Nynke Dekker Lab

Living matter *matters* at
the single-molecule level

Open projects
Summer and Fall of 2018

www.nynkedekkerlab.tudelft.nl

Description of the Nynke Dekker Lab

The Nynke Dekker Lab

The Nynke Dekker Lab (nynkedekkerlab.tudelft.nl) is a highly successful research laboratory focused on understanding the key cellular process of **nucleic acid replication** from a biophysical perspective in viral, bacterial, and eukaryotic systems. We perform our studies both using purified components in-vitro and inside living cells. To study in particular the dynamic aspects of replication, we make use of state-of-the-art **biophysics** (including cutting-edge techniques such as magnetic tweezers, flow-stretched DNA tethers combined with fluorescence microscopy, and super-resolution fluorescence in living cells) that is highly integrated with **biochemistry**. Studying molecular processes using these techniques requires broad expertise; our lab is composed of a multidisciplinary team of international scientists with backgrounds in quantitative biology, (bio)chemistry, or (bio)physics. If you are interested in contributing to a **mechanistic understanding of replication**, there are plenty of opportunities for exciting and challenging BEP and MEP projects available, as described below!

Department of Bionanoscience

The Nynke Dekker Lab is located within the Department of Bionanoscience (BN) at TU Delft. The Department operates at the interface between cell biology, single-molecule biophysics, and synthetic biology, and as such research in the Department ranges from the functioning of single cells in all their complexity down to the single-molecule level. Understanding the fundamental molecular processes is of crucial importance for diverse developments and applications involved in targeted therapeutics, biomedicine, diagnostics and alternative energy sources, among others. Scientific and social events at BN are a great opportunity to have fun while strengthen your knowledge.!

Becoming a student in the Nynke Dekker Lab

What types of students are we looking for?

How does it feel to create knowledge that will change textbooks for the next generation? If you are curious and strongly motivated to generate new knowledge, and willing to learn how to systematically do so systematically, then you are a qualified applicant. With a background in either molecular biology, genetics, biochemistry, biophysics, physics, or informatics, you will have much to contribute to our team-oriented, multidisciplinary studies. You can also simultaneously develop an expertise in another area while working with us. Most importantly, you will have the opportunity to develop your own ideas and hypotheses and thereby grow into an independent scientist or professional. As such, you will be accorded equal respect and responsibility to any group member.

What do we offer?

PhD students are fully integrated into our multidisciplinary team, gaining a unique experience at the frontier of research. The projects include all aspects of experimentation and data analysis. Every student will be guided to grow in his/her planning, experimental and presentation skills and become independent to a level where he/she can make a real

contribution to research at the cutting edge of science and through well recognised international scientific journals. Typically we have several students and postdocs in the group, allowing you to interact with your fellow colleagues scientifically as well as socially.

When can you start?

You can start at any time of the year. At present, we have open PhD and postdocs positions in different projects which we intend to fill within the next 6 to 12 months. If you too would like to start during outside of this period, please contact us well in advance.

How can you find out more about the projects?

We are driven by the idea that science, fun and intellectual freedom are inseparable. Do you want to know in detail about our research and projects, you are welcome to come for a coffee discussion and also take a lab tour! You may directly contact any of the PhD students/postdocs listed on the specific projects below, or e-mail Dr. Belen Solano Hermosilla (Research Manager, B.SolanoHermosilla@tudelft.nl) or Prof. Nynke Dekker (Group Leader, n.h.dekker@tudelft.nl) for a more general overview.

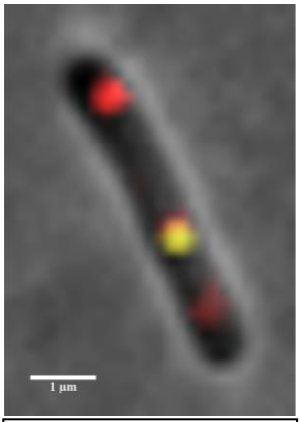
Current BEP and MEP Projects

1. Live cell imaging: understanding life and its processes via microscopy

All that life has to offer in function and diversity has a basis in how different cells and their components work together. The genetic information of the cell, DNA, provides a crucial template for all this, and any damage to this coded information can be detrimental to the organism.

- What is the goal of our research?

Our broad interest lies at the heart of understanding how the cell responds to DNA damage. The cell has the ability to harness many DNA repair pathways, depending on the type of damage, and understanding them in detail opens doors to understanding diseases when the pathways malfunction.



Super-resolution image of an E. coli bacterium containing labelled

- What tools do we use?

The bacterium *E. coli* is our experimental workhorse, involving genetic engineering and molecular biology. We use live cell, widefield fluorescence, confocal and super-resolution microscopy approaches to address our research. Interpreting such data relies on in-house and open source algorithms. In summary, in an interdisciplinary fashion we apply principles of physics to unravel biological mechanisms.

- What is the significance to society of what we do?

Antibiotic drug targets: With antibiotic resistance becoming a global phenomenon, our work on understanding bacterial replication and repair provides essential knowledge for the future / **DNA repair and cancer**: We enhance fundamental knowledge of DNA replication, errors in which are linked to the development of cancer / **Data analysis**: We develop novel analyses and algorithms to understand biological processes.

- What will your specific project look like?

We are looking for student colleague(s) interested in exploring how 'accessory helicases' function in the cell. While understood superficially so far, these helicases are believed to be critical players in DNA damage, in addition to the main replicative helicase that we know about. Evolution over thousands of years can be trusted on why a single helicase is not enough. You may choose to focus on either experimental microscopy or on quantitative data analysis

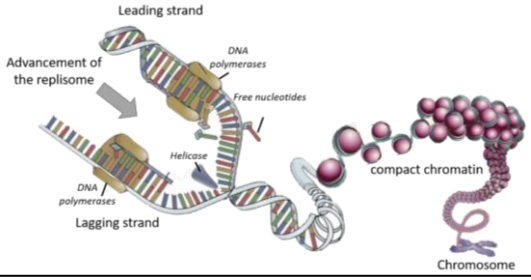
Contact
M.Sc. Sumit Deb Roy (s.debroy@tudelft.nl)
M.Sc. Filip Asscher, (bio)physicist and data analyst (f.m.asscher@tudelft.nl)

2. DNA replication: In vitro single-molecule studies of eukaryotic replication

Human beings copy a light-year's worth of DNA in their lifetimes. How this is mechanistically achieved remains under very active investigation.

- What is the goal of our research?

The replication of genomic DNA is one of the core processes that takes place during cell cycle progression and proliferation. It is performed by the replisome, a multi-protein complex that incorporates nucleotides into the genome with high fidelity while advancing and opening the double-stranded DNA. In eukaryotic organisms like ourselves, we still know little about how the replisome's proteins organize and interact in a dynamic manner to duplicate not only our genes, but also the compact chromatin environment in which they are embedded.



Replisome (polymerases, helicase, and other proteins) advancement while replicating DNA in the context of chromatin

- What tools do we use?

Due to recent advances in replisome reconstitution, we now have the opportunity to investigate the mechanics of DNA replication in eukaryotes *in vitro*. We employ state-of-the-art protein purification, protein labeling, fluorescence microscopy, magnetic tweezers, and nanofluidics to characterize the real-time dynamics of the replisome.

- What is the significance to society of what we do?

DNA repair and cancer: We enhance fundamental knowledge of DNA replication, errors which are linked to the development of cancer / **Protein labeling:** We engineer new proteins that permit the imaging of DNA replication. / **Advanced microscopy and data analysis**: We develop new imaging modalities, analyses, and algorithms to understand biological processes.

- What will your specific project look like?

We are looking for student colleague(s) interested in quantitatively exploring eukaryotic replication, including in the context of chromatin. While the overall features of eukaryotic replication are known, very little is known about the dynamics. At present, we have several projects available on experimental single-molecule microscopy, and one on quantitative data analysis. On bare DNA, we are studying the kinetics of replisome progression, the exchange dynamics between the two main polymerases, and the role of twist and torque in stalling the replisome. On chromatin, we are interested in the dynamics of histone displacement in front of the replisome and reassembly behind it, and the role the replisome plays in organizing that process.

Contact:
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