



Research assessment

Physics 2015-2021 Self evaluation report

Summaries and Case Studies

Summary Bionanoscience (BN)

At the Bionanoscience department we address fundamental questions in biology by using cutting-edge methods from physics and nanoscience. From single molecules to the full complexity of living cells and tissues, we want to answer questions about how life arises and is maintained at the molecular scale. Since our founding in 2010, we have grown into 18 independent groups that study a broad set of fascinating topics: how genomes are organised in time and space; mechanical properties of cells and tissues; how to build a synthetic cell; how nerve cells communicate; how to make gene editing safe; how to build self-healing materials—to name but a few. The potential for impactful fundamental discoveries is large, and answering the questions we pose promises to deliver novel strategies for drug design, delivery and therapy, as well as new ways of engineering and sustainably producing bio-based materials and compounds. To make real on these promises, we work interdisciplinary and bring together international experts using approaches and concepts from biology, physics, chemistry and (nano) engineering.

The department prides itself on its breadth of expertise: from theoretical biophysics, via single-molecule methods, to cell and tissue biology, and synthetic biology. We believe that scientific excellence is promoted by the freedom of individual groups to pursue curiosity-driven research and set their own research agendas. To foster excellence and ownership among our Principal Investigators (PIs), we operate a non-hierarchical department where all PIs have equal say in departmental decisions. Our flat structure offers scientists at all career stages excellent opportunities to grow, and we have been successful at attracting top international talent—almost doubling the number of groups over the reporting period.

We have also been exceptionally productive scientifically, and our work is typically cited twice the average number of times, across all the fields that we are active in. Our scientific achievements and ideas have been recognised by several prizes and awards to our members, including two Spinoza prizes and many large EU and NWO grants. We run the national Gravitation programme on Synthetic Cells, and we are a founding member of the Kavli Institute of Nanoscience Delft. Our department is diverse, with 44% female PIs and 44% PIs from outside the Netherlands. We will keep working on gender equality to ensure all our students and staff are exposed to brilliant scientist role models.

Over the next years we will continue our central pursuit of fundamental knowledge and understanding, but will also seek to translate our discoveries for direct societal impact. We are especially excited to take part in TU Delfts Health & Technology Convergence initiative with Erasmus MC, and are working to raise awareness among our members about opportunities for valorisation and collaboration with industry. Though our PIs are very successful in attracting personal funding, we will seek further financial security by increasing the diversity of funding sources. By fostering more collaborations within our department, Faculty and University, as well as with industry, we aim to increase our share of consortia and translational grants. To fully capitalise on the diversity of our department, we will continue work to increase social safety and inclusivity in all aspects of departmental life.



Case Study

Bionanoscience (BN)

Case study

Fagenbank (Phage Bank)

Antibiotic resistant bacteria are spreading across the globe at an alarming pace, rising from today's several hundred thousand lives claimed per year to an expected 10 million by 2050 (*Tackling drug resistant infections globally*, O'Neill, 2016). We risk being pulled back into a pre-antibiotic era, where average lifespans are cut short because bacterial infections cannot be controlled. To avert such a health catastrophe, the World Health Organization is strongly encouraging the development of alternative modalities to target antibiotic resistant bacteria.

Bacteriophage therapy and the Fagenbank

Bacteriophages are viruses specific to bacteria, and have evolved to target and kill their bacterial hosts (**Figure 4**). One promising alternative to antibiotics is therefore bacteriophage therapy, where carefully selected bacteriophages are used to target resistant bacterial species. This approach was eclipsed by standard antibiotic treatments in the West, but has been successfully used to treat bacterial infections for over 80 years in Poland, Georgia and Russia. As standard antibiotic treatments fail, bacteriophage therapy is making a comeback in the West. Bacteriophages exist for bacterial species of every kind, and can be isolated, characterised and stored for their potential use as therapeutics.

Seeing the potential for societal impact, the Brouns lab at the BN department started to promote bacteriophage therapy as a possible alternative to treat antibiotic resistant bacterial infections in 2017. In 2018 Stan Brouns founded the national Bacteriophage biobank *Fagenbank* (www.fagenbank.nl/english) to support investigations into the therapeutic uses of bacteriophages. The Fagenbank currently holds over 125 bacteriophages known to target resistant bacterial species, such as *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Some of the bacteriophages that the Brouns lab have isolated from wastewater have never been observed before, and have now been documented in scientific literature (Estrada-Bonilla 2021) and are included in the Fagenbank. The mission of the Fagenbank is to

Establish safe and effective bacteriophage therapies as a treatment method for antibiotic-resistant infections, and to investigate and prevent natural bacteriophage resistance.

The legal framework

The use of bacteriophages for medical purposes is in its infancy in the Netherlands, and the legal routes for therapeutic use still need to be established. Our collaborators at the UMC Utrecht are currently developing a compassionate-use protocol with their hospital pharmacists. Such a protocol is required by the Dutch health inspection authorities (IGJ) to implement personalised treatments of individuals suffering from a bacterial infection. Operating in accordance with the World Medical Association declaration of Helsinki, the protocol allows doctors to use unproven experimental medication with patient consent to potentially improve their life. Such a protocol is already in place in the Queen Astrid Military Hospital in Brussels, and will be adjusted for implementation in the Netherlands. The lead-in time to accomplish legal routes has been used by the Fagenbank to create a collection of bacteriophages for future use.

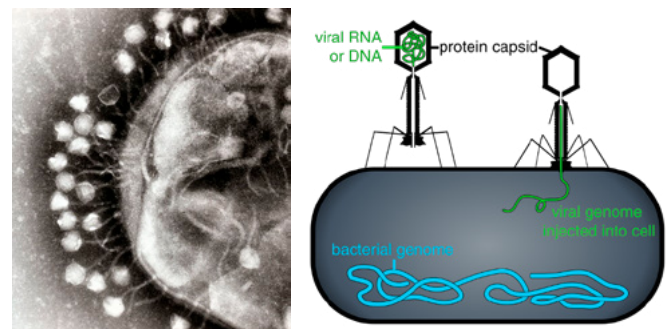


Figure 4: (left) Schematic representation of a bacteriophage infecting a bacterium by injecting the viral genome that will enable the viral replication that will eventually kill the bacterium. (Source: Wikipedia under the Creative Commons Attribution-Share Alike 3.0 Unported). (right) Electron micrograph of bacteriophages infecting a bacterium. (Source: Wikipedia under the GNU Free Documentation License).

The role of fundamental science

A limitation that needs to be assessed during clinical applications of bacteriophage therapy is the natural defences of the bacteria that can make them adapt and become resistant. The Brouns lab has a long history researching the fundamental mechanisms behind CRISPR-Cas and other bacteriophage defence mechanisms known to be present in the genomes of bacteriophage resistant bacteria (Egido, 2022). Using this expertise, we have recently reviewed potential forms of bacteriophage resistance together with our collaborators at the University Medical Centre Utrecht (Bonilla, 2021).



Currently, we are completing an experimental study funded by the European Research Council into the contribution of natural resistance mechanisms in clinical bacteriophage resistance strains. We continue to expand our collaborations with international scientific groups and Dutch academic hospitals and patient associations in the form of consortia, shared publications and exchange of strains and knowledge.

The importance of outreach

Examination at a clinical level and building a legislative framework to treat patients with bacteriophages requires awareness raising among the public and various stakeholders. To facilitate the therapeutic impact of the fundamental knowledge we develop about bacteriophages and bacteriophage resistance, we reach out to patients, students, medical doctors and other stakeholders. We promote bacteriophage therapy to the public through television, radio and the internet, and through articles aimed at specific target groups. Major media impact of our initiative was achieved in three episodes of a consumer TV programme called 'Zorg.nu' and 'Dokters van Morgen', each drawing over 1 million views ([link](#)). For high-school students, we have organised a bacteriophage workshop where students learned about the different aspects of developing phage therapy. For university students, we are developing a course dedicated to molecular virology.

Towards bacteriophage therapy in the Netherlands

To move bacteriophage therapy forward, we need to work on many fronts: from establishing the legal framework to advancing fundamental science. The combination of fundamental research into bacteriophages and bacteriophage resistance, reaching out and collaborating with different societal stakeholders, and creating a bacteriophage databank is crucial to one day establish bacteriophage therapy as a common therapeutic alternative. Drawing upon the diversity of the databank, research will show the potential and limitations of phage therapy, while and at the same time informing the further development of Fagenbank (**Figure 5**). Fagenbank itself will not only make research more efficient and straightforward, but also provide a tangible base to build towards the clinical use of bacteriophages.

References

Bonilla E, Costa AR, van den Berg DF, van Rossum T, Hagedoorn S, Walinga H, Xiao M, Song W, Haas PJ, Nobrega FL, Brouns SJJ. Genomic characterization of four novel bacteriophages infecting the clinical pathogen *Klebsiella pneumoniae*. DNA Res. 2021 Aug 25;28(4).
Egido JE, Costa AR, Aparicio-Maldonado C, Haas PJ, Brouns SJJ. Mechanisms and clinical importance of bacteriophage resistance. FEMS Microbiol Rev. 2022 Feb 9;46(1).

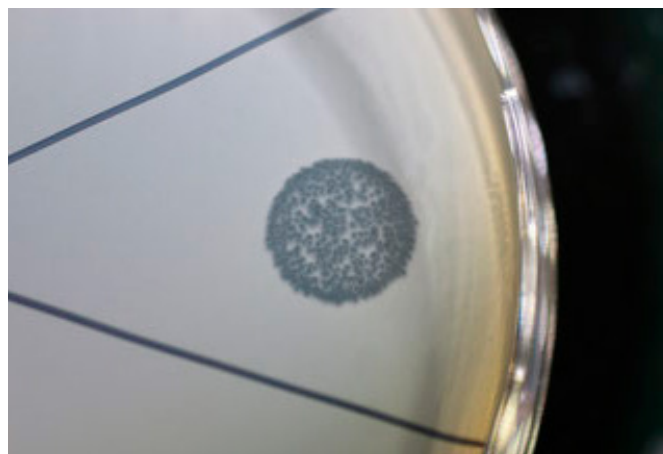


Figure 5: (left) The bacteriophages of the Fagenbank are stored at -80°C. (right) In petri dishes, bacteria normally grow very well they form a white layer. Putting a solution of a specific bacteriophage on a specific clearing spot allows us to see if the killing by the bacteriophage is effective.



Summary Imaging Physics

The mission of the Department of Imaging Physics is to elevate imaging sciences and their utility to society through cutting-edge science, engineering and design. In the domain of healthcare, we develop new instrumentation and new imaging modalities for applications from pre-clinical life sciences to clinical diagnostics, using light, electron, acoustic and magnetic imaging modalities. ImPhys researchers work at all levels of the pipeline of discovery, invention, development and analysis to enable insights in the fundamentals of imaging sciences and deliver technological breakthroughs to the clinic. In the domain of digital society, ImPhys generates innovation in sensing and precision metrology, with light and electron optics, and in instrumentation design. In both areas, computational imaging techniques and AI increasingly set the pace for progress.

Over the reporting period 2016-2021, the department has rejuvenated by attracting 7 tenure-track scientists, supported by several strategic (national and local) investment programmes. The attendant influx of novel research directions in imaging, ranging from in-vivo microscopy and neuro-imaging, to MRI physics and AI, functional ultrasound and single-photon detection technology, all hold the promise for breakthroughs in our targeted application domains. At the same time, we have reaped the fruits of our previous choice towards computational imaging, with important results published in the field of super-resolution microscopy, and new inroads and infrastructure created for soft X-ray lensless imaging and metrology.

Looking ahead, we are confident for the coming reporting period, with a better articulated vision on the ultimate societal goals of our work, next steps towards improving independence and ownership in our internal organisation, and the coming relocation to the new Applied Physics building. Most importantly, our confidence derives from the solid foundation of our research that lies in the scientific and technological skill set of our scientists in imaging methodologies.

The main strategic goals in the coming years are:

- Hire academic staff members in electron microscopy and applied optics in view of upcoming retirements Hagen and Urbach. Initiate public-private partnerships and organisation and alignment on the national level in these fields.
- Lead the health-tech convergence effort with regional partners in the areas of integrated advanced microscopy workflows, integrative neuromedicine, and deep MRI and ultrasound imaging.
- Stimulate the pursuit of personal grants, and encourage taking the lead in national and European consortium grants, in addition to straightforward participation in single-project grants supported by NWO or directly by partners in our research ecosystems.
- Support the growth of our cohort of tenure-track scientists to take up leadership in their respective fields and for the department and TU Delft as a whole.
- Achieve results in decreasing PhD duration towards the nominal 4 years.
- Continue on our path to achieve more open access, open source and open data in our science.
- Make next steps in improving diversity at all levels, including academic staff, support staff, postdocs and PhD candidates, and promote inclusiveness in our way of working.
- Change our internal departmental organisation to increase ownership and accountability of all the individual PIs for their own research and education, for their position in the international scientific landscape, and for their role in managing the department. At the same time, we aim to enable diverse and dynamic academic career paths for our scientists.
- Prepare for the relocation to the new Applied Physics building, so as to take full and direct advantage of the opportunities offered.



Case Study

Case study

Computational Imaging

History and background

Computational imaging is the field in which advances in optical technology are combined with reconstruction algorithms to create surprising new imaging systems architectures that can overcome fundamental imaging barriers. We have built a strong reputation in this field, based on strategic choices of our researchers in preceding reporting periods, and we consider it one of core strengths of the department. In particular the field of super-resolution microscopy, primarily based on single-molecule imaging, is vibrant in ImPhys. In this field, Rieger and Stallinga have made fundamental contributions to fast and accurate single-molecule spot fitting [1], resolution determination beyond the diffraction limit, and particle averaging. During the reporting period, both researchers were promoted to full professor, partly based on the success in their research lines (see **Table 1**). New approaches to imaging single molecules with a large numerical aperture optical system are closely related to novel technology for tightly focusing light spots with such optical systems. In that area Urbach, Pereira and part-time PI El Gawhary have advanced our understanding and led the way to novel optical metrology applications. An even more radical break from traditional optical imaging is to do away with lenses altogether, which is a necessity at low wavelengths (soft X-ray) where lenses simply do not exist. Urbach and part-time PI Coene drive our contributions to this field of lensless imaging, or ptychography as it is called, and develop advanced reconstruction algorithms to unscramble complex diffraction patterns for retrieving nanoscale object features.

Scientific interest and international positioning

The scientific drive to develop imaging techniques that allow to visualise smaller detail over a larger field-of-view at a smaller time scale is inspired by the realisation that imaging provides the most natural view (literally) on the otherwise invisible nano-world and is most instrumental for a human to understand a complex situation, regardless of the application area. Our scientific approach to enhance resolution in 3D imaging and sensing is by measuring data sets with maximum information content employing all properties of light: amplitude, phase, polarisation and wavelength.

We develop algorithms to enhance the signal-to-noise ratio (SNR) of imaging beyond the optical diffraction limit. In biology, many chemically identical structures are often present in a cell and can be imaged together, e.g. virus particles or macromolecular assemblies such as the nuclear pore complex (NPC). While each individual super-resolution recording of such a structure has poor SNR, the correct combination of all structures into one reconstruction enhances SNR and image resolution tremendously. We demonstrated this so-called particle averaging first on a fascinating toy example; the world's smallest TU Delft logo, made with DNA-origami technology (see **Figure 1** left), but also for the NPC, first in 2D and later in 3D [2][3][4]. Another major breakthrough was the use of patterned illumination in single-molecule imaging ("SIMFLUX") for a twofold improvement of localisation precision (see **Figure 1** right), where we made an initial point-scanning technique of the lab of Nobel laureate Stefan Hell suitable for single-molecule imaging over an extended field of view with a camera [5].

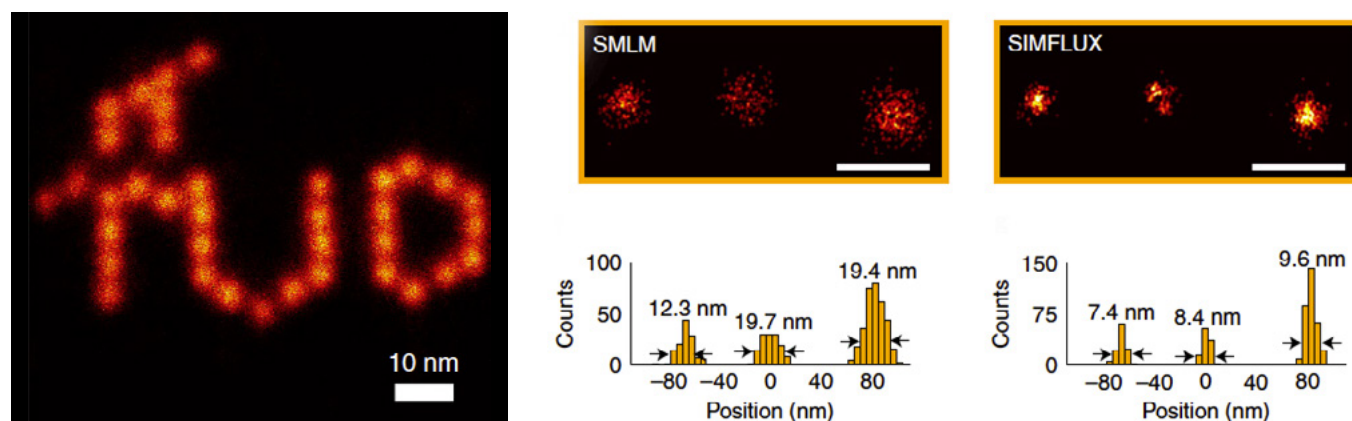


Figure 1: Left: Image of the world's smallest TU Delft logo, made by DNA-origami, combining data from 383 low-SNR single-molecule localisation images [2]. Right: SIMFLUX achieves a twice better localisation precision compared to standard SMLM, as indicated by the narrower localisation distributions [5].



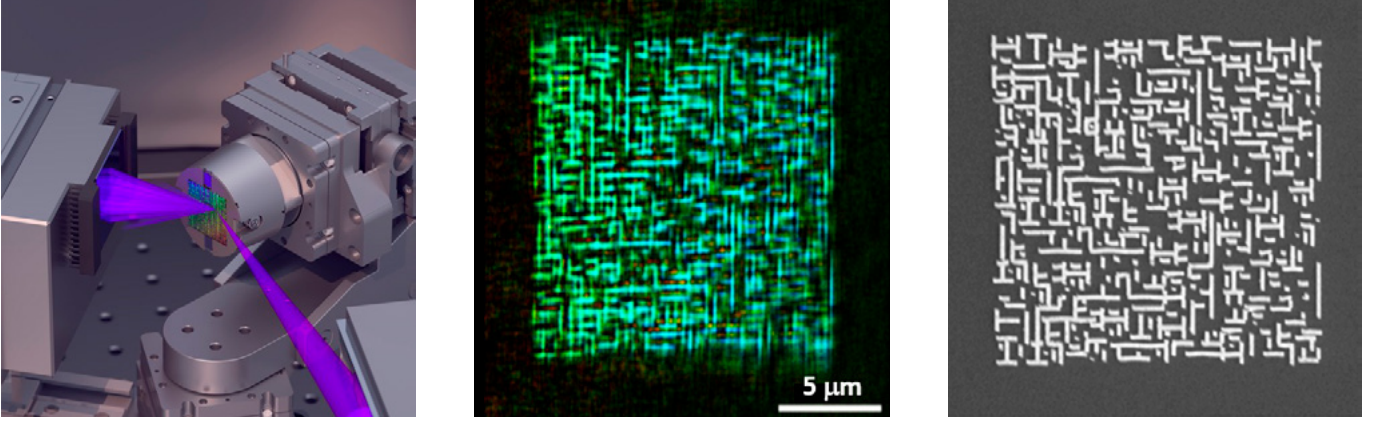


Figure 2. Left: Grazing incidence coherent illumination of a sample in the soft X-ray imaging set-up. Middle: Ptychography reconstruction at 50 nm resolution with our set-up. Right: Ground truth SEM image of the “Manhattan” structure.

We have realised a coherent soft X-ray source and setup in the department. A 100 W infrared laser generates by high-harmonic generation a record high photon flux of 1010 photons/s at a wavelength of 10 nm. High-quality mirrors are used to illuminate the sample under grazing angles of incidence and the diffracted light is detected with a 2K resolution EUV camera. One of the key goals of the setup is to investigate lensless imaging technology. **Figure 2** shows the grazing incidence principle, and a ptychography reconstruction we made of a test sample. Currently, we are making the step from lensless imaging of thin samples, to thicker, fully 3D samples. Here the effects of multiple scattering become so relevant that they must be taken into account in the reconstruction. Fast, accurate and efficient forward modelling of scattering beyond the so-called first Born approximation, is therefore a requirement. We recently made a significant step in this area by applying the mathematical technique of Padé approximants [7], which turns out to lead to an accurate and efficient representation of the scattered field (see **Figure 3**), and which moreover is very suitable for use in regularised reconstruction algorithms.

The scientific interest of our work in these fields not only derives from the scientific results, but also from the

prestigious funding we obtained (see also **Section 5** on accomplishments). In particular Rieger’s Vici project “Ultra-resolution with visible light”, and TTW-Perspective consortia Synoptics (lead Urbach) and LINX (lead Coene) stand out, where the LINX project actually made our soft X-ray infrastructure possible. Our position in the international scientific field has also enabled us to organise several key conferences (see also **Section 5** on accomplishments). The Quantitative Bioimaging Conference (2016) and the Single Molecule Localization Microscopy Symposium (2019) have both been hosted in Delft (Rieger, Stallinga), the Face2Phase conference series was launched by us, and we also managed to attract the bi-annual conference of the European Optical Society to Delft (Urbach, Pereira, Adam).

Nearly all our publications on the topic of nanoscale imaging for the life sciences had (inter)national co-authors from other universities or research institutes. This follows naturally from the interdisciplinary character of the research. While our expertise is on the imaging and analysis part, we need the input life-sciences part. Collaborators, but also other researchers in the life sciences often can directly use our open-source software.

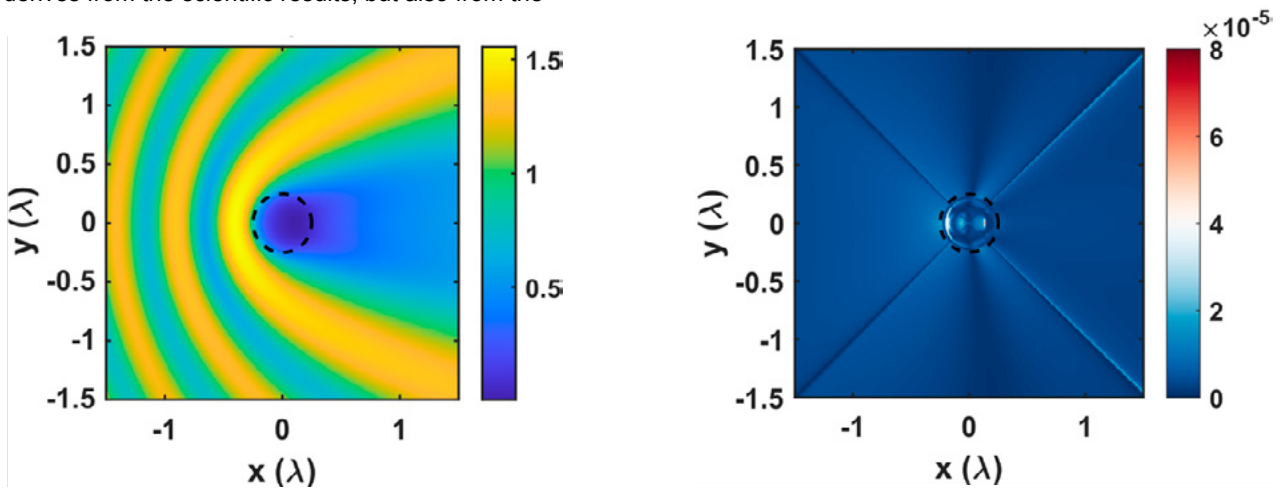


Fig. 3. Scattering by a 200-nm diameter cylinder made of silver of an incident plane wave of wavelength 400 nm coming from the left and polarised parallel to the axis of the cylinder [7]. On the left the intensity computed by the Padé approximant is shown while at the right the absolute error between the Padé approximant and the exact analytic solution is shown.



We have a strong international network of collaborators, mainly in Europe, but also in the US. We foster this network not only by interacting at conferences, but also by pro-actively looking for interesting samples and/or datasets, and by inviting foreign scholars to Delft to e.g. participate in PhD defences and give department seminars. To foster long-term collaborations, we exchanged 4 graduate and 5 undergraduate students with two US labs, each staying for three months.

Societal relevance and network

The continuous strive for smaller integrated circuits has led to the use of optical lithography at the soft X-ray or Extreme Ultra-Violet (EUV) wavelength of 13.5 nm. To comply with this downscaling, optical metrology for inspecting manufactured structures must now have resolution in the nm range, well below the diffraction limit of visible light. The need for nanoscale metrology is one of the primary drivers for the above efforts in computational imaging on the nanoscale. The interest from industry, from multinational ASML to SMEs and start-ups, but also from institutes like TNO and the metrology focused VSL, is apparent from the financial support to a wide range of projects. In the area of life sciences, our enabling imaging technologies target the field of molecular biology that works towards fundamental understanding of the molecular mechanisms of infectious diseases. Ultimately, the goal of that field is to achieve personalised treatment and monitoring of heterogeneous diseases such as cancer. Enabling breakthroughs in pre-clinical research with our imaging innovations is fostered by teaming up with researchers in academic medical centres, with regional partner Erasmus MC in a key role.

Future perspective

We foresee a bright future for the different fields in computational imaging, and we anticipate that researchers from ImPhys will continue to deliver innovations in the coming reporting period. New inroads originating from newly hired PIs Zadeh and Geertsema will aid in keeping this research line viable. Several new funding opportunities in this area have materialised already and are in different stages of the evaluation process. Very recently, an ERC Advanced Grant 2022 was awarded to Stallinga, building on recent results [5, 6], and a large health-tech convergence consortium with Erasmus MC and EUR on microscopy, led by Hoogenboom, received financial support. A large NWO TTW-Perspective proposal on 3D nanoscale imaging in semiconductor metrology and life sciences, driven by ImPhys, is currently under review.

References

(ImPhys researchers in boldface)

- [1] **C.N. Hulleman, R.Ø. Thorsen**, E.Kim, C.Dekker, **S.Stallinga**, and **B.Rieger**. Simultaneous orientation and 3D localization microscopy with a Vortex point spread function. *Nature Communications*, 12:5934, 2021.
- [2] **H.Heydarian**, F.Schueder, M.T. Strauss, B.v. Werkhoven, M.Fazel, K.A. Lidke, R.Jungmann, **S.Stallinga**, and **B.Rieger**. Template-free 2D particle fusion in localization microscopy. *Nature Methods*, 15:781-784, 2018.
- [3] **H.Heydarian, M.Joosten**, A.Przybylski, F.Schueder, R.Jungmann, B.v. Werkhoven, J.Keller-Findeisen, J.Ries, **S.Stallinga**, M.Bates, and **B.Rieger**. 3D particle averaging and detection of macromolecular symmetry in localization microscopy. *Nature Communications*, 12:2847, 2021.
- [4] **T.A.P.M. Huijben, H.Heydarian**, A.Auer, F.Schueder, R.Jungmann, **S.Stallinga**, and **B.Rieger**. Detecting structural heterogeneity in single-molecule localization microscopy data. *Nature Communications*, 12:3791, 2021.
- [5] J.Cnossen, **T.Hinsdale, R. Ø. Thorsen**, F.Schueder, R.Jungmann, C.S. Smith, **B.Rieger**, and **S.Stallinga**. Localization microscopy at doubled precision with patterned illumination. *Nature Methods*, 17:59-63, 2020.
- [6] C.S. Smith, J.A. Slotman, L.Schermelleh, **N.Chakrova**, S.Hari, Y.Vos, **C.W. Hagen**, M.Müller, W.van Cappelen, A.B. Houtsmuller, **J.P. Hoogenboom**, and **S.Stallinga**. Structured illumination microscopy with noise-controlled image reconstructions. *Nature Methods*, 18: 821-828, 2021.
- [7] **T.A. van der Sijs, O. El Gawhary**, and **H.P. Urbach**, Electromagnetic scattering beyond the weak regime: solving the problem of divergent Born perturbation series by Padé approximants. *Phys. Rev. Res.*, 2, 013308, 2020.



Summary Quantum Nanoscience

The Department of Quantum Nanoscience aims to open the quantum world for innovation. Through exploratory research, in both experiment and theory, on a wide variety of quantum physics manifestations, QN forms a fertile breeding ground for quantum innovation. The department is loosely organised into three themes—quantum matter, quantum transduction and quantum sensing—with each PI contributing to at least one theme. These themes are anticipated to spearhead the next generation of quantum technology that will help address the challenges of modern society.

The reporting period has been successful in terms of ground-breaking science and innovation. The department produced 819 research articles, 97 PhD candidates graduated successfully, and two companies were started. At an organisational level, we formally implemented the flat PI structure and finalised the establishment of the QuTech institute. We attracted new staff at both the assistant and associate professor level and doubled the number of female PIs.

In the coming years we will invest in our newly chosen research themes by attracting at least one PI and committing a sizeable fraction of our reserves we will cement our leading position in quantum matter, transduction and sensing.

Key objectives of the coming period are:

- Further strengthen internal cohesion and collaboration
- Initiate a large programme on Quantum Transduction by committing our reserves
- Increase diversity in our junior and senior staff
- Enhance our culture of inclusiveness
- Expand our Open Science activities
- Continue to optimise our organisational structure to find the best balance between PI independence and buy-in in the department through transparent and inclusive decision making
- Implement a new financial model
- Achieve a smooth transition to our new building



Case Study

Case study

Case study: QphoX

From fundamental research to industrial application

The future landscape of quantum information processing will most likely consist of various physical systems with particular favourable attributes for the storage, measurement and manipulation of quantum states. Anticipating the need to allow these systems to communicate with one another, the QN department actively pursues the theme of *quantum transduction*. Using technology that originated from basic research within that theme, in 2021 the start-up company QphoX was founded. By creating remote entanglement links between distantly separated quantum processors, QphoX aims to present the first viable solution for scaling the performance of today's most advanced quantum computers.

From microwaves to optics

In particular, QphoX focuses on transduction of quantum information between microwave-based quantum processors and fibre-optic network links. Leading candidates for (superconducting) quantum processors rely on microwave technology for on-chip interaction and readout. Scalability of such architectures is hindered due to wiring and heat-load constraints resulting from the required cryogenic environment, calling for an alternative means of communication. Optical fibres are proven technology for reliable, low heat-load, long-distance telecommunication.

QphoX products will offer bidirectional transduction between these two technologies, allowing for the entanglement of remotely located, high-fidelity microwave quantum processors over room temperature fibre-optic networks. As quantum hardware tends to operate at incompatible non-telecom frequencies, a notable challenge consists of wavelength conversion from a diverse set of quantum resources to a unified telecom frequency. With their *Quantum Modem*TM, QphoX will address this and other challenges currently prohibiting the development of a universal, scalable quantum internet.

Two-step conversion

Successful transduction of quantum states can only happen in a system that ensures high efficiency and minimal added noise. QphoX's technology is based on optomechanical crystals in the form of silicon nanobeams. These are coupled to optical waveguides and microwave piezoelectric circuits for interfacing with networks and processors, respectively.

The quantum transducers work by coherently interconverting microwave and optical photons through a mechanical intermediary resonator. As such, the electro-optic interaction is essentially split into two distinct interfaces:

- an electro-mechanical interface, enabled by the piezoelectric interaction in nanobeam material
- an opto-mechanical interface, realised by photo-elastic coupling

An immediate advantage of this technique is the reduction in optical power that is required with the consequence of drastically decreasing the absorption induced heating of the device and the noise added in the conversion process. The transduction process is, importantly, fully bidirectional. Transducing the microwave signal up to optical frequencies allows the qubit state to be accessed using ultra-sensitive optical photodetectors. This effectively replaces the readout coaxial cable and cryogenic amplifiers with a fibre-optical cable, drastically reducing the heat load to the dilution refrigerator per line.

Company profile

QphoX started in April 2021 with 2 M€ seed funds from several investors. In December 2021, it acquired an additional 6.5 M€ from the European Innovation Council (EIC) through their Accelerator grant instrument. The company, led by CEO Simon Gröblacher, currently has 10 employees and is located in the Applied Physics building. The initial portfolio will encompass several products: ultra-low power cryogenic microwave to optical power meters, single- to few-photon QPU optical readout modules, and a fully bidirectional *Quantum Modem*TM. With proof of principle already realised in 2018, the team are now working toward a product prototype (TRL6) of a microwave to optical quantum transducer.

Products developed by QphoX will enable technologies in the high-performance computing and quantum processing, and quantum networks market sectors. The total addressable market (TAM) for these sectors is estimated to reach USD \$65B by 2030. Customers of QphoX will consist of quantum processor manufacturers who require transduction solutions to produce large processors capable of running algorithms with real world applications. While QphoX has first-mover advantage, the company could face competition from future spinouts from various academic research groups.



Summary Radiation Science and Technology

The Department of Radiation Science and Technology aims to master the use of neutrons and ionising radiation for better materials, products and therapies for a healthy and sustainable world. Central to our expertise is the interaction of radiation with matter, and central to our research is the use of ionising radiation as a probe and tool. Our main radiation sources are the TU Delft research reactor, radionuclides (e.g., produced in our reactor) and the proton beam at HollandPTC.

We focus on Material Science for energy conversion and storage, Health Technology for imaging and radiation therapy, Nuclear Technology, and on the development of new instruments and sample environments. Our strategy is to focus on topics where the use of our radiation-based research infrastructure (neutrons, protons, electrons, positrons and gamma rays) gives us a leading edge. Examples are neutron depth profiling on lithium-ion batteries, neutron diffraction on materials as they are being synthesised, positron detection of atomic-scale defects, neutron imaging of objects, biomedical imaging, radionuclide production and therapy, proton therapy and the thorium molten salt reactor.

In the past five years we have rejuvenated our scientific staff by hiring five tenure-track assistant professors and made a successful transition towards a collaborative department of PIs organised in small disciplinary groups who form ad-hoc teams to address societal and scientific challenges. Our reactor and existing instruments have been upgraded and new instruments have been developed and installed. With the successful commissioning of the cold neutron source, expected in 2023, the capability and capacity of many of our instruments will increase strongly, leading to many new opportunities for materials research. This brings us in pole position for the future.

In the coming years we will continue to hire excellent scientists in the field of neutron science and radiation biophysics to strengthen our focus on materials science and health technology.

Our ambition is to explore new fields in materials science to which our expertise and instruments can uniquely contribute. The radiation biophysics position will bridge our expertise on internal radionuclide therapy and external radiation therapy and, together with our Convergence partners, combine these with other therapies like hyperthermia. We will continue to upgrade our sample environments towards more extreme conditions and towards operando and in-situ research to monitor processes in energy storage/conversion and in material synthesis processes. In the nuclear field, we will enforce our role as an independent advisor to the Dutch government, and as the main educator in the Netherlands of nuclear technology students and engineers.

Together with RID we aim to promote our radiation-related infrastructure in national and European research programmes and other large initiatives like the ESS. Our ambition is to take initiative and co-shape these programmes to enhance the valorisation of our expertise and infrastructure. As confirmed by the benchmark interviews, the declining number of research reactors in Europe and the increasing importance of small research reactors as a portal to large scientific infrastructure, increases the importance of a well-equipped reactor with easy access like we have in Delft.

We will continue to improve our academic culture by fostering a culture of inclusiveness and collaboration with sharing (Open Science / open data) as a leading principle. Our target is to hire a tenure-track assistant professor every two years and achieve gender balance in the department within ten years. In the next period, we want to establish a culture with our PIs and supervisors in which PhD candidates deliver approved theses within the contract term without excessive stress. On the financial side, we aim to achieve a net balance in the lump-sum, leaving more budget for new talent, larger start-up grants, advanced infrastructure and creative initiatives.



Case Study

Case study

Cast study: Next-Generation Lithium Batteries

As an example of a research strategy that benefits from the direct interaction with neutron instrument development, we discuss operando neutron depth profiling to study the behaviour of lithium in next-generation lithium batteries.

Societal relevance

The urgency posed by global warming to transform our fossil fuel-dependent society into one based on renewable energy sources creates grand scientific and technological challenges, one of them being energy storage. Batteries are now seen as key energy storage technology especially for electrification of transport and for short time-scale storage to stabilise the electrical grid when it is dominated by intermittent renewable energy sources such as sun and wind. As a result, the demand in Li-ion batteries is rising by approximately 20% per year, driving the search of safer, higher-performance, cheaper and more environmentally benign batteries. The Storage of Electrochemical Energy (SEE) group's material science programme within RST has been growing steadily in size and in quality during 2016 – 2020, including new battery directions such as solid-state batteries addressing safety issues (with publications in for instance Nature Materials (1), Joule (2), JACS (3) and Nature Communications (4)) and Na-ion batteries addressing critical material challenges (with publications in Science (5) and JACS (6)). Neutron-based characterisation methods and technique developments for battery research are a key ingredient of the SEE group, demonstrated by this case study on Neutron Depth Profiling (NDP) of lithium in batteries.

Li-ion batteries and Neutron Depth Profiling

Li-ion batteries are based on Li storage in the negative and the positive electrode, and Li-ion transport through the electrolyte membrane between these two electrodes. Understanding where and why the Li-ion transport is hindered is critical knowledge, as this determines how fast the battery can be charged and discharged. The second critical aspect is where and how much Li is irreversible captured, as this determines the cycle life of the batteries. However, monitoring the whereabouts of Li, a light element, is challenging, especially during battery (dis)charging. At RST it was realised that Neutron Depth Profiling (NDP) may be used to measure the Li density as a function of the (depth) position while cycling a battery. Early attempts in 2011 demonstrated that this can be achieved under in-situ conditions in thin films (microbatteries), revealing the Li movement within a battery upon charging/discharging.

An ERC Starting Grant allowed us to extend this technique to regular Li-ion batteries, including a liquid electrolyte, and to discover what relevant phenomena can be investigated with NDP. The sample environment was developed to perform operando NDP measurements in battery cell configurations that are representative for commercial Li-ion batteries, thus strongly extending the possibilities. It was demonstrated that operando NDP allows to monitor (1) the rate-limiting Li-ion transport process by locating Li-ion gradients that limit the maximum (dis)charge rate and (2) the evolution of inactive Li during battery cycling (causing capacity loss and end of life). Both processes are responsible for key performance parameters of batteries. This has provided substantial fundamental understanding in batteries and offers infinite possibilities for scientific and application driven studies in the rich diversity of battery chemistries that are being developed (electrodes and electrolytes).

Science and valorisation

An NWO Vici grant was awarded (2018), in part to further develop the operando NDP methodology to three dimensions and extending it to solid-state batteries (an emerging battery concept that requires battery stack pressure) and to use operando NDP to guide the development of new battery materials and solutions. For example, it has helped understand the impact of electrolyte formulations on next-gen Li-metal and Si anodes as well as in next-gen cathodes sulphur and Ni-rich NMC (publications in JACS (7), Nature Communications (8,9), Adv. Mat. (10) and Adv. En. Mat. (11) during 2016-2020). Becoming an important asset for battery research, the technique has contributed to international scientific collaborations, third-money stream collaborations (e.g., Shell, Leyden-Jar, RGS) and activities in large consortia projects (e.g., Big Map in the EU Battery2030+ programme in 2020, NWA-ORC BatteryNL in 2022, part of several EU proposals submitted in Battery2030+).

Developers and producers of battery electrodes have recognised the importance of the technique in understanding the transport and degradation processes, based on which direct collaborations have been set up (Leyden-Jar) and are being set up (E-magy, LionVolt, SAFT, ACC).



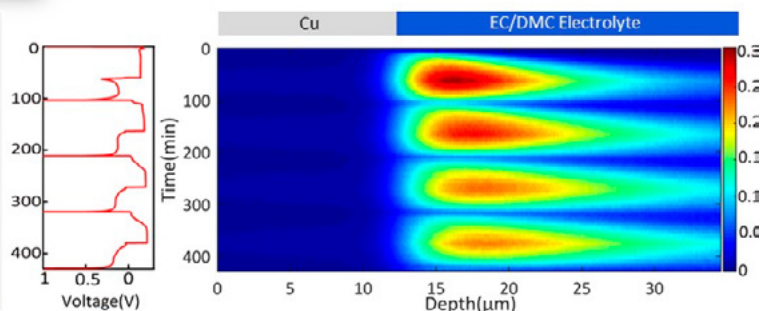
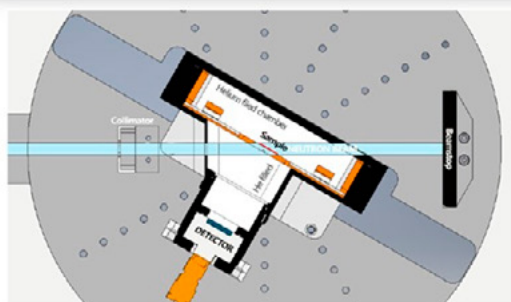
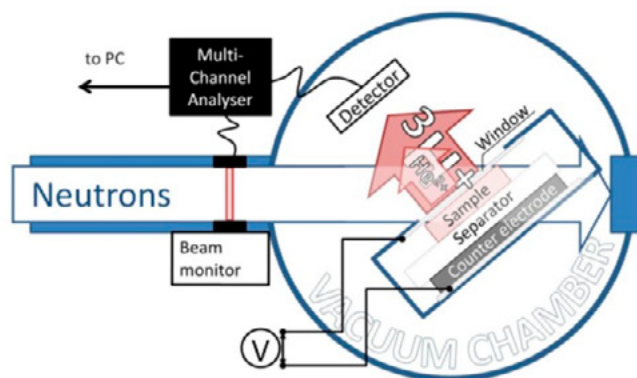


Figure. Top-left: Overview of the NDP instrument. Top-right: Schematic setup of operando NDP. Neutrons are captured by ^6Li , producing two charged particles with a well-defined energy ($^3\text{H}^+$ and $^4\text{He}^{2+}$) that are measured by a detector placed perpendicular to the battery. By measuring the energy loss of the charged particles, the depth of the Li can be determined based on the density of the materials. Bottom-left: Detailed schematic of the pouch cell battery holder with integrated detector for operando measurements. Bottom-right: Operando measurement of the Li-density (red is more dense, blue less dense) during four charge/discharge cycles of a Li-metal anode.

Projected developments of the RID-NDP setup

One of the next goals is to develop sample environments to enable analysis of solid-state batteries, which requires application of external pressure and temperature control. Especially applying pressure is challenging as the window between the Li of interest and the detector should be in the micrometre range. One approach in the running NWO-Vici project is to introduce a collimator, via which the detector can apply pressure on the solid-state battery under investigation, which will be further to be exploited in the recently granted NWA-ORC project (BatteryNL 2022).

A next step that is envisioned is to combine a collimator with a position-sensitive, energy-discriminating detector which enables 3D NDP, thus 3D imaging the Li in Li-ion batteries in a single shot. This would mean a significant step forward in Li imaging, currently only possible indirectly through neutron imaging, which is much more demanding in neutron flux, and can only be done with a limited time resolution and for a dedicated (not representative) battery design. In contrast, the 3D NDP concept allows to investigate standard battery pouch cells, opening a wealth of opportunities both scientifically as well as battery engineering related. It would provide unique insight into inhomogeneous lithiation of electrodes, a primary source of battery degradation, and into the charge transport limitations that determine the maximum charge rate. Currently the concept is under investigation and will be part of future proposals to realise the concept and its application to the field of batteries.

References:

1. Clarifying the relationship between redox activity and electrochemical stability in solid electrolytes. Schwietert, T. K., Arszewska, V. A., Wang, C., Yu, C., Vasileiadis, A., de Klerk, N. J. J., Hageman, J., Xu, Y., van der Maas, E., Kelder, E. M., Ganapathy, S., Wagemaker, M. & More Authors, 2020, In: **Nature Materials**. 19, 4, p. 428-435 8 p. IF: 47.6.
2. Revealing the Impact of Space-Charge Layers on the Li-Ion Transport in All-Solid-State Batteries. Cheng, Z., Liu, M., Ganapathy, S., Li, Z., Zhang, X., He, P., Zhou, H., Wagemaker, M. & Li, C., 2020, In: **Joule**. 4, 6, p. 1311-1323 13 p. IF: 41.2
3. Unravelling Li-Ion Transport from Picoseconds to Seconds: Bulk versus Interfaces in an Argyrodite Li₆PS₅Cl-Li₂S All-Solid-State Li-Ion Battery Yu, C., Ganapathy, S., De Klerk, N. J. J., Rosłóń, I., van Eck, E. R. H., Kentgens, A. P. M. & Wagemaker, M., 2016, In : **Journal of the American Chemical Society**. 138, 35, p. 11192-11201 10 p. IF: 16.4
4. Accessing the bottleneck in all-solid state batteries, lithium-ion transport over the solid-electrolyte-electrode interface Yu, C., Ganapathy, S., van Eck, E. R. H., Wang, H., Basak, S., Li, Z. & Wagemaker, M., 1 Dec 2017, In : **Nature Communications**. 8, 1, 1086. IF: 17.7
5. Rational design of layered oxide materials for sodium-ion batteries Zhao, C., Wang, Q., Yao, Z., Wang, J., Sánchez-Lengeling, B., Ding, F., Qi, X., Lu, Y., Wagemaker, M. & More Authors, 2020, In: **Science** (New York, N.Y.). 370, 6517, p. 708-711. IF: 63.1
6. Revealing High Na-Content P2-Type Layered Oxides as Advanced Sodium-Ion Cathodes Zhao, C., Yao, Z., Wang, Q., Li, H., Wang, J., Liu, M., Ganapathy, S., Lu, Y., Wagemaker, M. & More Authors, 2020, In: **Journal of the American Chemical Society**. 142, 12, p. 5742-5750 IF: 16.4
7. Spatiotemporal Quantification of Lithium both in Electrode and in Electrolyte with Atomic Precision via Operando Neutron Absorption Harks, P. P. R. M. L., Verhallen, T. W., George, C., van den Biesen, J. K., Liu, Q., Wagemaker, M. & Mulder, F. M., 2019, In: **Journal of the American Chemical Society**. 141, 36, p. 14280-14287 IF: 16.4
8. Operando monitoring the lithium spatial distribution of lithium metal anodes Lv, S., Verhallen, T., Vasileiadis, A., Ooms, F., Xu, Y., Li, Z., Li, Z. & Wagemaker, M., 2018, In : **Nature Communications**. 9, 1, 2152. IF: 17.7
9. Interface chemistry of an amide electrolyte for highly reversible lithium metal batteries Wang, Q., Yao, Z., Zhao, C., Verhallen, T., Tabor, D. P., Liu, M., Ooms, F., Kang, F., Wagemaker, M. & More Authors, 2020, In: **Nature Communications**. 11, 1, 4188. IF: 17.7
10. Review of Recent Development of In Situ/Operando Characterization Techniques for Lithium Battery Research Liu, D., Shadike, Z., Lin, R., Li, H., Liu, M., Ganapathy, S., Qin, X., Wagemaker, M., Yang, X. Q. & More Authors, 2019, In: **Advanced Materials**. 31, 28, 57 p., 1806620. IF: 32.1
11. Accelerating Battery Characterization Using Neutron and Synchrotron Techniques: Toward a Multi-Modal and Multi-Scale Standardized Experimental Workflow Atkins, D., Capria, E., Edström, K., Famprikis, T., Grimaud, A., Jacquet, Q., Johnson, M., Matic, A., Wagemaker, M. & More Authors, 2021, In: **Advanced Energy Materials**. 12, 17, 20 p., 2102694. IF: 29.7



