

From: UKRI Funding Service noresponse@funding-service.ukri.org
Subject: UKRI Funding Service - invitation to review a funding application APP36490: Conflict in the Brain: Understanding Sex and Context-Dependent Choices
Date: 22 May 2024 at 09:03
To: Alexander_Bates@hms.harvard.edu

US



UK Research
and Innovation

Funding Service

Dear Alexander Shakeel Bates,

We're inviting you to review a funding application for a UK Research and Innovation (UKRI) opportunity. We think your expertise will be crucial in reviewing the application and helping us assess whether it should receive funding.

Opportunity

OPP490: BBSRC Responsive Mode: 24RM2

Application

APP36490: Conflict in the Brain: Understanding Sex and Context-Dependent Choices

Application summary

Every day we are exposed to conflicting situations where we must prioritise one goal over others. Choosing the most appropriate action is crucial for life and can be impaired in neurological disorders like depression and schizophrenia. The brain's process of weighing and selecting between alternative options, known as 'action-selection', is not well understood. Furthermore, evidence shows sex biases in decision-making and sex-specific susceptibility to neuropathologies. **Hence, understanding how the brain makes decisions across contexts and genders holds important medical, economical, and societal benefits.**

Elucidating how different neurons contribute to optimal action-selection will help us advance our knowledge of how the brain works. Tackling this problem in mammals is challenging, due to the large number of neurons in the brain, but feasible in the fruit fly *Drosophila*. Flies have a brain of only 100,000 neurons, most of which have been mapped. Thanks to genetic tools, neurons can be observed and manipulated in flies with a level of temporal/spatial/genetic precision that is not possible in mammals. With these tools, we can study how the fly brain responds when there are conflicting options available, and how it chooses amongst them. For instance, how does a fly choose between feeding or escaping a predator? Where and how is this conflicting information evaluated in the brain to drive an appropriate action?

Using our novel behavioural assay, we found that flies abort feeding when danger is detected but ignore visual threats when experiencing severe hunger. Therefore,

the choice between feeding and fleeing is flexible and depends on the animal's hunger state. Moreover, we discovered a sexual dimorphism in this behavioural choice, with females requiring longer periods of starvation to shift their behaviour from escape to feeding.

Leveraging our pioneering behavioural assays, along with neurogenetic techniques and brain imaging, we aim to uncover the neural circuitry that dictates priority during this survival conflict. Moreover, having recently identified key neurons that mediate the choice between mating and fleeing or feeding, we are in a unique position to explore the universality of these mechanisms across various conflicts. Our work therefore provides an unprecedented opportunity to understand how flies integrate sensory cues to make these behavioural choices, and ask what it reveals about the way the brain functions across different contexts and sexes.

The proposed research is grounded in three objectives:

1. Compare and contrast circuit nodes for conflicts between feeding, mating, and escape.
2. Establish how internal hunger state influences cellular networks, activity and behaviour.
3. Characterise the neural and physiological basis of sex-specific behavioural prioritisation.

Outcome: This research will provide a mechanistic understanding of how the fly brain solves conflicts at a remarkable cellular and circuit-level resolution.

Impact: *Drosophila* research has greatly contributed to the field of neuroscience, uncovering universal properties of brain function present across species, including humans. Our work is poised to reveal fundamental principles of decision-making that might be shared across species. This knowledge could inform the development of AI-systems capable of autonomous decision-making and enhance our understanding of neuropathologies where decision-making is compromised. Our findings are expected to extend beyond neuroscience, impacting fields like biomedicine, computational biology, and psychology. This research aligns with the **BBSRC-Strategic Priorities**: "understanding the rules of life", "bioscience for an integrated understanding of health" and "the replacement-refinement-reduction (3Rs) in research using animals", by leveraging flies to address questions relevant to human-health and well-being.

Application team

- Dr Carolina Rezaval, University of Birmingham - **Project lead**

What happens next

If you accept the invite, you'll need to sign in to your UKRI Funding Service account, or create an account if you do not already have one.

Once you've signed in, you'll be able to view the application and submit your review.

How long do I have to complete my review?

You'll have 21 days from the day you agree to complete your review.

However, UKRI also sets a deadline by which time all reviews for an opportunity must be completed. This deadline may reduce your personal time limit of 21 days.

If your timeframe is not feasible, you can contact the council running the opportunity to request an extension:

- AHRC: operations@ahrc.ukri.org
- BBSRC: peer.review@bbsrc.ukri.org
- EPSRC: grants@epsrc.ukri.org
- ESRC: ESRCpeerreview@esrc.ukri.org
- MRC: peer.review@mrc.ukri.org
- NERC: researchgrants@nerc.ukri.org
- STFC: grantspolicy@stfc.ukri.org

If you're not sure which council to contact, or the funding Opportunity is being led by UKRI central, use the UKRI contact details at the foot of this email.

What is an expert reviewer?

The expert review stage (sometimes called the peer review stage) is an important part of our process. It gives fellow experts the chance to comment on and critique applications. This helps us understand the value of an application and decide which applications should receive funding.

Being an expert reviewer is a voluntary position. On average, reviews take between 2 to 6 hours to complete - but this varies depending on the reviewer and the application. We'll give you the guidance required to complete your review.

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You do not have to be an expert in every aspect of the application to be able to complete a review. For example, you may have expertise in the specific methodology but not the subject matter.

Being an expert reviewer also gives you exposure to new research ideas in your field and beyond.

Let us know if you can review this application

Respond to the invitation at: <https://ui.funding-service.ukri.org/review-invite/dbbbc7e2-3d57-45ef-8e91-cbe001a6df88>

You do not have to complete the review right now. Only agree to review this application if you are not aware of any conflicts of interest.

If you have more questions about reviewing this application, you can contact the council running the opportunity.

Thank you for your time and support.

Yours sincerely,

The UKRI Funding Service
Email: support@funding-service.ukri.org
Telephone: +44 (0)1793 547 490

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