

News from the Physics of Life Advisory Committee

The newsletter you are reading now is one of the initiatives of the Advisory Committee (in Dutch: werkgemeenschapscommissie WGC) Physics of Life to foster a lively community of biophysicists and affiliated researchers. The WGC's role in NWO is two-fold: sharing information from the NWO organization to you, the scientists in the lab. You can use this to your advantage when finding appropriate funding, when seeking new collaborations, or finding your way into the Dutch Physics of Life community. The other part of our mission is to represent the scientists in our field, such that our opinions and experiences are optimally incorporated into NWO's policy and funding schemes. Science is continuously evolving and we aim to keep Physics of Life active, innovating and well-funded.

With NWO Biophysics (previously known as Dutch Biophysics), we have our yearly conference that brings not only Dutch biophysicists together, but also international speakers, as well as a diverse group of scientists from affiliated Life Sciences, Chemistry and Physics. NWO Biophysics has a unique position in the ever-changing scientific landscape, and we hope that you will continue to enjoy this meeting. Regularly, we have discussions on how this meeting fits with other (NWO-organized) conferences, but as long as the turn-up is as large as it is now, the meeting clearly has a large support.

Recently, the WGCs were asked to reflect on the evaluation of the talent scheme (Veni-Vidi-Vici). Several suggestions for changes were proposed, including shifting focus to more applied research, explicit support for team-science, reduced support for the Vidi scheme, and better coordination with the ERC granting scheme. In our WGC advice, we pointed out that fundamental

science is heavily under-supported in the entire grant-landscape, and the talent-line is one of the few options to pursue basic, curiosity driven research. This should not change and if anything, more support is needed. We also pleaded for separate expertise panels to come to better informed decisions, and for simple procedures. Other WGCs gave similar advice to their representing tables. An NWO Working Group gathered input from many committee including the WGCs, Round Tables and Domain Boards and overall only minor changes are suggested and thus to largely maintain the current talent scheme. The NWO Executive Board will use this feedback to decide on the follow up. We will keep you updated on the matter.

In terms of NWO representation, we have experienced that the hierarchical advisory structure in which the Science domain is currently organized (WGCs, disciplinary Round Tables, ENW board) could be improved. We sometimes wondered what we as a WGC can contribute in this large organization and when asked for advice, the deadlines are often too short to consult our community. To shorten the lines in the organization, our WGC has proposed to include the chairs of the WGCs as members of the Physics Round Table. After consultation of the other WGCs who supported this proposal, the Physics Round Table forwarded it to the ENW board and they also agreed. So, in the near future you will be one step closer to the Physics Round Table, which makes it easier to reach out and to stay on top of current activities in NWO.

We hope that you continue to participate in our community and help us represent Physics of Life in the best possible way. You can do so by alerting colleagues to subscribe to our mailing list. It's not exclusive (you

can participate in multiple working groups). Since our field is closely associated with many other disciplines, it's not always obvious that you belong to the Physics of Life community or you may think that you fit better in another community. However, to make the point that Physics of Life has a broad constituency it is important that we organize ourselves in a tangible way. Registering to our newsletter is a small step to do so and

in return you will receive this newsletter a couple of times a year. We have a section on new colleagues, who can introduce themselves so we stay aware of new hires. If you have a new colleague, please let her/him know of this opportunity or send us an email. You may also advertise vacancies with a brief description and a link. And foremost: when you have any thoughts on our activities or those of NWO, let us know.

- Prof. John van Noort (chair; LEI)
- Dr. Kristina Ganzinger (AMOLF)
- Prof. Lukas Kapitein (UU)
- Dr. Nicholas Kurniawan (TU/e)
- Prof. Patrick Onck (RUG)
- Prof. Peter Peters (MU)
- Dr. Greg Stephens (VU)
- Dr. Rifka Vlijm (RUG)

For questions, ideas, announcements, new appointments, grants, and other news items, please contact:

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New appointments, vacancies, grants, prizes, and other news.

- In memoriam Claire Wyman. On 10 March Professor Claire Wyman passed away. Claire was Professor of Molecular Radiobiology at the Departments of Radiotherapy and Molecular Genetics at Erasmus MC, Medical Delta Professor and Program Director of Nanobiology. Our thoughts and sympathies are with her family and we highly appreciate her large contribution to the Dutch biophysics community. Not only has she been chair of our working group, she was also always present during biophysics conferences and asked critical and stimulating questions to further the field. We will miss her input.
- Dr. Markus Weingarth, Dr. Marvin Tanenbaum and Dr. Martijn Luijsterburg received an ERC Consolidator grant¹
- Prof. Carlijn Bouten, Prof. Sjoerd Stallinga, Prof. Siewert-Jan Marrink, Prof. Van Steensel and Prof. Van Oudenaarden received an ERC Advanced grant²
- Vacancy at Max Planck Institute of Molecular Cell Biology and Genetics (Dresden) for Custom Light Microscopy Developer and/or Biophysicist³.
- Alexander van Oudenaarden elected to the American Academy of Arts and Sciences⁴
- Postdoc vacancy: Discovering the biophysical basis of CAR T cell function. Research group of Kristina Ganzinger (AMOLF)⁵

¹ <https://erc.europa.eu/news/erc-2021-consolidator-grants-results>

² <https://erc.europa.eu/news/erc-2021-advanced-grants-results>

³ <https://www.mpi-cbg.de/join-us/open-positions/job-offer/custom-light-microscopy-developer-and-or-biophysicist>

⁴ <https://www.hubrecht.eu/alexander-van-oudenaarden-elected-to-the-american-academy-of-arts-and-sciences/>

⁵ <https://amolf.nl/jobs/postdoc-discovering-the-biophysical-basis-of-car-t-cell-function>

Events & meetings

What	When	Where	More information
International Mass Spectrometry Conference	27 August – 2 September	The Maastricht Exhibition & Congress Center	https://www.imsc2022.com/
EMBL Conference Transcription and chromatin	27 - 30 August	EMBL Heidelberg and Virtual	https://www.embl.org/about/info/course-and-conference-office/events/trm22-01/
NWO CHAINS 2022	21 and 22 September 2022	Koningshof, Velhoven	https://nwochains.nl/
NWO Biophysics 2022	10 and 11 October 2022	Koningshof, Velhoven	https://www.nwo.nl/en/meetings/dutchbiophysics
NWO Physics 2023	4 and 5 April 2022	Koningshof, Velhoven	https://www.nwo.nl/en/meetings/physicsveldhoven

New colleagues

Jorine Eeftens (RU)

My research focuses on understanding the physics of nuclear organization, in particular the organization of chromatin in space and time. I was introduced to the Dutch biophysics community during my PhD in the group of Cees Dekker at the TU Delft. My research focuse on using single-molecule techniques to elucidate the molecular mechanism of chromatin organizing proteins, in particular condensin. We discovered that these proteins are in fact motors that translocate along DNA.

After my PhD I moved to Princeton University to the group of Clifford Brangwynne, where I became interested in how another classical physics phenomenon might be implicated into chromatin organization: phase-separation. I focused on the interplay between condensates and epigenetic modifications, and got further interested in material properties of intracellular condensates, in particular viscoelasticity of the nucleolus.

Last September 2021, I joined the Radboud University Nijmegen as a tenure track assistant professor. Our lab aims to examine the functional relevance of the genome architecture and the biophysical mechanisms that drive it. We use a multifaceted and interdisciplinary approach, ranging from single-molecule biophysics to genomics and engineering. I am specifically interested in the role of histone modifications on chromatin folding, dynamics, compartment formation, and mechanical strength.

I am excited to be part of the Dutch Biophysics community again, and I look forward to meeting all of you in person soon.



David Dulin (VU Amsterdam)

I am a single-molecule biophysicist who build high-end microscopes to investigate life one molecule at a time. I apply both force and fluorescence spectroscopy techniques to study protein-nucleic acids interactions. My main research topic focuses on how RNA viruses, such as SARS-CoV-2, replicate and transcribe their genome.



I studied physics and math at University of Bordeaux in France, and move to Paris in 2006 to do my PhD thesis in single molecule biophysics under the supervision of Nathalie Westbrook and Karen Perronet (Institut d'Optique-University Paris-Sud) to study the bacterial ribosome elongation kinetics. In 2009, I started in the Nynke Dekker lab (TU Delft) as postdoc, where I pioneered new magnetic tweezers assays (real-time high-throughput and high-resolution magnetic tweezers) to investigate viral RNA polymerases from bacteriophage and human RNA viruses. In collaboration with Craig Cameron (State College, now UNC Chapel Hill, USA) and Martin Depken (TU Delft), we revealed the nucleotide addition cycle of human poliovirus RNA polymerase, and the mechanism of action of antiviral nucleotide analogs. In 2014, I moved to another postdoc in the Kapanidis lab at the University of Oxford, where I used single-molecule FRET to investigate bacterial initial transcription.

I moved in 2016 to FAU Erlangen-Nuremberg in Germany for my first PI position as junior group leader to investigate cellular transcription and RNA virus replication using single-molecule techniques. My lab achieved several innovations in nucleic acid constructs fabrication, magnetic tweezers stability and resolution. We leveraged these developments to achieve the first single molecule studies of the SARS-CoV-2 replication machinery, revealing its nucleotide addition cycle and a mechanism of action of Remdesivir. Since 2021, my lab moved to the Physics of Living System section at VU Amsterdam as assistant professor within the BaSyC consortium to build a synthetic cell. I am investigating bacterial transcription-translation coupling, while continuing my research on RNA viruses and antiviral drugs discovery. Since its inception, my lab has received several grants from the German Research Foundation (DFG) and NIH. I am very excited to be back in the Netherlands and collaborate with the vibrant Dutch biophysics community.

Granted projects NWO

Vici⁶

Transport in neurons

Prof. dr. L.C. Kapitein, Utrecht University

Long protrusions of neurons, axons, wire our nervous system. Their extreme length is enabled by motor proteins that transport cellular components over microtubules. Disruption of this process can result in disease. This research will use innovative microscopy to map the axonal roads and traffic rules in health and disease.

Filming the birth of intestinal tumors for finding new prevention methods

Prof. dr. J. van Rheenen, The Netherlands Cancer Institute

Preventing colorectal cancer is better than curing this disease. In this project, we will film the early steps of tumorigenesis and identify factors that can be targeted to decrease this risk. These experiments have the potential to identify novel ways to prevent or revert the risk of developing colorectal cancer.

Stop-fix-go: dealing with roadblocks on the gene-track

Dr. M.S. Luijsterburg, Leiden University Medical Center

Protein machines that read our genes get stuck on damage in the DNA template. DNA damage must first be repaired before these protein machines can continue. How this works is currently unknown. The researchers will use genetic, cell biological and genome-wide methods to unravel how these processes work.

Open Competition XS⁷

Unravelling neuronal growth cone mechanobiology via sub-micrometric fabrication and super-resolution microscopy

dr. A. Accardo (Delft University of Technology)

Comparing the growth of healthy and diseased neurons is fundamental to understand and tackle neurodegenerative diseases (e.g. Alzheimer's, Amyotrophic lateral sclerosis). The growth cone (GC) is a mechanosensitive structure, which probes the surrounding environment and connects neurons. To date, the GC has mainly been studied by employing unrealistic 2D bulky "petri-dish" configurations unable to mimic the brain microenvironment. We will pioneer a reproducible 3D GC model by combining 3D printed sub-micrometric biomaterials, able to simulate the geometrical and mechanical features in the brain, together with super-resolution microscopy. The results will pave the way for comparative studies involving diseased neurons.

Identification of proteins that protect DNA during extreme environmental conditions in diapaused killifish embryos and investigation of their application potential in human

prof. dr. E. Berezikov (Universitair Medisch Centrum Groningen)

Protection and repair of DNA is important to prevent cancer and delay ageing, and finding novel agents that can improve DNA protection in human is needed. African killifish *Nothobranchius furzeri* lives in ponds that dry out during a hot season. To survive the drought, killifish embryos enter into diapause, a low metabolic state with halted development, in which tissues and cells are highly protected from harsh environmental assaults by largely unknown mechanisms. This project will identify proteins that protect DNA from damage during diapause in killifish and test whether they can be used to improve DNA protection in human.

⁶ <https://www.nwo.nl/en/researchprogrammes/nwo-talent-programme/projects-vici/vici-2021>

⁷ <https://www.nwo.nl/en/news/twenty-six-groundbreaking-research-projects-launched-open-competition-domain-science-xs-2>

Innovative wound healing with 3D bioprinted living microalgae

dr. F. Gao (Wageningen University & Research)

Non-healing wound is a big social problem for 1-3% of the whole population, resulting in billions of medical care costs. Available wound healing dressing cannot solve the problem of bacteria colonization and local hypoxia, especially for chronic patients. An innovative idea of developing hydrogel dressing with photosynthetic microalgae is proposed to provide oxygen for faster skin-tissue repair and antibacterial exopolysaccharides. A microalga with high exopolysaccharides content will be three-dimensional bioprinted with hydrogel for wound healing dressing. The optimized dressing will be used for wound healing treatment with diabetic mice. This project will provide an innovative biological solution for wound healing.

Enlightening large nanogaps to visualize biomolecules

dr. O.S. Ojambati (University of Twente)

The most powerful optical microscopes have now reached a plateau in their performance. This is because they use fluorescent labels to image biological structures. The labels also affect the properties of these bio-structures. A way to solve this problem is to use a nanogap which is a very efficient way to concentrate light but it only works for small molecules. When nanogaps are made larger to fit in large structures, the efficiency drops. If this problem is solved, nanogaps can be used to image proteins and viruses. This proposal aims to solve this problem by shaping light.

High-throughput identification of bacterial RNA chaperone proteins

dr. D. Incarnato (University of Groningen)

RNA is a key molecule in most cellular processes. Many RNA's functions are mediated by its ability to form intricate structures, a process known as RNA folding. A group of proteins called RNA chaperones has been proposed to assist the RNA in this process. By studying how the loss of these proteins affects the structure of the RNA inside bacterial cells we aim to understand the rules governing RNA folding. As RNA folding regulates protein production, by focusing on RNAs involved in cell growth and survival we hope to identify new targets for the development of more effective antibacterial drugs.

Interfacing with the nervous system at single-cell resolution for the next generation of artificial retinas

dr. D.G. Muratore (Delft University of Technology)

The next generation of artificial retinas will rely on electronics capable of reproducing the natural pattern of activation of the different neuron types with single-cell and single-spike resolution. They will need to calibrate the stimulation parameters based on the recorded neural responses in a closed-loop manner. However, due to the complex electrode-tissue interface, a stimulation artifact corrupts the recorded neural activity at different electrodes, severely limiting the calibration process. Here, we propose a new mechanism suitable for implantable massively parallel interfaces to mitigate artifacts using linear models of the electrode-tissue interface and convex optimization algorithms.

Open Competition M⁸

Understanding Tubulin Detyrosination: Mechanism, Structure and Function

Prof. Thijn Brummelkamp & Prof. Anastassi Perrakis (Netherlands Cancer Institute/Netherlands Cancer Institute)

The skeleton of our cells consists largely of microtubules, polymers that consist of alpha and beta tubulin dimers. Microtubules play an important role in the transport of molecules within the cell and are also the target of commonly used therapeutics such as chemotherapeutics (taxanes). Microtubules are modified in various ways, giving them different properties. The first modification described is detyrosination but the responsible enzymes remained unknown. Now, after more than 40 years, we have discovered these enzymes allowing us to study their mode-of-action and the importance of this modification.

How do we package newly copied DNA?

Dr Francesca Mattioli (Hubrecht Institute)

Every day, billions of cells divide in our body. As the cells divide, they need to maintain their function to prevent the onset of diseases, such as cancer. Cell function is determined by the DNA and its packaging system. So, when cells divide, they need to inherit a copy of the DNA in the right packaging format. How this is controlled remains unclear. The team will visualize how key proteins responsible for packaging newly copied DNA perform their function. The work will provide fundamental knowledge on how to target this process in disease.

Molecular antibiotic fishing rods to decipher resistance

Dr Willem Velema (RU)

Antibacterial resistance is a major threat to human health worldwide. Here, we will decipher mechanisms that bacteria use to evade antibiotics. We will chemically modify antibiotic drugs to turn them into molecular fishing rods to catch RNA. After applying them to bacteria we will analyse what we caught, which can tell us how bacteria utilize RNA to

Gravitation⁹

IMAGINE!: Seeing and steering cells in our tissues

Full project title (IMAGINE! Innovative Microscopy and Guidance of Cells in their Native Environment)

The main applicants are Anna Akhmanova (UU), Peter Friedl (RadboudUMC), Jacco van Rheenen (NKI and Oncode Institute), Madelon Maurice (UMC Utrecht and Oncode Institute), Geert Kops (Hubrecht Institute and Oncode Institute) and Lukas Kapitein (UU). Also involved are researchers from TU Delft, TU Eindhoven, Prinses Máxima Centrum and ErasmusMC, and various microscopy centres, including the UU's Biology Imaging Center.

Cells, life's basic building blocks, have been extensively studied, but how cells self-organise into tissues and how molecular processes inside cells enable tissue formation is poorly understood. IMAGINE! will bring together biology and technology experts to address this major challenge by studying and manipulating cells at the molecular level in their native tissue environment. The programme will provide essential knowledge and tools for regenerative medicine, optimising therapies and repurposing existing drugs.

⁸ <https://www.nwo.nl/en/news/fourteen-innovative-research-projects-launched-through-open-competition-domain-science-m>

⁹ <https://www.nwo.nl/en/news/more-142-million-euros-groundbreaking-fundamental-research>

CURE4LIFE: Development and societal impact of stem cell based genetic medicines

For a number of rare genetic diseases, lifelong cure can be obtained by correcting the genetic defect in the patients' own blood stem cells. Many curative gene therapies do not reach patients for reasons other than a lack of treatment quality. The consortium proposes to develop platform infrastructure that can be used for many diseases rather than every time focusing on one approach unique for each disease. Simultaneously they address challenges regarding the regulation, reimbursement and public acceptance of these therapies in a knowledge hub for dialogue with society.

Consortium: Leiden University Medical Center, Erasmus MC, VU Amsterdam, Utrecht University, Leiden University, Avans University of Applied Sciences, UMC Utrecht, Radboud university medical center, Radboud University, Batavia Biosciences, ISHEO, Spierziekten Nederland, Prinses Beatrix Spierfonds, Miltenyi, Oscar Nederland, Foundation for Immune Disorders (SAS), Patiëntenvereniging voor Stofwisselingsziekten (VKS), Stichting Alexander, National Health Care Institute (Zorginstituut Nederland), IPOPI - International Patient Organisation for Primary Immunodeficiencies. Official secretary on behalf of the consortium: prof. dr. F.J.T. (Frank) Staal – Leiden University Medical Center (LUMC)

Amount awarded: 5.0 million Euro

CureQ: Predict, Delay & Cure polyglutamine(Q) caused neurodegeneration

There are over ten inherited neurodegenerative disorders that are caused by a similar DNA mutation, including Huntington's Disease. Recent trials are hopeful but also leave many questions. What is the best moment to start therapy? Can we predict age-of-onset more accurately, and do gene-carriers want to know this? Are there alternative therapeutic strategies possible that don't require repeated lumbar injections? What does this all mean for very young patients? Researchers from academia and biotech, neurologists, lecturers and patient foundations aim to answer these questions together, with a personalized treatment as the ultimate goal.

Consortium: Amsterdam UMC - Location AMC, Radboud university medical center, Erasmus MC, Hanze University of Applied Sciences, Leiden University Medical Center, VU Amsterdam, Princess Máxima Center for pediatric oncology, University Medical Center Groningen, Amsterdam University of Applied Sciences, Maastricht UMC+, Proefdiervrij, Campagneteam Huntington, Vico Therapeutics, ADCA/Ataxie Vereniging, VectorY, Vereniging van Huntington. Official secretary on behalf of the consortium: prof. dr. E.A.J. (Eric) Reits - Amsterdam UMC - Locatie AMC

¹⁰ <https://www.nwo.nl/en/researchprogrammes/dutch-research-agenda-nwa/research-along-routes-consortia-nwa-orc/awards-nwa-1>

NANOSPRESSO-NL: Local preparation of high-quality, personalized nucleic acid nanomedicines

NANOSPRESSO-NL specifically addresses the current mismatch between personalized therapeutic strategies and industrial centralized large-scale manufacture of medicines. The NANOSPRESSO-NL consortium is convinced that nucleic acid therapeutics are uniquely qualified for production in local hospital pharmacies in response to the needs of the individual patient. By switching towards a fully standardised platform formulation, quality control can be centred around the production process rather than the end product, quite similar to a popular method of decentralized high-quality espresso making.

Consortium: UMC Utrecht, University of Twente, Saxion University of Applied Sciences, Leiden University Medical Center, Princess Máxima Centre for pediatric oncology, Utrecht University, Leiden University, Solstice Pharmaceuticals B.V., CelluTx LLC USA, Anjarium Biosciences Switzerland, siTOOLS Biotech GmbH Germany, Lipoid GmbH Germany, Patiëntenvereniging Stofwisselingsziekten (VKS), Dutch Institute for Rational Use of Medicine (IVM), Karolinska Institute (Sweden), SINTEF (Norway), Val d'Hebron Hospital Spain, National University Singapore, European Technology Platform Nanomedicine (ETPN) (FR), Friedrich-Alexander- Universität Erlangen-Nürnberg (DE). Official secretary on behalf of the consortium: prof. dr. R.M. (Raymond) Schiffelers – UMC Utrecht

Large-Scale Neo-Cartilage Engineering: regenerative treatment technologies for osteoarthritis (LS-NeoCarE)

More than 1.5 million people in the Netherlands suffer from osteoarthritis – a degenerative joint disease. For many osteoarthritis patients, there is currently no treatment that can slow the disease process or cure it. Therefore, they struggle with pain and movement limitations every day. LS-NeoCarE wants to improve their lives by developing durable regenerative cartilage implants. These living implants are based on revolutionary stem cell, bioreactor, and 3D-printing technologies. Through the active involvement of researchers, industry, doctors, and patient organizations, the project creates support among both patients and doctors for applicability and with industry for marketing the developed implants.

Consortium: Eindhoven University of Technology, Leiden University Medical Center, UMC Utrecht, Utrecht University, Leiden University, Fontys University of Applied Sciences, University of Applied Sciences Utrecht, University of Applied Sciences Leiden, Regenerative Medicine Crossing Borders, Purac Biochem BV, Demcon, Scinus Cell Expansion BV, ASR Zorgverzekering, NC Biomatrix BV, Azar Innovations, Poietis France, Dutch Arthritis Foundation (ReumaNederland), patient participation arthritis Leiden LUMC (PPA-Leiden). Official secretary on behalf of the consortium: prof. dr. ir. K. (Keita) Ito – Eindhoven University of Technology