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
- $\bullet~{\rm FNR}$ '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).

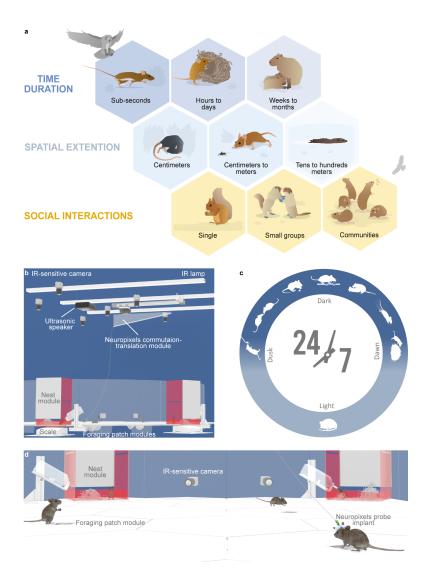


Figure 1: **a**: Example of natural behaviours in rodents that take place over different timescale, spatial extensions and involving different numbers of individuals.

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 tailored to nonstationary data, such as that generated in NaLoDuCo experiments.

Most of the neural data analysis methods that we will add to AEON require sorted spikes. We will adapt the offline spike sorting methods mentioned above to operate under the strict time constraints of real-time experiments (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.,

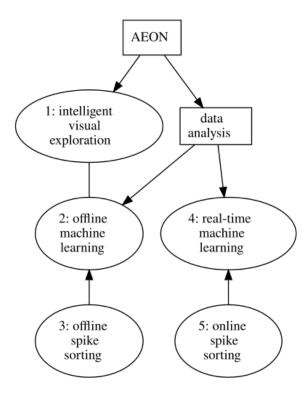


Figure 2: Specific aims

- 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.
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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. However, these very large datasets are of not much help without methods to visually explore and analyse them. We will disseminate a library of methods for visualisation and data analysis of NaLoDuCo experimental data. Sections 3.4.1 and 3.4.2 present offline and online data analysis methods, Section 3.4.3 discusses visualization methods, and Sections 3.4.4 and 3.4.5 elaborate on offline and online spike sorting methods.

3.4.1 Offline analysis methods

In Neuroscience we lack methods to characterise long-duration and continual time series, to learn from data whose statistical properties fluctuate over time, or to forecast time series over long horizons (e.g., hours, days, week or months). To develop such methods we need to address two major challenges, non-stationarity and computational efficiency, as we discuss below **We will create new implementations of methods adapted to function in non-stationary environments, and scaled to efficiently process very long time series.** If necessary, we will create new methods.

Initial list of methods to include in the library

We will initially add to the library methods that we are using at the GCNU/SWC and AIND to characterize mice behavioral and electrophysiological neural activity in NaLoDuCo foraging and odor learning experiments. Below we outline these methods, grouped by functionality (see also Table 1).

The first step in the analysis of NaLoDuCo foraging behavioural data is tracking multiple body parts in mice. For this we will use **deep learning** methods, as in SLEAP. Next, we will use the previous tracking outputs to infer mice kinematics with **linear dynamical models**, as in LDS. We will combine the tracking outputs with the kinematics inferences to infer behavioural states with **hidden Markov models**, as in MoSeq. Further, we will relate kinematics and behavioural states to the probability of foraging

events, like leaving a patch, with **generalized linear models** and **artificial neural networks**. NaLoDuCo experimental data allow to perform forecasting with much longer horizons than with conventional experimental data. We will do long-duration forecasting with **recusive neural networks** and **transformers**. The final step of the behavioural analysis will be to infer mice policy from behavioural measures with **inverse reinforcement learning**, as in HIQL.

The characterization of neural data will begin with the estimation of latent variables, to reduced the dimensionality of multielectrode recordings from hundreds or even thousands of neurons to a small number of latent variables, using latent variable models with linear and nonlinear latent dynamics, as in svGPFA and LFADS. We will use the estimated latent variables as inputs to infer neural states, using Hiden Markov Models, as in SSM. As with behavior, we will perform long-horizon forecasting with recursive neural networks and transformers. Next, we will decode mice position from hippocampal recordings, and study replay during long-duration foraging, with point process decoders, as in replay_trajectory_classification.

To better understand the relation between neural activity and behavior we will estimate latent variables underlying both behavior and neural activity with CEBRA and with RPM, a recent method developed at the GCNU.

Non-stationarity

Conventional offline methods used to characterize neural time series assume that the statistical characteristics of the modeled data do not change with time (i.e., that the probability of the data is time invariant – stationarity). This assumption may be valid for shorter experiments. However, for long-duration experiments, where animals learn and adapt, where their motivation fluctuates, and their activity is modulated by circadian, utradiem and peridiem rhythms, this assumption may not hold. In nonstationary environments, a non-adaptive model trained under the false stationarity assumption is bound to become obsolete in time, and perform sub-optimally at best, or fail catastrophically at worst. Below we briefly describe the type of methods we will use to adapt the disseminated methods to non-stationary environments.

The field of adaptive signal processing develops algorithms to characterize non-stationary systems (Haykin, 2002). In this field adaptations to specific algorithms have been developed to improve their performance in

Table 1: Data analysis methods to disseminate $\,$

Domain	Functionality	Method	Model Type
behaviour	multi-body-part	SLEAP	deep neural network
	tracking		
behaviour	kinematics infer-	LDS	linear dynamical system
	ence		
behaviour	kinematics infer-	LDS	particle filter
	ence		
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		RNN
	forecasting		
behaviour	long-duration		transformers
	forecasting		
brain	latents inference	svGPFA	Gaussian processes
brain	latents inference	LFADS	RNN
brain	state inference	SSM	hidden Markov model
brain	long-duration		RNN
	forecasting		
brain	long-duration		transformers
	forecasting		
brain	decoding	NA	point-process decoder
brain &	latents inference	RPM	Bayesian inference +
behaviour			deep neural network
brain &	latents inference	CEBRA	contrastive learning
behaviour			

non-stationary environments.

For example, the recursive least-squares algorithm (Haykin, 2002, Chapter 9) is an adaptation of the ordinary least square algorithm to perform linear regression with non-stationary data.

For non-linear regression using artificial neural networks, a very large number of strategies have been developed to address data non-stationarity. To mention a few, continual learning has introduced algorithms like Elastic Weight Consolidation (EWC) and Learning Without Forgetting (LwF) to allow models to adapt to changes over time without catastrophic forgetting. Also from this subfield is the Experience Replay (ER) algorithm that stores past data samples in a buffer and replays them alongside new data during training. A different type of strategy is used by ensemble methods (), which combine multiple models trained on different time windows to capture evolving data patterns.

Algorithms for **state-space models**, such as the Kalman filter, perform well in relatively simple non-stationary environments where data exhibit a Gaussian distribution with time-varying mean and covariance. However, in more complex settings with abrupt regime shifts or structured variability, more flexible approaches are required.

Switching state-space models, such as the switching linear dynamical system (SLDS) and the switching Hidden Markov model (sHMM), address discrete changes in system dynamics by adapting to different latent states. For tracking nonlinear and non-Gaussian processes, particle filters offer a powerful alternative by approximating posterior distributions through sequential sampling. Additionally, Bayesian online learning provides a principled framework for adapting probabilistic models to evolving data distributions, enabling continual adaptation in dynamic environments.

In the machine learning literature the study of non-stationary systems is done under the label of **concept drift** (), which refers to a change in the statistical properties of data that causes a model to perform poorly. Differently from adaptive signal processing, most methods developed to tackle concept drift are model agnostic and can be used with multiple machine learning models.

Concept drift can happen suddenly or gradually, and follow a periodic pattern where old concepts periodically reappear (e.g., circadian rhythm variations in neural firing rates). In such scenarios algorithms should remember previous contexts and re-instate them as soon as they reappear, overcoming catastrophic forgetting.

A basic strategy to address concept drift is to test for data distribution changes in data windows and retrain or update models when changes are detected. Several options exist for testing for distributional changes and for performing model updates. Alternatively, one could use ensemble methods that combine multiple models to mitigate the negative effects of drift (e.g., combine classifiers with different learning rates and weight them according to their accuracy. Most concept drift methods are designed for supervised learning, but methods such as clustering evolution, density estimation changes, and autoencoder-based monitoring can detect drift without labeled data.

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 and GPU computing address different bottlenecks in large-scale computation. GPUs are highly efficient at parallelizing operations within a single machine. They excel at matrix operations and batch processing. However, GPUs are limited by memory and cannot scale indefinitely when dealing with huge datasets that exceed the GPU memory. Distributed computing allows to split workload across multiple machines, overcoming memory and computational limitations. It is particularly useful for scaling to massive datasets (e.g., long-term time series recordings).

We will develop accelerated implementations of all methods in the library of methods to process NaLoDuCo experimental data (Section 3.4.1). These

implementations will use JAX¹ for model learning, inference, and numerical computation, Apache Spark² or Dask³ to distribute pre-processing and feature extraction, and Ray⁴ to distribute machine learning and deep learning functionality.

Thunder is a library developed in 2014 to 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, it includes methods to characterize behavior, while Thunder focuses on neural activity. Finally, Thunder implements simpler methods assuming independent and identically distributed data, while our library contains more sophisticated time series ones.

3.4.2 Online Machine Learning

3.4.2.1Outputs

- 1. Bonsai packages implementing real-time ML functionality for experimetal control
- 2. Documentation of these packages

Visual Exploration 3.4.3

3.4.3.1 Outputs

- 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

¹https://docs.jax.dev/ ²https://spark.apache.org/

³https://www.dask.org/

⁴https://docs.ray.io/

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.

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 (inkind) 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 (inkind) 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'.