2017

DANDRITE ANNUAL REPORT

AARHUS UNIVERSITY

DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

Words from the Director

Photo by the Novo Nordisk Foundation, Denmark

With our great pleasure, we present the 2017 annual report from DANDRITE.

The year 2017 was an exciting time of great neuroscience at DANDRITE ranging from molecular and cellular neuroscience to behavioral models and neurogenetics.

2017 marked the final year of the first 5-year period of DANDRITE and the very exciting news of approval by Lundbeckfonden of our application for an extension into a second 5-year funding period running until 2023. With a continuous development of advanced group leader programs and facilities, we saw a steady increase in the number of researchers that now exceeds 120 in the DANDRITE group leader and team leader laboratories. Several highly advanced research infrastructures are now in place and running, including in vivo two-photon imaging, cryo-electron microscopy for single-particle analysis, and voltage-clamp fluorescence microscopy and optogenetic light pulse modulation for high-content electrophysiology. A very significant fraction of the resources available to DANDRITE has been devoted to introducing these entirely new lines of research in Danish neuroscience. As a result, sweeps of pioneering publications were published in 2017 in leading journals such as Nature, Neuron, and Current Biology.

Six research groups at DANDRITE successfully proposed and established a center of excellence of the Danish National Research Foundation, PROMEMO – Center for Proteins in Memory. PROMEMO consists of Group Leader Sadegh Nabavi, Team leaders Hanne Poulsen and Magnus Kjærgaard, Affiliated Researcher Marco Capogna, and core group leaders Poul Nissen and Anders Nykjær (director) that through a multidisciplinary program will focus on the molecular mechanisms and microanatomy of synaptic plasticity that determine the persistence and associations of a memory. The PROMEMO program will introduce novel methods in synaptic tagging and protein research and will explore new targets for memory-associated disorders such as anxiety, depression, and dementia. It represents an exquisite example of a deep focus within the wide scope of neuroscience and broad mission of DANDRITE, and of how new expertise, approaches, and opportunities have emerged with DANDRITE.

Equally important, numerous postdoc fellowships and PhD stipends were awarded to the talent pool of DANDRITE and amounting so far to a total of 250 million DKK. I personally had the great honor of receiving the 2017 Novo Nordisk Prize.

We increased also our interaction with the Danish neuroscience community through appointment of four new affiliated researchers. This is a cornerstone of the DANDRITE strategy, and it pertains to our deep involvements in the NeuroCampus Aarhus initiative, the Danish Society for Neuroscience, and the Brain Prize activities supported by Lundbeckfonden, as well as many activities of cutting-edge biophysics and structural biology, as well as many international collaborations, speaker invitations, and exchange visits.

DANDRITE outreach activities extend to several, annual recurring events. One is the future student recruitment event: DANDRITE Encounters. Additionally, DANDRITE engages in public outreach such as Forskningens Døgn (the Festival of Research), Folkeuniversitetet (public outreach lectures), social media outlets, and a growing use of streaming such as video abstracts of important research papers.

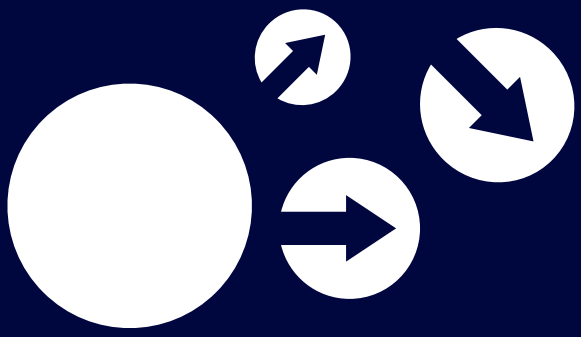
Entering the fifth year of DANDRITE operations, our first group leader evaluations have been initiated for a second 4-year funding period following the 5-year recruitment contracts. Group Leader Mark Denham was evaluated by an international review panel and extended in 2017. Coming up for review in 2018 will be also Anne von Philipsborn and Duda Kvitsiani.

We hope you will enjoy a few moments to learn more about our activities on the following pages.

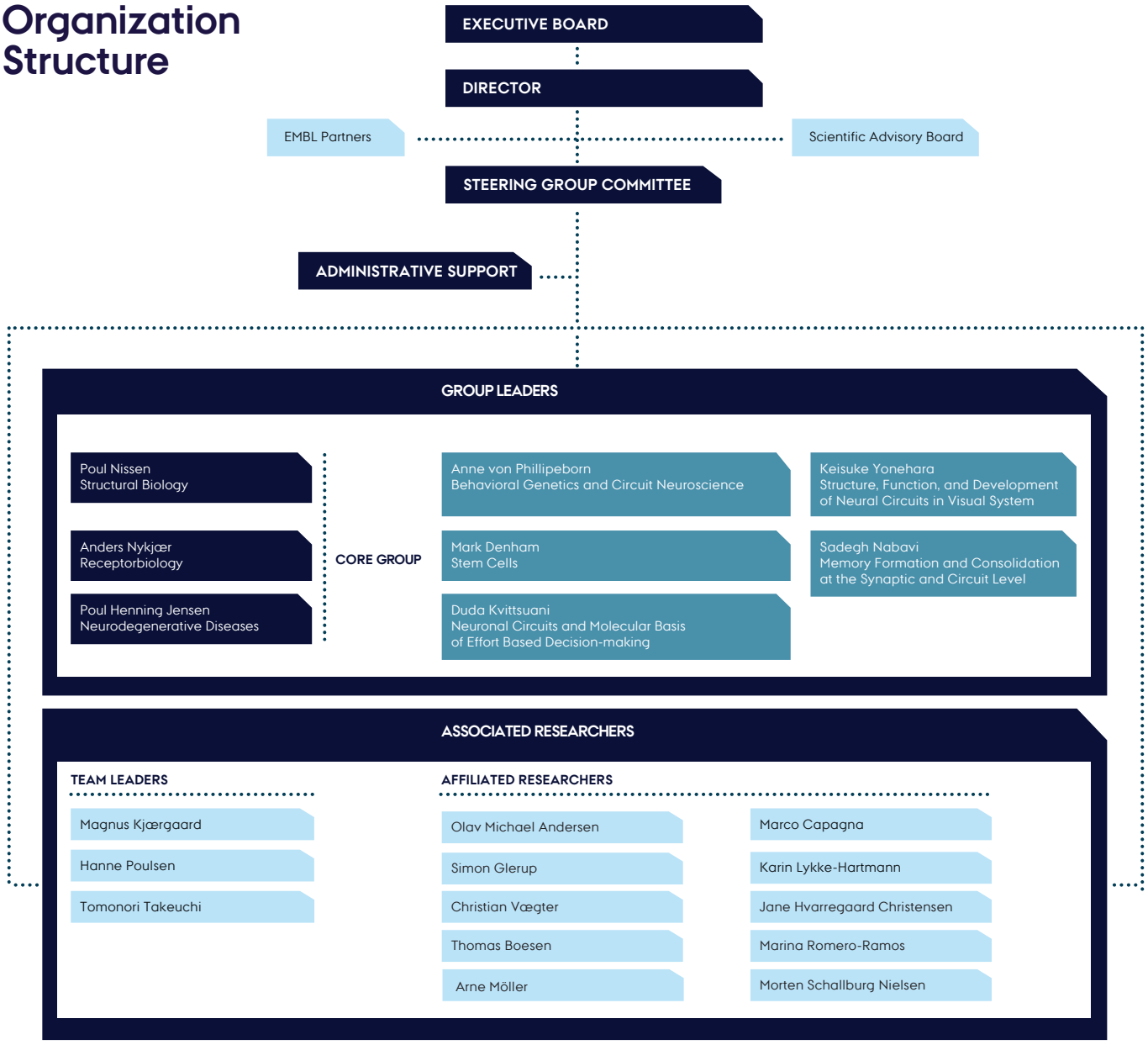
With my warmest regards,

Poul Nissen, Director and Core Group Leader

01 Organization Structure



Organization Structure



ASSOCIATED RESEARCHERS AT DANDRITE

Associate Membership serves as a strategic tool for the further development of DANDRITE's research focus areas and must be of mutual benefit. Selection criteria for associating a researcher is foremost on scientific excellence and scientific complementation.

A team leader holds a non-tenured junior group leader position/assistant professorship at Aarhus University. The appointment as DANDRITE team leader is for 3 years with possible extension for a total of maximum 6 years.

An affiliated researcher is typically an Aarhus University researcher with permanent position that is tightly associated to DANDRITE group leader(s) for mutual benefits on research aims (e.g. through joint grants/research centers, shared laboratories etc.). The affiliation can also support strategic structures of AU departments and infrastructures.

Executive Board

The Executive Board meets twice a year and consists of a chair, the deans of the Faculty of Science & Technology and the Faculty of Health, the Director of Research from Lundbeck-fonden and the DANDRITE core group leaders. The board members in 2017:

Chair: Clinical Professor **Jens Chr. Hedemann Sørensen**, Department of Clinical Medicine, Aarhus University (chair from December 2016)

Dean **Niels Christian Nielsen**, Faculty of Science and Technology, Aarhus University

Dean **Lars Bo Nielsen**, Faculty of Health Sciences, Aarhus University (new member from April 2017)

Director Professor **Poul Nissen**, DANDRITE

Professor **Anders Nykjær,** DANDRITE

Professor **Poul Henning Jensen**, DANDRITE

Director of Research **Anne-Marie Engel**, Lundbeckfonden (non-voting)

Administrative support by Chief Administrative Officer **Else Magård**, DANDRITE

DANDRITE Extended Business Meeting. Photo by Karen Bech-Pedersen

Management

STEERING COMMITTEE

The steering committee meets every Monday at 10-11 AM and consists of the director, the core group leaders and two representatives of the group leaders (internally elected for two-year terms). DANDRITE's administrative personnel also attends the meetings. The steering committee is responsible for strategic developments and implementation of research, the planning and coordination of activities, and the distribution of running budget. The steering committee will also be overseeing public dissemination and outreach of DANDRITE research and activities. The committee in 2017 consisted of the following members:

- Professor **Poul Nissen**, Director
- Professor **Anders Nykjær**
- Professor **Poul Henning Jensen**
- Group Leader **Duda Kvitsiani** (took over in August from Sadegh Nabavi)
- Group Leader **Keisuke Yonehara** (took over in August after Mark Denham)
- Chief Administrative Officer, **Else Magård**

Furthermore, the steering committee meetings are attended by:

- Communications Officer & Director PA, **Maria Thykær Jensen** (maternity cover)
- Communications Assistant & Director PA, **Karen Bech** (maternity leave during 2017)
- Scientific Coordinator & Professor PA, **Susanne Schousboe Sjøgaard**

MONTHLY EXTENDED STEERING COMMITTEE MEETING

Every second Monday of each month the steering committee meets for an extended steering committee meeting taking place from 10:30 AM to 11:30 AM. The extended committee consists of all group leaders and team leaders, spokespersons for each personnel category at DANDRITE. In 2017 the participants were:

- All DANDRITE group leaders
- All DANDRITE team leaders
- Affiliated Researcher spokesperson: **Simon Glerup** (first half year)
- Affiliated Researcher spokesperson: **Marco Capogna** (second half year)
- Postdoc spokesperson: **Hande Login** (first 11 month)
- Postdoc spokesperson: **Mette Richner** (from December)
- PhD student spokesperson: **Sara Buskbjerg Jager** (first half year)
- PhD student spokesperson: **Rikke Hahn Kofoed** (second half year)
- Technician spokesperson: **Benedicte Vestergaard**

MONTHLY COORDINATION MEETING

Monthly the DANDRITE core group leaders and chief administrator meet with the heads of the two hosting department (Thomas G. Jensen, Department of Biomedicine and Erik Østergaard Jensen, Department of Molecular Biology and Genetics) for coordination of activities, teaching, infrastructural matters, and strategies.

Administrative Support Team at DANDRITE. Photo by Morten Schallburg Nielsen

ADMINISTRATIVE SUPPORT TEAM
The Support Team aims at ensuring a cohesive, efficient and professional administration and research support for employees and students connected to DANDRITE. The Support Team strives for providing the framework needed for the single DANDRITE researcher to reach their full potential.

DANDRITE research encompasses interdisciplinary and translational activities, and therefore an important component in daily work and solving of administrative tasks is to bridge differences among various entities and cultures. The DANDRITE support team draws on the resources available from the university administrative divisions: AU Research Support and External Relations, AU Finance and Estates Project Development, AU HR, AU Student Administration and Services, AU IT, and Communication (Rector's Office). Furthermore, a tight collaboration and support is provided by colleagues in the two hosting departments and AU administration centers at Faculty of Health and at Faculty of Science & Technology.

TECHNICIAN NETWORK
The laboratory technicians from all research groups affiliated with DANDRITE meet 2-3 times per year, to facilitate exchange and alignment of know-how, administrative and regulatory procedures, practical information, and for informal networking. The technician spokesperson for the extended steering committee is elected by the network and communicates matters raised or discussed in the technician network or at the extended steering committee.

Part of Young DANDRITE at the SAB meeting & retreat in 2016

Young DANDRITE

– The PhD & Postdoc association at DANDRITE

The PhD & Postdoc Association at DANDRITE, "Young DANDRITE", facilitates interaction and unity among the PhD students and postdocs affiliated with DANDRITE.

The association meets several times a year for meetings and events, and ad hoc activities. In 2017, Young DANDRITE started a completely new initiative named "Rainbow Club" which is a unique seminar series club. The idea of the Rainbow Club seminars is to bring in inspiration from outside DANDRITE's typical research subjects and methodologies. The seminar layout is completely informal aiming for creativity and out-of-box thinking. Speakers are invited to introduce a selected topic in a basic, introductory manner, preferable in an entertaining format, to invite for interactive active discussions. To aid for the lively discussions, the seminars are followed by social gathering at which also the invited speaker takes part.

Also, Young DANDRITE are adding to DANDRITE's general social life by organizing evening get-togethers, nights out in town and by arranging entertainments and tournaments at festive occasions.

The PhD and postdoc spokespersons for the extended steering committee are also selected by Young DANDRITE.

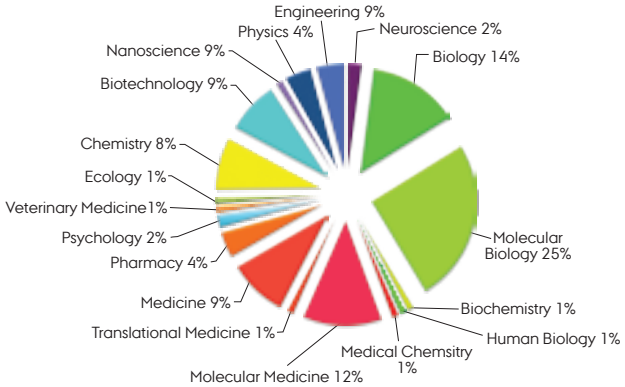


Figure 1: Students Educational Background.
Simple survey (sample size 97 participants): educational background of DANDRITE's students and employees. The interdisciplinary approach to Young DANDRITE's Rainbow Club initiative is reflected in educational backgrounds. Survey and graphic by PhD student Sophie Seidenbecher.

Current Young DANDRITE coordinators and PhD students: Juliane Martin, Katherine Patrice Gill, Milena Laban, Nathalie Krauth, and Emil Gregersen

Scientific Advisory Board

The scientific advisory board convenes biannually and provides independent advice on scientific and strategic matters, and evaluations of achievements, ideas and strategies. The scientific advisory board members are international, highly reputed researchers. Since the first advisory board meeting in Aarhus 2014, a second meeting was combined with the DANDRITE retreat September 2016 at the conference center Sandbjerg Manor.
The members of the scientific advisory board at DANDRITE are:

- Professor **Moses Chao**, New York University (NYU)
- Professor **Kathleen Sweadner**, Harvard Medical School
- Professor **Mart Saarma**, University of Helsinki
- Professor **Glenda Halliday**, Neuroscience Research Australia (NeuRA)
- Director **Matthias Wilmanns**, EMBL Hamburg
- Div. Director **Jan Egebjerg**, Lundbeck
- Professor **Rüdiger Klein**, Max-Planck-Institute of Neurobiology
- Professor **Carl Petersen**, École polytechnique fédérale de Lausanne EPFL

New members who will take part in the planned scientific advisory board meeting in May 2018:

- Professor **Ole Kiehn**, Univeristy of Copenhagen
- Professor **Yang Dan**, University of California, Berkeley

DANDRITE Affiliated Researchers

An Affiliated Researcher (AR) is typically an Aarhus University researcher with permanent position that is tightly associated to DANDRITE group leader(s) for mutual benefits on research aims (e.g. through joint grants/research centers, shared laboratories etc.). The affiliation can also serve to strengthen strategic infrastructures that are of key importance to DANDRITE. AR have qualifications and position at associate professor level or higher.

In 2017 four new AR joined DANDRITE, while six AR re-entered (after motivation and re-evaluation by DANDRITE steering committee). Thus, DANDRITE is proud to enter year 2018 with ten valuable associations:
Six Affiliated Researchers re-entered in 2017:

- Associate Professor Christian Vægter by March 2013
- Associate Professor Olav Andersen by March 2013
- Associate Professor Simon Glerup by March 2013
- Associate Professor Thomas Boesen by March 2013
- Associate Professor Arne Möller by November 2015
- Professor Marco Capogna by August 2016

Four new Affiliated Researchers joined in 2017:

- Associate Professor Jane Hvarregaard Christensen
- Associate Professor Karin Lykke-Hartmann
- Associate Professor Morten Schallburg Nielsen
- Associate Professor Marina Romero-Ramos

JANE HVARREGAARD CHRISTENSEN

Mental disorders - Genes and disease mechanisms
Our primary focus is to discover genetic risk factors and disease mechanisms in mental disorders. We study how core schizophrenia and autism risk genes involved in gene regulatory processes operate in the cell and the brain. We are also mapping novel risk genes in nocturnal enuresis (bedwetting). These are investigated along with genes causing rare disorders of the water balance to understand their interplay in regulating urine production, bladder activity and sleep.

KARIN LYKKE-HARTMANN

Atp1a3 disease knock-in mouse modeling
Autosomal dominant mutations in the human ATP1A3 gene encoding the neuron-specific Na+/K+-ATPase 3 isoform cause neurological diseases including rapid-onset dystonia-parkinsonism (RDP) and alternating hemiplegia of childhood (AHC). Main symptoms include hemiplegia, dystonia, ataxia, hyperactivity, epileptic seizures, and cognitive deficits. Mice harboring the D801Y mutation (3+/D801Y) were shown to represent several of the ATP1A3 disease-related symptoms including hyperactivity, increased sensitivity to chemically induced epileptic seizures, cognitive deficits, hypothermia-induced dystonia and ataxia.

MORTEN SCHALLBURG NIELSEN

Receptor mediated drug delivery to the brain
We are focusing on receptor trafficking in brain endothelial cells, to find effective ways to deliver drug from the blood to the brain. This year we have focused particular on the retrograde receptor MPR300 and we have found that this receptor has the ability to traffic from the luminal membrane at the blood side to the abluminal brain side. We are moreover focusing at characterizing the vesicular system in brain endothelial cells in order to understand receptor trafficking in better detail.

MARINA ROMERO-RAMOS

Study and characterization of the neurodegenerative event in Parkinson's Disease and the associated immune response
My lab works to understand the progressive changes related with the neurodegenerative process of α-synucleinopathies, such as Parkinson's Disease. We study early pathological changes induced by the mishandling of α-synuclein using in vivo modeling of the disease, behavioral tests, followed by anatomical analysis of brain pathology and the different cell populations relevant in disease using histological techniques. We also investigate the potential of novel neuroprotective strategies in different animal models of the disease. In addition, we apply the use of cytometry to analyze immune cell populations to understand the different cell populations as well as the proteins involved in the neuroinflammatory process of the diseases with an ultimate focus on describing novel targets for therapy and define disease biomarkers.

Highlights for 2017:
- Contributed to show: early synaptic dysfunction occurs during α-synuclein mishandling, prior to cell death, and that such event can be assessed in vivo using PET imaging ligands for VMAT2 (Phan et al., 2017)
- Contributed to show: immune system role in α-synucleinopathies and that the MHC-II system has a key role in the immune response associated to α-synuclein neurodegneration (Jimenez-Ferrer et al., 2017).
- Entered as Board Member of the Network for European CNS, Transplantation & Restoration (NECTAR)
- Editor of the Journal of Parkinson's Disease

OLAV MICHAEL ANDERSEN

Transport receptors in neurodevelopment and degeneration
We study the SORL1 gene and its translation product, SORLA during neurogenesis and neurodegeneration. SORL1 is associated with Alzheimer's disease, and we try to learn how genetic variations affect gene function, including alternative splicing and transcription, and why SORLA is downregulated in brain areas of patients with dementia. We develop new animal models to determine the physiological function of SORL1/SORLA, including a role during eye development and synaptic function in the neuroretina.

Highlights for 2017:
- Identified a new SORL1 splice variant that is two-fold down-regulated in AD brains
- The first SORL1 knockout minipig was born

THOMAS BOESEN

Cryo-EM on membrane transporters and receptors
I am involved in research projects centered on nanodisc technology and structural biology of membrane protein transporters and receptors. New avenues are cryo-EM data processing software development and implementation of new cryo-EM methods in DANDRITE projects. As cryo-EM Facility Manager at iNANO-AU, I enable easy access and training on equipment and in cryo-EM and negative stain methods for DANDRITE researchers. The iNANO cryo-EM facility is becoming an important strategic infrastructure in key DANDRITE projects.

Highlights for 2017:
- Establishment of cryo-EM facility at AU

MARCO CAPOGNA

Neuronal circuits of human and rodent cerebral cortex, amygdala and hippocampus
We define the neuronal circuits of human and rodent cerebral cortex and connected brain areas, as they are cellular regulators of cognitive process. We explore what neuronal circuitry guides emotional-dependent memory, and how it is modified in animal models of psychiatric disorders. Major focus is on GABAergic neuron types because of their critical role in controlling brain networks. We use electrophysiology, pharmacology, optogenetic, imaging and anatomy with Sadegh Nabavi and Duda Kvitsiani.

Highlights for 2017:
- Discovery that interneurons of the rodent amygdala are excited by serotonin/glutamate co-release from midbrain
- Discovery of nitric oxide-expressing GABAergic neurons of the rodent amygdala are activated by sleep
- Setting up of electrophysiological investigation of human cortical sections at AU

SIMON GLERUP

Protein sorting in neurological and metabolic disorders
The focus of our research group is cellular mechanisms of protein sorting with particular focus on two related receptor families; the sortilins and LDL receptor-related proteins and their role in lipid metabolism and neuronal function. We study this at the molecular and cellular level and in animal models. We also have a strong interest in the functional consequences of disease causing mutations located in the genes encoding the individual receptor proteins.

Highlights for 2017:
- Publication of study: "Heparan Sulfate Proteoglycans Present PCSK9 to the LDL Receptor" in Nature Communications
- Founding of the spin-out company Draupnir Bio
- Participation in panel discussion on scientific reproducibility together with key opinion leaders including editor-in-chief of Nature Methods at Alpbach meeting, Austria
- Recognized with The Jens Christian Skou Award 2017

ARNE MØLLER

Atp1a3 disease knock-in mouse modeling
The lab uses cryoEM to characterize 3D structures of membrane proteins. We set our focus on the analysis of the dynamics of trans-membrane transporters that actively translocate substrates through the lipid bilayer and neuronal surface receptors that are involved in trafficking and signaling. We are also pursuing methods development to improve EM-imaging and optimize the sample.

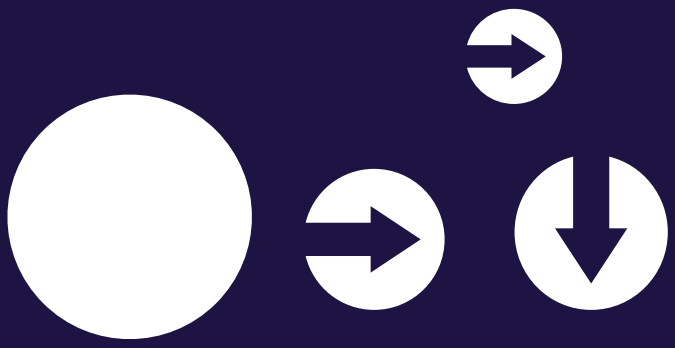
Highlights for 2017:
- Publication of study: "Hidden Twins: SorCS Neuroreceptors Form Stable Dimers" in Journal of Molecular Biology

CHRISTIAN VÆGTER

Nerve injury and neuropathic pain
The peripheral sensory neurons are completely covered by glial cells, with satellite glial cells (SCG) covering the neuronal soma and Schwann cells covering the length of the axon. It is therefore obvious that these glia cells play major roles in how the neurons function. Our aim is to understand how peripheral glia cells affect neuronal functionality in health but also following nerve injury or in diseases such as diabetes.

Highlights for 2017:
- Publication of study: "Isolation of Satellite Glial Cells for High-Quality RNA purification" in Journal of Neuroscience Methods (Jager et al., 2018)

02 Research Activities



Nissen Group

Structural and Functional Studies of Membrane Transporters in Brain

Professor
Poul Nissen

The Nissen lab investigates molecular mechanisms of membrane transport processes and higher-order structures of biomembrane functionalities in brain. Activities are mainly focused on cryo-electron microscopy, protein crystallography, biochemistry and biophysics, and include also collaborative studies through e.g. small-angle X-ray scattering, molecular dynamics simulations, super resolution microscopy, and electrophysiology. Main subjects of research focus on P-type ATPase ion pumps and lipid flippases, Na+ dependent transporters of neurotransmitters and chloride, and transmembrane Tyrosine kinase receptors. Derived activities include also structure based drug discovery. A major, long-term goal is to investigate and model higher-order networks in the Axon Initial Segment that integrates circuit inputs and generates the action potentials in firing neurons. Furthermore, synaptic structures associated with memory are being investigated within the PROMEMO center, and the molecular mechanism underlying direction-selective function in the visual system are being investigated with the Yonehara lab.

The P-type ATPase ion pumps and lipid flippases consume some 40-80% of ATP in the brain and maintain constantly the vital lipid distributions and ion and lipid gradients that potentiate e.g. ion channels, lipid bilayer dynamics, secondary transporters, and regulation of cell volume, ion homeostasis and pH control. Structural studies of Na,K-ATPase and Ca2+ ATPase reveal basic mechanisms of function and disease-mutations, ligand-induced inhibition, and of regulation by post-translational modifications. Chloride transporters are also being pursued to expand on the role of ionic gradients in brain.

Single-molecule studies by Fluorescence Resonance Energy Transfer on an engineered Ca2+-ATPase have revealed fundamental aspects of the transport mechanism and "hidden intermediates" outside crystal structures.

TRANSLATIONAL STUDIES

Effects and possible circumvention of neurological disease-related mutations of Na,K-ATPase are being approached as are interactions of Na,K-ATPase and Ca2+-ATPase with pathological fibrils/aggregates in neurodegenerative disorders. Studies of dysfunctional ATP7B in Wilson's disease take place in collaboration with the Danish Wilson's Disease Center at Aarhus University Hospital.

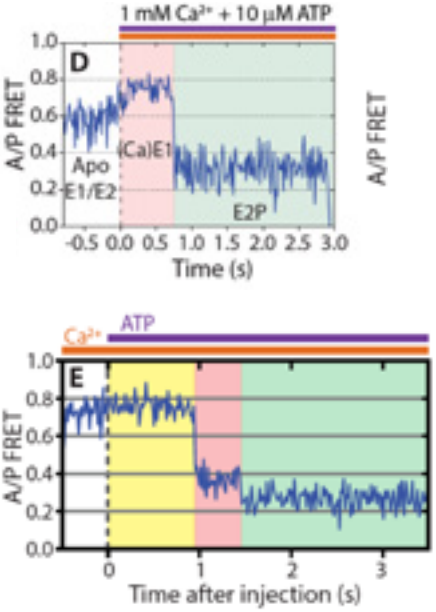


Fig. 1: Single-molecule Fluorescence Resonance Energy Transfer (FRET) traces of the Ca2+-ATPase LMCA1 reveal previously unknown insights into the mechanism of a molecular pump – how it is able to transport without leakage across a membrane (Dyla et al. 2017, Nature – collaboration with the Scott Blanchard lab, Weill-Cornell, and the Jens Peter Andersen lab AU).

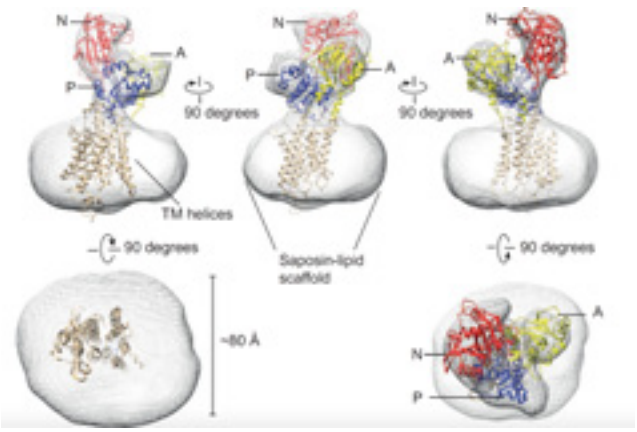


Fig. 2: Reconstitution of a membrane protein into saposin:lipid nanoparticles form samples that are suitable for electron microscopy studies (Lyons et al. 2017, Methods in Enzymology – collaboration with Jens Frauenfeld, Salipro Biotech)

Nissen group members on stairs in lab building.
Photo by Magnus Kjærgaard, DANDRITE

Selected publications 2017

Dyla M, Terry DS**, Kjaergaard M,** Sørensen TLM, Andersen JL, Andersen JP, Knudsen CR, Altman RA, **Nissen P**, Blanchard SB (2017). Dynamics of P-type ATPase transport cycle revealed by single-molecule FRET. *Nature* 551, 346-351

Azouaoui H, Montigny C, Dieudonné T, Champeil P, Jacquot A, Vázquez-Ibar JL, Le Maréchal P, **Ulstrup J, Ash MR, Lyons JA**, **Nissen P**, Lenoir G (2017). A High and Phosphatidylinositol-4-phosphate (PI4P)-dependent ATPase Activity for the Drs2p/Cdc50p Flippase after Removal of its N- and C-terminal Extensions. *J Biol Chem* 292, 7954-7970

Lyons JA, Bøggild A, **Nissen P**, Frauenfeld J (2017). Saposin-Lipoprotein Scaffolds for Structure Determination of Membrane Transporters. *Methods Enzymol* 594, 85-99

Personnel List Nissen Group

Assistant Professor **Joseph Lyons**
Assistant Professor **Esben Quistgaard**
Postdoc **Antoni Kowalski**
Postdoc **Michael Habeck**
Postdoc **Michael Voldsgaard Clausen**
Postdoc **Prasad Kasaragod**
PhD Student **Aljona Kotsubei**
PhD Student **Caroline Marie Teresa Neumann**
PhD Student **Jakob Ulstrup**
PhD Student **Jeppe Achton Nielsen**
PhD Student **Josephine Nissen**
PhD Student **Lars Sørensen**
PhD Student **Marlene Uglebjerg Sørensen**
PhD Student **Milena Laban**
PhD Student **Paula Szalai**
PhD Student **Samuel Hjorth-Jensen**
PhD Student **Sigrid Thirup Larsen**
PhD Student **Sofia Trampari**
Laboratory Technician **Anna Marie Nielsen**
Laboratory Technician L**otte Thue Pedersen**
Research Assistant **Dorota Focht**
Research Assistant **Temitope Ibironke Ayeotan**
Academic employee **Andreas Bøggild**
Academic employee **Christine Juul Fælled Nielsen**
Student Assistant **Sofie Stokkebro Schmøkel**
Communications Assistant (maternity cover) **Emilie Aagaard**
Communications Assistant (maternity cover) **Maria Thykær Jensen**
Communications Assistant & Personal Assistant **Karen Bech**
Group Leder Professor **Poul Nissen**

Jensen Group

Neurodegenerative Disease

Professor
Poul Henning Jensen

The Jensen group is studying how alpha-synuclein contributes to the neurodegenerative processes in Parkinson's disease, Lewy body dementia and multiple systems atrophy, which are hallmarked by prion-like spreading in the nervous system of intracellular aggregates of alpha-synuclein. This is investigated in studies of alpha-synuclein aggregates in vitro, in cell models, transgenic animals and human tissue and involves development of new tools and methods. A novel focus point is how the early phase of the degenerative process may contribute to patients' symptomatology by dysfunctional but still living neurons that offset normal circuitries.

The aim is with a therapeutic focus to characterize structures of aggregated alpha-synuclein species and determine how they impacts on cells with respect to cytotoxic and protective mechanisms, how cells decide on exporting certain aggregated species that facilitate the prion-like spreading in tissue. This involves risk factors from the environment, regulators of alpha-synuclein expression, neuroinflammation, alpha-synuclein strains, and susceptible homeostatic mechanisms like dysregulated calcium homeostasis and proteostatic factors like autophagy and unconventional secretion.
A key observation in 2017 was the demonstration of how the kinase PLK-2 rapidly can change brain levels of alpha-synuclein by regulating its transcription via exonic interactions (Kofoed et al., Neurobiology of Disease, 2017). Other focus areas was the expanded characterization of kinases regulating alpha-synuclein levels and function, the characterization of cell derived alpha-synuclein aggregates, the investigation of environmental factors affecting alpha-synuclein aggregation and our expansion of disease-modifying studies in mouse models of prion-like alpha-synuclein neurodegeneration. Marie Curie fellow Asad Jan joined our group with a project focusing on molecular mechanisms involved in the early prion-like spreading in our animal models. To expand our investigation of pathogenic structures of alpha-synuclein in vitro and in Parkinson brain tissue we were awarded two large collaborative grants from the Michael J Fox Foundation to establish collaborations with University of Southern Denmark, Max Planck Institute in Frankfurt, Germany, and Sydney University in Australia.

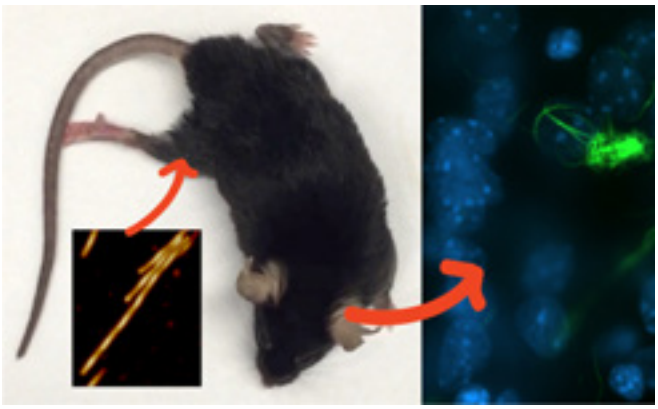


Fig. 1: Modeling α-synuclein aggregate-dependent neurodegeneration. Induction of progressive α-synuclein (AS) aggregate dependent neurodegeneration is initiated by injection of preformed AS fibrils into the hind limb muscle of AS transgenic mice. The preformed fibrils are visualized by atomic force microscopy. The degenerative process spreads through peripheral nerves, the spinal cord and into the brain. Here development of AS aggregates can be demonstrated in susceptible neurons by immunohistochemistry (right panel). Postdoc Nelson Ferreira heads the in-vivo modeling and the histological analysis of brain tissue is performed by PhD student Sara Elfarrash. Illustration by J. Wang and M. D. Dong, iNANO, AU

Jensen group members outside lab building.
Photo by Karen Bech-Pedersen, DANDRITE

Selected publications 2017

Kofoed RH, Zheng J, Ferreira N, Lykke-Andersen S, Salvi M, **Betzer C, Reimer L**, Jensen TH, Fog K, **Jensen PH** (2017) Polo-like kinase 2 modulates α-synuclein protein levels by regulating its mRNA production. *Neurobiol Dis.* Vol. 106, p. 49-62.

Personnel List Jensen Group

Assistant Professor **Cristine Betzer**
Postdoc **Asad Jan**
Postdoc **Fikret Emre Kapucu**
Postdoc **Louise Berkhoudt Lassen**
Postdoc **Nelson Ferreira**
PhD Student **Emil Gregersen**
PhD Student **Lasse Reimer**
PhD Student **Rikke Hahn Kofoed**
PhD Student **Sara Elfarrash**
Bioanalyst **Jette Bank Lauridsen**
Student Assistant **Linnea Sølbek Meier**
Group Leader **Poul Henning Jensen**

Nykjær Group

Receptor Biology

Professor
Anders Nykjær

Research activities of the Nykjær Group are focused towards the functional characterization of a family of neuronal type-1 receptors denoted Vps10p-domain receptors or sortilins. Members of this gene family, which comprises sortilin, SorCS1, SorCS2, SorCS3 and SorLA, predominate in neurons but are also present in specialized cell types outside the nervous system.

The receptors are multifunctional as they can bind a vast number of ligands including neurotrophins, receptor tyrosine kinases, amyloid precursor protein, and progranulin, and engage in cellular trafficking and signaling dependent on the cellular context. Accordingly, sortilin receptors have surfaced as risk genes in both psychiatric, neurological, and metabolic diseases.

We aim to understand the molecular mechanism by which the receptors control neuronal survival, differentiation, and functionality, and what goes wrong in mental disorders and neurodegenerative diseases. To achieve this, we take advantage of a broad repertoire of techniques including transgenic animal models, viral-mediated gene transfer, electrophysiology, mouse behavioral testing, cell biology, and advanced imaging systems and benefit from close collaborations with structural biologists and geneticists.

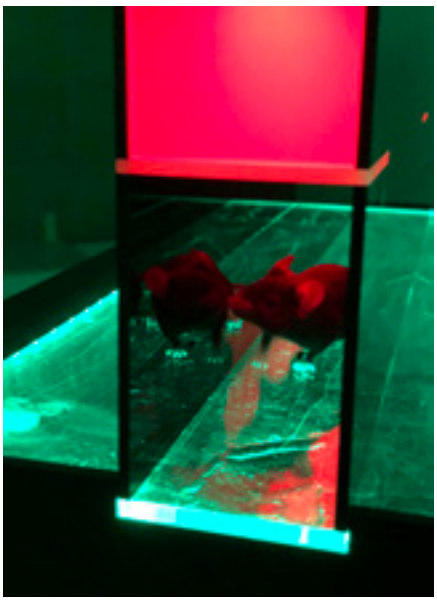


Fig. 2: Mouse analysed on a catwalk for evaluating motor symptoms of Huntington's Disease. Illustration by Anders Nykjær

Prion disease is a fatal neurodegenerative and self-propagating disorder caused by an abnormally folded isoform of the prion protein. The disease is characterized by progressive accumulation of anomalous prion protein in the brain through constitutive conformational conversion of the cellular and non-pathogenic form into the pathogenic variant. In a collaborative study, we demonstrated a critical role of sortilin in disease progression. We found that sortilin targets abnormally folded prion protein for lysosomal degradation, which is why mice devoid in sortilin accumulates the pathogenic prion protein variant leading to accelerated disease progression.

SorCS3 is genetically linked to psychiatric diseases including schizophrenia and major depression. In agreement, mice deficient in SorCS3 exhibit altered behaviour and perturbed synaptic functions that may be accounted for by enhanced mobility of postsynaptic AMPA receptors. SorC1, -2, and -3 can form homo- and heterodimers and ongoing studies aim to understand how dimerization may control their multitude of functions including synaptic transmission.

In 2017, Dr Nykjær together with other DANDRITE members established The Danish National Research Foundation Center PROMEMO (Proteins in Memory) (promemo.au.dk).

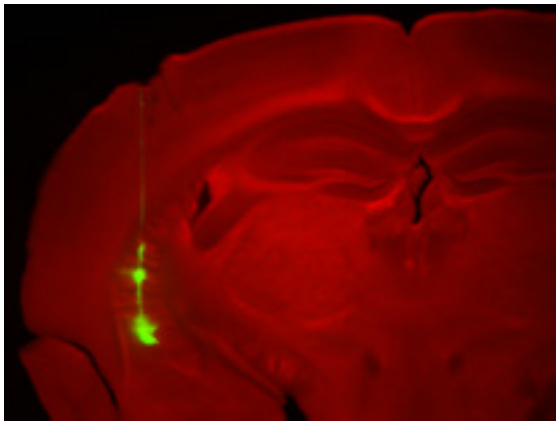


Fig. 1: Stereotactic injection of fluorophore-labelled beads (green) into the amygdala. Illustration by Mikhail Paveliev

Nykjaer group members on field trip to Mols Bjerge. Photo by nature guide Marianne Graversen at The Mols Laboratory

Selected publications 2017

Uchiyama K, Tomita M, Yano M, Chida J, Hara H, Das NR, **Nykjaer A**, Sakaguchi S (2017) Prions amplify through degradation of the VPS10P sorting receptor sortilin. *PLoS Pathogens*, Vol. 13, No. 6

Bundgaard CG, Andersen K, Riis S, **Nykjaer A**, Bølcho U, Jensen MS, Holm MM (2017) The sorting receptor SorCS3 is a stronger regulator of glutamate receptor functions compared to GABAergic mechanisms. *The Hippocampus*, p. 235-248

Januliene D, Manavalan A, Ovesen PL, Pedersen KM, Thirup S, **Nykjaer A**, Moeller A (2017) Hidden Twins : SorCS Neuroreceptors Form Stable Dimers. *Journal of Molecular Biology* Vol. 29, No. 19, p. 2907-2917

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Denham Group

Stem Cells

We study how the human nervous system develops and the processes involved in neural degeneration. To do this, we use human pluripotent stem cells, which have the unique ability to give rise to all cell types of the body and as such allows us the ability to investigate developmental or disease processes in a human context. Specifically, we are interested in the development of mesencephalic dopaminergic (mesDA) neurons, the cells that are particularly vulnerable in Parkinson's disease (PD) patients, and understanding the role of non-coding RNA in their specification. Furthermore, we are using patient-specific induced pluripotent stem cells (iPSCs) to generate disease susceptible neurons to model, in vitro, molecular events involved in Parkinson's disease. By combining in vitro activity analysis with next-generation sequencing, we aim to detect gene-expression changes between the various patient cell lines that are involved in early disease events. The overall goals are to identify new disease mechanism that may be used as alternative drug targets for treating Parkinson's disease and other neurodegenerative disorders.

MOLECULAR MECHANISMS CONTROLLING PARKINSON'S DISEASE SUSCEPTIBILITY

Within our lab, we have generated a bank of Parkinson's diseased iPSC lines reprogrammed from a diverse range of familial Parkinsonian patient skin samples (Fig. 1). With these cell lines, we are investigating genetic mechanisms that contribute to disease susceptibility. In particular, we are interested in the glucocerebrosidase (GBA) heterozygous mutation, a mutation that results in a compromised lysosomal/autophagic pathway. GBAhet mutations are the most significant risk factor for developing PD and is almost identical to idiopathic PD. However, not all GBAhet carriers acquire PD, and the reason for the variability in penetrance is unknown, as such we are investigating what mechanisms in addition to GBA regulate disease severity.

To date, we have successfully generated GBAhet derived-neurons from iPSCs and developed a culture system whereby we can detect deficits in synaptic activity compared to healthy control neurons (Fig. 2). Furthermore, we have seen changes in stress responses, and by performing RNA sequencing, we have identified a set of dysregulated genes in GBAhet derived-neurons. We are currently further investigating disease mechanisms that link these genes to PD by using CRISPR and multi-electrode array methods.

NON-CODING RNA AND THE REGULATION OF PROGENITOR CELL FATES

We are investigating the processes involved in stem cell fate, specifically factors involved in neural development. Numerous transcription factors that are known to be involved in dictating cell fate also play a critical role in maintaining cell identity and survival, however the regulatory mechanism that controls transcription factor expression is poorly understood. In particular, the role of circular RNA (circRNA) in regulating mesDA cell identity has to date not been described. We are therefore interested in understanding the contribution of non-coding RNA in mesDA neuron development. Recently we mapped the transcriptome from pluripotency to a mesDA neuronal identity and identified over two hundred circRNAs that are highly variable in expression across the developmental stages. Additionally, we have identified a miRNA that influences floor plate specification. We are now further investigating specifically what factors the miRNA is involved in regulating and what role these circRNA play during development. Overall determining how non-coding RNAs control cell identity is crucial not only for understanding developmental processes but also for understanding cellular homeostasis.

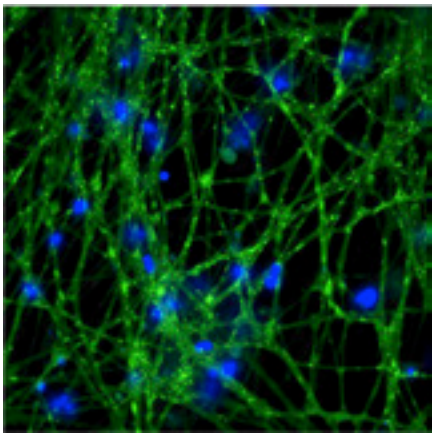

Fig. 2: Neurons derived from patient iPSCs
Illustration by Muwan Chen

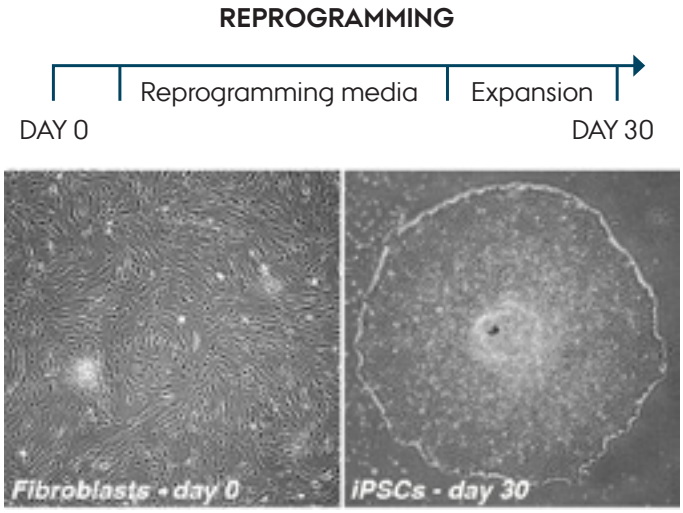

Fig. 1: 30 day sendai virus reprogramming protocol used to convert human patient fibroblast cells into induced pluripotent stem cells in defined media. Left image shows human fibroblast cells prior to reprogramming and right image shows a successfully reprogrammed cell colony.
Illustration by Susanne Buchholdt.

Denham group members in the campus park at Aarhus University.
Photo by Susanne Schousboe Sjøgaard, DANDRITE

Key publication

Chen M, Laursen SH, Habekost M, Knudsen CH, **Buchholdt SH**, Huang J, Xu F, Liu X, Bolund L, Luo Y, **Nissen P, Febbraro F, Denham M**. Central and Peripheral Nervous System Progenitors Derived from Human Pluripotent Stem Cells Reveal a Unique Temporal and Cell-Type Specific Expression of PMCAs. Front Cell Dev Biol., Vol. 6, no. 5

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Kvitsiani Group

Neuronal Circuits and Molecular Basis of Effort Based Decision-making

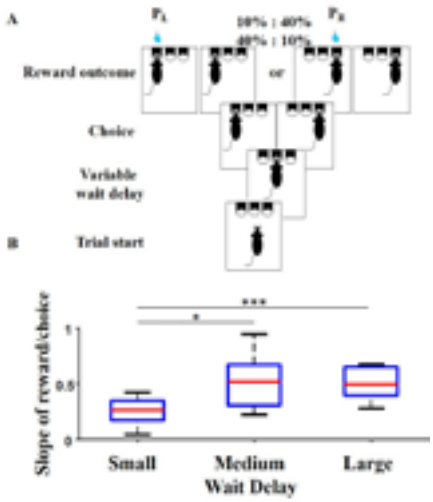


Fig. 1: A) Probabilistic reward foraging task. Mice start the trial by poking their noses into the center port, waiting different amounts of time, and making choices to the left or right side. Rewards come in a probabilistic way in those ports, and these probabilities change in blocks.
B) X-axis shows different delays and Y-axis – slope of Reward/Choice ratio from multiple sessions. The ratio is calculated by linear fit of a line to sum of Rewards divided by sum of Choices for a sliding window of 20 trials in a given session.
Illustration by Duda Kvitsiani

We investigate genetic and neural circuit mechanisms underlying decision-making in flies and rodents. The aim of our research is to build predictive and quantitative models of behavior that will help us uncover mechanistic insights into choices that animals make. The methods we use include molecular genetics, psychophysics, behavioral electrophysiology, and optogenetics. We ask a simple basic question: How do animals and humans choose better options? Our aim is to understand the biology of decisions on multiple levels: from molecules to neural circuits. In fruit flies we are undertaking genetic screens to discover single molecules controlling foraging decisions, using extracellular electrophysiology and cell-type specific recordings in rodents we investigate circuit level computations in the mouse brain that represent value. Overall, our long-term goal is to use ecology inspired quantitative behavioral models to guide and sharpen scientific questions.

MAJOR ACHIEVEMENTS

In the past year, we have studied probabilistic reward foraging decisions in fruit fly using closed loop optogenetic reward delivery system. This system allows us to study on a trial-by-trial basis how flies integrate option values into their choices. Using dense behavioral data from individual flies, we built predictive and generative computational models that extract hidden decision variables from observed behavior. The extracted variables, like value and learning rate, are used to see how flies behave when environmental statistics change. Our preliminary observation tells us that flies are sensitive to variance in the reward outcome and adjust their choices to maximize the reward income. We are in the process of verifying this result and gearing to test with various mutant lines if there are single genes or polymorphisms that can account for sensitivity to variance in foraging insects.

In mice, we have set up a similar reward foraging task (Fig. 1A) to examine how effort is integrated into choices. In this task animals initiate trial by poking into the center port, waiting a variable amount of time (effort manipulation) and choosing left or right side to collect probabilistic rewards. Reward probabilities change in blocks and the task of the animal is to adjust its choices to maximize the reward outcome. Our behavioral analysis showed that animals can adjust their choices according to reward probabilities. We can show that animals integrate delay effort into their choices by making more consecutive choices for previously rewarded side in long delay periods (Fig. 1B). We also carried out single unit recordings in the same animals to show that activity of the neural population in prefrontal cortical areas encode rewards and choices up to 5 trials back in history (Fig. 2). This data demonstrate that neurons in prefrontal cortex represent past using population code rather than single neurons.

FUTURE PLANS, PROJECTS, AND GOALS

In the future, we aim to dissect the contribution of single neurons to decision making and learning in behaving animals. For this, we are developing single cell stimulation tool to manipulate activity of individual neurons at will. My lab in collaboration with Henrik Stapelfeldt's lab at Aarhus University is developing a patterned light stimulation tool via multimode optical fibers to activate individual neurons with natural patterns of ensemble activity in behaving animals. This collaboration also includes groups at Hungarian Academy of Science (Zoltan Somogyvari and Balazs Hangya's labs) in Budapest. Our set up (Fig. 3) is able to deliver phase modulated wavefront of light in living brain tissue together with the high-density electrophysiological recording system.

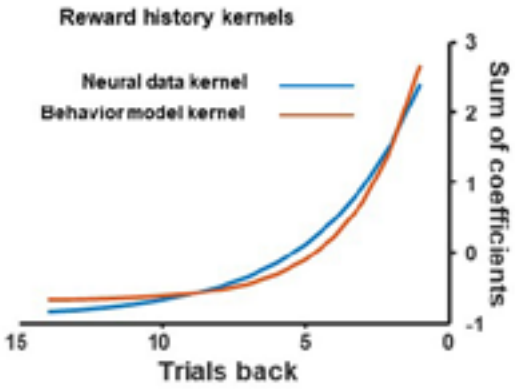
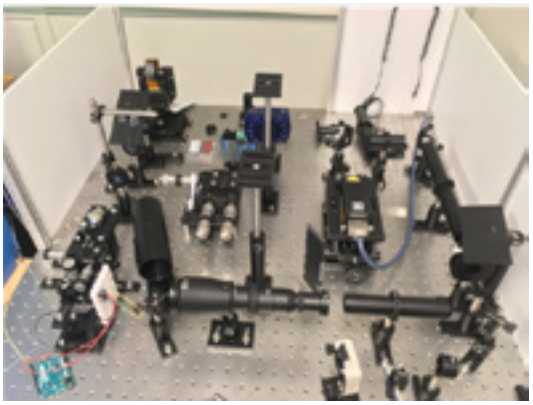


Fig. 2: Average of all predictors from neural population analysis using regularized regression (in blue) and behavioral analysis (in red) for left choices, showing similar decaying kernels. Illustration by Duda Kvitsiani



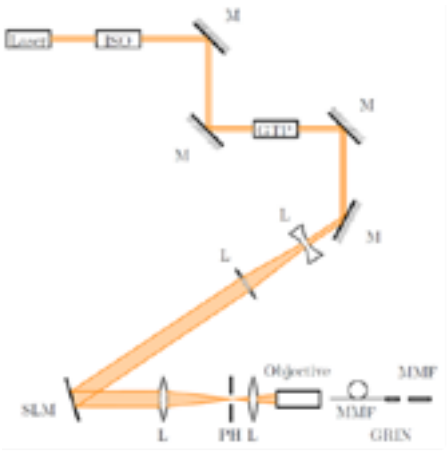


Fig. 3: Generating focus using the SLM- spatial light modulator and CCD camera. Top panel: Schematics of experimental setup consisting of laser, ISO-optical isolator, GTP-light polarizer, M-mirror, L lenses for beam expansion, SLM, PH-pinhole, Objective- focusing light onto the MMF- multimode fiber.
Bottom panel: View of the optical set up. Photo and illustration by Duda Kvitsiani

Kvitsiani group members in park at Sandbjerg Manor. Photo by Susanne Schousboe Sjøgaard, DANDRITE

Key publication

Kvitsiani D, Ranade S, Hangya B, Taniguchi H, Huan Kepecs A (2012) Distinct behavioural correlates and network interactions of two interneuron classes in mouse prefrontal cortex. *Nature* June 20; 498(7454):363-6.

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Group Leader **Duda Kvitsiani**

Nabavi Group

Memory Formation and Consolidation at the Synaptic and Circuit Levels

Memories are formed by changes in the strength of connections between neurons, a process known as synaptic plasticity. Our lab studies the neurobiological processes that contribute to differences in the strength of our memories. Following is a brief description of our current projects.

SYNAPTIC TAGGING AND CAPTURE
Synaptic tagging and capture is a dominant hypothesis that describes how a strong memory can stabilize a weak memory if they coincide within a short time window. Combining optogenetics and classical conditioning, we are aiming to test this by implanting a weak memory in the amygdala and stabilize it with an long-term potentiation (LTP) protocol. We have been able to use channelrhodopsin to design a conditioning protocol that produces a weak memory, an essential requirement for the feasibility of the project. We are attempting to manipulate two overlapping populations of synaptic terminals, namely thalamic and cortical auditory projections to the amygdala.

PLASTICITY-RELATED PROTEINS
A hallmark of persistent memories is that they depend on protein synthesis. We aim to find the proteins that are required for making long-term memories. In order to do this, we are using a novel biochemical technique that can specifically label newly synthesized proteins. We used this technique successfully in slices, being able to detect newly synthesized synaptic proteins. However, the use of our biochemical technique in vivo proved to be a challenge, as we failed to detect the newly synthesized proteins. To improve our labelling method, we are collaborating with Dr. Muttenthaler (Vienna) and Dr. Yates (California).

SIGNALS FOR UNCONDITIONED STIMULI
To understand how emotional stimuli contribute to memory strength, we aim to identify the pathways that transmit such stimuli. To do this, we use associative fear circuit in the amygdala wherein by pairing a neutral stimulus (e.g. a tone) with an aversive unconditioned stimulus (e.g. a foot-shock) a long-lasting tone-driven fear memory is formed. To identify the inputs for aversive stimulus we use an activity dependent virus based retrograde labelling method. This approach directs us to the amygdala-projecting circuits that have been activated during an emotional event (Fig. 1). Complementary to this, we use multi-fibre photometry to monitor the activity of the multiple brain regions including neuromodulatory circuits during aversive and rewarding memory formation.

STRUCTURAL STUDIES
In collaboration with Drs. Kjærgaard and Nissen, we are investigating the phosphorylation pattern of the C-tails of dopamine receptor D1 and Beta-2 adrenergic receptor and their relevance to the G protein-coupled receptor signalling pathways mediated by adapter protein arrestin. We complement experimental works with molecular modelling.

ANXIETY IN PARKINSON'S DISEASE (PD)
We are using a mouse model for PD that shows anxiety. Intranasal application of a neuropeptide had anxiolytic effects in our mouse model. Our next step is to identify the circuits that underlie the observed anxiety in PD models. For the development of this project, we rely on a collaboration with Dr. Jensen.

SYNAPTIC DEPRESSION IN MEMORY DECAY
The mechanisms underlying memory decay have been largely neglected, in part due to the technical difficulties as the process occurs in a much slower time scale. We test the hypothesis of whether synaptic depression is a substrate for weakening memories. This is based on our previous works, where we demonstrated: A) induction of long-term depression (LTD) weakens a memory; B) beta-amyloid, a causative agent in Alzheimer's disease, induces synaptic depression through a mechanism similar to LTD; C) pre-synaptic release of glutamate can induce an NMDAr-dependent LTD if the calcium influx through the receptor is blocked. We test our hypothesis using optogenetic viral approaches combined with pharmacological block of calcium influx through NMDARs.

INNATE FEAR
In addition to memory-based behaviors, we are interested in innate behaviors with the emphasis on innate fear. What intrigues us is that learned fear and innate fear engage overlapping circuits in the amygdala, the brain's fear center. By using a model of visual innate fear in mice, we found an increase in the cellular activation within the amygdala (Fig. 1 & 2). These results suggest that the amygdala is involved in a circuit processing visual stimuli-inducing innate fear. We are currently investigating different possibilities to tease apart the brain circuits for the visual innate fear, with an emphasis on identifying the properties of neurons activated by innate fear in the amygdala and their downstream target circuits.

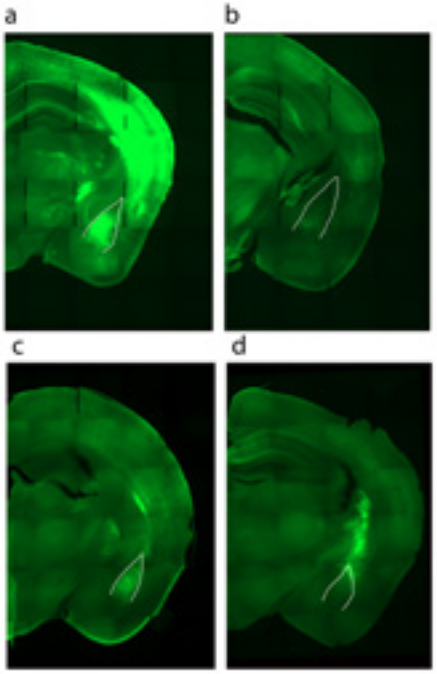

Fig. 1: Activity dependent labelling of the amygdala neurons in Arc-cre transgenic mice exposed to a foot-shock (a) or an innate fear (c). Note, few fluorescently labeled neurons in the control groups (b & d), which received the same treatment as the test groups but have not been exposed to the aversive stimuli. The white line marks the Amygdala region. Illustration by Nathalie Krauth and Noemie Mermet-Joret

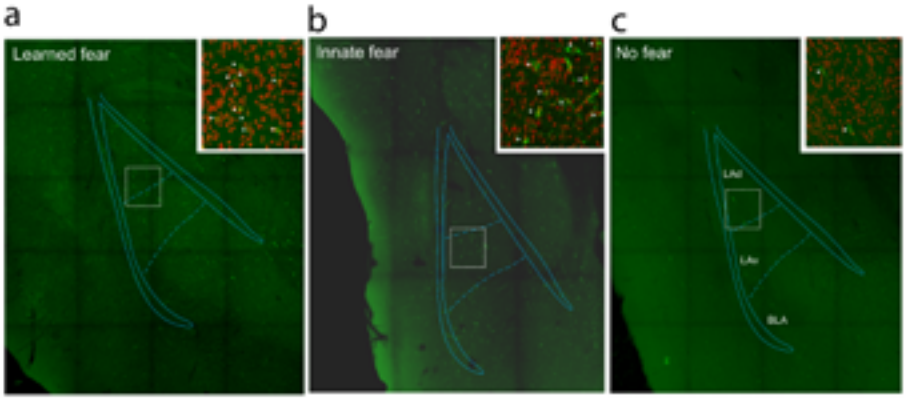

Fig. 2: Activity dependent labelling of the amygdala neurons using c-fos staining in mice exposed to a foot-shock (a) or an innate feat (b). Note, few immono-flouorescently stained neurons in the control groups (c), which received the same treatment as the test group but have not been exposed to the aversive stimuli. The top corner boxes are the magnification of the small dash-lne boxes. Different regions of the amygdala are labeled accordingly. LAd: Dorsal part of the lateral amygdala. LAv: Ventral part of the lateral amygdala. BLA: Basolateral amygdala. Illustration by Noemie Mermet-Joret

Nabavi group members in the campus park at Aarhus University. Photo by Susanne Schousboe Sjøgaard, DANDRITE

Key publication

Nabavi S, Fox R, Proulx CD, Lin JY, Tsien RY, and Malinow R (2014) Engineering a memory with LTD and LTP. *Nature* 511, 348-352

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Philipsborn Group

Behavioral Genetics and Circuit Neuroscience

We are interested in how the nervous system generates and controls behavior- at the level of genes and molecules, cells and neuronal circuits. Our model system is *Drosophila melanogaster*, which has a relatively small and stereotyped nervous system, but displays complex and fascinating behaviors.

By studying the neuronal circuits underlying Drosophila behavior, we aim at understanding general principles of motor control. We focus on circuits for motor pattern generation and the architecture of neuro-muscular networks, as well as the mechanisms of higher order coordination of complex motor behaviors and behavioral sequences.

As a model behavior, we use Drosophila reproductive behavior and male courtship. Identified neurons are dedicated to generation of male courtship song, an elaborately patterned acoustic signal. We investigate how the sex-specific song pattern is generated, and how the song circuit is modulated during other motor behaviors. We use audio recording as a highly sensitive, high throughput measurement for motor behavior at millisecond timescale as well as genetic tools for neuronal activity imaging and optogenetic activation and silencing in intact animals.

Simultaneously, we scrutinize the genetic and molecular basis of circuit dynamics. We are interested in genes pivotal for computational performance and configuration of ensembles of interconnected neurons, namely, genes encoding ion channels, membrane transporters and molecules implicated in neuromodulation.

MECHANISMS OF MULTIFUNCTIONAL MOTOR CONTROL

Multifunctional motor systems produce distinct output patterns dependent on behavioral context, posing a challenge to underlying neuronal control. Flies use their wings for flight and the production of a patterned acoustic signal, the male courtship song, employing in both cases a small set of wing muscles and corresponding motor neurons. We investigated the neuronal control mechanisms of this multifunctional motor system by live imaging of muscle ensemble activity patterns during song and flight and establish the role of a comprehensive set of wing muscle motor neurons by functional manipulations. Song and flight rely on distinct configurations of neuromuscular activity, with most, but not all flight muscles and their corresponding motor neurons contributing to song and shaping its acoustic parameters. The two behaviors are exclusive, and the neuronal command for flight overrides the command for song. The neuromodulator octopamine is a candidate for selectively stabilizing flight, but not song motor patterns.

MECHANISMS OF MOTOR PATTERN GENERATION AND GABAergic SIGNALING

Almost all behavior is shaped by both excitatory and inhibitory neuronal control. We find that GABAergic inhibitory signaling impacts on song motor behavior on multiple levels, tuning fine motor structure, intensity and overall coordination of the behavior. With cell specific RNAi mediated knock- down of genes involved in GABAergic signaling, we are elucidating the mechanisms of inhibitory control and its role in pattern generation. Our efforts are directed at integrating data from genetic and neuronal screens and at building a model of how the song pattern is generated at the level of interneurons. We are establishing connectivity patterns of the various circuit components by GRASP (Gfp reconstitution across synaptic partners) and neuronal epistasis experiments.

Publications 2017

Heinze S and **von Philipsborn A** (2017) Editorial: Recent advances in insect neuroethology: from sensory processing to circuits controlling internal states. *Current Opinion in Insect Science*, 24

Ellendersen BE and **von Philipsborn A** (2017) Neuronal modulation of D. melanogaster sexual behaviour. *Current Opinion in Insect Science*, 24:21-28

Fielderling F, Weschenfelder M, Fritz M, **von Philipsborn A**, Bastmeyer M, Weth F (2017) Ephrin-A/EphA specific co-adaptation as a novel mechanism in topographic axon guidance. *eLIFE*, 6:e25533

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Philipsborn group members in the old library. Photo by Maria Thykær Jensen, DANDRITE

BEHAVIORAL HIERARCHY AND COORDINATION
– STATE DEPENDENT ACTION SELECTION
How do different behaviors interact and influence each other on a circuit level? During courtship, some behavioral elements are combined and others exclude each other or occur in a preferred sequence. We discovered that dependent on the state of the animal and the behavior it is engaged in, activation of neuronal classes has drastically different motor outcomes. By using optogenetic circuit interrogation, we explore the neuronal and genetic basis of state dependent action selection, aiming at identifying circuits and neuromodulators for behavioral hierarchy and coordination. Our findings highlight inhibition as an important mechanism for structuring behavioral sequences, ensuring appropriate, context dependent response to sensory stimuli.

SEX SPECIFIC MOTOR CIRCUITS FOR COMMUNICATION
We discovered that during reproduction, not only male, but also female flies use rhythmic acoustic signals for communication. We find indication that female sound production is correlated with male ejaculate quantity and/or quality, i.e. reproductive potential. Females lack most of the male's song neurons and show differential gene expression, which might explain striking differences in the motor output shaped to produce sex-specific sound patterns.

MOLECULAR AND CELLULAR MODELS FOR NEUROLOGICAL DISEASE IN *DROSOPHILA*
Fundamental mechanisms of nervous system function on the molecular, cellular and circuit level are conserved and shared across vertebrates and invertebrates. *Drosophila* is a convenient and genetically accessible in vivo model for analyzing the effect of pathological mutations on neuronal physiology. For example, we are currently collaborating with Hanne Poulsen at DANDRITE to study disease causing mutations of ATP1A3 in a *Drosophila* model system and with Poul Henning Jensen to explore calcium dynamics during alpha-synuclein mediated neurodegeneration.

Fig. 1: *Drosophila* courtship song. A male fly sings to a female by extending and vibrating one wing. Song is recorded by small microphones: the oscillogram shows sine and pulse bouts. Photo and illustration by Anne von Philipsborn

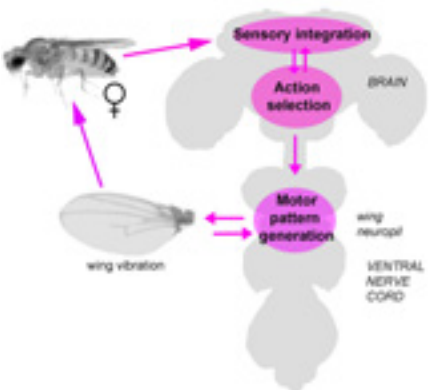


Fig. 2: Schematic of the neuronal circuits for courtship song. Illustration by Anne von Philipsborn

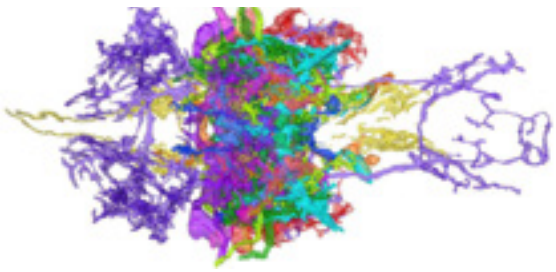
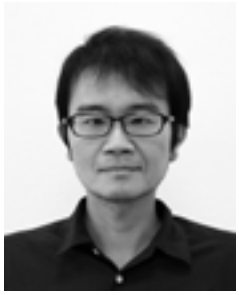


Fig. 3: Reconstruction of 3D arborization patterns of wing motor and premotor interneurons contributing to the patterning of wing movements. Illustration by Anne von Philipsborn

Yonehara Group

Structure, Function, and Development of Neural Circuits in Visual System



The Yonehara group investigates the structure, function and development of neural circuits using mouse visual system as a model. We are seeking to address the following questions:

1. How are sensory signals processed by neuronal circuits?
2. What is the function of individual cell types in computation and behavior?
3. What are the genetic and activity-dependent mechanisms of circuit development?

We address these questions mainly by focusing on visual circuits across retina, superior colliculus, thalamus and visual cortex of mice. The logic of our research plan is to first identify a computation performed by a given neuronal circuit comprising distinct cell types in the adult brain. Second, to investigate how the computation is performed by linking the activity and synaptic connectivity of individual cell types in the circuit to the computation that the circuit achieves. Third, to examine the role of individual cell types in transforming the sensory input into output behavior. Finally, to study the genetic mechanisms by which the elementary circuit motifs are assembled, and how its dysfunction can lead to disease.

COMPUTATION OF VISUAL MOTION
The direction of visual motion is first extracted by retinal direction-selective circuits and further processed in downstream areas such as thalamus or visual cortex. We are identifying novel circuit motifs that could explain how direction selectivity and velocity preference are created in different types of retinal direction-selective cells with 2-photon calcium (Fig. 1) or glutamate imaging (Fig. 2). Furthermore, we are exploring a causal link between retinal and cortical motion computation by in vivo 2-photon calcium imaging (Fig. 3) in mice in which retinal direction selectivity is disrupted. Through these experiments, we aim to understand fundamental principles underlying sensory processing.

SENSORIMOTOR TRANSFORMATION
The superior colliculus is one of the main recipients of retinal output and mediates visually-guided behaviors based on visual saliency. However, it remains unknown how visual signals from individual retinal ganglion cell types are processed by collicular neurons to achieve specific computations relevant to behaviors. Recently we have identified several transgenic mouse lines in which specific collicular cell types are labeled. Using these mouse lines, we are characterizing the response properties, neuronal connectivity of individual types of collicular neurons, and dissecting the role of these neuron types in visually-guided behaviors.

DEVELOPMENT OF SPATIALLY ASYMMETRIC NEURONAL CONNECTIVITY
We use retinal direction-selective circuits as a model to study how spatially asymmetric neuronal connectivity is assembled by genetic mechanisms. Very recently, we published results showing that congenital nystagmus gene FRMD7 is a key molecule for establishing spatially asymmetric inhibitory input from an inhibitory amacrine cell type to the direction-selective cells in the retina (Yonehara et al., Neuron, 2016). Our aim is to understand key mechanisms underlying the establishment of neuronal polarity and synaptic specificity by further investigating the role of FRMD7 signaling cascades in the inhibitory amacrine cell type.

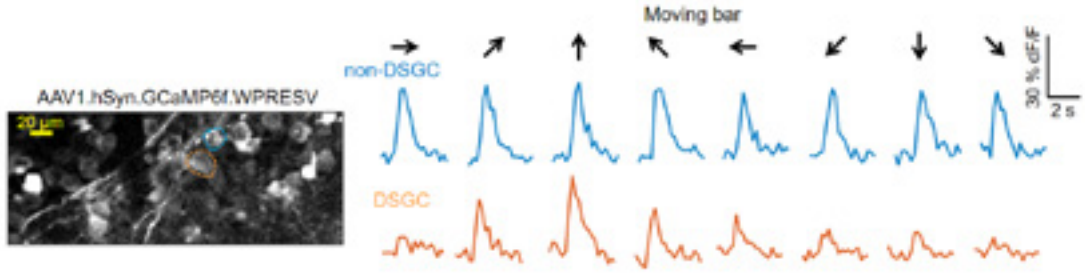


Fig. 1: Exo vivo 2-photon calcium imaging of retinal direction-selective ganglion cells (DSGCs) and non-DSGCs labeled with GCaMP6 in response to moving bar stimulus. Illustration by Akihiro Matsumoto

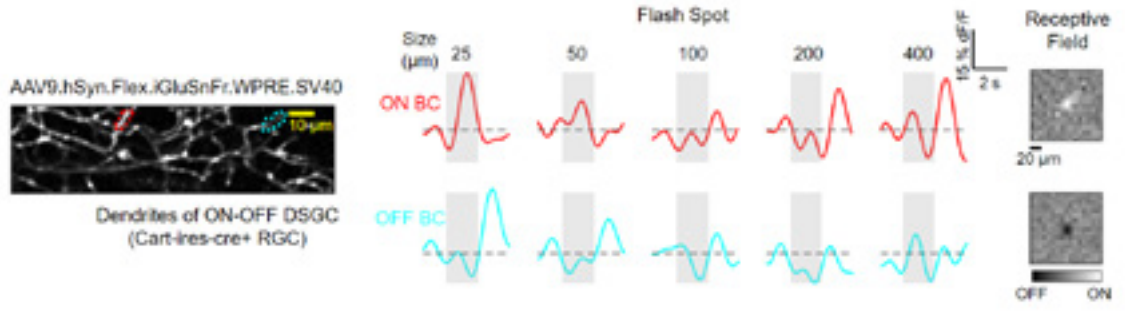


Fig. 2: Exo vivo 2-photon glutamate imaging of the dendrites of retinal DSGCs labeled with iGluSnFr in response to flash spot. Receptive fields of individual bipolar cell (BC) input are mapped by reverse correlation method. Illustration by Akihiro Matsumoto

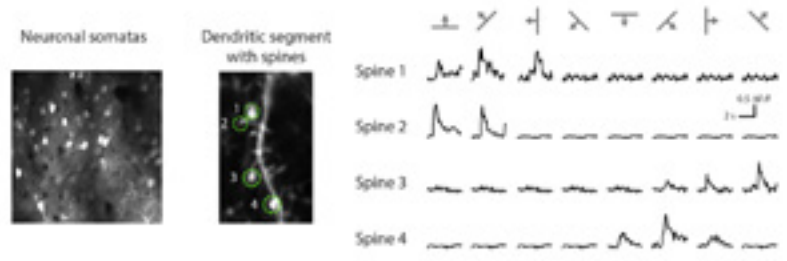


Fig. 3: In vivo 2-photon calcium imaging of neuronal somatas and dendritic spines labeled with calcium indicator GCaMP6 in an anaesthetized head-fixed mouse. Illustration by Rune Rasmussen

Selected publications 2017

Glangetas C, Massi L, Fois GR, Jalabert M, Girard D, Diana M, **Yonehara K**, Roska B, Xu C, Lüthi A, Caille S, Georges F (2017) NMDA-receptor-dependent plasticity in the bed nucleus of the stria terminalis triggers long-term anxiolysis. *Nature Communications*, Vol. 8, 14456

Rompani SB, Müllner FE, Wanner A, Zhang C, Roth CN, **Yonehara K**, Roska B (2017) Different Modes of Visual Integration in the Lateral Geniculate Nucleus Revealed by Single-Cell-Initiated Transsynaptic Tracing. *Neuron*, Vol. 93, No. 4

Rasmussen R, **Yonehara K** (2017) Circuit Mechanisms Governing Local vs. Global Motion Processing in Mouse Visual Cortex. *Frontiers in Neural Circuits*, Vol. 11, No. 109

Personnel List Yonehara Group

Assistant Professor **Szilard Sajgo**
Postdoc **Akihiro Matsumoto**
Postdoc **Ana Oliveira**
Postdoc **Yutaka Shimizu**
PhD Student **Monica Dahlstrup Sietam**
PhD Student **Ole Søndergaard Schwartz**
PhD Student **Rune Rasmussen**
External Consultant **Zoltan Raics**
Laboratory Technician **Bjarke Thomsen**
Laboratory Assistant **Misugi Yonehara**
Group Leader **Keisuke Yonehara**

Kjærgaard Team

Synaptic Plasticity and Intra-cellular Signaling Complexes in Memory Formation

Team Leader
Magnus Kjærgaard

We are interested in understanding how proteins in the post-synaptic density modulate the dynamics of synaptic proteins and signalling pathways. These proteins are crucial for memory formation but are difficult to study due to their flexibility. We use a range of biophysical techniques including NMR spectroscopy and single molecule FRET spectroscopy to answer mechanistic questions about brain proteins.

A key mechanism of memory formation is the modulation of ionotropic glutamate receptors by their intra-cellular ligand occupancy and phosphorylation state. The intra-cellular domains of these receptors coordinate many binding partners and affect the conductivity of the channels, but are difficult to study by traditional structural techniques as they are flexible and devoid of fixed structures, so-called intrinsically disordered proteins. We use spectroscopic and biophysical techniques to study the interactions of the intra-cellular domains of the NMDA receptor with post-synaptic proteins. We particularly focus on understanding the effects of phosphorylation by two kinases: CaMKII that provide a mechanism for long-term memory by acting on a switch and PKA that is activated by neuromodulators in emotionally significant events.

Receptor activation leads to different downstream events depending on the cellular context, e.g. which other signaling pathways are active. Large flexible molecular assemblies called signaling complexes organized by scaffolding proteins coordinate signaling pathways. These complexes connect receptors to enzymes and substrates. The signaling complexes act as molecular matchmakers by determining which molecules encounter each other. We would like to understand quantitatively how such signaling complexes work at the molecular level. To this end, we have developed a quantitative assay for measuring effective concentrations in signaling complexes, which is likely to be crucial to understand kinase activity in signaling complexes. Furthermore, we develop model systems for understanding the role of synaptic scaffolding proteins that coordinate the supra-molecular structure of signaling pathways.

Key Publications

Dyla M, Terry D, **Kjærgaard M**, Sørensen T, Andersen JL, Andersen JP, Knudsen CR, Altman R, **Nissen P**, Blanchard S (2017) Dynamics of P-type ATPase transport cycle revealed by single-molecule FRET. *Nature*, Vol. 551, No. 7680, p. 346-351

Shammas SL, Kumar S, Garcia GA, **Kjaergaard M**, Horrocks MH, Shivji N, Mandelkow E, Knowles TPJ, Mandelkow EM, Klenerman D (2015) A mechanistic model of tau amyloid aggregation based on direct observation of oligomers *Nature Communications*. 6:7025

Lešmantavičius V, Dogan J, Jemth P, Teilum K, **Kjaergaard M** (2014) Helical Propensity in an Intrinsically Disordered Protein Accelerates Ligand Binding. *Angew. Chem. Int. Ed. Engl Vol. 53, no. 6, p. 1548-51*

Personel List Kjærgaard Team

Postdoc **Agnieszka Jendroszek**
Postdoc **Charlotte Skovgaard Sørensen**
Postdoc **Mateusz Dyla**
Postdoc **Xavier Warnet**
PhD Student **Sara Basse**
Team Leader **Magnus Kjærgaard**

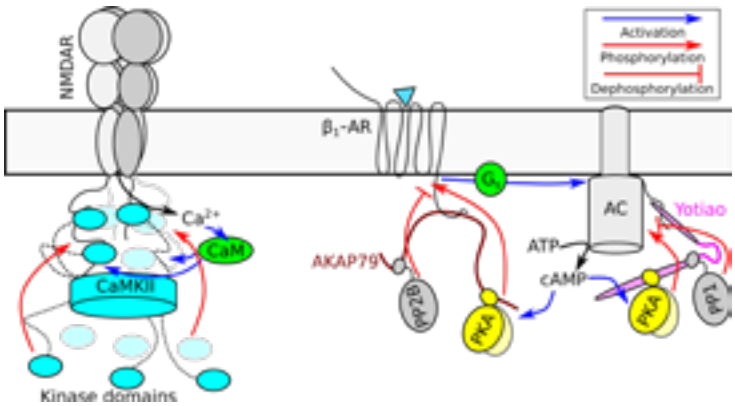
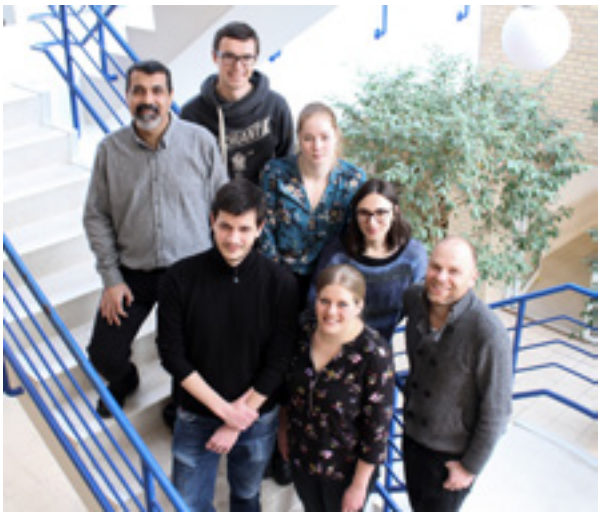
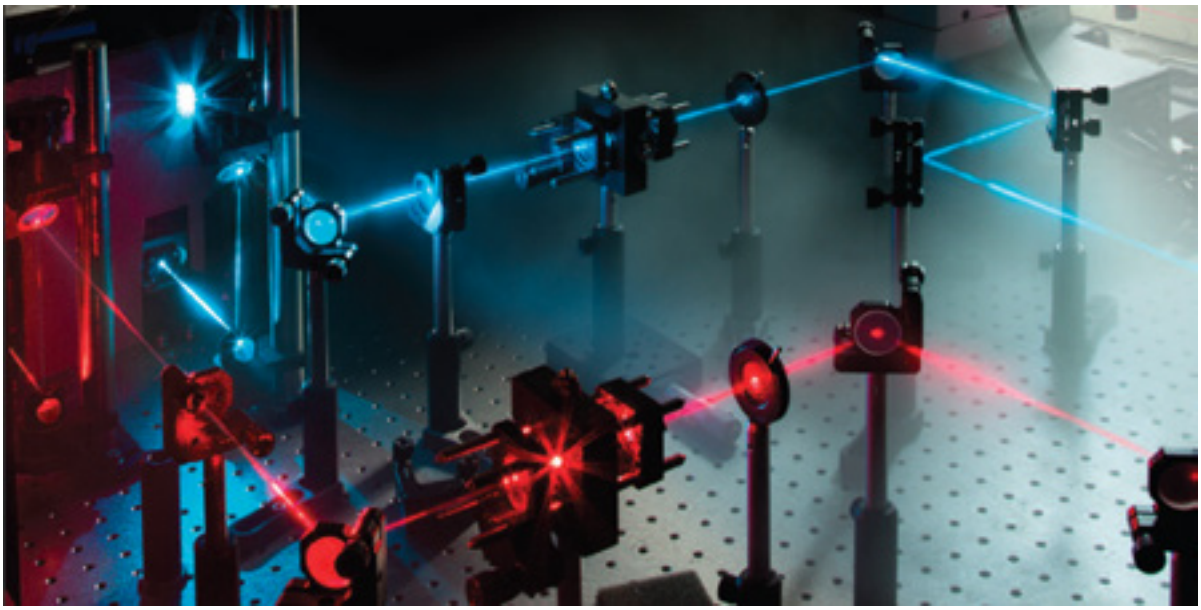


Fig. 1: Signalling complexes coordinate subsequent molecules inside a signalling pathway. Illustration by Magnus Kjærgaard.



Kjærgaard team members on stairs in lab building. Photo by Karen Bech-Pedersen, DANDRITE

Fig. 2: Single molecule FRET microscope allows structural interrogation of individual molecules. Courtesy of Mathew H. Horrocks, Cambridge University.



Poulsen Team

Electrophysiology of Electrogenic Transporters and Ion Channels

Team Leader
Hanne Poulsen

For us to sense temperature - or light or sound or smell - the signal from the outside world has to be translated into an electrical signal that our neurons can interpret and react to. In Poulsen Team, we study membrane proteins important for neuronal signaling and transport in order to understand their basic mechanisms and the physiological consequences it has if they do not function optimally.

We use electrophysiological methods to study membrane proteins, including voltage-clamp fluorometry (VCF), where protein movements are correlated with protein activity with millisecond resolution. For this, we make membrane proteins containing the fluorescent unnatural amino acid Anap. We incorporate Anap in sodium/potassium ATPase, TRP channel and the Gaba transporter GAT-1.

Using our new VCF set-up, we find that we can increase the time resolution when investigating the sodium/potassium ATPase and are able to distinguish the release of the individual sodium ions. We therefore expect to obtain VCF results, which will elucidate the detailed mechanism of how sodium ions are released from the pump.

TRP channels are channels that are responsible for sensing of temperature, but also react to chemical compounds such as menthol or capsaicin. We are interested in how a channel can responds to such different stimuli. Electrophysiology and VCF are obvious methods to investigate response variation as we can measure the effect of the stimuli and further are able to determine which parts of the channel moves when situated to a particular stimuli.

In 2018 a new PhD project is started in collaboration with DANDRITE Group leader Keisuke Yonehara. In this project, a specific disease causing mutation in the sodium/potassium ATPase 3 gene (called the CAPOS mutation) is investigated. This mutation is known to cause deafness and blindness. The effect of the mutation on the sodium/potassium ATPase function will be studied using electrophysiology and the physiological effects will be studied in a mouse model.

In 2017, the group has been part of starting up the Center for Proteins in Memory, PROMEMO, which is funded by the Danish National Research Foundation. The contribution to the center will be electrophysiological characterization of transporters and channels involved in memory, such as the NMDA receptors.

Fig. 1: Two-electrode voltage clamping. The two glass electodes are in a *Xenopus laevis* oocyte, and the external buffer is controlled at the inlet to the left. Photo by Hanne Poulsen

Poulsen team members in the laboratory. Photo by Hanne Poulsen

Publications 2017

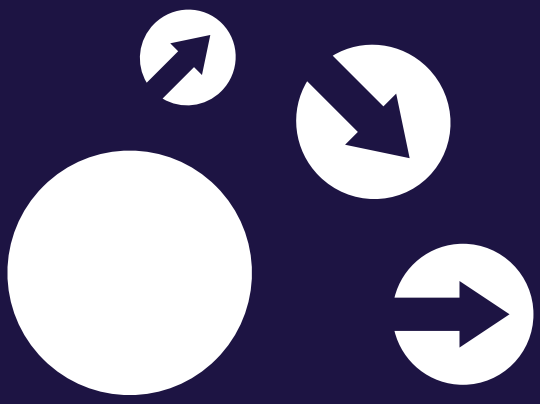
Poulsen H (2017) Ins and Outs of the Na, K-ATPase. *Biophysical Journal,* Vol. 112, No. 3, Supplement 1.

Clausen MV, Hilbers F, **Poulsen H** (2017) The structure and function of the Na,K-ATPase isoforms in health and disease. *Frontiers in Physiology,* Vol. 8, No. JUN, 371.

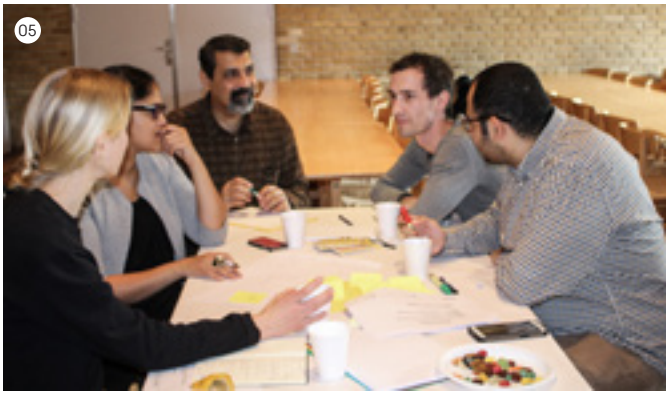
Personnel List Poulsen Team

Postdoc **Helle Bakke Krog**
PhD Student **Mette Ozol**
PhD Student **Saida Said**
Team Leader **Hanne Poulsen**

03
Events, Visitors, Guests & Seminars



EVENTS, VISITORS, GUESTS & SEMINARS



01 **DECEMBER**
EVENT: **AIAS Conference: *Fear: Brain, Behaviour, Society***, at Aarhus University. Organizer: **Magnus Kjærgaard**

02 **NOVEMBER**
SEMINAR: **Joint KJELDGAARD & DANDRITE Lecture**, Professor **Jozsef Csicsvari,** Institute of Science and Technology, Vienna, Austri, T*he role of the hippocampus in spatial learning*

03 SEMINAR: **DANDRITE Lecture**, Professor **Jens Christian Schwamborn**, Developmental and Cellular Biology group, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, *Human brain organoids as in vitro model for Parkinson's disease.*

04 SEMINAR: **DANDRITE Topical Seminar,** Postdoctoral Researcher **Povilas Uzdavinys**, Tampere University of Technology, Finland, *Establishing the molecular mechanism of sodium/proton exchangers*

05 EVENT: **DANDRITE Workshop: *How to communicate your research through video*** by Nordic EMBL Communications Officer **Annabel Darby** and Communications Assistant **Maria Thykær Jensen**

06 EVENT: **DANDRITE Extended Internal meeting**, inaugural talks by DANDRITE's newly appointed affiliated researchers; Associate Professors **Jane Hvarregaard Christensen**, Associate Professors **Karin Lykke-Hartmann**, Associate Professors **Marina Romero-Ramos**, Associate Professors **Morten Schallburg Nielsen**

07 GUEST: PhD student **Alena Salasova**, Karolinska Instituttet, Sweden (9 months)

08 **OCTOBER**
SEMINAR: **Joint KJELDGAARD & DANDRITE Lecture**, Professor **Radu Aricescu**, MRC Laboratory of Molecular Biology, Cambridge University, United Kingdom. *Structural Insights into GABAA Receptor Gating Mechanisms*

09 SEMINAR: **DANDRITE / NeuroCampus Aarhus Lecture**, Director & Principal Investigator **Jinhyun Kim**, Center for Functional Connectomics, Korea Institute of Science and Technology (KIST), *mGRASP for mapping mammalia synaptic circuit at multiple scales*

10 EVENT: **Young DANDRITE Rainbow Club**: ***Consciousness***, with Professor **Morten Storm Overgaard**, Center of Functionally Integrative Neuroscience (CFIN), Aarhus University

11 SEMINAR: **Joint KJELDGAARD & DANDRITE Lecture**, Senior Lecturer **Marcus Stensmyr**, Functional zoology, Lund University, Sweden, *Drosophila olfactory neuroecology*

Group photo from the 8th Annual Network Meeting of the Nordic EMBL Partnership for Molecular Medicine.
Photo by Jouko Siro

12 **SEPTEMBER**
EVENT: **8th Annual Network Meeting of the Nordic EMBL Partnership for Molecular Medicine**, hosted by Institute for Molecular Medicine Finland, FIMM, Hotel Rantapuisto, Finland

13 GUEST: Erasmus Intern **Michaela Orlová**, Comenius University in Bratislava, Slovakia (4 months)

14 SEMINAR: **AU Summer School in crystallography: CryoTEM Tomography Lecture**, Associate professor **Elizabeth R. Wright**, EMORY University School of Medicine, Atlanta, USA, *Advances in Structural Virology via Cryo-Electron Tomography*

15 **AUGUST**
EVENT: **BrainStem Summer Symposium**, at Aarhus University. Co-organizer: **Mark Denham**

16 GUEST: Erasmus student **Iker Rivas González**, The University of the Basque Country, Spain (5 months)

17 GUEST: Trainee **Emilía Sif Ásgrímsdóttir** (4 month)

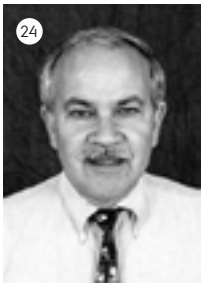
18 EVENT: **DANDRITE Master Class**, Associate professor **Elizabeth R. Wright**, EMORY University School of Medicine, Atlanta, *Principles and Practices of Phase Plate Cryo-Microscopy*

19 SEMINAR: **DANDRITE Topical Seminar**, Postdoc **Machteld N. Verzijden**, Dept. Bioscience, Aarhus University, *Stress and mate choice: how common environmental stressors affect the outcomes of mating encounters in Drosophila fruit flies*

20 **JULY**
SEMINAR: **DANDRITE Topical Seminar**, Postdoctoral Researcher **Emre Fikret Kapucu**, Tampere University of Technology, Finland, *How do we interpret the neuronal talking among populations? Information Extraction Methods from Microelectrode Array Measurements of Neuronal Networks*

21 EVENT: **Young DANDRITE Rainbow Club: Epigenetics,** discussion lead by PhD student **Sophie Seidenbecher** and PhD student **Juliane Martin**

22 GUEST: Student Intern **Line Cecilie Hansen** (1 month)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23 GUEST: PhD student **Thibaud Dieudonné**, The Institute for Integrative Biology of the Cell (I2BC), France (1 month)

24 GUEST: Visiting researcher Professor **William C. Merrick**, Biochemistry Department, Case Western Reserve University, USA (4 months)

JUNE

25 SEMINAR: **DANDRITE Topical Seminar,** Dr. **Andrew Lin**, University of Sheffield, United Kingdom, Sparse coding for odour-specific memories through balanced excitation and inhibition

26 SEMINAR: **DANDRITE Topical Seminar,** Dr. **Jacob K. Dreyer**, Center for Neuroscience, University of Copenhagen, *The swiss-army-knife dopamine model: A model for reinforcement learning, ADHD, and Parkinson's disease*

27 SEMINAR: **DANDRITE Topical Seminar**, Assistant Professor **Karl Farrow**, KU Leuven, Belgium, *Routing visual information through the superior colliculus*

28 SEMINAR: **Joint DANDRITE, iPSYCH & iSEQ Seminar,** Professor **Wayne Chen**, University of Calgary, Canada, *The Ryanodine Receptor Store-Sensing Gate: from Structure to Cardiac and Neurological Disorders*

29 SEMINAR: **DANDRITE Lecture**, Professor **Hilmar Bading**, Interdisciplinary Center for Neurosciences (IZN), University of Heidelberg, Germany, *The good and the bad of NMDA receptor induced calcium signaling*

30 EVENT: **Young DANDRITE Rainbow Club**: ***Let's start simple: Diving into Quantum Mechanics***, with Postdoctoral Researcher Pinja Haikka, Dept. Physics, Aarhus University

MAY

31 SEMINAR: **DANDRITE Topical Seminar**, PhD student **Sandra Eltschkner**, Rudolf Virchow Center for Experimental Biomedicine, University of Würzburg, Germany, *Targeting fatty acid synthesis II proteins for drug development*

32 SEMINAR: **DANDRITE Topical Seminar**, **Valérie Coronas**, Laboratory of Signalisation and Transports Ioniques Membranaires (STIM), University of Poitiers, France, *Regulation of neural stem cells by the microenvironment*

33 EVENT: **STRING/Cytoscape Workshop**, by Professor **Lars Juhl Jensen**, Disease Systems Biology, Center for Protein Research, University of Copenhagen

34 SEMINAR: **DANDRITE Topical Seminar**, Associate professor **David Gloriam**, Dept. Drug Design and Pharmacology, University of Copenhagen. *GPCR ligand identification and crystallization*

35 SEMINAR: **DANDRITE Topical Seminar**, Professor **Robert Malinow**, Dept. Neuroscience, University of California, San Diego, USA, *Synapses in health and disease*

36 GUEST: Principal Investigator **Balázs Hangya**, Institute of Experimental Medicine, Hungarian Academy of Sciences, Hungary (one week)

NCA Neuroscience Day 2017. More than 450 people participated. Photo by Lars Kruse, AU Photo

Professor Maiken Nedergaard

Professor Richard Morris

37

EVENT: **Neuroscience Day 2017:** ***Let's Rethink Memory.*** Organized by NeuroCampus Aarhus.
Keynote lecturers:

- Brain Prize Winner Professor **Richard Morris**, University of Edinburgh
- Professor **Maiken Nedergaard**, University of Copenhagen

Presentations by:

- Professor **Dorthe Berntsen**, Aarhus University
- Professor **Gregers Wegener**, Aarhus University Hospital
- Associate Professor **Ditte Demontis**, Aarhus University
- Associate Professor **Carmela Matrone**, Aarhus University
- CEO **Kim Baden-Kristensen**, Brain+
- Vice President Neurodegeneration and Biologics **Jan Egebjerg**, Lundbeck A/S
- Professor **Elvira Brattico**, Aarhus University
- **Julie Rubow** and **Bjørn Jakobsen**: "Life with Alzheimer's Disease"

Festival of Research 2017 – FASCINATING RESEARCH, with DANDRITE research groups attending. In picture: PhD student Emil Gregersen and PhD student Sara Elfarrash.
Photo by Maria Thykær Jensen, DANDRITE

Prize celebration. From right: Poul Nissen, Emmanuelle Charpentier, and Virginijus Siksnys. Photo by Novo Nordisk Fonden

Poul Nissen received the 2017 Novo Nordisk Prize for his pioneering studies of the structure and function of ion pumps. Photo by Novo Nordisk Fonden

38 GUEST: Aarhus University Research Foundation Guest Researcher **Thomas Lykke-Møller Sørensen**, Principal Beamline Scientist: Diamond Light Source (6 months)

APRIL

39 SEMINAR: **DANDRITE Topical Seminar**, Professor **Guillermo Montoya**, The Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, *Crystal structure of the Cpf1 R-loop complex after target DNA cleavage*

40 EVENT: **Festival of Research 2017 – FASCINATING RESEARCH,** DANDRITE research groups attending. In picture: PhD student **Emil Gregersen** and PhD student **Sara Elfarrash**

41 SEMINAR: **DANDRITE Lecture**, Professor **Botond Roska**, Friedrich Miescher Institute for Biomedical Research (FMI), Switzerland, *The first steps in vision: cell types, circuits and repair*

42 GUEST: Nordic EMBL Communications Officer **Annabel Darby** (3 days)

43 EMINAR: **DANDRITE Topical Seminar**, Postdoctoral Researcher **Mikhail Paveliev**, University of Helsinki, Finland *A role for the extracellular matrix in neurotrophic factor signaling?*

44 SEMINAR: **DANDRITE Topical Seminar,** Assistant Professor **Kristian G. Andersen**, The Scripps Research Institute, & Member at the Broad Institute of MIT and Harvard, *From Ebola to Zika – Tracking large-scale outbreaks using infectious disease genomics*

MARCH

45 SEMINAR: **DANDRITE Topical Seminar**, PhD Student **Akihiro Matsumoto**, Dept. Psychology, University of Tokyo, Japan. *Processing of global motion image by local clusters of retinal ganglion cells*

46 EVENT: **Celebration**, Professor **Poul Nissen** received the 2017 Novo Nordisk Prize. The 2017 Novo Nordisk Prize award was marked with two celebration events: at Novo Nordisk headquarter in Bagsværd, Denmark and at Aarhus University. At the Bagsværd celebration, furthermore the 2017 Novozymes Prize was awarded for two researchers: Professor **Emmanuelle Charpentier**, former scientist at the Swedish node of the Nordic EMBL Partnership, The Laboratory for Molecular Infection Medicine Sweden (MIMS) and Professor **Virginijus Siksnys**, Vilnius University, Lithuania.

DANDRITE Encounters 2017. Group leaders Mark Denham presents to visitors. Photo by Maria T. Jensen, DANDRITE

DANDRITE Encounter 2017 was visited by local AU students and DIS students from US. Photo by Maria Thykær Jensen, DANDRITE

48 49 50 51 52 53 54 55 57

47 **FEBRUARY**
EVENT: **DANDRITE Encounters 2017**, at Aarhus Institute of Advanced Studies, Aarhus University

48 GUEST: Erasmus student **Harm Ruesink**, University of Groningen, The Netherland (5 months).

49 GUEST: Erasmus student **Damián Carvajal Ibáñez**, University of Barcelona, Spain (5 months) student.

50 GUEST: Erasmus student **Cármen Maria Leal Vieira**, Portugal (5 months)

JANUARY

51 SEMINAR: **DANDRITE Topical Seminar**, PhD student **Rune Berg**, University of Copenhagen, *Neuronal population activity involved in motor patterns of the spinal cord: spiking regimes and skewed involvement*

52 SEMINAR: **DANDRITE Topical Seminar**, Senior Research Fellow **Zoltan Somogyvari**, Wigner Research Centre for Physics, Hungarian Academy of Sciences, Hungary, *Determination of spatio-temporal input current patterns of single hippocampal neurons based on extracellular potential measurements*

53 GUEST: PhD student **Andrea Moreno**, University of Edinburgh, United Kingdom.

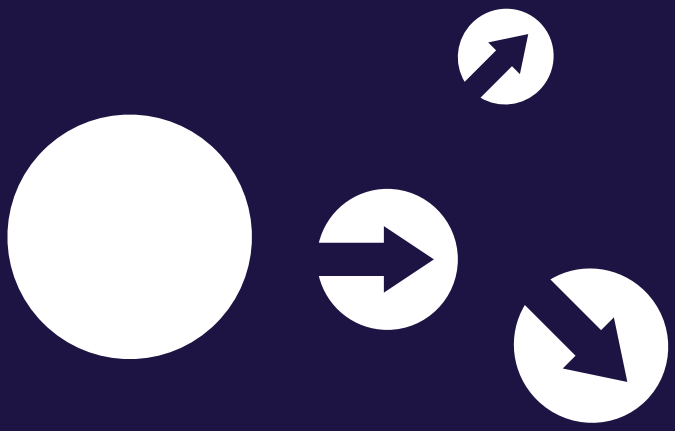
54 SEMINAR: **DANDRITE Topical Seminar**, Principal Investigator **Balázs Hangya**, Institute of Experimental Medicine, Hungarian Academy of Sciences, Hungary, *Tonic and phasic properties of central cholinergic neurons in sensory detection*

55 SEMINAR: **DANDRITE Topical Seminar,** Postdoctoral Researcher **Matt Swulius**, Grant Jensen's lab, California Institute Of Technology, Caltech, USA, *Exploring native cellular structure by cryo-electron tomography, correlated cryo-fluorescence microscopy and focused ion beam milling*

56 GUEST: Intern student **Satoshi Toyama**, Nara Medical University, Japan (4 months)

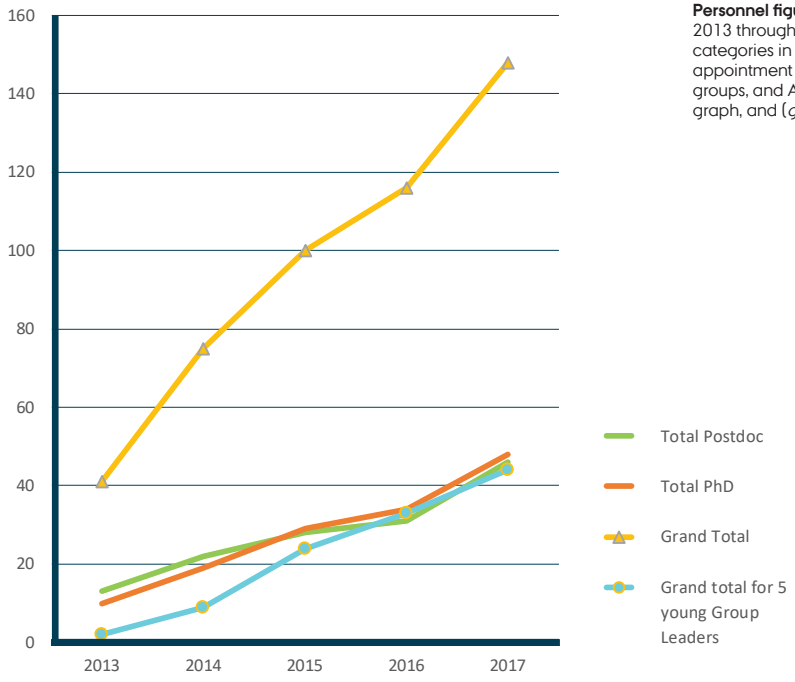
57 SEMINAR: **DANDRITE Topical Seminar,** Postdoctoral Researcher **Michael Habeck**, Steve Karlish Laboratory, Weizmann Institute of Science, Israel, *Functional effects of specific lipid binding to Na, K-ATPase*

04
Personnel



Personnel

Each of the five young group leaders during 2017 continued the successful establishment and build-up of their groups with students, technical support staff, postdoctoral fellows, of which many have also received individual fellowships. Additionally, all groups have attracted several summer students, interns, and research visitors from EU, Denmark, as well as rest of the World. Furthermore, DANDRITE increased our interaction with the Danish neuroscience community through appointment of four new affiliated researchers in 2017.

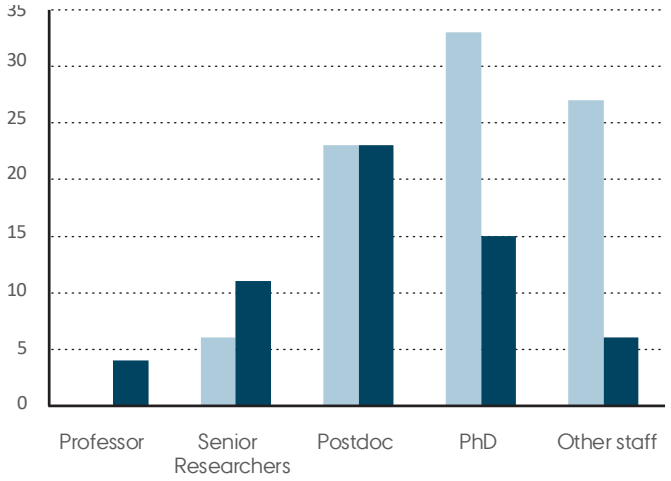


Personnel figure 1: Graphic representation of personnel progression 2013 through 2017. Graphs summarize with: (*blue dots*) all appointment categories in the five recruited DANDRTITE groups, (*yellow triangles*) all appointment categories in the eight DANDRTITE groups, plus Team Leader groups, and Affiliated Researcher groups, (*red*) all PhD students from yellow graph, and (*green*) all postdocs in yellow graph

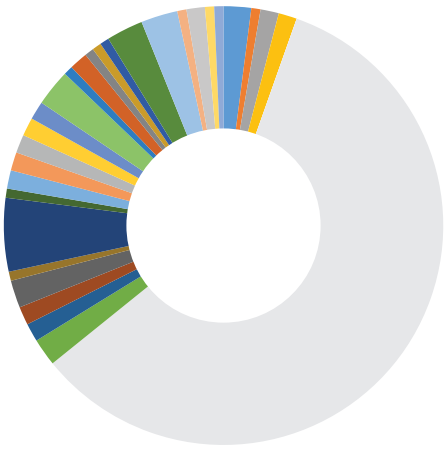
COUNT AND PERCENTAGES OF PERSONNEL EMPLOYED AND AFFILIATED DURING 2017 GROUPED BY APPOINTMENT CATEGORY AND GENDER

DANDRITE Personnel categories	Female	Male	Total
Professor		4	4
Senior Researchers	6	11	17
Postdoc	23	23	46
PhD	33	15	48
Other staff (Laboratory Technician, Research Assistant, and administration)	27	6	33
Grand Totalt	89	59	148
% Male/Female	60	40	100

Personnel figure 2: Count and percentages of personnel employed and affiliated during 2017 grouped by appointment category and gender.

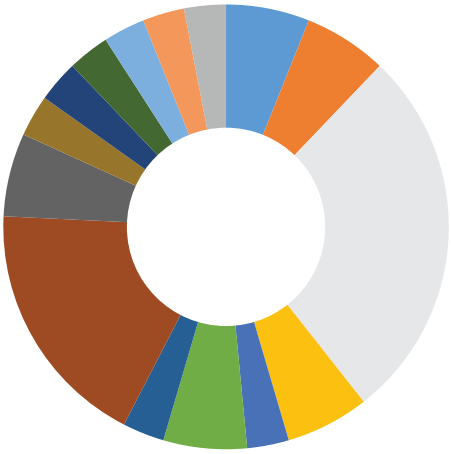


Personnel figure 3: Employment categories & gender distribution for personnel 2017



Personnel figure 4: Count of all employees and affiliated group members 2017 grouped by nationality

Australia
Belgium
Canada
China
Denmark
Egypt
Estonia
Finland
France
Georgia
Germany
Greece
Hungary
India
Iran
Ireland
Italy
Japan
Latvia
Mexico
Netherland
Nigeria
Norway
Poland
Portugal
Romania
Spain
Sweden
Turkish



Personnel figure 5: Count of all employees and affiliated group members 2017 grouped by nationality

Australia
China
Denmark
Egypt
Estonia
France
Georgia
Germany
Iran
Ireland
Italy
Latvia
Mexico
Netherland
Spain

Grants for Aarhus Universit Hosted Research Activities

1 Postdoc **Mette Richner**: *Sortilin i neuropatisk smerte* DKK 0.2 million, Dagmar Marshalls Foundation

2 Affiliated Researcher **Simon Glerup**: *Ildsjæle-initiativ* DKK 0.1 million, Aarhus University

3 Assistant Professor **Szilard Sajgo**: *The role of individual retinal ganglion cell types in visual computations and behaviours* DKK 1.6 million, Marie Skłodowska-Curie fellowship

4 PhD Student **Nathalie Krauth**: *Travel grant* DKK 3.000, The Danish Society for Biochemistry and Molecular Biology

5 Assistant Professor **Camilla Gustafsen**: *Travel grant* DKK 24.000, Lundbeckfonden

6 PhD Student **Rikke Hahn Kofoed**: *Travel grant* DKK 3.000, Danish Society for Biochemistry and Molecular Biology

7 PhD Student **Mariam Gamaledin**: *1/3 PhD Stipend: Identifying Proteins Essential for Making Memories Long-lasting* DKK 0.5 million, Graduate School of Science and Technology, Aarhus University

8 PhD Student **Angela O'Sullivan**: *EMBL Advanced Training Centre Corporate Partnership Programme Fellowship* DKK 1.500, EMBO

9 Group Leader **Keisuke Yonehara**: *Lundbeckfonden running cost grant* DKK 0.5 million, Lundbeckfonden

10 Group Leader **Poul Henning Jensen**: *IMPRiND – Inhibiting Misfolded protein Propagation in Neurodegenerative Diseases*, DKK 1.5 million, Innovative Medicines Initiative 2

11 Group Leader **Poul Nissen**: *Novo Nordisk Prize* 2017 DKK 2.5 million, Novo Nordisk Foundation

12 Group Leader **Anders Nykjæ**r: *Functional characterization of the multiple sclerosis risk gene SORCS3: a novel drug target* DKK 0.25 million, Foundation for Research in Neurology

13 PhD Student **Maimaitili Muyesie**r: *1/3 PhD Stipend: Understanding the molecular mechanisms involved in the early disease states across the various familial Parkinson's mutations* DKK 0.5, Graduate School of Health, Aarhus University

14 Team Leader **Magnus Kjærgaard**: *DFF-Research Project 1: Antibody engineering facilitated by avidity* DKK 2.6 million, Danish Council for Independent Research (DFF - FTP)

15 PhD Student **Giulia Monti**: *1/3 PhD Stipend: A novel SORL1 splice variant with profound impact on Alzheimer's Disease etiology*, DKK 0.6 million, Graduate School of Health, Aarhus University

16 Team Leader **Magnus Kjærgaard** and Group Leader **Poul Nissen**: *Research Project 2: Regulation of plasma-membrane calcium pumps – from single molecules to structures* DKK 6.0 million, Danish Council for Independent Research (DFF – FNU)

17 Group Leader **Sadegh Nabavi**: *Research Project 1: Mapping the Neural Circuit for an Innate Fear Behaviour* DKK 2.6 million, Danish Council for Independent Research (DFF - FNU)

18 Group Leader **Poul Nissen**: *RAtionalising Membrane Protein crystallisation – RAMP*, DKK 3.5 million, Horizon2020, ITN

19 PhD Student **Rune Rasmussen**: *PhD Scholarship: Circuit mechanisms of target-specific computation in mouse visual cortex* DKK 1.6 million, Lundbeckfonden

20 Group Leader **Anders Nykjær**: *DFF-Research Project 2: Functional characterization of the Alzheimer's Disease and type 2 diabetes risk gene SORCS1* DKK 5.1 million, Danish Council for Independent Research (DFF)

21 Group Leader **Anders Nykjær**: Center of Excellence: Center for Proteins in Memory – *PROMEMO* DKK 62.0 million, Danish National Research Foundation (DNRF)

22 Team Leader **Hanne Poulsen**: *Generation of CAPOS mouse* DKK 0.1 million, GEMM (MRC Harwell)

23 PhD Student **Sara Raquel Almeida Ferreira**: *1/3 PhD Stipend: Involvement of the CD163 receptor in the α-synuclein induced neurodegeneration in Parkinson's disease* DKK 0.5 million, Graduate School of Health, Aarhus University

24 Group Leader **Poul Henning Jensen**: *Alpha-synuclein oligomers, conformation specific MJF14 antibody and their interrelations. New applications, structure and functional analyses* DKK 3.7 million, Michael J. Fox Foundation for Parkinsons's Research

25 Postdoc **Asad Jan**: *Blocking the prion-like disease propagation in Parkinson's disease and related disorders – model development and identification of cell-autonomous and cell non-autonomous factors,* DKK 1.6 million, AIAS-COFUND Marie Curie Fellowships

26 PhD Student **Pernille Thomasen**: *Travel grant* DKK 11.350, EMBO short term fellowship

27 Associate Professor **Lone Pallesen**, *Microglia and sortilin – regulation of neuropathic pain* DKK 164.000, Riisfort Fonden

28 Affiliated Researcher **Marina Romero-Ramos**: *Project Grant* DKK 120.000, Parkinsonforeningen

29 Group Leader **Poul Henning Jensen**: *Mechanistic investigation of the neuroprotective effect of caffeine in prion-like alpha-synuclein models – identification of therapeutic targets* DKK 261.000, Parkinsonforeningen

30 Affiliated Researcher **Simon Glerup**: *Jens Christian Skou Prisen* DKK 100.000, Aarhus University

31 Affiliated Researcher **Marco Capogna**: *Lundbeckfonden running cost grant* DKK 0.5 million Lundbeckfonden

32 Affiliated Researcher **Marina Romero-Ramos**: *Project Grant: the role of peripheral immune cells in the neurodegenerative process associated to Parkinson's disease*DKK 0.6 million, Novo Nordisk Foundation

33 Group Leader **Keisuke Yonehara**: *Lundbeckfonden running cost grant* DKK 0.5 million, Lundbeckfonden

34 Team Leader **Hanne Poulsen**: *Brain prize winner collaborative grant* DKK 2.6 million, Lundbeckfonden

35 Group Leader **Mark Denham**: *Project grant: A novel Stem Cell model for Parkinson's disease: Investigating genetic and environmental interactions* DKK 120.000, Bjarne Saxhofs Foundation facilitated by the Parkinsons Association

36 Research Student **Pardis Zarifka**r: *Oxytocin attenuates anxiety caused by pathological changes in the neurocircuitry of the Amygdala in Parkinsons Disease* DKK 140.000, Danish Society for Neuroscience (DSfN) & Lundbeckfonden

37 Group Leader **Poul Henning Jensen**: *Using MJF-14 antibody to uncover novel a-synuclein in Parkinson's disease and MSA* DKK 1.2 million, Michael J. Fox Foundation for Parkinsons's Research

38 Associate Professor **Lone Pallesen**: *Microglia in neuropathic pain* DKK 100.000, Dagmar Marshalls Foundation

39 PhD Student **Sara Basse Hansen**: *PhD fellowship: Calcium Transport at Atomic Resolution and by Single Molecules* DKK 444.000, Boehringer Ingelheim Fonds

Patents

Postdoc Mikhail Paveliev obtained patent: C Protamine In Treatment Of Neuronal Injuries, co-inventors: Rauvala H, Paveliev M, Kujapanula J, Rouhiainen A, Kulesskaya N. Application N14/899,924. Allowed for issuance as a patent by United States Patent and Trademark Office on 10/16/2017

Affiliated Researcher Thomas Boesen obtained patent: Nanodisc comprising ice nucleating proteins, co-inventors: Boesen T, Finster K, Ling M, Temkiv, T. Patent number: EP17162310 March 2017

Spin-off Company

Affiliated Researcher Simon Glerup set out with the start-up company Draupnir Bio (https://scale-updenmark.com/2017/11/30/draupnir-bio/). Draupnir Bio has set out to develop novel types of medicine to fight cholesterol related diseases such as cardiovascular disease by using a new mechanism of action.

Invited Talks

DECEMBER

Poul Nissen: *The use of advanced neutron and X-ray technologies in drug discovery*, LINX meeting at Leo Pharma A/S, Copenhagen, Denmark

Poul Nissen: *The use of advanced neutron and X-ray technologies in structural biology*, Annual meeting of LINX (Linking Industry to Neutrons and x-rays), Copenhagen, Denmark

Affiliated researcher Marina Romero-Ramos: *CD163+ cells as modulators of the immune response related to Parkinson's' Disease*, NECTAR 2017 - 27th Annual meeting of Network for European CNS Transplantation & Restoration, Dublin, Ireland

Andrea Moreno (Sadegh Nabavi's group): *Erasing fear memories by pharmacological manipulation*, Conference: FEAR: Brain, Behaviour, Society, Aarhus Institute of Advanced Studies, Aarhus University, Denmark

Affiliated Researcher Marco Capogna: *Fear and sleep: key role of amygdala GABAergic neurons*, Conference: FEAR: Brain, Behaviour, Society, Aarhus Institute of Advanced Studies, Aarhus University, Denmark

NOVEMBER

Anne von Philipsborn: *Neuronal circuits for fly sexual behaviour*, University of Sheffield, United Kingdom

Affiliated Researcher Jane Hvarregaard Christensen: *Genetics of nocturnal enuresis – new progress*, Danish Pediatric Society, Middelfart, Denmark

Poul Nissen: *Structure and mechanism of membrane transporters of the P-type ATPase family, 4th* Shanghai Tech SIAIS BioForum – Advances and Perspectives in Integrative Biology of Cellular Processes, Shanghai, China

Poul Nissen: *Structure and mechanism of membrane transport proteins*, University of Copenhagen, Denmark

Affiliated Researcher Arne Möller: *A structural perspective on neuroreceptors: Visualising sortilins by cryoEM*, SFB-Seminar, Goethe Universität Frankfurt, Germany

Poul Nissen: *Maintaining a leading position within Life Science*, Technology Day – Towards a World-Class Science & Engineering Region, Danish Academy of Technical Sciences, Copenhagen, Denmark

Poul Nissen: *Structural biology using neutrons*, Nordic-EMBL-ESS workshop on structural biology, Lund, Sweden

Mark Denham: *Modelling Parkinson's Disease with Stem Cells*, The Parkinson Association, Denmark

Keisuke Yonehara: *Cell-type-based mechanisms of vision in the mouse*, Aarhus University, Denmark

Juliane Martin (Duda Kvitsiani's group): *Time to decide: how decision time affects choices*, Brain Prize Meeting, Hindsgavl Castle, Denmark

Junior Lopez (Duda Kvitsiani's group): *Abstract representation of value in prefrontal cortex*, Brain Prize Meeting, Hindsgavl Castle, Denmark

OCTOBER

Niels Sanderhoff Degn (Anders Nykjær's group): *SorCS2 as a modifier of disease progression in Huntingtons disease*, Brain Prize Meeting, Hindsgavl Castle, Denmark

Mikhail Paveliev (Anders Nykjær's group): *Microstructure of the complex of GABAergic synapse with perineuronal net*, Brain Prize Meeting, Hindsgavl Castle, Denmark

Poul Nissen: *The evil twin and other translations*, CoLuAa XXV 2017 Conference, University of Copenhagen, Denmark

Poul Henning Jensen: *Have we missed a critical phase for reduced cytosolic calcium during alpha-synuclein aggregate-dependent neurodegeneration?* University of Helsinki, Finland

Affiliated Researcher Arne Möller: *Cryo-EM of membrane proteins: Challenges and Perspectives*, CEF-Seminar, Goethe Universität Frankfurt, Germany

Affiliated Researcher Morten S. Nielsen: *Advanced light microscopy of the BBB – Methods,* Challenges and Results, Gordon Museum of Pathology, King's College London, United Kingdom

Anne von Philipsborn: Neuronal circuits for fly sexual behaviour, Panum Institute, University of Copenhagen, Denmark

Anne von Philipsborn: *Neuronal circuits for fly sexual behaviour*, Maiken Nedergaard's laboratory, Center for Translational Neuromedicine, University of Copenhagen, Denmark

Affiliated Researcher Jane Hvarregaard Christensen: *International nocturnal enuresis biobank (INEB) projects*, International nocturnal enuresis biobank – 1st steering committee meeting, Hindsgavl Castle, Denmark

SEPTEMBER

Poul Nissen: *The Structure and Mechanism of P-type ATPases*, The 15th International Conference on Na, K-ATPase and Related Transport ATPases, Otsu, Japan

Affiliated Researcher Marco Capogna: *Role of GABAergic neurons on hippocampal-amygdala network*, Brain Research Institute, Zurich, Switzerland

Mikhail Paveliev (Anders Nykjær's group): *Microstructure of the complex of GABAergic synapse with perineuronal net*, Brain Extracellular Matrix and Glia in Health and Disease, Voronezh, Russia

Poul Nissen: *Structure and Mechanism of P-type ATPase transporters*, Conference: Dynamics of Membrane Systems, Collaborative Research Centre 1208, University of Düsseldorf, Germany

Poul Henning Jensen: *Joining IMI – The academic experience*, Nordic Life Science Days 2017, Malmø, Sweden

Poul Henning Jensen: *Cellular models of MSA*, Meeting: 20 years of alpha-synuclein in Parkinson's Disease and related synucleinopathies, Athens, Greece

Affiliated Researcher Arne Möller: *Cryo-EM of membrane proteins: Challenges and Perspectives, 6th* Caesar international conference, Bonn, Germany

Anders Nykjær: *Regulated sortilin-shedding balances synaptic input and emotional state*, Institute of Biotechnology, University of Helsinki, Finland

Anders Nykjær: *Functional genomics screens and analyzing big data – SorCS1 in diabetes*, Discussion leader at round table discussion, 8th Annual Network Meeting of the Nordic EMBL Partnership for Molecular Medicine, Helsinki, Finland

Susanne Schousboe Sjøgaard (Anders Nykjær's group): *Science Communication*, Discussion leader at round table discussion, 8th Annual Network Meeting of the Nordic EMBL Partnership for Molecular Medicine, Helsinki, Finland

Poul Nissen: *DANDRITE – Danish Research Institute of Translational Neuroscience*, Director's overview, 8th Annual Network Meeting of the Nordic EMBL Partnership for Molecular Medicine, Helsinki, Finland

Keisuke Yonehara: *Cell-type-specific computations and disease in the visual system*, University of Helsinki, Finland

AUGUST

Anne von Philipsborn: *Motor control and action selection during Drosophila sexual behaviour*, Lund University, Sweden

Poul Henning Jensen: *Parkinson's disease and synucleinopathies – what to model, why and how?* BrainStem Summer Symposium, Aarhus Institute of Advanced Studies, Aarhus University, Denmark

Muwan Chen (Mark Denham's group): *Investigating the role of Alpha-Synuclein in GBA1 iPSC-derived neurons*, BrainStem Summer Symposium, Aarhus Institute of Advanced Studies, Aarhus University, Denmark

Poul Nissen: *Structure and mechanism of membrane transporters studied through protein engineering*, Benzon Symposium no. 63: New Paradigms of Protein Engineering, Copenhagen, Denmark

JULY

Anne von Philipsborn: *Motor control and action selection during Drosophila sexual behaviour*, University of Wuerzburg, Germany

JUNE

Affiliated Researcher Marina Romero-Ramos: *The Dynamic Immune Response in PD,* Gordon Research Conference: Parkinson's Disease, Maine, USA

Poul Nissen: *Can we bridge between different levels of neuroscience?* Annual Meeting at Dept. Molecular Biology and Genetics, Aarhus University, Denmark

Poul Nissen: *Snapshots and dynamics of membrane proteins and biomembranes*, Neutrons in Structural Biology 2017, Grenoble, France

Anders Nykjær: *Sortilin receptors in mental disorders and plasticity,* 2nd Nordic Neuroscience Meeting, Stockholm, Sweden

Affiliated Researcher Marco Capogna: *Key role of GABAergic neurons on amygdala networks*, 2nd Nordic Neuroscience Meeting, Stockholm, Sweden

Poul Nissen: *Membrane transporters in the brain*, Erice International School of Crystallography, Italy

MAY
Affiliated Researcher Marco Capogna: *Role of GABAergic neurons on amygdala networks*, Academy of Sciences, Budapest, Hungary

Keisuke Yonehara: *Cell-type-specific computation and disease in the visual system*, Max Planck Institute of Neurobiology. Martinsried, Germany

Sadegh Nabavi: *Synaptic plasticity: from molecule to behavior,* School of Medicine, University of Tasmania, Hobart, Australia

Poul Henning Jensen: *Early decisive calcium changes in Parkinsons disease & Mouse models of prion-like synuclein patholgy*, Annual Meeting at Danish Society for Neuroscience - Neurodegenerative diseases, Nyborg, Denmark

Rikke Hahn Kofoed (Poul Henning Jensen's group): *PLK-2 regulates a-synuclein phosphorylation and mRNA expression*, Annual Meeting at Danish Society for Neuroscience - Neurodegenerative diseases, Nyborg, Denmark

Anders Nykjær: *SorCS2 is required for BDNF-dependent hippocampal plasticity and memory formation*, Neuroscience Day 2017, Aarhus University, Denmark

APRIL
Poul Henning Jensen: *Reduced cytosolic calcium caused by SERCA activation is an early and pathogenic event in neurodegeneration caused by alpha-synuclein oligomers,* 13th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PDTM 2017), Vienna, Austria

Affiliated Researcher Marco Capogna: *Key role of GABAergic neurons of amygdala and hippocampus in health and disease*, Neurobiology, The University of Southern Denmark, Odense, Denmark

MARCH
Poul Nissen: *How do membrane transporters switch sides?* ETH, Dept. Biochemistry, Zürich, Switzerland

Keisuke Yonehara: *Congenital nystagmus gene Frmd7 is necessary for estaglishing a neuronal circuit asymmetry for direction selectivity*, The Annual Meeting of the Physiological Society of Japan, Hamamatsu, Japan

Poul Henning Jensen: *Presentation of Workpackage 2 contribution on cell models of prion-like alpha.synuclein spreading*, Kick-off meeting for the Innovative Medicines Initiative (IMI), Oxford, United Kingdom

Poul Nissen: *Pumps and circumstances*, Novo Nordisk Prize Lecture, Aarhus University, Denmark

Poul Nissen: *Pumps and circumstances*, Novo Nordisk Prize Ceremony, Novo Nordisk A/S, Denmark

Affiliated Researcher Arne Möller: *Know your Detergents! or Back to Blobology*, Universität Potsdam, Germany

Affiliated Researcher Simon Glerup: *Panel discussion on scientific reproducibility*, Affinityproteomics, Alpbach, Austria

Poul Nissen: *How do membrane transporters switch sides and get away with it? EMBO Workshop* - Towards Novel Therapies: Emerging Insights from Structural and Molecular Biology, Groningen, Netherlands

Affiliated Researcher Marco Capogna: *GABAergic neuron diversity in the hippocampus-amygdala*, Centre for Cognitive and neural systems, Edinburgh, Scotland

FEBRUARY
Duda Kvitsiani: *Foraging decisions in flies and mice*, Institute of Experimental Medicine, Budapest, Hungary

Poul Nissen: *Structural and Functional Studies of Biomembranes*, Inaugural lecture as Affiliated Professor, University of Copenhagen, Denmark

Anders Nykjær: *NeuroCampus Aarhus*, Site Visit by Edinburgh University, Aarhus University, Denmark

JANUARY
Affiliated Researcher Marco Capogna: *Pharmacology of dis-inhibitory circuits in the human cerebral cortex*, Dept. Pharmacology, Oxford, United Kingdom

Anders Nykjær: *Signalling of NGF and prof NGF through the NGF receptor system in NP and OA*, PAINCAGE meeting, Pisa, Italy

Pictures from the inauguration of the Center for Proteins in Memory – PROMEMO

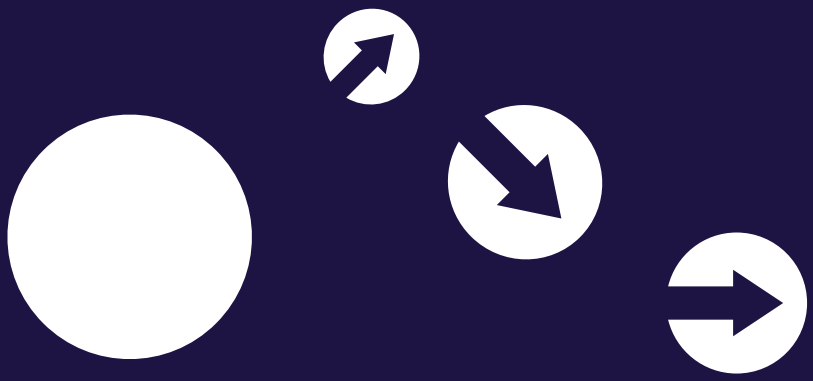
DNRF board member Professor Eero Vuorio in conversation with AU Dean of Health Faculty and representatives from The Lundbeckfonden.
Credits: Ida Jensen, AU Photo.

The keynote speakers of the Minisymposium on Memory. From the left, Prof Sumantra Chattarji, and Prof Clive R. Bramham with Center Leader Prof Anders Nykjær.
Credits: Susanne Schousboe Sjøgaard

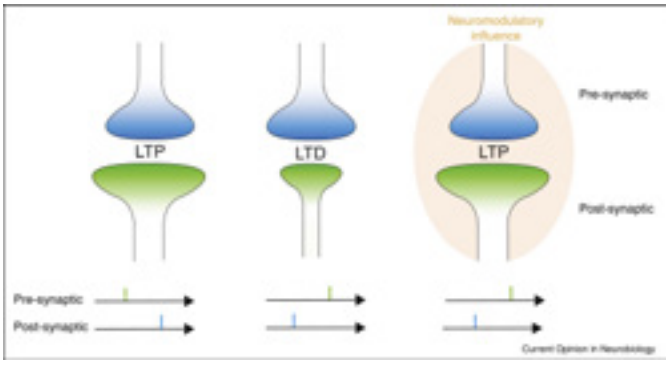
Center Leader Professor Anders Nykjær

Center Leader Professor Anders Nykjær. Photo by Ida Jensen

05 Publications



Publications



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1 **Andersen N, Krauth N, Nabavi S** (2017) Hebbian plasticity in vivo: relevance and induction. *Current Opinion in Neurobiology*, Vol. 45, p. 188-192

2 Azouaoui H, Montigny C, Dieudonné T, Champeil P, Jacquot A, Vázquez-Ibar JL, Maréchal P, **Ulstrup J**, Ash M, **Lyons JA**, **Nissen P**, Lenoir G (2017) A High and Phosphatidylinositol-4-phosphate (PI4P)-dependent ATPase Activity for the Drs2p/Cdc50p Flippase after Removal of its N- and C-terminal Extensions. *Journal of Biological Chemistry*, Vol. 292, p. 7954-7970

3 Blans K, Hansen MS, Sørensen LV, Hvam ML, Howard KA, **Möller A**, Wiking L, Larsen LB, Rasmussen JT (2017) Pellet-free isolation of human and bovine milk extracellular vesicles by size-exclusion chromatography. *Journal of Extracellular Vesicles*, Vol. 6, No. 1, 1294340

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11 Lazzaro VD, Rothwell J, **Capogna M** (2017) Noninvasive Stimulation of the Human Brain: Activation of Multiple Cortical Circuits. *The Neuroscientist*, p. 1-15

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14 **Ellendersen BE, von Philipsborn A** (2017) Neuronal modulation of D. melanogaster sexual behavior. *Current Opinion in Insect Science*, Vol. 24

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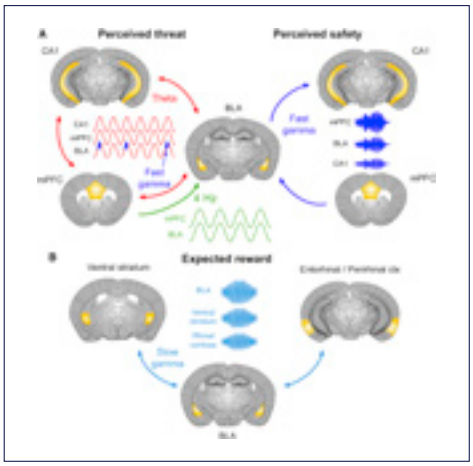


Review
Synaptic Plasticity, Engrams, and Network Oscillations in Amygdala Circuits for Storage and Retrieval of Emotional Memories

4

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20 **Glerup S**, Schulz R, Laufs U, Schlueter K (2017) Physiological and therapeutic regulation of PCSK9 activity in cardiovascular disease. *Basic Research in Cardiology*, Vol. 112, No. 3, 32

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22 Gustafsen C, Olsen D, Vilstrup J, Lund S, Reinhardt A, **Wellner N**, Larsen T, Andersen CBF, Weyer K, Li J, Seeberger PH, Thirup S, Madsen P, **Glerup S** (2017) Heparan sulfate proteoglycans present PCSK9 to the LDL receptor. *Nature Communications*, Vol. 8, No. 1, p. 503

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25 Heinze S, **von Philipsborn A** (2017) Editorial overview: Recent advances in insect neuroethology: from sensory processing to circuits controlling internal states. *Current Opinion in Insect Science*, Vol. 24, p. iv-vi

26 Isaksen TJ, Kros L, Vedovato N, Holm TH, Vitenzon A, Gadsby D, Khodakhah K, **Lykke-Hartmann K** (2017) Hypothermia-induced dystonia and abnormal cerebellar activity in a mouse model with a single disease-mutation in the sodium-potassium pump. *PLOS Genetics*, Vol. 13(5)

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28 **Januliene D**, Manavalan A, **Ovesen PL**, **Pedersen KM**, Thirup S, **Nykjær A**, **Moeller A** (2017) Hidden Twins : SorCS Neuroreceptors Form Stable Dimers. *Journal of Molecular Biology*, Vol. 29, No. 19, p. 2907-2917

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30 Jimenez-Ferrer I, Jewett M, Tontanahal A, **Romero-Ramos M**, Swanberg M (2017) Allelic difference in Mhc2ta confers altered microglial activation and susceptibility to α-synuclein-induced dopaminergic neurodegeneration. *Neurobiology of Disease*, Vol. 106, p. 279-290

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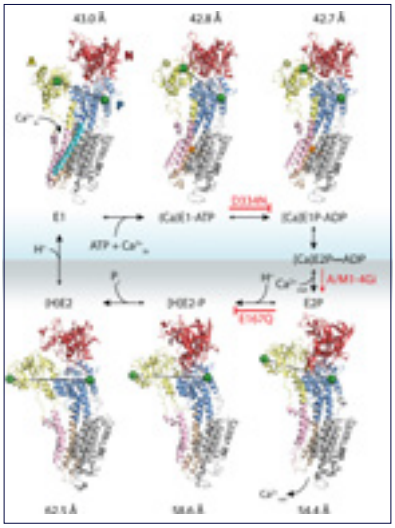

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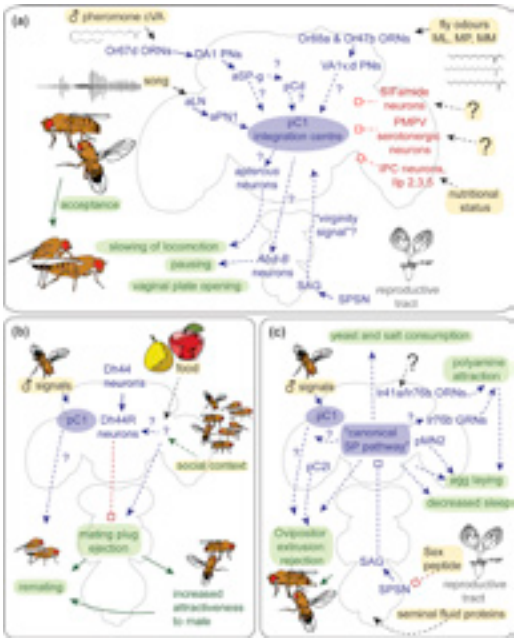

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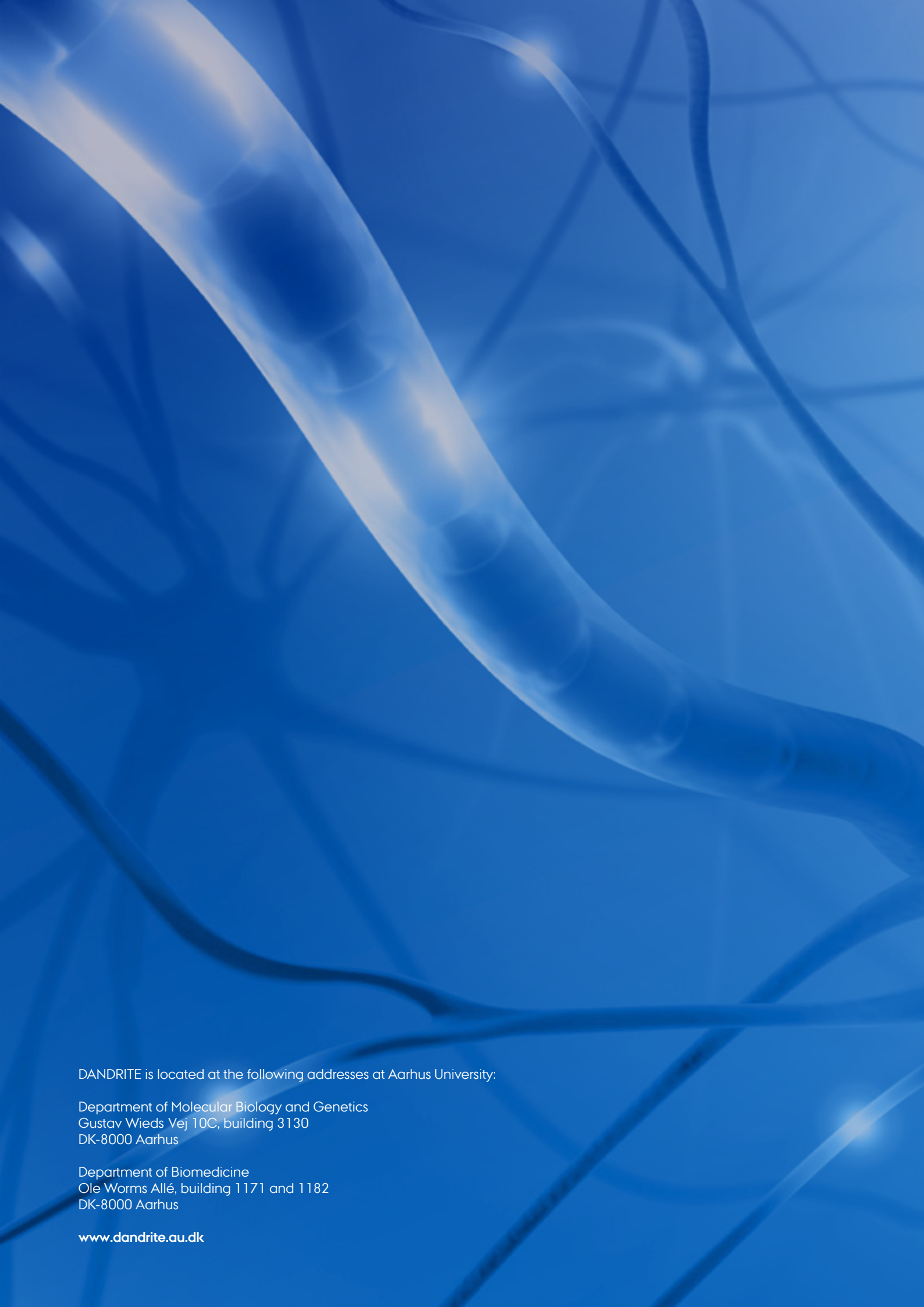

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