S.V.N.B. HOOKE

STUDY ASSOCIATION NANOBIOLOGY

BEP/MEP Event

14 November 2019

CONTENTS

INTRODUCTION

Dear Reader,

Welcome to the BEP/MEP event of 2019!

This event was created for the purpose of exhibiting the research groups that Nanobiology Bachelor and Master students have a chance to be a part of, so that when the time comes they can make an informed decision for which lab to join. Congratulations, you have now taken the first step towards choosing your end project!

In this booklet you will find some information concerning the subject matter, participants, and contact information of these groups. Speak to as many as you please! If you wish to learn more about the basics of BEP or MEP, the next few pages of this booklet contain some general information on how to get started. You can also visit the stall manned by Serge Donkers. He will be happy to answer all your general questions.

We wish you the best of luck, and don't be afraid to approach Anouk or me if you have any questions!

Kind regards,

Annemieke Mathissen
Commissioner of Education of S.V.N.B. Hooke

GENERALINFORMATION

There are multiple important things that you need to know about doing a Bachelor or Master End Project. A summary can be found on the following pages.

Disclaimer: S.V.N.B. Hooke cannot be held responsible for any mistakes. No rights can be derived from this information.

A Bachelor End Project is worth 20 ECTS. A Master End Project is worth 44 ECTS.

There are several requirements before you can start you BEP:
- You need to have finished your first year
- You need to have at least 60 ECTS from year 2 and/or 3.

Concerning Internship and Master end project within the Master:
- At least one of these should be followed within the Bionanoscience department or within Erasmus MC.
- Both may be followed within the Bionanoscience department but not within the same group (same PI).
- Both may be followed within the Erasmus MC but not within the same group (same PI).

GENERALINFORMATION

Step-by-step guide for your BEP/MEP:

1. Orientation

- Visit the BEP/MEP event organized by the Hooke board.
- Search for projects on the websites of research groups.
- Visit the departments and different research groups.

2. Preparation

- Find a supervisor for your project. You can find a greenlist of approved supervisors on the Bachelor and Master Nanobiology Brightspace pages.
- Fill in the BEP/MEP application form. This form should by signed by your supervisor and Serge or Tanja.
- Send the application form to thesisoffice-tnw@tudelft.nl

3. Start with your project!

All information, including a grading scheme, can be found on brightspace and in the study guide. For Brightspace go to: *Brightspace TU Delft > enroll in course Thesis Office Applied Sciences > Content > BSC End Projects / MSc End Projects*

If you have further questions, you can contact the following people:

Academic counsellor:

Tanja Hilkhuijsen: studieadviseur-nb@tudelft.nl

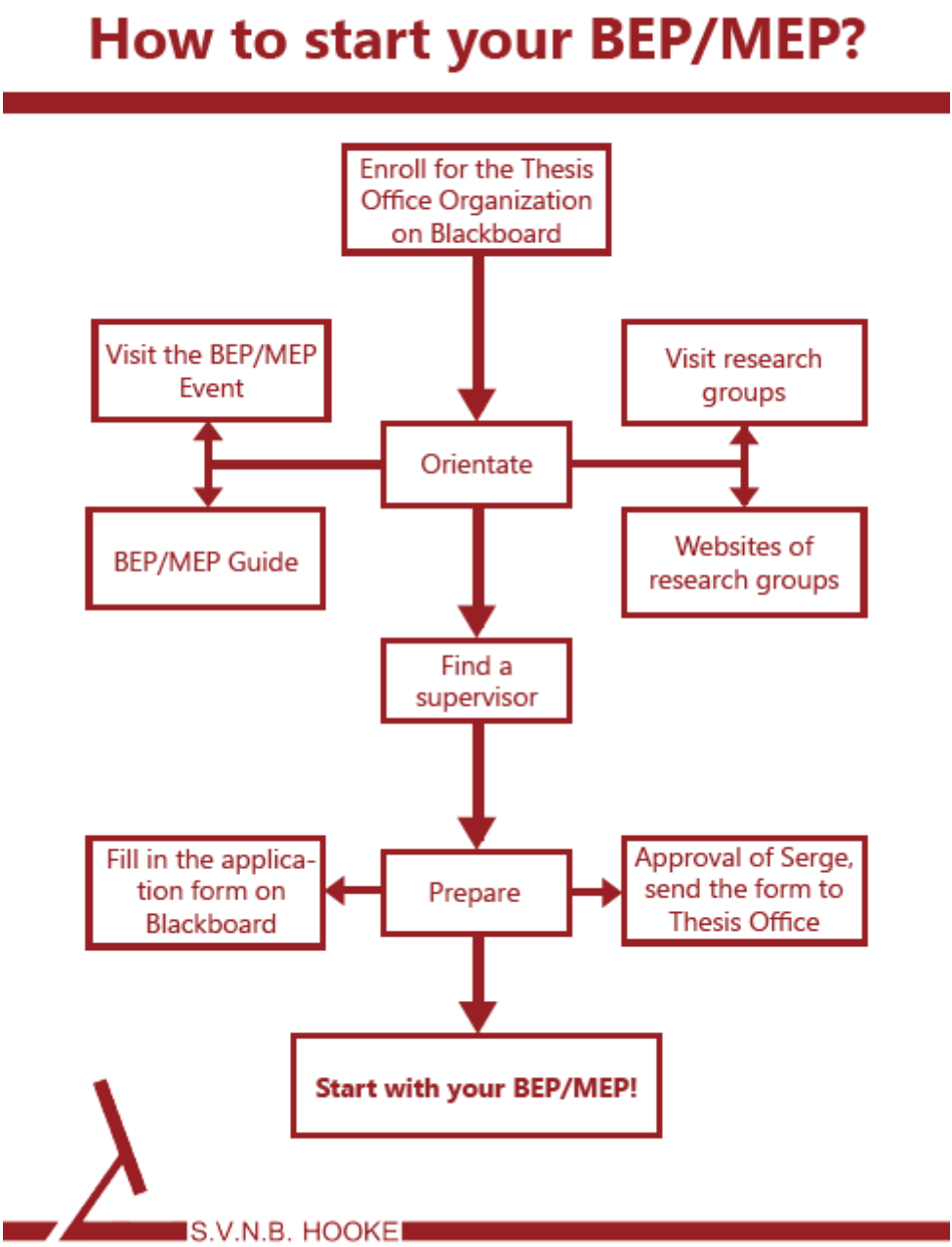
Programme coordinator:

Serge Donkers: s.p.donkers@tudelft.nl

Thesis office Applied Sciences:

thesisoffice-tnw@tudelft.nl

FLOW CHART


How to start your BEP/MEP?
Enroll for the Thesis Office Organization on Blackboard
Visit the BEP/MEP Event
Visit research groups
Orientate
BEP/MEP Guide
Websites of research groups
Find a supervisor
Fill in the application form on Blackboard
Prepare
Approval of Serge, send the form to Thesis Office
Start with your BEP/MEP!

RESEARCH GROUPS DELFT

Aubin-Tam Group, Bionanoscience

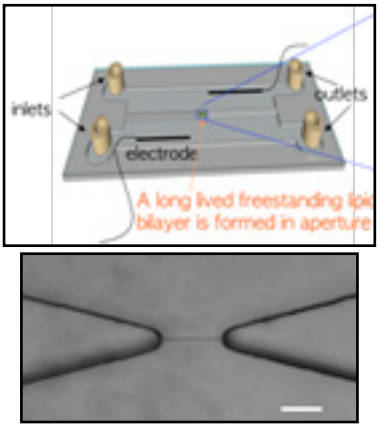
CONTACT: M.E.Aubin-Tam@tudelft.nl

The Aubin-Tam group (Bionanoscience department) is interested in the relationship between structure and mechanics in biological molecules and biological materials.

Master End Project #1:

Freestanding membrane in microdevice, a tool to study biological nanomachines

This project involves making new kinds of microdevices that enable the formation of a lipid membrane. A method developed in the Aubin-Tam group enables easy access to both sides of the membrane. One goal is to form membranes of controlled composition, such as with different kinds of lipid molecules on each leaflet. The activity of single biological nanomachines that can pierce the membrane will then be measured.



A microfluidic device is custom-designed in our group in order to form stable free-standing membranes. A picture of the membrane is shown.

Master End Project #2:

Single-molecule tracking of a protein degradation machine with optical tweezers

The membrane protein FtsH unfolds and degrades other proteins. In this project, single FtsH protein complexes with be studied while they degrade a protein substrate. Optical tweezers will be used to track the activity to this protein in real-time for the first time, enabling us to gain insight on its mechanism of action.

Cees Dekker Lab, Bionanoscience

CONTACT: c.dekker@tudelft.nl
WEBSITE: ceesdekkerlab.nl

We are an explorative experimental biophysics group that aims to uncover new concepts in a variety of biological research areas from single molecules to single cells. In the past decade, our focus was on single-molecule (mostly single-DNA) biophysics using solid-state nanopores, high-speed AFM, and optical/magnetic tweezers – with research ranging from DNA translocation through nanopores to DNA-supercoiling studies of nucleosomes and DNA repair proteins. This continues with exciting current research such as the processing of DNA by structural maintenance of chromatin (SMC) proteins, DNA sequence dependence of supercoiling, and development and use of novel nanopore methodologies such as plasmonic and biomimetic nanopores for protein sequencing.

Recently our research expanded from single molecules to single cells on chip, particularly studying chromosome structure and cell division of bacteria. We use nanofabrication to shape cells in fluidic microstructures and study the intracellular distribution of DNA and proteins, e.g., the cell-division-regulating Min proteins. A major future direction is the development of a 'bottom up biology', i.e., disentangling how biological complexity and functionality emerge from components. We use microfluidics to reconstitute proteins and DNA in fluidic nanochambers and liposomes on chip. We aim to realize minimal synthetic cell-division systems that will be a key part of synthetic cells. Furthermore we aim to build chromosomes from the bottom up.

Research highlight

One example of our recent research projects is the single-molecule biophysics work on condensin: We recently provided unambiguous evidence that the SMC protein complex condensin has a motor function by which it extrudes loops of DNA. Using single-molecule imaging, we showed the formation of large DNA loops by single condensin complexes, providing direct evidence for a loop-extrusion mechanism for the spatial organization of chromosomes.

See: M. Ganji, I.A. Shaltiel, S. Bisht, E. Kim, A. Kalichava, C.H. Haering, C. Dekker, Real-time imaging of DNA loop extrusion by condensin, Science 360, 102 (2018)

Some other highlight papers:

- F. Wu, A. Japaridze, X. Zheng, J.W.J. Kerssemakers, C. Dekker, Direct imaging of the circular chromosome in a live bacterium, Nature Commun. 10, 2194 (2019)
- S. Deshpande, F. Brandenburg, A. Lau, W.K. Spoelstra, L. Reese, S. Wunnava, M. Dogterom, C. Dekker, Spatiotemporal control of coacervate formation within liposomes, Nature Comm. 10, 1800 (2019)
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- A.W. Bisson-Filho, Y.-P. Hsu, G.R. Squyres, E. Kuru, F. Wu, C. Jukes, C. Dekker, S. Holden, M.S. VanNieuwenhze, Y.V. Brun, E.C. Garner, Treadmilling by FtsZ filaments drives peptidoglycan synthesis and bacterial cell division, Science 355, 739-743 (2017)

Student projects

We welcome BEP and MEP students to join this cutting-edge research. Information and a list of open projects can be found at https://ceesdekkerlab.nl/come-join-us/student-projects/

Youk Lab, Bionanoscience

CONTACT: h.youk@tudelft.nl

Our lab's main interest is in understanding how living systems bidirectionally transition between being alive and being either truly dead or seemingly dead. We aim to identify all the ways in which these transitions can occur, in hopes of finding common principles that underlie them. We are particularly interested in principles that allow life to be restarted after it has nearly/completely ceased. Our studies use microbes and mammalian cells (e.g., yeasts and mouse embryonic stem cells). We combine experimental and theoretical approaches.

The big talk of embryonic stem cells

How often do you make your own decisions, and how often do you trust on all others around you for that?

We looked how cells from an early mouse embryo do this by growing and differentiating them into specialized cells on a large laboratory dish (10-cm). In turned out, as we discovered, that all cells on the dish first talk to each other when deciding on a new fate – by secreting and sensing signalling molecules in their environment – to find out with how many they are before continuing their endeavor. The population of cells stays alive and can expand and differentiate on the dish if it is large enough while it surprisingly dies as a whole if there are not enough cells on the dish. Interestingly, deciding on a fate requires these cells to "quorum-sense" for survival – making it a matter of life and death.

Resuming mummified life at the push of a button

Several organisms are able have their lives halted in a dried state and then resume their lives after being rehydrated. These organisms include unicellular organisms such as yeast and some species of bacteria and some multicellular organisms such as a desert plant, eggs of a shrimp, and water bears (tardigrades). However, these organisms are rare exceptions as most cells and multicellular organisms cannot be revived after they are desiccated. A poorly understood question is what principles enable some organisms to restart their lives from a desiccated state after they are rehydrated.

By addressing this question, we may be able to desiccate and then revive numerous unicellular and multicellular organisms for which this is not yet possible. In our work, we used the budding yeast as an easy-to-cultivate model organism. After desiccating budding yeasts, we explored various features that they exhibit as they recover from their dried state, including restarting of metabolism and gene expression and resuming of cell replication.

Nynke Dekker Lab, Bionanoscience

CONTACT: N.H.Dekker@tudelft.nl, B.P.SolanoHermosilla-1@tudelft.nl

Description of the Nynke Dekker Lab

Our research focus (http://nynkedekkerlab.tudelft.nl) lies on understanding the key cellular process of **DNA/RNA replication** in viral, bacterial, and eukaryotic systems. To study dynamic aspects of replication in vitro but also in living cells, we make use of state-of-the-art **biophysics** (magnetic and optical tweezers, integrated with fluorescence microscopy and super-resolution fluorescence in living cells) highly integrated with **biochemistry**. We are an international multidisciplinary team with backgrounds in quantitative biology, (bio) chemistry, or (bio)physics. At present, we have exciting and challenging BEP/MEP projects available in:

1) *Live cell imaging*

At the heart of the project is improving the fundamental knowledge of DNA replication and repair, whose malfunctioning is related to the development of cancer.

2) *In vitro single-molecule studies of eukaryotic DNA replication*

Human beings copy a light-year's worth of DNA in their lifetimes. How this is dynamically achieved by the core proteins composing the replisome is the main focus of our project.

Idema Group, Bionanoscience

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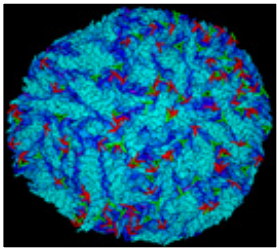
Biology is often highly nonlinear, which is good news for life: many actors together can accomplish what a few cannot, not just for lack of individual strength, but because the whole really is more than the sum of its parts. In our group, we study how collective dynamics of many particles, affect the function and behaviour of the living system they are part of.

Available projects in 2019-2020 include:



- The dynamics of bacterial colony growth and defect formation.
- Flow of active particles through narrow openings.
- Differentiation in growing eukaryotic tissues.
- Membrane-mediated interactions between curved proteins.
- Self-organization of polymers adsorbed on membranes.

More information on all projects at idemalab.tudelft.nl.

Jeremy Brown Lab, Radiation Science and Technology

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Dr. Brown is a recently established PI at TU Delft who focuses on improving our understanding of radiobiology at multiple length scales and, in turn, increase the clinical efficacy of radiotherapy. Possible research projects span from exploring DNA damage induction and complexity from different ionising radiation sources, to the development of biological response predictive frameworks aimed at assisting clinicians in incorporating the impact of hypoxia and radiosensitising drugs into patient specific treatment planning approaches. Depending on the potential student's interest, custom projects can also be developed in collaboration with other researchers at Erasmus MC, TU Delft and abroad.

Projects involve: biological system and response model development, Monte Carlo modelling of radiation transport and biological damage, radiobiology experiments, radiation chemistry experiments, live cell imaging, and image analysis.

Carroll Lab, Imaging physics

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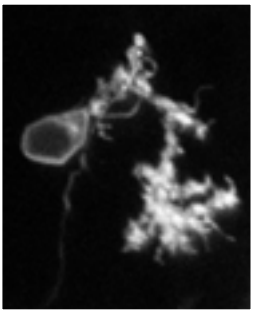
A very basic, but extremely challenging, question about the brain is how do networks of neurons generate behavior? My team adresses these questions using zebrafish as a small animal model for brain development. Many length scales and time scales relevant to brain function. Often the equipment needed to image processes at different scales does not currently exist. We do the engineering work necessary to image synapse function and development in living zebrafish embryos, and connect this to nanoscale maps of synapse structure using electron techniques.

Image analysis of 3D structure of neurons



Neurons are the most complex cell types in the body. We use fluorescence labelling techniques to visualize individual neurons in the zebrafish brain. Neurons can then be imaged by light microscopy techniques, like confocal laser scanning or light sheet microscopy. From images of the same neuron on different days of development, we want to quantify changes in the shape of the neuron. This BEP/MEP project will implement the latest generation of 3D neuron tracking and volume rendering software to develop an image analysis pipeline.

Virtual reality platform for brain imaging in zebrafish

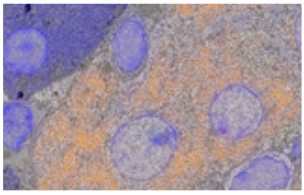
The goal of this project is develop a "virtual reality" environment to add to our custom light sheet microscope. The environment will consist of a miniature movie screen, and a software (in matlab or python) to adapt movies to test the vision of the larval zebrafish, e.g., simulating optic flow that makes the fish believe it has control over its environment. While the fish is engaged in virtual reality, we will simultaneously image brain activity using fluorescence from genetically-encoded calcium indicators. This approach has proven useful for connecting brain activity to behavior.

Hoogenboom Lab, Imaging physics

CONTACT: j.p.hoogenboom@tudelft.nl

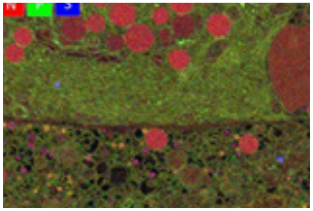
Molecular reactions dictate life up to the level of cells, organs, and organisms, compassing orders of magnitude and developing a staggering structural heterogeneity. Microscopes are essential for investigations but no microscope technique can provide the full picture of (live) molecules and underlying biological structure over all relevant length scales. My group is developing new techniques and microscopes to address this issue and integrate all capabilities in one microscope.

Building biomolecular Google Maps



Electron microscopy images structure of cells and tissue with nanometer-resolution, but at very low throughput and without information on molecular content. We are developing new techniques based on parallel scanning with multiple beams, integration of light and electron microscopy, and development of dedicated probes and labels to allow fast, high-resolution imaging over multiple length scales. In this way we want to build an atlas or "Google Maps" for life, zooming in and out on tissue from millimetres to molecules.

New superresolution techniques to visualize proteins in tissue



When fluorescence images are overlaid or integrated with electron microscopy images, the diffraction limit precludes molecular fluorescence localization at the resolution of the electron image. We are inventing new techniques to visualize proteins and other biological molecules in color at electron microscopy resolution and we collaborate with microscopists in medical centers to apply these techniques on their tissue samples. Student projects in our lab can involve experimental work, construction and design of experimental set-up, and data analysis and programming (artificial intelligence).

Daan Brinks Lab, Imaging physics

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WEBSITE: www.brinkslab.org

Image the brain at work

In my lab, we work on technologies to understand brain function, and apply those in neuroscientific research. We develop tools with roots in physics, biochemistry, optics, mathematics and nanofabrication and we're interested in how brain cells work on every level, from biophysical principles to consequences in behavior and from subcellular compartments to complete organisms.

Our work focuses on Voltage imaging, the direct transduction of changes in membrane voltage into a fluorescent signal. This allows faithful recording of the fast electrical dynamics of many neurons in parallel and is set to revolutionize our understanding of network dynamics, plasticity and memory formation in the brain.

One of the projects in my lab tackles the challenge voltage imaging deep in the living brain. For this, we evolve fluorescent voltage sensitive proteins optimized for multiphoton imaging, using a new single-cell selection technique. This allows us to screen mutant libraries of proteins directly for brightness, voltage sensitivity, and membrane trafficking in neurons. We have projects involving research into the molecular biology of the protein engineering, the photocycle dynamics of different families of proteins, their application in vitro and vivo to answer fundamental biophysical and neuroscience questions, the challenges of high bandwidth deep-tissue imaging and the modeling of neural dynamics.

Another aspect of electrical dynamics that we're interested in is the possible effect of membrane voltage changes on embryonic development. For this, we develop a technique called absolute voltage imaging that allows tracking of subtle changes in membrane voltage in groups of cells as they undergo specialization, for instance in developing zebrafish embryos.

Finally, we're interested in nanoscopic imaging of activity at synapses. We are looking into different ways of enhancing the signals of fluorescent voltage sensing proteins at synapses with a combination of genetic and chemical technologies on the one hand, and nanoparticles and plasmonics on the other hand.

RESEARCH GROUPS ROTTERDAM

Riccardo Fodde Group, Pathology

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Cancer Stem Cells

In organs like the intestine, skin, and blood, highly dynamic processes take place where aged cells are continuously being replaced by new ones. Adult stem cells located within these tissues and organs are responsible for this critical turnover. Stem cells give rise to more specialized cells which are programmed to take care of specific functions (e.g. digest food and absorb nutrients; deliver oxygen to distant tissues; etc.) and to eventually die after a defined lag of time. Within these high turnover tissues a tightly controlled equilibrium is maintained so that new cells are generated to replace the dying ones. In order to maintain this equilibrium even in situations of stress (e.g. inflammation, wounding, etc.), stem cells are not alone. They are usually surrounded by other specialized cells which form a niche that insulates stem cells and mediates their response to external cues. This is of great relevance as upon tissue injury stem cells need to increase their production to balance cell loss in response to signals from the niche.

We believe that this so called hierarchical organization of our normal tissues and organs is conserved within tumor masses with cancer stem cells (CSCs) at the very top of this hierarchy. Likewise, the niche of CSCs is essential to determine their capacity to proliferate, invade surrounding tissues, and eventually colonize distant organ sites, the so-called metastases. By comparing normal and cancer stem cells and by studying the CSC niche, we hope to identify key molecular and cellular mechanisms to be specifically targeted in future therapies.

Cancer Computational Biology and Bioinformatics

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Dr. Harmen van de Werken
Erasmus MC Be330A
010-7044467

The Erasmus MC Cancer Computational Biology Center (CCBC) facilitates ICT and bioinformatics for research and clinic. In addition, the CCBC develops new computational algorithms, analysis methods and visualization tools in the field of computational biology to gain insights in cancer biology with the ultimate goal to improve patient treatment.

Cancer onset, progression and drug resistance mechanisms are driven by hereditary and somatically acquired genomic aberrations. Many cancer driver genes and their coding changes but more than 98% of the somatic DNA mutations in cancer occur in non- coding areas of the human genome and their contribution towards cancer cell behavior is still enigmatic. The CCBC interrogate the entire cancer coding genome, as well as, its regulatory part including promoters, enhancers, silencers and regions generating non-coding RNAs to gain insight in their contribution to cancer progression and mechanisms of drug-resistance. Moreover,we aim to develop novel tools that visualization of the result and may improve patient stratification[1].

Currently, we have access to the world-wide the largest metastatic Whole Genome Sequencing data sets with matched RNA-seq data from breast (Currently, n > 600), prostate cancer patients (n > 400)[2,3] among others solid cancers. These comprehensive data sets will give us the opportunity to unravel novel biology including interaction of DNA elements, regulatory mechanisms, but also aberrant splicing and fusion gene detection. We apply next to state-of-the-art bioinformatics, statistical analyses and Machine Learning methods to interrogate these rich data source.

We will compare the results to primary cancer and integrate our data with publicly available data sources from ChIP-seq and 3D chromosome conformation capture assays[4,5] to reveal (non-coding) drivers of cancer initiation and progression and importantly drug-resistance[6].
Ultimately, we will apply this gained knowledge to improve patient stratification.

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Department of Developmental Biology

CONTACT: h.mirabontenbal@erasmusmc.nl

Research projects at the Department of Developmental Biology (Erasmus MC) are related to the epigenetic regulation of genes and sex chromosomes during the life cycle, focusing on their regulation during the generation of gametes that fuse to form the totipotent zygote, and during differentiation of stem cells, in vivo and in vitro. Epigenetics involves heritable modifications of DNA or associated proteins, leading to altered regulation of gene expression, without modification of the genetic code. Female somatic cells in placental mammals and marsupials have two X chromosomes, whereas males carry only one X and the male-determining Y chromosome. The X chromosome is gene-rich, but the Y chromosome carries few genes that are mostly involved in male sex determination and fertility. The dosage inequality of X-linked genes between males and females is compensated via inactivation of one of the two X chromosomes in female cells, through a process called X chromosome inactivation (XCI) that takes place in the early stages of embryo development. The long non-coding, X-linked RNA Xist is crucial for XCI and is up-regulated from the future inactive X chromosome, coating it and recruiting factors involved in silencing and altering its chromatin state. Once this process is complete, the inactive X chromosome can be recognized as a so called Barr body, and will remain inactive throughout further development and into adulthood. Only in the germline when oocytes are formed and the inner cell mass of blastocysts just before implantation, both X chromosomes are active. In XY males on the other hand, the sex chromosomes are both normally active in somatic cells, but become silenced during the prophase of the first meiotic (reductional) division through an epigenetic regulatory process named meiotic sex chromosome inactivation (MSCI). Our department aims to unravel the mechanisms of XCI and MSCI control, maintenance and reversal. In addition, we want to understand how gene expression has proceeded during development and cancer by making use of a novel technique we have developed to analyse DNA methylation. To reach these aims, we use genetically modified mouse models as well as mouse embryonic stem cells (ESCs) carrying different deletions of the X chromosome.

Students can participate in ongoing projects that will involve state of the art microscopy techniques, use of advanced gene editing tools in stem cells, and general molecular biology techniques. The results obtained in our Department will contribute to our understanding of basic aspects of fundamentally important processes such as gametogenesis and cell differentiation in general, and can thus be relevant to basic researchers in these fields, but also to clinicians and pharmaceutical companies trying to understand and find better treatments for X-linked diseases, cancer and infertility.

Houtsmuller Group and Optical Imaging Centre

CONTACT: a.houtsmuller@erasmusmc.nl

Super resolution microscopy (nanoscopy)and time lapse imaging of gene transcription and DNA repair.

The proteins involved in gene transcription or DNA repair, often accumulate in tiny active structures on DNA, which are typically smaller than a micrometer. We are interested in 1) the distribution of different types of proteins inside these structures, 2) the order in which they accumulate, and 3) the time they spend inside. More important, we aim to understand how these features relate to the functions of the various proteins.

To investigate this, we make use of confocal time lapse imaging and super resolution imaging of cells expressing transcription and repair proteins either tagged with fluorescent proteins (time lapse) or cells stained with fluorescently tagged antibodies against the protein under surveillance (single molecule imaging). In addition, we apply various quantitative methods to make microscopic measurements, such as FRAP and FRET. All the techniques above were introduced in the BSc course Microscopy/Nanoscopy.

Aleksandra Badura Lab, Neuroscience

CONTACT: a.badura@erasmusmc.nl

When we reach for a piece of cutlery we rarely take time to scan the full content of the drawer. We merely put a hand in, and nine out of ten times we immediately locate what we were looking for.

But sometimes we do not — that is when most of us will take advantage of behavioral flexibility, an ability to adapt cognitive processing strategies to face new and unexpected conditions. However, in some disorders characterized by repetitive and stereotyped behaviors this adaptation does not occur at all – a person with autism will likely keep on opening and closing the same drawer. But how is this richness of flexible behavior or the lack thereof determined by the brain?
The Neural Networks Underlying Behavioral Flexibility group aims to understand how cerebello-cortical brain activity translates into behaviors that adapt to ever-changing environments. We are particularly interested in uncovering the mechanisms of maladaptive perseverative behaviors characteristic of autism spectrum disorder. To that end we employ a wide range of techniques, from behavioral assays through imaging to modeling.

Profile analysis of autism-like behaviour scores
Genes and environment can contribute to the development of autism, which complicates the study of its underlying neural substrates. In our lab, we simulate this variability by studying behaviour in different mouse models of autism. We created a pilot multi-parametric matrix to register experimental behavioural scores. In this project, we want to further develop our approach by integrating all our models' scores into one single platform. This will allow us to compare groups and identify common behavioural traits, or combinations of behaviours, across experimental models, i.e., to develop a "behavioural fingerprint" for each autism model.

Registration and quantification of volumetric and structural differences in MRI data:
We have a particular interest in investigating the role of the cerebellum in autism and are using different mouse models for our studies. We have recently discovered a novel autism risk gene and generated a mouse model from it. We are currently imaging the brains of these animals with a state-of-the-art 15 T MRI scanner to study anatomical anomalies. We are looking for a student to develop a 3D brain analysis for reconstructions for volumetric and structural comparisons.

Modelling brain connectivity in mouse models of autism:
Brain functional ultrasound (fUS) is a novel technique that enables visualization of doppler signals representative of blood-flow changes. In our lab, we use this technique to explore brain connectivity alterations in mice models of autism. We record brain activation signals during resting-state and brain stimulation paradigms, together with mouse movement dynamics, which we then model into 3D representations. We are looking for a student who can help us improve our modeling systems and integrate network and movement dynamics data, to analyse how connectivity is altered in different models of autism.

If you are interested in any of our projects, come by our poster to hear more from the researchers involved!

Chris de Zeeuw Lab, Neuroscience

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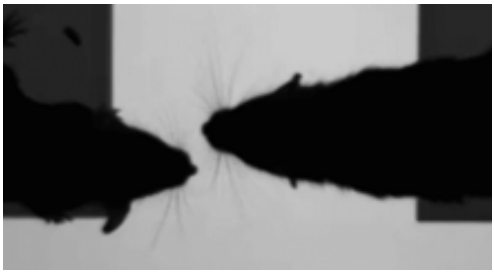
Cerebello-cortico-striatal interplay during a cognitive flexibility task in autism spectrum disorder

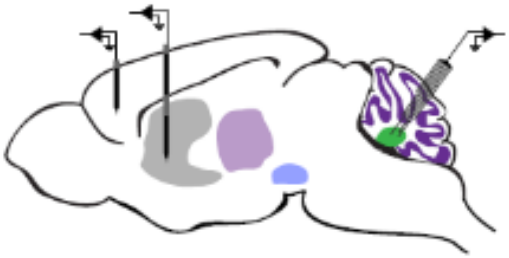
Project:
Autism spectrum disorder (ASD) is a highly prevalent neurodevelopmental disorder characterized by social deficits and cognitive inflexibility. These higher-order functions rely on coordinated neuronal activity across many brain regions and networks. Coordinated activity in the cortico-striatal network is crucial for social behavior and cognition[1,2] and its dysfunction contributes to the deficits characteristic of ASD[2-4]. However, evidence reveals a crucial role for the cerebellum in the pathogenesis of (ASD)[5]. The cerebellum is extensively and reciprocally connected to cortico-striatal networks and can potently affect cerebral network activity[6]. How cerebellar injury or dysfunction can cause a disorder associated with abnormal cortico-striatal functioning remains however unknown.

The aim of this project is to unravel deficits in cerebello-cortico-striatal network dynamics related to the core characteristics in autism: ***social deficits*** and ***cognitive inflexibility*** by setting up analyses and software to analyze the data and with the possibility of learning to perform behavioral and electrophysiological experiments.



Social Interaction

Cognitive flexibility



Electrophysiology

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Bosman and Romano, Neuroscience

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Walking patterns all over the world

Key words: data, walking, coding

Impaired movement can result from a large number of causes. All over the world, many mouse models have been developed to study common as well as rare causes for impaired walking. In our department, we have developed the "ErasmusLadder" as an automated test for gait abnormalities in mice. The ErasmusLadder is now commercially available and is being used by research groups all over the world. Thanks to collaborations with the company that makes and sells the ErasmusLadder as well as with multiple research groups using the ErasmusLadder, we have now access to the gaiting pattern of many different mice. For each mouse, the condition (genetic or acquired) is known and can be linked to deviations in the normal gaiting pattern. The goal of this project is to develop a predicting algorithm: if I tell you how a mouse walks, can you tell me what type of mutation he has?

You never move alone

Key words: behavioural analysis, neuroscience, coding

Over the last decade or so, our understanding of how the brain encodes movements has rapidly expanded. However, most of our knowledge relates to single types of behaviour, like walking or the movements of arms or eyes, but you seldom move alone: while walking, you are also breathing, looking and maybe waving to a friend. In many cases, muscle groups are involved in multiple movements at the same time, requiring a strict coordination by the brain. We have reasons to assume that the cerebellum is a key area in creating these coordinated patterns. We have recorded neuronal activity in the cerebellum of mice while making high-speed videos of multiple behaviours. During this project, you will analyse these signals and investigate which neuronal signal is specific for which type of movement or for their synergies.

Neural coordination of voluntary vs. reflexive movements

Keywords: neuroscience, electrophysiology, behavioural analysis

For this project, you will study the whisker system of mice. This has become probably the prime model system for studying the integration of motor commands with sensory feedback.

Mice can move their whiskers voluntarily when exploring their environment, but they also have whisker reflex: a fast forward sweep upon touch. We have recorded neuronal activity in the cerebellum during both movements and we have found that the same neurons are differently involved in the two types of movement. This project entails the further analysis of this initial finding and relates to a hot topic in neuroscience: state-dependent brain activity. The latter implies that the same neurons have different relations between their firing rate and movement depending on the behavioural state of the animal. Our pilot observations indicate that this can become very interesting, so this is the time to join!

Perception and prediction of time

Keyword: time-perception, prediction, neuronal activity

To better react to external events, our nervous system continuously seeks predictable patterns. Periodic events are easy to predict but which are the brain areas involved in the perception of time and computation of the prediction is largely unknown. Using the newest techniques in neuroscience, we record and selectively manipulate the brain activity in the regions that we think are involved in time perception and time prediction. Further development of this project could include the potential impact of dopamine in the perception of time.

Sequential activation of neurons in the cerebellum

Keyword: neuronal activity, motor control, cross-correlation

The cerebellum fine-tunes the activation of muscles to generates smooth movements to an extent that still far to be reproduced in robots. How do the neurons are activated in space and in time during motor control? Using neuronal activity recording and optogenetic stimulation techniques we can first unravel the sequences in which the neurons are activated and then reproduce those sequences to evaluate their impact on behavior. Understanding the computational mechanisms that neurons use for the fine-tuning of the body movements could provide useful insights for robotics.

Kerstin Wendt, Cell Biology

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Cohesin functions and malfunctions

Cells depend for the stability of the genome on the cohesin complex. This large ring-shaped complex tethers sister DNA strands together to allow a correct segregation of the chromosomes during cell division. Using a similar mechanism, cohesin establishes loops in the chromatin fiber. These structures help to pack the about 2 m DNA in human cells into the cell nucleus and regulate gene activity by steering promoter-enhancer communication.

Mutations and Misexpression of cohesin complex subunits or cohesin regulators are frequently found in different cancer types and also cause developmental defects in human.

Great progress has been made in the past years by us and others to understand these functions of cohesin at the molecular but also genome-wide scale. However, a large number of fundamental questions are still unresolved. Below some projects are outlined to tackle those questions.

In our group we use a wide panel of methods and techniques such as Imaging (Super resolution imaging, live cell imaging, single molecule localization with dSTORM), methods to study chromatin folding (4C, T2C, HiC) or to identify genomic binding sites (ChIP-sequencing), as well as basic cell biology and biochemistry approaches such as mass spectrometry. Our model systems are cultured human cells that we engineer with CRISPR genome editing, eg. to allow visualization of proteins or DNA regions with fluorescent tags or allow rapid depletion of the proteins. Further, we also use cells obtained from patients to study the role of cohesin in disease.

Project examples:

How many cohesin rings are necessary to form a chromatin loop? (collaboration with Johan Slotman and the OIC)

- Perform single molecule localization imaging (dSTORM and similar) and data analysis to understand how many cohesin complexes colocalize with CTCF on chromatin.
- Visualize cohesin complexes that are forming loops in live and fixed cells.

How do the cohesin/CTCF binding sites that form the chromatin loop find each other?

- Cohesin is thought to slide along the chromatin fiber. We want to visualize its track by specifically marking the chromatin-bound proteins that are touched by cohesin and investigate them using ChIP-sequencing and correlate this with exiting ChIP-seq data.

Frank Grosveld Lab, Cell Biology

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We are interested in the very early decisions that regulate choices between (e.g the cardiac and hematopoietic) cell lineages, the establishment of hematopoietic stem cells and the differentiation of these stem cells to the erythroid lineage. This process is regulated through specific gene transcription patterns during development and is controlled by transcription factors networks that become activated or inactivated in response to external cues. Developmental decision as to what identity (tissue) any given cell will assume is taken at the single cell level. However, despite genome-wide biochemical approaches, the spatiotemporal dynamics of such developmental decisions is only partially understood. The nature of such decisions will be studied at the single cell level through the development of novel technology and its application. Furthermore the regulation of transcription occurs within the context of the 3D space of the nucleus and is also controlled by it. Presently the spatiotemporal dynamics of genomic interactions and their relation to functional multi-dimensional interactions are only partially understood. The plasticity and dynamics of enhancer-promoter interactions and their relation to transcription factories will be visualized in single live cells and the function of different Transcription factors (TFs) in establishing these interactions will be assessed.

Main projects

The study of hematopoietic networks during development using a combination of novel single cell -Omics techniques, biochemistry, informatics and (live) image analysis using super high resolution microscopy and dynamic light sheet microscopy of live cells.

The study of 3D genome structure and transcription factory formation during the cell cycle and differentiation

The Grosveld Lab is interested in transcriptional regulation and more specifically in visualizing the 3D dynamics of transcription factors and their target genes during cellular processes, such as the cell cycle and embryonic development.
For 2020, we have two available Master projects.

Topic 1: Transcription factor binding kinetics during mitosis of mouse embryonic stem cells
It has been shown that during mitosis some transcription factors remain bound to the chromatin, whereas other transcription factors are depleted. We have previously created a cell line in which a transcription factor was tagged with a fluorescent colour and we have shown that this transcription factor remains on mitotic chromatin during live cell imaging. Using biochemical approaches, other research groups have reported that this transcription factor only binds a subset of its interphase binding places during mitosis (around 50%). We would like to investigate whether this transcription factor has mitosis-specific DNA binding kinetics. The Master student will synchronize mouse embryonic stem cells, perform single molecule imaging during different cell cycle stages and model the imaging data.

Master Project: Develop a novel cell stage specific single particle tracking method.

Topic 2: Monoallelic integration of genomic locus trackers in mouse embryonic stem cells
We have previously established a system with which we can visualize genomic loci by inserting repetitive arrays next to our locations of interest. The theoretical minimal distance between two visualization arrays required for their successful separation during live cell imaging is the equivalent of 15 kilo-basepairs of DNA, however, this has never been experimentally validated. We would like to test this theoretical distance by creating a multitude of cell lines with a single construct. The Master student will integrate two arrays in a single genomic location and induce the cis-spreading of one of the two arrays by a transposase, isolate individual single colonies and analyse the images acquired during live cell imaging.

Master Project: Determine the minimal linker distance required for distance measurements between two fluorescent genomic loci by employing transposase-mediated *cis* spreading.

Niels Galjart, Cell Biology

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Control of cellular dynamics by microtubules and their interacting proteins

Microtubules (MTs) are cytoskeletal elements that are essential to maintain cell structure and shape, and that are also involved in many dynamic cellular processes, including cell division, cell attachment and migration, and differentiation. MT behaviour is regulated by various microtubule-associated proteins (MAPs). At this BEP/MEP event we present our work on two MAPs.

The **first** project is on mammalian **CLASPs**, which are MT plus-end tracking proteins (+TIPs) that associate specifically with the ends of growing MTs. CLASPs control MT behaviour as well as MT interactions with other cellular structures, and they do this downstream of important signalling pathways. As such CLASPs are major regulators of cellular polarity. Recent data implicate CLASPs also in RNA biology. Here, we ask what the relationship is between these two functions, and hence between MTs and RNA. This question bears medical relevance, as mutations in the CLASP genes in man give rise to neuronal and heart defects.

The **second** project is on **KIF2A**, a member of the kinesin family of MT motor proteins. KIF2A is thought to be a MT depolymerase, that induces MT catastrophe by "peeling off" tubulin at the ends of MTs. Our in vitro data suggest additional functions for KIF2A, that may explain its role during the end stage of cell division, called cytokinesis, when KIF2A is abundantly present on so-called midzone MTs, which regulate the separation of daughter cells. Here, we ask what the role is of KIF2A during mitosis, and in particular cytokinesis. This question bears medical relevance, as mutations in KIF2A in man give rise to microcephaly, or "smaller brain", and this is thought to be due to defective mitosis in neuronal precursor cells.

To address our questions we have targeted the Clasp and Kif2a genes in mouse embryonic stem cells with fluorescent markers and affinity tags. We will use these lines to perform imaging studies, applying state-of-the-art techniques such as fluorescence light sheet microscopy, to describe the localization, and understand the dynamic behaviour and conformation of CLASPs and KIF2A in living cells. Studies are combined with -omics approaches, to characterize the network of proteins and nucleic acids to which CLASPs and KIF2A bind. Studies are further complemented by in vitro MT reconstitution assays, where we use purified CLASPs, KIF2A, and other proteins, to study their dynamic behavior in isolation, and by CRISPR/Cas9-based genome engineering to introduce mutations and describe phenotypes in cells.

Computational Methods for Quantitative Colocalization Analysis of Actinin and CLASP2

Cardiomyocytes (CMs) are the muscle cells that make up a large part of the heart. They are responsible for heart contraction, which enables the pumping of the blood, and hence of oxygen, through the body. The basic contraction unit of the CM is the sarcomere, a repeating unit positioned between two Z lines, that contains the contractile actomyosin filaments and associated proteins.

Microtubules (MTs) are another major cytoskeletal system, whose function in CMs is not well characterized. MT plus-end tracking proteins (+TIPs), which bind to the growing end of MTs, regulate MT function. Recently we showed that CLASP2, a +TIP with an important function in the heart, localizes near sarcomeres in a typical pattern. In order to understand its localization, we want to quantitatively analyze the localization of CLASP2 in CMs.

The project will focus on development of a co-localization method (with implementation in Python or as a plugin for ImageJ), capable of automatically depicting the distribution of CLASP2 depending on the distance between z-discs for different experimental condition.

Joyce Lebbink, Molecular Genetics

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In our laboratory we combine molecular biology, structural and functional biochemistry, single molecule analysis and quantitative approaches to study mechanisms of molecular machines on DNA:
•How do DNA mismatch repair proteins communicate between different sites on DNA?
•Which physicochemical properties determine stable DNA binding by the CRISPR-Cas9 nuclease?
•How can we exploit Cas9 as in vitro tool to study DNA mismatch repair?

Projects
•To in vitro reconstitute reaction steps of the MMR pathway using purified proteins MutS, MutL, MutH and/or UvrD on specific mismatch-containing DNA substrates.
•To correlate time-resolved function of the MMR system to different characteristics such as protein structure using mutational and 3-D structure analysis;
•To monitor kinetics of protein-DNA complex formation using surface plasmon resonance.
•To study the architecture of these complexes using scanning force microscopy.
•To describe quantitative behavior using Monte Carlo simulations.

Miao-Ping Chien Lab, Molecular Genetics

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Single cell technology for cancer biology
Our group develops technologies to tackle the complex biological challenges in cancer research such as tumor metastasis and therapy resistance. These technologies are a mix of advanced/custom microscopes, quantitative image analysis, photochemistry, single cell technologies (single cell genomics, transcriptomics and proteomics) and cancer biology.
One of the main problems in cancer research is lack of understanding of the underlying mechanisms of cancer driver cells or cancer stem-like cells. To address this issue, we design and build our own microscope setups that allow high-throughput fast imaging of 2D and 3D samples with high spatial (single-cell) resolution; in combination with single cell identification assays developed in our group, we can

identify aggressive cancer cells based on time-resolved, quantitative measurements. We also create single cell isolation techniques that allow precise single cell isolation based on any complex criteria via a combination of optics and photochemical methods.
Furthermore, we apply and develop suitable single cell next-generation sequencing and proteomic technologies to profile the genomic, transcriptomic and proteomic signatures of aggressive cancer cells. Based on the sequencing or proteomic data, we create and apply analysis algorithms and mathematical modeling to best identify the variant genes and proteins that drive the aggressiveness in these cancer cells; this allows us to identify suitable therapeutic targets.

Jeroen Essers Lab, Molecular Genetics

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HeartCHIP II

What do we want to do? What will we deliver
HeartCHIP will develop a novel in vitro heart failure (HF) model for preclinical drug discovery and efficacy testing based on high content microfluidic Organ-on-Chip technology. Prevalent genetic mutations will be introduced with gene editing CRISPR/CAS9 system in human induced pluripotent stem cells, which will be differentiated into cardiomyocytes. Integration of non-destructive functional microscopy and detection biomarkers will ensure a high-content platform for drug efficacy screening.
Why do we want to do it?
The heart's inability to meet circulatory demands heart failure (HF) is a serious medical condition with a prevalence of 1-2% in developed countries. Pharmaceutical companies need predictive in vitro models for HF patient groups as alternatives for animal models for cost-effective and successful drug development. Current models do not mimic the human heart sufficiently. The HeartCHIP project answers this unmet medical need.
What is the project goal? What will be the main result of the project?
The aim of the HeartCHIP project is to develop a novel, physiologically relevant, in vitro disease model to test the efficacy of novel drugs to treat different symptoms of HF. HF is a chronic, progressive condition in which the heart muscle is unable to meet the circulatory demands. Most in vitro models only consider the heart muscle cells

(cardiomyocytes, CM), but the HeartChip projects aims to develop a reconstructed 3D heart culture with human CMs, endothelial cells (EC) and myofibroblasts (MF) for in-depth characterization of compounds (complex-HFoC).

Claire Wyman, Molecular Genetics

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Quantitative single-molecule analysis of the nuclear dynamics of DNA Repair proteins in living cells

We aim to understand fundamental principles that determine complex biological processes. We currently focus on the process of double-strand DNA break repair in relation to genomic (in)stability, carcinogenesis and radio- and chemotherapy. We develop and apply new methods from single molecule imaging to live cell microscopy for quantitative analysis of detailed molecular function. Although our focus is fundamental knowledge, the mechanistic information we reveal are needed both to understand molecular causes that promote tumor formation, and to design of strategies specifically sensitizing rapidly dividing cells to anti-cancer treatments based on DSB induction.

Projects may include: protein biochemistry, molecular biology, scanning force microscopy imaging, live cell imaging, super resolution microscopy and image analysis in many forms.

[Bacherlor/Master] 3D imaging and analysis of single-molecule tracking data:

Part 1: Extracting 3D information from 2D images

The main idea is to use a modern supervised deep learning methods in order to estimate 3D coordinates of moving objects (proteins, molecules or other intracellular structures) using only 2D time-lapse images.

Relevant literature:

Deep-STORM: super-resolution single-molecule microscopy by deep learning - https://www.osapublishing.org/optica/abstract.cfm?uri=optica-5-4-458

To increase SNR by using neural networks: Content-aware image restoration: pushing the limits of fluorescence microscopy -

https://www.nature.com/articles/s41592-018-0216-7 and
http://csbdeep.bioimagecomputing.com/

Part 2: Extending the DL-MSS analysis to 3D
The main idea is to further extend the recently developed method for analysis of BRCA2 dynamics, where recurrent neural networks are combined with multi-scale spectrum (MSS), for analysis of 3D trajectories. The available real data includes 3D time-lapse sequences acquired using microscopes at Janelia, as well as the data obtained in Part 1 of this project.
Relevant literature:
Marloes' MSc thesis "BRCA2 mobility analysis using Deep Learning and the Moment
Scaling Spectrum "
https://www.youtube.com/watch?time_continue=65&v=Lj9TafL3WEc

[Bachelor] Spatial analysis of single-molecule tracking data
The main idea it to develop a methodology for modelling, analysis and quantification of spatial distributions and clustering patterns of different types of motion patterns using the tracking data extracted from time-lapse fluorescent microscopy imaging. The developed techniques (e.g. based on Ripley's K-function or t-SNE) will be used to accurately quantify differences in spatial distributions of proteins in cells without/with DNA damage and different mutants.

[Bachelor/Master] Extending the DL-MSS method
Part 1 Comparison of the developed DL-MSS method with existing techniques
The idea is to compare the performance of the existing motion analysis and motion clustering methods based on Bayesian inference with the DL-MSS method.
Part 2 Extension of the DL-MSS method with prior information
The idea is to introduce more prior information (experimental parameters in terms of localization uncertainty, track length, etc.) in the DL-MSS method during the training of the neural networks and study the improvements in the performance.
Part 3 Self-Learning DL-MSS method
The goal is to extend the ML-MSS analysis and develop a self-optimizing iterative procedure, which eliminates the necessity for specification of any user-defined parameters.

Relevant literature:
Variational Algorithms for Analyzing Noisy Multistate Diffusion Trajectories - http://elflab.icm.uu.se/lore/ref/BiofysJ-2018-Linden.pdf
HMM-Bayes https://www.ncbi.nlm.nih.gov/pubmed/26192083
Marloes' MSc thesis "BRCA2 mobility analysis using Deep Learning and the Moment Scaling Spectrum"
https://www.youtube.com/watch?time_continue=65&v=Lj9TafL3WEc

You can find more information on our research and project at:
https://www6.erasmusmc.nl/moleculargenetics/researchandfaculty/faculty/wymanlab/?lang=en

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Our lab is primarily interested in homologous recombination (HR) – a fascinating biological mechanism, present in all living organisms and fundamental to life as we know it. HR is also important for human health, as on the one hand, it protects against cancer, and on the other hand, can be targeted to cure cancer. Central to the HR reactions in vertebrates is the breast cancer associated protein 2 (BRCA2). Despite being one of the most studied human proteins, it is still surrounded by many mysteries. We aim to understand how BRCA2 operates by methods spanning all levels of organisation: from single molecule scanning force and high-resolution microscopy, chromosomal and cellular reporter systems, and up to creating mouse models by genomic engineering. One important source of insight are the proteins BRCA2 is physically associated with, and we discovered several previously undescribed interactions of BRCA2, including with completely uncharacterized proteins. Lack of any knowledge about the function of these novel proteins provides a completely open field for exciting experiments, both laboratory and computational: creating genomically engineered cell lines using CRISPR/Cas9, modelling protein structure and mapping interaction interfaces, analyzing molecular phylogeny, studying protein complexes using mass spectrometry, purifying recombinant proteins to raise antibodies and to perform biochemical experiments. At the same time, the connection to BRCA2 gives high chances that these exploratory studies will be of immediate relevance for human health.

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The role of DNA damage and transcription stress in aging.

Keywords:
genomics, transcriptomics, bio-informatics, modelling, transcription, aging, DNA damage

Introduction:
Aging is a complex process in which many molecular and cellular processes play a role. We are focusing on the role of DNA damage and associated transcription stress. By developing new genomics/transcriptomics methods and bio-informatics tools, we found that accumulating DNA damage in aging blocks transcription, which in turn can control many processes that are altered in aging. My lab aims at understanding the role of DNA damage and associated transcription stress in aging at the level of molecules, cells, tissues and organisms.

Bio-informatics projects for students:
HIV & Aging: HIV patients under anti-retroviral drug treatment appear to have an accelerated aging phenotype. We will study the impact of HIV and anti-retroviral drugs on aging by analyzing liver, kidney, heart and cortex mRNA-Seq data from humanized immune system mice with and without HIV and/or anti-retroviral drug treatment.
Evolution of transcription stress in aging: Transcription stress by DNA damage is mostly visible in long genes. Using bio-informatics and mathematical modeling we will isolate the conserved long genes, categorize function, model DNA damage load on genomes and predict functional outcomes in aging.
Nanopore Sequencing: We will use the power of nanopore sequencing in combination with bio-informatics and machine learning to develop new methods to detect pre-mRNAs, monitor de novo RNA synthesis and DNA damage.

P.S.: As a bonus you will also learn how to feed our lab pet axolotls (-;

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The consequences of DNA damage on transcription

Keywords:
DNA damage, Aging, Cancer, Transcription, Transcription coupled repair

Methods:
Live-cell imaging (e.g. time-lapse confocal, FRAP, DNA damage kinetics using confocal microscopy), quantitative proteomics, CRISPR/Cas9, modeling.

The eukaryotic genome is transcribed by RNA polymerase 2 (Pol 2). Pol 2 mediated transcription is a tightly controlled process to ensure correct temporal and spatial regulation of gene expression, which is crucial for proper cell function. However, the DNA template that is transcribed by Pol 2 is compromised on a daily basis by numerous types of DNA-damaging factors. DNA damage can block or strongly impede Pol 2 mediated transcription. If these transcription-blocking DNA lesions (TBLs) are not properly resolved, this will severely disrupt cellular homeostasis due to the disturbed synthesis of new RNA molecules. In addition, TBLs may result in genome instability, severe cellular dysfunction or premature cell death, which finally may result in DNA damage-induced accelerated aging. Cells counteract these harmful effects by specifically removing TBLs by transcription-coupled repair (TCR), thereby safeguarding transcription. The severe developmental, neurological and premature aging features observed in patients with inherited TCR defects underscore the biological relevance of TCR and show the involvement of TBLs in the aging process.

The main research focus of my lab is to investigate the precise consequences and impact of DNA damage that blocks transcription. Over the years, my lab has identified several factors that play important roles in this repair pathway (for example, Schwertman, Nature Genetics, 2012; Dinant, Mol. Cell, 2013; Tresini, Nature, 2015).

Thus far surprisingly little is known about the regulation of transcription or what exactly happens with Pol 2 following the induction of transcription-blocking DNA damage. To study how transcription is inhibited upon DNA damage, or how it is restarted following repair of the DNA damage we have generated a cell line expressing GFP-tagged Pol 2 at endogenous levels (Steurer, PNAS, 2018).

We use a combination of innovative live-cell imaging approaches with advanced proteomics and CRISPR/Cas9-mediated genomic approaches to identify new factors involved in the regulation of this pathway and to obtain a better understanding of the molecular mechanisms how cells cope with transcription blocking DNA damage.

Example Master End Project #1:

Effects of different types of DNA damage on transcription:
This project involves making testing the effects of different types of DNA damage (e.g. chemotherapy, oxidative damage) on transcription. This project will involve a lot of live-cell imaging, FRAP analysis and modeling of the acquired microscopic data to obtain new insight on the effects of DNA damage on transcription of microdevices that enable the formation of a lipid membrane. A method developed in the Aubin-Tam group enables easy access to both sides of the membrane. One goal is to form membranes of controlled composition, such as with different kinds of lipid molecules on each leaflet. The activity of single biological nanomachines that can pierce the membrane will then be measured.

Master End Project #2:

Regulation of transcription coupled repair:
DNA damage that blocks transcription is efficiently recognized and excised from our genome. However how the DNA damage is exactly removed from the chromatin remains largely unknown. In this project we will study for proteins that might be involved in the last critical step of this important repair reaction. The students will generate new fluorescent knock-in cell lines and develop new imaging tools to study the function of these new factors.

Julie Nonnekens Group, Molecular Genetics

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Radiobiology of radionuclide therapy

Molecular radionuclide therapies (MRT) are revolutionizing treatment of patients with metastasized cancers. During MRT, radioactively labeled compounds are targeted to the cancer cells via specific tumor binding. Once bound to the tumor cells, the radionuclides will induce DNA damage leading to cancer cell death. Currently, more cancer patients are being treated with MRT than ever before. However, it is clear that some patients are being over-treated (resulting in toxicity) or under-treated (no tumor regression). This indicates the clinical need for therapy improvement. Our lab focused on gaining a better understanding of the radiobiology, i.e. of the biological effects of ionizing radiation of MRTs. By using this knowledge, we can significantly contribute to increasing the effectiveness of MRTs by providing evidence in favor of one treatment method or regimen over another. In order to answer our research questions, we are using a variety of models and tools. From 2D cultured cells and ex vivo cultured human tumor slices to xenografted mice. This broad range of models allows us to study different aspects of MRTs. We use several cellular assays, immunohistochemistry of human tumor tissue or mouse organs, confocal live-cell microscopy and small animal imaging (SPECT, MRI, optical).

Upcoming Events

YER Workshop - *November 26*

sign up now via: www.yer.nl/hooke

Master's Open Day EUR - *November 30*

Excursion Baseclear - *January 9*

Gupta Case Study - *March 17*

Multiple Day Excursion - *March 20-22*

To stay updated on events and activities, visit the Hooke website!

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