

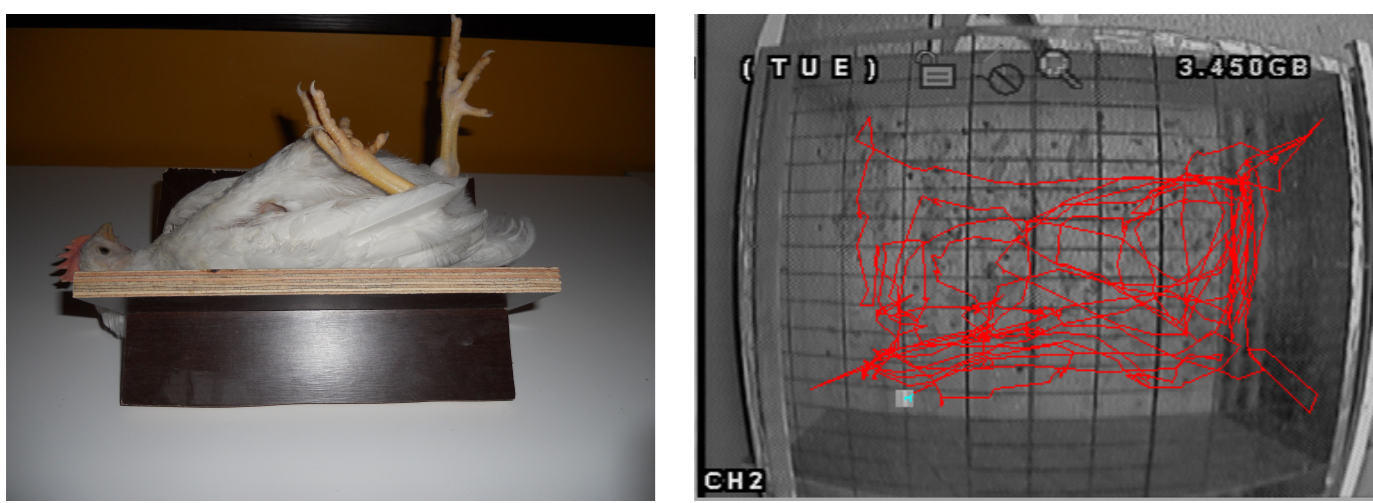
Quantitative trait genes for fearful behaviour in an intercross of wild and domestic chickens

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An advanced intercross is a powerful system for mapping quantitative traits differing between domesticated White Leghorn layers and Red Junglefowl, the wild progenitor. We use genetic mapping of gene expression traits, eQTL mapping, to narrow down the list of candidates generated by quantitative trait locus mapping.

We performed quantitative trait locus (QTL) mapping of the outcomes of three test situations – open field, social reinstatement, and tonic immobility – in 572 birds of the eighth generation of a White Leghorn x Red Junglefowl advanced intercross. The tests were performed twice, and several variables from each test were mapped. The birds were genotyped on 652 SNP markers. Mapping was performed with one and two dimensional scans with Haley Knott regression.



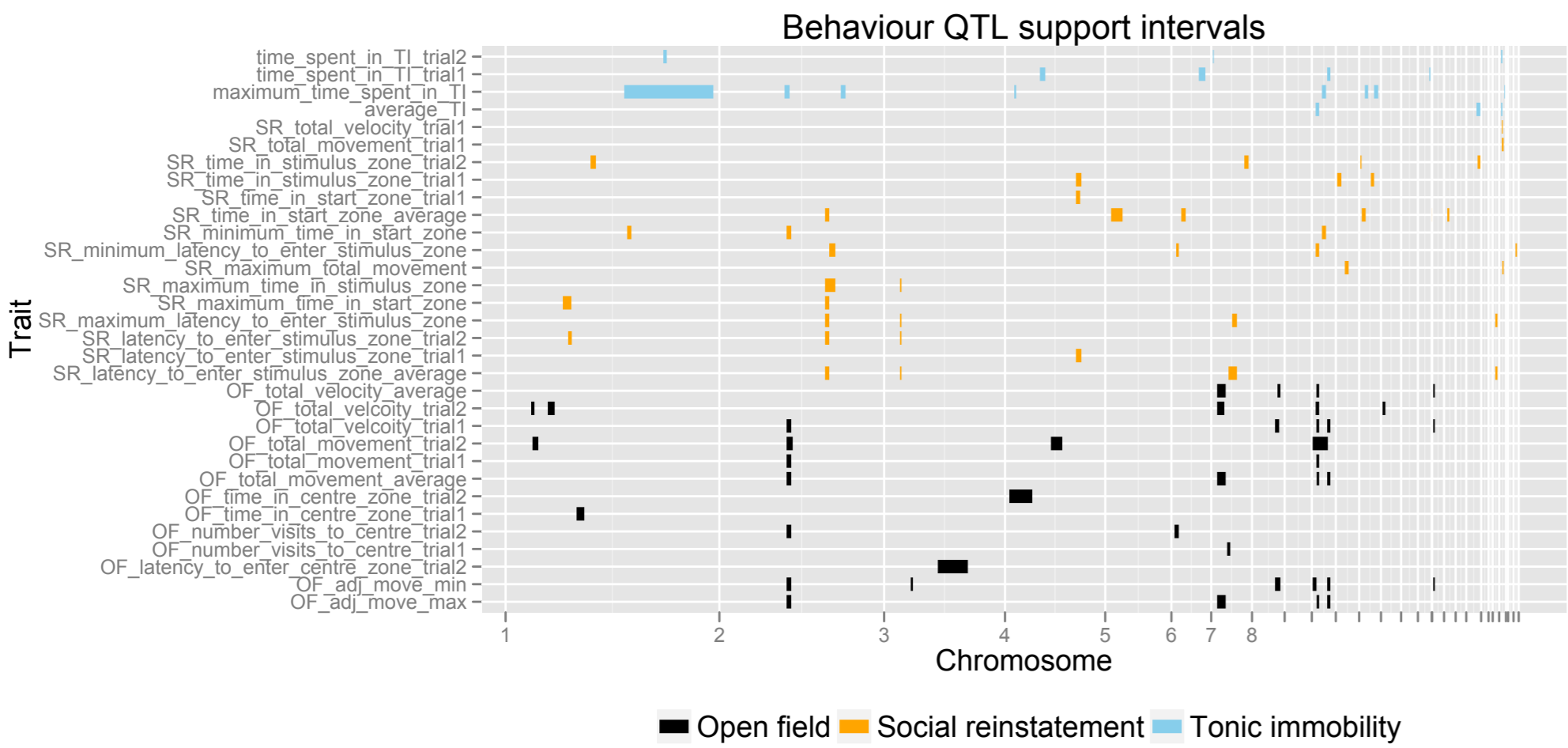
A subset of the cross, 129 hypothalamus samples, were used for eQTL mapping. Gene expression was measured with custom NimbleGen microarrays, covering all known chicken genes, and a database of chicken ESTs. We detected 535 local cis-eQTL and 99 trans-eQTL. Expression QTL that overlapped with behaviour QTL were tested for correlation between the behaviour and gene expression traits to identify candidate genes. We detected 16 such genes out of over 200 that have eQTL overlapping behaviour QTL.

The plots below show LOD (logarithm of the odds) curves of behaviour and gene expression traits in two such cases: a social reinstatement an tonic immobility QTL on chromosome 1, and two proximal open field QTL on chromosome 10.

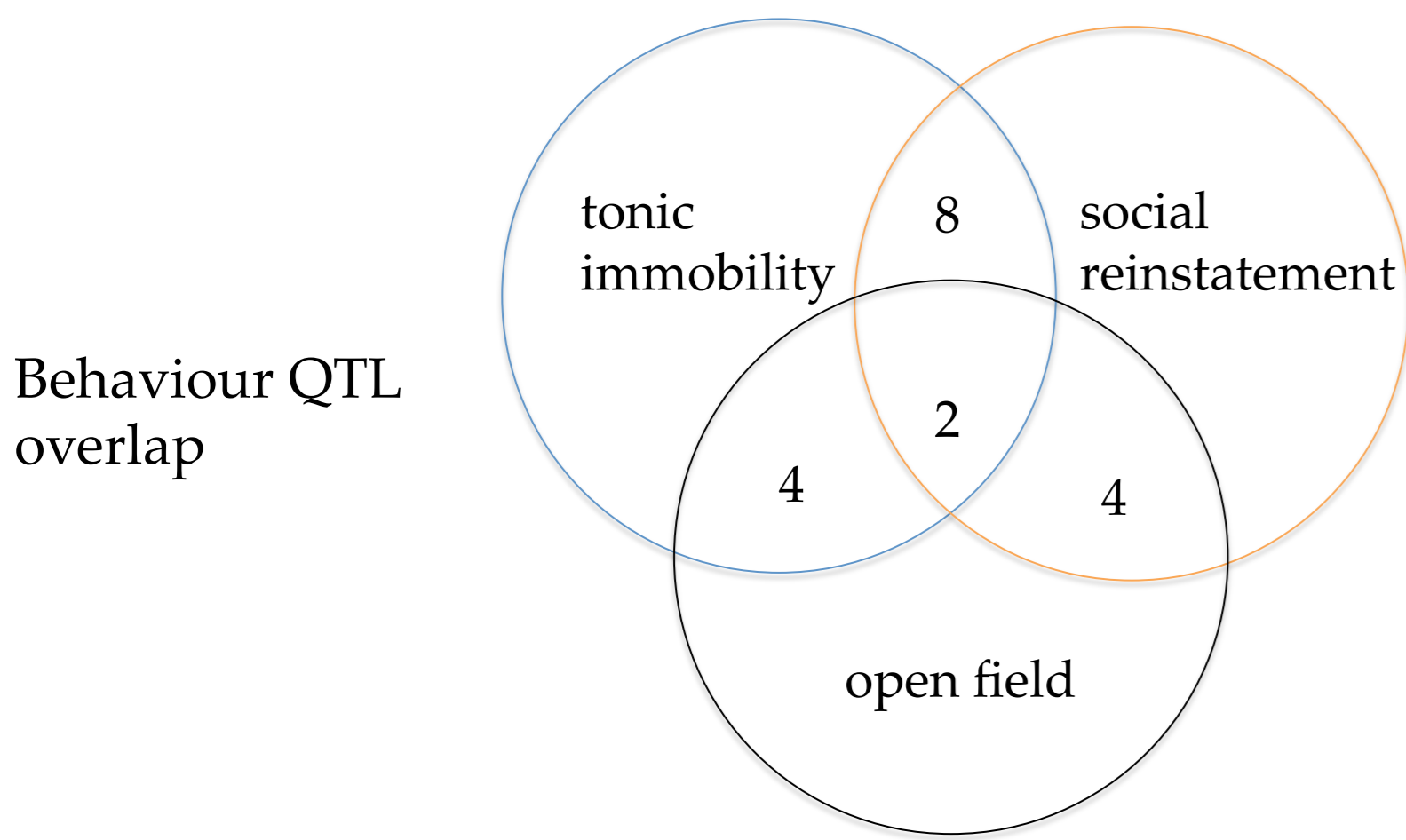
Finally, we applied structural equations modelling, using the NEO software (Aten et al, 2008), to test whether the partial correlations of the genetic markers, gene expressions and behaviour traits are consistent with a causal effect of the gene. A set of alternative models (causal model, marker -> expression trait -> behaviour; reactive model, marker -> behaviour -> expression trait; independent cauastion etc) were fit to the data and compared.

Some of the behaviour QTL could not be detected in the smaller sample size (129 individuals) of the eQTL data set. Therefore, this analysis was not applied to those genes. Eight genes in five QTL regions on chromosomes 1, 2, and 10 were supported by the structural equations model. In several cases, our analysis still highlighted more than one alternative candidate for the QTL.

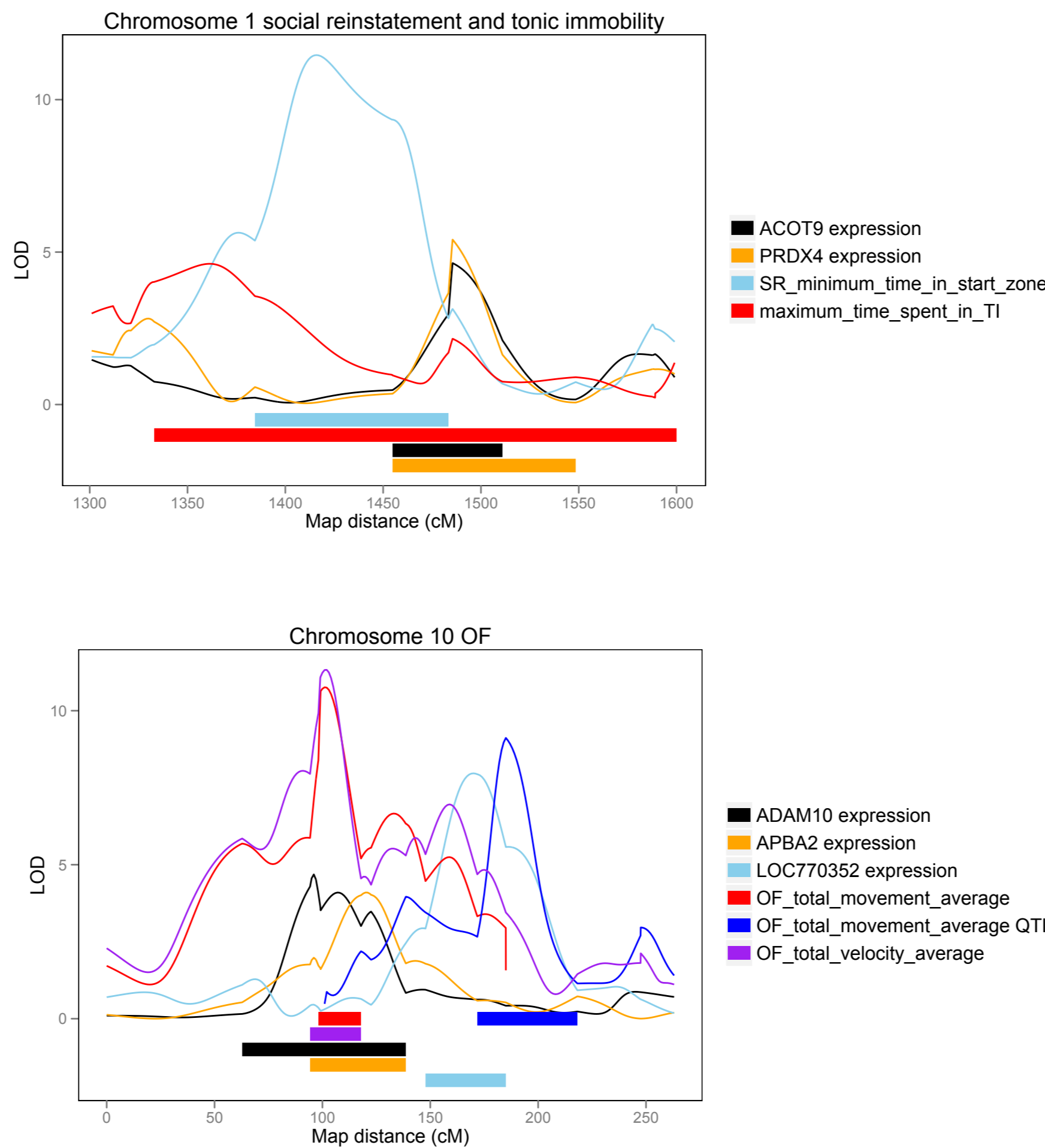
genes in QTL regions



We identify ~ 40 QTL regions, some of which appear to have pleiotropic effects in two or three of the test situations. As expected, fearful behaviour has a polygenic genetic architecture, and the detected QTL have small to moderate effects.



eQTL overlap and trait correlation

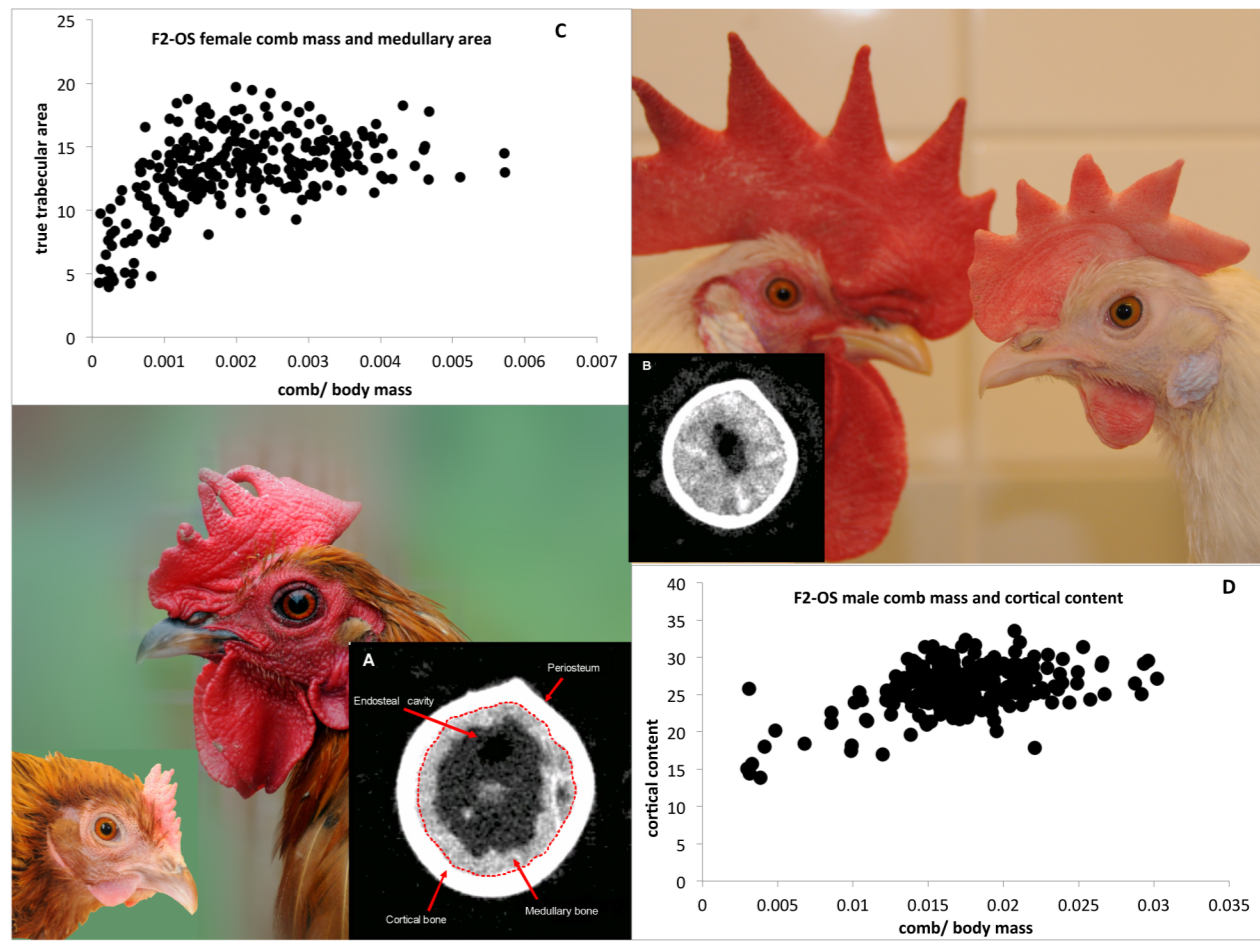


structural equations modelling

gene	description	traits	chr
ACOT9	ACOT9 acyl-CoA thioesterase 9	SR	1
		TI	1
		SR	10
SRPX	Sushi repeat-containing protein	SR	1
PRDX4	peroxiredoxin 4	SR	1
		TI	1
TTRAP	TRAF and TNF receptor-associated protein	SR	2
603866246F1	unknown EST	SR	2
ADAM10	A Disintegrin and metalloproteinase domain-containing protein 10	OF	10
LOC770352	unknown	OF	10
APBA2	Amyloid beta A4 precursor protein-binding family A member 2	OF	10

Of brains, combs, and bones

The common theme of my PhD project is building on the results of quantitative trait locus mapping to find quantitative trait genes for domestication phenotypes in the chicken. To that end, eQTL mapping has been, or is in the process of being, applied to study fearful behaviours, comb size, and bone allocation—divergent traits between wild and domestic chickens.



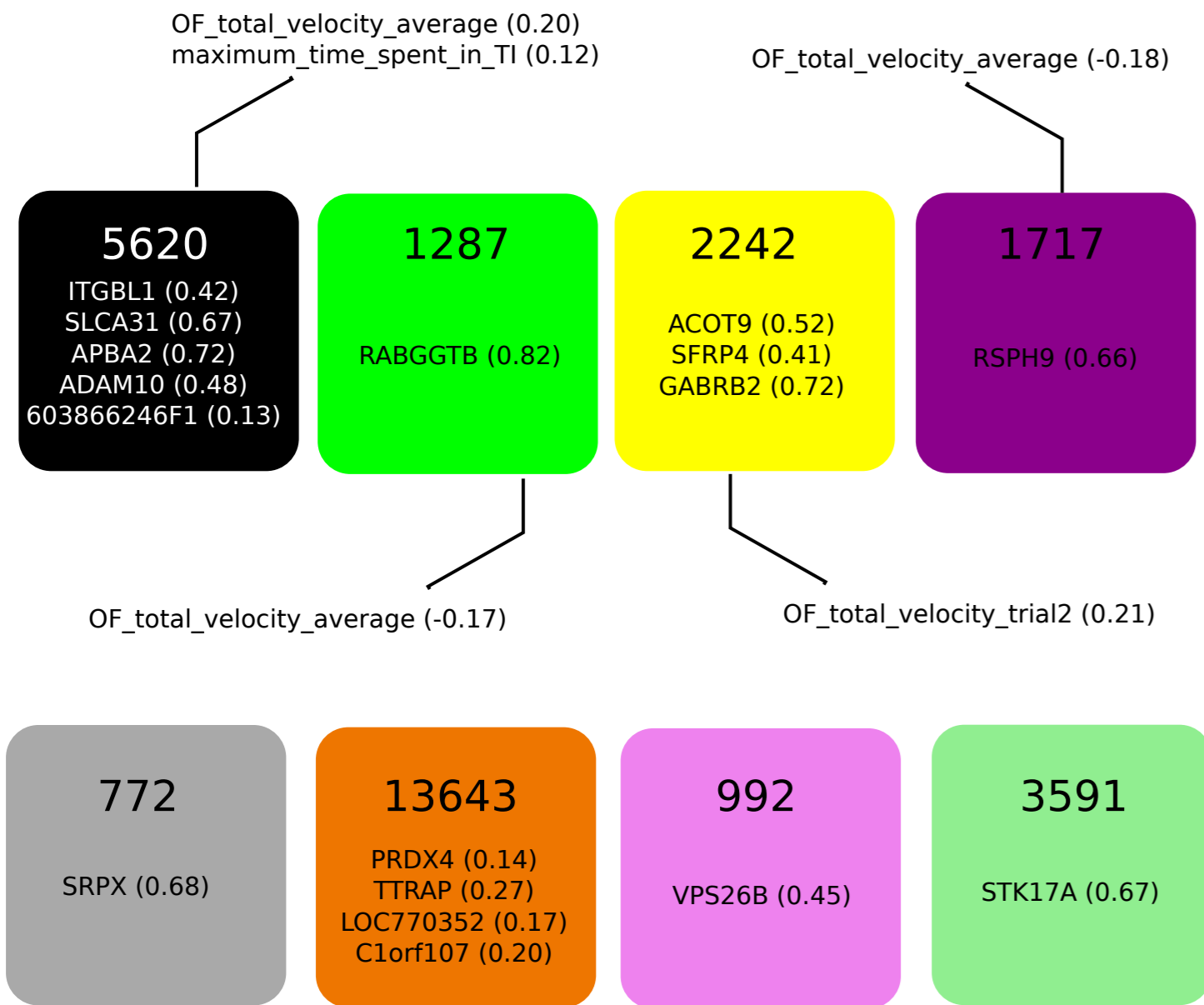
The next step is to use cell culture based models to investigate the genes singled out by mapping and gene expression, and to study their association with quantitative traits in chicken populations.

Weighted coexpression network

We constructed a weighted coexpression network based on scaled Pearson correlations, and clustered genes into modules with hierarchical clustering (Langfelder & Horvath, 2008). Out of 53 modules, eight contain at least one the 16 correlational candidate genes.

Four of those modules have a correlation to the trait value, and show a positive relationship between module memberships and trait correlation, indicating the expression of this module might be relevant for the trait.

The figure shows the number of probesets in the module, the correlation between the gene in question and the module expression profile (in brackets), and the associated quantitative traits with their correlation to the module expression profile.



References:
Aten J, Fuller T, Lusis A, & Horvath S (2008) Using genetic markers to orient the edges in quantitative trait networks: The NEO software. BMC Systems Biology 2(1):34.
Langfelder P & Horvath S (2008) WGCNA: an R package for weighted correlation network analysis. BMC Bioinformatics 9(1):559

We find genetic and gene expression evidence for several quantitative trait genes for tonic immobility, social reinstatement, and open field behaviour.

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