Contents

1 Summary

Word limit: 550

In plain English, provide a summary we can use to identify the most suitable experts to assess your application.

We usually make this summary publicly available on external-facing websites, therefore do not include any confidential or sensitive information. Make it suitable for a variety of readers, for example:

- opinion-formers
- policymakers
- the public
- the wider research community

Guidance for writing a summary Clearly describe your proposed work in terms of:

- context
- the challenge the project addresses
- aims and objectives
- potential applications and benefits
- its relevance to the BBSRC long-term research and innovation priorities and, if applicable Responsive Mode Spotlight areas

2 Core team

List the key members of your team and assign them roles from the following:

- project lead (PL)
- project co-lead (UK) (PcL)
- specialist
- professional enabling staff
- research and innovation associate
- technician
- researcher co-lead (RcL)

Only list one individual as project lead.

UKRI has introduced a new addition to the 'specialist' role type. Public contributors such as people with lived experience can now be added to an application.

Find out more about UKRI's core team roles in funding applications and our eligibility guidance.

3 Application questions

3.1 BBSRC schemes

Word limit: 1

Indicate the scheme through which you are applying.

In the text box, copy the number corresponding to the scheme you are applying through. These are:

1. standard (no scheme)
2. Industrial Partnership Award (IPA)
3. LINK
4. Brazil (FAPESP)
5. Luxembourg (FNR)
6. NSF-Bio

Additional guidance

This is for administrative purposes to help the initial application processing.

Please follow the scheme specific guidance below and upload the additional documents listed as a single PDF no larger than 8MB:

IPA or LINK:

- a letter from your institution's technology transfer office outlining the management of outputs from the proposed research

FAPESP:

- FAPESP proposal form
- FAPESP consolidated budget form
- FAPESP letter of eligibility

FNR:

- CVs of international collaborators
- FNR ‘INTER’ budget form
- FNR ‘INTER’ cost justification

NSF-Bio:

- US biosketches
- US budget forms

3.2 BBSRC remit classification

Word limit: 1

Your application will be considered by one of our four research committees made up of independent experts. Indicate which you feel would be best placed to assess your application.

In the text box, write only the letter (in uppercase) corresponding to the committee you feel would be best placed to assess your application. These are:

A animal disease, health and welfare

B plants, microbes, food and sustainability

C genes, development, and science, technology, engineering and maths (STEM) approaches to biology

D molecules, cells and industrial biotechnology

Additional guidance:

This is for administrative purposes to help the initial application processing. We will check your choice and make a final decision as to which committee will assess your application.

3.3 Vision

Word limit: 550

What are you hoping to achieve with your proposed work?

What the assessors are looking for in your response

Explain how your proposed work:

1. is of excellent quality and importance within or beyond the field(s) or area(s)
2. has the potential to advance current understanding, or generate new knowledge, thinking or discovery within or beyond the field or area
3. is timely given current trends, context, and needs
4. impacts world-leading research, society, the economy, or the environment

You may demonstrate elements of your responses in visual form if relevant. Further details are provided in the Funding Service. References may be included within this section.

3.3.1 Context

Conventional systems neuroscience experiments are typically short in duration and often place significant constraints on subjects behaviours to simplify data analysis. However, these restrictions may limit our ability to observe critical aspects of brain function and behaviour that only manifest in more naturalistic and extended conditions.

At the Sainsbury Wellcome Centre (SWC) and Gatsby Computational Neuroscience Unit (GCNU) we are pioneering **Naturalistic, Long-Duration, and Continual (NaLoDuCo) experiments** in mice that span weeks to months. During these experiments, we collect high-resolution behavioural and neural recordings in naturalistic settings (Figure 1).

To support this endeavor, we are developing the **AEON platform**, an innovative set of hardware and software tools for NaLoDuCo experimental control, data store and access. We are using this platform to investigate the neural basis of foraging behavior in mice over prolonged periods of time (Campagner et al., 2024).

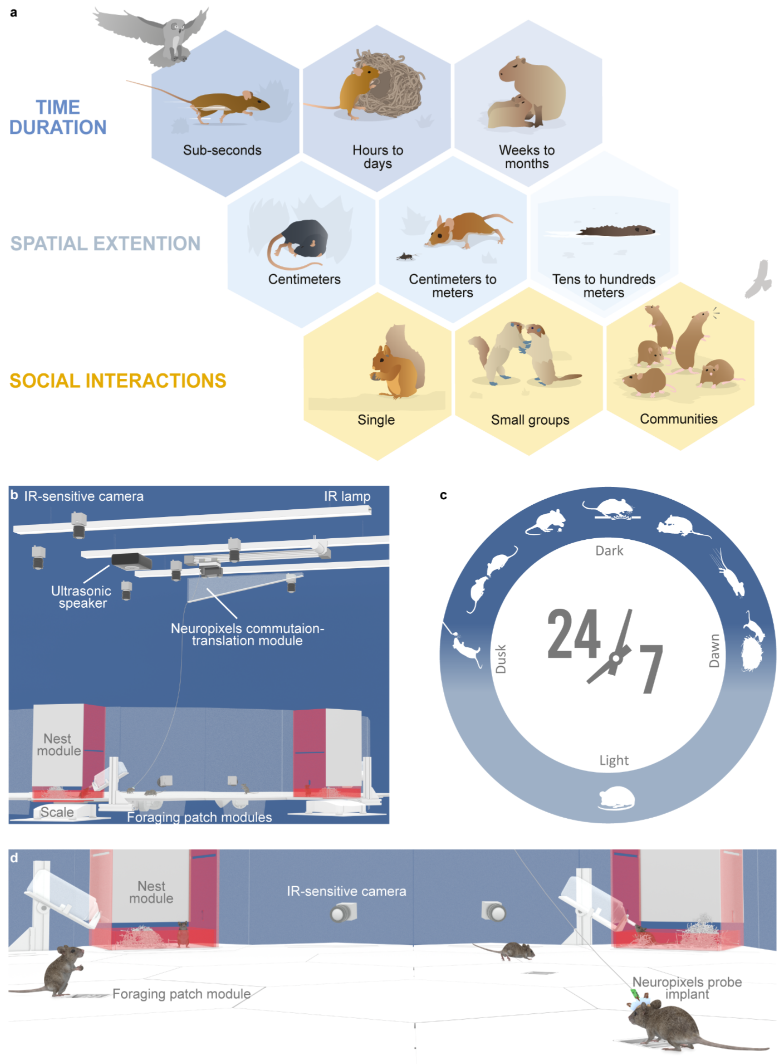

Figure 1: **a**: Example of natural behaviours in rodents that take place over different timescale, spatial extensions and involving different numbers of individuals.
b-d: Close-up views of one possible configuration of the Aeon environment in which naïve mice and mice chronically implanted with Neuropixels probe can live while expressing a variety of natural behaviours including exploring, drinking, escaping, foraging, nesting, sleeping, eating and interacting socially.

Our US partner, the **Allen Institute for Neural Dynamics (AIND)** is also performing NaLoDuCo experimentation, using the AEON platform, studying naturalistic olfactory learning over weeks to month outside conventional task structures (Fink et al., 2024).

NeuroGEARS Ltd, our industrial partner, is a UK-based company supporting academic institutions implementing innovative technology for scientific investigation. It is the main developer of the **Bonsai** software ecosystem for experimental control (Lopes et al., 2015), used by thousands of scientists around the world, and powering the AEON platform. NeuroGEARS has played a central role in the development of the AEON platform, and provides services to both the SWC and the AIND.

NaLoDuCo experimentation will enable researchers to explore neural mechanisms underlying ethological behaviours in naturalistic environments over months, for the first time. The experiments will shed new light on a wide range of poorly understood neural mechanisms, including how the brain structures complex behavioural sequences as a function of the animal needs, learning, adaptation, sleep-dependent memory consolidation and social dynamics. **The data generated from NaLoDuCo experiments represent an entirely new resource in neuroscience**, with the potential to drive breakthroughs and discoveries that are beyond the reach of traditional experiments.

While **naturalistic, long-duration, or continuous** neuroscience experiments have been conducted in the past (Nagy et al., 2023; Ho et al., 2023; Ray et al., 2025; Weissbrod et al., 2013; Dhawale et al., 2017; Newman et al., 2024), to the best of our knowledge, **we are the first ones to integrate all three of these features in a single experimental paradigm**.

This emerging paradigm of long-duration experimentation is poised to become mainstream in the coming years. However, experiments spanning weeks to months generate massive datasets—often reaching hundreds of terabytes—posing significant challenges in data acquisition, management, distribution, visualization, and analysis. To address these challenges, we (GCNU, SWC, AIND, and NeuroGEARS Ltd) will collaboratively extend the AEON platform with functionality to **visualise and statistically analyze previously collected NaLoDuCo experimental data on the cloud**, and to **perform real-time machine to enable the intelligent control of NaLoDuCo experiments**.

3.3.2 Specific aims

Data generated by NaLoDuCo experiments will be of general interest to the neuroscience community. **We want to share our NaLoDuCo foraging and odor learning recordings and allow other groups collecting this type of data to share their own.** However, this dissemination is not trivial, as datasets are of the order of hundreds of terabytes, and it will take users several days to download them over standard Internet connections.

Instead of bringing data to users, we will bring users to data, by storing datasets in the cloud (or in institutional clusters), and providing **cloud software to allow users to visually explore and statistically analyse behavioural and neural NaLoDuCo datasets where they live** (1 and 2 in Figure 2).

Our statistical analysis of neural time series will require knowledge of the spiking activity of single units; i.e., spike sorting. In long-duration experiments with freely moving animals spike sorting is a challenging problem, because movements of recording probes change the shape of spike waveforms over time and complicate the assignment of spikes to units based on their waveforms. We will address this problem by developing **spike sorting methods for long-duration, continual and high-channel-count recordings** (3 in Figure 2).

Funded by a BBSRC award we are adding machine learning functionality to Bonsai in order to enable a new type of experimentation controlled by advanced machine learning inference on behavioral and neural recordings (Bonsai.ML, Guilbeault et al., 2025). We have developed this functionality for conventional short duration experiments. We will add to Bonsai.ML **real-time machine learning functionality for processing nonstationary data**, such as that generated in NaLoDuCo experiments.

Most of the online neural data analysis methods that we will add to AEON require sorted spikes. We will adapt the previous offline **spike sorting methods for long-duration experiment to operate in real-time** (5 in Figure 2).

References

Campagner, D., Bhagat, J., Lopes, G., Calcaterra, L., Ahn, J., Almeida, A., Carvalho, F. J., Cruz, B., Erskine, A., Lo, C., Nguyen, T. T.,

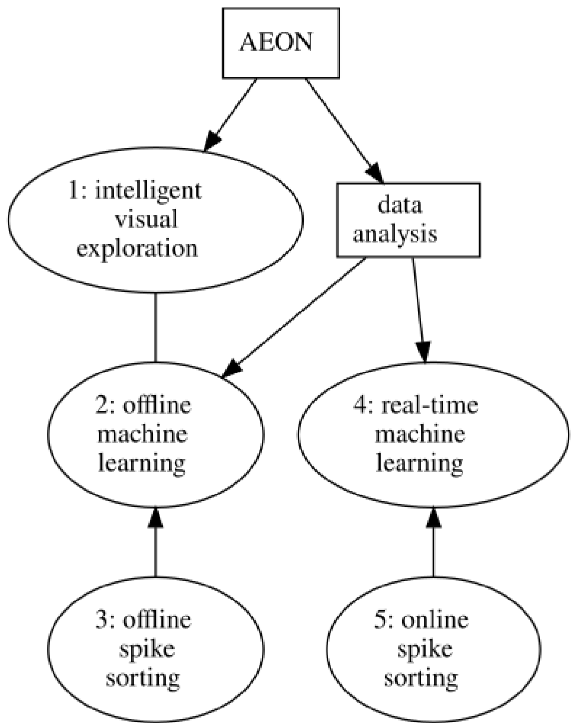

Figure 2: Specific aims

Pouget, A., Rapela, J., Ryan, T., Reggiani, J., and Group, S. S. F. B. W. (2024). Aeon: an open-source platform to study the neural basis of ethological behaviours over naturalistic timescales. https://www.sfn.org/-/media/SfN/Documents/NEW-SfN/Meetings/Neuroscience-2024/Abstracts-and-Sessions/Abstract-PDFs/SFN24_Abstracts-PDF-Posters_SAT_PM.pdf.

Dhawale, A. K., Poddar, R., Wolff, S. B., Normand, V. A., Kopelowitz, E., and Ölveczky, B. P. (2017). Automated long-term recording and analysis of neural activity in behaving animals. *Elife*, 6:e27702.

Fink, A. J., Hogan, M., and Schoonover, C. E. (2024). Olfactory investigation in the home cage. *Neurobiology of Learning and Memory*, 213:107951.

Guilbeault, N., Lopes, G., and Rapela, J. (2025). Bonsai.ml: machine learning for intelligent experimental control. https://bonsai-rx.org/machinelearning/.

Ho, H., Kejzar, N., Sasaguri, H., Saito, T., Saido, T. C., De Strooper, B., Bauza, M., and Krupic, J. (2023). A fully automated home cage for long-term continuous phenotyping of mouse cognition and behavior. *Cell Reports Methods*, 3(7).

Lopes, G., Bonacchi, N., Frazão, J., Neto, J. P., Atallah, B. V., Soares, S., Moreira, L., Matias, S., Itskov, P. M., Correia, P. A., et al. (2015). Bonsai: an event-based framework for processing and controlling data streams. *Frontiers in neuroinformatics*, 9:7.

Nagy, M., Naik, H., Kano, F., Carlson, N. V., Koblitz, J. C., Wikelski, M., and Couzin, I. D. (2023). Smart-barn: Scalable multimodal arena for real-time tracking behavior of animals in large numbers. *Science Advances*, 9(35):eadf8068.

Newman, J. P., Zhang, J., Cuevas-López, A., Miller, N. J., Honda, T., van der Goes, M.-S. H., Leighton, A. H., Carvalho, F., Lopes, G., Lakunina, A., et al. (2024). Onix: a unified open-source platform for multimodal neural recording and perturbation during naturalistic behavior. *Nature Methods*, pages 1–6.

Ray, S., Yona, I., Elami, N., Palgi, S., Latimer, K. W., Jacobsen, B., Witter, M. P., Las, L., and Ulanovsky, N. (2025). Hippocampal coding of identity, sex, hierarchy, and affiliation in a social group of wild fruit bats. *Science*, 387(6733):eadk9385.

Weissbrod, A., Shapiro, A., Vasserman, G., Edry, L., Dayan, M., Yitzhaky, A., Hertzberg, L., Feinerman, O., and Kimchi, T. (2013). Automated long-term tracking and social behavioural phenotyping of animal colonies within a semi-natural environment. *Nature communications*, 4(1):2018.

3.4 Approach

Word limit: 3,300

How are you going to deliver your proposed work?

What the assessors are looking for in your response

Explain how you have designed your approach so that it:

1. is effective and appropriate to achieve your objectives
2. is feasible, and comprehensively identifies any risks to delivery and how they will be managed
3. uses a clearly written and transparent methodology (if applicable)
4. summarises the previous work and describes how this will be built upon and progressed (if applicable)
5. will maximise translation of outputs into outcomes and impacts
6. describes how your, and if applicable your team's, research environment (in terms of the place and relevance to the project) will contribute to the success of the work

You may demonstrate elements of your responses in visual form if relevant.

Please make sure to check sizing and readability of the image using 'read view' prior to submission. Further details are provided in the Funding Service.

References may be included within this section.

Within the 'Approach' section we also expect you to:

- provide a detailed and comprehensive project plan including milestones and timelines in the form of an embedded Gantt chart or similar (please make sure to check sizing and readability of the image using 'read view' prior to submission)

BBSRC's action plan for EDI outlines our commitment to removing barriers to participation in our programmes, ensuring investments do not inadvertently prevent access or usage by individuals from minority groups, for example disabled researchers.

To this end, applications should identify how accessibility and inclusiveness in the widest sense have been incorporated into the design of the project. For example, you may wish to reference relevant institutional strategies and policies which support equality, diversity, and inclusion as they relate to access to equipment and facilities and indicate how the proposed project has been designed and will be delivered with broad access in mind.

We have collected unprecedented NaLoDuCo datasets at the SWC and AIND, comprising continuous, multimodal recordings over weeks to months. However, the scientific value of these massive datasets cannot be fully realized without robust tools for visual exploration and analysis. To address this need, we will develop and disseminate an open-source library of methods for the visualization and analysis of NaLoDuCo experimental data.

This library will include tools for both offline and online analysis (Sections 3.4.1 and **??**), visual exploration (Section 3.4.3), and scalable offline and real-time spike sorting (Sections 3.4.4 and 3.4.5). Together, these methods will make NaLoDuCo data more accessible, interpretable, and actionable for the neuroscience community.

3.4.1 Offline Analysis Methods

Modern neuroscience lacks robust methods to characterize long-duration and continual time series, especially in settings where the statistical properties of the data evolve over time. This limitation present a methodological gap that must be addressed in order to unlock the scientific potential of NaLoDuCo experiments.

To bridge this gap, we will develop and disseminate a software library containing new implementations of machine learning methods specifically tailored to: (1) operate effectively under **non-stationary** conditions, and (2) scale to **very long time series**.

3.4.1.1 Initial List of Methods to Include in the Library

We will initially populate this library with new implementations of methods already in use at the GCNU, SWC, and AIND to analyze neural and behavioral time series from NaLoDuCo foraging and olfactory learning experiments in mice. These methods span multiple domains—kinematics, neural dynamics, behavioral state segmentation, forecasting, and joint modeling—and are designed to work together within an integrated analysis pipeline. We described these methods below and summarise them in Table 1.

Behavioral Analysis: The first step in behavioral analysis involves multi-body-part tracking. For this, we will use **deep learning-based pose estimation** methods such as SLEAP, which enable accurate and efficient tracking of multiple unmarked mice across long recording sessions.

From the tracked poses, we will infer continuous kinematic variables using **linear dynamical systems (LDS)**, including particle filter-based variants to handle uncertainty and measurement noise. These kinematic features will be used to infer discrete behavioral states with **Hidden Markov Models (HMMs)**, as implemented in tools such as MoSeq.

We will relate these inferred states and kinematic variables to foraging-related outcomes—such as patch-leaving decisions—using both **generalized linear models (GLMs)** and **deep neural networks**. These models will allow us to capture both interpretable and high-capacity representations of behavioral decision-making processes.

To recover the latent strategies guiding animal behavior, we will apply **inverse reinforcement learning** methods such as HIQL, which estimate the underlying reward functions and policies based on observed actions.

NaLoDuCo recordings uniquely support behavioral forecasting over extended horizons—ranging from hours to days—far beyond what is feasible in conventional short-duration experiments. To capitalize on this, we will apply long-horizon forecasting models using **recurrent neural networks (RNNs)** and **transformer architectures**, which are well-suited to modeling long-range temporal dependencies.

Neural Data Analysis: Analysis of high-density electrophysiology will begin with **latent variable modeling** to reduce the dimensionality of population neural recordings. We will use both linear and nonlinear latent dynamics models, including svGPFA, which uses Gaussian processes, and LFADS, a deep generative model based on recurrent neural networks.

The resulting low-dimensional trajectories will be used to infer discrete neural states via **HMMs**, using methods such as SSM. For neural activity forecasting across long durations, we will again employ **RNNs** and **transformers**, which can model complex temporal structure in spiking activity.

We will also decode the animal's position from hippocampal spike trains using **point-process decoders**, enabling the analysis of spatial coding and replay phenomena during naturalistic foraging behavior. We will build on existing implementations such as replay_trajectory_classification.

Joint Neural-Behavioral Modeling: To understand the interactions between neural dynamics and behavior, we will use models that extract **shared latent representations** from both domains. These models will help reveal how cognitive and behavioral states are jointly encoded in neural activity.

We will adapt Recognition-Parametrized Models (RPM), a Bayesian approach developed at the GCNU, which infers latent variables that explain multiple observation streams through highly nonlinear relationships. We will also use CEBRA, a state-of-the-art contrastive learning framework designed for multimodal representation learning, to discover temporally and semantically aligned neural-behavioral structure.

3.4.1.2 Non-stationarity

Many conventional methods for analyzing neural and behavioral time series assume that the underlying data-generating processes are stationary—that is, their statistical properties remain constant over time. While this assumption may be acceptable in short-duration experiments, it breaks down in long-duration and continual recordings. In such settings, animals learn and adapt, their internal states and motivations fluctuate, and their behavior and physiology are influenced by biological rhythms such as circadian, ultradian, and infradian cycles. These changes induce non-stationarity in the data, making models that assume stationarity progressively less reliable or even obsolete.

To address this challenge, we will adapt and develop methods that are explicitly designed to operate in non-stationary environments. Our approach draws on techniques from multiple domains, including adaptive signal processing, machine learning, and Bayesian inference.

Adaptive Signal Processing. The field of adaptive signal processing has produced robust methods for modeling linear systems with time-varying dynamics (Haykin, 2002). The recursive least-squares (RLS) algorithm, for example, is a well-known adaptation of the ordinary least squares algorithm that continuously updates model parameters to perform linear regression under non-stationary conditions. We will use RLS to study time-varying relations between behavioral states, as inferred by hidden Markov models, and

Table 1: Initial data analysis methods to disseminate

Domain	**Functionality**	**Method**	**Model Type**
behaviour	multi-body-part tracking	SLEAP	deep neural network
behaviour	kinematics inference	LDS	linear dynamical system
behaviour	kinematics inference	LDS	particle filter
behaviour	state inference	SSM	hidden Markov model
behaviour	regression		generalized linear model
behaviour	regression		deep neural network
behaviour	policy inference	L(M)V-IQL	reinforcement learning
behaviour	long-duration forecasting		RNN
behaviour	long-duration forecasting		transformers
brain	latents inference	svGPFA	Gaussian processes
brain	latents inference	LFADS	RNN
brain	state inference	SSM	hidden Markov model
brain	long-duration forecasting		RNN
brain	long-duration forecasting		transformers
brain	decoding	NA	point-process decoder
brain & behaviour	latents inference	RPM	Bayesian inference + deep neural network
brain & behaviour	latents inference	CEBRA	contrastive learning

foraging visit durations.

Continual Learning. The field of continual learning develops adaptive methods for artificial neural networks. In classic continual learning, a model learns a sequence of discrete, well-defined tasks. But in NaLoDuCo experimentation, as in many real-world settings there are not specific task boundaries. So methods that do not require task boundaries are needed. They are studied by the subfield of task-free continual learning and include online regularization (which constrain the update of relevant weights), experience replay (which maintain a small, representative buffer of past samples) and ensemble methods (which combine the predictions of multiple individual models with, for example, different learning rates). We will use these techniques, for example, to train pose tracking models on month-long continuous recordings.

Adaptive State-Space Models. In state-space modeling, the Kalman filter provides a principled way to handle non-stationary Gaussian processes with drifting mean and covariance. More flexible approaches are needed when data exhibit abrupt regime shifts or complex latent dynamics. Switching state-space models, such as Switching Linear Dynamical Systems (SLDS) and Switching Hidden Markov Models (sHMMs), model discrete changes in underlying system dynamics. For nonlinear, non-Gaussian signals, particle filters approximate the posterior distribution through sequential sampling. Bayesian online learning techniques offer a general framework for continually updating model parameters as new data arrive. Using these techniques we will build models that robustly infer kinematics over months.

Concept Drift in Machine Learning. In the machine learning literature, non-stationarity is often framed under the concept of *concept drift*, which refers to changes in the joint distribution of inputs and outputs over time. Such drift can take various forms—sudden, gradual, or cyclical (e.g., re-emergence of behavioral patterns linked to circadian or ultradian rhythms).

Techniques for handling concept drift generally fall into three categories: (1) *detection methods*, which monitor for significant changes in data distribution; (2) *adaptation methods*, which incrementally update models using strategies such as sliding windows, online learning, or ensemble-based approaches; and (3) *forgetting mechanisms*, which allow models to discard outdated information while retaining relevant past knowledge.

We will apply techniques from the concept drift literature to models that fall outside the previous categories of focus (e.g., linear models, artificial neural networks, and state-space models). In particular, we will explore their use in building Recognition-Parametrized Models (RPMs) to estimate joint behavioral and neural latent variables over timescales of weeks to months.

In summary, robust analysis of NaLoDuCo datasets requires models that continuously adapt to evolving data distributions. Our offline analysis framework will integrate both established adaptive algorithms and cutting-edge methods from continual learning and concept drift to meet this challenge.

3.4.1.3 Computational efficiency

Neural and behavioral data analysis is most effective when computations are performed quickly, ideally in real time. Slow computations discourage data exploration and hinder scientific discovery. The large dataset sizes generated by NaLoDuCo experimentation pose a significant challenge for fast data analysis.

To overcome this limitation, we will combine distributed and GPU computing. Distributed computing is a paradigm in which tasks and data are divided across multiple computers. Instead of relying on a single powerful machine, distributed computing accelerates processing by executing multiple parts of a computation in parallel. GPU computing is a parallel computing approach that uses Graphics Processing Units (GPUs) to accelerate computational tasks. Unlike traditional Central Processing Units (CPUs), which execute a few complex operations sequentially, GPUs consist of thousands of smaller cores optimized for executing many operations simultaneously. Distributed computing allows to split workload across multiple machines, overcoming memory and computational limitations. It is particularly useful for scaling to massive datasets.

For distributed computing to deliver substantial speed improvements, computations must be decomposable into independent parallel tasks. Due to their serial dependencies, time series models are difficult to decomposed in this manner. Still, time series models can benefit from distributed computing infrastructures, as many parts of time series pipelines are parallelizable, like preprocessing steps (e.g., filtering, feature extraction, normalization) or parallel model evaluation across hyperparameter sweeps. In addtion, when datasets are too large to fit in memory, distributed computing (e.g., with Ray, Dask, or Spark) can Distribute I/O and preprocessing, train models in parallel on different subsets (e.g., one model per animal or time window) and run hyperparameter sweeps or model variants in parallel. Furthermore, even with serial dependencies GPU acceleration significantly speeds up the processing of each item in the time series, specially when large matrix operation are involved.

We will develop accelerated implementations of all methods in the library. These implementations will use JAX for model learning, inference, and numerical computation, Apache Spark or Dask to distribute pre-processing and feature extraction, and Ray to distribute machine learning and deep learning functionality.

Related to this item is the library Thunder, which accelerate the analysis of large scale neural data. It was pioneering by introducing the use of distributed computing in neural data analysis. Our library is different from Thunder in that, besides analyzing large scale neural data, it processes continual recordings, and needs to overcome non-stationarity problems. In addition, Thunder implements simpler methods assuming independent and identically distributed data, while our library contains more sophisticated time series ones.

3.4.1.4 Deliverables

1. repository containing implementations of machine learning algorithms for offline processing NaLoDuCo experimental data, adapted to operate in non-stationary environments, and optimized to perform at scale when running on public clouds or institutional high-performance-computing clusters.

2. SWC NaLoDuCo foraging dataset storred in DANDI.

3. deployment of the methods in 1 in Amazon EC2 instances, to allow users to analyze on the cloud the datasets in 2.

3.4.2 Real-Time Machine Learning Methods

3.4.2.1 Real-Time Machine Learning in Neuroscience

Real-time machine learning (RTML) is now widely used across many disciplines.

For example, in climate and environmental monitoring, RTML supports real-time detection of floods and wildfires using satellite and sensor data, and predicts extreme weather events from streaming radar and temperature data.

In food delivery, RTML predicts delivery times using live traffic, restaurant queues, and historical patterns, and dynamically plans optimal routes for drivers and shoppers.

Despite its potential, RTML remains underutilized in neuroscience. This is surprising given its promise for next-generation experiments involving navigation, learning, and dynamic control (NaLoDuCo).

Real-time experimental design verification. Neuroscience experiments typically rely on offline analysis. These analyses often uncover flaws in data collection only after experiments are complete, requiring multiple iterations.

This is impractical for long-duration experiments that span weeks or months. A better approach is to perform real-time analysis and adapt experimental protocols dynamically when issues are detected.

Intelligent neuromodulation. Brain activity can be modulated optically, chemically, or electrically. Traditionally, such interventions are scheduled at fixed times or based on simple behavioral cues.

A more sophisticated method uses inferences from machine learning to guide modulation. For example, a scientist may hypothesize that a peak in a latent neural variable (derived from prefrontal cortex activity) signals a decision to forage. By estimating this latent variable online and forecasting its peak, the scientist can optogenetically inactivate the relevant neural population just before the predicted peak. If this prevents the mouse from initiating foraging, the hypothesis is supported.

Intelligent data storage. As NaLoDuCo experiments increase in duration and data richness, storing all raw data becomes unfeasible. Intelligent real-time data pruning becomes essential.

For instance, in a large arena monitored by ten high-resolution cameras, it is more efficient to store footage only from the cameras actively observing the mouse. Real-time probabilistic tracking can guide this, saving all footage when tracking confidence is low, and selectively saving when confidence is high.

3.4.2.2 Bonsai and Bonsai.ML

Bonsai is a widely used software ecosystem for experimental control in neuroscience (Lopes et al., 2015).

With support from the BBSRC, we are building infrastructure for intelligent experimentation through the Bonsai.ML package.

Bonsai.ML currently includes online machine learning models such as linear regression, linear dynamical systems, hidden Markov models, and Bayesian point-process decoders. In collaboration with researchers at SWC and UCL, we apply these models to neuroscience challenges including receptive field estimation, foraging behavior analysis, behavioral state inference, and hippocampal position decoding.

However, Bonsai.ML models assume data stationarity, which is incompatible with NaLoDuCo experiments (see Section 3.4.1). We are adapting these models for non-stationary settings using techniques described in Section 3.4.1.2.

These new machine learning modules for real-time control in non-stationary environments will be released as part of the open-source Bonsai.ML package.

At SWC and AIND, Bonsai is a core part of our experimental infrastructure. In partnership with scientists at both institutions, we will deploy these RTML methods in state-of-the-art NaLoDuCo neuroscience experiments.

3.4.2.3 Deliverables

1. A repository of real-time machine learning methods for experimental control in non-stationary environments.

2. Collaborative publications with SWC and AIND researchers reporting scientific findings from NaLoDuCo experiments using non-stationary Bonsai.ML methods.

3.4.2.4 Real-Time Machine Learning in Neuroscience

Real time machine learning (RTML) is currently used across many disciplines. For example, in climate and environmental monitoring it is used for real-time flood or wildfire detection from satellite or sensor data, and for predicting extreme weather events using streaming radar and temperature data. Another example is food delivery where RTML is used for predicting delivery time based on live traffic, restaurant queues, and historical patterns and dynamic route planning for drivers and shoppers.

However, there are very few applications of RTML in neurosciences. This is surprising, since the potential of RTML for neuroscience is enormous, specially for NaLoDuCo experimentation.

Real-time experimental design verification. Offline analysis is the standard in neuroscience. These analyses often reveal deficiencies in the data collection process and scientists carry out multiple iterations of an experiment until they converge to the desired one. This modus operandi is not adequate for long-duration experimentation, as it would not be practical to perform several iterations of months long experiments. One solution would be to perform analysis online, and update the experiment design if the online analysis reveals deficiencies.

Intelligent neuromodulation. Brain activity can be modulated optically, chemically and electrically. Most commonly this modulations is done at fixed experimental times, or based on simple behavioural or neural observations. A better approach is to guide neural manipulations based on inferences from advanced machine learning methods. For example, a scientists may hypothesize that a peak in a neural latent variable, inferred from a prefrontal cortex population, signals the moment when mice decide to begin a foraging bout. To test this, she estimates latent variables online from prefrontal cortex activity, and use them to forecast when this peak will occur. She then optogenetically inactivates the neural population before the forecasted time. Because inactivation prevented the mouse from initiating a foraging bout, her hypothesis is supported.

Intelligent data storage. As the duration of NaLoDuCo experiments become longer, and the richness of the behavioural and neural recordings become larger, it will be unfeasible to store all raw data. We will be forced to intelligently decide, in real time, subsets of data to discard.

For instance, if we are recording videos from a mouse foraging in a large arena with ten high-resolution cameras, it would save considerable storage if at any time we only save videos from cameras capturing the mouse. This could be done by tracking the position of the mouse in real time with probabilistic machine learning methods. Then, when the confidence of the tracking is high, we would only save videos of cameras capturing the mouse at the tracked position, but when the confidence is low, we would save all videos.

3.4.2.5 Bonsai and Bonsai.ML

Bonsai is a software ecosystem for neuroscience experimental control used by thousands of scientists around the world (Lopes et al., 2015). Funded by the BBSRC we are building software infrastructure to enable intelligent experimentation in the Bonsai.ML package. We have integrated into Bonsai.ML several online machine learning models (e.g., linear regression, linear dynamical systems, hidden Markov models, Bayesian point-process decoders) and, in collaboration with scientists at the SWC and UCL, we are applying these models to neuroscience problems (e.g., estimation of visual receptive fields, inference of foraging mice kinematics, inference of behavioral states, position decoding from hippocampal mice activity).

Bonsai.ML methods assume stationarity that, as discussed in Section 3.4.1, is not suitable for NaLoDuCo experimentation. We will adapt these methods to operate in non-stationary environments using the techniques outlined in Section 3.4.1.2.

The new advanced machine learning methods for intelligent experimental control in non-stationary environments will be openly disseminated as new modules of the Bonsai.ML package.

At the SWC and at the AIND we use Bonsai for experimental control. In collaboration with scientists at both institutes, we will use the new RTML methods to process non-stationary data in state-of-the-art neuroscience NaLoDuCo experiments.

3.4.2.6 Deliverables

1. repository of real time ML methods for neuroscience experimental control adapted to work in non-stationary environments.

2. publications with scientists at the SWC and AIND reporting findings in NaLoDuCo experiments using non-stationary Bonsai.ML methods.

3.4.3 Visual Exploration

Visualizations are essential for extracting insight from any dataset. Given the scale of NaLoDuCo datasets, downloading them locally is impractical.

Therefore, visualization methods must operate where the data resides—either in the cloud or on institutional compute clusters.

We will develop visualization functionality for both continuous datasets (Section 3.4.3.1) and epoched datasets, where epochs are anchored around events identified by advanced machine learning methods (Section **??**).

3.4.3.1 Continuous Visualizations

Continuous visualizations will enable users to seamlessly explore large-scale behavioral and neural datasets spanning weeks to months. Users should be able to fluidly zoom out to gain a high-level overview (e.g., across an entire month) and zoom in to inspect millisecond-level detail. Our goal is to provide an interactive experience analogous to Google Maps—where one can zoom from a global perspective down to individual buildings—with time series data.

To achieve this, we will employ a combination of tiling, hierarchical storage, and streaming techniques:

Multi-Resolution Tiling.

- Large volumetric and time series datasets will be preprocessed into tiles at multiple spatial and temporal resolutions.
- When the user zooms into a specific time or spatial window, only the relevant tiles at the appropriate resolution will be rendered, minimizing latency and resource use.

Hierarchical Storage.

- Data will be organized using hierarchical file formats (e.g., Zarr, HDF5) that support chunked access and multi-resolution storage.
- These formats allow efficient random access to specific subsets of data and integration with modern data infrastructure.

On-Demand Streaming.

- Visualizations will stream data dynamically based on the user's current view, leveraging cloud infrastructure to deliver data at the required resolution and scale.

- We will develop custom APIs for real-time access and transformation of neural and behavioral data streams.

3.4.3.2 Epoched and Interactive Visual Analytics

A key strength of our platform is its support for **epoched visualization and interactive, closed-loop visual analytics**, which together enable the discovery and refinement of neural and behavioral patterns in long-duration datasets.

Epoched visualizations are essential for analyzing data around events of interest—such as decision points, sensory cues, or machine learning-inferred transitions. These visualizations will support:

- Grouping trials or epochs by event type, time of day, or machine learning-inferred state
- Overlaying neural, behavioral, and environmental variables aligned to key event markers
- Flexible sorting and filtering of epochs to uncover context-dependent patterns

We will implement interactive interfaces that allow researchers to define, explore, and compare arbitrary epoch-based segments. These will support exploratory data analysis as well as hypothesis-driven comparisons across conditions, individuals, and time periods.

Machine Learning-Defined Events. A core feature of our system will be the ability to align epochs not just to experimenter-defined events, but also to latent state transitions inferred via unsupervised methods (e.g., hidden Markov models, behavioral clustering, inverse reinforcement learning). This will support deeper investigation into emergent patterns in long-duration, naturalistic behavior.

Closed-Loop Analytics. There will be a *closed-loop interaction* between visualizations and machine learning algorithms: algorithmic outputs will generate new visualizations, and visual insights will guide further machine learning analysis, forming an iterative discovery cycle. This process allows the visualization platform to function not just as a display tool, but as a central component in data-driven scientific inquiry.

In this loop:

- **Machine learning algorithms** extract latent states, classify behaviors, infer structure, or forecast dynamics from NaLoDuCo data.
- These outputs feed into the visualization engine to generate novel views (e.g., state-aligned rasters, dynamic embeddings, attention maps).
- **Users explore these visualizations interactively**, discovering unexpected, task-agnostic, or contextual patterns.
- New queries and insights drive further rounds of machine learning analysis—closing the loop.

This design enables researchers to co-develop computational models and scientific hypotheses iteratively, with human insight and machine inference deeply intertwined.

3.4.3.3 Software Stack for Interactive Visualizations

To support scalable, cloud-based, and interactive visualization of NaLoDuCo datasets, we will develop our system using a modern and modular software stack optimized for high performance, extensibility, and ease of integration with existing neuroscience infrastructure.

Frontend (User Interface).

- **React.js** will serve as the primary framework for building a dynamic, modular, and responsive web-based interface.
- Visualization components will leverage libraries such as **D3.js**, **Plotly**, and **Deck.gl** to render interactive time series, raster plots, and behavioral trajectories at scale.
- For GPU-accelerated rendering of large datasets, we will use **WebGL** and related technologies such as **regl** or **Three.js**.

Backend (Computation and Data Services).

- The backend will be written in **Python**, using **FastAPI** or **Flask** to serve data and model outputs to the frontend.
- Time series pre-processing, tiling, and downsampling will be handled via **NumPy**, **Xarray**, and **Dask** to enable scalable, distributed processing.
- For storage, we will use chunked, cloud-native formats such as **Zarr** and **HDF5**, which allow efficient retrieval and hierarchical access to long-duration recordings.
- Machine learning integration will rely on **PyTorch**, **scikit-learn**, and model serving frameworks such as **TorchServe** or **ONNX Runtime**.

Cloud Infrastructure.

- The system will be deployable on commercial or academic cloud platforms (e.g., AWS, GCP, or institutional clusters).
- For orchestration of services, we will use **Kubernetes**, enabling auto-scaling and distributed deployment of visualization and ML services.
- **Docker** containers will ensure reproducibility and portability across environments.
- The visualization system will integrate directly with the **DANDI Archive** for cloud-native access to neurophysiology data.

Data Interoperability.

- All tools will be compatible with **Neurodata Without Borders (NWB)** and follow FAIR data principles.
- The system will expose APIs for programmatic access to raw and derived data, enabling integration with existing tools like **Bonsai**, **CaImAn**, or **napari**.

This software stack ensures that our visualization tools will be performant, scalable, and usable across a wide range of environments, from local lab systems to cloud-based scientific platforms.

3.4.3.4 Deliverables

1. visualisations for continuous behavioural and neural recording
2. visualisations for epoched behavioural and neural recording
3. visualisations for model outputs
4. indexing system to support intelligent visualisations
5. deployment of the above items to allow users to visualise NaLoDuCo DANDI datasets on the cloud

3.4.4 Offline spike Sorting

3.4.4.1 Outputs

1. Repository with implementations and benchmarking of offline spike sorting algorithms for long-duration recordings

3.4.5 Online spike Sorting

3.4.5.1 Outputs

1. Repository with implementations and benchmarking of online spike sorting algorithms

References

Haykin, S. S. (2002). *Adaptive filter theory.* Pearson Education India.

Lopes, G., Bonacchi, N., Frazão, J., Neto, J. P., Atallah, B. V., Soares, S., Moreira, L., Matias, S., Itskov, P. M., Correia, P. A., et al. (2015). Bonsai: an event-based framework for processing and controlling data streams. *Frontiers in neuroinformatics*, 9:7.

3.5 Applicant and team capability to deliver

Word limit: 1,650

Why are you the right individual or team to successfully deliver the proposed work?

What the assessors are looking for in your response

Please ensure the current job titles of the core team members are included here to ensure eligibility can be established for the core team roles assigned. Find out more about UKRI's core team roles in funding applications and our eligibility guidance.

Evidence of how you, and if relevant your team, have:

- the relevant experience (appropriate to career stage) to deliver the proposed work
- the right balance of skills and expertise to cover the proposed work
- the appropriate leadership and management skills to deliver the work and your approach to develop others
- contributed to developing a positive research environment and wider community

You may demonstrate elements of your responses in visual form if relevant.

Further details are provided in the Funding Service.

The word limit for this section is 1,650 words: 1,150 words to be used for R4RI modules (including references) and, if necessary, a further 500 words for Additions.

Use the Résumé for Research and Innovation (R4RI) format to showcase the range of relevant skills you and, if relevant, your team (project and project co-leads, researchers, technicians, specialists, partners and so on) have and how this will help deliver the proposed work. You can include individuals' specific achievements but only choose past contributions that best evidence their ability to deliver this work.

Complete this section using the R4RI module headings listed. Use each heading once and include a response for the whole team, see the UKRI guidance on R4RI. You should consider how to balance your answer, and emphasise where appropriate the key skills each team member brings:

- contributions to the generation of new ideas, tools, methodologies, or knowledge
- the development of others and maintenance of effective working relationships
- contributions to the wider research and innovation community
- contributions to broader research or innovation users and audiences and towards wider societal benefit

Additions

Provide any further details relevant to your application. This section is optional and can be up to 500 words. You should not use it to describe additional skills, experiences, or outputs, but you can use it to describe any factors that provide context for the rest of your R4RI (for example, details of career breaks if you wish to disclose them).

Complete this as a narrative. Do not format it like a CV.

References may be included within this section.

The roles in funding applications policy has descriptions of the different project roles.

3.6 Project partners

Add details about any project partners' contributions. If there are no project partners, you can indicate this on the Funding Service.

A project partner is a collaborating organisation who will have an integral role in the proposed research. This may include direct (cash) or indirect (in-kind) contributions such as expertise, staff time or use of facilities. Project partners may be in industry, academia, third sector or government organisations in the UK or overseas, including partners based in the EU.

If you are applying via the IPA or LINK scheme, please include details of industry partners here.

If applying under the BBSRC-NSF lead agency scheme, please include details of your US partner here.

Add the following project partner details:

- the organisation name and address (searchable via a drop-down list or enter the organisation's details manually, as applicable)
- the project partner contact name and email address
- the type of contribution (direct or in-direct) and its monetary value

If a detail is entered incorrectly and you have saved the entry, remove the specific project partner record and re-add it with the correct information.

For audit purposes, UKRI requires formal collaboration agreements to be put in place if an award is made.

3.7 Project partners: statement of support

Word limit: 3,000

Only complete a statement of support if you have named project partners in the project partner section above. A statement is required to be provided from each partner you named in the 'Project partners' section.

If you are applying via the IPA or LINK scheme, please include details of industry partner support here.

What the assessors are looking for in your response

A project partner is a collaborating organisation who will have an integral role in the proposed research. This may include direct (cash) or indirect (in-kind) contributions such as expertise, staff time or use of facilities.

Each statement should:

- confirm the partner's commitment to the project
- clearly explain the value, relevance, and possible benefits of the work to them
- describe any additional value that they bring to the project

Ensure you have prior agreement from project partners so that, if you are offered funding, they will support your project as indicated in the 'Project partners' section.

For audit purposes, UKRI requires formal collaboration agreements to be put in place if an award is made.

Do not provide a statement of support from host and project co-leads' research organisations.

Do not provide a statement of support from collaborators. Contributions from collaborators not listed as project partners can be outlined in 'Applicant and team capability to deliver'.