Project Details	
Project Code	MRCNMH25Br Purple
Title	Using machine learning to investigate the role of cell assemblies in processing traumatic experiences and the development of post-traumatic stress disorder
Research Theme	Neuroscience & Mental Health
Summary	Groups of neurons known as cell assemblies become active during our daily experiences and reactivate over time, including during sleep. Whilst this reactivation is known to be important for the processing and consolidation of memory, little is known of how this occurs in the context of a traumatic experience. This project aims to develop machine learning algorithms to identify cell assemblies and track their reactivation during wake and sleep after a trauma-like experience in rats. This will provide essential insights into how traumatic experiences are processed within the brain and how this contributes to the development of post-traumatic stress disorder.
Description	Over 80% of people experience a traumatic event during their lifetime; of these, up to ~10% develop post-traumatic stress disorder (PTSD), suffering distressing flashbacks, avoidance, hyperarousal, and nightmares. Crucially, current therapies fail to deliver long-term control of symptoms in ~50% of sufferers. Defining determinants of vulnerability to PTSD and designing novel, biologically informed prevention and treatment strategies is essential. Sleep supports “offline” processing of daily experience; its disruption can therefore contribute to the maladaptive memory processing that hallmarks PTSD. Cell assemblies, groups of neurons that temporally and functionally organise to encode information, that are active during learning, reactivate during sleep. This occurs when the coordination of network oscillations including ripples, spindles, and slow-waves, optimise limbic-cortical dialogue and tune the integration of memory into long term storage. Replay of hippocampal place cell sequences during non-rapid eye movement sleep (NREM) supports consolidation of spatial memories. In contrast, there is significant evidence from human studies that REM sleep, and theta activity, are instrumental in processing emotional memories and reducing emotional tone. However, sleep reactivation in this context has only been partially explored and no studies have assessed this in relation to trauma. Your project will involve computational neuroscience and the development of machine learning algorithms to optimise the detection of cell assemblies that become active during trauma exposure in a rat model of PTSD. Detecting cell assemblies during trauma exposure and tracking assembly reactivation across time including during sleep, will provide essential insights into how traumatic memories are processed, pinpointing precise temporal and anatomical targets for therapeutic intervention. Further, there are currently no methods to assess trauma-related intrusive memories or nightmares in animals, which are both key symptoms of PTSD. Although it is unclear whether replay of task-related activity during sleep (or wake) represents conscious recollection of the event, evidence suggests replay is related to memory retrieval. Identifying the frequency of assembly reactivation after trauma exposure may reveal unique differences between vulnerable and

	resilient animals, providing novel evidence of 'intrusion-like' activity and further improving translatability to human psychopathology. Your project will involve an interdisciplinary team and collaboration between Bristol, Pisa and Cardiff. This project can be broadly split into three primary areas with increasing opportunity for independence and student ownership and direction throughout. Objective 1: The introduction of Neuropixels silicone probes, with over 900 electrode recording sites, has provided a step change in the number of neurons we can record from in freely behaving animals. While giving the opportunity to better characterize ongoing mental processes, the analysis of datasets of this size comes with computational challenges. Co-supervisor Dr Russo has previously developed a machine learning algorithm to detect cell assemblies across multiple timescales and lag constellations. The first aim of your project will be to develop this algorithm further, tailoring it to the analysis of large datasets. To this aim, you will be encouraged to actively propose and develop new approaches and test them with the supervision of Dr Russo. After validating the new algorithm, you will apply it on existing Neuropixels data (provided by co-supervisors Dr Purple, Dr O'Neill and Prof Jones) to track assembly reactivations across time. Objective 2: We will collect new Neuropixels data, recording from limbic areas of the rat brain, during exposure to a predatory threat, trauma-like paradigm. Subsequent recordings will also be conducted during sleep and free behaviour over the course of a week. Using your improved algorithm, you will analyse cell assembly activations and reactivations during these recordings. This will allow us to answer key questions such as: Do trauma-related assemblies reactivate during specific stages or oscillations of sleep? How do assembly reactivation patterns differ between animals that go on to develop PTSD-like phenotypes and animals that remain resilient? Objective 3: The final objective will test the potential to manipulate cell assembly reactivation. You will work with Dr Purple, Dr O'Neill and Prof Jones to develop an intervention (e.g. conditioned auditory stimulation or optogenetics) to interrupt or enhance cell assembly reactivation, providing key insight into their causal effects on the development of PTSD-like phenotypes. Whilst an interest in computational neuroscience and coding with Matlab/Python is essential for this project, the degree of involvement you have in conducting the in-vivo experiments and collecting data is flexible and dependent on your own research direction and interests. Location: You will primarily be based at the University of Bristol with regular meetings with other co-supervisors taking place online. Initial training and development of the algorithm will require considerable (but flexible) research visit/s to Sant'Anna School of Advanced Studies in Pisa.
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