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2022

Professor
Mark van Loosdrecht

The Novozymes Prize

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Mark van Loosdrecht

Nomination of **Mark van Loosdrecht**

Wastewater treatment is a brilliant example of how biotechnology percolates many sectors of modern society. Professor Mark van Loosdrecht exemplifies how first-class science can combine with inventions and process development to solve major societal challenges such as ensuring clean water ecosystems, recycling of valuable and finite resources and solutions to mitigate climate change.

Mark van Loosdrecht obtained his PhD from Wageningen University, The Netherlands in 1988 in the field of environmental engineering. Ever since, he has conducted his research at the Delft University of Technology. When Mark van Loosdrecht started his work, wastewater treatment heavily relied on physical and chemical methods, which were not only costly but sometimes also poorly effective for the removal of environmental pollutants such as phosphates and nitrogen-containing compounds. The first major success of Mark van Loosdrecht was the biological-chemical phosphorus and nitrogen removal or BCFS® process, which significantly improved denitrification and phosphorus-removal by combining biological nitrogen removal with chemical precipitation of phosphorus. The removal of phosphorus from wastewater is not only important in relation to avoid eutrophication of natural water ecosystems, but as a limited resource the recovery of phosphorus is critical.

Mark van Loosdrecht focused his work on understanding the microbial transformations that take place in the wastewater treatment plants at the molecular level. Very importantly, he introduced the concept of metabolic modelling in open systems and mixed cultures. The result of this work was that many environmental key processes could be handled very quantitatively and with a distinct degree of predictability.

A major breakthrough occurred when Mark van Loosdrecht realised the importance of the physical association of the bacteria that thrive in wastewater treatment plants and how he could harness this association to control and optimise the biological processes. He thus continued his inventive path combining science and technology with creating a process he dubbed “SHARON” for Single reactor system for High activity Ammonium Removal Over Nitrite. SHARON reactors can perform the denitrification of sewage streams taking advantage of the bacterial anaerobic ammonium oxidation (Anammox), in which nitrite and ammonium ions are converted directly into nitrogen and water and thus avoid the production of nitrous oxide. This is particularly important as nitrous oxide is a highly

potent greenhouse gas (GHG), and thus this concept is of utmost relevance in order to limit release of GHGs, thereby mitigating climate change. To underline the importance of the work, Mark van Loosdrecht's fundamental research not only decrypted these anaerobic redox reactions but he also applied this knowledge to design the process parameters for true large-scale operation.

Another major discovery within wastewater treatment was when Mark van Loosdrecht observed that phosphate-removing bacteria could be assembled into granules rather than loose biofilms and that this property could be used to produce "granular" sludge with much improved sedimentation properties thereby avoiding subsequent use of clarifiers and sludge recycle pumping. This technology, called Nereda®, requires significantly less chemicals and energy when compared with conventional activated sludge systems. Again, this was a result of in-depth fundamental understanding of the microbial community involved in these processes combined with physical science and process engineering expertise. A great example of the interdisciplinary research of Mark van Loosdrecht.

Full scale reactors based on Mark van Loosdrecht's research and design are now in operation or under construction on almost all continents. Most scientists would be more than satisfied with this amazing set of biotechnological achievements and their immediate application in real operations. This is not how Mark van Loosdrecht functions. As a true engineer, he is constantly driven by the quest for novel applications that combine science and biological wastewater treatment. His latest efforts focus on a seemingly simple but in fact extremely interesting question: could wastewater treatment not only remove pollutants in an economical way, but could the bacteria of the sludge also produce valuable by-products?

To make progress towards this goal, Mark van Loosdrecht is now investigating the exopolysaccharides produced by sludge bacteria and the ways they can be isolated to manufacture valuable materials for the circular economy. The research has resulted in a demonstration plant for the production of Kaumera Gum. The immense variety of structures and properties that polysaccharides can adopt augurs well for Mark van Loosdrecht's relentless pursuit of biotechnological solutions to solve some of the great challenges of our time!

The successful technology contributions of Professor Mark van Loosdrecht have been accompanied by a very prolific scientific production of more than 880 papers and this has propelled environmental microbiology to unprecedented heights of international recognition. With an h-index of 126 he is one of the most influential leaders in environmental biotechnological science today. He has contributed to the next generation of environmental biotechnologists by being a tremendous mentor for young scientists. Mark van Loosdrecht has supervised the graduation of 65 PhD students and is currently mentoring 15 active PhD students.

Professor Mark van Loosdrecht is being awarded the 2022 Novozymes Prize for developing biotechnological solutions that are revolutionising wastewater treatment and resource recovery. His outstanding research in environmental biotechnology and microbial ecology has led to the design of innovative solutions for removing biological pollutants. The profound impact of Professor van Loosdrecht's inventions is clearly evident from numerous full-scale reactors and systems operating worldwide.

About Mark van Loosdrecht

1988	PhD, Environmental Engineering, Wageningen University
1988	Assistant Professor, Department of Biochemical Engineering at TU-Delft
1999	Anthonie van Leeuwenhoek Professor at TU-Delft
2003	Chair Professor and head of the section, Environmental Biotechnology at TU-Delft
2012	Lee Kuan Yew Prize
2013	Gravitation Award
2014	Spinoza Award
2018	Stockholm Water Prize

Using bacteria to convert wastewater sludge into valuable resources

The development of new technologies for biological wastewater treatment is turning our view of sludge upside down. According to Dutch environmental biotechnologist Mark van Loosdrecht, treating wastewater will become good business in the future. He will receive the 2022 Novozymes Prize for his pioneering work in copying and reusing nature's mechanisms in wastewater treatment and resource recovery – transforming sludge into valuable resources.

Today, about two thirds of the world's population are guaranteed clean drinking-water. Fortunately, this percentage is rising. However, global threats such as pollution through fossil fuels, climate change with droughts and floods, increasing population, increasing urbanisation and lack of investment in infrastructure, including wastewater treatment, are threatening this trend. The demand for water has never been greater, and water has therefore never been higher on the political agenda. The focus in wastewater treatment for decades has been on developing even better physical and chemical methods, but Dutch microbiologist Mark von Loosdrecht has focused on the biological aspects. "Development in environmental technology is almost exclusively the preserve of engineers, and they are not that concerned about what all the microorganisms in the water do," explains Mark van Loosdrecht, Professor in Environmental Biotechnology at Delft University of Technology, The Netherlands. "They call it sludge and just want to get rid of all the impurities. What I am trying to do is understand the bacteria and their interactions instead and, with their help, try to recover all the valuable nutrients from the wastewater. Wastewater treatment can therefore actually become good business rather than an increasing expense for countries globally."

Come and work for me – but somewhere else

Most people think of sludge as a disgusting sticky mass that needs to be discarded. But this semi-solid material from industrial processes, from wastewater treatment and from our toilets actually contains many valuable substances, and with a little help from microorganisms, it can become a valuable resource. For Mark van Loosdrecht, the dream of transforming it started more than 30 years ago – not as a dream of saving the world but through fascination about the often hidden valuable properties of bacteria.

"During my very first studies of bacteria, while completing my education in Environmental Engineering at Wageningen University & Research, I investigated how bacteria interact with surfaces. It rapidly dawned on me that when engineers study bacteria, they often do not have very good control over the conditions under which the bacteria were grown or the actions of the bacteria themselves. Conversely, as a microbiologist, I did not want to study bacteria alone. I wanted to do both," says Mark van Loosdrecht.

Actually, Mark van Loosdrecht got somewhat tired of academia and had agreed with Sef Heijnen, whom he had met while studying for his PhD degree, that he would apply for a job at Gist-Brocades, where Heijnen worked. However, in the meantime Heijnen had returned to academia.

"He said: 'Yes, you can still come and work with me, but somewhere else,'" he recalls.

"Wastewater treatment is ideal for studying microbial ecology because it is a diverse microbial ecosystem in which many properties can be studied."

Somewhere else was Delft University of Technology, and the topic was developing water and wastewater treatment processes. Ever since he changed directions in 1988, Mark van Loosdrecht has worked in the same place and on the same interdisciplinary topics: integrating microbiology and engineering and integrating research and practice.

"Wastewater treatment is ideal for studying microbial ecology because it is a diverse microbial ecosystem in which many properties can be studied. Further, when you discover things in the lab, you can often evaluate them easily in practice. This often generates new questions that are taken back to the lab. So this is where science and technology can help each other," explains Mark van Loosdrecht.

Combining science and engineering

Researchers in the Netherlands quickly realised the advantages combining fundamental knowledge of the capabilities of bacteria and their interaction with wastewater treatment.
"The field was back then essentially very conservative. Those who studied wastewater treatment optimised filters to remove all the impurities. Those who studied bacteria usually studied a specific type of bacterial culture to determine how it behaves. We decided instead to focus the research on the bacterial communities naturally found in wastewater that help to purify it," explains Mark van Loosdrecht.

The use of microorganisms to purify water dates back more than a century, when British researchers found that oxygenating wastewater could remove harmful nitrogen-containing compounds such as ammonia. They called this activated sludge, and only much later realised that it was the living organisms in the wastewater that had been activated. The discovery kick-started an interest in understanding how these organisms function and help to remove nitrogen and phosphorus compounds along with other harmful compounds from wastewater.

"We realised in earlier studies that cultivating pure cultures of bacteria in the laboratory tends to change their properties so that they no longer resemble their naturally occurring ancestors. So even if bacteria could be isolated that could remove a specific substance, other aspects of their behaviour change. The organism is not behaving anymore as it was when it was mixed with the wastewater, where the conditions were completely different and where they coexisted and interacted with many other organisms," recalls Mark van Loosdrecht.

Very efficient method

Mark van Loosdrecht and colleagues therefore decided to study the bacteria under their natural conditions in the wastewater in order to foster and cultivate the relevant organisms. A more dynamic and selective enrichment technique was therefore required – and this became very successful within a few years.
"The discharge of phosphates into surface water leads to

eutrophication and blooming of algae, which was a huge problem at the time. We refined, adopted and further developed an existing process into an efficient technology by integrating chemical and biological removal. This resulted in an optimal combined system for efficient nutrient removal with minimal energy usage to be obtained," says Mark van Loosdrecht.

In 1998, this BCFS® process for phosphorus recovery became the first of a series of new wastewater treatment processes developed by Mark van Loosdrecht, his team in Delft and Dutch water utilities. In the same year, the researchers also developed a particularly efficient method to remove ammonia – one of the main sources of nitrogen pollution, alongside nitrogen oxides.

"Ammonia pollution can have substantial effects on both human health worsening cardiovascular and respiratory diseases and the biodiversity through the accumulation of nitrogen in plant species. Another major nitrogen source, nitrous oxide, remains


Photo: Marcel Krijger

in the atmosphere for 114 years before being removed naturally. One tonne of N_2O affects global warming almost 300 times that of 1 tonne of C_2O," explains Mark van Loosdrecht.

A perfect match

Over the years the researchers had searched for biological means to solve the nitrogen issues. In the early 1990s Mark van Loosdrecht's research colleagues in Gijs Kuenen's research group had surprisingly found bacteria that could convert ammonia and nitrite directly into nitrogen gas – the ANAMMOX® (anaerobic ammonium oxidation) process.

"By skipping several steps in the nitrogen cycle, this bacterial process saves a lot of time, chemicals and energy. However, for the process to take place, an acceptor of an electron is needed, so the bacteria can donate electrons from ammonium to nitrite," adds Mark van Loosdrecht.

By studying the bacterial communities in detail, Mark van Loosdrecht and his colleagues became instrumental in gaining a better biological understanding of the ANAMMOX® process, and in 1998 the development of the SHARON (single-reactor system for high-activity ammonium removal over nitrite) process became the launching pad for a huge breakthrough, which solved the central issue with the ANAMMOX® process, the lack of an electron acceptor.

"In the SHARON process we take advantage of the growth rate differences between *Nitrosomonas*, which oxidise ammonium to nitrite and *Nitrobacter*, which can further oxidise the nitrite to nitrate. By favouring *Nitrosomonas*, the product from the SHARON process is nitrite, an electron acceptor, so the SHARON process can then efficiently be used to scale up the ANAMMOX®

process and directly convert nitrite into nitrogen gas," explains Mark van Loosdrecht.

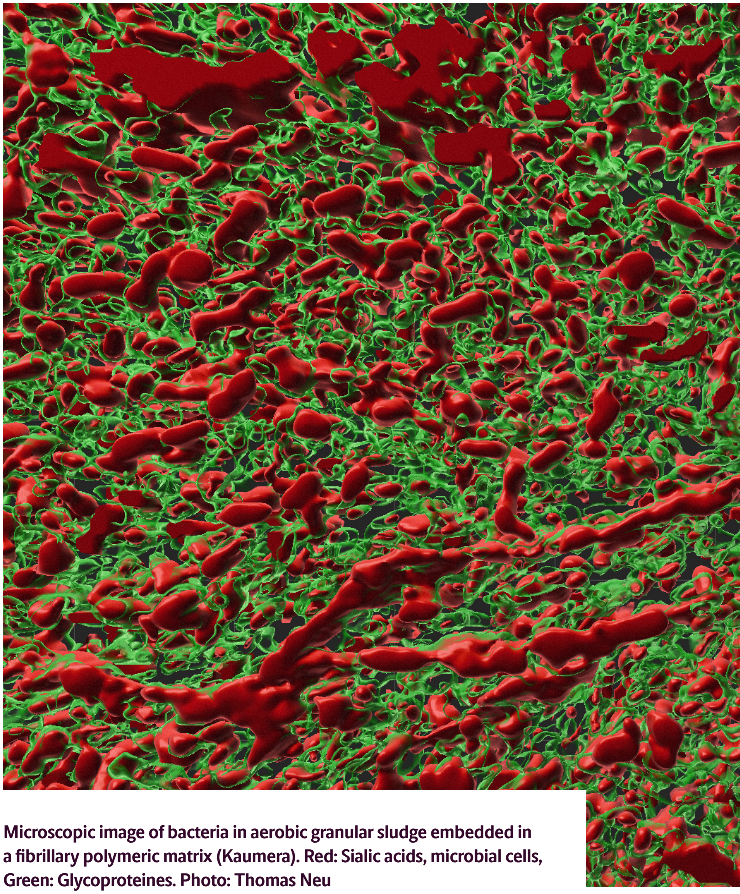
Training bacteria

In the following years, while SHARON and ANAMMOX® plants were implemented worldwide, Mark van Loosdrecht took wastewater treatment to the next level by studying other natural microbial processes in sludge, combining his experience in wastewater treatment with his knowledge about the physical interactions between bacteria on which he had focused at the start of his career.

"When bacteria grow together, they can make very fluffy structures, as in conventional wastewater treatment, or compact structures that much more easily separate from the cleaned water. The structure formation appeared to be more a physical than biological process, where slow-growing bacteria enable the right conditions to be created for compact structures. Coincidentally, the phosphate-removing bacteria are such bacteria. We thereby converted the activated sludge into small granules that contain various layers of these bacteria trained to perform a specific function," says Mark van Loosdrecht.

By cultivating granular sludge on wastewater, Mark van Loosdrecht and colleagues could now not only improve the treatment of wastewater. Once the water is pure, the granules settle at the bottom of the tanks and can be reused. The big advantage here was time. Conventionally activated sludge settles at about 1 metre per hour, whereas the smoother and denser bacterial granules managed 1 metre in 4 minutes. The researchers dubbed the technology Nereda® – derived from the Nereids, mythical Greek water nymphs.

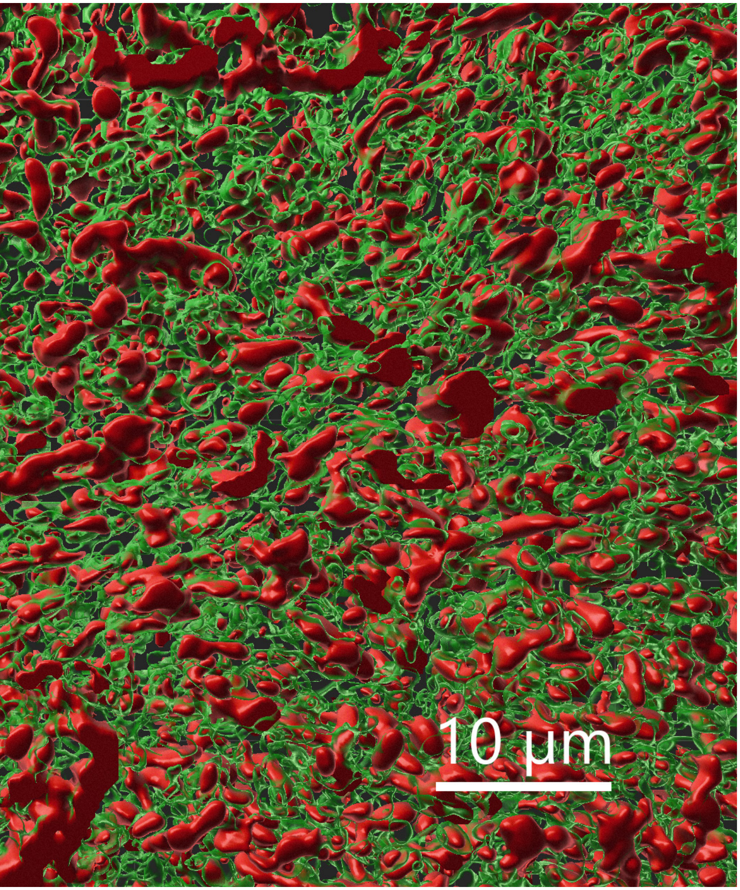
"Making these processes mechanically simpler and cheaper requires deep understanding of the complex interaction between biology and process technology. Nereda® requires much less space and uses half as much energy as conventional methods. The principles of forming granular sludge are based on physics, but in the end the bacteria do the job," explains Mark van Loosdrecht. It again emphasise the importance of interdisciplinary research.



Microscopic image of bacteria in aerobic granular sludge embedded in a fibrillary polymeric matrix (Kaumera). Red: Sialic acids, microbial cells, Green: Glycoproteines. Photo: Thomas Neu

Jewellery from the toilet

The fascination for new knowledge has been absolutely crucial in driving Mark van Loosdrecht and his colleagues towards their new remarkable discoveries. An example of how curiosity, economics and social responsibility can often be integrated is vivianite, a hydrated iron phosphate mineral. In 2016, scientists discovered that it could help solve one of the greatest challenges in wastewater treatment – phosphate discharge, which is an environmental problem but phosphorus is also a limited resource.



“Phosphorus recycling is crucial for creating a sustainable circular economy and balance in nature. Iron binds phosphate as vivianite, which can then be removed with a magnetic separator. Vivianite can be used as a fertiliser. The curiosity towards how iron behaves in a wastewater treatment process has led to an interesting innovation stimulating a circular economy. We need to be more curious and think outside the box,” says Mark van Loosdrecht.

Although the vision of Mark van Loosdrecht and his colleagues in Delft of turning sludge into economically profitable resources has not yet been achieved, they are now closer to realising their long-standing dream. They have discovered several substances with a possible market potential by analysing the Nerada® granules, such as Kaumera Nerada® Gum, a sustainable biopolymer.

“There is already a market for this biopolymer, which in combination with clay has proven to be comparable to some of the existing fibre-reinforced plastics – and with even better fire-retardant and heat-resistant properties. The material is actually so attractive that a colleague has started making jewellery from Kaumera Nerada® Gum. Its beautiful pearly lustre can remind us of things that can be made from what we flush down the toilet today,” concludes Mark van Loosdrecht.

The 2022 Novozymes Prize is being awarded to Mark van Loosdrecht, Professor in Environmental Biotechnology at Delft University of Technology, Netherlands.

The Novozymes Prize Committee

The Novozymes Prize aims to raise awareness of basic and applied biotechnology research. The prize is awarded to recognize outstanding research or technology contributions that benefit the development of biotechnological science for innovative solutions. It is awarded for a predominantly European contribution. Prize recipients must have a current position at a public or non-profit research institution in a European country. They may have any nationality.

The Novozymes Prize Committee awards the prize based on the nominations received. Anyone can nominate a candidate for the prize. The prize is awarded annually and is accompanied by DKK 5 million. DKK 4.5 million is a funding amount for the Prize recipient's research, while DKK 0.5 million is a personal award.

The Novozymes Prize is awarded by a prize committee that selects the successful candidate based on scientific achievements after a confidential nomination and review process.

The members of the Novozymes Prize Committee are appointed by the Novo Nordisk Foundation Board of Directors. The 2021 Committee comprised the following seven members:

Professor Bernard Henrissat, Chair
Professor Jens Nielsen
Professor Gunnar von Heijne
Professor Johanna Buchert
Professor Dame Carol Robinson
Professor Detlef Weigel
Senior Vice President of Biotech Claus Felby, representing the CEO

The award event usually takes place in the spring at the Novo Nordisk Foundation Prize Celebration, at which the Novo Nordisk Prize is also awarded.

In addition, in celebration of the award, the recipient gives a lecture lasting about 1 hour at his or her workplace. Before the end of the year, the recipient and the Foundation arrange an international symposium within the scientific field of the Prize recipient.

Candidates for the Novozymes Prize can be nominated by the Prize Committee and former Prize recipients. In addition, a call for nominations is published in the spring, and candidates can be nominated based on this call.

The Committee meetings thoroughly discuss the nominated candidates with regard to their research contribution and impact, and a comprehensive bibliometric report is produced. A few candidates are then selected for thorough international peer review. Based on the international peer reviews, the Committee reaches a decision about the year's Prize recipient.







Previous recipients of

The Novozymes Prize

2015–2021

2015	Professor, Director Bernard Henrissat
2016	Professor Jens Nielsen
2017	Professor Emmanuelle Charpentier
	Professor Virginijus Siksnys
2018	Professor Gunnar von Heijne
2019	Professor Dame Carol Robinson
2020	Professor Detlef Weigel
2021	Professor Peer Bork

Novo Nordisk Fonden

Tuborg Havnevej 19
2900 Hellerup
Denmark

Phone: +45 3527 6600

nnfond@novo.dk
www.novonordiskfonden.dk/en/

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Cover photo: Marcel Krijger

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