients record system. That is to make the health care easier and more efficient. It is nice to meet the patients you are working for."

*"A mishmash of Eastern and Western sounds, I reckon that this resembles my character."*

"I love the pieces from Vagif Mustafazadeh. He is a fantastic composer. His work is often a mishmash of Eastern and Western sounds. I reckon that this also resembles my character. If you ask me for a specific style, then the Phrygian scale is my favourite. It is used in many Turkish songs, but it has been used by the Ancient Greeks as well. There you have it: music is universal and does not have "artificial" edges."

*As we know, the best stories arise from spontaneous conversations. Therefore, mRNA likes to yield the floor to members of S.V.N.B. Hooke, who all indubitably have magnificent stories to share. We used a Mersenne Twister and linked the outcome to the membership database. We asked this person to write a column about a topic of personal preference.*

```
>> rng('shuffle');
>> randi(nr_leden)

ans =

    220
```

## LIFE

The wind was blowing softly and from time to time, you could see the sun shining through the clouds. It was at a moment like this, that a little green stem popped out of the earth. With a beautiful yellow flower on top, Narcissus arrose. And as days were passing by, word spread about Narcissus' greatness and not only the flowers along the river, but also the Daffodils on the hill talked about him. You could say that life was going pretty well for Narcissus.
But then, everything changed.
As nights became longer and the world around them turned orange, the flowers started to worry for their lives. But not Narcissus. Narcissus was convinced that among all the flowers, he would certainly never have to worry, because he was the best. Clouds became masters of the sun and Narcissus experienced a new kind of feeling. A frosty feeling covered his leaves during the night and during the day, Narcissus became hungry. "How could this have happened?" was the only thought in his pretty little head. "How could nature not have prepared me for this? Why am I so fragile, was I not the greatest?" Even as Narcissus was on the brink of dying, he tried not to give up on life. Days were passing by and just when he wanted to give up, he felt a soft sunbeam tickling his leaves. He knew his days of suffering were to end soon. He knew he could be great again. But above all, he knew he had to learn how to survive in his shape-shifting pretty little world.

Nicki Jansen

# SOLUTIONS TO THE PUZZLE

## ANNOUNCEMENTS OF THE PRIZE WINNERS

### Solutions to the challenges of the previous edition

Freshman: As long as you could make 'Okazaki', it is alright.

Bachelor: This image (Nova NanoSEM, Magnification: 2000x) is from the BSc thesis of Melina Dekker, in which she produced a material from cellulose and calcium oxide.

Master: This problem was borrowed from Prof Dr A. Houtsmuller's thesis: "Three Dimensional Analysis of Mitotic Prophase Chromosomes".

We had multiple submissions and decided to award two prizes. One for the best numerical and one for the best analytical.

Dirk Kruit had the best numerical solution. Max Betjes was able to calculate the mean square and won the analytical prize. An honourable mention goes to Kristian Blom, who solved it for the mean, but submitted too late.

### An outline of the solution to the Master problem is given here:

This problem contains point P and Q with distance d in a circle S. For this problem we can take volume as a measure for the distribution.

(1) $P(d) = \frac{M_d\{PQ\}}{M\{PQ\}} = \frac{M_d\{PQ\}}{M\{P\} \cdot M\{Q\}} = \frac{M_d\{PQ\}}{V_S^2} = \frac{M_d\{PQ\}}{\frac{16}{3}\pi R^2}$

For an arbitrary P with distance i from the origin of S, and variable distance d, all the points Q lie on the sphere Pd. As long as this sphere is inside S, the area of the sphere is equal to:

(2) $M_{d,i}\{PQ\} = \int_0^{\pi} 2\pi d^2 \sin(\phi) \mathrm{d}\phi = 4\pi d^2$

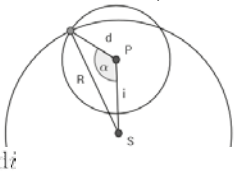
If however d + i > R, the sphere Pd will go outside S (see image). This constraint can be expressed as:

(3) $0 < \phi < \alpha(i,d) = \arccos \frac{i^2 + d^2 - R^2}{2id}$

Resulting in:

(4) $M_{d,i}\{PQ\} = \int_0^{\alpha(i,d)} 2\pi d^2 \sin(\phi) \mathrm{d}\phi = 2\pi(1 - \cos(\alpha(i,d)))d^2$

(2) and (4) now describe both the area of this sphere. We can now integrate the area of the sphere over the radius to get the total volume of this sphere, while it is kept in S.




(5) $M_{d,i}\{PQ\} = \int_0^{R-d} M_{d,i,2}\{PQ\} \mathrm{d}i + \int_{R-d}^{R} M_{d,i,4}\{PQ\} \mathrm{d}i$

After multiplying with the total volume of P, we get what we want.

(6) $M_d\{PQ\} = \int_0^{R-d} M_{d,i,2}\{PQ\} \cdot M_i\{PQ\} \mathrm{d}i + \int_{R-d}^{R} M_{d,i,4}\{PQ\} \cdot M_i\{PQ\} \mathrm{d}i$

Everything filled in.

(7) $M_d\{PQ\} = 8\pi^2 d^2 \left( \int_0^{R-d} \int_0^{\pi} i^2 \sin\phi \, \mathrm{d}\phi \, \mathrm{d}i + \int_{R-d}^{R} \int_0^{\alpha(i,d)} i^2 \sin\phi \, \mathrm{d}\phi \, \mathrm{d}i \right)$

The first term of the formula is only applicable when d < R, otherwise Pd is always outside S.

Worked out this will end up as this surprisingly simple polynomial:

(8) $P(d) = \frac{M_d\{PQ\}}{M\{PQ\}} = \frac{3}{R^3}d^2 - \frac{9}{4R^4}d^3 + \frac{3}{16R^6}d^5$

With this polynomial one can calculate quite easily the mean, mode, and variance.

However, the mean alone could directly be calculated with Kristian's method:

$$\bar{d}(p_1,p_2) = \int_{r_1=0}^{R} \int_{r_2=0}^{R} \int_{\theta=0}^{\pi} \frac{9}{2} \frac{r_1^2 r_2^2}{R^6} \sin\theta \sqrt{r_1^2 + r_2^2 - 2r_1 r_2 \cos\theta} \, \mathrm{d}\theta \, \mathrm{d}r_2 \, \mathrm{d}r_1 = \frac{36}{35} R$$

## APPLIKON BIOTECHNOLOGY
## ADVANCED BIOREACTOR SYSTEMS

"Providing reliable solutions for the bioprocess market that will enable an improved quality of life." That is the mission of Applikon Biotechnology, a world leader in developing and supplying advanced bioreactor systems, from lab-scale in microliter volumes to production systems of several thousand liters.

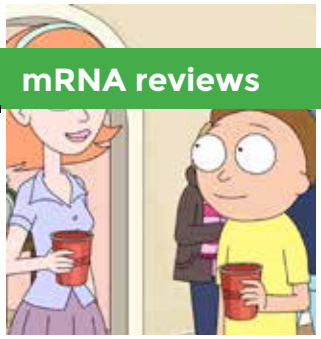
*"This strategy is also anchored in the company name: 'Appli' is deducted from the English 'to apply'; and the last part 'kon' is used in a lot of city names in Switzerland."*

Founded in 1973 as a subsidiary of Pieterman BV, this medium sized company lives by its motto "a step ahead" to differentiate them from other suppliers. Their focus on bioreactors only allows them to produce state-of-the-art equipment resulting in a steady growth to the top position of the worldwide laboratory bioreactor market. The basis of their new product development lies in their strong cooperation with leading international universities and institutes. Applikon also represents products of other foreign firms, mainly products based on biotechnology. Three groups of specialists support these activities, application research, training and project group. This strategy is also anchored in the company name: "Appli" is deducted from the English "to apply"; and the last part "kon" is used in a lot of city names in Switzerland.

In April 2017, Applikon Biotechnology announced its expansion into Japan through a partnership with Sanyo Trading Scientific Instruments.


Fragments and image retrieved from applikon-bio.com.

# RICK AND MORTY



**Rick and Morty, an animated tv show that started in 2014, is considered by many as the *crème de la crème* of running tv spectacles. Protagonist Rick Sanchez, a genius scientist, and his grandson Morty Smith explore many universes and worlds with Rick's remote teleportation device. With Rick and Morty, things are always exactly as you would expect them to be: just completely random, yet unorthodox circumstances. The mRNA did a review on one episode to give a quick look into their universe.**

S02E07 starts with a family conversation about a killer vampire at Morty and Summer's high school. Everybody seems shocked at the confirmed existence of vampires, except for Jerry Smith, absorbed by his smartphone. This arena reminds us of how affordable it has become not to pay attention, like, at all, any time. Beth Smith does not agree and soon an argument develops between the middle agers, who are immediately taken on an intergalactic trip to a specialised world for couples therapy by Rick.

We nanobiologists like it small, so you can imagine that when Tiny Rick comes into scene, everyone is having a blast. Tiny Rick? Yeah, if you want to hunt a vampire at a high school, you just have to transfer your consciousness into a younger clone of yourself. Unfortunately, the teenage clone becomes a very nasty version of himself, probably a phenomenon known to your parents.

Summer Smith, usually the living definition of pop culture and all that is wrong in western modern culture, takes up the role of the wise woman we always hoped would be somewhere hidden inside her, and she tries to make Tiny Rick reasonable again and repatriate his mind into the old man he is.


Meanwhile, Jerry and Beth are shown the subconscious versions of each other, scanned from their brains through an EEG. These versions, a naked worm and a monstrous spider, team up and try to destroy the couples therapy base and dominate the world. Will Jerry and Beth ever escape? Will Rick ever be old again? And will you, dear reader, come watch the third season of Rick and Morty with us sometime? We, at least, can't wait.

A-jerry-el Morty-na

## WHAT'S NEXT?

Labcourse 2.....27/06
Linear Algebra 1.....04/07
Physical Biology of the Cell 1.....05/07
Analysis 3.....06/07
Biomolecular Programming.....07/07

Journal Club.....29-30/06
Computational Science.....4-6/07
Bioinformatics.....05/07
Image Analysis.....07/07

High-Speed Simulations.....05/07
Systems Neurobiology.....06/07

Retakes.....14-18/08
IntroN.....18-20/08