Green Computer Networks  
Reparing the retina by gene therapy  
Piet Borst, a life full of science
First time lucky?

The response to the first edition of Amsterdam Science was overwhelming! Many of our colleagues congratulated us with the content of the magazine and the nice “look and feel” of the printed version. The magazine landed on the reading tables of research institutes, but also in hotel lobbies, Ministries, the Amsterdam municipality office, Brussels and many other unexpected places. Our mission to make the first edition of Amsterdam Science visible was a great success. To our surprise, even the response to the puzzle was almost instantaneous and we received very elaborate solutions, including in the form of a computer script that could be used to solve the riddle. Let’s see how the new puzzle is received.

Not just the paper version, but also the website received compliments and was visited frequently in the first weeks of its existence online. Of course, although a great start, Amsterdam Science #1 was not perfect and we received very useful feedback on both the magazine and the accompanying website.

As you can see in Amsterdam Science #2, this has resulted in format changes for the magazine: the page size is slightly larger to accommodate a larger font and boost the size of the images, both measures aiming at making reading more relaxed and comfortable. On the website we worked on the online submission form and have clarified our selection criteria for contributions. This led to more submissions made directly to the magazine, meaning that the second issue not only covers all disciplines, but also contains contributions from institutes other than the two universities who initiated the Amsterdam Science project.

Further expansion in the circle of contributing institutes is an explicit goal for the next issues, and inviting and recruiting more partners to the editorial board from outside the UvA or VU is a key step on this path. New board members are needed as, after enthusiastic and much-valued service, Monalisa, Dorota, Jeroen and Anne are stepping down in the closing stages of their PhD project or Master study. Also on behalf of our readers, we sincerely thank them for their inspiring contributions and wish them well with their careers.

On the cover and on the centrefold you will find amazing images and with the help of all contributing authors we can bring you a kaleidoscopic overview of what Amsterdam Science has to offer. Enjoy the second issue, one that we feel proves that the magazine’s winning streak is more than a case of first time lucky!

On behalf of the Editors-in-Chief,
Michel Haring
The spectacular images taken by the Hubble Space Telescope have fascinated two generations of professional astronomers and the general public alike. Hubble is celebrating its 25th birthday, which is truly exceptional for a space-based observatory, and all its glory is still going strong. Astronomy researchers still fiercely compete to get observation time using Hubble. How else could NASA and ESA celebrate this event than by releasing this new spectacular image (and even a fly-through movie), of the enigmatic star cluster Westerlund 2 (see magazine cover)? This star cluster harbours some of the hottest, brightest, and most massive stars in our Galaxy, illuminating the remains of the clouds of gas and dust out of which they were formed. UvA astrophysicist Selma de Mink, a newly hired assistant professor at the Anton Pannekoek Institute, is one of the rare places where we can study massive stars.

Although massive stars are vast—typically outnumbered, they play many premier roles in astrophysics. The very first stars that formed in the Universe after the Big Bang are thought to be very massive. The Universe was still dark and filled with neutral hydrogen. The hot radiation from the first massive stars ionized this gas, making the Universe transparent again, bringing an end to the cosmic dark ages. Since then, multiple generations of massive stars have fuelled the primordial hydrogen into heavier elements, such as the oxygen that now allow life on Earth. Understanding how massive stars live their life is a small but crucial step in understanding our own cosmic history.

Hubble has been crucial for our understanding of how massive stars live their lives. Taking images of these objects, Hubble can gather data in wavelength regions shielded from Earth’s atmosphere, such as the ultraviolet, where hot, massive stars emit most of their light. Fortunately, Hubble takes data in the near-infrared region, which allows us to see through the dusty gas clouds that typically surround them. Above all, the superstar Westerlund 2 is one of the rare places where we can study massive stars.

The most striking part of the cover image is the dusty cloud visible on the lower left: when looking closely one can distinguish pillars of dust, which are places where lower-mass stars similar to our Sun are being formed. Understanding the formation of massive stars is therefore one of the rare places where we can study the birth of our own Sun. On top of that they tend to hide in very dense regions obscured by gas and dust. This makes it very challenging to study them. Fortunately Westerlund 2 is one of the rare places where we can study massive stars.

The star cluster Westerlund 2 is visible in the centre of the image as a dense clump of stars that appear to be red. In reality the stars are extremely blue and hot, shining so much of their light through these dusty clouds that we see them as red. In reality the stars are extremely blue and hot, shining so much of their light through these dusty clouds that we see them as red. In reality the stars are extremely blue and hot, shining so much of their light through these dusty clouds that we see them as red.
An interview with Piet Borst, clinical biochemist, cancer researcher and former director of the Netherlands Cancer Institute

A life full of science

Organizing an interview with professor Piet Borst turns out to be easy: “Being a retired professor means that I have oceans of time, please come by!” When we arrive in the main Hall of the Antoni van Leeuwenhoek Hospital in Amsterdam-West, professor Borst himself comes to meet us: “People tend to get lost when they have to find their way to the laboratory, that is why I rather pick up my guests myself”. The interview takes place in his room in the Netherlands Cancer Institute. After he serves us a cup of coffee we quickly switch from professor to “Piet”, as he likes to keep things informal. And he likes to talk… So we need to guide him to our questions, otherwise he would bury us in anecdotes and science facts. Given that he is eighty-one and still active in scientific research we set out to discover the secret of his success.

How did you come to choose your research fields of biochemistry and molecular biology?

“It was just coincidence that brought me there! I never planned my career, everything happened by chance. Originally, I wanted to be a doctor and do clinical research. My father was a professor of internal medicine in Amsterdam, an excellent physician and researcher with an empathic attitude towards his patients. He was the ideal role model and this drove me towards a study in medicine. While I was waiting for a training position as medical doctor I had some time to kill and I decided to train myself in lab work and doing research. My father advised me to contact a young professor in Biochemistry at the University of Amsterdam: Bill Slater. I worked in his lab for four months and continued my studies in medicine afterwards, just as planned. However, a few months later, when I was doing the training internship for my medical studies I got a call from Slater: some doctor quit a research project and Slater wanted me to continue that work. But I was just in the middle of my medical training! It didn’t seem a good idea at first. Well, Slater convinced me to do it, and so I did. It turned out that I really liked doing the research, and so it happened that I completed my PhD thesis on metabolism of mitochondria (the energy generating organelles of the cell) in the lab of Bill Slater, while I simultaneously finished my study in medicine and became a physician.”

So in 1963 you were both a medical doctor and a researcher. What did you want to do next?

“I wanted to become an endocrinologist, a doctor specialized in hormones. There was a very good endocrinologist in Leiden, Queirodo, and I applied for a trainee position, but again the fact that there was a waiting list changed my career path. Through Slater I came in contact with a Nobel prize winner in America, Severo Ochoa, who worked on nucleic acids. For two years I lived in New York and studied the multiplication of bacterial...
"Biologists have to deal with the unique differences between each organism, and the randomness of nature."

"A group in Belgium studying the trypanosoma parasites was looking for something specialised for the DNA present in their microorganisms. They asked me and I said yes. I had two drivers for joining them. First, I did not think that the people working on it was incredibly talented - arrogant, that was what I was thinking then, I lost that now - soised they start in this area with one PhD student I think has a good chance to complete with the rest of the world. Second, it was a good thing that the research was relevant, in the sense that it directly contributed to solving health threats. Relevant, applied research, was that a thing that the students were looking for at that time."

So you think applied research is more relevant? "No, that's not true! You should not underestimate the importance of fundamental research. Fuyo do fundamental research, ultimately it will always lead to knowledge that can be applied in such a way that society can benefit from it. Sometimes people don't realise that all the big revolutions in for example technology and health care are the result of fundamental research, funded by governments. Fundamental research is more relevant at first - its purpose was just the gathering of knowledge but, then suddenly, it turned out to be of great interest! Fundamental research is of utmost importance."

"Just as a hungering cell eats itself, we are gradually consuming all the fundamental knowledge we built up in the past..."
Self-learning search engines

→ How does a search engine such as Google know which search results to display? There are many computing algorithms that generate search results, but where do they come from? We developed a new probabilistic method for quickly comparing large numbers of search algorithms by examining the results users click on. Our study was presented at SIGIR 2015, the 38th international conference on information retrieval, held in Santiago (Chili) last summer.

Interleaving Developers of web search engines constantly create hundreds of alternative search algorithms, all of which aim to find the best possible match between a user’s information need and web pages. It is vital for both the search engine and the user to know which of these algorithms produces the best results. A straightforward way to compare search algorithms is through interleaving, a sorting method by which the search engine analyses the users’ click behaviour to determine a prefer- ence between two alternative algo- rithms. After the user has typed in a query, the unique results of two search algorithms (blue and red in the Figure) are interleaved alter- natingly (from top to bottom, and displayed to the user as a single list). If the user then clicks on a result found by one search algorithm (red), the algorithm analysis infra that in this particular case the al- gorithm generating the selected result produces the desired result, but the other one. By scaling up this type of inference to cover millions of users, the search engine automatically learns which algorithms yield the best results.

Multileaving 1.0 Interleaving is, however, limited by the fact that only two algorithms can be compared at a time, and the use of combinations of comparisons may therefore be required to deter- mine which one of hundreds of existing algorithms really works the most effectively. So-called multileaving methods, which have been developed at the University of Amsterdam, allow multiple al- gorithms to be compared simul- taneously. In earlier work, we did so by combining the results from many lists of results at once (in the example of blue and red lists, imagine also adding orange and green lists, etc.). The multileaved result list that is shown to the user is then a mix of results from many search algorithms — a multi-coloured list. We keep track of where each of the results comes from (their colour), and, as with interleaving, we observe which search algorithm (colour) attracts most clicks from users. Again, the search algorithm that receives most clicks wins. Typical- ly, since this has been established, the search engine will complete- ly switch over to the victorious search algorithm for all its users and queries.

Next step: probabilistic multileaving Our newest method takes multileaving a step further. While we still combine the results from many search algorithms into a sin- gle multileaved result list, we do so probabilistically. Instead of alternatingly picking results from each of the lists, always working from the top-ranked downwards, we now define a (high) probabil- ity that the top-ranked result is picked, leaving a non-zero prob- ability that a lower ranked result is selected instead. By making the multileaved list probabilistic, we ensure that any combination of search algorithms (coloured lists) could have resulted in the multileaved list that is shown to a user. This has the major advan- tage that we can retrospectively evaluate any search algorithm, us- ing a multileaved result list that has already been shown to a user. In other words, it now becomes possible to reuse old combinations of multileaved result lists and users’ clicks to keep evaluating new search algorithms. As can be expected, the search algorithms that originally contributed results to the multileaved result list, or algorithms that are very similar, can be evaluated with higher con- fidence than very different search algorithms. However, even work- ing at lower confidence levels, it is a major advantage of our prob- abilistic multileaving method that new search algorithms that were not even invented when the multileaving took place can be eval- uated retrospectively. This way, our method can identify the best search algorithms much faster, enabling search engines such as Google to self-improve much more efficiently.

→ In the early 1900s, it was well known that the same fossils could be found in the rocks of different continents. At first, geologists thought the bridges were invoked to explain fossils from different continents, such as the homi- nos, a Permian fern which fossil- sils were found in Africa, South America and Australia. However, there was no trace of the land bridges was found. Alfred Wegener (1880 – 1930) was a German geophys- ical, and geophysicist, realised that the outline of the continents, 200 meters below present sea level, fitted together like the pieces of a giant jigsaw puzzle. “The conti- nents must have shifted,” Wegener said. “South America must have lain alongside Africa and formed a unified block.” Before their separation, the continents were fused together in what he named the ‘Urkontinent’ – now known as Pangaea. “The parts must have become increasing separated over a period of millions of years,” Wegener wrote. He suggested that the ‘Urkontinent’ was pulled apart by the centrifugal force from the Earth’s rotation and that the conti- nents drifted apart with speeds of up to 10 cm per year until reaching their current positions.

In 1915, Wegener published his paper “Die Zerstörung der Kon- tinent und Ozeane” (The Origin of Continents and Oceans), which was greeted with great scepticism. The mechanism involving cen- trifugal forces proved erroneous, and in the end it took until the 1970’s for the theory of continental drift (plate tectonics) to be accep- ted. Mapping the topography of the ocean floor, the geologist Marie Tharp (1920 - 2006) discovered a chain of mountains splitting the large ocean basins in two. Tharp and the geologist Bruce Heeney (1944 - 1977) recognized that the mid-ocean ridges were lines along which the oceanic crust was split- ting apart, thus confirming the continents we walk on today as stone drafts, drifting through the Earth as fast as our nails grow.

“Plate tectonics is still an active field of scientific inquiry in itself and important to understanding today’s variety of landforms. For instance, researchers in the De- partment of Earth Sciences at the Vrije Universiteit Amsterdam are studying the mechanisms leading to the formation and modification of new continental crust. This research is leading to improved es- timations of the timescale of sea-level development and its variations, and to understanding of the relationships between magmatic processes and crustal growth.”

The Computational Geo-Ecology group of the University of Amster- dam is interested in how tectonic structure, due to tectonic collisi- ons and the resulting rock and mountain formation, influences the configuration of landforms and their diversity, as well as the distribution of quaternary mate- rials and soils.

The Royal Society of London held the world’s first symposium on plate tectonics only as recently as 1964. If Wegener had reached the age of 64, he would have been invited as a guest of honour, as although Wegener’s mechanism and rates of continental drift have since been corrected, his creativ- ity and originality are still part of the picture of continents on the move. Wegener was the first to think that the continents we walk on today as stone drafts, drifting through the Earth as fast as our nails grow.

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The war within our DNA

Testing Einstein’s general relativity with neutron stars

The theory of general relativity, as proposed by Albert Einstein, offers the simplest description of particle motion in extreme gravitational fields. It is in correspondence with astronomical observations. Applying it to accurately describe the orbits of GPS satellites around Earth has helped me pinpoint my grandmother’s house on more occasions than I would like to admit.

In my Earth’s gravitational field, my grandmother’s house qualifies as weak when viewed on an astronomical scale. To prove the universality of general relativity, we need to test its predictions in more extreme environments.

Lense-Thirring precession

In the framework of general relativity, a rotating object drags along and deforms spacetime. YouTube’s enthusiastic physics teachers have helped me visualize this by pouring their marble collection onto a sheet of paper. Any straight line will stretch out over a horizon. (Well, almost, it’s the so-called GR治安.) The spinning marbles will form a deformed perfect spacetime fabric and slightly twist it. In a way, the amount of twist depends on how fast the marbles spin. General relativity predicts that under certain circumstances the gas that falls onto the neutron star will precess. This phenomenon will precess, or ‘wobble’ (like a spinning top) due to the twisting of spacetime. This is called the Lense-Thirring precession, that offers a possible solution for the quasi-periodic features we see in the X-ray signals. The precise pattern of the features is predicted to correlate with the spin of the neutron star, and also with the rate at which the gas orbits the neutron star. By comparing the observational findings with theoretical predictions we are now able to test general relativity under extreme gravitational conditions.

Testing general relativity

In previous research at our institute, this test was carried out by examining the X-ray signal from three neutron stars. A correlation remarkably close to the theoretical prediction was found. Surprisingly, no effect due to the rotation rate of the three stars could be discovered. In my Master’s thesis, I re-examined these findings in an extended data set containing 21 X-ray sources and indeed found correlations. However, these are significantly different from what the theory predicts. Although the correlations vary among sources, this variation cannot be ascribed to the different rotation rates of the neutron stars investigated.

It is only fair to note that the theory predictions take single gas particles into account that reside in a vacuum, while real gas flows are more complex entities, involving, for example, hydrodynamic processes. Apart from this reason for a deviation between observation and theory, magnetic effects and precession — due to the fact that a neutron star (just like the Earth) need not be a perfect sphere — can also affect the signal we are observing.

My research fields speculation about what the mechanisms might be that cause the different types of variability we see in the X-ray emission from accreting neutron stars. Lense-Thirring precession is still thought to contribute, but to what degree, and whether general relativity indeed offers the simplest description of particle motion in gravitational fields remains to be seen.

General relativity has helped me pinpoint my grandmother’s house on more occasions than I would like to admit.

Do not hallucinate.
Putting Higgs on the scales

We regularly hear of computing experimental data from the two big experiments at the Large Hadron Collider (LHC) in Geneva—called ATLAS and CMS. However, when data from these experiments are combined, the results can be especially powerful.

No one will have missed the LHC's recent discovery of the Higgs particle, which completes a vital part of the Standard Model of subatomic physics, providing an explanation as to why we (and all other matter) weigh anything at all. But how much does the Higgs particle itself weigh? The ATLAS and CMS teams joined forces to measure the Higgs mass with unprecedented accuracy, an endeavour involving researchers at Nikhef, the National Institute for Subatomic Physics in Amsterdam, and the UvA via their work on ATLAS. As a PhD researcher, I was heavily involved in the analysis that appeared in the premier physics journal Physical Review Letters in May 2015.

When Higgs particle decay, they send out other elementary particles we can detect. My ATLAS team and our CMS colleagues merged the analyses of two such decays: one into two particles known as Z bosons ("ZZ" decay), and one into two photons ("gamma gamma" decay). Merging these decays enabled a highly accurate estimate of the Higgs mass. Particle physicists like to express mass in energy units (referring to the famous equation by Einstein relating energy and mass), and all the Higgs particle weighed in at 125.09 million electron volts, which is more than two atoms of iron taken together.

This value was measured with an uncertainty of only 0.27%. Run 1 of the LHC, which just started, is expected to enable a further squeezing of the experimental uncertainties, but the present number already shows that the Higgs mass is very special. With this value, either our universe is not stable and close to a phase transition, or the Standard Model is wrong. Thus rather than being finished, the Higgs story is only just beginning.

Right now, networks are becoming directly programmable from applications. From individual users can decide on the paths followed by the data and on the type of services provided by the various internet nodes. This new mode of operation goes under the name of Software-Defined Network (SDN). Computer scientists recognize the possibilities offered by SDNs: they want to identify and implement novel algorithms, leading to faster, more secure, and more responsive networks. Indeed, the uses, SDNs offer the possibility to create "green" networks, i.e., networks possessing a smaller energy footprint, while maintaining the same level of performance. Green networks are in fact one of the elements required to make energy efficient software defined computing ecosystem, also known as Green ICT. Networks, computing clouds, physical devices and software programs can all be tuned to be more energy efficient, both individually and in combination with one another.

Research by the SNE group at the UvA focuses on green networking in cloud-based environments: a systematic literature review, ACM Computing Surveys 47, 4 (2015), available online at http://dl.acm.org/citation.cfm?id=2764644

Green computer networks

Green computer networks are only the fabric supporting the communication and data movements, as we no longer want to waste energy this way. Thanks to new technologies such as Software-Defined Network (SDN), the networks of the future will operate differently than today. For the people and companies interested in exploiting these new possibilities and aiming for a greener ICT, the internet will no longer be just a black box that cannot be adjusted.

"Computer networks; smaller energy footprint, same performance"


References

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Hans van Kranenburg, Computer scientist and co-founder of the SNE group at the UvA, is now looking at the integration of all these components to allow distributed applications running in clouds to programme SDNs. Her initial work has already resulted in a groundbreaking paper called “Energy efficient networking solutions in cloud-based environments: a systematic literature review” in the prestigious Journal ACM Computing Survey.

Groen Netwerken

The SNE group has been involved in several national and international collaborations on this topic. Among them, two projects were rooted in Amsterdam: the ‘Green Software’ and ‘Greening the Cloud’ projects, both of which also involved the participation of the Vrije Universiteit Amsterdam (VU) and the Amsterdam University of Applied Sciences (IvA). These joint efforts highlight the leading role Amsterdam and other Dutch cities are now using to search in the subject of sustainable computing.
In the greenhouse of the Amsterdam Science Park tomato plants can be found in abundance. Under a microscope it becomes clear that their green parts are covered with hair-like structures, called trichomes. The ‘heads’ of some of these trichomes function as small chemical factories, producing toxic and volatile substances. If we touch the plant, these cells rupture and volatile compounds are released, causing the characteristic tomato odour. In nature, herbivores foraging on the plant cause the release of tomato volatiles, which serve as the plant’s ‘cry for help’ and attract the enemies of the herbivore. The Plant Physiology group of the UvA investigates the potential of these natural defence compounds in wild and cultivated tomato plants.
Repairing the retina: a gene-therapeutic approach

Blindness is a debilitating disease that affects millions of people worldwide. Scientific advancement is, however, laying the foundations to combat such conditions using retinal prostheses as well as cell- and gene-therapeutic approaches. The first step on the road to developing any therapy is to understand the underlying disease mechanisms and how they might be manipulated. For over a decade our group has tried to answer these fundamental questions using mice that mimic hereditary blindness, providing a platform from which we have developed therapeutic tools for their treatment. Now, using gene therapy, we have successfully replaced faulty genes in our mouse models. By doing so we were able to change the disease’s natural course, leading to improved retinal functionality.

The retina and hereditary blindness

The retina is a multilayered tissue at the back of the eye, which receives light cues that then travel through the optic nerve to be interpreted by the brain. The retina contains seven cell types, including the light-sensitive photoreceptors and the neural support Müller glial cells (see Figure). The photoreceptors are of two types - rods, for vision in dim light, and cones, for higher light levels and colour vision. There are over 160 genes associated with hereditary eye diseases. We focus on two genes, CRB1 and CRB2, which are involved in the control of cell-cell adhesion between photoreceptors and Müller glial cells. Mutations in the human CRB1 gene lead to disruption of this adhesion resulting in both congenital and early-onset diseases such as Leber Congenital Amaurosis and Retinitis Pigmentosa - eye disorders that cause visual impairment.

CRB fundamentals

The CRB1 and CRB2 proteins have similar structures and are localised at junctions between the photoreceptors and the Müller glial cells, residing at the outer limiting membrane (which is the multilayered layer at the top of the Figure). Loss of CRB proteins leads to a dysregulation of the cell cycle during retinal development and subsequently to disruption of adhesion between the Müller glial cells and photoreceptors. This results in retinal degeneration, resulting in disease.

Which genes to target in which cells?

With a better understanding of the molecular basis of CRB-related retinal diseases we set out to create possible gene therapy tools. We used mice with different levels of retinal integrity to verify whether we could bring back proper adhesion, leading to improved functionality. In gene therapy a faulty gene is replaced with a ‘healthy’ copy. In our case, we packaged a correct version of either CRB1 or CRB2 into viral particles that were then injected into the diseased retina. Our system was cell-specific, meaning that we were able to target the correct gene to certain cell types in the retina, namely the Müller glial cells and/or photoreceptors. Success was measured in terms of improved retinal function and the preservation of its architecture as compared to control models. When targeting both cell types with the CRBs packaged viral particles, signs of a recovery were clear. However, when targeting either Müller glial cells or photoreceptors alone, no improvement was found, suggesting that the CRBs need to be present in both cell types to mediate their adhesion. Furthermore, when targeting the two cell types either individually or together with CRBs instead of CRB1, we found reduced retinal function. In fact, we observed an immune reaction, which was initially surprising, as the eye is generally considered to be immune privileged, meaning it is more likely to tolerate foreign antigens. We believe that the injected human CRBs was rejected, most probably due to the influence of the diseased retina.

Hypothesis vs. reality: moving into the future

While our research has made a case for targeting multiple cell types at the same time and highlighted possible immune reactions, long-term efficacy issues in clinical gene therapy for other retinal disease genes have been identified as well. Recent clinical retinal gene therapy trials have shown that this approach may only provide a temporary benefit, lasting three years. In addition, treating patients whose eyesight has already started to degenerate presents a further challenge, mainly to slow down the photoreceptor cell’s death. However, providing any benefit and extending vision even for a few years is still a step in the right direction.

After our initial experiments, we now need to test the long-term efficacy of their therapy and its potential use in congenital blindness. We hope to be moving towards pre-clinical testing at the end of 2016, thereby and I had to pinch myself a few times to realize this was real. When I asked my wife later that day the only thing we could both do for some 20 minutes was cry.

After this event and the associated media hype many, many invitations followed to present and share this amazing story. For me the absolute highlight of this was an invited presentation at the TED annual conference in Vancouver in March. The presentation was put online and has been viewed some 900,000 times.

This story of successive opportunities coming my way begins in August 1976 when I entered the ‘Roeterseiland’ building of the UvA to start studying astrophysics. For my graduation research project Professor Ed van den Heuvel put me in touch with a group in Leiden: they needed somebody practical/computer-oriented for a collaborative project with MIT. This worked well and I got asked to do my PhD in Leiden. Afterwards I spent some years in the lab with no clear options for the future. In 1995 I got asked to join ESA and this eventually led me to managing XMM-Newton, Mars Express, Venus Express, Rosetta and now Gaia; all amazing science missions.

FRED JANSEN

Of first contact studied Astrophysics at the UvA. He obtained his PhD at Leiden University on a study of X-ray radiation originating from solar flares. He worked at the Netherlands Institute for Space Research (SRON) and the European Space Agency (ESA) in the XMM-Newton mission. After that he was project scientist at ESA’s Maks Experiment for X-ray and Gamma Astronomy and mission manager of both XMM-Newton and Rosetta. Rosetta was launched in 2004, rendezvous with the comet 67P two years later and releasing the Philae lander to make the first-ever soft landing on a comet.

The past two years have been the most tiring, difficult and rewarding ones in my scientific career. In May 2013 I was asked to join the Rosetta mission as mission manager – the person carrying overall responsibility for the project. The objective: to deliver this scientific mission of the European Space Agency (ESA) to the comet 67P/Churyumov-Gerasimenko, escort it for 16 months and land its Philae probe on the comet. Fifteen months and a lot of difficult decisions, compromises, travel and incredibly hard work later, I found myself in our control centre in Darmstadt, Germany along with 200+ media teams from all over the world, streaming live from there to events all over Europe, including one at the Parcs des Sciences in Paris – with the French president Hollande. To cut a long story short, we successfully landed on the comet that day and I had to pinch myself a few times to realize this was real. When I asked my wife later that day the only thing we could both do for some 20 minutes was cry.

After this event and the associated media hype many, many invitations followed to present and share this amazing story. For me the absolute highlight of this was an invited presentation at the TED annual conference in Vancouver in March. The presentation was put online and has been viewed some 900,000 times.

This story of successive opportunities coming my way begins in August 1976 when I entered the ‘Roeterseiland’ building of the UvA to start studying astrophysics. For my graduation research project Professor Ed van den Heuvel put me in touch with a group in Leiden: they needed somebody practical/computer-oriented for a collaborative project with MIT. This worked well and I got asked to do my PhD in Leiden. Afterwards I spent some years in the lab with no clear options for the future. In 1995 I got asked to join ESA and this eventually led me to managing XMM-Newton, Mars Express, Venus Express, Rosetta and now Gaia; all amazing science missions.

This past summer, some 39 years later, my son, together with hundreds of others, went to the ‘Roetersland’ for the introduction week as the start of his own university study. If, as a society, we want to get the best out of these young people, opportunities will have to exist for them to experience ‘thinking outside of the box’, to learn, grow and realise their own potential. If we don’t manage to do this, part of the investment in them will be lost.

References


→ Figure

Mouse retina that originally lacked CRB1 genes were injected with a fluorecently labelled human CRB1 vector into mouse. This gene therapeutic approach preserves the healthy retinal architecture, resulting in robust and well-organized layers.

→ References

PETER M. QUINN

Retinal Degenerative Diseases at the Netherlands Institute for Neuroscience, Amsterdam.

FRED JANSEN

Of first contact studied Astrophysics at the UvA. He obtained his PhD at Leiden University on a study of X-ray radiation originating from solar flares. He worked at the Netherlands Institute for Space Research (SRON) and the European Space Agency (ESA) in the XMM-Newton mission. After that he was project scientist at ESA’s Maks Experiment for X-ray and Gamma Astronomy and mission manager of both XMM-Newton and Rosetta. Rosetta was launched in 2004, rendezvous with the comet 67P two years later and releasing the Philae lander to make the first-ever soft landing on a comet.

“[…]“I had to pinch myself a few times.””
A 'spin-off' is a company that is formed on the basis of a specific scientific invention. Spin-off companies make it possible for fundamental knowledge that is developed by institutes to make its way to society, resulting in top quality jobs.

Science spin-offs
Amsterdam 2015

Disclaimer: although the utmost care has been taken, omissions or inaccuracies can be possible, due to the highly dynamic nature of the start-up landscape.
Microbes strike back. How bacteria develop antibiotic resistance

NADINE HÄNDEL PhD student in the Molecular Biology group of the Swammerdam Institute for Life Sciences (2015), UvA.

How do bacteria develop antibiotic resistance?

Main mechanisms of antibiotic resistance in bacteria. Genetic changes in proteins that are targeted by the antibiotic (induced drug target), acquisition of new genes encoding resistance proteins (in other words: to express a gene), a gene first has to be copied into RNA in a process known as 'transcription'. When or in what quantity a protein has to be produced is determined largely by the number of mRNA molecules that are transcribed from a particular gene. Using a whole-genome mRNA expression analysis, we identified permanent changes in expression levels of certain genes in resistant cells. These permanent changes in transcription levels of certain genes were neither dependent of initial antibiotic treatment nor fixed by the antibiotic. Thus, regulation at the transcriptional level (quantitative differences between different numbers of mRNA) appears to be just as important as genetic changes. Resistance conferred by mutations (qualitative changes: mutated protein) and environmental factors produce increasing amounts of certain proteins ("upregulation") could be directly linked to antibiotic resistance, for instance the ampC gene, encoding for β-lactamase, an enzyme that can break down the penicillin-class of antibiotics such as amoxicillin. We found that this gene is approximately 100-fold overexpressed in E. coli cells that have become resistant to amoxicillin.

Finally, we discovered that genes coding for important global regulators have not been described before in the context of antibiotic resistance, played an important role in the de novo acquisition of drug resistance. Some of these upregulated genes remained at a high level of expression even when antibiotics were removed from the culture medium.

Roads to Rome. Combining information from the genetic and transcriptional level during the acquisition of enrofloxacin resistance in E.coli, we were able to show that de novo resistance to antibiotics is brought about by a complex interaction of cellular processes, involving both changes in transcription levels and DNA point mutations. Bacterial cells have a remarkable capacity to develop resistance to antibiotics in various ways that are reminiscent of the old saying ‘All roads lead to Rome’, or, in this case, ‘All roads lead to bacterial resistance to antibiotics’.

Overall, our data could be deployed to optimise current treatment strategies based on the combination and alternation of different classes of antibiotics. Indeed, recent studies indicate that the use of drug cycling or alternating antibiotic treatment strategies slow down the evolution of resistance. Clearly, there still is much potential in optimising current treatment protocols to slow down de novo acquired resistance in microbes and to gain control over the development and spread of antibiotic resistance.

“Antibiotic resistance cell”

Reports on antibiotic-resistant pathogenic microbes are rising alarmingly in the last decade. Figure 1. The behind the data are patients infected with antibiotic-resistant microbes and dwindling susceptible organisms, such as the World Health Organization (WHO), raised the alarm about the increasing number of drug-resistant microbes. The European Commission estimated in 2011 that within the EU antimicrobial resistance in pathogenic microbes caused 25,000 human deaths annually and extra healthcare costs and productivity losses of at least € 1.5 billion per year. Bacteria can become resistant through three main mechanisms: Figure 2: (1) Physiological adaptation. For example, bacteria can increase the expression of transport proteins that actively extrude antibiotics out of the cell or increase expression of an antibiotic degrading enzyme; (2) Genetic adaptation – due to mutations in their DNA, cells can become less sensitive to antibiotics that originally inhibited its cellular processes; (3) Temporal transfer of resistance genes from other bacteria. To curb thecontaminating antibiotic use and the misuse of antibiotics worldwide, new strategies are urgently needed that counteract the development and spread of resistance. We studied the relationship between antibiotic use and the development of resistance, using laboratory cultures of the bacteria Escherichia coli. This is a very well-studied gram-negative bacteria commonly found in the human gut, and an established model organism for bacteria in general.

Resistant E. coli

It is very likely that the transformation from antibiotic-sensitive to antibiotic-resistant cells, E. coli was made resistant by stepwise increase of environmental stress. Prior to genetic adaptation, the concentration of drug concentrations was observed for different classes of antibiotics within only 14 days. For example, the minimum inhibitory antibiotic concentration is a measure of drug sensitivity increased 12-fold for the fluoroquinolone antibiotic enrofloxacin. Enrofloxacin is an antibiotic that is more commonly known as Baytril and is often used for the treatment of our infections in domestic animals. During a 1-month study, E. coli cultures could adapt to a 100-fold increase in the concentration of enrofloxacin.

Thus, we could double the antibiotic concentration in the culture medium almost every day without killing the sensitive cells. Eurofloxin normally performs its antibiotic task by blocking two key enzymes involved in bacterial DNA replication. The resistant E. coli population contained genetic mutations specifically in these two key enzymes. In the resistant population, enrofloxacin can no longer bind to these two key enzymes, so they actively continue to ferment the nutrient and grow. Resistance, however, comes at a cost, as the resistant bacteria have a slightly lower growth rate in the absence of the antibiotic. At low sub-lethal concentrations, antibiotics can trigger specific mechanisms that allow for intentional error-prone DNA replication. This response, aptly named ‘SOS response’, transiently increases the mutation rate of the bacterial DNA. Under non-stressed conditions, the mutation rate in E. coli cells is already well adapted to their current conditions. Under stressful conditions, cells apparently have a remarkable capacity to develop resistance to antibiotics in various ways that are reminiscent of the old saying ‘All roads lead to Rome’, or, in this case, ‘All roads lead to bacterial resistance to antibiotics’. Therefore, we studied the relationship between antibiotic use and the development of resistance, using laboratory cultures of the bacteria Escherichia coli. This is a very well-studied gram-negative bacteria commonly found in the human gut, and an established model organism for bacteria in general.
Spotlight on friction at the atomic scale

Our approach involves the preparation of molecules that can be chemically attached to the surface. These molecules are quite special; on their own they do not fluoresce, but as soon as they are brought in contact with another surface they light up. As machines are getting ever tinier, and their moving parts must as well, they increasingly suffer from friction. This makes the kind of insight that our new method can deliver important for further successful miniaturisation of moving parts.

1. The first experiment I ever did was... for a project in high school, where we had to recreate a laser show. We deflected a laser beam with two mirrors. The perpendicular vibrations of the beam formed the ingredients of our own laser show, but first we had to find the right frequency of these vibrations.

2. My constant source of inspiration is... my father. He was always there for me, stimulated me in my development, encouraged me to move into science and supported my passion for sport.

3. One book that I recommend to all young scientists is... Flatland: A Romance of Many Dimensions by Edwin A. Abbott. It’s a combination of a mathematical essay, in which the concept of dimensionality is brilliantly elaborated, and a satirical novella criticizing society in Victorian times.

4. If I headed the Ministry of Science the first thing I would change is... to allocate more money to fundamental research. The impact of our scientific findings on society is an important measure, but before we get there, fundamental science is key to it all. Therefore, the general direction and goals for the future of science should be set by the academic community itself.

5. If I had to change roles with a famous person for one day, I would choose to be... captain of a Volvo Ocean Race boat. This year’s race was particularly exciting as the boat speeds were barely differing among the boats, so that all boats were within each other’s range of sight even in the middle of the Pacific Ocean. And I enjoy competing!

6. I am most creative when... I take some break after being stuck or unable to track down the bugs in my programmes.

7. If I could choose my field of study and university once again I would choose... Astronomy in Hawaii. For a long time I doubted between studying Astronomy or Theoretical Physics. Luckily, the Bachelor’s programme in Amsterdam combines them both, so I was able to postpone this decision, but for my Master’s I eventually went for Theoretical Physics.

8. If I were a famous person for one day, I would... own a laser show, but first we had to recreate a laser show. We deflected a laser beam with two mirrors. The perpendicular vibrations of the beam formed the ingredients of our own laser show, but first we had to find the right frequency of these vibrations.

9. When I am not being a scientist I am mostly... a watersports fanatic! Most of my time off I spend on competing in sailing races on traditional Frisian barges (skûtsjesilen in Frisian) or playing water polo.
Ocean currents complicate climate models

Fossils of marine microorganisms, such as planktic foraminifera, are among the cornerstones of palaeoclimatological studies. Up to now, it has been assumed that data on the local temperature and salinity of the ocean derived from the analysis of their calcareous shells represent ocean conditions above the location where they were sedimented. Together with an international team of researchers, we have—in our recent Nature Communications paper—reported that this assumption is far from correct.

We used high-resolution ocean circulation models to assess the current-induced spatial footprint of planktic foraminifera, validating the models by means of the analysis of fossil foraminifera shell data from two widely separated sediment core locations. The results clearly show that foraminifera in a particular sediment core, which is generally assumed to give us the record of the palaeoclimatic conditions at that location, may originally come from areas up to several thousands of kilometres away. This in turn means that the historic temperatures inferred from the sediment cores may be off by as much as 1.5-3.0 °C.

Therefore, one has to be cautious with interpreting historic oceanic temperatures from planktic foraminifera, as they originate from much larger areas than previously thought, and thus reflect an ocean state significantly different from that at the core site. This observation is both a stark warning for palaeo-oceanographers, and a powerful tool for improving climate interpretation, as since the 1950s, the earth’s climate history has been reconstructed from the fossil shells of living and settling foraminifera. In fact, the present study is the first rigorous investigation of the trajectories of living and settling foraminifera. This research was a successful collaboration between European, Australian and US institutes in which two research communities—palaeo-climatologists and ocean modellers—joined forces to solve a long-standing problem.

“The powerful tool for improving climate interpretation”

By completing a jigsaw puzzle during the official opening on September 15, Senior Vice President of Qualcomm Nangaj R. Kshetri and UvA Rector Dympna van den Boom marked the start of a new public-private partnership between Qualcomm and the Informatics Institute of the University of Amsterdam: the ‘QUVA’ lab.

The mission of the QUVA lab is to perform world-class research on ‘deep vision’. Deep-vision software should automatically interpret what happens where, when and why in videos and images, with the aid of ‘deep learning’. Deep learning is a form of machine learning with neural networks, which is inspired by how human neurons process information in the brain (see text box). Research projects in the QUVA lab will focus on learning to recognize objects in images from a single example, on personalized event detection and automatic interpretation of videos, and on privacy-preserving deep-learning tools. The aim will be to publish research results in the best academic journals, and where possible to secure novel findings in patents. The agreement between the UvA and Qualcomm will be for a period of five years and will involve the participation of 15 to 20 researchers.

One billion processors Qualcomm Technologies, Inc. is the world-leading provider of processors and radio technology for mobile devices and especially smartphones. The company ships over one billion processors annually, which includes wireless radio processors (GG/GGG, WIFI, Bluetooth) as well as the CPUs, GPUs and DSPs that integrate into the Qualcomm ‘Snapdragon’ system-on-a-chip, which make your mobile devices so fantastic. Bringing computer vision together with machine learning—with an emphasis on mobile and embedded-use cases—will foster new approaches to more intelligence in smartphone cameras, robotics, automotive and Internet-of-Everything applications.

The establishment of the QUVA lab was motivated by Qualcomm’s acquisition of Envision Technologies during the Summer of 2014. Envision was a spin-off company of the Informatics Institute of the UvA, founded and led by Arnold Smeulders. It has now become Qualcomm Research Netherlands, with its R&D team focusing on computer vision by learning. With Qualcomm Research Netherlands and the QUVA lab both located in the Informatics Institute at the Amsterdam Science Park, the development of further collaborative projects is facilitated, enabling academic research in computer vision and deep learning in Amsterdam.

Deep learning

A deep-neural computer network receives data for instance in the form of an image. It starts this image with small templates (e.g., parts of objects) that generate ’feature maps’ after one layer of processing. Features represent the activity of ‘neurons’ that get activated if a template finds a match somewhere in the image. These fields of activities then are scanned again for suspicious correlations by new templates in the second layer of the network, resulting in new feature maps, and so forth. Where neurons in lower layers usually search for edges, neurons higher up in the hierarchy are sensitive to more abstract concepts covering a larger area of the image, such as an entire face. The final layers are trained to detect and classify the objects present in the image (for more details: read the ‘video story’ item in the first issue of Amsterdam Science).

In recent years, new deep-learning algorithms have seen the light of day, but their backbone is still an algorithm invented in the eighties, known as ‘error backpropagation’. In contrast to the feedforward processing of information necessary to detect and classify objects in images, the learning updates that tune the parameters of the network run backward through the network, computing how each template needs to change in order to make the network perform better. This is iterated millions of times until the updates converge. ‘Yoshua Bengio’, one of the founding fathers of the field, delivered a keynote address on deep learning during the opening of the QUVA lab on 15 September 2015.
The lifelong learner.

> Become a life long learner

“Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young.” These are the words of Henry Ford, who acknowledged the importance of continuous learning at any age. However, in daily life, formal learning for many of us is restricted to the first quarter of our lives. From primary school onwards we spend time in classrooms and lecture halls in order to enrich our selves with knowledge. And then, all of a sudden, we are at the point of graduation, ready (or not) to take the step into working life. Luckily for the studious amongst us, more and more initiatives arise to make education easily accessible, also for those who have long said goodbye to university. And both UvA and VU science faculties - riding the wave of the lifelong-learning trend - offer different formal and less formal ways of schooling. Below, two examples:

Summer School Programming

Over the summer, when many students enjoy their holidays, part of the UvA’s Faculty of Science building is turned into a large computer lab. This past summer, more than eighty participants signed up for a week of workshops to improve their skills in programming language Ruby. One of the participants was Niels Mulder, a strategic consultant at PostNL: “I have always had an interest in programming, it is one of my hobbies. In my search for an opportunity to learn a new programming language I came across the UvA Summer School. It appealed to me that you spend a week here at the Faculty. It is great for the contact with lecturers and participants that you share an interest with.”

The Its Academy

Working as a science teacher? Another initiative of the UvA and VU outside the regular educational programmes is the Its Academy, where “thi is for ‘informatics, technology and science”. This academy offers ongoing training for high-school teachers in the science domain. Conferences, masterclasses and networking meetings are organised to support high schools in the region and contribute to a better fit between secondary and academic education.

So, whether you wish to improve your career perspective, keep your brain fit or relive the student experience, there is always a good reason to become a lifelong learner.

> For more information

www.itsacademy.nl

> More information

→  Info

ELINE VAN DILLEN
Department of Communication, Faculty of Science, UvA.

“...build a portfolio and a network, and show what my research at Yahoo is about. It involves better understanding of user goals and considering the differences between machine models and people’s perspectives on the world around them. Design and social expectations have a crucial impact, and it’s fascinating to research that in practice. After my PhD at the Informatics Institute of the University of Amsterdam, I moved to Stockholm to work at Mobile Life, an academic-industrial research collaboration focused on mobile systems and the Internet of Things. Mobile Life gave me the opportunity to coordinate projects on mobile and human-robot interaction. This experience gave me a much broader perspective on playful design and human and emotional aspects of interactions. As a next step, I decided to immerse myself in the centre of tech, the San Francisco Bay Area. I joined Yahoo, where I’ve since then worked on mobile, personalisation and search. My academic background has been very beneficial here, in knowing how to combine technical studies into a bigger picture and develop a big picture understanding.”

Henriette Cramer
Research scientist at Yahoo

> How people interact with systems that proactively try to anticipate their needs: that is, in short, what my research at Yahoo is about. It involves better understanding of user goals and considering the differences between machine models and people’s perspectives on the world around them. Design and social expectations have a crucial impact, and it’s fascinating to research that in practice.

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Moving into industry has been extremely worthwhile, as I gained invaluable experiences working with actual products and end-to-end data collection. The people, resources and data are incredible, and your research has the potential to impact millions of users. Beyond the sheer concentration of tech, a big difference between the Bay Area and the Netherlands is the much higher tolerance for professional risk. Failure isn’t seen as the end of the world, it’s a learning opportunity (even though you better make sure you learn fast!). Ambitions are bigger and resources are much more readily available, both in terms of funding and expert advice. I’d love to see more resources for start-ups and interaction design research in Amsterdam, as it can be a great place to work and especially live.

G/_ns Hateboer
European Patent Attorney at DeltaPatents

→  Starting as a biology student at the Vrije Universiteit Amsterdam, I found out I needed a mix of skills and was too shy to work in a lab. So I instead switched careers by moving to the Netherlands Cancer Institute to become a PhD student. After a postdoc period working in a lab in Milan for two years I came back to the Netherlands. That was then when I started to have doubts about spending the rest of my working life in the lab. Coincidently, at that very same time I was writing two patent applications, which really caught my interest. I decided to completely switch careers by moving to the Intellectual Property (IP) department of Crucell in Leiden, where I was trained to become a Dutch and subsequently European Patent Attorney.

I have never regretted the move. For me it is absolutely the best of both worlds: with a scientific back- ground in genetics, medicine and biology, I fully understand the drive that scientists have to do research. On the other hand, I now understand how to protect that knowledge, how to transfer it to a level at which it becomes ‘patentable’, and how to deal with other (sometimes really big) parties that may either be in competition with or highly interested in the new developments. It is simply awesome to be instrumental in that process.

My job consists of a lot of different tasks: I write new patent applications, I communicate with the European patent office and foreign agents to get patents approved, and together with inventors I identify new innovations. Furthermore, I am involved in determining the ‘freedom to operate’ for parties that question whether their technology is part of a patent that is already filed. To stay well informed, I have to continuously keep up with the intellectual property legislation. And now and then I share this knowledge when teaching in courses about the (biotechnology) patenting process.”

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“Failure isn’t seen as the end of the world...”
puzzle

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Short information about magazine

Amsterdam Science gives Master’s students, PhD students and researchers 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.

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Citizen science tracks bird behaviour: the Vogel het uit! project

Using your smartphone to contribute to scientific research is possible with Vogel het uit!, a citizen science project connected to our research on bird behaviour. We use a flexible, high-tech GPS Bird Tracking System – the UvA-BiTS – to tag birds and study their daily movements. This system gives us a wealth of information on where and when birds travel, but not on why birds prefer certain locations in the Netherlands. As an interdisciplinary team connected to the University of Amsterdam we therefore developed a communication plan and with it won the 2013 Academic Year Prize organised by NWO, NRC Media, the KNAW and VPRO/NTR. The prize allowed us to create a smartphone app, an accompanying website and social-media outlets where anyone can follow and contribute to our research.

The main goals of the project were to engage the general public in scientific research, to collect information that could help us understand why tagged birds frequent certain locations; and to increase our knowledge of bird behaviour. Through the Vogel het uit! app, we collect data for five different bird species. Locations visited by tagged birds for which we need more information about their surrounding environment can be easily found with the app. Our requests to app users vary from taking pictures of potential food sources or specific landscape features (like temporary water bodies) to counting the number of birds present. For example, our tracking data have revealed that certain places in the city and in the countryside are very popular with lesser black-backed and herring gulls. We would like to understand why, considering that both types of gulls are marine species.

Since the launch of Vogel het uit! in May 2014, many people have become active participants in scientific research. The information we have received until now is useful for generating more insight into how birds interact with their environment. For example, for gulls visiting Amsterdam from their colony on Texel, app users have sent us pictures of busy locations in the city showing possible food sources. Bird-count data have revealed how some sites, while not attracting a large number of gulls on a regular basis, seem to be personal favourites of particular gulls. Data collection and interpretation is still an ongoing activity, but even now we can definitely conclude that thinking out of the box by placing research in the public arena can yield new insights and increased public participation in science.