Project Details	
Project Code	NMH27Br Cahill
Title	Cerebellar orchestration of social behaviour
Research Theme	Neuroscience & Mental Health
Project Type	Other
Summary	The cerebellum is increasingly recognised to contribute to behavioural flexibility and social cognition. Cerebellar changes are also a major risk factor for developing Autism Spectrum Disorders (ASD). The student will determine the role of specific cerebellar networks in dynamic social behaviour. We will refine novel tasks of social perception and communication and apply them to study social behaviour in genetically modified mice that have altered cerebellar function. Combining behavioural neuroscience, in vivo electrophysiology, and circuit dissection this work will establish how social behavioural is regulated by the cerebellum and how this process is altered in a mouse model of ASD.
Description	Background: The importance of the cerebellum to regulate social behaviours is increasingly becoming apparent. The behavioural tests that are traditionally used to measure social behaviour in genetically modified mice have to compromise on the capacity for natural interaction in order to have tight experimental control and for ease of measurement of behaviour. These limitations restricted our ability to capture the richness and dynamics of natural social behaviour. We have recently developed an advanced deep learning-based pipeline, that is well suited to reveal the diversity of social behaviour. This gives the chance to understand the circuit basis of complex social behaviour processing over longer periods of time. The student will use mice that carry a conditional mutation of TSC1 gene specially in the Purkinje cells of the cerebellum, which leads to dysfunction of the circuit and social behaviour alterations. The student will compare these mice to littermate controls to understand the recruitment and necessity of brain networks downstream of the cerebellum, like the prefrontal cortex (PFC), for social responding using sophisticated viral-based techniques to track and manipulate neural circuits. The mice will be recorded in their home cage environment to provide longitudinal, potentially more ethological, assessment of their sociability. This will be complemented by developing sophisticated behavioural tasks to assess the communicative nature of social behaviour, including the impact on interaction partners and social reciprocity. Our central hypothesis is that the cerebellar exerts an influence over the PFC when contexts shift, signalling that a new mental state and behaviour needs to be engaged in order to adapt to the current context (behavioural state switching, for e.g. rule changes and prediction violations in social contexts). We predict the neural correlates of this representation in the PFC will be influenced by disruption of the cerebellar inputs, leading to impairments in adaptive social behaviour. Our team has the strategic expertise to support the student in the success of the project. Dr Cahill provides expertise in refining behavioural assays to enhance sensitivity of social behaviour measurements (Mediane, Anastasiades and Cahill, 2026). Dr Anastasiades provides expertise in precise circuitry manipulation of the

	PFC (e.g. Anastasiades and Carter 2021). Dr Rule develops mathematical models (e.g. Rule, O'Leary 2022) and data processing workflows (e.g. Rule, Chaudhuri-Vayalambrone et al. 2023) linking neural activity to behaviour. Dr Chadderton provides expertise in in vivo electrophysiology, and cerebellar neural representations of behavioural states (Pemberton, Chadderton and Costa, 2024). Prof Isles provides expertise in neurodevelopmental brain and behavioural phenotyping, and is the lead of the UKRI:MRC National Mouse Genetic Network cluster MURIDAE. He will further contribute strategic expertise in the use and interpretation of genetic mouse models. Ultimately, this work will address the key question: How does the cerebellum influence behavioural state switching during complex, naturalistic social interactions? Overarching Objectives: 1. Characterise cerebellar–prefrontal circuit engagement during social context shifts 2. Compare mutant mice with controls to establish how cerebellar dysfunction alters social interactions, linking neural circuit dysfunction to impaired behavioural adaptation 3. Formalise with computational modelling whether the transition between social and non-social states are less sensitive to social cues, and how this relates to the quality of the neural representations. Feasibility The proposed research will be fully supported by the existing infrastructure in the host laboratories. As such the major expenses will be animal costs and consumables. Some behavioural testing and circuit manipulations in this mouse model have been investigated by the host teams (e.g. Mediane, in preparation) which lays a solid basis for this research to build upon. Degree of Challenge, Strategy for impact: A challenge in the field of social behaviour research is bridging the understanding from the genetic, circuit and behavioural levels, this requires high-dimensional datasets. The proposal seeks to move beyond static measures of behaviour to understand dynamic, context-dependent state transitions, which are inherently difficult to define and quantify. Exposure to a multi-institutional, multidisciplinary supervisory team strengthens the training outcomes for the student. The proposed collaborative project offers excellent synergy for this work as the Cahill and Anastasiades groups (Bristol) already collaborate, whilst the addition of Rule and Chadderton (Bristol) develops a focus on how cell firing patterns in social processes can be formalised into theoretical models of brain function. The addition of behavioural and neurodevelopmental genetics expertise from the Isle group (Cardiff) will systematically investigate relations between earlier life stages and adult phenotypes. This would afford the student with a holistic research approach to develop priority In Vivo skills to investigate social behaviour, alongside insight into computational models / neurodevelopmental genetics. Disentangling developmental from acute circuit contributions to behaviour is not trivial, so the student would draw on these mentors to refine existing tasks, and choose chemogenetic approaches to alter brain circuits. We also actively collaborate with industry (Boehringer

	Ingelheim, Roche, Compass Pathways Neumora), so the student will learn about industry science and translational model refinement.
Can be completed part time?	Yes
Supervisory Team	
Lead Supervisor	
Name	Dr Emma Cahill
Affiliation	Bristol
College/Faculty	Life Sciences
Department/School	Psychology and Neuroscience
Email Address	emma.n.cahill@bristol.ac.uk
Co-Supervisor 1	
Name	Dr Paul Anastasides
Affiliation	Bristol
College/Faculty	Life Sciences
Department/School	School of Psychology and Neuroscience
Co-Supervisor 2	
Name	Dr Paul Chadderton
Affiliation	Bristol
College/Faculty	Life Sciences
Department/School	School of Psychology and Neuroscience
Co-Supervisor 3	
Name	Professor Anthony Isles
Affiliation	Cardiff
College/Faculty	Centre for Neuropsychiatric Genetics and Genomics Canolfan y Cyngor Ymchwil Feddygol ar gyfer Geneteg Niwroseiciatrig a Genomeg
Department/School	Medicine
Co-Supervisor 4	
Name	Dr Michael Rule
Affiliation	Bristol
College/Faculty	Engineering
Department/School	School of Engineering, Mathematics and Technology