DBI^2 Annual report

Year 1 | October 2022 – September 2023

DBI²
DUTCH BRAIN
INTERFACE INITIATIVE

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Acronym

NS: Neuroscience specific aim

CS: Computation specific aim

TS: Technology specific aim

CL: Closed-loop

Nat-B Lab: Naturalistic Behaviour Laboratory

PI: Principal Investigator

SAB: Scientific Advisory Board

SteerCo: Steering Committee

WP: Work Package

TI: Temporal Interference

RU: Radboud University

TU Delft / TUD: Delft University of Technology

YTC: the Young Talent Council

NIN: The Netherlands Institute for Neuroscience

UMCU: The University Medical Center Utrecht

Erasmus MC: Erasmus University Medical Center

PD: Parkinson's disease

DBI² Introduction

The **Dutch Brain Interface Initiative (DBI²)** seeks to enhance our understanding of brain functions and brain-environment interactions by leveraging the development of a new generation of effective and minimally disruptive brain-machine interfaces. DBI² combines an integrated methodological platform including computational, software and hardware elements, geared towards facilitating long-term closed-loop manipulations and brain monitoring in a naturalistic setting, with a neuroscience research program encompassing three main goals:

- *To understand the common principles of global brain dynamics and feedback interactions between brain areas subserving cognition.*
- *To make a major advance in closed-loop feedback control of the brain that is enabled by novel computational and technological advances, to devise effective, ecological, minimally invasive ways to influence brain dynamics, towards new practicable avenues for therapy and cognitive enhancement.*
- *To understand how animal behaviour is generated, by studying the brain during complex, free-flowing interactions between the animal and the environment, and between animals under increasingly natural conditions. For this, we will study the brain in a naturalistic environment throughout different life stages using computational simulations, novel neurotechnology and advanced behavioural monitoring and tracking building on advances in machine learning, breaking away from the highly restricted laboratory experiments that are conventional in neuroscience, and allowing us to answer long-standing neuroscience questions.*

We will tackle these goals with a tight integration between neurotechnology, systems/cognitive neuroscience and computational neuroscience, which this consortium brings together. We will develop and leverage an **integrated platform for manipulating brain activity** based on its neural context (by means of closed-loop stimulation) and environmental context (animal behaviour, in unprecedentedly wild-like conditions, and characterized in an expressive and detailed fashion). The platform will include custom-developed neurotechnology for brain monitoring and perturbation, as well as novel ways for applying artificial intelligence (neural networks, biophysical modelling, advanced statistics) to the study of the brain.

Closed-loop and naturalistic behaviour are two emerging trends in neuroscience research. Our program will be the first to combine the two, providing an **unprecedented window into how information is encoded and processed**. By better controlling neural variability and testing the developed devices against a much wider array of behavioural conditions than currently used, this methodological approach will also enable brain interfaces of unmatched reliability and effectiveness.

DBI² is a broad consortium, leveraging the world-class expertise in Dutch neuroscience, neurotechnology and computational sciences. It also has the goal of being **the centre of gravity of a new Dutch School of Neuroscience and Neurotechnology**, connecting scientists in fundamental and engineering disciplines in (technical) universities and research institutes across the country. The large presence and role assigned to mid-career and young scientists ensures that this school will be a long-lasting player in the Dutch research landscape.

The consortium organisation

The consortium includes researchers with an extensive track record in neuroscience, computational neuroscience, control theory, and electrical engineering towards the fusion of neuroscientific and microsystems, computing architectures, and technological goals. Here below we formulate their track record in terms of collaborative and embedded systems, grouped in the **neuroscience, computation, and neurotechnology** areas. Each of these groups is represented as a work package.

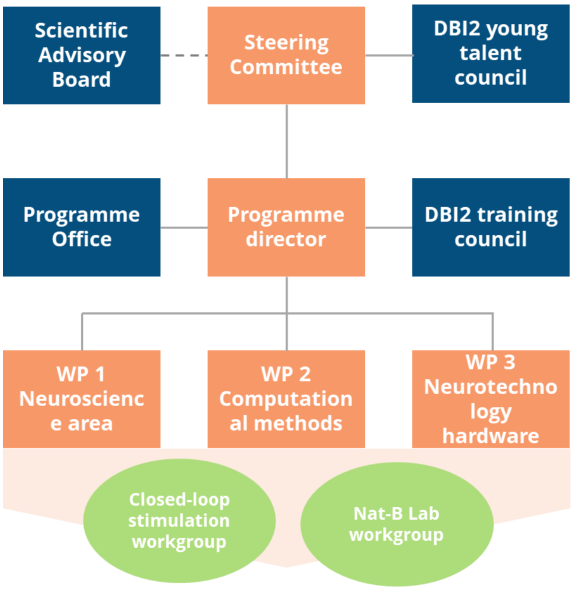

Figure 1 DBI² Governance structure

Figure 1 provides an overview of the DBI² governance structure.

The **Steering Committee** is the highest governing body of the DBI² consortium, consisting of the Programme Director and seven members representing the participating institutions. Additionally, the Steering Committee includes one non-voting member from the Young Talent Council to ensure a broader perspective.

Francesco Battaglia, the **Programme Director**, spearheads the strategic management of the program. His efforts are supported by the Programme Office.

The **Young Talent Council (YTC)**, an integral part of the consortium, is made up of two postdocs and five PhD students. These members are elected for a three-year term by their peers among all PhD students and postdocs in the consortium. The YTC aims to empower young researchers by giving them a voice in both the operational and strategic management of the consortium. This initiative fosters enhanced synergy across DBI² and its participating institutions through a bottom-up approach.

Prioritizing the training of the next generation of scientists is fundamental to DBI², securing the project's enduring legacy. The **Training Council**, led by Fleur Zeldenrust and Martin Vinck from Radboud University, is charged with organising the training program. They collaborate closely with the YTC to refine and expand the programme, ensuring it meets the needs of its participants.

The consortium's main external advisory body is the **Scientific Advisory Board (SAB)**. The SAB provides guidance on all consortium aspects, including research strategy, international competitiveness, organization, and knowledge transfer, to maintain and enhance the consortium's effectiveness.

The **Programme Office**, crucial for day-to-day operations, includes a Programme Manager and a Scientific Coordinator. The Programme Manager is responsible for communication, data management, dissemination, financial administration, and various project management tasks. Meanwhile, the Scientific Coordinators focus on overseeing the consortium's scientific collaborations and assisting the Programme Managers with dissemination activities, ensuring a cohesive and collaborative environment within DBI².

Work packages and Workgroups

Work in DBI² is organized into three main areas: **Neuroscience** (**Work Package 1**), **Computational Methods** (**Work Package 2**) and **Neurotechnology Hardware** (**Work Package 3**). The Neuroscience area encompasses methods development, validation and scientific aims. The aims of the Computational Methods and Neurotechnology Hardware areas are designed to support at least one Neuroscience aim.

Efforts on the two principal methodological innovations, closed-loop analysis and study on naturalistic behaviour, are undertaken by the **Closed-Loop Stimulation Workgroup** and the **Nat-B Lab Workgroup** respectively. Each workgroup comprises researchers from all three work packages to encourage collaboration across different areas.

1. Annual report summary

DBI² has started in October 2022. This document reports on the first year of scientific, and project management activities from October 2022 to September 2023, which represented the setting up and ramp-up phase of the project.

We present here the achievements from the reporting period and the plans for the upcoming project phase. This report reflects the organizational structure of DBI², which is reflected in the following structures:

- Work packages
  - Neuroscience
  - Computational methods
  - Neurotechnology hardware
- Two cross-package workgroups
  - Nat-B Lab workgroup
  - Closed-loop stimulation workgroup
- Programme Office
  - Networking & outreach activities
  - Programme management
  - Training

2. Achievements – Highlights and progress

2.1 Work Packages

The first year was mainly busy with hiring top talent for all work packages and the inventory research phases. We successfully hired 5 Postdocs, 10 PhD candidates and 2 lab managers, one AI engineers. Besides, bridges between these researchers and the rest of the DBI² PIs and researchers have been built.

2.1.1 Work Package 1 | Neuroscience

Below Table 1 is the key scientific goal of WP 1 (Work Package 1), as stated in the project proposal.

NS 1	*How do global brain dynamics during sleep determine dreams and memory processes?*
NS 2	*How do spontaneous activity and environmental factors affect brain development?*
NS 3	*How can visual perception guide decision-making?*
NS 4	*How can the brain support active perception and voluntary action?*
NS 4-1	*Cortical and subcortical contributions to active perception (How can the brain support active perception and voluntary action?)*
NS 4-2	*Descending cortico-cerebellar loops (How can the brain support active perception and voluntary action?)*
Ns 4-3	*Ascending cortical-subcortical loops (How can the brain support active perception and voluntary action?)*
NS 5	*What are the principles of human closed-loop brain interfaces for vision and action?*
NS 5-1	*NS 5-1 Brain interface to restore vision for the blind (What are the principles of human closed-loop brain interfaces for vision and action?)*
NS 5-2	*NS 5-2 Brain interface for locked-in patients (What are the principles of human closed-loop brain interfaces for vision and action?)*
NS 6	*What are the brain circuits of social transmission of emotion?*
NS 7	*How do emotions propagate in a social group?*

Table 1. Overview of the WP 1 Neuroscience specific aims

In the initial year of DBI², the focus was primarily on identifying and establishing pertinent collaborations, as well as on developing and refining the methodology, experimental setups, and conditions necessary for testing the central hypothesis and conducting experiments related to rodent work in NS1, 2, 4-2, 4-3, 6, and 7. Furthermore, this period was devoted to recruiting candidates who would play a significant role in driving the projects forward. As a result, eight junior researchers were hired during the first year in WP 1.

Regarding setting up the experimental conditions, the following efforts have been made:

NS 2 (PIs: Olafsdottir, Hoebeek)

- Building and testing the continuous rodent tracking paradigm
- Building analysis routines for the cylinder-rearing task
- Analysing two cohorts of mice with early brain damage for the cylinder-rearing task
- Implementation of wireless electrophysiological recordings in rodents (mice, rats)

NS 6 (PIs: Gazzola, Olafsdottir, Hoebeek, Battaglia)

- Building the ultrasound imaging setup for the recording of emotional contagion in rats, while at the same time monitoring behavioural responses, such as body and tail movements, running, pupil dilation and facial expressions. The setup will also allow for closed-loop implementations.
- Testing the impact that body motion has on data quality, and optimization of the data analysis pipeline, including registration of images across animals and to the reference atlas.
- Testing the impact of tail shock and the quality of the ultrasound imaging, which is necessary to test the self-experience of pain, but that is potentially a source of noise on the images.
- Obtaining pilot ultrasound imaging data during emotional contagion
- Initiating a collaboration with NERF in Belgium, which will allow for simultaneous ultrasound imaging recording of two awake and interacting (despite the head fixation) animals.
- Optimizing the pipeline for automated pupil dilation and facial expression analyses
- Acquired Neuropixels 2.0 for simultaneous recording from two brain regions, and designed the implant for chronic implantation.
- Integration of a head-mounted video camera for facial recordings into the Neuropixels chronic implant in rats.
- Obtaining pilot data from the newly built Neuropixels system from ACC, prelimbic and infralimbic during emotional contagion, and bilateral hippocampus for social fear learning testing

NS1 (PIs: Vinck, Battaglia)

- Developing machine learning algorithms for the detection of cortical (K-complexes) and hippocampal (sharp wave/ripples) states for closed-loop suppression
- Defining the behavioural paradigm for testing recent and remote spatial memories in mice, which will be used to probe the effect of closed-loop cortical state disruption.
- Acquisition and setting up of an ONIX data acquisition system for closed-loop stimulation

NS7 (PIs: Gazzola, Vinck, Battaglia)

- Testing pipelines to analyse rat's vocalization during mother-pup interactions.
- Determining the best pipeline to analyse entropy in mother-pup interactions.
- Analysing existing data to understand whether early life stress affects emotional contagion.
- Optimising analyses pipeline of a digital version of Paxinos rat brain atlas to automatically perform cell counting of the region of interests
- Initiating a collaboration with Karim Benchenane in Paris to add heart rate variability in the characterization of an emotional state

NS4-2 and 4-3 (PIs: de Zeeuw, Narain)

- Development of a new electrophysiology experimental set-up
- Refinement and optimisation of existing behavioural tests

NS5-2 (PIs: Ramsey, van Steensel)

- Building and testing an offline speech decoding model using intracranial human brain data.
- Preparing a transition to an online closed-loop setting for speech decoding in a person with a brain implant
- Developing a map of speech motor programs on the sensorimotor cortex to inform the speech decoding models.

Pipelines and knowledge developed over NS 1, 2, 6 and 7 are already discussed and in part shared across the different groups and locations. Several collaborations within WP 1 have been reinforced and developed, e.g. between the following pairs of groups.

- Battaglia and Gazzola;
- de Zeeuw and Narain;
- Hoebeek and Olafsdottir;
- Vinck and Battaglia

Concerning the non-human primate and rodent work described in NS3 (PIs: Pennartz, Roelfsema, Vinck) and NS5-1 (PIs: Roelfsema, Pennartz), the following was achieved:

- Acquisition of several components for the development and implantation of several high channel-count (MRI-compatible) electrode implants. Experiments will be run with these next-generation implants in non-human primates.
- Acquisition of one monkey, which will be trained and used in experiments in the coming years.
- Improvement of the existing experimental setup to train two monkeys.
- Initiation of the training and preparation of the two monkeys for experiments in the coming years.
- Development of perceptual and multisensory rodent (mouse) tasks in combination with multi-electrode recordings and optogenetics
- Selection and acquisition of an all-optical setup for 2-photon imaging and optogenetics in task-performing mice
- Validation of cortex-wide optogenetic scanning technique in combination with visual detection task.

Collaboration between WP 1 and other work packages has also been reinforced and developed over the first DBI² year. In particular:

- Between WP 1 and WP 3 (e.g. Gazzola's lab and Giagka's lab for testing the transparency of new bio-electrical material to ultrasound imaging; Gazzola and Serdijn for the development of miniaturized vocalization sensors)
- Between WP 1 and WP 2 (e.g. Tangermann's lab and the following WP1's lab: Battaglia, Stella, Ramsey, van Steensel, Kappen; Vink and van Gerven; Ramsey and van Gerven for human brain decoding models)

2.1.2 Work package 2 | Computational methods

Table 2 lists the scientific goals for WP 2 (Work Package 2) were defined in the project proposal.

CS1	*Feature extraction of neural and behavioural data*
CS1-1	*Automated behavioural recognition | Detection, characterization and segmentation of states (key PIs: van Gerven, Tangermann)*
CS1-2	*Neural decoding / "Brain reading" (key PIs: van Gerven, Güçlü, Tangermann)*
CS1-3	*Nonlinear dynamical systems and manifold learning (PIs: Narain, van Gerven)*
CS2	*Computational models for the development and validation of neural closed-loop control*
CS2-1	*Neural Models: single neuron and ensemble models (key PIs: Zeldenrust, Jafarian)*
CS2-2	*Model validation of closed-loop feedback control | Stability and plasticity (key PIs: van der Helm, Jafarian, Schouten, Kappen, van de Ruit)*
CS2-3	*Machine learning and control theoretical methods for neural control (key PIs: van Gerven, Tangermann, Kappen, van der Helm, van de Ruit)*
CS3	*Implementation*
CS3-1	*Neural Data Analysis | Neurophysiological data acquisition, extraction, and inference (key PIs: Strydis, van Gerven, Battaglia)*
CS3-2	*Edge computing (key PIs: Strydis, Serdijn, Battaglia)*

Table 2 Overview of the WP 2 Computational Methods specific aims

The WP 2 team's contributions span across the original goals, with notable advancements in the fields of neuroscience and computational modelling.

CS 1-1 (PIs: van Gerven, Güçlü)

- Neural system identification using Stuart-Landau oscillator models
- Development of framework for simulation of neural systems, alongside the initiation of a neuroscience-dedicated software package
- Initial development of software stack for on-chip learning
- Postdoc submitted a paper on modelling as the first author. PhD candidate Siddharth Chaturvedi submitted a paper on optimal foraging.
- Yuzhen Qin submitted a paper on simulating epileptic seizures.

CS 1-2 (PIs: Tangermann)

- Two publications on unsupervised decoding models and transfer learning frameworks for BCI datasets further contribute to this domain.
- Development of DAREPLANE software platform, signifies a concerted effort toward adaptive brain stimulation.

CS 1-3 (PIs: Narain)

- Developed a new manifold learning technique, Riemannian Alignment of Tangent Spaces (RATS) that advances low-distortion low-dimensional embeddings of topological objects.
- Published findings in Nature Communications, detailing functional classification of heterogeneity in neural activity within the cerebellar cortex.
- Invited review on Neural Manifolds accepted at Nature Neuroscience
- One DBI^2 project presented at Cosyne 2023 and two projects presented at Cosyne 2024

CS2-1 (PIs: Zeldenrust)

- Developed models of whisker system to understand the complex roles of the brain stem and thalamus beyond traditional views as mere relay stations.
- Demonstrated the importance of heterogeneity and diversity in neural properties for enhancing the computational capacity of networks through increased dimensionality of neural response.
- Highlighted the potential role of neuromodulators like dopamine in augmenting computational abilities by affecting specific subsets of neurons.
- Provided foundational insights for the development of closed-loop experiments to further explore neural processing.

CS2-1 (PIs: Heida)

- Investigation of freezing of gait in Parkinson's: Focused on understanding the mechanisms behind the freezing of gait and the effects of cueing as a therapeutic intervention.
- Development of mouse model: appointed a PhD student to develop a mouse model for studying the freezing of gait.
- Computational modelling of neuronal network: Conducted computational models to explore the neuronal network involved in gait, contributing to understanding the underlying mechanisms.

CS2-2 (PIs: Jafarian, van der Helm, Schouten, van de Ruit)

- Obtaining approval for an fMRI-EEG validation study
- Validation of 4D EEG setup
- Development of a linear state space brain connectivity model to analyse cortical activity during motor tasks.

CS2-3 (PIs: Strydis, Battaglia, Serdijn)

- Specification and design of extended OpenEphys-2 system, imbued with high-speed GPU support.
- Development and successful integration of OpenEphys-2 extensions for AI-algorithm support and closed-loop control using GPU platforms and GPUDirect high-speed links.
- Validation and evaluation of extended OpenEphys-2 system (ongoing), development of DBI2 use-case descriptions and future steps.
- Initial literature study and exploration of surrogate modelling for the reduction of biologically plausible brain models into AI-fueled (and neuroODE-based), energy-efficient kernels as single-neuron and network model stand-ins.

Overall, the WP 2 team's interdisciplinary efforts across different universities and research groups illustrate a comprehensive approach to tackling the complexities of neural processing, computational modelling, and the development of therapeutic interventions for neurological disorders.

2.1.3 Work package 3 | Neurotechnology hardware

Table 3 delineates the scientific goals of WP 3 (Work package 3) defined in the project proposal.

TS1	*Hardware for the naturalistic behaviour (Nat-B) lab; system integration*
TS2	*Microfabricated multi-modal neurostimulator technology for ensembles of neurons and single-cell resolution*
TS3	*Flexible ultrasound-phased array design for ultrasound-based stimulation of deep brain circuits*
TS4	*Pliable/flexible/stretchable freely floating active electrode array technology*
TS5	*Electronics for large-scale (100,000+) single-cell resolution bi-directional neural interfaces*
TS6	*Directional magnetostatic wireless power and data transfer*
TS7	*Using non-linear cell properties to arrive at effective electrical stimulation using beamforming at multiple frequencies*
TS8	*Specification, design & piecemeal implementation of DBI2 final platform components including CPU-FPGA partitioning/coupling aspects, as well as algorithmic aspects (spike sorting, signal processing, deep learning, DSS etc.)*
TS9	*Microchips to be placed above the dura mater for focused ultrasound brain stimulation and functional ultrasound neuronal recording with high-spatial resolution and whole-brain coverage.*
TS10	*Pliable/flexible/stretchable freely floating active electrode array technology for longitudinal (chronic) use*
TS11	*Electronics for fully-implantable brain imaging*
TS12	*Thermal energy harvesting and subcutaneous ultrasound wireless power transfer electronics*
TS13	*MRI and US compatibility of multiple and multimodal stimulation modalities and minimizing the interference*
TS14	*Advanced DBI2-platform aspect design; security provisions for reliable chip operation, wireless communication, implant-to-cloud continuum etc.*

Table 3 Overview of WP3 Neurotechnology hardware specific aims, (TS 9 - 14 are to be executed in the 2nd phase of the DBI², which is from Year 6 till Year 10)

In the pursuit to develop next-generation electroceuticals/neurotech and to perform research at the convergence of biology and electronics, we have now made concrete steps towards the realisation of a biological measurement lab. The lab will facilitate the much-needed ‘bridge’ between disciplines and allow for functional (in vitro, ex vivo) testing of our microelectronic devices on/with live biological material. In May 2023 we hired a biologist/laboratory manager (Chris S. Vink, PhD) who will be responsible for establishing and operating the lab. He commenced his role in September 2023.

In the 1st phase of DBI², i.e., the first 5 years, the scientific work in WP 3 is subdivided into 8 tasks (TS1 to TS8). The progress on these tasks is reported below.

- TS1: System integration into the Open E-Phys hardware for the naturalistic behaviour lab: The work has started in year 1 with the setting up of a next-generation “ONIX” system. We have begun to rewrite hardware drivers and other software components to enable fast implementations of machine learning algorithms (using GPUs) in the context of closed-loop electrophysiology experiments.
- TS2: Multi-modal neural interfaces for increased specificity and energy-efficiency
  In the past year, TS2 has made foundational strides in the development of neural interfaces for multimodal brain interaction. We've expanded our team by hiring a postdoctoral researcher (Christos Pavlou, PhD) and two master students specializing in the fabrication of these advanced interfaces based on graphene. The design phase of the graphene-based neural interfaces has been concluded, and it is now (Feb. 2024) in the midst of the fabrication process.

Initial efforts were showcased at the first general assembly of the DBI² project (Sep. 26/27, 2023) and the Microelectronics Research Day at TU Delft (Nov. 9, 2023), reflecting the commitment to academic excellence and collaborative research. A partnership with the company Bi/iond has been established to utilize their state-of-the-art facilities for biocompatibility testing, marking a significant collaboration that leverages external expertise and resources.

- TS3: Flexible ultrasound phased arrays for ultrasound-based stimulation of deep brain circuits
  This task started in Year 2.
- TS4: Conformally coated miniaturised active implants for long lifetimes
  This task started in Year 2.
- TS5: Electronics for massively parallel neural interfaces
  - A PhD student (Arash Akhoundi) has been hired.
  - A review of literature focused on on-chip compression and processing of neural recordings has been conducted. The chosen approach involves utilizing compressive ADC (Analog-to-Digital Converter) in conjunction with a Neural Signal Processor.
  - The Wired-OR read-out scheme has been chosen as the compressive readout strategy, and its scalability is analysed across various datasets. The findings of this analysis are published in The IEEE Transactions on Biomedical Circuits and Systems journal [https://doi.org/10.1109/TBCAS.2023.3292058].
  - A neural signal processor, designed to be compatible with the Wired-OR output, has been developed for spike sorting utilizing the spatial feature space. The chip has been sent for fabrication, and simulation results indicate a reduction of more than 10 times in power consumption and area usage compared to other state-of-the-art solutions.
- TS6: Directional magnetostatic wireless power and data transfer
  Achievements for Year 1:
  - A PhD student (Kimia Ahmadi) has been hired;
  - A literature survey on wireless power transfer methods has been conducted; and
  - a suitable wireless power transfer technique has been selected: optical (instead of magnetostatic) wireless power transfer.
- TS7: Technology for effective electrical stimulation using beamforming at multiple frequencies:
  - A PhD student (Paria Mansourinezhad) has been hired;
  - In the first year, the focus of our research was to investigate the impact of uncertainties in brain tissue conductivities on the intensity of the temporal interference electric field at the target site, specifically the right hippocampus. Utilizing a highly detailed head model, the MIDA model, we introduced probability distributions for six major tissue conductivities. Subsequently, we conducted Monte-Carlo simulations to perform a comprehensive uncertainty analysis. The findings revealed a crucial insight: uncertainty in tissue conductivities resulted in a notable decrease in the targeting accuracy of TI stimulation. Specifically, we observed a decrease from 87% to 65% in accurately targeting the right hippocampus. Interestingly, non-targeted regions remained relatively consistent at 18%.
  - Building upon these findings, our next objective is to delve deeper into understanding which conductivity values contribute more substantially to uncertainties in the resultant electric field. This endeavour aims to better incorporate uncertainties into experimental setups, enhancing the robustness of simulations and subsequently improving the reliability of conclusions drawn from experiments.
- TS8: closed-loop, neuro-controller platform for the Nat-B lab
  This task started in Year 2.

2.2 Workgroups

2.2.1 Nat-B Lab Workgroup

Over the first year of DBI², much effort has been made to have a first drawing of the NAT-B Lab environment with a list of measures that will be taken, at least during the first use of this environment. This process was done in collaboration with colleagues from several Dutch universities to think of ways in which the NAT-B Lab environment could be used in the future as a facility for the NL and Europe. A consortium has been built for this purpose, and a grant application will be submitted in April 2024. DBI² will remain the driving force for the development of techniques that will allow neuronal and physiological online (and close-loop) recordings. The NAT-B Lab environment will serve as a testbed for these advances. The PIs and affiliated researchers involved at this stage are Battaglia, Olafsdottir, Englitz, Hoebeek, Witter, Gazzola, Keysers, Serdijn, and Michon. Below is a list of practical and technical achievements over the first year:

- Design of a smaller version of the Nat-B environment (suitable to host a rat litter and track the behaviour of the dam and the pups), including video and RFID-based position tracking, ultrasound vocalization recording and localization, and electrophysiology recording. One PhD student has been hired to work at this (who started in Year 2)
- Identification of one interim platform for electrophysiological recording (while we wait for the devices developed in WP3) in the Evolocus data loggers
- Integration of the ultrasound vocalization localization system HyVL (from affiliated researcher Englitz) in the NAT-B technological environment
- Integration of automated video-tracking efforts across labs (mostly RU, NIN, UMCU).

2.2.2 Closed-Loop Stimulation Workgroup

A Cross WP workgroup has been constituted to speed up the development of the first closed-loop electrophysiology experiment. The activities that took place in Year 1 were the following:

- Acquisition and deployment of an ONIX Open-Ephys data acquisition system (PI Strydis, Battaglia
- Analysis of the Open Ephys hardware and software and design of a software interface capable of running complex GPU machine learning-oriented workflow in the signal processing loop of the data acquisition system (PI Strydis)
- The design of a behavioural task for the testing of hypotheses of the effect of different closed-loop disruptions of cortical activity on memory. An affiliated PhD has been recruited for this work (PIs: Battaglia, Vinck, in collaboration with SAB member McNaughton)
- The design of pattern recognition algorithms for the detection of activity phenomena in the cortical local field potential. (PIs: Vinck, Battaglia)

2.3 Programme Office

The programme manager, Soo Kyung Shin was hired in February 2023 to lead the DBI^2 project management, event organisation, communication and data management. The following progress has been made by the Programme office in Year 1.

2.3.1 Networking and Outreach

Since the programme was in its initial phase, the DBI^2 programme office focused primarily on internal networking opportunities. To gain a deeper understanding of the research plan and laboratory setups between different groups, the programme office organised site visits and meetings at TU Delft, UMC U, NIN, and Erasmus MC. Besides, the programme office organised a meetup of junior researchers in August 2023 to introduce each other and discover new collaboration opportunities. The first Annual Retreat, held in September, provided a valuable opportunity for DBI^2 consortium members to network and refine the collaboration plan as well.
Externally, as part of networking efforts, the DBI^2 consortium reached out to the ESDiT (Ethics for Socially Disruptive Technology) programme. ESDiT is one of the Gravitation research programmes launched in 2020. One of their research lines, Human Conditions, delves into philosophical questions regarding BCI. In July 2023, DBI^2 and ESDiT agreed to collaborate on organizing academic workshops and possibly a public outreach event in the coming years. Joel Anderson, the leader of the Human Conditions research line, has been invited to join as a member of the Scientific Advisory Board (SAB). This collaboration is expected to provide an opportunity for the DBI^2 consortium to reflect on ethical concerns in the early research phase.

2.3.2 Programme management

From March 2023 onward, the high-level programme governance structure has settled. The Steering Committee meeting is held monthly. Meeting documents and action lists have been systematically maintained. The first Data Management plan was produced and submitted to NWO. In February 2023, MS Teams was introduced as an internal communication channel, and OneDrive was chosen to store documents. However, due to accessibility issues for non-RU users, Slack replaced MS Teams, and SufrDrive was adopted instead of OneDrive in November 2023.

3. Plan for the next period (Year 2 | Oct 2023 – Sep 2024)

3.1 Work Packages

3.1.1 Work Package 1 | Neuroscience – Year 2 Plan

Main activities

In general, Year 2 will continue to include optimisation of experimental set-ups and integration of a variety of technologies for neural recording that will allow for new data to be recorded. It will also allow for the finalisation of work performed in Year1, and to offer some new hiring opportunities. More specifically the following actions will be taken:

NS2 (PIs: Olafsdottir, Hoebeek)

- Two more cohorts for analysis in cylinder rearing task
- Refinement of automatization for cylinder rearing task
- First cohort(s) of animals with early brain damage in Live Mouse Tracker
- Literature research on social behaviour in juvenile mice (together with a BSc student)
- Writing custom analysis routines for social interactions in juvenile mice for Live Mouse Tracker
- First electrophysiological recordings in juvenile animals
- Set up wireless recording in pre-weaning rat pups.
- Set up home cage video and audio recording; along with RFID tracking, to chart the development of behaviour and dam-pup interactions - starting from birth and continuing up to ~8 weeks.

NS6 (PIs: Gazzola, Olafsdottir, Hoebeek, Battaglia)

- Setting up a harm aversion paradigm with water droplets grasping
- Setting up a working and sharable pipeline for the analyses of facial expressions both in head-fixed and freely moving rodents (head-mounted camera)
- Having a method Biorxiv paper on the ultrasound set-up
- Writing the first ultrasound manuscript on emotional contagion
- Having pilot data on ultrasound simultaneous recording during emotional contagion
- Setting up a learning paradigm with three freely moving rats, and prepare for electrophysiology or wireless calcium imaging recording
- Finalising the Neuropixels dataset for the in-depth characterisation of the neuronal responses during the emotional contagion
- Testing ultrasound transparency of bio-compatible electrodes made by the group of V. Giagka

NS1 (PIs: Vinck, Battaglia)

- Validation of behavioural protocol for testing recent and remote spatial memories (including testing the role of the hippocampus with pharmacogenetic inhibition)
- Setting up and validation of closed-loop stimulation paradigm on the Onix system
- Experiments testing how closed-loop suppression of cortical state may differentially affect recent and remote memories.

NS3 (PIs: Pennartz, Roelfsema, Vinck)

- Testing of a new type of electrode that targets the LGN
- Testing of a new method to measure consciousness elicited by electrical microstimulation in monkeys during fMRI measurements
- Testing of consciousness elicited by electrical stimulation of SEEG electrodes or grids in patients that are implanted for epilepsy
- Operational deployment of an all-optical setup for 2-photon imaging and optogenetics in vivo

- First results on cortex-wide optogenetic scanning technique in combination with visual detection task.

NS7 (PIs: Gazzola, Vinck, Battaglia)

- Writing the manuscript on the effect of early life stress on emotional contagion
- Writing the manuscript on the digital Paxinos rat atlas for automatic cell counting
- Integrating the measure of heart rate into experimental designs and testing to understand whether it would be an informative measure to characterise different types of stress
- Implementation of an auditory tracking system

NS4-2 and 4-3 (PIs: de Zeeuw, Narain)

- Tackling the descending cerebrocerebellar circuit by studying the contributions of the cerebral cortex to cerebellar function that are mediated via the inferior olive.
- Aim at understanding how supervised learning can be implemented not just in the cerebellum but through brain-wide control.

NS5-2 (PIs: Nick Ramsey, van Steensel)

- Completing the implementation of the online closed-loop speech decoding in a locked-in person with a brain implant
- Testing online speech decoding in a locked-in person with a brain implant

NAT-B lab

- Testing whether we could record vocalisation through a subcutaneous microchip

Main outputs

NS2 (PIs: Olafsdottir, Hoebeek)

- Publication on automatisation of cylinder rearing task
- Analysis results from two more cohorts in the cylinder-rearing task.
- Custom analysis routines for social interactions in juvenile mice.
- First electrophysiological recordings in juvenile animals.
- Development of wireless recording set-up for pre-weaning rat pups.
- Comprehensive data on home cage video, audio recording, and RFID tracking to chart behaviour and dam-pup interactions from birth up to ~8 weeks.

NS6 (PIs: Gazzola, Olafsdottir, Hoebeek, Battaglia)

- Method paper on the ultrasound setup to be published on bioRxiv.
- First manuscript on ultrasound studies of emotional contagion.
- Pipeline for the analysis of facial expressions in animals.
- Pilot data on ultrasound simultaneous recording during emotional contagion.
- Neuropixel dataset for in-depth characterisation of neuronal responses during emotional contagion.

NS1 (PIs: Vinck, Battaglia)

- Validation results of behavioural protocols for spatial memory testing.
- Implementation and validation of a closed-loop stimulation paradigm on the Onix system.
- Findings on the effects of closed-loop suppression of cortical state on recent and remote memories.

NS3 (PIs: Pennartz, Roelfsema, Vinck)

- Testing results for a new type of electrode targeting the LGN.
- New methods for measuring consciousness during electrical micro-stimulation in fMRI in monkeys.
- Results from tests of consciousness using electrical stimulation in epilepsy patients.
- Initial findings from the all-optical setup for in vivo 2-photon imaging and optogenetics.
- First results on cortex-wide optogenetic scanning in visual detection tasks.

NS7 (PIs: Gazzola, Vinck, Battaglia)
- Manuscript on the effect of early life stress on emotional contagion.
- Manuscript on the digital Paxinos rat atlas for automatic cell counting.
- Integration of heart rate measures into experimental designs for stress characterisation.
- Implementation of an auditory tracking system.

NS4-2 and 4-3 (PIs: de Zeeuw, Narain)
- Research findings on the contributions of the cerebral cortex to cerebellar function via the inferior olive.
- Insights into the implementation of supervised learning through brain-wide control.

NS5-2 (PIs: Nick Ramsey, van Steensel)
- Completion of online closed-loop speech decoding in a locked-in person with a brain implant.
- Testing of online speech decoding in a locked-in person with a brain implant.

3.1.2 Work package 2 | Computational methods – Year 2 Plan

Main activities

The van Gerven group (Radboud University) plans to evaluate the approach developed in Year 1, towards goals CS1-2 and CS2-3, focusing on the framework for modelling and controlling simulated neural systems, using real-world datasets. They also intend to extend this approach to model multiple neural populations and develop a method for the analysis of modelled systems. Furthermore, they will conceptualise and develop a proof of concept for a new multi-agent foraging virtual environment using end-to-end parallelisation methodology with JAX. Assistant Professor Yuzhen Qin will continue theoretical studies on vibrational control in network systems (towards CS2-2) and investigate the origins of epilepsy through the lens of network pathology to gain deeper insights. Moreover, strategies for brain stimulation aimed at mitigating excessive synchronisation in epileptic brains will be explored by harnessing vibrational control theory (towards CS2-3). Umut Altin, the AI Engineer will work on deep learning inference and training using a System-on-Chip implementation (CS3-2). A postdoc is projected to be hired soon. The postdoc will work on enabling machine-learning applications throughout DBI² based on recent machine-learning advances in the van Gerven group.
The Tangermann group (Radboud University) plans to hire a PhD candidate and set up a simulation environment for closed-loop parameter optimisation. (CS2-2)

In Year 2, **the Narain group (Erasmus MC)** is preparing a manuscript detailing their discovery of how the cerebellar cortex encodes temporal statistics of prior distributions. Additionally, they are in the process of developing their first closed-loop cortical stimulation setup and hiring a postdoc to further this research goal. Another manuscript is being prepared to share their discovery of cortico-cerebellar interactions in closed-loop motor timing behaviours. (CS2-1)

The van der Helm Group (TU Delft) is gaining insights into the validity of 4DEEG assumptions using neural network models from December 2023 until the end of December 2024. Additionally, they will collect data for fMRI-EEG validation of the 4DEEG methodology in April and May 2024. This will be done with the help of a PhD candidate and postdoc starting in September and December 2023. From the second half of 2024, they will work on the frequency domain description of cortical information flow, followed by pilot testing of temporal interference stimulation with TU Eindhoven (Rob Mestrom, WP 3). (CS1-3, CS2-2, 2-3)

In the upcoming period, **the Heida group (Twente University)** will set up the lab for experimental studies on freezing/gait problems in a Parkinson's disease (PD) mouse model. They are in search of the best PD model to use, such as 6OHDA or other models, to identify Parkinson-related gait problems and test the effects of cueing. Additionally, they will establish the lab with a video/tracking system and experimental protocols to test gait patterns in mice (CS1-3). Furthermore, a CCD proposal (animal experimentation ethical approval) will be written and submitted.

Year 2 Main outputs

The van Gerven Group (Radboud University)
- Publication on control of network systems.
- Publication on understanding epilepsy from a network-pathology perspective.
- Two academic papers on system identification for neural systems.
- Publishing the first version of the current in-development package for modelling in neuroscience.
- GitHub repositories for modelling neural systems, modelling natural behaviour and FPGA compilation.
- Development of a Deep Learning inference and training compiler for System on Chip (publication in progress).

The Tangermann Group (Radboud University)
- Identification of collaboration scenarios for closed-loop parameter optimisation.

The Narain Group (Erasmus MC)
- Publication on implicit/explicit learning in cortico-cerebellar closed-loop
- Publication on Riemannian Alignment of Tangent Spaces
- Open-source code for RATS on Github
- Publication on temporal statistics in cerebellar cortical representations
- One patent application to be submitted.

The van der Helm, van de Ruit Group (TU Delft)
- September 2024: First results of fMRI validation of the 4DEEG approach.
- December 2024: First frequency domain description of cortical information flow.
- December 2024: Insights into the validity of 4DEEG assumptions.

The Heida Group (Twente University)
- Completion of research and educational plan of Matthijs Hulsebos by the end of April 2024.
- Approval of DEC proposal around September 2024.
- Setting up the lab environment for mouse research around August 2024.

3.1.3 Work package 3 | Neurotechnology hardware – Year 2 plan

Main activities

The Year 2 research plan focuses on developing and refining neural interface technologies. A technician will design a head-stage for animal vocalisation recording. Efforts in graphene-based neural interfaces include prototype creation, performance characterisation, and biocompatibility testing aiming for preclinical trials. Two PhD candidates will respectively work on calibrating ultrasound phased arrays for brain stimulation and studying neuromodulation effects. Further tasks involve validating a spatial spike sorting chip, exploring optical wireless power transfer, enhancing Temporal Interference (TI) stimulation through conductivity analysis, and improving the Open-Ephys platform with GPU acceleration and developing a new spike-sorting algorithm, potentially for use with memristor chips. Below are the detailed research activities per research aim.

- Task TS1: A technician will be hired for this position and a first demonstrator of a headstage that will enable the recording of vocalisation of group-housed animals will be designed.
- Task TS2:

  We will concentrate on three primary activities critical to advancing our graphene-based neural interface technology:
  - Our initial objective is to fabricate the first prototype of our graphene-based neural interface device. This milestone will serve as a tangible proof-of-concept and a springboard for iterative development and refinement. This prototype will be offered to the consortium for collaborative experiments.
  - Our second action involves an in-depth characterisation of the graphene-based neural interfaces' performance. We will employ established techniques such as UV-Vis transparency, cyclic voltammetry (CV), current-sensing ion-selective electrode (CIS), and signal-to-noise ratio (SNR) assessments. This characterisation is crucial for fine-

  - tuning the device's functionality and for ensuring its reliability and effectiveness in real-world applications.
  - In Vitro Biocompatibility Tests: Concurrently, we aim to rigorously evaluate the compatibility of our neural interfaces with living neural tissues. Through a comprehensive series of in vitro tests, we intend to establish a biocompatibility index. Our goal is to achieve a threshold exceeding 95%, which will affirm the interfaces' safety and efficacy, thereby paving the way for subsequent preclinical trials.
- Task TS3: A PhD student has been appointed (Samuel Desmarais), who will start his research by
  - studying methods for calibration two-dimensional ultrasound beamforming from two-dimensional ultrasound phased-arrays with non-uniform curvatures.
  - The outcome will be a flexible and conformable two-dimensional ultrasound phased array that can focus accurately in three dimensions despite not having a flat geometry. The calibration will be optimised for the flexible and conformable array to be placed under the skull of a mouse, following its curvature, for high-precision and high-spatial reconfigurability brain stimulation in freely moving animals.
  - We will submit the fabrication method of the array to IUS 2024 (April 12 2024 deadline), and then
  - expand it to the "IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control" journal with the acoustic validation of the calibration method.
  - Meanwhile, we will seek collaborators within DBI2 for in vivo experiments towards the demonstration of high-precision brain stimulation, for which the outcome can be a publication in the journal "Ultrasound in Medicine and Biology".
- Task TS4: A PhD student has been appointed (Niloufar Behzadpour), who will start her research by
  - setting up an experimental platform to investigate the effect of US neuromodulation together with electrical stimuli on brain tissue
- Task TS5:
  - We will conduct measurements on the Spatial Spike Sorting chip across diverse datasets to validate the simulation results regarding sorting accuracy and power usage;
  - We will develop an algorithm to utilise the outcomes of the spatial spike sorting process for adjusting the Wired-OR wiring scheme aims to enhance recording precision and enable targeted cell group activity recording; and
  - We will Initiate both the simulation and implementation phases of the reconfigurable Wired-OR system.
- Task TS6:
  - We will write a review paper on concepts of optical wireless power transfer methods;
  - We will investigate the use of commercially available photovoltaic (PV) cells and the applicability of PV cells under investigation at another department of TU Delft to design and implement the first optical wireless power transfer receiver based on off-the-shelf components;
  - We will design a first prototype for the optical transmitter design;
  - We will conduct optoelectronic simulations with COMSOL Multi-Physics of the optical wireless link; and
  - We will design, implement and opto-electronically test a first head-mounted optical receiver.
- Task TS7:
  We will provide stronger evidence regarding the focused stimulation nature of TI stimulation and its efficacy, initiating the pathway toward the practical integration of TI in clinical settings. To this end, we will conduct an uncertainty analysis to examine the impact of variations in brain tissue conductivities on the resulting Temporal Interference electric field at the modelling and simulation level. To enhance experimental and clinical results, numerical techniques such as the finite element method (FEM) are commonly employed to simulate the electric fields generated by TI stimulation. These numerical simulation techniques heavily depend on the electrical conductivities of brain tissues. However, accurately representing the tissue conductivities in these models presents a challenge due to disparities in brain tissue conductivities reported in the literature. These disparities arise from variations in measurement techniques, experimental protocols, and individual

differences among subjects, making it difficult to predict the electric field of TI stimulation with precision.

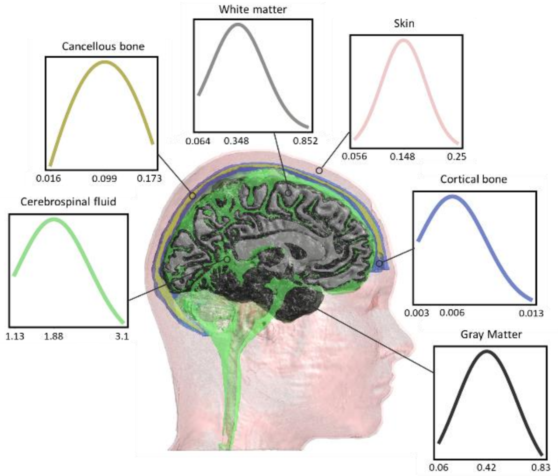

Figure 2 Conductivity distributions per tissue in S/m

- Task 8:
    - A postdoc (River Betting) has been hired.
    - We will extend the Open-Ephys 2.0 platform with GPU acceleration (initial working setup, limited throughputs);
    - We will develop a spike-sorting algorithm running on a microPCB for mouse neural recording;
    - (potentially) this algorithm will be ported to a memristor chip

Main outputs

- Milestones/deliverables
    - First prototype of our graphene-based neural interface device (TS2)
    - A flexible and conformable two-dimensional ultrasound phased array that can focus accurately in three dimensions despite not having a flat geometry (TS3)
    - Experimental platform to investigate the effect of US neuromodulation together with electrical stimuli on brain tissue (TS4)
    - Spatial Spike Sorting Chip (TS5)
    - Prototype of an optical wireless power transmitter for the Nat-B Lab (TS6)
    - Prototype of a head-mounted optical wireless power receiver for use on freely moving animals in the Nat-B Lab (TS6)
    - Open-Ephys 2.0 platform extended with GPU acceleration (initial working setup, limited throughputs) (TS8)
    - spike-sorting algorithm running on microPCB for mouse neural recording (TS8)
- Journal papers:
    - Journal paper on the in-depth characterization of the graphene-based neural interfaces' performance (TS2)
    - Journal paper on the flexible and conformable two-dimensional ultrasound phased array with the acoustic validation of the calibration method, to be submitted to IEEE TUFFC (TS3)
    - Journal article detailing the development and performance evaluation of a compressive ADC combined with a spatial spike sorting chip (TS5)
    - Review paper on optical wireless power transfer to freely moving rodents, such as can be found in the Nat-B lab (TS6)
    - M. A. Siddiqi, D. Vrijenhoek, L. P. L. Landsmeer, J, van der Kleij, A. Gebregiorgis, V. Romano, R. Bishnoi, S. Hamdioui, C. Strydis, A Lightweight Architecture for Real-Time Neuronal-Spike Classification, ACM Computing Frontiers 2024, Ischia, Italy. (TS8)
- Presentations:
    - Presentation at the GRC Neuroelectronic Interfaces, March 10-15, Galveston, TX, USA (Vasso Giagka and Christos Pavlou)

- Presentation at the NeurotechEU workshop on "Electrode development for human recordings" in Bonn, May 16-17 (Vasso Giagka, invited)
- Presentation: From Solid State to BioPhysics XI: From Basic to Life Sciences Conference, Cavtat, Croatia, June 9-15 (Vasso Giagka, invited)
- Presentation at the 2024 MRS Fall Meeting & Exhibit, December 1-6, 2024, in Boston, MA, USA (Vasso Giagka, invited)
- Presentation at the nanoGe Conference on Bioelectronic Interfaces: Materials, Devices and Applications (CYBIOEL24), Oct. 22-25, Limassol (Cyprus) (Wouter Serdijn, invited)
- IUS 2024 (TS3)
- Poster presentation at the BeNe Brain Stimulation Congress, Nijmegen, November 16-17, 2023 (TS7)

3.2 Workgroups

3.2.1 Nat-B Lab Workgroup

Main activities

- Testing whether we could record vocalisation through a subcutaneous microchip
- If the funding proposal to build Nat-B Lab environment is accepted by NWO, start with the construction of the habitiats.
- Integration of video, RFID, ultrasound tracking, and electrophysiology in one environment
- Joint development of video tracking workflows (multi-camera, including RFID information)

Main output

- Results from testing vocalisation recording through a subcutaneous microchip.
- Proof of concept of the first NAT-B environment
- Technical report on information integration

3.2.2 Closed-Loop Stimulation Workgroup

Main activities

- Setting up the first platform for CL electrophysiology, based on the ONIX system, with pilot experiments in the mouse
- Setting up and demonstrating online processing from high dimensional data (e.g. Neuropixels probes) with GPU-implemented machine learning models
- Implementing spike sorting-based algorithms for online neural ensemble activity geometry characterisation (based on methods developed in CS1-3)
- Implementing LFP-level CL control algorithms

Main output

- Paper on GPU-based real-time processing of neural data
- Conference presentation of the first proof of concept CL experiments

3.3 Programme Office

3.3.1 Networking and Outreach

Main activities

In Year 2, the roundtable event titled 'The Future of Neurotechnology' will be organised in collaboration with the INTENSE consortium. The event is planned to be held in conjunction with the joint DBI^2 and INTENSE retreat in September 2024. The Roundtable will include a panel discussion followed by a question-and-answer session with the audience, which will consist of members from the DBI^2 and INTENSE consortia. Furthermore, the event will be streamed online to allow public access.

Additionally, plans are underway for a workshop in collaboration with the ESDiT consortium, indicating a commitment to fostering educational and collaborative opportunities within the scientific community.

In terms of networking, a proposal is under consideration to organize an event that connects the academic and business sectors, aiming to enhance collaboration and innovation across different industries.

The FENS Forum 2024, sets for June 2024, will see participation from some DBI^2 researchers at the level of their individual labs. Besides, the company of DBI^2 PI, Lucas Noldus will be presented as an exhibitor. Looking ahead, the possibility of consortium-level representation will be explored for the 2026 conference, reflecting a strategic approach to engagement and collaboration within the scientific community.

Main output

- Organization of two public events: Roundtable: The Future of Neuroscience, and Workshop with ESDiT.

3.3.2 Programme management

Main activities

In Year 2, the programme office will focus on expanding a stable governance structure to the Work Packages levels. Regular work package meetings will be organised. Additionally, we will establish milestones for the programme to track our progress and ensure alignment with our objectives.
As part of our efforts to build a strong community and facilitate synergy among the labs within DBI^2, we will publish a bi-monthly internal newsletter. This newsletter will serve as a platform for sharing updates, achievements, and opportunities for collaboration among team members. Furthermore, to enhance the visibility and awareness of DBI^2 activities among external stakeholders, we will publish a bi-annual public newsletter. This outreach initiative is aimed at keeping our partners, collaborators, and the wider scientific community informed about our progress and breakthroughs.

To improve internal communications and address accessibility issues for individuals not affiliated with RU, we will introduce Slack as our new internal communication tool, replacing MS Teams. This change is expected to facilitate smoother, more inclusive interactions among all consortium members, regardless of their institutional affiliations.

Main output

- A new internal communication channel will be introduced.
- Milestones per Work package, Workgroup, and programme level will be produced.
- Dissemination and communication plan will be published.
- Newsletter will be published bi-monthly internally. The public version of the newsletter will be published bi-annually.

3.3.3 Training for junior researchers

Main activities

From Year 2, DBI^2 training activities will be conducted through two main channels: 1) Lab Visits and Mini-Lectures, and 2) a Training Week targeting junior researchers within the consortium.

Lab Visits and Mini-Lectures are hosted by DBI^2 Principal Investigators (PIs) and consist of 1-2 day visits aimed at acquiring specific knowledge and familiarization with lab setups at hosting sites. These visits are scheduled to occur three times per year. In Year 2, RU, NIN, and TU Delft are set to host these sessions.

The Training Week, organised by and for junior researchers, is a comprehensive one-week retreat led by the Young Talent Council with support from the programme office. Scheduled for the end of April at

Soeterbeeck (near Nijmegen), the week will feature a mix of lectures, hands-on workshops, and a one-day hackathon, designed to enhance both knowledge and practical skills.

Additionally, the programme office is exploring a collaboration with NeurotechEU, a trans-European network renowned for excellence in brain research and technologies. This partnership could enable DBI^2 researchers to develop and participate in specialised training modules hosted on the NeurotechEU platform, potentially including access to NeurotechEU's training lab and other relevant training resources.

Main output

- Lab visit + mini-lectures at 3 sites
- Training week
- A collaboration strategy with NeurotechEU

4. SWOT analysis

	Helpful to achieve the objectives	Harmful to achieve the objectives
Internal origin	**S**trengths • Diverse, state of the art expertise • Collaborative nature	**W**eaknesses • Coordination difficulty • Insufficient funding • Some technological challenges Actions: • The programme manager's working hours have been increased since Year 2. • Regular work package and workgroup meetings to collaborate on common goals and to align on priorities. • Securing additional funding • Fining alternatives to tackle technological weakness
External origin	**O**pportunities • New funding to build Nat-B Lab • Novel technologies to acquire (also via new affiliated researchers)	**T**hreats • Funding cut • Regulatory changes in animal experiments and clinical trials • Public perception and trends • Competition Actions: • The programme office has been in contact with the funding agency since Year 1 to gain insight into mid-term evaluation criteria. Additionally, the programme manager regularly participates in workshops with other Gravitation programme managers to share best practices and other useful information. • Information sharing with public

Table 4 SWOT analysis summary

Strengths
The strength of the DBI² consortium is characterised by the presence of diverse expertise. Also, strong junior talents have been onboarding to the consortium. Real collaborative work has been initiated in clusters within the consortium. The collaborative nature of the project is significant, polling a wide range of expertise from Neuroscience, Computational solutions and Neurotechnology. DBI²'s multidisciplinary approach not only fosters innovation but is also an imperative part of delivering the main outputs of the project.

Weaknesses
Coordination challenges:
Managing a project with numerous stakeholders can lead to logistical and communication challenges combined with limited resources in the programme office. In response to that, the working hours of the programme manager has been increased from 24 hours per week to 32 hours. While the diversity in expertise leads to a variety of solutions, achieving sufficient cohesiveness to fulfil overarching goals may prove challenging. Different priorities and interests within the consortium can influence the research focus, potentially leading to a conflict of interest. The DBI² consortium is attempting to minimise such risks by establishing work packages and workgroups involving multiple institutes with diverse expertise. These groups convene regularly to collaborate on common goals and to align priorities.

Insufficient funding:
The Gravitation funding is not sufficient to support the full-scale implantation of the Nat-B Lab. Without additional funding, the DBI^2 consortium can only deliver the technology to set up the Nat-B Lab but not the Lab itself, which will limit our technology development and valorisation after the closure of the DBI^2.

Technological weakness:
A weakness of temporal interference (TI) could be that its targeting possibilities prove to be insufficient. To overcome this challenge, a systematic investigation of TI targeting, combined with 4D-EEG techniques (van de Ruit, van der Helm, TUDelft) will be set up to validate target engagement in a small group of volunteers.

Opportunities:
To secure the resources to build a Nat-B Lab setup, a new project proposal is under preparation. The ambition is to set the Netherlands in a leading position in ecologically valid laboratory animal research. Furthermore, we aim to continue our affiliated researcher program, to acquire novel technologies and expertise.

Threats:
GO-NOGO moment
The Gravitation funding for the DBI^2 is guaranteed only for the first 5 years of the programme. Funding for phase 2 (Year 6- Year 10), depends on evaluation at a GO-NOGO moment after year 5. Without that extension, the DBI^2 consortium will not be able to deliver the overarching goals of the programme: an integrated Brain-Machine platform to manipulate brain activities.
Successful mid-term review is imperative to prevent such funding cuts, thus the programme office is in contact with the other project managers sponsored by the same Gravitation funding programme to gain more insight into the midterm review process from NWO. The preliminary feedback from other programme managers has been reflected in the programme governance.

Regulatory changes:
Shifting attitudes, at the national and institutional levels, related to animal research and clinical trials, could impose additional constraints on obtaining ethical approval, lab space, and institutional support.

Public perception and social trend
DBI^2 is in the field of “socially disruptive technology”, which is often subjected to negative public opinion or social movements. This is especially pertinent as corporate-led BCI developments, such as Neuralink, garner constant public attention with limited information, thereby raising significant ethical questions and groundless fears among the public. Consequently, this can lead to decreased financial support and increased regulatory scrutiny. In order to provide balanced information on state-of-the-art Neuroscience and BCI technologies, the DB^2 consortium's dissemination activities include media involvement and public workshops.

Competition:
DBI^2 is not the only research consortium focusing on developing brain-computer interface technology. The progress from other research programmes in countries such as Germany, the U.S., China, South Korea, and Japan, can overshadow the DBI^2 impact to be recognised.

5. Overall outlook and conclusions

The first year of such a vast, extended, and intricate project necessitates substantial groundwork in terms of organising both the scientific framework and the governance structure. This includes recruiting new junior talent and enhancing the cohesion among members in a highly diverse consortium, many of whom had not met before.

We have achieved this through numerous online and in-person meetings, highlighted by a highly successful and well-attended retreat in 2023. The two workgroups focused on Closed-loop technologies and the analysis of Naturalistic behaviour are pivotal in the project's development. They are forging closer connections among researchers across the three work packages through well-defined, "proof of concept" subprojects. The initial outcomes from these workgroups are expected by the end of Year 2.

Significantly, the community surrounding DBI² is expanding, both through the mechanisms for affiliated researchers and through new grant applications, as well as collaborations with other projects like INTENSE, ESDiT, and organisations including Neurotech-NL and NeurotechEU. In doing so, we are beginning to fulfil the vision of DBI² as a central node for neurotechnology and neuroscience research in the Netherlands.

In Year 2, we anticipate the emergence of the project's initial results. We expect to see deliverables from WP 2 and WP 3 and will begin to explore their application in experimental settings and potential therapeutic scenarios. We will also witness a significant increase in the number of active junior members, who have already shown great enthusiasm for interdisciplinary collaboration. Additionally, a comprehensive training program for these junior researchers is taking shape.

We view DBI² as a thriving community with a bright future, promising significant contributions to the field.

Appendix A. DBI² Consortium members in Year 1

Table 5 Full list of DBI2 people in Year 1

Full name	Organization	Academic position	Main Work package	Role
Chris de Zeeuw	Erasmus MC	Full professor	WP 1 Neuroscience	PI
Christos Strydis	Erasmus MC	Associate professor	WP 2 Computational methods	PI
Devika Narain	Erasmus MC	Associate professor	WP 2 Computational methods	PI
Luca Mangili	Erasmus MC	PhD	WP 1 Neuroscience	PhD
Staf Bauer	Erasmus MC	PhD	WP 1 Neuroscience	PhD
Christian Keysers	NIN	Full professor	WP 1 Neuroscience	Affiliated researcher
Floor Nelissen	NIN	PhD	WP 1 Neuroscience	Affiliated researcher
Frederic Michon	NIN	Postdoc	WP 1 Neuroscience	Affiliated researcher
Laura Hammock	NIN	Lab manager	WP 1 Neuroscience	Lab manager
Maureen van der Grinten	NIN	PhD	WP 1 Neuroscience	PhD
Pieter Roelfsema	NIN	Full professor	WP 1 Neuroscience	PI
Sjoerd Murris	NIN	Postdoc	WP 1 Neuroscience	Postdoc
Valeria Gazzola	NIN	Associate professor	WP 1 Neuroscience	PI
Ahmed Elgazzar	Radboud University	Postdoc	WP 2 Computational methods	Postdoc
Angela Zordan	Radboud University	PhD	WP 1 Neuroscience	PhD
Antoine Wellink	Radboud University	Other	Not applicable	Other
Bernhard Englitz	Radboud University	Associate professor	WP 1 Neuroscience	Affiliated researcher
Bert Kappen	Radboud University	Full professor	WP 2 Computational methods	PI
Cem Uran	Radboud University	Postdoc	WP 1 Neuroscience	Postdoc
Federico Stella	Radboud University	Assistant professor	WP 1 Neuroscience	PI
Fleur Zeldenrust	Radboud University	Associate professor	WP 2 Computational methods	PI
Francesco Battaglia	Radboud University	Full professor	WP 1 Neuroscience	PI
Hauður Freyja Ólafsdóttir	Radboud University	Assistant professor	WP 1 Neuroscience	PI
Jeroen Bos	Radboud University	Senior researcher	WP 1 Neuroscience	PI
Lennart Verhagen	Radboud University	Assistant professor	WP 2 Computational methods	Affiliated researcher
Lucas Noldus	Radboud University	Full professor	Not applicable	PI
Marcel van Gerven	Radboud University	Full professor	WP 2 Computational methods	PI
Martin Vinck	Radboud University	Full professor	WP 1 Neuroscience	PI
Michael Tangermann	Radboud University	Associate professor	WP 2 Computational methods	PI
Nasir Ahmad	Radboud University	Assistant professor	WP 2 Computational methods	Affiliated researcher
Paul Verschure	Radboud University	Full professor	WP 1 Neuroscience	Affiliated researcher

Sander Keemink	Radboud University	Assistant professor	WP 2 Computational methods	Affiliated researcher
Siddharth Chaturvedi	Radboud University	PhD	WP 2 Computational methods	PhD
Sookie Sookyung Shin	Radboud University	Non academic project member	Not applicable / Project manager	Non academic project member
Umut Altin	Radboud University	AI engineer	WP 2 Computational methods	Non academic project member
Umut Guclu	Radboud University	Assistant professor	WP 2 Computational methods	PI
Yasemin Atil	Radboud University	Non academic project member	Not applicable / Project manager	Non academic project member
Yuzhen Qin	Radboud University	Assistant professor	WP 2 Computational methods	PI
Alfred Schouten	TU Delft	Full professor	WP 2 Computational methods	PI
Arash Akhoundi	TU Delft	PhD	WP 3 Neurotechnology hardware	PhD
Chris Vink	TU Delft	Lab manager	WP 3 Neurotechnology hardware	Non-academic project member
Christos Pavlou	TU Delft	Postdoc	WP 3 Neurotechnology hardware	Postdoc
Dante Muratore	TU Delft	Assistant professor	WP 3 Neurotechnology hardware	PI
Frans van der Helm	TU Delft	Full professor	WP 2 Computational methods	PI
Ioannis Kyriazis	TU Delft	PhD	WP 2 Computational methods	PhD
Kimia Ahmadi	TU Delft	PhD	WP 3 Neurotechnology hardware	PhD
Mark van de Rui t	TU Delft	Assistant professor	WP 2 Computational methods	PI
Matin Jafarian	TU Delft	Assistant professor	WP 2 Computational methods	PI
Tiago Costa	TU Delft	Assistant professor	WP 3 Neurotechnology hardware	PI
Vasso Vasiliki Giagka	TU Delft	Assistant professor	WP 3 Neurotechnology hardware	PI
Wouter Serdijn	TU Delft	Full professor	WP 3 Neurotechnology hardware	PI
Paria Mansouri Nezhad	TU Eindhoven	PhD	WP 3 Neurotechnology hardware	PhD
Rob Mestrom	TU Eindhoven	Assistant professor	WP 3 Neurotechnology hardware	PI
Elena Offenberg	UMC Utrecht	PhD	WP 1 Neuroscience	PhD
Freek Hoebeek	UMC Utrecht	Full professor	WP 1 Neuroscience	PI

Julia Berezutskaya	UMC Utrecht	Postdoc	WP 1 Neuroscience	Postdoc
Laurens Witter	UMC Utrecht	Assistant professor	WP 1 Neuroscience	PI
Mariska van Steensel	UMC Utrecht	Assistant professor	WP 1 Neuroscience	PI
Nick Ramsey	UMC Utrecht	Full professor	WP 1 Neuroscience	PI
Ciska Heida	Universiteit Twente	Associate professor	WP 2 Computational methods	PI
Cyriel Pennartz	Universiteit van Amsterdam	Full professor	WP 1 Neuroscience	PI
Sarvenaz Fatapour (left the project after 3 months)	Erasmus MC	PhD	WP 2 Computational methods	PhD
Zhoushi Liu (left the project after 9 months)	Erasmus MC	PhD	WP 1 Neuroscience	PhD

Table 6 Members of Scientific Advisory Board

Full name	Organization	Academic position	Related work package	Role
Alex Gomez-Marin	Instituto de Neurociencias in Alicante	Associate professor	WP 1 Neuroscience	SAB
Bruce Mcnaughton	University of California	Full professor	WP 1 Neuroscience	SAB
Georges Gielen	Katholieke Universiteit Leuven	Full professor	WP 3 Neurotechnology hardware	SAB
Maria Asplund	Chalmers University of Technology	Full professor	WP 3 Neurotechnology hardware	SAB
Julijana Gjorgjieva	Technical University of Munich	Full professor	WP 2 Computational methods	SAB
Ewelina Knapska	Nencki Institute	Full professor	WP 1 Neuroscience	SAB
Taufik Valiante	University of Toronto	Associate professor	WP 1 Neuroscience	SAB
Maneesh Sahani	University College London	Full professor	WP 2 Computational methods	SAB
Joel Anderson	Universiteit Utrecht	Full professor	Not applicable	SAB

Table 7 Total number of DBI2 people per role and work package (September 2023)

Role in DBI²	NA	WP 1 Neuroscience	WP 2 Computational methods	WP 3 Neurotechnology hardware	Grand Total
Affiliated researcher		5	3		8
Non-academic project member	3	1	1	1	6
PhD		5	2	3	10
PI*	1	13	13	5	32
Postdoc		3	1	1	5
SAB	1	4	2	2	9
Grand Total	5	31	22	12	70

* PI includes Full professor, Associate professor, Assistant professor, and Senior researcher.

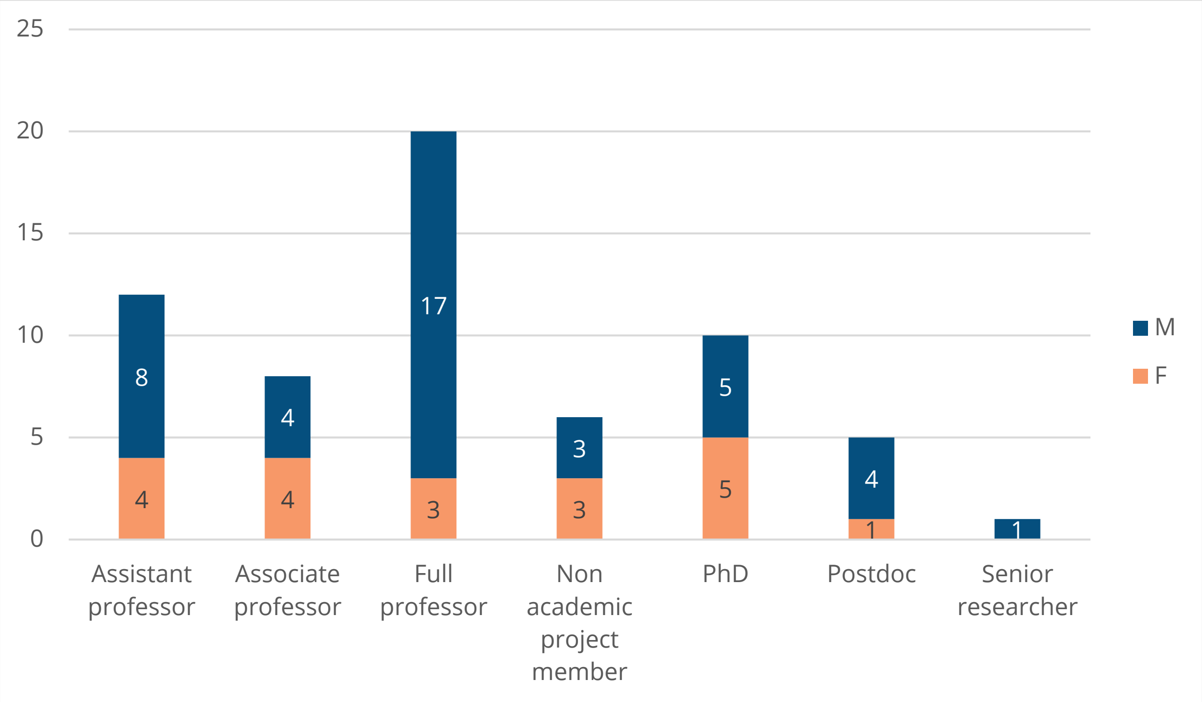

Figure 3 Gender distribution of the DbI2 in Year 1

The Figure 3 overview does not include affiliated researchers.

Appendix B. New development during Year 1

Table 8 New equipment and lab setup established during Year 1

Name	Organisation	WP	Please describe the new equipment or the new lab setup
Chris de Zeeuw	Erasmus University Medical Center	WP 1 Neuroscience	E-phys set up
Freek Hoebeek	University Medical Center Utrecht	WP 1 Neuroscience	Video analysis hardware (cameras) and software for movement analysis; Live Mouse Tracker system; Hardware for in vivo electrophysiology
Pieter Roelfsema	Netherlands Institute for Neuroscience	WP 1 Neuroscience	Several components were acquired for the development and implantation of several high channel-count (MRI-compatible) electrode implants. Experiments will be run with these next-generation implants in non-human primates. One monkey was acquired in August, which will be trained and used in experiments in the coming years.
Christos Strydis	Erasmus University Medical Center	WP 2 Computational methods	Open-ephys 2.0 card (borrowed from Radboud University), housed in a new desktop computer along with a newly acquired Nvidia GPU.
Francesco Battaglia	Radboud University	WP 1 Neuroscience	ONIX advanced ephors setup for closed-loop experiments

Table 9 New enhancement made during Year 1

Name	Organisation	WP	Details
Chris de Zeeuw	Erasmus University Medical Center	WP 1 Neuroscience	Behavioral and E-phys set up
Freek Hoebeek	University Medical Center Utrecht	WP 1 Neuroscience	Movement analysis was scored by hand/eye, which cost a lot of time (and thus money). Now we're able to run the analysis in more detail, faster and automated
Pieter Roelfsema	Netherlands Institute for Neuroscience	WP 1 Neuroscience	We improved the setup to train two monkeys, preparing them for experiments in the coming years.

Appendix C. Research output produced during Year 1

Table 10 Research output produced during Year 1

Name	Organisation	WP	Details
Chris de Zeeuw	Erasmus University Medical Center	WP 1 Neuroscience	- The Sleep Quality- and Myopia-Linked PDE11A-Y727C Variant Impacts Neural Physiology by Reducing Catalytic Activity and Altering Subcellular Compartmentalization of the Enzyme. Sbornova I, van der Sande E, Milosavljevic S, Amurrio E, Burbano SD, Das PK, Do HH, Fisher JL, Kargbo P, Patel J, Porcher L, De Zeeuw CI, Meester-Smoor MA, Winkelman BHJ, Klaver CCW, Pocivavsek A, Kelly MP. Cells. 2023 Dec 14;12(24):2839. doi: 10.3390/cells12242839. - Accessible and reliable neurometric testing in humans using a smartphone platform. Boele HJ, Jung C, Sherry S, Roggeveen LEM, Dijkhuizen S, Öhman J, Abraham E, Uvarov A, Boele CP, Gultig K, Rasmussen A, Vinueza-Veloz MF, Medina JF, Koekkoek SKE, De Zeeuw CI, Wang SS. Sci Rep. 2023 Dec 18;13(1):22871. doi: 10.1038/s41598-023-49568-2. - The sleep quality- and myopia-linked PDE11A-Y727C variant impacts neural physiology by reducing catalytic activity and altering subcellular compartmentalization of the enzyme. Sbornova I, van der Sande E, Milosavljevic S, Amurrio E, Burbano SD, Das P, Do H, Fisher JL, Kargbo P, Patel J, Porcher L, De Zeeuw CI, Meester-Smoor MA, Winkelman BHJ, Klaver CCW, Pocivavsek A, Kelly MP. bioRxiv. 2023 Nov 17:2023.11.16.567422. doi: 10.1101/2023.11.16.567422. Preprint. - Heterogeneous encoding of temporal stimuli in the cerebellar cortex. De Zeeuw CI, Koppen J, Bregman GG, Runge M, Narain D. Nat Commun. 2023 Nov 21;14(1):7581. doi: 10.1038/s41467-023-43139-9. - Whisker kinematics in the cerebellum. Zhai P, Romano V, Soggia G, Bauer S, van Wingerden N, Jacobs T, van der Horst A, White JJ, Mazza R, De Zeeuw CI. J Physiol. 2024 Jan;602(1):153-181. doi: 10.1113/JP284064. Epub 2023 Nov 21. - Synaptic mechanisms for associative learning in the cerebellar nuclei. Broersen R, Albergaria C, Carulli D, Carey MR, Canto CB, De Zeeuw CI. Nat Commun. 2023 Nov 20;14(1):7459. doi: 10.1038/s41467-023-43227-w. - Swept-3-D Ultrasound Imaging of the Mouse Brain Using a Continuously Moving 1-D-Array-Part II: Functional Imaging. Generowicz BS, Dijkhuizen S, Bosman LWJ, De Zeeuw CI, Koekkoek SKE, Kruizinga P. IEEE Trans Ultrason Ferroelectr Freq Control. 2023 Dec;70(12):1726-1738. doi: 10.1109/TUFFC.2023.3330343. Epub 2023 Dec 14. - Human brain mapping using co-registered fUS, fMRI and ESM during awake brain surgeries: A proof-of-concept study. Soloukey S, Collée E, Verhoef L, Satoer DD, Dirven CMF, Bos EM, Schouten JW, Generowicz BS, Mastik F, De Zeeuw CI, Koekkoek SKE, Vincent AJPE, Smits M, Kruizinga P. Neuroimage. 2023 Dec 1;283:120435. doi: 10.1016/j.neuroimage.2023.120435. Epub 2023 Oct 30. - A common cause for nystagmus in different congenital stationary night blindness mouse models. Hölzel MB, Kamermans W, Winkelman BHJ, Howlett MHC, De Zeeuw CI, Kamermans M. J Physiol. 2023 Dec;601(23):5317-5340. doi: 10.1113/JP284965. Epub 2023 Oct 21. - Swept-3-D Ultrasound Imaging of the Mouse Brain Using a Continuously Moving

			1-D-Array-Part I: Doppler Imaging. Generowicz BS, Dijkhuizen S, De Zeeuw CI, Koekkoek SKE, Kruizinga P. IEEE Trans Ultrason Ferroelectr Freq Control. 2023 Dec;70(12):1714-1725. doi: 10.1109/TUFFC.2023.3318653. Epub 2023 Dec 14. - Cerebellar nuclei: Associative motor learning in zebrafish. Broersen R, Canto CB, De Zeeuw CI. Curr Biol. 2023 Aug 21;33(16):R867-R870. doi: 10.1016/j.cub.2023.07.018. - How inhibitory and excitatory inputs gate output of the inferior olive. Loyola S, Hoogland TM, Hoedemaker H, Romano V, Negrello M, De Zeeuw CI. Elife. 2023 Aug 1;12:e83239. doi: 10.7554/eLife.83239. - Purkinje cell microzones mediate distinct kinematics of a single movement. Blot FGC, White JJ, van Hattem A, Scotti L, Balaji V, Adolfs Y, Pasterkamp RJ, De Zeeuw CI, Schonewille M. Nat Commun. 2023 Jul 19;14(1):4358. doi: 10.1038/s41467-023-40111-5. - Case report: High-resolution, intra-operative µDoppler-imaging of spinal cord hemangioblastoma. Soloukey S, Verhoef L, Generowicz BS, De Zeeuw CI, Koekkoek SKE, Vincent AJPE, Dirven CMF, Harhangi BS, Kruizinga P. Front Surg. 2023 Jun 5;10:1153605. doi: 10.3389/fsurg.2023.1153605. eCollection 2023. - cAMP-EPAC-PKCε-RIM1α signaling regulates presynaptic long-term potentiation and motor learning. Wang XT, Zhou L, Dong BB, Xu FX, Wang DJ, Shen EW, Cai XY, Wang Y, Wang N, Ji SJ, Chen W, Schonewille M, Zhu JJ, De Zeeuw CI, Shen Y. Elife. 2023 Apr 26;12:e80875. doi: 10.7554/eLife.80875. - The integrated brain network that controls respiration. Krohn F, Novello M, van der Giessen RS, De Zeeuw CI, Pel JJM, Bosman LWJ. Elife. 2023 Mar 8;12:e83654. doi: 10.7554/eLife.83654. - Myopia control in Mendelian forms of myopia. van der Sande E, Polling JR, Tideman JWL, Meester-Smoor MA, Thiadens AAHJ, Tan E, De Zeeuw CI, Hamelink R, Willuhn I, Verhoeven VJM, Winkelman BHJ, Klaver CCW. Ophthalmic Physiol Opt. 2023 May;43(3):494-504. doi: 10.1111/opo.13115. Epub 2023 Mar 7. - Functional imaging of the exposed brain. Soloukey S, Vincent AJPE, Smits M, De Zeeuw CI, Koekkoek SKE, Dirven CMF, Kruizinga P. Front Neurosci. 2023 Feb 9;17:1087912. doi: 10.3389/fnins.2023.1087912. eCollection 2023. - A Systematic Review of Direct Outputs from the Cerebellum to the Brainstem and Diencephalon in Mammals. Novello M, Bosman LWJ, De Zeeuw CI. Cerebellum. 2022 Dec 28. doi: 10.1007/s12311-022-01499-w. Online ahead of print. PMID: 36575348 Review.
Freek Hoebeek	University Medical Center Utrecht	WP 1 Neuroscience	Video data of rodent movements during cylinder rearing test

Michael Tangermann	Radboud University	WP 2 Computational methods	Transfer Learning between Motor Imagery Datasets using Deep Learning-- Validation of Framework and Comparison of Datasets P Guetschel, M Tangermann arXiv preprint arXiv:2311.16109 UMM: Unsupervised Mean-difference Maximization J Sosulski, M Tangermann arXiv preprint arXiv:2306.11830 An embedding for EEG signals learned using a triplet loss P Guetschel, T Papadopoulo, M Tangermann arXiv preprint arXiv:2304.06495 Perspectives of implementation of closed-loop deep brain stimulation: from neurological to psychiatric disorders S Groppa, G Gonzalez-Escamilla, G Tinkhauser, HI Baqapuri, B Sajonz, ... Project dareplane for closed-loop deep brain stimulation M Dold, J Pereira, M Janssen, M Tangermann Brain Stimulation: Basic, Translational, and Clinical Research in …
Dante Muratore	Delft University of Technology	WP 3 Neurotechnology hardware	P. Yan et al., "Data Compression Versus Signal Fidelity Tradeoff in Wired-OR Analog-to-Digital Compressive Arrays for Neural Recording," in IEEE Transactions on Biomedical Circuits and Systems, vol. 17, no. 4, pp. 754-767, Aug. 2023, doi: 10.1109/TBCAS.2023.3292058.
Pieter Roelfsema	Netherlands Institute for Neuroscience	WP 1 Neuroscience	Roelfsema, P.R. (2023) Solving the binding problem: assemblies form when neurons enhance their firing rate – they don't need to oscillate or synchronize. Neuron, 111, 1003-1019. Papale, P., Wang, F., Morgan, A.T, Chen, X., Gilhuis, A., Petro, L.S., Muckli, L., Roelfsema, P.R. and Self, M.W. (2023) The representation of occluded image regions in area V1 of monkeys and humans, Curr. Biol. 33, 3865-3871. doi: 10.1016/j.cub.2023.08.010
Martin Vinck	Radboud University	WP 1 Neuroscience	Software for detection of sharp wave ripple events by postdoc Cem Uran
Christos Strydis	Erasmus University Medical Center	WP 2 Computational methods	Paper: J.L.F. Betting, C.I. De Zeeuw, and C. Strydis, "Oikonomos-II: A Reinforcement-Learning, Resource-Recommendation System for Cloud HPC," in 2023 IEEE 30th International Conference on High Performance Computing, Data, and Analytics (HiPC), 2023
Francesco Battaglia	Radboud University	WP 1 Neuroscience	1. Sotomayor-Gómez B, Battaglia FP, Vinck M. SpikeShip: A method for fast, unsupervised discovery of high-dimensional neural spiking patterns. PLOS Computational Biology. 2023 Jul 31;19(7):e1011335.
Marcel van Gerven	Radboud University	WP 2 Computational methods	1 ElGazzar, A. and van Gerven, M. Universal differential equations as a common modeling language for neuroscience, ArXiv preprint arXiv:2403.14510, 2024. 2. Chaturvedi, S., ElGazzar, A. and van Gerven, M. A dynamical systems approach to optimal foraging. BioRXiv. 2024.

Appendix D. Financial Overview

Financial overview in Year 1 (Oct 2022-Sep 2023)

Table 11 Year 1 Total budget overview

Planned budget (kEUR)			
Personnel	Non-personnel	Total requested	Co-funding
€ 1,066.83	€ 716.09	€ 1,782.92	€ 671.13

Table 12 Year 1 Total subsidy received

Grant received (kEUR)	Inflation correction (kEUR)	Total subsidy (Grant+inflation correction) (kEUR)
€ 2,225.95	€ 74.35	€ 2,300.30

Table 13 Year 1 Total costs and delta

Actual costs (kEUR)		Total actual costs (kEUR)	Delta (kEUR)
Actual personnel costs	Actual non-personnel costs		(Total subsidy-Total actual costs)
€ 623.50	€ 134.66	€ 758.16	€ 1,542.15

Due to delayed hiring across all DBI² organizations, a significant gap has emerged between the total received subsidies and the actual costs incurred. This gap is regarded as a result of deferred spending. Consequently, no specific action is planned at this moment.