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Nobel Science

Feringa, Zernike and the Groningen tradition

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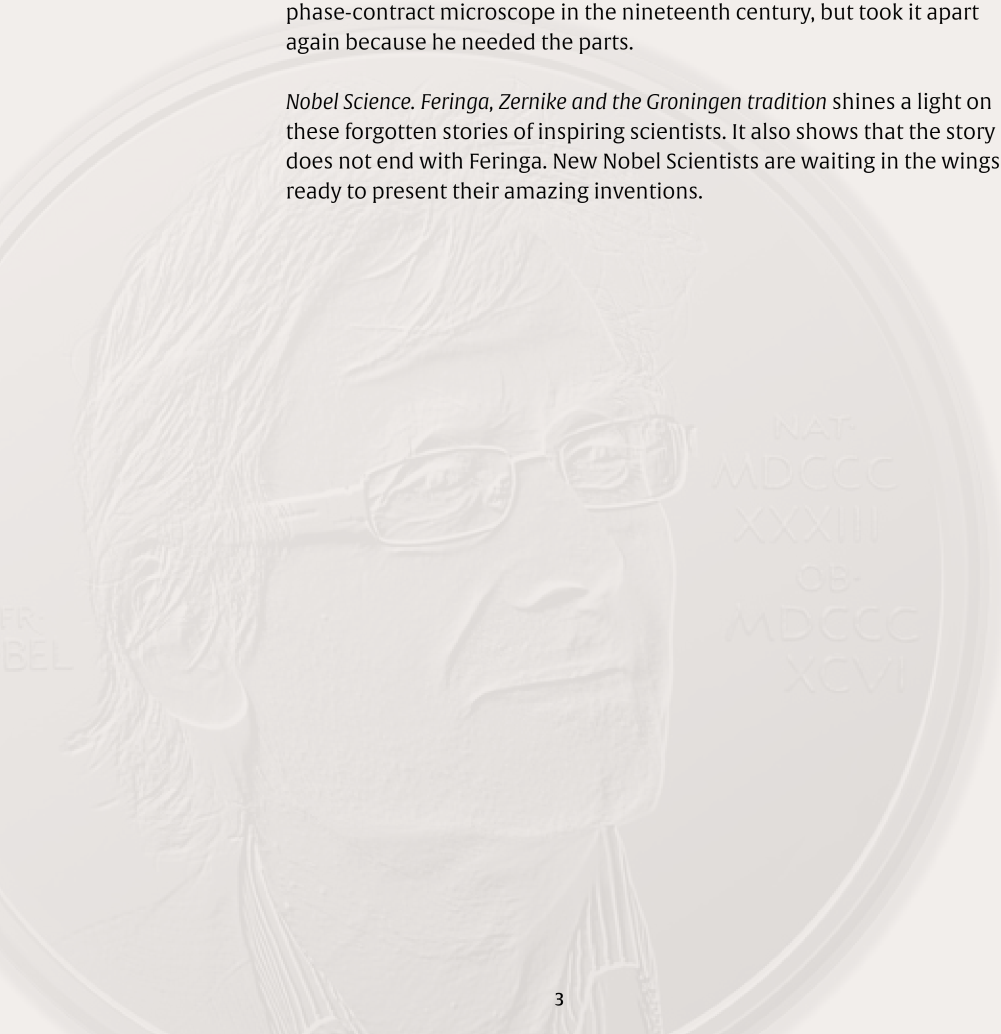
Inleiding

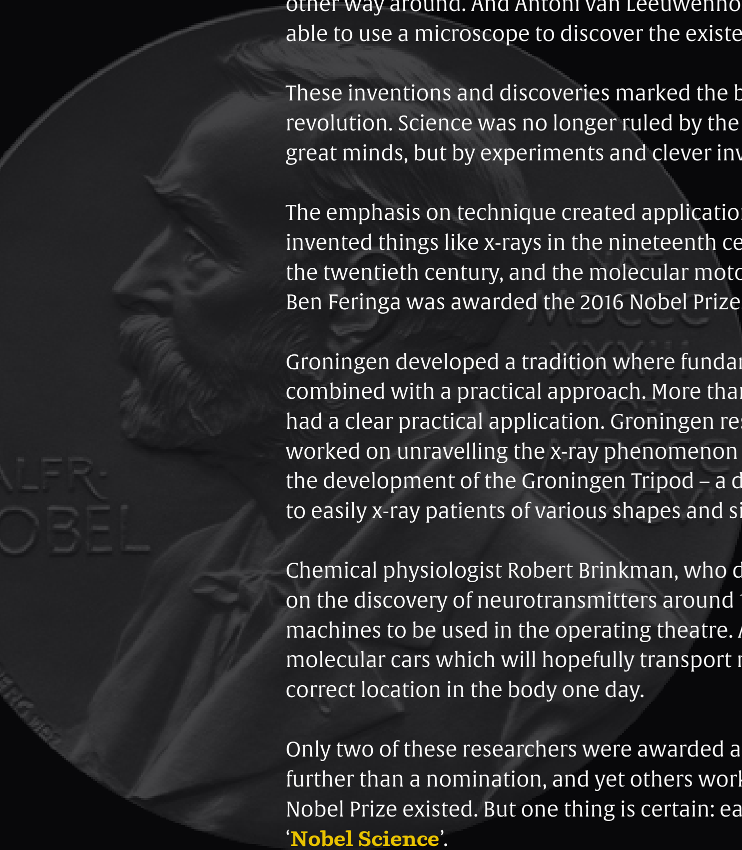
The 2016 Nobel Prize for Chemistry winner, Ben Feringa from Groningen, calls himself a ‘molecule tinkerer’. He plays with the Lego’s that nature has provided him and makes new molecules, molecular motors that did not exist before.

But Feringa is not the only one. Groningen has a long tradition of scientists making great discoveries while tinkering or playing. Think for example of Frits Zernike who would scour the Physics Laboratory at night, looking for materials for his inventions, which included the phase-contrast microscope. Or Jacobus Laurentius Sirks who made a precursor to that phase-contract microscope in the nineteenth century, but took it apart again because he needed the parts.

Nobel Science. Feringa, Zernike and the Groningen tradition shines a light on these forgotten stories of inspiring scientists. It also shows that the story does not end with Feringa. New Nobel Scientists are waiting in the wings, ready to present their amazing inventions.



A Groningen tradition



What if Hans Lipperhey, the spectacle maker from Middelburg, had never discovered that he could grind a lens to enable him to look into the distance? Galileo would never have been able to use an improved version of that lens to study the sun and planets a year later, and he would never have discovered that the earth revolves around the sun rather than the other way around. And Antoni van Leeuwenhoek would have never been able to use a microscope to discover the existence of minuscule life.

These inventions and discoveries marked the beginning of the scientific revolution. Science was no longer ruled by the philosophic theories of great minds, but by experiments and clever inventions.

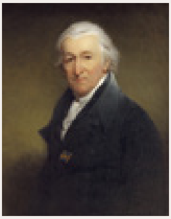
The emphasis on technique created application-oriented scientists who invented things like x-rays in the nineteenth century, artificial kidneys in the twentieth century, and the molecular motor, for which RUG chemist Ben Feringa was awarded the 2016 Nobel Prize.

Groningen developed a tradition where fundamental research was combined with a practical approach. More than once, these discoveries had a clear practical application. Groningen resident Hermanus Haga who worked on unravelling the x-ray phenomenon in 1896 was also involved in the development of the Groningen Tripod – a device that enabled doctors to easily x-ray patients of various shapes and sizes.

Chemical physiologist Robert Brinkman, who did groundbreaking work on the discovery of neurotransmitters around 1930, developed many machines to be used in the operating theatre. And Ben Feringa developed molecular cars which will hopefully transport medication straight to the correct location in the body one day.

Only two of these researchers were awarded a Nobel Prize, others got no further than a nomination, and yet others worked in fields for which no Nobel Prize existed. But one thing is certain: each one of them engaged in '**Nobel Science**'.

1 | Martinus van Marum (1750-1837)



A REVOLUTIONARY ELECTROSTATIC GENERATOR

Martinus van Marum (1750-1837) became known as the first director of the Teylers Museum in Haarlem and the man who invented the largest electrostatic generator in the world, which he had built in 1784 and which is still housed in the museum. Van Marum was able to generate no less than 330,000 volts using the machine and he used it for testing for a decade.

He concluded, among other things, that electricity, which no one understood at the time, was 'one liquid' that only flowed in one direction, something that was heavily debated at the time. Van Marum was able to make his observations by creating sparks so large that he could literally see the beams jumping from one conductor to another, branching out along the way.

Van Marum laid the foundation for the machine in Groningen. Van Marum was distraught to find out that not he, but Wijnold Munniks succeeded him in 1771. Van Marum was so disappointed that he threw himself into a new research field: electricity.

Together with his friend Gerhard Kuyper, he experimented for four years until he had developed a new kind of electrostatic generator. He experimented abundantly and wrote a book about it: '*Verhandeling over het elektrizeeren*' ('A treatise on electrification').

The publication was received enthusiastically, both at home and abroad. However, Van Marum left for Haarlem. There he became director of the '*Kabinet van Natuurlijke Zeldzaamheden van de Hollandsche Maatschappij*' – which later became the Teylers Museum.

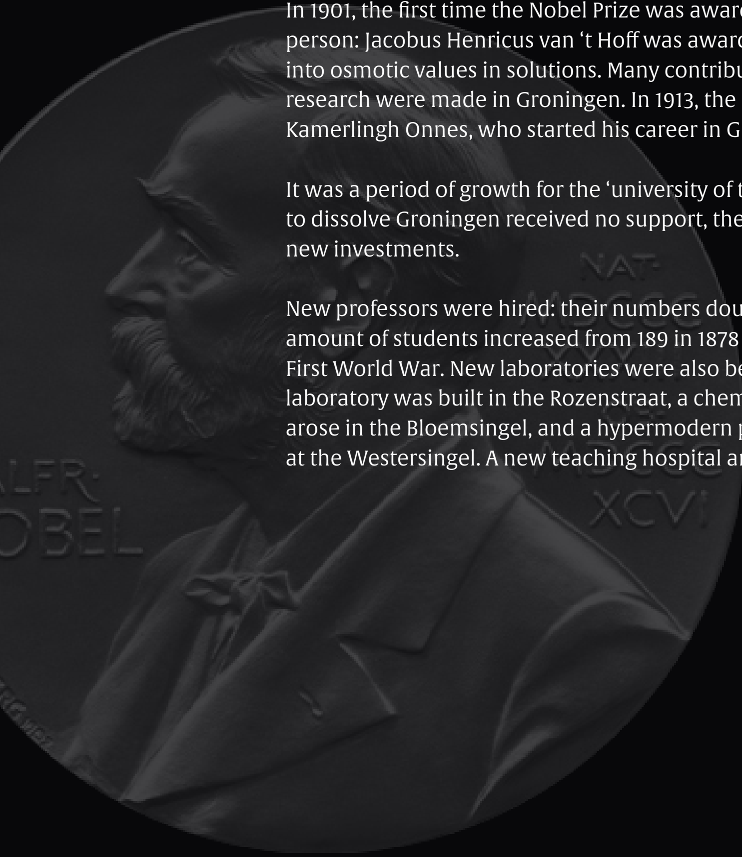
The electrostatic generator

The big problem electrostatic generators faced around 1775 was the leakage of voltage due to the humidity in the air. In addition, the leather pads used to electrically charge the discs would wear down quickly, resulting in an uneven voltage being generated.

Van Marum solved the issue with the pads by rotating them in a tub filled with quicksilver. The glass discs were covered in gum resin to improve conductivity.

His experiments were not always without risk. During one experiment under a bell jar, Van Marum accidentally created oxyhydrogen, which promptly exploded and 'destroyed it [the bell jar] with such violence that the shock, which took place in an upstairs room, made the windows of the entire house and even the basement rattle as though a large amount of gun powder had been ignited'.

Early tinkerers



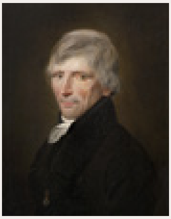
The fast scientific developments in the nineteenth century engendered a strong worldwide faith in progress. It was the time of the telegraph, the telephone, the steamboat, and the electric motor. The Netherlands, too, experienced a second ‘golden age of science’.

In 1901, the first time the Nobel Prize was awarded, it was won by a Dutch person: Jacobus Henricus van ‘t Hoff was awarded the prize for his research into osmotic values in solutions. Many contributions to this field of research were made in Groningen. In 1913, the prize was awarded to Heike Kamerlingh Onnes, who started his career in Groningen in 1875.

It was a period of growth for the ‘university of the North’. After a proposal to dissolve Groningen received no support, there were opportunities for new investments.

New professors were hired: their numbers doubled from five to ten. The amount of students increased from 189 in 1878 to 611 right before the First World War. New laboratories were also being built. A new botanical laboratory was built in the Rozenstraat, a chemical and physiological lab arose in the Bloemsingel, and a hypermodern physic laboratory was built at the Westersingel. A new teaching hospital arose at the Oostersingel.

2 | Pieter de Riemer (1769-1831)



FROZEN CROSS-SECTIONS

If anyone in 1800 wanted to view the anatomical specimens prepared by Pieter de Riemer (1769-1831), they would have to go to him personally. Whenever there was a sufficient amount of people interested, he invited them over for a visit. These visits started at eight in the evening and could easily last until two in the morning, 'since he points out and runs through everything, the entire workings of the human body, which he knows as well as the equipment of a warship', one of his contemporaries wrote in January 1819.

His collection of over 2,000 specimens made him one of the most well-known anatomists of his time. After his passing, King William I donated them to the University of Groningen.

De Riemer became famous partly because of his invention of the Frozen Section Technique, which enabled him to make precise cross-sections of the body from 1818 onwards. Up until then, anatomical education had been dependent on specimens preserved in formalin. 'Never will I forget the surprise I felt at the frozen corpse before me that I had sawn open, and at being able to see the internal organs calmly lying in the same.'

The frozen section

The Frozen Section Technique is simple and effective. The tissue that needs cutting – to see if it contains any abnormalities, for example – is first frozen and then cut and fixed.

This offers advantages for modern medicine too. The technique works faster than the traditional method, which has long fixing times. That is why it is still used when a quick definitive answer is needed, for example in oncology research.

3 | Heike Kamerlingh Onnes (1853-1926)

BUILDING A PENDULUM IN THE BASEMENT

When he was still a student in Groningen, Heike Kamerlingh Onnes designed a functioning Foucault pendulum. A tricky job, because the smaller the pendulum, the more difficult the design. Not just practically – the movement of the pendulum twists the rope – but also theoretically – it takes complicated maths.

During his assistantship at the university of Heidelberg in 1872, he was asked to create such a pendulum. He was tasked with using it to calculate the university's geographical coordinates. It turned out to be an enormous job, and in spite of numerous experiments, he was unable to figure it out.

Back in Groningen, he decided to keep working on the problem. He expected to figure it out within the year. However, it ended up taking him three years of hard work in a peat-storing shed in the basement of what was then the Academy building.

'When I was looking for a place to hang a cardanic pendulum where it would be free from vibrations I could find nothing other than the wall of a small peat-storing shed. [...] After much debate about authority, I was finally allowed to lift a few tiles out of the floor to hammer in some poles; I was also allowed, at my own expense, to install a stove in this humid place, and lead the stovepipe outside through a window.'

He got his PhD in 1879 for the pendulum he had built in this 'cyclops cave'.

Afterwards he left Groningen to become a professor of experiment physics in Leiden. There, in 1908, he managed to liquefy helium gas. He was awarded the Nobel Prize in Physics in 1913. Three years later he discovered that metals such as quicksilver, tin, and lead become superconductors at low temperatures. He was awarded the Nobel Prize in Physics in 1913.

Foucault pendulum

Foucault's pendulum is a pendulum, usually built quite large, that demonstrates the rotation of the earth. The pendulum is suspended from a great height with a weight at the bottom which keeps it in motion. After a while, the pendulum's movement relative to the plane beneath it changes. At the equator, the pendulum does not move at all. At the poles, the pendulum makes a full 'rotation' in exactly one day.

Kamerlingh Onnes managed to be precise to the seventh percentile. This was so precise that experimentation with the pendulum all but stopped.

4 | Jacobus Cornelius Kapteyn (1851-1921)

ASTRONOMER WITHOUT A TELESCOPE

When the Groningen astronomer Jacobus Cornelius Kapteyn (1851-1921) was appointed professor of astronomy in 1878, nothing could have predicted he would one day become one of the most important astronomers in the world. There were no funds left for employees or instruments, and certainly not for an observatory. In desperation, he turned to research into the connection between tree rings and climate.

But then Kapteyn found some unique photos of the night sky, taken by David Gill in Cape Town. They had been taken by astronomer David Gill, who operated an observatory in Cape Town. Gill was doing something that had never been done before: instead of drawing the stars onto a map, he took pictures. He had hoped to determine the position of the stars based on the photo plates, but a lack of money and manpower had prevented him from doing so.

Kapteyn made a virtue of necessity and built a unique instrument to analyse these photos and map the night sky. In seven years' time, he analysed the position and exact brightness of all 454,875 dots on the glass negatives. It made him the greatest astronomer of his time. 'This work of Kapteyn offers a remarkable example of the spirit which animates the born investigator of the heavens', wrote the American astronomer Newcomb.

Experts agree that, had a Nobel Prize for astronomy existed, Kapteyn would certainly have been awarded it.

Secretly, Kapteyn detested the data collecting. Later in his life, he wrote: 'There is a sort of fate which makes me do all my life long just what I want to do least of all.'

The parallactic instrument

Kapteyn's 'parallactic instrument' has nothing to do with 'parallax' – the phenomenon that a far-off object like the moon seems to move with you when you move, but a nearby object like a tree doesn't. It is merely called that because Kapteyn attached his instrument to the base of a parallactic telescope.

The instrument has a telescope with the same focal length as the telescope that was used to take pictures of the night sky in Cape Town. An assistant can point the telescope at a star and observers can read its relative position using the protractors. It is like taking a really large telescope and measuring the sky star by star.

5 | Sibrandus Stratingh (1785-1841)

THE FIRST ELECTRIC CAR AND A BOAT

All of Groningen turned out on 22 March, 1834. And for good reason, because Groningen professor Sibrandus Stratingh was driving through the city's streets in a steam-powered carriage of his own design.

People were incredibly enthusiastic about the invention. They thought 'that when this machine is refined and finished, such a carriage will not only be usable on the newer roads of stone and rock, but it will even be able to withstand the extremely uneven cobbled streets'.

King William I was interested as well and awarded the professor a grant to develop the machine. He even visited Stratingh's laboratory.

Nevertheless, the professor shifted his attention to other types of engines. Because in spite of the proof of concept he had shown with the steam-powered engine, he was also busy working on something even more revolutionary: a car powered by an electric motor.

This little cart was capable of driving for twenty minutes and could transport 1,5 kilos in addition to its own weight of 3 kilos. Stratingh believed that this electrical power 'will in general be preferable over all other power, even [...] steam power. [...] That the same will also be more suitable as a form of transportation'.

Stratingh even made a little boat, which he is said to have sailed around the canal behind his house in 1840. This made him the inventor of the very first electric boat.

In 1841, the old professor died suddenly, only 55 years old.

Electric motor

Stratingh was not the only scientist to work on electric motors. Hungarian Anyos Jedlik designed the first electric motor in 1827. And the American Davenport even created a little electric cart in 1834 – perhaps at the same time that Stratingh had a model in his laboratory. However, Davenport's car could not be driven. Stratingh's cart could.

Sibrandus Stratingh took inspiration from an electric motor designed by the German scientist Moritz von Jacobi. He created an electric motor using straight magnets, but Stratingh realised that a curved magnet would generate twice as much energy.

6 | Jacobus Laurentius Sirks (1837-1905)

THE TINKERING RECTOR

Jacobus Laurentius Sirks (1837-1905) was kind of an outsider on the scientific scene in Groningen. He never became a professor: he was ‘merely’ the rector of the city’s Stedelijk Gymnasium. He was also a brilliant physicist.

He was a teacher, ‘a formidable man who had the ability to teach any course, and he was one of the best rectors this school has ever had’, a 1943 memorial book for the Stedelijk Gymnasium says. ‘His standing among the students was increased by the rumours about the physics experiments he performed in the attic of his house at the Heerestraat.’

His experiments with the refraction of light attracted the attention of the established order of physicists. In 1892, the University of Groningen awarded him an honorary doctorate, on the recommendation of Groningen professor Hermanus Haga.

Less than a year later, Sirks designed the very first interference microscope: a microscope based on the same principles as the phase-contrast microscope for which Zernike was awarded the Nobel Prize in 1953.

Just like Zernike’s microscope, this device made it possible to observe transparent, living objects. Sirks was also able to measure differences in thickness many times smaller than with a normal microscope.

But his device went practically unnoticed. Sirks published a paper on his findings, but took his revolutionary microscope apart after he had used it. He needed the lenses for his next experiments.

Interference microscope

French physicist Jules Jamin designed an interferometer in 1856, which split beams of light and put them together again using mirrors, in order to measure small differences in length. There was one located in Haga’s laboratory, where Sirks spent much of his time. Sirks’ interference microscope combined the interferometer and a microscope.

His device was extremely sensitive to vibrations, but in 1892, Hermanus Haga had a special, vibration-free laboratory built at the Westersingel. Special experiments could be done in this lab, but only there.

They faced another problem in the form of the light source. Sirks used a sodium flame, which made ‘extreme demands of the skill and stamina’ of the observer. Sodium burns extremely hot and bright.

7 | Hermanus Haga (1852-1936)

X-RAY PROFESSOR IN A SUPER LAB

Three months after Wilhelm Röntgen announced his 'new, unknown type of radiation' to the world in 1895, the first x-rays were on display in Groningen. Their creator: Hermanus Haga (1852-1936), professor of physics. The objects he had x-rayed were a frog and a compass box. A short time later, he showed an x-ray he took of his brother's hand during a meeting of the Royal Society of Science (available for viewing in the museum's upstairs room).

However, it was his subsequent research with his employee Cornelis Harm Wind that was truly groundbreaking. In 1899 he was the first person to prove that x-rays behave like light – i.e., a wave – and he determined the radiation's wavelength. Unfortunately, practically no one believed him, and other people were unable to replicate his results.

This was due to Haga's ultramodern laboratory at the Westersingel, which had been built to be almost entirely iron-free. It was also almost entirely vibration-free, because it had deliberately been built on top of a former bastion, where the ground was extremely compact.

The lab was an ideal place for research into x-rays. Haga passed the radiation through a narrow crack and took pictures that showed a 'fan effect'. This allowed Haga to not only infer the radiation's wave characteristics, but also its wavelength. However, the scientific community blamed the effect on sloppy development of the pictures.

It was not until 1912 – thirteen years later – that the German physicists Von Laue, Friedrich, and Knipping came up with the same results via a different method. Von Laue was awarded the Nobel Prize for his work.

In later years Haga studied the structure of crystals using radiation, the way Von Laue had as well. He was finally recognised for his work in the field of diffraction: in 1921 he was made an honorary member of the Dutch Society for Electrical Engineering and Radiology. By that time, Wind had passed away.

X-ray diffraction

Max von Laue, who was awarded the Nobel Prize in 1914, realised in 1912 that he could use a crystal as a natural grid. He directed x-rays to hit copper sulphate. By doing so, he confirmed the rays' wave characteristics, as well as the crystals' grid structure.

X-ray diffraction is mainly relevant to crystallography. The radiation can be directed at a crystal, and the electron cloud around the atoms causes the rays to be scattered. The pattern this causes can be seen as the crystal's fingerprint.

8 | Antonie Cramer (1822-1855)

A MAN WITH KEEN EYES

Antonie Cramer dreamed of becoming a doctor. Sadly, his health was so poor that he was forced to stick to research.

Cramer mainly concentrated on the workings of the eyes, in particular the way they focus themselves. A letter recently recovered from one of his books showed that he experimented quite a lot with seals' eyes.

He had well-known Groningen instrument builder Willem Deutgen make an ophthalmoscope, a microscope he used to study the working eye. It enabled him to prove that the eyes focus by means of the lens – something that no one knew around 1850.

Cramer entered his discovery into a contest organised by the Dutch Society of Sciences in November of 1851. He won the gold medal in 1852, but it took a while before he published any papers.

This nearly caused his downfall: in the interval, famous ophthalmologist Hermann von Helmholz (1821-1894) from Königsberg had also got into the problem and solved it in a manner almost identical to Cramer. He reported this to the Berlin Academy of Sciences in February of 1853, before Cramer published any papers.

Fortunately, the Utrecht professor of medicine and physiology F.C. Donders used his reputation to help him out. He had noticed Cramer's earlier research into the ocular lens. When Cramer's paper was published, he wrote about it at length, which allowed Cramer to take the credit for his discovery.

Antonie Cramer died in 1855. He was 32 years old.

Ophthalmoscope

Antonie Cramer's ophthalmoscope was a revolutionary invention. With this ophthalmoscope, the researcher views a mirror through a small lens. The mirror reflects the test subject's eyes. The test subject has to then look at a thin wire or stare into the distance, changing the curve of the eye's lens.

9 | M.E. Mulder (1847-1928)

ANOTHER MAN WITH KEEN EYES

M.E. Mulder was a passionate ophthalmologist. In 1897, he founded his Institute for Eye Patients in Groningen, across from the hospital at the Munnekeholm.

Mulder was the first ophthalmologist in Groningen, and several years later he became the first private instructor in the field. He wanted to focus on the poor and needy country people. 'Especially the poor have the greatest need, because they are plagued by an infinitely larger number of eye diseases than those better off', he said fierily.

The clinic opened with nine beds. People were usually treated as outpatients. The poor received free treatment, with all other patients paying one guilder.

Mulder quickly ran out of room in his clinic and he built a new facility with sixteen beds at the Zuidersingel – the current Ubbo Emmiusstraat. Mulder refused to be part of the existing old hospital. He said his patients needed 'light and air'.

When he retired in 1913, his clinic performed 225 surgeries each year, treated over 300 patients, and had fifty appointments a day.

Astigmometer

Mulder developed an improved astigmometer. It was an early version of the machine opticians nowadays use to measure people's vision. In 1903, he described his new astigmometer in the *Klinische Monatsblätter für Augenheilkunde*.

The astigmometer, nowadays called an ophthalmometer, consisted of two long slats with lenses mounted on them which could be rotated and moved. It enabled the eye doctor to measure the curve of the cornea and determine which lens was best suited to the patient.

Mulder's device was extremely useful. The ophthalmologist could turn and secure the lenses very precisely. Mulder also used larger lenses, which allowed the patient to determine the most suitable one more easily.

10 | Nicolaas Jacobus Boerma (1871-1962)

FORCEPS LIKE A FOX TERRIER

Obstetrics was a field near Nicolaas Jacobus Alphonsus Frederik Boerma's (1871-1962) heart. In 1905, he debuted his custom designed forceps, to the great benefit of mothers and children.

Boerma studied in Groningen, started his practice there in 1904, and was the head of the department at the teaching hospital. Forceps already existed when he was there, but the question is how painless and safe these forceps deliveries were. Initially, Boerma used the common tool, Naegele's forceps, but he had some misgivings. 'When one sees the damage done to the children's heads, and the way young, inexperienced people abuse the pinching quality of the forceps, I cannot help but wish for something different, something that does no harm, something better', he wrote.

And so he developed a shorter, more easily manageable type. 'It is good and has a grip like a fox terrier', Boerma said.

Boerma did not stay in Groningen. In 1920, he was asked to start a midwifery school in Medan, in the Dutch East Indies. Although the school took a long time to set up, he did start a clinic with an obstetrics office attached.

When he returned to the Netherlands in 1933 he settled in The Hague, where he passed away in 1962.

The forceps

Many assisted deliveries in Groningen were done with Naegele's forceps until well into the twentieth century.

Boerma's forceps prevented doctors from pinching the tongs as much, allowing them to focus more on pulling. It meant they did not do damage as easily as before. The tongs were smaller which meant they were less painful for the mother. Finally, the 'pocket model' made it practical: it could fit into a bag and could be easily disinfected by being sterilised in a pot of boiling water.

'This way, the assisted delivery hurts no more than if the head came out naturally, and sometimes the patients are not even aware the forceps have been used', an enthusiastic user described them.

11 | Johan Huizinga (1872-1945)

AUTUMN AT THE DAMSTERDIEP

The most important historian in the Netherlands, Johan Huizinga (1872-1945), was born in the Oosterstraat in Groningen. He was the son of physiologist Dirk Huizinga and would grow up to become the founder of the history of mentalities. But if it were not for a walk down what was then the Damsterdiep, *Autumn of the Middle Ages* might never have existed.

The year was 1907. 'In the afternoon hours, when my wife's time was taken up by the care for our little children, I often took walks on my own to the outskirts of town which back then led straight to the wide, flat Groningen countryside. On one such walk along or close to the Damsterdiep, on a Sunday I think, I had a flash of insight: I saw the late Middle Ages not as an announcement of things to come, but as a dying off of what had gone by', he wrote. It was an 'epiphany'.

It would take more than a decade before *Autumn* was actually published. Huizinga's wife died of a brain tumour in 1914 and he fled the city in 1915 to become a professor in Leiden.

From that moment onward, his star was on the rise. *Autumn of the Middle Ages* came out in 1919. It was a unique work, not just because of the innovative outlook on history, but also because of the broad approach to his theme. For Huizinga, it was not just the story, but also the way he told it was important. He wanted to make his narrative come alive.

His fame increased when he gained national acclaim in 1935 with *In the Shadow of Tomorrow*. In this book, he warned people of the totalitarian stupidity he saw happening around him.

He died in 1945, several weeks before the Dutch liberation.

Autumn of the Middle Ages

Before Johan Huizinga's work, the late Middle Ages were mainly considered to be a time of decay, or a precursor to the Renaissance. Huizinga abandoned that vision. As far as he was concerned, the Middle Ages had their own spirit and character. His style, as well as the literary force of his works, inspired many of the historians after him.

Huizinga also introduced the concept of 'historical sensation': the feeling historians get when he gets in touch with the past. It formed the core of his historical vision.

12 | Gerard Heymans (1857-1930)

THE MAN WHO EXPERIMENTED

It may sound unbelievable, but Gerard Heymans (1857-1930) started his career as a philosopher. But as soon as he was appointed professor of philosophy and psychology in 1890, he started to shape the brand new discipline. At the core of his vision? Experiments.

Heymans was the very first person to build a psychological laboratory in his house at the Stationsstraat. It was not until the fire in the Academy building in 1906 that he was able to embed his work at the university. He asked for, and received, his own lab in the new building which was opened in 1909. It was there that Heymans performed his famous experiments with Arend van Dam.

This student claimed he possessed telepathic abilities. Starting in 1920, Heymans tested this claim with a set of advanced tests. Van Dam would sit in a room covered with cloth. He had to stick his hand through a curtain and select a single square that the researcher was thinking of from a 48-square 'chess board'. The researcher himself sat in a room above and observed the goings-on through a little window.

Van Dam was right 60 out of 180 times. And so, Heymans claimed, the possibility of telepathy had been proven.

Recent researchers have criticised this method, however. Are we sure that Van Dam could absolutely not see the researcher? Could the latter have unintentionally given sound signals, even just through the creaking of his chair? Yet these experiments are characteristic of the systematic, experimental manner in which Heymans approached his research in a time where that was not a matter of course.

Heymans also made a name for himself with 'Heyman's cube'. This was a personality model he based on extensive research using questionnaires. It was another method that was well ahead of its time.

Heymans' cube

Heymans thought that personality consisted of three fundamental characteristics: the degree of emotionality, activity, and impulsiveness. The way these three characteristics relate to each other determines who we are.

The psychologist had general practitioners draw up more than two thousand personality descriptions and 'arranged' these in a cube. He checked the results on the basis of famous people's biographies. And that is why nowadays we can take a test using Heymans' method and find out that our personality strongly matches Napoleon's or Dostoevsky's.

13 | Albert van Giffen (1884-1973)

THE FATHER OF DOLMENS

In Drenthe, people lovingly called him '*'t Spittertien*' ('the Digger'). Again and again, they watched as archaeologist Albert van Giffen (1884-1973) tirelessly worked, excavating cemeteries and terps.

Others called him the 'father of dolmens', because he spent 1918 mapping, excavating, documenting, and often restoring the run-down dolmens in the Netherlands.

But Van Giffen's most important contribution to the field of archaeology was his 'quadrant' or 'wedge' method. It is a clever way of extracting as much information from a site with as little digging – and therefore as little damage – as possible.

Even now, the method is an international standard in archaeology. But Van Giffen was a practical man and as such, he did not publish many papers. Because of this, he did not receive much recognition for his insights. This once led to an occasion where a German female archaeologist visiting one of Van Giffen's excavation sites in 1943 started telling him about the German method: 'In Germany we always work according to the quadrant method...'

Van Giffen is said to have listened stony-faced to the woman explaining the method he himself had developed.

Van Giffen died in 1973 in Zwolle and was buried in Diever, near dolmen D52. When Van Giffen owned the estate *De Heezenberg*, this dolmen was practically located in his backyard.

The quadrant method

Before Van Giffen introduced his quadrant method, archaeologists would often excavate the entire site, layer by layer. While this meant that the objects had been removed, the context was forever lost.

Van Giffen would dig both vertical and horizontal trenches, creating a three-dimensional view of the structure of a site. The largest part of the site stays untouched, preserving the information. There is a reason he used '*Die Tatsachen bleiben, die Interpretation schwänkt*' as a motto for his thesis: 'The facts remain the same, but the interpretation can change.'

The power of Groningen

Chemistry's importance to medical research was hardly a given before 1900. But that changed with the arrival of Hartog Jacob Hamburger in 1901. The discoverer of physiological saline introduced a new research field: chemical physiology. Hamburger studied the body at the cell level and encouraged his students to do the same.

He got future Nobel Prize winner Albert Szent-Györgyi to come to Groningen, who isolated vitamin C in the basement at the Bloemsingel 1 – although no one knew about it at the time. Hamburger's student Robert Brinkman played a key role in the discovery of neurotransmitters.

The very same Brinkman then set the standard for an important new trend. Groningen scientists developed artificial organs such as the artificial kidney, the artificial lung, and the heart-lung machine.

To this day, Groningen is a pioneer in the field of transplant medicine, especially for the liver and the lungs.

14 | Hartog Jacob Hamburger (1859-1924)

FROGS AND PHYSIOLOGICAL SALINE

Almost everyone in the world has been exposed to a ‘physiological saline solution’ at one time or another in their lives: a solution of 9 grams of salt in 1 litre of water. It can be used to rinse eyes of a harmful substance or as a drip in the hospital for people who have lost a lot of blood. This solution is ‘isotonic’: the pressure on the cell walls is the same on the inside as on the outside.

While the solution is well-known, its discoverer Hartog Jacob Hamburger is not. Hamburger studied chemistry and medicine in Utrecht. After that, he taught at the University of Veterinary Medicine for years. And in spite of a heavy course load he would work on his research in the evenings. ‘Late in the evening we could often hear the sound of the gas motor in his laboratory.’

He also discovered how the lymphatic system works and achieved immortality with the ‘Hamburger shift’: the phenomenon that some molecules can pass through the membranes of red blood cells. This was important, because arterial blood absorbs different substances than ‘normal’ blood. When Hamburger came to Groningen in 1901, it was the start of a new research discipline: chemical physiology.

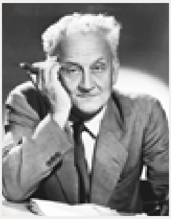
But perhaps his most important contribution was the fact that he hired future Nobel Prize winner and vitamin C discoverer Albert Scent-Györgyi when the latter had broken off relations with his professor in Leiden after a conflict. Why did he do this? He needed someone who could operate on dogs without immediately killing them.

Physiological salt

Early on in his career, Hamburger came across Cohnheim’s experiments. As early as 1869, Cohnheim had discovered that if a frog’s blood is replaced by a 0.6 percent saline solution, the animal continues to live for several days. It was concluded that this saline solution was harmless and from 1881 onwards it was used on people as a drip.

Hamburger discovered an essential difference between the cells of mammals and amphibians: a mammal’s cells would swell up when a 0.6 percent saline solution was injected into them. The perfect ratio was found to be 0.9, and it is used to this day.

15 | **Albert Szent-Györgyi** (1893-1986)



A MYSTERIOUS SUBSTANCE

It was pure coincidence that brought future Nobel Prize winner and discover of Vitamin C Albert Szent-Györgyi come to Groningen in 1922 to Groningen. A physicist from Leiden had made him come to the Netherlands in 1922, but the collaboration did not succeed: he fancied the scientist's wife.

Luckily he met Groningen physiologist Hartog Jacob Hamburger and he got the Hungarian a basement office at Bloemsingel 1. There, Szent-Györgyi studied biological oxidation. He suspected there was a connection between Addison's disease, which causes kidney failure and a darkening of the skin, and the discolouration of apples and bananas. He was trying to find a substance that was present in both the adrenal gland and in fruit.

He would grind up the kidneys of slaughtered cows and dry out the gunge with an exsiccator. Once, this led to chaos when he tried to speed up the process using an electric heater. 'We had barely closed the door behind us or there was a thunderous crash inside and the basement hallway we were in became dark. As we carefully opened the door, we saw the ruin of glass shards mixed with parts from the electric heater.'

Eventually he isolated a substance he believed to be essential for the human metabolism – now known as cortisol. However, no one in Groningen was interested in it.

His last experiments in Groningen failed: on Sinterklaas night (5 December) he had removed the adrenal glands from six cats and had tried to keep them alive using the mysterious substance, but all animals perished. Frustrated, he destroyed his lab and decided to quit scientific research.

A scholarship to Cambridge ensured that he was not lost to science. After a year, he returned to Hungary to become professor of medical chemistry at the University of Szeged.

Vitamin C

That sauerkraut or tangerines could prevent scurvy had been clear since the eighteenth century. However, no one had succeeded in isolating the substance responsible.

Initially, even Szent-Györgyi did not recognise the substance he had isolated in Groningen. And although he figured out its chemical structure at Cambridge, his discovery was shelved. It was not until 1933 that his mysterious substance was discovered to be Vitamin C. Szent-Györgyi was awarded the Nobel Prize in 1937.

16 | Robert Brinkman (1894-1994)

IMPULSIVE INVENTOR

During his final class in 1956, professor Robert Brinkman said that in actuality, he had been an 'impulsive amateur' all his life. But, he immediately added, 'I have no regrets, because this attitude has made most of my life an adventure'.

Everyone who knew him knew he was always bursting with ideas. He was also impatient: he always wanted his assistants to immediately get started on every new idea he had.

But he was certainly no amateur. Just like future Nobel Prize laureate Szent-Györgyi, he was one of Hamburger's students, who wanted to know how processes in the body went. His research on neurotransmitters drove British researcher and Nobel Prize laureate Henry Hallett Dale to do his own – celebrated – research. But Brinkman wanted to put his knowledge into practice.

In addition to his fundamental research, Brinkman created many useful machines that made their way into the operating theatre. He came up with the 'cyclops': a device he could use to keep an eye on oxygen saturation in the blood, and the 'Brinkman carbovisor', which was able to register the amount of carbon dioxide in the air patients breathed out. And let us not forget the reflection oximeter, which was used to study the cause and effect of acute oxygen deprivation.

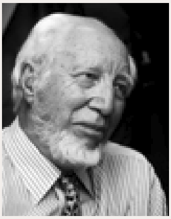
Before he introduced his discoveries in the operating theatre, he would try them out on himself. He could 'lie motionless for hours on an examination table, surrounded by equipment, a bit in his mouth preventing him from speaking, and he would never blame his assistants if they hurt him through clumsiness of carelessness during these experiments'.

Neurotransmitters

Brinkman researched 'humoral stimulus transfer'. Pharmacologist Otto Loewi posited the existence of a 'vagus substance'. Brinkman wanted to prove the existence of this substance. He connected the heart of a live frog to the stomach of a second frog. By stimulating the vagus nerve fibres near the heart, he could also make the stomach contract. With this, he had definitively proven the existence of Loewi's substance.

Henry Dallett Dale continued the research and eventually discovered the actual vagus substance, which we now know to be acetylcholine. It won him a Nobel Prize.

17 | Willem Kolff (1911-2009)



AN ARTIFICIAL KIDNEY CONSTRUCTED FROM A BOMBER PLANE

While he was still training to be an internist, Willem Kolff encountered a 22-year-old patient with kidney failure. The man had not urinated for days, and even his breath smelled of urine. He started convulsing, fell into a coma, and died.

Kolff was so affected by his death and the fact that he had been powerless, that he vowed to develop an artificial kidney that would be able to filter urea from the blood.

Some inroads into dialysis had already been made. Scientists had filtered dogs' blood, discovered the anti-clotting agent heparin, and in 1938 it became known that cellophane made a great membrane. But a working dialysis machine had not yet been created.

Kolff set to work. Together with his supervisor Brinkman, he constructed several test devices, but the war threw a spanner into the works. Kolff left Groningen and started working at the city hospital in Kampen.

However, he did continue working on his artificial kidney: he took the drum of a Groningen model and placed it horizontally rather than vertically. He also added a pump, which he had salvaged from an old Ford Model T, and he built a base out of the remnants of a German bomber plane.

It wasn't until 1943 that he developed the first working artificial kidney in the world. However, he did not yet manage to save lives at first. Sixteen patients died, until finally, in 1945, a terminally ill patient survived.

After the war, Kolff wanted to leave Kampen. Several universities, including Groningen, considered appointing him professor, but none of them did.

Eventually he emigrated to America and set up a laboratory in Salt Lake City. There, he developed an artificial heart, an artificial lung, and a disposable artificial kidney.

Artificial kidney

The kidneys are the body's purification plant: they filter fluids, waste products, and toxins from the blood and transport it out of the body via urine. If they fail, the fluids and waste products start building up, killing the patient. An artificial kidney dehumidifies the body and cleans the blood by running it through the artificial kidney outside the body. It is filtered through a membrane that allows the fluids and waste products to pass but not the blood cells.

18 | Jan Homan van der Heide (1926-)
19 | Joop Dorlas (1925-)

A HEART-LUNG MACHINE IN THE ATTIC

Around 1955, the light in the attic of the Groningen Surgery clinic could often be seen burning late at night. Under its rafters, three men would still be at work: technician P.A. Rijksamp, anaesthesiologist Joop Dorlas, and surgical assistant Jan Homan van der Heide.

They were working on building a heart-lung machine. They would do many experiments with cow's blood from the abattoir, and on dogs – delivered to them by the dog catcher. Their goal was to cool the blood of the animals to such an extent that they became slightly hypothermic, just like patients during open heart surgery. However, in these surgeries, the entire patient was cooled. Homan van der Heide and Dorlas would extricate the blood from the body in order to bring its temperature down.

They also attempted to build an oxygenator. This would ensure the exchange of oxygen and carbon dioxide in the blood while the blood flow had been stopped.

After two years of experiments they finally succeeded in building the 'cirrestor': a working heart-lung machine. In 1957 it was used for the first time on the European mainland: a seven-year-old girl received successful surgery.

Groningen became a pioneer in the field of thoracic surgery: surgery of the heart and lungs. Under Homan van der Heide's leadership an internal pacemaker was developed, which was successfully implanted into a patient in 1962.

Moreover Homan van der Heide – called 'Ho' by his residents – turned out to be a true student of Brinkman. He came up with the 'perforated needle' and even the 'pacemaker antenna'. He also felt that a doctor should always know how to improvise. He once saved the life of a 14-year-old Polish boy by creating a retractor on the spot: he took a sharp metal operating pin and bent it into the shape of a paperclip.

Heart-lung machine

When a patient's heart needs to be stopped during surgery, the heart-lung machine ensures the blood flow and oxygenation of the blood.

Many people were working on heart-lung machines in the 1950s. However, oxygenating the blood turned out to be difficult. While Robert Brinkman's oxygenator did oxygenate the blood, it also caused gas bubbles and damaged the blood.

Homan van der Heide and Dorlas solved the problem in 1957 by using the recently discovered low flow principle. This meant that only a small part of the heart pump volume had to be taken over by the machine.

20 | Jan Snijders (1910-1997)

THE MAN WITH THE INTELLIGENCE TESTS

Jan Snijders almost became a priest. But TBC contracted while he was at school made it impossible for him to become what he wanted most: a missionary. But when he encountered both psychology and his future wife Nan Oomen during his studies, he abandoned the priesthood. He left priesthood in 1938, only to become one of the most well-known Dutch test psychologists. His greatest feat: the Snijders-Oomen Nonverbal intelligence scale (SON) which he developed together with his wife in 1943. It was the first test that was not based on language competence.

Nan Oomen developed this SON test in 1943 for deaf children. She felt that the regular tests put deaf and deaf-mute children at a disadvantage, because that test required language skills. At Jan's insistence, the pair married before she received her doctoral degree, to ensure that the test would have the same name that she would have for the rest of her life: Snijders-Oomen.

After this, Snijders left for Groningen to become a professor. Nan became scientific senior lecturer at the Audiological Institute of the Groningen university.

After the first SON was a success, the married couple came up with a version that worked for both deaf and hearing children. A third version in 1975 split the test into one version for children aged seven to seventeen, and one for toddlers.

In addition to the SON, Snijders also created other tests, including the Groningen Intelligence test for adults in the sixties. This test also measured the various aspects of intelligence through sums, logical reasoning, and spatial skills.

Snijders worked as a professor in Groningen until 1975. His personal involvement in the tests slowly decreased over time. After his retirement, he focused on Higher Education for the Elderly (HOVO).

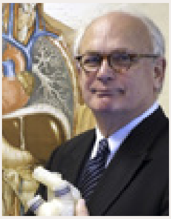
The SON

The Snijders-Oomen Nonverbal intelligence scale was revolutionary in 1943. The SON is a systematic set of abstraction tests based on blocks and pictures.

Children have to create mosaics, put pictures into different categories, or complete an image so the whole makes logical sense. The test is mainly suitable for people who have trouble with language or speaking. It is also very useful for immigrants.

Several countries use the SON, including China. It is easy because the test does not need to be translated.

21 | Gerhard Rakhorst (1946-)



SUSTAINING ORGANS

Gerhard Rakhorst used to be a veterinarian. But his association with the inventor of the artificial kidney, Willem Kolff, led him to become the inventor of the heart pump, which sustains a damaged heart, as well as the Organ Assist, which keeps organs 'alive' until they can be transplanted.

In the second year of his studies, Gerhard Rakhorst wrote a letter to a laboratory in Salt Lake City. He had read an article in the papers about a girl who was dying of a defective heart valve. Rakhorst thought, 'Why can't we make a new one out of plastic?' This is exactly what they were working on in Salt Lake City.

What Rakhorst failed to realise was that he had written a letter to the famous Willem Kolff. The inventor of the artificial kidney not only had him flown over, but he also put him to work.

In Salt Lake City, Rakhorst worked on the artificial heart and returned a year later with his wife – it was their honeymoon. He even had the chance to stay, because Kolff had arranged for a grant. But Rakhorst refused, to Kolff's dissatisfaction. 'I had been offered a great practice in Apeldoorn.'

It was not until the 1980s that science lured him back. Rakhorst got his PhD and when the Groningen university needed a senior staff member in the department of biomedical technology, he made the switch.

Inspired by his experiences in Salt Lake City, Rakhorst started working on a catheter pump that could be inserted into a vein. This pump could sustain the heart for several days, allowing it to recover from a heart attack or serious surgery.

A heart pump

The core of the invention is a valve, which allows blood to be pumped both ways through one single tube. When the valve is closed, the blood flows in the direction of the heart. When the valve is open, it ends up in the coronary arteries.

He worked out the idea, from a simple plastic tube with a valve put together using iron wire, to the eventual actual device: the pulsecath. But Rakhorst did not stop there. Because if you could keep a heart going, could you do the same with kidneys, lungs, or a liver?

That is exactly what his second big invention, the Organ Assist, does. The condition of kidneys is maintained and lungs that would have been discarded before are transplantable after several hours. In 2014 in England a patient was saved with an 'upgraded' liver.

22 | Sijbren Otto (1968-)

LIFE IN A TEST TUBE

Sijbren Otto really wanted to be a palaeontologist. But he opted for chemistry because of the job prospects. Now, he makes a molecule with which he is attempting to create life. In a test tube.

Otto studied and received his PhD in Groningen. He worked in Pennsylvania and Cambridge for a while, but returned home. It was there that he made a discovery, in 2010, that would change his career.

It started when one of his PhD students, sort of by accident, discovered a molecule which could replicate itself. What was particularly amazing was the fact that the molecule could repeat this process indefinitely. The molecules consist of a ring with small 'protrusions' that stack to form strings. When stirred, the strings break. And then they grow again, until they run out of building blocks.

Otto realised that there was potential to research the creation of life as defined by NASA: a sustaining chemical system capable of undergoing Darwinian evolution.

By adding other building blocks, he could create mutations. Sometimes the rings become a bit bigger, and sometimes a bit smaller. Otto also discovered that smaller rings appear in one kind of solution, while bigger ones do better in another kind. In other words: the rings respond to their environment.

In 2016, Otto introduced death to the system. He 'kills' molecules by removing them or by adding fluid that breaks them down to their basic forms.

Did Otto discover life? After all, do his molecules not live, die, and evolve? Otto himself does not think so. One thing is still missing: his molecules are not yet self-sustaining.

A human being is alive. So is a rabbit. However, when Otto stops feeding his molecules, they disintegrate. Until his molecules are able to fend for themselves, he won't call them 'life'. But, he emphasises, 'it is a grey area'. Put a man on the moon and he too will die. So who knows?

Life

Scientists believe that life arose from the 'primordial soup' during the earth's creation. In this cauldron of erupting volcanoes and comets hitting the earth, more complex compounds slowly came into being.

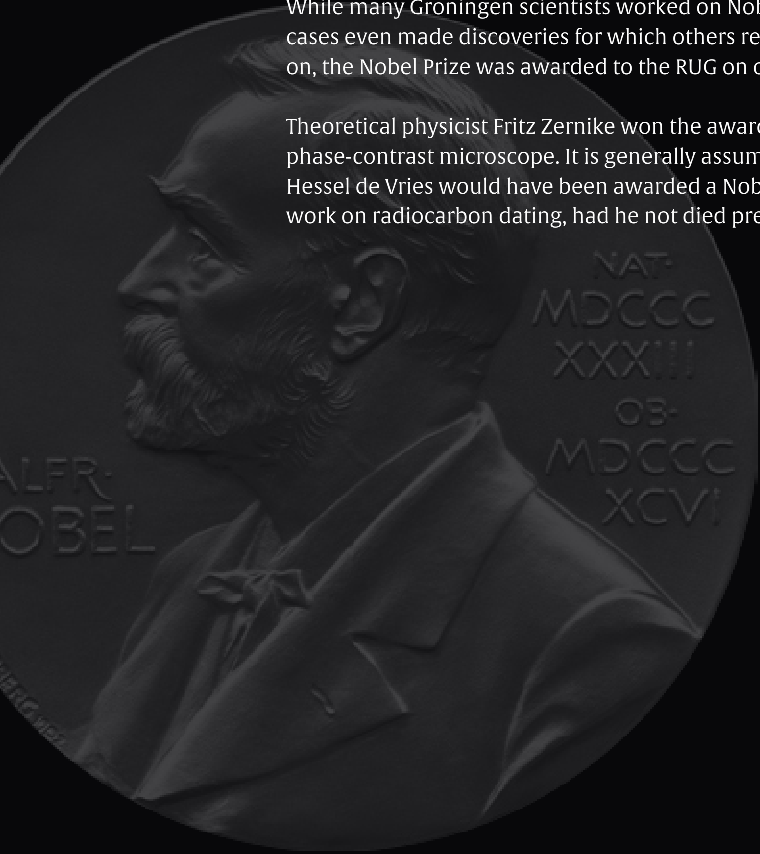
Until now, scientists always tried to recreate that primordial soup. Otto's experiment approaches the problem from a different direction. He simply starts with a single molecule in a test tube.

A Nobel prize in Groningen

The Nobel Prize is the highest honour a scientist can be awarded. It's not about the money – the winner receives 8 million Swedish kronor, a certificate, and a medal – but rather about the global recognition for their amazing scientific achievements.

While many Groningen scientists worked on Nobel Science and in some cases even made discoveries for which others received a Nobel Prize later on, the Nobel Prize was awarded to the RUG on only one other occasion.

Theoretical physicist Fritz Zernike won the award for the invention of the phase-contrast microscope. It is generally assumed that his colleague Hessel de Vries would have been awarded a Nobel Prize in 1960 for his work on radiocarbon dating, had he not died prematurely.



23 | Hessel de Vries (1916-1959)

UNSUNG HERO OF RADIOCARBON DATING

It wasn't even Groningen resident Hessel de Vries himself who realised how important radiocarbon dating would become. Famous archaeologist Albert van Giffen had come across the American physicist Willard F. Libby's discovery from 1949 and asked De Vries to research the method.

Initially, De Vries was not very enthusiastic. But Van Giffen wanted to use radiocarbon to date foundation poles that he had excavated at the Martini churchyard.

De Vries quickly discovered there were flaws in Libby's method. He improved upon it by basing it not on pure carbon, but on carbon dioxide. He then measured the foundation poles as being 1,000 years old rather than the 2,000 years Libby had calculated. Other laboratories confirmed De Vries' results several years later, cementing his international fame.

Moreover, in 1958 he posited that the amount of radiocarbon in the atmosphere is not always stable and proved this using the growth rings in trees. This meant that some specimens were much older than people initially thought.

In 1959, everything seemed to be going his way. A new laboratory was built just for him, which included a 25-metre deep, radiation-resistant pit. And the Third International Radiocarbon Conference was held in Groningen.

A personal catastrophe ended his career and his life. Rejected by his secretary with whom he was in love, he murdered her in 1959 and committed suicide. Had that not happened, he would have undoubtedly shared the Nobel Prize for Physics with Libby a year later. He is known as the unsung hero of radiocarbon dating.

Radiocarbon dating

Radiocarbon dating is done by measuring the – radioactive – radiocarbon that organisms absorb into their metabolism from the atmosphere. When a life ends, that exchange ends as well, and the isotope starts decaying at a steady pace.

By measuring the amount of radiocarbon in a specimen and comparing it to the amount of radiocarbon in the atmosphere, we can determine the age of the specimen very precisely.

24 | Frits Zernike (1888-1966)

THE FIRST NOBEL PRIZE FOR GRONINGEN

In 1930, Frits Zernike was working on a light refraction experiment in his laboratory at the Westersingel. He liked to work at night and would tinker with his own devices and prototypes. He had had this predilection for putting together his own devices since he was a boy, when he made a telescope out of an old pair of binoculars, a table leg, and a gramophone motor in order to photograph comets.

More than once he combed his colleagues' drawers and cabinets looking for parts. Supposedly, this is the reason he was not allowed his own key to the laboratory and he would sometimes sneak in via the roof of the bicycle shed.

This time he was using a Rowland diffraction grating: a metal plate with little cracks that reflected light. Suddenly he noticed that two light beams were unequal. They were in a different 'phase' – they refracted differently.

It was the onset of the development of the phase-contrast microscope, an invention that led to a revolution in cellular biological research. Zernike was awarded the Nobel Prize for his discovery in 1953.

Although Zernike attained his fame with the phase-contrast microscope, he has many more achievements to his name. For example, he also invented the sensitive galvanometer, which was able to measure very weak electrical current. The Delft firm of Kipp and Sons took the device into production.

Phase-contrast microscope

The phase-contrast microscope (available for viewing in the upstairs room) makes use of the principle that light is refracted differently by different materials. A phase-contrast microscope uses that 'phase' difference and enhances it. This makes it possible to make transparent cells visible under a microscope. Before the discovery of the phase-contract microscope, people were only able to view 'dead' cells that had been coloured in.

Not everyone was convinced of the importance of the microscope right away, however. When Zernike presented his idea in 1932 to a German microscope manufacturer, they were critical: 'If this had any practical value we would have invented it ourselves a long time ago.'

During the Second World War, it was the Wehrmacht who recognised the importance of Zernike's discovery and made use of it. After the war, his invention finally received the attention it deserved.

25 | Ben Feringa (1951-)

MOLECULE TINKERER

It's a good thing that Ben Feringa didn't take over his parents' farm in Barger-Compascuum. Because the man who invented the first molecular motor in 1999 and the first molecular car in 2011 was awarded the Nobel Prize in 2016. He shares the prize with the Frenchman Jean-Pierre Sauvage and the Briton Sir James Fraser Stoddart.

Feringa has been fascinated with molecules ever since he constructed his first, very simple, molecule when he was a chemistry student. The realisation that where there was nothing there now was something awakened a drive in him that has never left him. 'You can wake me up any time for a beautiful molecule', he likes to say.

During research into molecular switches in the 1990s, he came across a molecule that was making a half-turn when exposed to light. Feringa realised that if he could make the molecule make an entire turn, he would have a nanomotor.

He finally succeeded in creating one in 1999. His first motor in 1999 made one turn per hour. 'Proof of concept' was the most important thing – it could be done.

The molecules he is making now make ten million turns per hour. Feringa hopes to be able to use them to transport medication through the body. He is also working on smart surfaces: a layer that repairs itself under the influence of light.

As far as Feringa is concerned, we are on the threshold of a new kind of science. 'In spite of all the medication, cars, and smart phones in existence, we have only seen a fraction of the molecular world.'

Nanomotors

Nanomotors are machines that are just a few millionths of a millimetre big. Feringa's motor has two rotor blades and a double carbon compound that serves as an 'axis'. An ultraviolet pulse loosens the compound just for a little bit, which causes the blade to make a half-turn. And then another one.

The famous nano 'four wheel drive' from 2011 had four motors attached to a compound piece – the body. It allowed Feringa to convert a rotating movement into a linear one.

In 2014, he designed a nano wind park, based on a molecule from 2005. In this park, the molecules are placed on a layer of gold. Because the windmills work together, interaction with the macro world becomes possible. A drop of water can shrink and expand under the influence of Feringa's wind park.

Another Nobel Prize

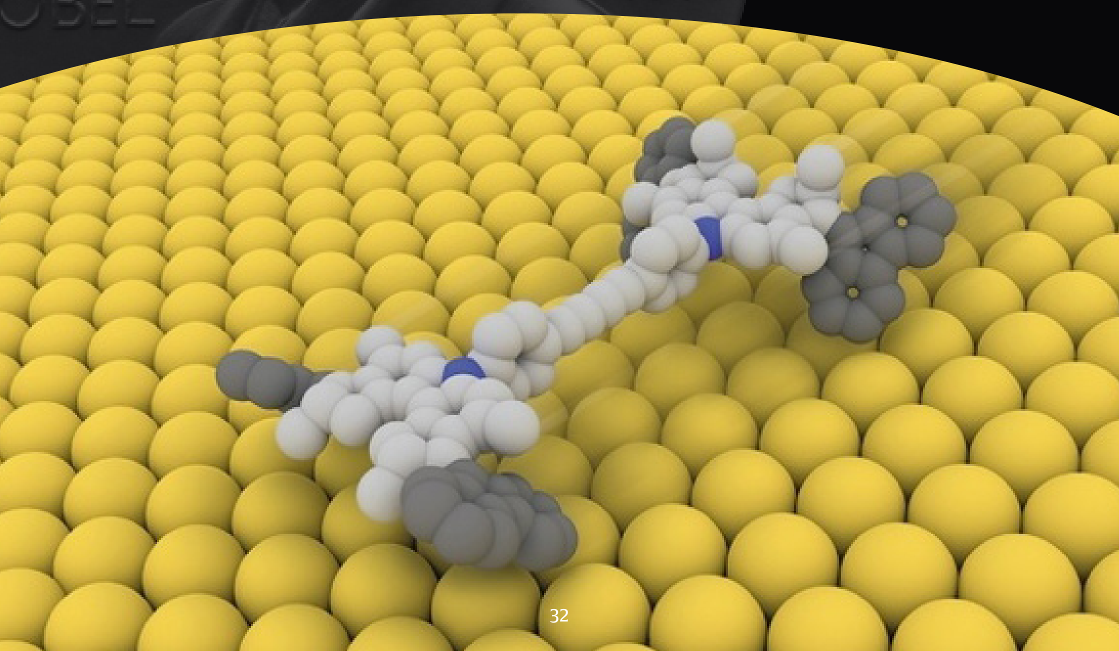
Until now, only two people have ever been awarded more than one Nobel Prize. The honour first fell to Marie Curie, and later to the American chemist Linus Carl Pauling.

However, Jean-Pierre Sauvage, one of the chemists who were awarded the Nobel Prize for the molecular motors together with Feringa, made an interesting remark. 'Those motors are just part of what he does. He might even win yet another Nobel Prize in a different field.'

Feringa and his group are also working on molecular switches: think of antibiotics you can switch 'on' or 'off' by using light. 'On' when it has reached the 'sick spot'. 'Off' when it leaves the body.

They also developed a molecule with a 'door'. Think of it as a little pouch with a pore than opens and closes under the influence of light. You can put medication inside the pouch.

Finally, Feringa's group is working on a project where they catch catalytic agents in a 'nanocage': it is so small that you can count the molecules inside it. The processes in that cage will probably be more efficient than in the macro world. It can teach us how catalysing agents work and how we can make chemical reactions more environmentally friendly.



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