BEP/MEP booklet

BSc and MSc Nanobiology

BEP/MEP event 2023

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General information for BEP students

Bachelor End Project: in short

- 20 ECTS (i.e., ~3 months full time or 5 months part time).
- All approved groups are on the green list.
- Consists of literature study, research work, thesis writing, and final presentation and defense.

Prerequisites

To start your BEP, you should have completed all courses from the first year of Nanobiology. In addition, you have to have 60 ECTS from the second and third year combined; this can include your minor.

Resources

- The Brightspace page Thesis Office Applied Sciences.
- The BEP/MEP database and booklet.
- The websites of individual supervisors.
- TU Delft Writing Centre.

Best practices

- Do not only consider the content of the project, but also the **overall feeling** of the lab. It is important that you feel safe to ask questions. It may help to discuss with multiple supervisors before choosing a project.

- You might have a preference in **supervision**: would you like to have frequent meetings or do you prefer to discuss more infrequently? Think about this before discussing with your potential supervisors.

- When discussing potential BEPs, also think of **practical issues** such as lab space, resources, lab activities, etc. that might aid you during the process.
- Hand in the **BEP application form** before starting your BEP. This may help catch potential issues in an early stage. Your supervisor should sign it and you can send it to info-bsc-nb@tudelft.nl afterwards.
- Keep in mind that the goal of a BEP is **not to generate results**: your BEP should be a learning experience, so make sure to take time to discover how you work best.
- If you need help, **don't be afraid to ask**! Your supervisor should be your first point of contact, but you can always contact our academic counsellor Tanja Hilkhuijsen if you need additional support.
- To alleviate the writing stage, it can be helpful to **write sections** of your BEP as you are going through the process.

General information for MEP students

Master End Project: in short

- 42 ECTS (i.e., ~7-8 months full time).
- All approved groups are on the green list.
- Consists of literature study, research work, thesis writing, and final presentation and defense.

Prerequisites

To start your MEP, you should have completed at least 35 ECTS of Nanobiology MSc courses; this can include your electives. Moreover, you have to complete both Project Development courses (NB4510 and NB4520) before starting your MEP. Between your broadening research project and your MEP, at least one should be completed within a research group included on the green list.

Resources

- The Brightspace page Thesis Office Applied Sciences.
- The BEP/MEP database and booklet.
- The websites of individual supervisors.
- TU Delft Writing Centre.

Best practices

- Do not only consider the content of the project, but also the **overall environment** of the lab. It is important that you feel safe to ask questions. It may help to discuss with multiple supervisors before choosing a project.

- You might have a preference in **supervision**: would you like to have frequent meetings or do you prefer to discuss more infrequently? Think about this before discussing with your potential supervisors.
- When discussing potential MEPs, also think of **practical issues** such as lab space, resources, lab activities, etc. that might aid you during the process.
- To pick a group, it might help to look into the places where graduates of that specific group **ended up**. Do you see yourself going a similar route?
- Hand in the **MEP application form** before starting your MEP. This may help catch potential issues in an early stage. Your supervisor should sign it and you can send it to info-msc-nb@tudelft.nl afterwards.
- If you need help, **don't be afraid to ask**! Your supervisor should be your first point of contact, but you can always contact our academic counsellor Tanja Hilkhuijsen if you need additional support.
- To alleviate the writing stage, it can be helpful to **write sections** of your MEP as you are going through the process.

Project Development Course

NB4510 and NB4520

Are you a new MSc Nanobiology student?

Then we look forward to seeing you at the Project Development Course!

This course is compulsory and carries a weight of 10 ECTS, scheduled to run in the third and fourth quarters of 2023/24. Throughout this course, we will provide you with essential (soft) skills to ensure your preparedness for the commencement of your MEP, enabling you to maximize your research-focused time effectively. At the MEP event, we will provide you with more information and answer your questions.

IMPORTANT: Start looking for your potential MEP supervisors early so that you can make the most of this course. It is required that you have a potential MEP supervisor already by 11th February, 2024.

We look forward to seeing you soon!

Your course coordinators:

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Robert-Jan Palstra, r.palstra@erasmusmc.nl
Shringar Rao, s.rao@erasmusmc.nl

Erasmus MC

Baarends Lab

Department Developmental Biology

Principal investigator Willy Baarends

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Human *in vitro* oogenesis: bridge technology gaps, improve protocols, enhance knowledge

BEP MEP

Supervisor: Ilse de Bruin, i.debruin@erasmusmc.nl

Human oogenesis is hard to study *in vivo*, because it mostly occurs during the fetal period, bringing both technical and ethical difficulties. That's why we focus on creating an in vitro differentiation model of human oogenesis to be able to study all aspects of egg cell development. We are culturing immature germ cells and optimizing differentiation protocols for oocyte development, while checking expression levels using qPCR and immunostaining / confocal microscopy. Furthermore, we study X chromosomal dynamics during germ cell specification, which can be analyzed by for example RNA FISH / confocal microscopy. Lastly, we analyze recombinase locations of homolog pairing during meiotic prophase I in human oocytes, using the superresolution microscopy technique dSTORM and analysis in Fiji / R.

Techniques

- IPS culture and differentiation,
- Co-culture systems with mouse primary material
- RNA extraction and RNA FISH
- cDNA synthesis
- qPCR
- dSTORM and confocal microscopy
- Data analysis in R
- Immunofluorescence staining

In vitro differentiation towards the human fetal ovarian soma

BEP
MEP

Supervisor: Nina Dartée, n.dartee@erasmusmc.nl

Development of reproductive cells (gametes), oocytes in females, relies on the support of somatic granulosa cells (GCs). GCs encapsulate premature oocytes, forming a follicle that enables the progression of oocytes through the first stages of meiosis. We aim to model in vitro gametogenesis by producing the female reproductive by combining hiPSC-derived granulosa-like cells and hiPSC-derived oocytes. My project focusses on differentiating the supporting cells in vitro. To find and understand the signals that guide granulosa cell differentiation, we are analyzing sequencing data and creating reporter cell lines for large scale condition testing. Furthermore, we are testing 2D and 3D cell culture conditions and assessing methylation and transcriptome status of pluripotent and differentiated cells in vitro and in vivo to recapitulate the fetal ovary as accurately as possible.

Techniques

- IPS culture and differentiation
- Co-culture systems with mouse primary material
- DNA and RNA extraction
- cDNA synthesis
- (q)PCR and gel electrophoresis
- Bacterial work (e.g. transfection)
- Confocal microscopy
- Big data analysis (e.g. single cell and bulk RNA sequencing, methylation sequencing) in R

Badura Lab

Department	Neuroscience
Principal investigator	Aleksandra Badura
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Cerebello-cortical networks in Shank2 mouse model of Autism Spectrum Disorder

~~BEP~~ MEP

Pathogenic SHANK2 variants are extraordinarily rare in the general population but estimated to occur in 0.15%-0.3% of all individuals diagnosed with Autism Spectrum Disorder (ASD). SHANK2 is therefore regarded as a high-confidence ASD risk gene. Heterozygous loss-of-function mutations within the SHANK2 gene show very high prevalence in ASD diagnosis, often accompanied by other deficits.

Previous studies showed that human neurons with SHANK2 mutations make more functional excitatory connections relative to controls, and our own studies identified strong behavioral deficits in Shank2 deficient mice including. We also have preliminary data that shows altered functional brain connectivity in Shank2 mice. However, it is not known if the altered connectivity and behavioral deficits are the result of increased excitation in the cerebello-cortical network. Thus, in this project, we will investigate if the activity of the mPFC, primary motor cortex and cerebellar Crus1 is elevated in Shank2 mice while performing cognitive flexibility tasks.

Techniques

- Shank2 mouse model
- Intracranial surgery
- Viral injections

- *In vivo,* awake electrophysiology
- Calcium imaging
- Behavior and functional connectivity
- Prediction models

Can damage to the cerebellum lead to structural changes in the neocortex?

~~BEP~~ MEP

Injury to the cerebellum is the only risk factor that is quantitatively comparable to that of having an identical twin with autism, consistent with the fact that deficits have been reported after cerebellar injury. These findings point to a role for cerebellar dysfunction in the etiology of cognitive disorders, but explaining how they fit into models of autism has been difficult. The most parsimonious hypothesis is that during development cerebellum shapes the development of cortical areas involved in cognition and social interaction. Recent studies show that functional changes restricted to the cerebellum indeed cause behavioral change. However, many questions remain on the regionality of these changes, their critical periods and their effect on functional networks.

Here, we will answer these questions by performing lesion studies in mice at critical time points to investigate the causal role of specific cerebellar regions in shaping cortical anatomy and cerebello-cortical resting state networks. We will quantify changes to dendritic and synaptic densities in the neocortex following cerebellar insult. We will also study the impact of cerebellar lesions on cerebello-cortical resting state networks and white matter tracts.

Techniques

- Viral injections
- Confocal imaging and analysis
- 3D reconstruction
- (UHF-MRI) 7T in vivo imaging
- MRI data analysis

Cilia and signal transduction

Department Cell Biology

Principal investigator Gert Jansen

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Molecular mechanism of neuronal cell fate maintenance

BEP MEP

To maintain their proper functioning, cells must maintain their fate. However the molecular mechanisms that maintain cell fate are not well understood. We study this process in the ASE salt sensing neurons of C. elegans. We recently identified a transcription factor that contributes to ASE fate maintenance. In this project we will study the function of the transcription factor using molecular genetics, imaging techniques and behavioral assays.

Techniques

- C. elegans culture
- Crosses
- Microinjections
- CRISPR/Cas9 genome editing
- Auxin induced protein depletion
- PCR
- Fluorescence microscopy
- Chemotaxis assays

Further reading

Traets, J.J.H., et al. (2021). *eLife*, *10*, e66955. DOI: 10.7554/eLife.66955.

Computational Biology & Bioinformatics in Immunology and Cancer

Department Immunology

Principal investigator Harmen van de Werken

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Various projects related to computational biology & bioinformatics in immunology and cancer

BEP MEP

The CBBI group's scientific endeavors are firmly rooted in four fundamental pillars:

Integrating Big Data with Clinical Data: Leveraging advanced statistical learning methods, including Machine and Deep Learning, to enhance clinical decision-making. Our innovative approaches have allowed us to accurately predict the severity of COVID infections and forecast the metastatic spread of solid tumors, such as skin cancer.

Exploring Disease Onset and Development: Using Big Genomic Data to gain insights into the initiation and progression of various diseases, uncovering new avenues for scientific exploration. We've successfully unraveled genomic alterations in prostate, bladder, and neuroendocrine cancers, as well as examined gene expression changes in the immune response of Sjögren Syndrome. Additionally, we've delved into single-cell genomic analysis in Hepatitis B patients.

Developing Cutting-Edge Algorithms: We frequently design novel algorithms to extract critical biological information from Big Genomic and Cellular Data. Our algorithms can identify clustered mutations on the genome and even predict genome folding in three dimensions.

Empowering Scientific Data Processing: We develop tools and implement algorithms for high-end scientific data processing, enabling the visualization of extensive genomics datasets.

Our student projects are seamlessly integrated into ongoing research initiatives, drawing from one or more of the aforementioned CBBI pillars. For instance, we are currently engaged in a project to enhance the prognosis of skin carcinoma metastasis by harnessing genomics, imaging, and clinical data through machine learning techniques. We are also dedicated to deepening our understanding of immune diseases in collaboration with 12 countries within the EU ImmunAID consortium. Furthermore, we have access to extensive Whole Genome and Transcriptome datasets from cancer patients through the Hartwig Medical Foundation. These datasets allow us to investigate drug resistance causes, as well as interactions between the immune system and cancer. Moreover, we have numerous other projects related to the immune system, cancer, and Big Data.

Techniques

- Computational algorithms
- Artificial intelligence
- Machine learning techniques
- Visualization tools

Further reading

Van de Werken, H.J.G. et al. (2012). *Nature Methods, 9*, 969–972. DOI: 10.1038/nmeth.2173.
Van de Geer, W.S., et al. (2022). *Bioinformatics, 38*, 1437–1439. DOI: 10.1093/bioinformatics/btab809.

DNA repair mechanisms and disease

Department Molecular Genetics

Principal investigator Hannes Lans

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DNA repair responses to anti-cancer chemotherapy

DNA damaging chemotherapeutic drugs are clinically widely applied to kill cancer cells. Within cells, an elaborate network of DNA repair mechanisms protects against this type of DNA damage, to safeguard genomic integrity and ensure that essential processes such as replication and transcription can continue. In this project, we investigate the function and activity of known and new DNA repair proteins and mechanisms that are needed to detect and remove chemotherapy-induced DNA damage. Knowledge of these mechanisms is essential to understand how cancer treatment can be improved.

Techniques

- Cell culture
- DNA repair assays
- Live cell confocal imaging
- Western blot
- CRISPR-Cas9
- Immunoprecipitation

Further reading

Slyskova, J., et al. (2018). *Nucleic Acids Research, 46*, 9537-9549 DOI: 10.1093/nar/gky764.

DNA repair research for tumor therapy optimization

Department Molecular Genetics

Principal investigator Dik van Gent

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Optimizing predictive ex vivo assays for lung cancer

BEP MEP

Supervisor: Zhongli Chen, z.chen@erasmusmc.nl

There are several different options for treatment of lung cancer with chemotherapy, targeted therapy and immunotherapy. However, there is currently no option to select the best treatment for each individual patient. Therefore, we are developing methods to grow small pieces of lung tumors in the lab and investigate how they react to various treatments. Projects encompass optimizing growth conditions and treatment schedules, as well as developing methods to allow automatic analysis of microscopic images before and after treatment.

Techniques

- Tissue culture
- Immunofluorescence (confocal) microscopy
- Automatic image analysis

Further reading

Zhang, W., et al. (2019). *Prostate*, *79*(4), 390-402. DOI: 10.1002/pros.23745.

Essers Lab

Department Molecular Genetics

Principal investigator Jeroen Essers

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Feasibility of animal mouse models for testing of novel proton therapy delivery technique

BEP
MEP

Supervisor: Kelvin Ng Wei Siang, k.ngweisiang@erasmusmc.nl

Patients treated with radiotherapy for squamous cell anal and vulva carcinoma usually suffers from grade 3 or higher acute radiation dermatitis and gastrointestinal toxicity. A possible way to mitigate these effects could lie in the application of particle micro beamlets. To investigate the effects from the technique, animal studies could be carried out.

We propose a study to investigate the feasibility of animal mouse models for quality assurance and testing of the novel proton therapy delivery technique on patients with squamous cell anal and vulva carcinoma. This project will explore the induction of excess skin flaps with sweat glands and tumor genesis in mice by genetic or surgical modifications through a literature study. The student shall look into equivalent mouse tumor models that resembles anal and vulva cancer in humans. Additionally, the student makes recommendations on the experimental setup for dosimetric verification of a novel delivery technique of proton beams using equivalent animal phantom models, to assess quality assurance and safety of the technique. In this multidisciplinary project, you will work closely with a qualified medical physicist expert (dr. ir. Kelvin Ng Wei Siang) and radiobiologist expert (dr. Jeroen Essers).

Techniques

- Setting up experimental design with phantoms
- Data extraction
- Treatment planning
- Data analysis

Further reading

Gillespie, M.A., et al. (2021). *Oncology Reviews, 15*(1), 511. DOI: 10.4081/oncol.2021.511.

Human X chromosome inactivation and X-linked neurodevelopmental disorders

Department Developmental Biology

Principal investigator Cristina Gontan

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Establish a human XCI system and identify skewing due to X-linked mutations

~~BEP~~ MEP

Asymptomatic female carriers of mutations in genes like RNF12 linked to Neurodevelopmental Disorders (NDD), exhibit significant skewing in X Chromosome Inactivation (XCI). This skewing results in the inactivation of the X-chromosome carrying the mutated allele. We propose that this phenomenon is driven by the action of the ubiquitin ligase RNF12 during human XCI, rather than being a result of negative secondary selection during neurogenesis.

In this study, We aim to validate this hypothesis by generating a dual fluorescent reporter system to monitor XCI in female induced pluripotent stem cells. Confirming this hypothesis would significantly enhance our understanding of this phenomenon related to NDD mutations and shed light on XCI-skewing mechanisms in general.

Techniques

- Cell culture of hiPSCs
- Generation of transgenic lines using CRISPR-Cas9
- Molecular cloning
- DNA and RNA isolation
- Fluorescent in situ hybridization (FISH)
- Immunofluorescence

Human X chromosome inactivation and X-linked neurodevelopmental disorders

- Western blotting
- Microscopy
- Neuronal differentiation

Further reading

Frints, S.G.M., et al. (2019). *Molecular Psychiatry, 24,* 1748–1768. DOI: 10.1038/s41380-018-0065-x.

Identifying RNF12 substrates and mutations mediating NDD in RNF12 male patients

~~BEP~~ MEP

Supervisor: Kyra Swildens, k.swildens@erasmusmc.nl

RNF12 mutations cause NDD in male patients, probably because RNF12 target-proteins are not/less degraded and affect brain development. Here I aim to identify RNF12 target-proteins during neurogenesis. To explore future therapeutic avenues, I will test whether antisense RNA-mediated knock-down, with antisense oligonucleotides (ASOs), of RNF12 targets complements (potential) defects observed during neurogenesis of RNF12 mutant PSCs. For diagnostic and scientific purposes, I will test new RNF12 patient mutations for their effect on RNF12 activity.

Techniques

- Cell culture of hiPSCs and neuronal differentiation
- Generation of transgenic lines using CRISPR-Cas9
- Molecular cloning
- DNA and RNA isolation
- Fluorescent in situ hybridization (FISH)
- Immunofluorescence
- Microscopy

Further reading

Frints, S.G.M., et al. (2019). *Molecular Psychiatry, 24,* 1748–1768. DOI: 10.1038/s41380-018-0065-x.

Kanaar Lab

Department Molecular Genetics

Principal investigator Roland Kanaar

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Dynamic organization of DNA repair proteins at damage sites

~~BEP~~ MEP

Supervisor: Maarten Paul, m.w.paul@erasmusmc.nl

Our research group aims to determine how proteins work together to achieve precision and control in Homologous Recombination (HR) DNA repair. We focus on the nanomachinery composition, architectural arrangement, and how these are controlled in time and space. Our multidisciplinary approach moves beyond determining highly detailed but static structure to learn how proteins work together in complex and dynamic assemblies that accomplish the work in living cells. We use advanced live-cell imaging and analysis tools to determine the in vivo diffusive behavior of specific proteins and functional complexes in mammalian cell nuclei. We also use super-resolution microscopy to define the organization of repair proteins that accumulate in high local concentration at break sites and relate organization to function.

Techniques

- Live-cell imaging
- Single-molecule tracking
- Super-resolution microscopy (TIRF/dSTORM)
- Image analysis (Fiji) & data analysis (R/Python/Matlab)
- Molecular cloning
- CRISPR/Cas9

Further reading

Paul, M.W., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.02.20.527475.

Laboratory of population genomics

Department Internal Medicine

Principal investigator Jeroen van Rooij

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Polygenic risk scores in cancer disease prevention

~~BEP~~ MEP

Genetic risk scores include summing up many genetic risk variants for a certain disease. For example, the 313 genetic variants identified to influence risk of breast cancer. In this project, we build prediction models based on these genetic variants to inform population screening, treatment decisions and use the biological mechanisms these variants are expected to influence to inform drug development.

Techniques

- Bioinformatics
- Epidemiology
- Translation/implementation science
- Machine learning applications

Further reading

Lakeman, I.M.M., et al. (2020). *Genetics in medicine, 22*(11), 1803–1811. DOI: 10.1038/s41436-020-0884-4.

Combining multiple genomic layers in neurodegenerative brain samples

~~BEP~~ MEP

In this project we have collected DNA, RNA and proteomic data from multiple post-mortem brain samples of dementia patients. Most of these datasets have been analyzed separately, but additional insights are to be gained by multi-omic data analyses. We focus mostly on frontotemporal dementia, which is different from Alzheimer's disease, and small (n=20) datasets with large numbers of measured genes/proteins (20k/5k, on average). This is a collaboration with the department of Neurology.

Techniques

- Bioinformatics
- Statistics
- Molecular biology
- Machine learning

Further reading

Mol, M. O., et al. (2022). *Acta neuropathologica communications, 10*(1), 190. DOI: 10.1186/s40478-022-01499-1.

Marteijn group

Department Molecular Genetics

Principal investigator Jurgen Marteijn

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Effects of DNA damage on transcription

BEP
MEP

Our lab studies the effects of DNA damage on transcription, how this transcription-blocking DNA damage is repaired and how this contributes to aging and age-related diseases. We have different interesting projects using live cell imaging , gene editing and proteomics techniques to identify new factors involved in this process and to better understand the repair mechanisms.

Techniques

- CRISPR/Cas9
- Live cell imaging
- Image analysis
- Cell culture
- Proteomics
- Single molecule imaging
- DNA damage induction

Further reading

Steurer, B., et al. (2022). *Nature Communications, 13*(3624). DOI: 10.1038/s41467-022-31329-w.
Van Toorn, M., et al. (2022). *Molecular Cell, 82*, 1343–1358. DOI: 10.1016/j.molcel.2022.02.020.

Miao-Ping Chien Lab

Department Molecular Genetics

Principal investigator Miao-Ping Chien

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Microscopy-based functional single cell sequencing for cancer biology

~~BEP~~ MEP

In Dr. Chien's lab, we develop single cell technologies combining optical imaging, biomedical and bioinformatics methods to address biological questions, particularly in cancer biology and immuno-oncology. There are two potential projects: one is to apply our microscopy-based functional single cell sequencing method to study the effect of fibroblasts on clonogenicity of cancer cells; another one is to help develop a spatial -omic profiling technology and apply it to investigate the interplay of cancer cells and tumor microenvironment.

Techniques

- Advanced imaging
- Image analysis
- Single cell sequencing
- Bioinformatics

Further reading

You, L., et al. (2022). *Nature Biomedical Engineering, 6*, 667–675 DOI: 10.1038/s41551-022-00853-x.

Multisensory Integration in the Auditory System

Department	Department of Neuroscience
Principal investigator	Aaron Wong
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Website	https://neuro.nl/research/wong

Molecular and functional profiles of auditory neurons with single cell transcriptomics data

BEP MEP

The inferior colliculus is a key subcortical integration center in the auditory system. Despite its importance, a proper molecular characterization of its highly heterogeneous cell types is still lacking. This project aims to fill this urgently needed gap by performing state-of-the-art single cell transcriptomics analysis on inferior colliculi from mice. We will first make use of a recently published open spatial transcriptomics data ("Allen Brain Cell Atlas") in combination of dimensionality reduction bioinformatics tools to identify molecularly defined sub-populations within the inferior colliculus and other auditory nuclei. A natural extension of the project would be to characterize the electrophysiological properties of a selected neuronal sub-population that process non-auditory information, and relate these properties with an in-depth characterization of their gene expression profiles.

Techniques

- Analysis of single cell transcriptomics data in R
- Immunohistochemistry and/or in situ hybridization techniques on brain tissue
- In vivo viral labelling OR patch-clamp electrophysiology in brain slices

Further reading

Oliver, D.L. (2005). Neuronal organization in the inferior colliculus. In J. A. Winer and C. E. Schreiner (Eds.), The inferior colliculus (pp. 69–114). New York: Springer.

Hearing touches and vibrations: investigating multi-sensory integration in auditory midbrain

~~BEP~~ MEP

Supervisor: Blom Kraakman

Sensory systems allow us to detect the world around us. The inferior colliculus (IC) is a major station of the ascending auditory pathway, but interestingly also receives inputs from somatosensory regions such as the somatosensory cortex, dorsal column nuclei and trigeminal nuclei. However, what information these connections convey and their function remain mysterious. In this project, you will target somatosensory neurons in the IC and characterize their activities in physiological experiments. Further identification can be done using a combination of viral tracers and optogenetics. The identification of somatosensory stimuli that best activate these somatosensory neurons will aid in distinguishing between competing hypotheses (e.g. suppression of self-generated sounds or to aid in orientation to sounds) in the function of this circuit.

Techniques

- Microsurgery techniques (and viral injections)
- Multielectrode recording (combined with optogenetics)
- Data analysis and programming in Matlab, with utilization of openly available packages (e.g. Kilosort)

Further reading

Lesicko, A.M.H. et al. (2016). *Journal of Neuroscience, 36*, 11037–11050. DOI: 10.1523/JNEUROSCI.4134-15.2016.
Straka, M.M. et al. (2015). *Neuroscience, 300*, 325–337. DOI: 10.1016/j.neuroscience.2015.05.032.

Neural dynamics lab

Department Neuroscience

Principal investigator Devika Narain

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Neural control of movements using brain machine interfaces

~~BEP~~ MEP

Several years ago, we discovered a novel neural code that hints at a neural mechanism for controlling the tempo of movements i.e. whether you deliberately play a music composition slowly or quickly or strike a tennis return hard or not. A major undertaking in our lab is building neural interfaces to utilize and manipulate this code with the long-term goal of restoring movement control in patients. In this project, we will use a combination of closed-loop engineering and systems neuroscience to collect and analyze neurophysiological data from rodent brain-machine interfaces.

Techniques

- Machine learning
- Neuroelectrophysiology
- Closed-loop engineering
- Optogenetics

Further reading

Wang, J., et al. (2018). *Nature Neuroscience, 21*, 102-110. DOI: 10.1038/s41593-017-0028-6.

Implicit and explicit learning as a window into interareal brain communications

~~BEP~~ MEP

As explained in the recent book 'Thinking, Fast and Slow', in cognitive neuroscience, it has long been maintained that the acquisition of implicit processes is automatic and rapid, whereas, learning of explicit processes is believed to require more effort and is slower. Interestingly, exactly the opposite is true in motor neuroscience where learning of implicit processes is known to be slower than explicit learning. Here we report that in time perception, which often straddles cognitive and motor learning, implicit timing is learned more rapidly than explicit temporal metrics. This project entails the analysis of existing neurophysiological data underlying these behaviors. If interested, students can also be trained on electrophysiological techniques and experimental procedures (optional).

Techniques

- Machine learning
- Dimensionality reduction
- Optional: electrophysiology, surgery and behavioral training

Further reading

Ma, Q., et al. (2023). *Social cognitive and affective neuroscience, 18*(1), nsac044. DOI: 10.1093/scan/nsac044.

Neurocomputing Lab

Department	Neuroscience
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Unsupervised models of cerebellar plasticity (PF-PC plasticity in the cerebellar loop)

~~BEP~~ MEP

The olivocerebellar system consists of multiple feedback and feedforward loops. One of the main loops that we are interested in consists of the "Parallel Fiber (PF) - Purkinje cell (PC) - Deep Cerebellar Nuclei (DCN) - Inferior Olive (IO) - Purkinje cell" loop. Most theories of cerebellar function are based on the coincidence of PF-PC signals with the activity arriving via the climbing fiber (CF) from the IO, as these signals modulate the PF-PC synapse. Hence, there is particular interest in investigating plasticity at the PF-PC synapse. We start by looking at plasticity with a simplified loop (no excitatory/inhibitory interneurons and Golgi and basket cells). This closed loop model of the cerebellar circuit will consist of a mixture of spiking neurons and conductance based neurons (Hodgkin-Huxley), with a model of synaptic plasticity to study how incoming signals change the cerebellar circuit.

Techniques

- Modelling neurons
- Data analysis

Reconstruction and analysis of realistic olivocerebellar networks

BEP
MEP

Currently we have small (~1000 cell) biologically realistic networks of the inferior olive and cerebellum. We are currently expanding these networks to the scale of realistic mouse networks to recreate the mouse olivo-cerebellar loop of motor control to study motor control and learning bottom-up, while at the same time increasing the level of morphological model detail. This will require efficient use of a large amount of computational resources. The neuronal clustering behaviour in these large-scale simulations will then be analyzed either by in-house developed statistical methods or something you come up with yourselves during the project.

Techniques

- Statistical methods
- High-speed scientific computation

The influence of plasticity on cluster formation in the Inferior Olive

~~BEP~~
MEP

As said before, the neurons of the inferior olivary nucleus can be modelled as coupled nonlinear oscillators and the synchronization between neurons is thought to play an important role in motor control feedback. Apart from various parts of the brain that are able to specifically modulate this synchronization behaviour via glomerular synapses, the inferior olive itself is also able to change the connection strength of dendro-dendritic gap junctions over time via various plasticity methods. This conductance modulation will change how cells synchronize and is expected to have a key role in motor learning and motor feedback tuning. Your task will be to quantify the effect of various models of plasticity, including spike-timing dependent plasticity (STDP), on

dynamical cluster formation in the inferior olive and then to connect this to motor control and learning.

Techniques

- Modelling of dynamical systems
- Analysis of synchronisation

Homeostasis: How do neurons change to stay the same?

BEP
MEP

One of the fundamental differences between artificial neural networks and biological neural networks is that in the latter the neurons adjusts its own intrinsic properties to maintain functionality. Neurons maintain complex regulatory protein expression (i.e., ion channels) as a function of their activity. The molecular pathways involved in this regulation are only now beginning to be unveiled. This project studies the processes maintaining equilibrium either from a mathematical or a biological perspective. We model with a variety of neuronal types (Purkinje neurons, Inferior Olivary cells), and simulate them at various levels of detail.

Techniques

- Modelling neurons and networks
- Data analysis

Neuromotor control lab

Department Neuroscience

Principal investigator Vincenzo Romano

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Cerebrocerebellar interactions underlying the coordination of complex behaviour

BEP
MEP

To make precise movements, our big and small brain (cerebrum and cerebellum) constantly exchange electrical signals. Thus far, studies have only examined the big and small brain separately, or in relation to one body part. Therefore, we lack a comprehensive understanding of how we control simultaneous movements of multiple body parts. With a new freely moving system that we have developed, we aim to reveal how these two brain cortices work together during natural behaviour.

Techniques

- Electrophysiological recordings of single unite and local field potential in freely moving mice.
- Quantification and correlation of the mouse movement in the 3D space with neuronal activity.

Nitika Taneja Lab

Department Molecular Genetics

Principal investigator Nitika Taneja

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Dynamics of chromatin re-organization upon DNA replication stress

~~BEP~~ MEP

Our lab investigates local and spatial re-organization of chromatinized replication forks in response to replication stress. We use a combination of super-resolution imaging, genomics and proteomics based approaches to understand the complex mechanisms of chromatin regulation in maintaining replication fork stability in normal as well as cancer cells.

Techniques

- Single molecule chromatin fibre technology, ChromStretch (developed & patented by the lab)
- Next-generation sequencing technologies: Hi-C and specialized technology, Rep-HiC (developed by the lab)
- DNA combing technology
- Automated quantitative imaging based cell cytometry
- Super-resolution STED microscopy
- Biochem-based tech: ChIP, IP/Co-IP, WB, proteomics

Further reading

Gaggioli, V., et al. (2023). *Nature Cell Biology*, *25*, 1017–1032. DOI: 10.1038/s41556-023-01167-z.

Lo, C.S.Y., et al. (2021). *Science advances, 7*(19), eabe7804. DOI: 10.1126/sciadv.abe7804.

Uruci, S., et al. (2021). *International journal of molecular sciences, 22*(16), 8850. DOI: 10.3390/ijms22168850.

Radiobiology of radionuclide therapy

Department Molecular Genetics

Principal investigator Julie Nonnekens

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Radiation biology of radioactive anticancer treatment

BEP MEP

Various preclinical projects available all focusing on gaining a clear view of how cancer cells respond to radioactive anticancer treatment with the goal better understand the dose-effect relationship. Our goal in the long run is to predict upfront whether a patient can be successfully treated or not.

Techniques

- Molecular biology (cell culture, microscopy, molecular techniques, etc.)
- Computational biology (Monte Carlo simulations, deep learning based image analysis, etc.)

Sensorimotor integration lab

Department Neuroscience

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You will never walk alone

BEP MEP

Every step you make is like a piece of art, and requires quite some effort from your brain. This is most likely not a problem for you, but for elderly people, walking and keeping balance are getting more and more difficult. Falls and resultant bone fractions cause a major loss of quality of life. Apart from normal aging, walking is also compromised in many diseases, muscular as well as neurological. To walk, your brain needs to integrate sensory input and motor output, and this is a computationally heavy task requiring the cooperation of multiple brain regions. Will you join our lab in decoding the information processing shared by multiple brain regions?

Techniques

- Machine learning and pattern recognition
- MEP only: behavioural experiments (in mice or patients)

Further reading

Jaarsma, D., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.08.29.555378.

Swallow this one

~~BEP~~ MEP

If you would make a list of all your amazing skills, on which place would you put swallowing? Good chance that you

underestimate how important this is! In many neurodegenerative diseases, problems with swallowing are life threatening. Yet, the neurobiology of swallowing is relatively unexplored. After studying multiple behaviours related to the face, understanding swallowing will be the next challenge for our lab. Will you contribute to setting this up, in patients and mouse models?

Techniques

- EMG recordings
- Acoustic recordings
- Machine learning

Further reading

Krohn, F., et al. (2023). *eLife, 12*, e83654. DOI: 10.7554/eLife.83654.

Spatiotemporal dynamics of the learning brain

BEP
MEP

Recently, we have identified a crucial pathway in the brain that is required to learn to make decisions based on environmental cues. For this project, we will study how different parts of the brain contribute to this pathway. This is a unique chance to understand how you learn to understand.

Techniques

- Machine learning and pattern recognition
- Fourier analysis
- MEP only: electrophysiological recordings in learning mice

Further reading

Bina, L., et al. (2021). *Cell Reports, 37*(11), 110116. DOI: 10.1016/j.celrep.2021.110116.

Sensorimotor Neuroscience and Biorobotics

Department	Neuroscience
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Understanding motor control by decoupling the brain from the body

~~BEP~~ MEP

Supervisor: Lucas Mensink, l.mensink@erasmusmc.nl

Neural control of movement demands understanding of the body's passive mechanics. For example, passive mechanisms such as (short-range) muscle stiffness contribute ~30-90% of the required load when standing upright. This variability results from dynamic factors such as thixotropy and viscosity arising from the binding and release of cross-bridges. Computational models describing these dynamic changes in passive muscle properties have been proposed. However, direct testing of passive properties in vivo is obscured by neural modulation. Our project aims to use nerve-blocking anesthesia to paralyze lower-limb muscles, disconnecting them from neural control. The focus is on characterizing the different mechanisms that dynamically affect passive ankle properties during standing balance and understanding the effect on control of the system.

Techniques

- Nerve-blocking
- Ultrasound
- Electromyography
- Musculoskeletal modelling
- Robotics

Further reading

Sakanaka, T.E., et al. (2018). *PLoS One, 13*(3), e0193850. DOI: 10.1371/journal.pone.0193850.
Tisserand, R., et al. (2022). *PNAS Nexus*, 1(4), pgac174. DOI: 10.1093/pnasnexus/pgac174.

Unlearning how to stand: probing human motor control through transforming standing balance

~~BEP~~ MEP

Supervisor: Matto Leeuwis, m.leeuwis@erasmusmc.nl

Human motor control must continuously adapt, both to abrupt perturbations and progressive changes. The central nervous system (CNS) maintains intended motion patterns by altering the control scheme and reweighting or transforming inputs. The CNS could even control standing balance when the relation between applied forces and whole-body angle was mirrored using a robotic balance simulator. Here, the relation between required ankle torque and sensory information was normal for proprioceptive signals but mirrored for vestibular and visual signals. Based on recent observations, we hypothesize that the CNS may be similarly able to control balance using transformed proprioceptive information. In this project, you will quantify human learning of sensorimotor transformations and test to what extent the CNS can transform different sensory inputs.

Techniques

- Robotics
- Musculoskeletal modelling
- Computational motor control
- Electromyography
- Sensory stimulation

Further reading

Forbes, P.A., et al. (2016). *Journal of Neuroscience, 36*(45) 11510-11520. DOI: 10.1523/JNEUROSCI.1902-16.


TU Delft
Delft
University of
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Aubin-Tam Lab

Department Bionanoscience

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Microfluidics for the formation of free-standing asymmetric lipid bilayers

~~BEP~~ MEP

The goal of this project is to develop a novel, robust method to form stable asymmetric freestanding lipid membranes. Cell membrane asymmetric structure controls several biological phenomena like enzyme activities, vesicle budding, signal-transduction, etc. Specifically, it affects the membrane's mechanical properties such as bending rigidity which directly controls protein folding and activity. Mechanical properties of asymmetric membranes also contribute to cell morphogenesis and vesicle formation.

Techniques

- How to design and fabricate microfluidic chips
- Working with lipids and making artificial asymmetric cell membranes
- Fluorescent microscopy and image processing
- Data analysis

3D patterning of photosynthetic living materials

~~BEP~~ MEP

Nature fabricates materials with remarkable properties, having the ability to grow, move and sense their environment. Such dynamic and interactive materials are in strong contrast with man-made synthetic materials, which are far less functional

and which tend to require a large energy input for their fabrication and use. For this reason, a recent trend in materials science is to use living organisms for materials fabrication. Living cells themselves are now also incorporated in materials to form so called living materials. A precise and dynamic 3D organisation of materials is important both in synthetic engineered devices and in living organisms (mammals, plants, etc.), and represents an important sought-after feature of living materials.

Techniques

- 3D patterning
- Tuning material properties of the matrix
- Pulse amplitude fluorescence measurements
- Cell count and cell morphology assessment

Production of biomimetic materials with the use of microorganisms

~~BEP~~ MEP

Biomaterials in the natural world provide an abundant source of inspiration for the design of novel high-performance materials. Nacre consists of stacked layers of calcium carbonate ($CaCO_3$) separated by thin 20nm layers of sticky elastic biopolymer. This layered confers exceptional mechanical properties. Our approach is to exploit synthetic biology to self-assemble artificial nacre with bacteria.

Techniques

- Biomimetics
- Measurement of mechanical properties
- Synthetic biology

Fibrous flagellar hairs as mechanosensors during swimming

~~BEP~~ MEP

The green microalgae Chlamydomonas reinhardtii has long served as the model organism for studies on the structure, assembly, and function of eukaryotic flagella. Decades ago, their flagella were observed to possess nanometer thick fibers known as mastigonemes. These structures were believed to enhance flagellar thrust, but our recent study proved otherwise. Specifically, we found that mutants lacking these structures swim at the same speed and generate the same hydrodynamic thrust. However, the mutants without mastigonemes were observed to swim more erratically, with significantly higher rates of turning. These observations, along with a recent report of mastigonemes being physically connected to the axonemes of the flagella (Liu, et al 2020 J Cell Biol), lead us to hypothesize that these structures may function as mechanosensors that help regulate swimming behavior.

Techniques

- High speed fluorescence microscopy
- Cell culturing
- Delivery of molecular dyes
- Microfluidic device design
- Molecular biological tools
- Image analysis

Bauer Group

Department Bionanoscience

Principal investigator Marianne Bauer

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Sensing in plants

BEP
MEP

This project will explore the regulatory precision and sensing in published plant datasets. Depending on interest, we will use either published data from sequencing in seedling data sets or responsed to stimuli from sunflower seedlings. Using either simple Bayesian inference or a delayed-embedding framework for data analysis, we will infer how variable the seedlings are, and whether and with how much data we can infer the stimulus. This project will be the first in a series targeted at understanding plant adaptation.

Techniques

- Numerics/computation
- Data analysis
- Probability distribution
- Some information theory

Further reading

Greenwood, M., et al. (2022). *Molecular Systems Biology, 18,* e10140. DOI: 10.15252/msb.202010140.
Rivière, M. & Meroz, Y. (2023). *Biophysics and Computational Biology, 120*(42), e2306655120. DOI: 10.1073/pnas.2306655120.

Information in neuronal stimuli

BEP
MEP

We are proposing a theoretical Masters project to analyse traces of neuronal activity of a system of connected neurons in culture in comparison to mouse cortex. The aim of this project is to identify information- theoretical or statistical quantifiers that could serve as indicators for different experimental conditions. The long-term goal is to investigate if particular cells within the same culture, between different cultures or compared to the cortex are uniquely recognizable, and if they can be assigned correctly to their environment. (This project is together with the Daan Brinks Lab.)

Techniques

- Numerics/computation
- Statistical physics (Ising models)
- Entropy calculations (no previous knowledge required)

Further reading

Tian, H., et al. (2021). BioRxiv. DOI: 10.1101/2021.11.22.469481.
Palmer, S.E., et al. (2015). *PNAS, 112*, 6911. DOI: 10.1073/pnas.1506855112.

Noise in gene regulation

BEP
MEP

This project will involve polymer simulations (Brownian dynamics) with clustering molecules, to investigate how molecules can affect contact statistics of different parts of a polymer (corresponding to enhancers and promoters) in various synthetic and natural contexts. Using simulations as well as simple analytical calculations, we will try to see how these contacts affect the noise in the enhancer. The project will further involve stochastic simulations of the enhancer in order to investigate how an enhancer should optimally respond to different stimuli.

Bauer Group

Techniques

- Brownian motion simulations
- Stochastic simulations
- Data analysis

Further reading

Bintu, L., et al. (2005). *Current Opinion in Genetics & Development, 15*(2), 116-124. DOI: 10.1016/j.gde.2005.02.007.
Bauer, M. (2022). *Biochemical Society Transactions, 50*(5), 1365-1376. DOI: 10.1042/BST20220333.

Biophysics of reconstituted cytoskeletal systems

Department Bionanoscience

Principal investigator Marileen Dogterom

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The interaction between the TubR-LOV2 protein, tubC centromeric DNA, and TubZ filaments

BEP MEP

Supervisor: Beatriz Orozco, b.e.orozcomonroy@tudelft.nl

With the aim of building a DNA segregation mechanism for a synthetic cell using bacterial cytoskeleton filaments, this project consists of testing the interaction of the engineered light-switchable protein TubR-LOV2 (fusion of the adaptor protein TubR with the light-responsive LOV2 domain) with tubC centromeric sequences and TubZ bacterial cytoskeleton filaments. TIRF microscopy and image analysis will be employed to assess the interaction among these components and the dynamicity of the filaments. Additional experiments, such as mass photometry or gel electrophoresis, may be used in conjunction with microscopy to optimize experimental parameters like the ratio at which the components interact more efficiently.

Techniques

- TIRF microscopy
- Mass photometry

Further reading

Aylett, C.H.S. & Löwe, J. (2012). *PNAS, 109*(41), 16522-16527. DOI: 10.1073/pnas.1210899109.

Olivi, L., et al. (2021). *Nature Communications, 12*(1), 4531. DOI: 10.1038/s41467-021-24772-8.

Control aster positioning in droplets

BEP
MEP

Supervisor: Yash Jawale, y.k.jawale@tudelft.nl

Correct positioning of the (mitotic) spindle is an essential process in cell division, as its position plays an important role in determining the division plane and hence the size of the daughter cells. The spindle consists of two microtubule asters (growing from centrosomes) exerting forces.

You will attempt to learn how the microtubule aster positions inside a 3D cell-like confinement, and how the force balance changes in response to constraints of the environment and additional components.

Objectives:

1. Encapsulate minimal asters inside a droplet;
2. Quantify aster position as a function of protein concentration and droplet size;
3. Study the effect of organelle-like structures, by adding crowding, LUVs or nucleus, and motor proteins;
4. Simulate aster positioning.

Techniques

- Microfluidics to encapsulate microtubule asters inside droplets
- Advanced microscopy techniques and image analysis tools
- Cytoskeleton simulation tools such as CytoSim to make predictions

Further reading

Roth, S., et al. (2019). *bioRxiv.* DOI: 10.1101/770602.

Spatio-temporal control of spindle positioning (simulations)

BEP MEP

Supervisor: Yash Jawale, y.k.jawale@tudelft.nl

Correct positioning of the (mitotic) spindle is an essential process in cell division. Although in vitro reconstitution methods provide much insight into spindle positioning, they are not sufficient to study the complete spectrum of force balances. We therefore turn to simulations to better understand spindle positioning and predict what affects the force balance.

Objectives:

1. Simulate spindle assembly and monitor involved forces;
2. Study the effects of cell shape and size;
3. Study the effects of force generators (such as motor proteins) at the cortex and in the cytoplasm;
4. Mimic events in the cell division process using spatial and temporal cues in the simulations;
5. Find conditions for asymmetric spindle positioning.

Techniques

- Simulations to answer research questions.
- CytoSim (a cytoskeleton simulation tool).

Further reading

Roth, S., et al. (2019). *bioRxiv.* DOI: 10.1101/770602.

Controlling lipid liquid-liquid phase separation on membranes

BEP MEP

Supervisor: Yash Jawale, y.k.jawale@tudelft.nl

Lipid domains play an important role in organizing proteins on the cell membrane. The cellular membrane consists of different lipids, and via interactions between the lipids, they

can form clusters (domains) with each other and thus create lipid phase separation. As some proteins bind to specific lipids, the formation of lipid domains on membranes can be used to recruit and organize these proteins.

Objectives:

1. Find and tune the different lipid types and their ratios required to create lipid phase separation on 2D membranes (and on 3D membranes);
2. Optimize the size and number of lipid domains;
3. Add spatial and temporal control on phase separation using light.

Reconstituting microtubule dynamics inside micro and nanochannels

Supervisor: Nemo Andrea, n.andrea@tudelft.nl

We have developed microfluidic devices with micro and nanochannels that we want to use for liquid-phase EM. Not much is known about microtubule growth behaviour in extreme confinement (high surface to volume ratio) like in nanochannels. The project would involve investigating the growth dynamics of microtubules in micro and nanochannels and comparing them to macroscopic flowchannels that is already well established. Increasing the complexity of the reconstituion by studying effects of adding microtubule-binding proteins or other filaments (e.g. actin) would also be an option. The project would involve the reconstitution of the system (finding the right conditions and concentration), imaging the system on a fluorescence microscope, working with microfabricated chips and data analysis in Python or Julia.

Techniques

- Fluorescence microscopy
- In vitro reconstitution
- Data analysis
- Optional: data management with Git and Git-Annex.

Cees Dekker Lab

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A ground-breaking adventure in the fascinating world of pattern formation

~~BEP~~ MEP

Supervisors: Eva Bertosin & Sabrina Meindlhumer, e.bertosin@tudelft.nl & s.meindlhumer@tudelft.nl

Pattern formation is a phenomenon that appears at all biological levels, from pattern-forming proteins used for cell division to the stripes on the animal fur. How do these pattern-forming systems work? To answer this question, we're not just exploring, but actively creating these captivating phenomena using the power of DNA nanotechnology. Imagine crafting stunning patterns from the simplest of systems!

You will work in a multidisciplinary experimental environment and also in close collaboration with experts in the theory and modelling of pattern formation.

We are looking for an independent, creative, and passionate Master student (starting preferably in January 2024) ready to craft stunning and mesmerising patterns from scratch! Let your curiosity lead the way and join us on this exciting exploration!

Techniques

- Designing DNA strands
- Testing the system using fluorescence microscopy
- Performing bulk fluorescence measurements
- Understanding the relation between our artificial systems and biological ones

Building a living cell from scratch using microfluidics

BEP
MEP

Supervisor: Bert van Herck, b.vanherck@tudelft.nl

Throughout the course of evolution life has developed a staggering complexity at the cellular level. To shed light on the fundamental blueprint of a cell and get a better understanding of the governing principles of cellular life, we are aiming to build a synthetic cell from the bottom-up using molecular building blocks (www.basyc.nl).

More specifically, we developed a microfluidic technology, Octanol-assisted Liposome Assembly (OLA), to produce cell-sized (5–20 μm) liposomes in our lab. These liposomes can be immobilized using microfluidic traps for further manipulations. In the past, we already succeeded in mimicking the form of rod-shaped bacteria by squeezing the liposomes into narrow confinements. Further, liposome growth was established by recruiting lipids from the external environment, and liposome division was induced by colliding them against well-defined microfluidic structures. Now the time has come to combine these modules into an integrated lab-on-a-chip system to establish a dynamic cycle of growing and dividing liposomes, mimicking a continuous life cycle of a living cell.

Techniques

- Microfluidic setup
- Basic light- and epifluorescence microscopy
- On-chip production of synthetic cells

Protein sequencing with nanopores

BEP
MEP

Supervisor: Justas Ritmejeris, j.ritmejeris@tudelft.nl

Nanopore technologies have been used by astronauts aboard the International Space Station and biologists travelling across the far reaches of the Earth to study DNA at the single-

molecule level. However, analyzing the protein composition of cells at the single-molecule level, while an extremely valuable diagnostic tool, remains a difficult task. In this project we are taking important steps in developing nanopore technologies for proteomics.

Currently, we are exploring methods inspired by nanopore DNA sequencing. This approach involves attaching a small piece of protein (peptide) to a DNA strand to form a peptide-oligo conjugate (POC) which is pulled through a nanopore by a DNA motor enzyme. By measuring the ion current through the pore as the peptide moves through it, we can distinguish individual amino acids and detect important post-translational modifications! Our group has pioneered the proof-of-concept of this method, but engineering and data analysis breakthroughs are needed to push this technology to the next stage!

Techniques

- Wet lab
- Handling data sets

The ring of power: Building a biomimetic nuclear pore complex with DNA origami

BEP
MEP

Supervisor: Eva Bertosin & Anders Barth, e.bertosin@tudelft.nl & a.barth@tudelft.nl

The nuclear pore complex (NPC) is a huge, ring-shaped protein system inserted into the nuclear membrane that allows only certain macromolecules to translocate into the nucleus. It is an incredibly complex system that we aim to study using a bottom-up approach.

Our goal is to build a NPC from scratch by combining different NPC proteins (nucleoporins) grafted inside a ring-like DNA

origami structure. This approach gives us precise control over the stoichiometry and the positioning of individual proteins. We utilize this platform to study the arrangement and structural dynamics of the FG-nucleoporins in the pore on the single-molecule level.

Techniques

- Designing, folding and assembling DNA origami rings
- Protein functionalization of the DNA origami structure
- Gel electrophoresis
- Mass photometry
- Fluorescence correlation spectroscopy
- Fluorescence microscopy
- Transmission electron microscopy

Electron Nanoscopy Lab

Department Bionanoscience

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Deep learning for cryo-EM image processing

BEP
MEP

Supervisor: Maarten Joosten, m.j.joosten@tudelft.nl

Cryo-EM is a technique that is heavily dependent on the computational algorithms that allow us to pick, classify and reconstruct particles to obtain a 3D representation of a protein or protein complex. The images are noisy and heterogeneous, making it very challenging to find robust computational solutions. We therefore often work with simulated data to test the capabilities of our algorithms. This data needs to be as realistic as possible. In this project you will evaluate how good our simulated data is and optimise it by applying machine learning. You will (learn to) work with Python to build image processing scripts, build neural networks and run them on our high-performance computing environment. You will also get experience working with cryo-EM image processing software, and there are possibilities to complement computational work with work on the microscope and/or in the wetlab.

Techniques

- Cryo-EM
- Image processing
- Machine learning/AI
- Neural networks
- Structural biology

Further reading

Zhong, E. D., et al. (2021). Nature methods, 18(2), 176–185. DOI: 10.1038/s41592-020-01049-4.

Resolving the structural mechanisms of GBP heterodimer formation

~~BEP~~ MEP

Supervisor: Lennart Pagani, l.l.pagani@tudelft.nl

Guanylate-binding proteins (GBPs) are key components of cell-autonomous immunity and protect host-cells from intracellular pathogens by encapsulating bacteria and initiating bacteriolysis and inflammation. The seven GBP orthologues are hierarchically recruited to the bacterial membrane via heterodimerization, but direct molecular evidence is missing. Hence, structural information of GBP heterodimers would be very valuable in our goal to understand the role of GBPs in cellular self-defence. In this project you will try to isolate a GBP heterodimer (GBP1-GBP3) and to resolve the structure by cryo-EM. Within this project you can learn how to clone, culture cells, purify protein and all the other basics of biochemistry. Additionally, you can learn the basics of cryo-EM and image processing.

Techniques

- Cryo-EM
- Fluorescence microscopy
- Protein biochemistry
- Structural biology
- Biophysical characterisation
- Cell culture

Further reading

Kuhm, T., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.03.28.534355v1.

Elucidating the membrane-binding mechanism of human GBP4

~~BEP~~ MEP

Supervisor: Lennart Pagani, l.l.pagani@tudelft.nl

Guanylate-binding proteins (GBPs) are key components of cell-autonomous immunity and protect host-cells from intracellular pathogens by encapsulating the bacteria and initiating bacteriolysis and inflammation. For decades it has been known that GBP1/2/5 bind membranes through the C-terminal end by having a lipid-moiety attached post translation, yet the membrane-binding mechanism of their family members (GBP4/6/7) is still completely unknown. Through bioinformatic analysis we believe the latter all bind bacterial membranes through amphipathic helices at the C-terminal end. In this project you will try to experimentally show how these GBPs binds membranes. Within this project you can learn how to clone, culture cells, purify protein and all the other basics of biochemistry.

Techniques

- Cryo-EM
- Fluorescence microscopy
- Protein biochemistry
- Structural biology
- Biophysical characterisation
- Cell culture

Further reading

Kuhm, T., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.03.28.534355v1.

Visualizing antibacterial protein coats at high resolution

~~BEP~~ MEP

Supervisor: Clémence Taisne, c.m.taisne@tudelft.nl

In our lab a key project focuses on studying guanylate-binding proteins (GBPs) involved in cytosolic host defense against intracellular bacteria. Certain pathogens like Salmonella hyphimurium and Shigella flexneri evade vacuoles to thrive in the cell cytosol. Host cells counteract this by recruiting GBPs around pathogen membranes. Using cryo-electron microscopy, our lab has solved the structure of GBP1 and its binding with lipopolysaccharides (LPS). This project aims to further characterise this interaction through high-resolution fluorescence and electron microscopy obtained in infected cells. Using cryo-tomography and super-resolution imaging you will visualise the GBP1 coat binding around different gram-negative bacteria, shedding light on an intricate host defense mechanism that is crucial in the fight against intracellular pathogens.

Techniques

- Cryo-EM/ET
- Fluorescence microscopy
- Cell culture
- Microbiology
- Infection biology

Further reading

Kuhm, T., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.03.28.534355v1.

Grussmayer Lab

Department Bionanoscience

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Quantitative imaging of cytoskeletal crosstalk at the nanoscale

BEP MEP

Supervisor: Moritz Engelhardt;
In collaboration with Koenderink lab

Master project to establish new multicolor super-resolution imaging to unveil the nanoscopic cytoskeletal structures (actin, microtubules and intermediate filaments) of cells as well as their interaction (crosstalk) and relate it to their active mechanical behaviour. You will optimize multicolor imaging and focus on quantitative network analysis of multicolor super-resolved networks at the nanoscale or on extending imaging from 2D to 3D. At a later stage, we will investigate how different surface micropatterning influences cytoskeletal crosstalk. This is a joint Kavli Institute for Nanotechnology Delft funded project between the Koenderink Lab and the Grussmayer Lab @BN/AS.

Techniques

- Cell culture and labelling
- State-of-the-art super-resolution microscopy methods
- Advanced image analysis
- Visualization and presentation of experimental data
- Micropatterning of surfaces for controlled cell adhesion

Grussmayer Lab

Gentle super-resolution imaging for tissue

BEP

MEP

In collaboration with the Smith Lab at 3mE

Master project super-resolution imaging for optically "complex" biomedical samples by combining Super-resolution optical fluctuation imaging on a new light sheet microscope (SOLEIL) with adaptive optics. Joint TU Delft Bioengineering Institute funded project between the Smith Lab @DCSC/3ME and the Grussmayer Lab @BN/AS.

Techniques

- Cell culture and labelling
- State-of-the-art super-resolution microscopy methods
- Adaptive optics
- Data simulation
- Adaptive optics algorithm
- Microscopy hardware for simultaneous 3D imaging

Koenderink Group

Department Bionanoscience

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Cytoskeletal crosstalk in confined cancer cells

~~BEP~~ MEP

Supervisor: Anouk van der Net, j.j.p.vanderNet@tudelft.nl

Confinement parameters of extracellular matrix in the local tumor microenvironments can impact tumor cell migration strategies and therefore also invasion efficiency and metastatic potential. To better understand the effect of confinement on cancer cell morphology and mechanics, we use live-cell confocal microscopy to study the localization of different cytoskeletal networks and their crosstalk in genetically manipulated cancer cells that are confined on 2D micropatterns that mimic 3D collagen migration tracks. Via image analysis, we aim to elucidate strategies employed by cancer cells to survive extreme confining conditions via the cytoskeletal networks.

Techniques

- Micropatterning
- Live-cell confocal microscopy
- Mammalian cell culture
- Electroporation
- Image analysis

Further reading

Ndiaye, A.B., et al. (2022). *Frontiers in Cell and Developmental Biology, 11*(10), 882037. DOI: 10.3389/fcell.2022.882037.

Building a living cell from scratch using microfluidics

~~BEP~~ MEP

Supervisor: Bert van Herck, b.vanherck@tudelft.nl

To shed light on the fundamental blueprint of a cell and get a better understanding of the governing principles of cellular life, we are aiming to build a synthetic cell from the bottom-up using molecular building blocks. Towards this end, we use a microfluidic technology, Octanol-assisted Liposome Assembly, to produce cell-sized liposomes. This project will focus on the expansion of this microfluidic technology in order to obtain a lab-on-a-chip system to establish a cycle of growing and dividing liposomes, mimicking a continuous life cycle of a living cell. In this experimental and multidisciplinary project, you will gain experience working in a wetlab, learn how to operate a microfluidic setup, and perform fluorescence microscopy-based experiments.

Techniques

- Microfluidics
- Fluorescence microscopy
- Image analysis

Further reading

Deshpande, S., et al. (2016). *Nature Communications, 7*(10447). DOI: 10.1038/ncomms10447.

Establishing programmable liposome fusion to enable synthetic cell growth

BEP MEP

Supervisor: Bert van Herck, b.vanherck@tudelft.nl

To accomplish sustained growth and division, synthetic cells must expand their membrane surface. Providing extra lipids from the outside is a necessity to supply additional membrane area. We are developing a membrane fusion protocol based

on complementary DNA strands with a cholesterol tag to induce binding and fusion between GUVs and LUVs. To characterize this process, we use fluorescence imaging (confocal laser scanning, FRET, FLIM) and quantitative image analysis. The project will focus on the development of a content mixing and a leakage assay to further assess vesicle fusion. Further, we plan to integrate this fusion system into a microfluidic device to improve our control over the experimental parameters.

Techniques

- Confocal fluorescence microscopy
- FRET
- FLIM
- Image analysis
- Microfluidics

Further reading

Lira, R.B., et al. (2019). Biophysical Journal, 116(1), 79-91. DOI: 10.1016/j.bpj.2018.11.3128.

Mechanobiology of in vitro cartilage tissues

BEP
MEP

Supervisor: Irene Nagle, i.nagle@tudelft.nl

In connective tissues, cells are embedded in a support matrix composed of a complex 3D network of extracellular macromolecules and proteins. Cells receive various biophysical stimuli through this extracellular matrix (ECM) such as topographic cues or mechanical stimulation. For instance, chondrocytes, specialized collagen-secreting cells responsible for the maintenance of cartilaginous tissues within joints, are constantly exposed to mechanical loading (compression, shear). This project aims at understanding the interplay between cell behaviour and ECM properties using in

vitro model systems based on 3D cultures of chondrocytes in cartilage-mimicking hydrogels and/or the influence of controlled external loading on the cell response. The goal is to gain insights into chondrocyte mechanobiology in healthy but also in diseased conditions.

Techniques

- Light microscopy
- Mammalian cell culture
- Mechanical testing in the context of biological tissues

Further reading

Muntz, I., et al. (2022). Physical Biology, 19(2), 021001. DOI: 10.1088/1478-3975/ac42b8.

Engineering an actin cytoskeleton in synthetic cells for electroporation

BEP
MEP

Supervisor: Nikki Nafar, n.nafar@tudelft.nl

This project focuses on the role of the actin cytoskeleton in electroporation, a key technique for delivering materials into cells. Electroporation uses electric pulses to destabilize the cell membrane, but the underlying actin cytoskeleton, a complex structural network, might significantly influence this process. You will employ the eDICE technique to create an actin cortex within synthetic cells and then modify this structure using actin-binding proteins. The aim is to understand how these alterations impact the synthetic cells' response to electroporation.

Techniques

- GUV fabrication (eDICE: emulsion droplet interface crossing encapsulation)
- Fluorescent (+ super-resolution) microscopy
- Electroporation

Further reading

Perrier, D.L., et al. (2019). *Scientific Reports, 9*(1), 8151. DOI: 10.1038/s41598-019-44613-5.

Model intercellular bridge with septin and other proteins

~~BEP~~ MEP

Supervisor: SaFrye Reese, s.d.r.mxreese@tudelft.nl

In the intercellular bridge, proteins are important for the recruited and organized in the intercellular bridge. In our group, we use cell-sized giant unilamellar vesicles (GUVs) as a model to investigate biological proteins spatiotemporal interactions in a bottom-up approach. By utilizing microfluidic traps, the geometry of the plasma membrane is altered to investigate the shape deformations. Experimentally you can learn about encapsulation of proteins, such as septin and anillin, to model the intercellular bridge. Additionally, you can improve the quantification of the co-localization of multiple proteins to each other or the membrane.

Techniques

- Protein encapsulation
- Confocal microscopy
- Image analysis
- Python coding

Further reading

Panagiotou, T.C., et al. (2022). Cell Reports, 40(9), 111274. DOI: 10.1016/j.celrep.2022.111274.

Evolutionary approach to building a synthetic cell

BEP
MEP

Supervisor: Marijn van den Brink, m.vandenbrink@tudelft.nl

We aim to build a synthetic cell via a directed evolution approach. We express small but smart DNA libraries inside liposomes using a cell-free expression system (PURE system) and sort the vesicles displaying improved phenotypes, so we can identify the responsible genotypes. Because the genetic modules essential to a synthetic cell are linked to multidimensional phenotypes, including dynamic behaviours, cell shapes and protein localizations, we are developing an imaging-based vesicle selection technique. Possible student project directions: (1) develop microscopy-based method to sort gene-expressing liposomes (wet lab), (2) perform directed evolution experiments to optimize synthetic cell modules (wet lab), (3) train and test AI-based object detection/video classification algorithms (dry lab).

Techniques

- Cell-free gene expression
- Liposome preparation
- Microscopy
- Flow cytometry
- PCR/qPCR
- DNA library design and synthesis

Further reading

Abil, Z. & Danelon, C. (2020). *Frontiers in Bioengineering and Biotechnology, 8*, 927. DOI: 10.3389/fbioe.2020.00927.

Idema group

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Mechanics of tissue development

~~BEP~~ MEP

During development, tissues undergo large conformational changes. As part of such changes, tissues sometimes behave as a solid, and sometimes as a fluid. In this project, we'll study the mechanics of a developing tissue, built from cells that we describe with a 'sticks and balls' model (representing the nucleus and cytoskeleton of each cell). We already know that this model can correctly predict the geometric pattern of the cells in an actual tissue, and that non-adhering cells flow like soap bubbles when we shear them. In this project, we will study the effect of cell division on tissue. As always, we will aim to predict the outcome of similar tests in experiments.

Techniques

- Simulations
- Data analysis

Further reading

Van Drongelen, R., et al. (2018). *Journal of Theoretical Biology, 454*, 182-189. DOI: 10.1016/j.jtbi.2018.06.002.

Interactions between crawling cells

BEP
MEP

The 'sticks and balls' model of project 1 allows us to create not only growing but also crawling cells. In this project, we will study the interaction between such crawling cells, and see if and how excluded volume and transient adhesion interactions cause the cells to exhibit nontrivial collective dynamics. While we will initially do our simulations in an empty environment, the next step will be to include patterns, resembling extracellular material and ultimately other tissue that the cells are moving through.

Techniques

- Simulations
- Data analysis

Further reading

Van Drongelen, R., et al. (2018). *Journal of Theoretical Biology, 454*, 182-189. DOI: 10.1016/j.jtbi.2018.06.002.

Bacterial colony growth and shape

~~BEP~~
MEP

Bacterial colonies grow through repeated growt h-and-division cycles. Rod-shaped bacteria do so by elongating along their long axis, defining a clear local orientation. However, after a couple of division rounds, the global orientation is lost, and orientational defects appear. In this project, we'll study how the properties of the colony, like the defect density, correlation length, and colony shape, are affected by the bacterial properties, such as their growth protocol ('adder' and 'sizer' models) and their interactions, to figure out which of these we can induce directly from experimental observations of growing colonies.

Techniques

- Simulations
- Data analysis

Further reading

Los, R., et al. (2022). *arXiv.* DOI: 10.48550/arXiv.2003.10509.

Oscillation-induced phase separation in bacterial colonies

BEP
MEP

Some species of swimming bacteria can oscillate: they repeatedly flip the direction in which they are moving by 180°. While this behaviour may appear counterproductive for colony spreading, earlier work has shown that it can actually help a colony boundary move faster, by better aligning the bacteria inside. In this project, we'll study what happens when we mix two species of oscillating bacteria together. We expect that under the right conditions, these bacteria can phase-separate, much like the motility-induced phase separation observed in self-propelling systems.

Techniques

- Simulations
- Data analysis

JZ Group

Department Bionanoscience

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Stochastic simulations of phase separation in the polarisation network of budding yeast

BEP MEP

Although the relevant proteins in the polarisation network of budding yeast have been clearly identified, including their mutual interactions, there is increasing experimental evidence that some of the components can form characteristic structures and aggregates under special conditions. The origin of these structures, and their potential function in the network is unclear, and currently under experimental and computational investigation. This project uses stochastic computational methods to simulate the reaction-diffusion system of the polarisation network, and explore potential scenarios, to interrogate the potential function of these liquid-like structures of proteins. (This project is largely inspired by the experiments of the Laan Lab).

Techniques

- Stochastic simulations (Gillespie algorithm)
- Theory of phase separation
- Statistical mechanics in general
- c++ programming (not essential)
- Data analysis using python

Collective swimming behaviour of *C. Reinhardtii* and the influence on their environment

BEP
MEP

Swimming algae and bacteria show a very different, and much more complex dynamic behaviour than 'passive' diffusing solutes. While the swimming behaviour of bacteria like Pseudomonas A. are rather well described by a 'run-and-tumble motion', the individual swimming behaviour and decision making of single algae is still under investigation, and is much more complex, let alone their flocking behaviour and the influence on the environment such as other diffusing particles and swimmers. This project uses simulation methods to find relations between the individual swimming behaviour of algae and their collective properties. In particular how flocks of swimmers can influence diffusing particles and the medium they are suspended in. (This project is largely inspired by the experiments in the group of Marie-Eve Aubin).

Techniques

- Molecular Dynamics-like simulation of swimmers
- MD-like simulations of passive particles

Living soft matter

Department Chemical Engineering

Principal investigator Pouyan Boukany

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Using 3D microfluidics to mimic the tumor microenvironment

~~BEP~~ MEP

The tumor microenvironment (TME) is a central player in local cancer cell invasion and metastasis. Its unique biomechanical and biophysical characteristics dynamically change due to the influence of tumor cells, thereby promoting tumor growth and invasion. The role of relevant physical cues on cancer cell invasion through a complex TME remains widely unknown. This project aims to develop new microfluidics to replicate the intricate characteristics of TME in a controlled and scalable manner for research and therapeutic development.

Techniques

- Microfluidics
- Confocal Imaging
- Cell culture

Further reading

Mehta, P., et al. (2022). *Trends in Cancer, 8*(8), 683-697. DOI: 10.1016/j.trecan.2022.03.006.

A first step towards high throughput micro-fluidic aspiration and electroporation device

BEP MEP

Supervisor: Sophie de Boer, S.S.M.deBoer@tudelft.nl

Efficient delivery of genetic materials into cells is a crucial aspect of gene-editing technologies. Electroporation, a

promising method, involves creating temporary pores in the cell membrane through high-voltage electric pulses. However, the factors influencing its efficiency remain poorly understood, primarily due to the complexity of living cells and use of overly simplified models like giant unilamellar vesicles (GUVs).

An often overlooked component is the role of the actin cytoskeleton, a dynamic network of polymers located beneath the cell membrane. It is pivotal in regulating diverse biological functions, one of which is providing structural support to maintain cell shape. Research has shown that the actin cytoskeleton is disrupted and may also play an active role in the pore dynamics during electroporation of the cell membrane. However, our knowledge of the underlying biophysical mechanisms of this process is limited.

This project aims to uncover the biophysical interactions between electroporation and the actin cytoskeleton.

Techniques

- Microfabrication of a microfluidic-aspiration-and-electroporation (MFAE) device
- Extract material properties from data
- Confocal Imaging

Further reading

Muralidharan, A., et al. (2022). *Bioelectrochemistry, 147*, 108197. DOI: 10.1016/j.bioelechem.2022.108197.

Stiffness of cancer tissue impacts efficacy of immune therapies: 3D-printing meets T-cells

BEP
MEP

Supervisor: Mahdiyeh Nouri, m.nourigoushki@tudelft.nl

Imagine a world where cancer can be treated with remarkable success using the body's own immune system. T-cell therapy, a revolutionary approach that engineers immune cells to

target cancer, has made significant strides in treating blood cancers. However, its efficacy against solid tumors, like those in breast or bone tissues, has been limited. The reason? Neglecting the impact of the mechanical properties of cancer tissues on T-cell behavior.

Our MSc thesis project, "Stiffness of Cancer Tissue Impacts Efficacy of Immune Therapies: 3D-Printing Meets T-Cells," endeavors to bridge this critical knowledge gap. We aim to engineer 3D-printed micro-scaffolds that mimic the mechanical and morphological properties of breast cancer tissue. Through this, we will explore how these properties influence T-cell proliferation and responses. This innovative project blends the bioengineering of T-cells with the fabrication of a 3D tumor microenvironment in vitro.

Techniques

- Bioprinting
- Cell culture
- Confocal Imaging

Medical Imaging

Department Imaging Physics

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Protein engineering of gas vesicles for multiplexed biomolecular ultrasound imaging

BEP
MEP

Supervisor: Dion Terwiel & Byung Min Park, d.terwiel@tudelft.nl

Ultrasound imaging has recently entered the biomolecular imaging field with the discovery of gas vesicles (GVs) as ultrasound contrast agents. GVs are gas-filled cylindrical protein nano-structures (50nm x 500nm) found in cyanobacteria who use them for floatation. Their genetic encodability allows them to fulfill a similar function to GFP in optics: to connect detectable signals to cellular and molecular processes. Contrary to optics however, ultrasound imaging is capable of penetrating into opaque tissue. We at the Maresca lab are involved in the effort to expand the toolkit for gas vesicles as contrast agents. This project is mainly concerned with finding a consistent strategy for engineering gas vesicle sizes and population heterogeneity, with the aim of enabling multiplexed imaging of cellular processes in a single organism.

Techniques

- Molecular biology (PCR, transformation etc.)
- Protein expression and purification
- Ultrasound imaging
- Nanopore particle size analysis
- TEM

Further reading

Heiles, B. (2021). *Neuroscience, 474,* 122-133. DOI: 10.1016/j.neuroscience.2021.03.011.

Menzel Lab

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3D-Nanoprinting for improved fiber reconstruction with scattered light

BEP
MEP

In collaboration with the Accardo Lab (3mE, TU Delft)

Computational Scattered Light Imaging is a highly promising new imaging technique, which allows to disentangle highly complex nerve fiber networks in the brain. However, it has mostly been used to generate 2D fiber maps, as tissue samples with well-defined 3D fiber orientations are not available. In this project, we will generate 3D-printed tissue phantoms with different fiber geometries (e.g. crossing fibers, inclined fibers, fibers with different diameters) and measure them with our setup. In this way, we want to validate and improve the current reconstruction of fiber structures from measured scattering signals. The project is a joint TU Delft Bioengineering Institute funded project.

Techniques

- Two-photon polymerization
- Scanning electron microscopy
- Scattered light imaging
- Image analysis

Exploiting tissue composition with polarized light scattering

In brain tissue sections, an interesting effect has been observed: Some regions let more light through when the light is polarized parallel to the nerve fibers. Other regions let more light through when the light is polarized perpendicular to the nerve fibers. In this project, we will study to what degree this effect is caused by scattering and how it can be used to distinguish between different tissue compositions. Apart from brain, we will measure biological tissues with other types of fibers (muscle, collagen) to see if they show similar effects.

Techniques

- Polarization microscopy
- Scattered light imaging
- Tissue histology
- Image analysis

Analyzing nerve fiber size in brain samples using scattered light of different wavelengths

~~BEP~~ MEP

Computational Scattered Light Imaging (ComSLI) is a promising new imaging technique that resolves densely interwoven nerve fibers and their crossings with micrometer resolution, by exploiting scattering of visible light. While other techniques require dedicated equipment and time-consuming raster-scanning, ComSLI can be performed with a simple LED light source and camera.

It is expected that the scattering of light depends on the feature size relative to the wavelength. In this project, we will systematically compare scattering signals obtained from ComSLI measurements with different wavelengths on various brain tissue sections, to better understand how they are related

to the underlying nerve fiber sizes, and how these measurements can be used to estimate the fiber sizes.

Techniques

- Scattered light imaging measurements
- Automated signal and image analysis (using ImageJ/Python)

Further reading

Menzel, M., et al. (2021). *Frontiers in Neuroanatomy, 15*, 767223. DOI: 10.3389/fnana.2021.767223.

Confidence map for scattered light imaging measurements of fibrous tissue samples

~~BEP~~ MEP

Currently, measurement results from Computational Scattered Light Imaging (ComSLI) are mostly compared qualitatively because a quality measure is missing. This makes it difficult to optimize measurement parameters or make informed statements about differences between samples. Also, the measured scattering signals are only interpreted by a simple peak-finding algorithm - the strength and clarity of the signals are not taken into account. In this project, we will develop a quality measure to better quantify the results of ComSLI (scattering patterns, line profiles, etc.), and develop a confidence map to indicate how reliable the computed fiber orientations are. We will identify questionable outliers by taking regional information and information from surrounding pixels into account.

Techniques

Signal and image analysis (using ImageJ and Python)

Further reading

Menzel, M., et al. (2021). *NeuroImage, 233,* 117952. DOI: 10.1016/j.neuroimage.2021.117952.

Development of a combined fluorescence and scattered light imaging system

~~BEP~~ MEP

Computational Scattered Light Imaging (ComSLI) stands as a novel and emerging imaging method capable of distinguishing intricately entangled fibers (nerves, collagen, etc.) and their intersections at a micrometer scale, utilizing the scatter of visible light.

Whole-slide fluorescence microscopy is a specialized form of fluorescence microscopy that allows for the scanning and digitization of an entire microscope slide with high throughput. It has significant applications in pathology, allowing for the rapid screening and analysis of tissue samples.

Techniques

- Optical system development (scattered light imaging, fluorescence imaging)
- Automated image accusation (e.g., using Python)

Further reading

Menzel, M., et al. (2021). *NeuroImage, 233,* 117952. DOI: 10.1016/j.neuroimage.2021.117952.

Rivenson, Y., et al. (2019). *Nature biomedical engineering, 3,* 466-477. DOI: 10.1038/s41551-019-0362-y.

Molecular Neurobiology

Department Bionanoscience

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Cell adhesion molecules at the synapse

BEP
MEP

In our research group we aim to understand how neurons form circuits. Intact neuronal circuits are at the basis of learning and memory. Damaged neuronal circuits can cause memory loss and behavioral or motor skills disorders. We use techniques from biochemistry, biophysics and cellular biology to address questions such as: How do neuronal circuits develop over time? Which molecules are important players in this process? What is the molecular basis of neuronal recognition?

Techniques

- Molecular biology (cloning)
- Biochemistry (protein purification)
- Biophysics/structural biology (protein characterization, electron microscopy)

Further reading

Gogou, C., et al. (2023). *BioRxiv.* DOI: 10.1101/2023.10.27.564434.

Neurophotonics lab

Department Imaging Physics

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Creating sensors for Voltage imaging

BEP
MEP

Supervisor: Marco Post, m.g.post@tudelft.nl

Voltage imaging allows recording 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, computational evolution, the photocycle dynamics of different families of proteins and their application *in vitro* and *in vivo* to answer fundamental biophysical and neuroscience questions.

Techniques

- Molecular biology (cell culture, microscopy, molecular techniques, etc.)
- Computational biology (Monte Carlo simulations, deep learning based image analysis, etc.)

Further reading

Adam, Y., et al. (2019). *Nature, 569*(7756), 413-417. DOI: 10.1038/s41586-019-1166-7.
Meng, X., et al. (2023). *ACS Physical Chemistry, 3*(4), 320-333. DOI: 10.1021/acsphyschemau.3c00003.

Absolute voltage imaging for investigation of embryonic development

~~BEP~~ MEP

Supervisor: Zhenzhen Wu, z.wu-3@tudelft.nl

We're interested in 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. We have projects involving the creation of new sensors, investigating their trafficking behavior in zebrafish, and acquiring and analyzing this new type of data.

Techniques

- Cloning
- Fluorescence lifetime imaging
- Data processing
- Zebrafish embryos

Further reading

Brinks, D., et al. (2015). *Biophysical journal, 109*(5), 914–921. DOI: 10.1016/j.bpj.2015.07.038.

Nanoscopic optogenetics

BEP MEP

Supervisor: Qiangrui Dong, q.dong@tudelft.nl

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. The BEP/MEP projects here focus molecular biology and biochemistry, for instance testing linkage of nanoparticles to membrane proteins.

Techniques

- Organic chemistry
- Cloning
- Cell and tissue engineering
- Fluorescence imaging

Further reading

Locarno, M. & Brinks, D. (2023). *American Journal of Physics, 91,* 538. DOI: 10.1119/5.0094967.

Simulations and machine learning for voltage imaging

BEP MEP

Supervisor: Rui Silva, Alejandro Castaneda, Laurens Engwegen

The lab has a theoretical branch where we develop Machine learning/AI algorithms to analyze the rich multidimensional data voltage imaging provides. we develop automated protocols to address excitable tissue to learn about, manipulate and implant electrical dynamics; and we model neural dynamics to understand the effect disease models have on the electrical dynamics we can observe with voltage imaging.

Techniques

- Reinforcement learning
- Physics-based AI
- Mathematical models of (networks of) neurons

Single Molecule Imaging lab

Department Imaging Physics

Principal investigator Hylkje Geertsema

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Lamin network in human cells visualized with super-resolution

BEP

MEP

To keep our body healthy, cells continuously adjust to stress responses, such as DNA damage, nutrient deficiency and mechanical stress. Recently, the lamin family of cytoskeletal proteins have emerged as a key regulator of cell response to intrinsic and environmental stimuli. Lamins form a fibrous meshwork underlying the inner nuclear membrane. And we are interested in how this protein meshwork looks like and responds at the molecular level within the living cell. We use advanced fluorescence microscopy techniques to visualize those protein structures to get a very accurate peek inside human cells. Those techniques comprise DNA-PAINT, expansion microscopy and live cell imaging. So if are you looking for a diverse, multidisciplinary project… then we are happy to hear from you!

Techniques

- Super-resolution fluorescence microscopy
- Human cell culture
- Live cell imaging
- Gene-editing
- Image and cluster analysis
- Expansion microscopy

Further reading

Nmezi, B., et al. (2019). *PNAS, 116*(10), 4307-4315. DOI: 10.1073/pnas.1810070116.

M'Saad, O. & Bewersdorf, J. (2020). *Nature Communications, 11(3850).* DOI: 10.1038/s41467-020-17523-8.

Sostaric group

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Protein interactions in 3D

~~BEP~~ MEP

In collaboration with Liedewij Laan

Protein-protein interactions (PPIs) are essential for functioning of any living cell. While some proteins form strong interactions, other PPIs are of a transient nature, forming interactions of varying strength and time duration. Moreover, a cell may modulate binding affinity of a protein:protein pair by, e.g., changing the amounts of proteins or introducing/removing post-translational modifications. In this project, we will use bioinformatics to explore PPIs in yeast polarity protein network. Our starting point will be the proximity labelling data (TurboID), where interactors of selected polarity network proteins were identified. Our aim will be to distinguish different types of interactions and learn more about this network.

Techniques

- Mass spectrometry data analysis
- Performing simultaneous folding and docking of proteins using AlphaFold2-based tools
- Prediction of binding affinities

Further reading

Branon, T.C., et al. (2018). *Nature, 36*(9), 880-887. DOI: 10.1038/nbt.4201.

Bryant, P., et al. (2022). *Nature Communications, 13*, 1265. DOI: 10.1038/s41467-022-28865-w.

RNA distribution clustering

BEP
MEP

In collaboration with Marianne Bauer

T cells play an important role in our immune system. To be able to effectively clear tumors and viruses, they have to switch from resting to activated state. We previously built distribution profiles of RNAs among different ribosome-bound states, which are a proxy for RNA translation. In this project, we want to learn which types of distributions RNAs follow and how they change upon T cell activation. To this aim, we will cluster RNA distributions based on their shape. We will first cluster profiles with a constraint of Gaussian distributions in each cluster. For comparison, we can use an information-theoretic clustering and k-means. In parallel, we will investigate what distributions fit best the currently found clusters, and variations over conditions.

Techniques

- Data-analysis methods
- Interpretation of clustering results through the data, as well as through a mathematical analysis

Simulating dynamics of lipid bilayers

~~BEP~~
MEP

In collaboration with Marie-Eve Aubin-Tam

Biomolecular systems are not static but rather in constant motion. Molecular dynamics (MD) simulations give us a glimpse into molecular movements on an atomic scale and allow us to analyze dynamic events in biologic al systems. In this project, we will use computational biology tools, MD simulations in particular, to gain a better understanding of dynamic behavior and of quantitative properties of lipid bilayers. We will build several different lipid bilayers (both of homogeneous and heterogeneous compositions), surround them by water and ions, and simulate these systems to analyze

properties such as lateral diffusion of lipids, among others. Ultimately, the results from MD simulations will be integrated with (already obtained) measurements of bilayers' properties from the wet lab.

Techniques

- Building molecular systems
- Molecular dynamics simulations trajectory analysis

Further reading

Marrink, S.J., et al. (2019). *Chemical Reviews, 119*(9), 6184-6226. DOI: 10.1021/acs.chemrev.8b00460.

Spatial distribution of RNA molecules

BEP
MEP

In collaboration with Wolkers group (Sanquin, A'dam UMC)

T cells play a central role in human immune system by combating viruses and tumors. When they encounter a cell that needs to be cleared, T cells become activated and produce specific set of proteins, called cytokines, which are vital for target cell clearance. In this project, we will explore the spatial distribution of cytokine RNAs in human T cells. We will analyze 3D microscopy images of T cells in which positions of individual cytokine RNA molecules were captured by smFISH (single molecule fluorescence in situ hybridization). More specifically, we will investigate distances between RNAs, whether they're forming clusters, polarization of RNA spots within the cells, as well as distribution of nuclear RNAs with respect to transcription sites.

Techniques

- Programming
- Analysis of 3D microscopy images

Further reading

Stueland, M., et al. (2019). *Scientific Reports, 9*, 8267. DOI: 10.1038/s41598-019-44783-2.