

Report on the thesis and viva of Jonathan Krohn  
"Genes Contributing to Variation in Fear-Related Behaviour"  
Examiners: Prof. Martien Kas (external) and Dr. Andrew Morris (internal)

The thesis of Jonathan Krohn describes the application of novel Bayesian methods for modelling complex relationships between genotype, environment, expression and phenotype, to the identification of genes contributing to variation in fear-related behaviours in a mouse model. First, the thesis considers the use of Bayesian sparse partitioning to identify gene-by-sex interactions that contribute to fear-related behaviours, and contrasts results with "Bagphenotype", a frequentist approach to detect gene-environment interactions. There is overlap in gene-sex interactions identified by the two approaches, and positive correlation between metrics that assess the strength of evidence of in favour of association. Next, the thesis considers a variety of approaches to generate gene co-expression networks. These approaches are applied to gene expression data from the hippocampus, and the networks used to search for gene ontology enrichments and map QTL for the network modules. Two of the modules were enriched for nervous system components, but were not clearly associated with fear-related behaviours. Finally, the thesis applies novel Bayesian methodology, using sparse instrumental variables, to model the relationships between hippocampus gene-expression and fear-related behaviour phenotypes, to assess the evidence for "causality" as opposed to "undirected association"

The thesis represents a substantial and high-quality piece of work, and the methodology and results of these analyses have already been published or are under review. The thesis makes use of state-of-the-art statistical modelling techniques, and we consider that it will provide a valuable contribution to the genetics research community, particularly in the utility of Bayesian methodology in the investigation of the complex relationships between gene, environment, expression and phenotype.

Jon defended his thesis in a three hour viva on 6 September 2013. He clearly demonstrated that the work presented in the thesis was his own, and showed expertise in both the methodological and analytical aspects of his project. The viva was an interesting and enjoyable discussion between the candidate and examiners.

On completion of the viva, the examiners highlighted a number of minor corrections to the thesis. These consisted primarily of minor typographical errors, minor figure adjustments to improve readability, minor re-structuring of the presentation of the discussion of results in Chapters 3, 4 and 5, and additional discussion points (investigated during the viva) to be included in Chapter 6. Jon received the list of minor corrections on 17 December 2013. The revised version of the thesis was received by the examiners and the corrections subsequently approved on 23 December 2013.

After submission of the minor corrections, the examiners are happy that Jon's thesis and performance in the viva meet the standard required for the award of the degree of Doctor of Philosophy.