BEP/MEP Event

14 November 2018

S.V.N.B. HOOKE

Study Assocation Nanobiology

TU Delft

Erasmus MC
Universitair Medisch Centrum Rotterdam

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Introduction

Hi fellow Nanobiologists,

In a while you have to choose what Bachelor/Master End Poject you're going to do. Well, the best choice you've already made… Coming to this event! I think this event is the best opportunity to orient yourself across the BEP/MEPs offered in the nanobiological field. So please look around, visit interesting presentations and view posters of the labs you could do your project at. My main message for today: don't be afraid to talk to some of the research groups about their research and BEP/MEP opportunities. As such you'll get a much better idea of which projects suit you and which do not. I hope you learn a great deal today and get a somewhat clearer future on your interests and career path. Enjoy!

Sweet Regards,

Tim Zonjee
President of Cohecie 4

General Information

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: Cohecie 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 36/48 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.

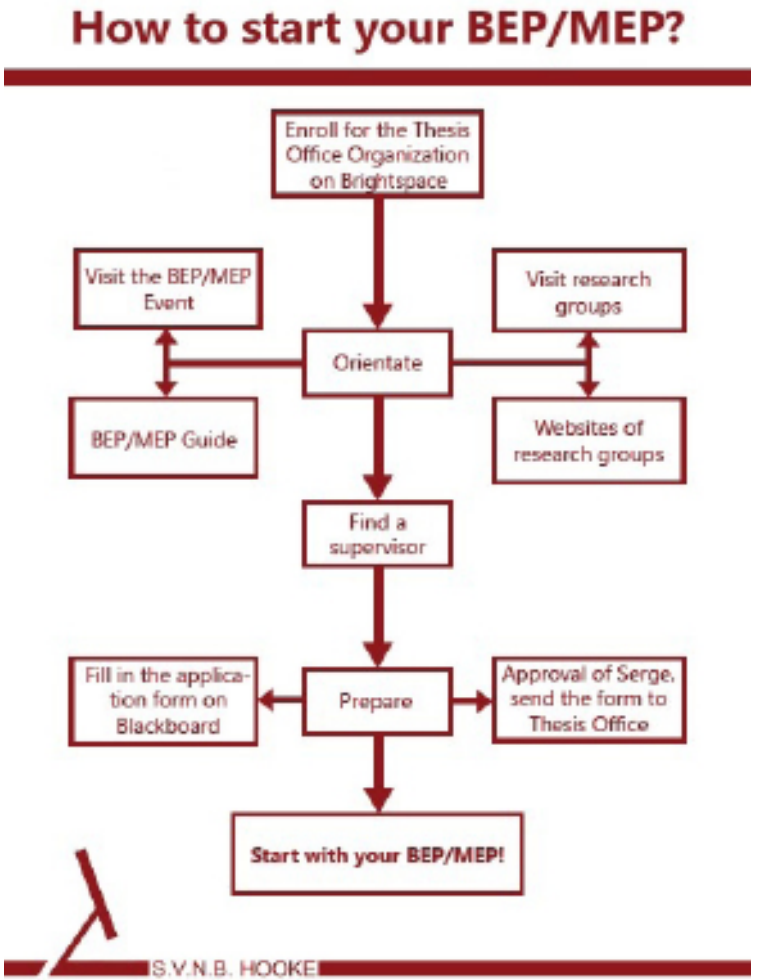
Concerning Internship and Master end project within the Master:
• At least one of these should be followed within the Bionanoscience department or within Erasmus MC.
• Both may be followed within the Bionanoscience department but not within the same group (same PI).
• Both may be followed within the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

Step-by-step guide for your BEP/MEP:
1. Orientation
• Visit the BEP/MEP event organized by the Cohecie.
• 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 Brightspace.
• Fill in the BEP/MEP application form. This form should be 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



Research Groups Delft

Daan Brinks Lab

Contact: D.Brinks@tudelft.nl

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 GEVIs optimized for two-photon (2P) imaging, using a new single-cell selection technique. This allows us to screen mutant libraries of GEVIs directly for brightness and photostability under 2P-excitation, voltage sensitivity, and membrane trafficking in neurons.

Optimized GEVIs and excitation protocols will then be used to investigate for instance memory formation. As an example, we know that procedural memory formation in the cerebellum, as well as more convoluted 'states' in the hippocampus, cannot be fully captured by correlated activity as measured in calcium dynamics. The hypothesis is that correlated timing and shapes of individual action potentials in different cells in the network play a role here, which we will resolve.

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 the potential application of minimally invasive techniques. Targeting genetically selected cell populations expressing channelrhodopsin with through-the-skull non-ballistic illumination, and detecting electrical activity with a new kind of quantum magnetometer (which has been shown to be able to detect individual action potentials in individual neurons from a distance of several mms) could prove a fantastically fruitful niche between the high resolution but cumbersome measurements on single cells using optical imaging, and the easier but significantly lower resolution measurements of fMRI or ultrasound. We're looking into the development this technology in collaboration with the lab of Eugene Polzik at the Niels Bohr institute in Copenhagen.

Cees Dekker Lab

Contact: A.Fragasso@tudelft.nl

Nanopores are unique tools that allow for label-free high-throughput single-molecule investigation of biomolecules such as DNA, proteins, and peptides chains. The principle of interrogation for nanopore sensing derives elegance from its simplicity: a nanopore, which can be either biological or artificially made, defines a nanoscale sensing volume through which biomolecules can be probed on passage, usually via an ionic-current readout.

As a group working at the crossroads of nanotechnology and biology, we use nanopores as biophysical tools to study biomolecular transport in a variety of ways. Projects range from DNA and protein sequencing, to biomolecular trapping and mimicking of Nuclear Pore Complexes.

Meijer Lab

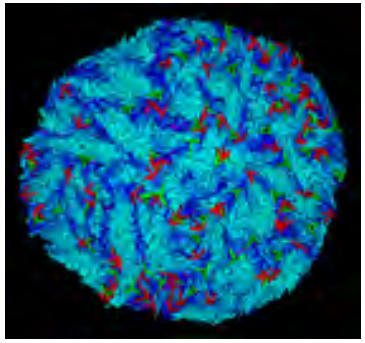
Contact: D.H.M.Meijer@tudelft.nl

The Meijer group investigates the development of the central nervous system. We use molecular and cellular techniques to discover the mechanisms of neural diversity and neural circuitry formation. We specialize in cell-fate choice, neuronal partnering and the tripartite synapse. Recent work has focused on neuronal partnering, and synapse formation in particular. At the molecular level, synapse formation is enabled by cell-adhesion molecules that interact across the synapse. At present, many individual proteins have been identified that contribute to synaptic cell adhesion, but it is unclear how these individual proteins team up in macro-molecular complexes to organize synapse formation and function. Teneurins, a family of type II transmembrane proteins, have been characterized as synaptic cell adhesion molecules (CAMs) and are instrumental in the formation of neural circuits, including visual and memory circuitry. Previously, we determined the cryo-EM structure of Teneurin3 ectodomain in monomeric form. This reconstruction revealed a surprising novel fold for mammalian proteins. The structure contains a YD-shell topped with a beta-propeller similar to bacterial toxins, but it also harbors additional N- and C-terminal domains. Future studies for this project entail the functional implications of the Teneurin domain architecture in developing neural circuits.

Please, come visit our poster to discuss our research and potential student projects.

Idema Group

Contact: T.Idema@tudelft.nl



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 a¬ffect the function and behaviour of the living system they are part of.

Available projects in 2019 include:

- The dynamics of bacterial colony growth and defect formation.
- Flow of active particles through narrow openings.
- Deformations of tissues under applied stress.
- Differentiation in growing eukaryotic tissues.

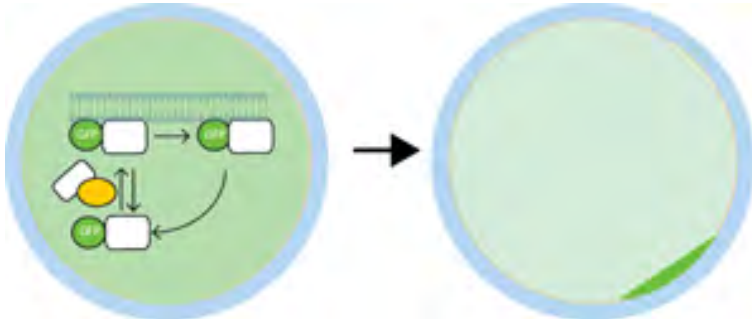
More information on all projects at idemalab.tudelft.nl.

Laan Lab

Contact: L.Laan@tudelft.nl

The Laanlab is a young, multidisciplinary, international lab, which focusses on how a network of proteins can both be highly precise on cell cycle timescales and simultaneously very adaptable on evolutionary timescales. We focus on the essential biomolecular network for polarity establishment in budding yeast, which is one of the best understood molecular networks in eukaryotic cells, allowing for a quantitative description. Roughly there are three research lines in my lab:

1) We use experimental evolution in combination with growth rate assays, whole genome sequencing, and modelling to investigate how the network for polarity establishment evolves.
2) We combine live cell microscopy, flow cytometry and modelling to understand how the molecular details of the symmetry breaking network affects its function and evolvability.
3) To find basic network structures, which facilitate evolution, we build minimal networks in vitro. We will enclose purified components in lipid droplets and study how symmetry breaking changes with an increasing number of components.



Based on your interest and the current state of the research in the lab you will together with us design a BEP or MEP project within one of these research lines. Different idea's within the research interest of the lab are more than welcome as well.
Please visit our website for more info: laanlab.tudelft.nl, Or contact Liedewij: l.laan@tudelft.nl

Brown Lab

Contact: J.M.C.Brown@tudelft.nl

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

Rieger Group

Contact: B.Rieger@tudelft.nl

At TU Delft, our research team works on Computational Microscopy in light and electron microscopy. It comprises the combination of imaging physics and image processing to surpass fundamental limitations imposed by physics on image formation. Our main application area is in life sciences at the molecular level, with the most notable research activity at the moment in localization or super-resolution microscopy, an area also known as optical nanoscopy. The team aims to develop techniques that offer the highest spatial (and temporal) resolution in microscopic imaging. With this aim, we place ourselves in between purely curiosity and application-driven research. Currently we are developing experimental and theoretical means to enable localization microscopy at cryogenic temperature.

Joo Lab

Contact: C.Joo@tudelft.nl

In the Joo lab we use cutting-edge single-molecule fluorescence tools to identify biomolecules and to study their working mechanisms on the nanometer scale. More specifically we are interested in how small RNAs mediate gene silencing (RNA interference) and how anti-viral defense is performed (CRISPR immunity and DNA interference). In addition, for studying the influence of DNA or RNA sequence on these processes we are developing a high-throughput method combining single-molecule experiments with next-generation DNA sequencing. Last but not least, we are developing a highly sensitive single-molecule technique for protein sequencing which can be applied to detect low-abundant proteins in single cells

Carroll Group

Contact: E.C.M.Carroll@tudelft.nl

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.

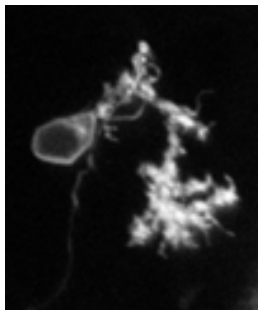


Image analysis of 3D structure of neurons

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.

In vivo efficacy study of radiation therapy dose rate effects in zebrafish

The main goal of this project is to explore the radiobiological effects of different irradiation dose rates, and establish a basis for future radiotherapy experiments with the use of Zebrafish. A pilot study will be performed to test the effects of high and low dose-rate irradiations in zebrafish embryos, as assessed by a combination of intravital imaging and pathological analysis of tissue damage. We are looking for a highly creative, enthusiastic student with both good experimental and numerical skills, who would be interested in designing and building a completely new experimental setup from scratch, as well as performing and evaluating measurements with his/her own device.

Nynke Dekker Lab

Contact: B.P.SolanoHermosilla-1@tudelft.nl

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!

The Nynke Dekker Lab is located in 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.!

Delft Bioinformatics Lab

Contact: T.Abeel@tudeft.nl

The Delft Bioinformatics Lab
We create computational tools to gain biological insight through analysis of high-throughput molecular biology data. We have a strong affinity for algorithms, machine learning and data analytics, and a profound interest in novel biomolecular technologies. Our application areas span biomedicine, microbiology, and plant research.

THEMES

Genome and genomic variation
Advances in technology have made it possible to read the whole DNA of an organism in fragments. We address algorithmic challenges related to assembling the reads into complete genomes, comparing genomes, and characterizing genomic variation.

Genome assembly: haplotype reconstruction, aneuploid/polyploid genome assembly, long-read assembly for repeat-rich genomes/regions;
Variant prediction: allele specific variant calling, tissue specific somatic variant detection;
Pangenome graphs: construction, analysis and visualization of pangenome graphs as an alternative to single-genome linear references, enabling improved structural variant detection.

Gene regulation
We analyze spatial and temporal changes in genome-wide profiles of regulatory elements under various conditions to decipher gene regulation and disruptions involved in disease.

Pathway prediction: automated identification and analysis of regulatory pathways across tissues, patients, single-cells (RNA-seq, TF ChIP-seq);
Gene essentiality: detection of essential genes, synthetic lethal interactions, redundant genotypes from perturbation screens (siRNA/shRNA, CRISPR/Cas9);

Epigenetic regulation: influence of epigenomic landscape on diverse biological processes (chromatin compaction, histone marks, …);
Single-cell: identification of cell populations (scRNA-seq), integration of multi-panel mass cytometry measurements (cyTOF).

APPLICATION DOMAINS

Microbial genomics
Medical: genotypes of antibiotic resistance in pathogenic bacteria, DNA-based diagnostics of complex bacterial infections.
Industrial: mutations affecting yield and conversion efficiency.

Cancer research
Novel therapeutic targets: identification of regulators of disrupted pathways, genes essential for cancer cell survival, synthetic lethal interactors.
Genotype redundancy: detection of genotypes leading to similar regulatory signatures.

Neurobiology and neurological disease
Aging research: representation of multivariate phenotypes of neurodegeneration, and genotypephenotype association via burden tests or graphical models in Parkinson's and Alzheimer's disease.
Brain atlases: analysis of transcriptome patterns across brain regions and development stages in
autism, migraine, Duchenne muscular dystrophy.

CONTACTS

Gene regulation, cancer: Joana Gonçalves
http://joanagoncalves.org (joana.goncalves@tudelft.nl)

Pangenome graphs, microbial genomics: Thomas Abeel
https://www.abeel.be/ (t.abeel@tudelft.nl)

Genome analysis, neurobiology: Marcel Reinders
m.j.t.reinders@tudelft.nl

Aubin-Tam Group

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

The Aubin-Tam group (Bionanoscience) is interested in:

- Fabrication of biomineralized composite materials. Most living organisms fabricate composite materials. Due to their intricate and hierarchical structure, biocomposite materials present improved material properties. We use micro-organisms to fabricate biomimetic materials combining stiffness and toughness.
- Mechanical processes at the cell membrane. We study how individual biomolecules/cells respond to external stimuli to better understand molecular mechanisms. We design, develop and use biophysical assays to track dynamical cellular processes occurring at the cell membrane.

In 2019, we have the following projects available:

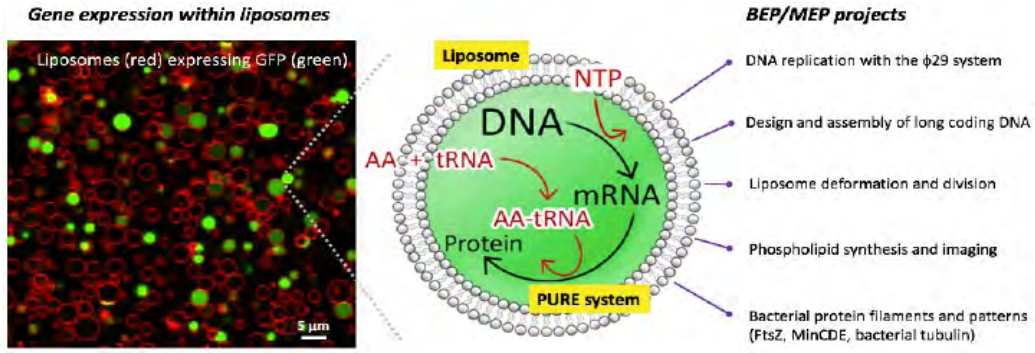
- Master Project: Resolving the dynamics of single contractile nanomachines. With single-particle fluorescence and electrophysiology approaches, we seek to resolve the dynamics of contractile machines (e.g. bacteriophages).
- Bachelor Project: Flagellar biolocomotion. Implement and use neural networks for image recognition of flagella in high-speed movies.
- Master Project: Flagellar biolocomotion at the microscale, studies on single cells. Direct measurement of the flow generated by flagellar motion, with the use of optical tweezers.

Feel free to contact us, as other projects related to the research themes described above might also be available.

Christophe Danelon Lab

Contact: C.J.A.Danelon@tudelft.nl

Our group is engaged in the long-term effort to construct a minimal cell using a bottom-up approach. The core architecture of our minimal cell model consists of a cell-free gene expression system – the PURE system – encapsulated inside a lipid vesicle (liposome) compartment. Using in-liposome synthesis of proteins from DNA templates, we aim to reconstitute four essential cellular modules: DNA replication, vesicle growth through lipid biosynthesis, liposome division, regeneration of the gene expression machinery.



Research groups Rotterdam

Claire Wyman Lab

Contact: C.Wyman@erasmusmc.nl

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

Aleksandra Badura Lab

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 in the environment. What is fascinating is that even in this simple example humans will employ different strategies that are highly heterogeneous in a way that depends on individual characteristics. Psychologists refer to these characteristics as personality traits. One person might first check every corner of the cutlery drawer, and someone else might just ask for help. However, in some disorders characterized by repetitive and stereotyped behaviors this adaptation to changes in conditions 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 in vivo electrophysiology, virtual reality and calcium imaging to modeling.

Ten Berge Lab

Contact: D.tenBerge@erasmusmc.nl

The ten Berge group studies the cellular and molecular mechanisms that govern the creation and self-renewal of pluripotent and adult stem cells.
Every adult mammal, including humans, is constructed from many millions of cells, each specialized into muscle, blood, bone or other cell types. During this specialization, each cell builds up a memory that permanently records the type of the cell. This starts very early in embryonic development, a few days after fertilization. However, the early embryonic cells already possess a cellular memory, inherited from the male and female gametes that produced the embryo. Before the cells acquire the ability to make all cell types of the embryo, a property called pluripotency, they must erase this old cellular memory.

Cellular memory consists of epigenetic modifications of the genomic DNA. Signals, such as growth factors, that regulate the differentiation of the cell leave a trace in these modifications that lead to permanent changes in gene expression. We study which epigenetic changes occur during the induction of pluripotency in the embryo, which molecular mechanisms take care of these changes, and how these are linked to the embryonic processes that simultaneously take place, such as implantation in the uterine wall, growth and pattern formation. This research can provide us with many new insights into the formation of pluripotency, in the epigenetic mechanisms that regulate pluripotency and cell differentiation, and in early embryonic development. Moreover, it will provide insight into the mechanisms by which pluripotent cells regulate gene expression in the absence of normal epigenetic mechanisms. Such alternative mechanisms have also been observed in cancer cells, and our research may therefore lead to a better understanding of the role of epigenetic mechanisms in cancer. More information, including about student projects, can be found on our web page: https://www.erasmusmc.nl/cellbiology/research/research-groups/berge/

Chien Lab

Contact: M.P.Chien@erasmusmc.nl

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 techniques (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.

Bremen Lab

Contact: P.Bremen@erasmusmc.nl

Optical coherence tomography (OCT) is a 3D optical imaging technique. Traditionally OCT has been used for the visualization of anatomical structures. A typical application is the ophthalmological assessment of the eye and retina. In addition to providing structural information, the OCT technique can be extended to provide a depth resolved measure of neuronal activity (fOCT). The basic operating principle of fOCT is interferometry. Rays from a low-coherence light source are separately projected onto a reference mirror as well as onto the tissue under study, the combination of the reflected light from both sources creates an interference pattern that can then be analyzed. Depending on the hardware specifications fOCT achieves a range of several millimeters, e.g. spanning the cortical column, and a spatial resolution of several micrometers, i.e. down to the cellular level. Therefore, fOCT is a promising technique for large-scale mapping of brain activity along the depth axis. So far, fOCT has been successfully employed to study the functional architecture of cat visual cortex and rat olfactory bulb. In your project you will study the processing of audiovisual integration in individual layers of sensory cortices in collaboration with the group of Dr. van der Heijden.

Approach: All fOCT measurements take place in the setup of Dr. van der Heijden. To establish the basic experimental and analysis pipelines, first, you will measure subcortical and cortical activity to simple auditory stimuli. Note that the interpretation of the fOCT signal is facilitated by the clear tonotopic, i.e. sound frequency-based, organization of the auditory system. Additionally, extracellular neurophysiological recordings will allow you to correlate neuronal voltage signals with the optical fOCT signals. After successful completion of these measurements you will apply fOCT to measure cortical activity under audiovisual stimulation. Of particular interest for these measurements is the spatiotemporal activity pattern evoked by visual (auditory) inputs into cortical columns of auditory (visual) cortex. Techniques: 1) Optical coherence tomography of the cerebral cortex in anaesthetised Mongolian gerbils 2) Neurophysiology with multi-site silicone probes in anaesthetised Mongolian gerbils 3) Matlab for digital signal processing, and data analysis

Marteijn Lab

Contact: J.Marteijn@erasmusmc.nl

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 transcritpion. 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. For example, the exact mechanisms how transcription is inhibited upon DNA damage, or how it is restarted following repair of the TBLs remains largely enigmatic. 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.
If you are interested, please contact me by email to discuss the possibilities for an internship in my lab.

Demmers Lab

Contact: J.Demmers@erasmusmc.nl

Project background | The proteasome is a huge multi-subunit protein degradation machinery in the cell. It degrades damaged proteins by proteolysis. Proteasomes are part of a major mechanism by which cells regulate the concentration of particular proteins and degrade misfolded proteins. The degradation process yields peptides that can then be further degraded into amino acids and used in synthesizing new proteins. Proteins are tagged for degradation with a small protein called ubiquitin. The tagging reaction is catalyzed by enzymes called ubiquitin ligases, resulting in a polyubiquitin chain that is bound by the proteasome, allowing it to degrade the tagged protein.

What are you going to do? | In our lab, we study the proteasome by using combinations of biochemical and cell biological methods, and state-of-the-art mass spectrometry based quantitative proteomics (SILAC). In this project the role of the individual components of the proteasome will be studied by monitoring the quantitative and qualitative changes in the global proteome that occur after selective removal of each individual component by RNAi. What are we looking for? | We are looking for motivated BSc or MSc students in Chemistry, (Medical) Biology, Biotechnology, Life Sciences or any related field, who are available for an internship of at least 6 months. A background in cell biology and biochemistry and/or analytical chemistry (preferably mass spectrometry) is recommended. What's in it for you? | In this research project you will learn modern mass spectrometry based proteomics techniques (nLC-MS) and get the opportunity to work with the most recent high-end mass spectrometers yourself. In addition, you will become familiar with biological and biochemical approaches and cell culturing to study proteasome (dys)functioning. Together, this will provide you with a solid background and expertise that will be very useful for your further career, in science or in industry. Obviously, there is the opportunity to (co-)publish the work if it turns out to be successful. Interested? Please send your CV and a motivation letter to Dr. Jeroen Demmers. For more information visit our website www.proteomicscenter.nl.

Van Gent - Kuijten Project

Contact: D.VanGent@erasmusmc.nl and/or M.Kuijten@erasmusmc.nl

The DNA damage response is a powerful tool of the cell to protect the genome by preventing replication of genetic mutations. A well-known defect in DNA repair is caused by mutations in one of the BRCA genes, present in several hereditary breast and ovarian cancers. BRCA proteins are essential for DNA repair via Homologous Recombination (HR), making these cancers hypersensitive to PARP1 inhibition. However, PARP inhibitor resistance may occur. We are developing reporter constructs to assess HR proficiency in single breast cancer cells in a 3D breast cancer model as a tool to select PARP inhibitor sensitive tumors and to monitor resistance development.

The project involves the use of molecular biology, cell biology, imaging and programming techniques to study DNA repair in live 3D cell models. Methods we are using include 2D and 3D cell culture, genetic modification of cells (including cloning of the constructs and transfections), confocal imaging of live/fixed 2D/3D cell cultures. Moreover, we need to develop an imaging analysis tool to assess subcellular structures in a 3D cell model.

Kanaar Lab

Contact: O.Zelenskyy@erasmusmc.nl

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 microscopy experiments, through 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 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.

Lebbink Lab

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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 properties determine stable DNA binding by the CRISPR-Cas9 nuclease?
- How can we exploit Cas9 as in vitro tool to study DNA mismatch repair?

Techniques and approach: mutation, protein purification, in vitro reconstituted DNA repair and nuclease assays, surface plasmon resonance, fluorimetry, Monte Carlo simulations

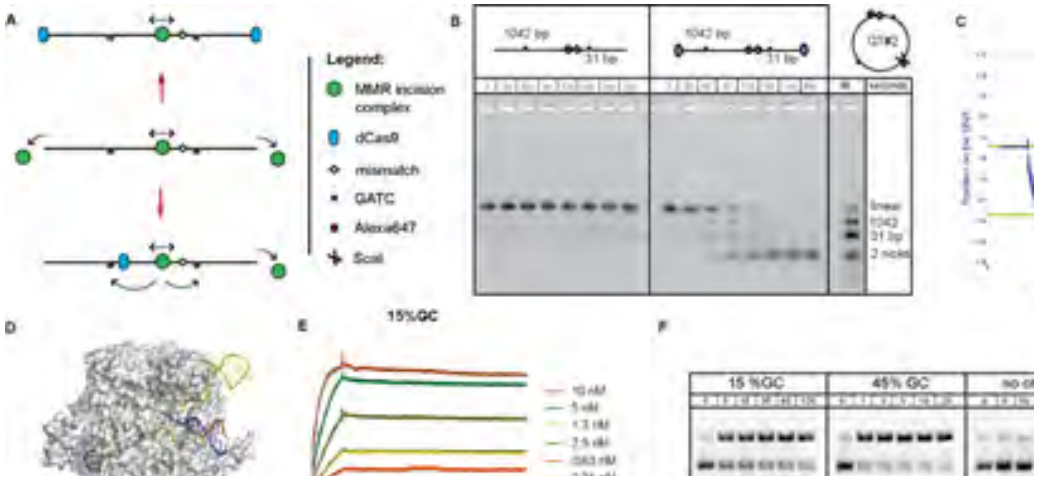

Figure 1: Structural biochemistry of DNA mismatch repair and CRISPR-Cas9.
A) Scheme depicting diffusive behavior of MMR complexes on DNA during early steps of repair. B) Effect of dCas9 end-blocks on the strand incision activity during MMR. C) Monte Carlo simulation predicting position of MutS and incision of DNA in time. D) Structure of Cas9 (grey) bound to RNA (yellow) and DNA (blue and orange). E) Kinetics of binding of dCas9 to DNA. F) DNA incision by nCas9.

Mulugeta Lab

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Cellular development and differentiation is a tightly controlled process. This tight control involves several genes that are organized in different gene regulatory networks (biological circuits) to regulate the expression of genes within their network or beyond. Unravelling the systems biology relationship and dynamics of such biological circuits remains a challenge. Recent advances in massive parallel genome editing and single cell DNA and RNA sequencing now make it possible to study these biological circuits in unprecedented detail. By applying state of the art techniques and developing new approaches, we aim to deconstruct the regulatory network of signalling and transcription factors (TFs) during development. Our main biological questions include:

1. What is the dynamics of the regulatory network of signalling pathways and TFs in mouse embryonic stem cells (mESCs) and their neural and hematopoietic cells after differentiation?
2. How do signalling pathways crosstalk in embryonic stem cells before and after differentiation?
3. How do signalling pathways crosstalk with core TFs in embryonic stem cells and during their differentiation?

The project is multi-disciplinary combining many of branches of biology (molecular biology, developmental biology and biochemistry) with computer science and mathematical modelling.

We are looking for students with strong interest in:

1) Dry lab experiments (bio-informatics and computational biology)
2) Wet lab experimental work that involves:

- stem cell differentiation in cell culture (mESC and induced pluripotent cells)
- gene perturbation experiments (via CRISPR/Cas)
- single cell RNA and DNA sequencing

Department of Developmental Biology

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After fusion of sperm and egg, the emerging zygote represents a naïve state which allows descendants of this cell to contribute to all cell types in the developing embryo. Prior to initiation of new life, epigenetic information needs to be reset. The processes that lead to the establishment and erasure of epigenetic information are highly complex and extremely relevant with respect to human disease. In the midst of the global epigenetic turbulence that accompanies early embryonic development, the newly formed embryo has to immediately assess its number of X chromosomes, to ensure activation of the dosage compensation mechanism in female embryos, by inactivating one of the two X chromosomes. Only when primordial germ cells enter meiosis, in the embryonic ovary, this inactivation is reversed, and two active X chromosomes support oogenesis. In contrast, in the male germ line, entry of meiosis is accompanied by inactivation of X and Y.

Our research is focussed on sex chromosome epigenetics during the life cycle, and in stem cells. By performing a BEP/MEP project in our lab you will contribute to one of the ongoing research lines in the Department of Developmental Biology. Current topics are for example: High resolution microscopy to understand chromosome pairing in meiosis, application of a new tool that can be used to detect genome wide DNA methylation patterns or to retrospectively detect gene expression patterns in stem cells, by analyses of differentiated cells, Use of CRISPR-Cas technology to identify new regulators of X chromosome inactivation in female stem cells, or work on the project that aims to identify genes involved in sex determination in the mole vole that lost its Y chromosome (ellobius lutescens). We also use, and are setting up new in vitro models to study aspects of early development and gametogenesis. You will be supervised by Joost Gribnau, Willy Baarends or Hegias Mira Bontenbal, as well as by current PhD students and postdocs in the lab. Together, all our projects aim to gain new basic insight into essential developmental processes, and the results will lead to the generation of useful new (in vitro) models to unravel epigenetic mechanisms involved in reprogramming, genome integrity, development of disease and infertility. We hope to meet you in our lab! Joost Gribnau, Hegias Mira Bontenbal, and Willy Baarends

Wendt Lab

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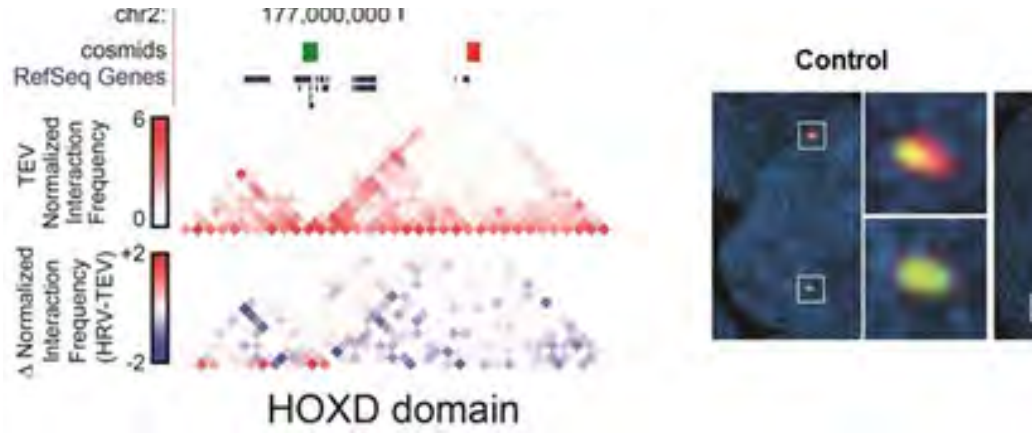
Cohesin and chromatin organization

The regulation of gene activity is crucial for embryonic cells to develop into a body with numerous different tissues. Here regulatory elements such as promoters and enhancers play a role. Recent advances in techniques studying the three-dimensional organization of the chromatin fiber in the cell nucleus revealed that the folding of the chromatin fiber is also of great importance for regulating gene activity and steer developmental processes.

Our research interest is to understand which proteins are involved in shaping the 3D-architecture of the human genome. Our previous research revealed that the cohesin complex and the chromatin insulator protein CTCF play very important roles. However, the molecular mechanisms when and how loops are formed are only poorly understood. Further, mutations in the cohesin complex and its regulars are observed in rare human developmental syndromes and rather frequently in cancer. The mechanisms how these mutations cause the disease and whether changes in chromatin structure are involved are still unclear.



We are using different methods to investigate the interactions of the chromatin fiber:

Chromatin conformation capturing (4C, T2C, HiC)
Imaging (DNA FISH)
Currently we establish live cell labelling and imaging of chromatin structures.

Other essential methods in the lab are:

Chromatin immunoprecipitation (ChIP), also combined with next generation sequencing (ChIP-seq)
Identification of novel binding partners with immunoprecipitation and mass spectrometry
CRISPR/Cas9 genome editing to generate model cell lines carrying patient mutations
Engineering of degron tags into the endogenous proteins with CRIPSR/Cas9 to allow rapid protein depletion
Biochemistry and different cohesin functional assays
Imaging of immunostained cells and live cells carrying fluorescent markers

We are always looking for curious and motivated students who want to unravel the mysteries of chromatin organization.
Please get in contact: k.wendt@erasmusmc.nl
Lab webpage: www.erasmusmc.nl/cellbiology/research/research-groups/wendt

HeartCHIP Project

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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).

Vermeulen Lab

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Research in our group at the department of Molecular Genetics of Erasmus MC is focused on elucidating the molecular mechanism and regulation of nucleotide excision repair and its impact on human health. This important DNA repair mechanism protects organisms against DNA damage-induced carcinogenesis and premature aging. In our lab, we apply a multidisciplinary approach, including state-of-the-art confocal microscopy and proteomics, to improve our understanding of its molecular mechanism. Research questions that we currently aim to answer are:

Which proteins (and posttranslational) modifications participate in and regulate NER?
How does NER protect against cancer? Can knowledge about NER be used to treat cancer?
What is the impact of DNA damage on transcription and how is this signaled?
How do heredity mutations in NER genes affect health?
How does DNA repair act within chromatin?
How does NER function within different cell types?
How is the interplay of NER with other DNA repair pathways regulated?

We are looking for ambitious students interested in elucidating molecular mechanisms of DNA repair. Students typically work on their own project, with daily supervision by a PhD student or postdoc. For more information, visit our website at www.vermeulenlab.com or email to w.vermeulen@erasmusmc.nl.

Program

16:30	Welcome	foyer
17:00 - 17:45	Presentations *Serge Donkers* *BEP student* *MEP student*	CO-1
16:30 - 18:30	Information market	foyer & OWR10
18:30	Drinks	't Vat