

Project Details	
Project Code	MRC21NMHCa Zhang
Title	The connectomics of Alzheimer's risk: characterising brain temporal network dynamics in young adults at increased genetic risk for late-onset Alzheimer's disease
Research Theme	Neuroscience & Mental Health
Summary	Using advanced imaging and novel mathematical approaches, we will identify spatio-temporal brain networks that show altered dynamics in young adults with genetic risk for Alzheimer's disease. The PhD will provide grounding in network neuroscience — an evolving field using network theories to study the brain across multiple scales and modalities.
Description	<p>To reduce the burden of cognitive decline in neurodegeneration, a key challenge is to understand genetic influences on brain functions at the preclinical stage. This PhD focuses on the strongest genetic risk factor for Alzheimer's disease: the $\epsilon 4$ allele of the APOE gene. We will establish, decades before the onset of clinical symptoms, whether young APOE-$\epsilon 4$ carriers show selective changes in brain network dynamics compared to non-carriers. Novel findings of network alternations in young APOE-$\epsilon 4$ carriers could help develop preventative interventions in early life. Our innovative data-driven approach combines:</p> <ul style="list-style-type: none"> [1. Unique resources from a longitudinal birth cohort] This project links to a £1.8m MRC-funded multi-centre study, which will recruit >200 APOE-$\epsilon 4$ carriers and non-carriers (age 26~28) from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort for comprehensive brain-imaging and cognitive testing, with 204 participants completed to date. ALSPAC contains detailed demographical and neuropsychological data from >14,000 pregnancies since 1991. [2. Cutting-edge brain-imaging] We will integrate advanced multi-modal imaging to quantify brain networks: (1) high resolution (200 μm) 7T structural MRI for precise segmentation of brain regions; (2) high-gradient diffusion-weighted MRI for modelling structural connectivity; and (3) ultra-high-field 7T functional MRI (fMRI) for measuring temporal networks during rest and movie viewing. [3. Exciting opportunities for new mathematical approaches] Starting with the static structural connectivity of each individual, we will use fMRI data during rest to quantify brain functional connectivity as time-varying networks. This allows measuring whole-brain functional connections as well as their dynamic changes over time. We will use the temporal-topological structure of these networks to identify network dynamics that show alternations in APOE-$\epsilon 4$ carriers. By relating the network measures to fMRI data acquired during free-viewing of movies, we will further identify the emergence of the atypical network dynamics essential to the known behavioural phenotype in APOE-$\epsilon 4$ carriers (i.e., impaired scene perception), thus contributing new knowledge on the systems level mechanisms by which genetic factors influence cognition. Further added value includes (1) a GW4 supervisory team with interdisciplinary expertise in imaging (Cardiff) and network dynamics (Exeter, Bath), (2) three collaborators who are international experts in network sciences (Prof. Naoki Masuda, USA; Prof. Lorenzo Livi, Canada) and cognitive neuroscience (Prof. Kim Graham, Cardiff) and (3) the strong feasibility from being linked to a large MRC-funded study,

	including support from geneticists and fieldworkers at Bristol. Beyond academic beneficiaries, outcomes will be disseminated to the public through regular engagement events. Together with our GW4 collaborators, we will also seek opportunities to disseminate your research to clinicians, carers, and patients.
Supervisory Team	
Lead Supervisor	
Name	Dr Jiaxiang Zhang
Affiliation	Cardiff
College/Faculty	College of Biomedical and Life Sciences
Department/School	Cardiff University Brain Research Imaging Centre and School of Psychology
Email Address	zhangj73@cardiff.ac.uk
Co-Supervisor 1	
Name	Dr Marc Goodfellow
Affiliation	Exeter
College/Faculty	College of Engineering, Mathematics and Physical Sciences
Department/School	Mathematics
Co-Supervisor 2	
Name	Professor Andrew Lawrence
Affiliation	Cardiff
College/Faculty	College of Biomedical and Life Sciences
Department/School	Cardiff University Brain Research Imaging Centre and School of Psychology
Co-Supervisor 3	
Name	Professor Tim Rogers
Affiliation	Bath
College/Faculty	
Department/School	Department of Mathematical Sciences
Co-Supervisor 4	
Name	Professor Kim Graham
Affiliation	Cardiff
College/Faculty	College of Biomedical and Life Sciences
Department/School	Cardiff University Brain Research Imaging Centre and School of Psychology