

Complex Genetic Architecture of the Chicken Genome

An Example of *Growth1* QTL Region

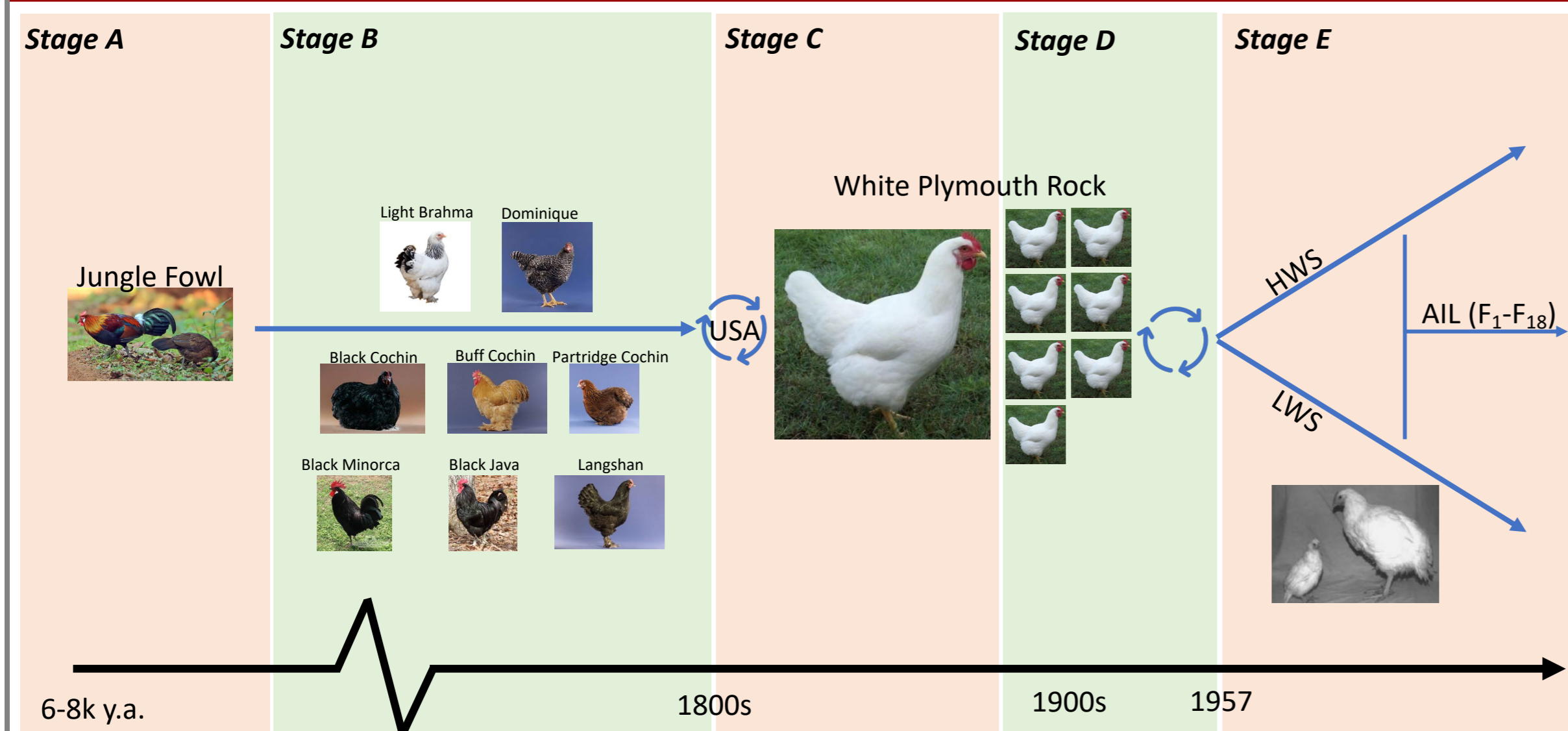
Jen-Hsiang Ou, Tilman Rönneburg, Carl-Johan Rubin

Department of Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden

ABSTRACT

Chicken body weight is an essential trait in both commercial and research, and it is known to be controlled by multiple effects. Virginia Chicken Lines were introduced with bi-directional selected lines (high-weight, HWS / low-weight, LWS) and as advanced intercrossed lines generated from the 41st generation of HWS and LWS. While accumulating recombination in each generation, extending generation to F₁₈ provided a higher resolution for GWAS and variance-heterogeneity GWAS. This research discovered that haplotype and epistasis effects caused the complex genetic architecture in the *Growth1* QTL region. Two major peaks were detected from GWAS, and the haplotype-based association study carried out similar results while providing a more vital significance. Statistical epistasis results suggested that there is a local interaction network in which interaction effects play an essential role in this region.

VIRGINIA CHICKEN LINES



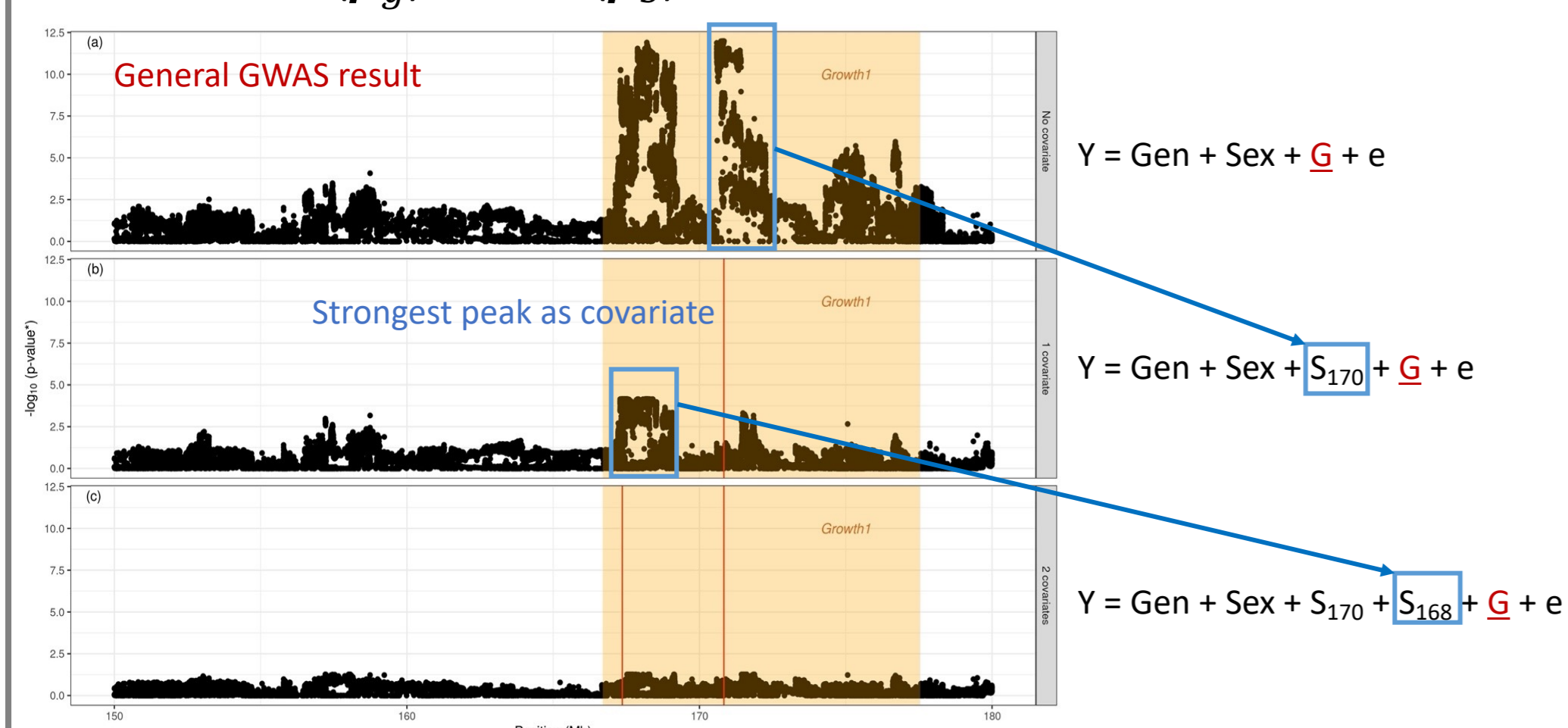
- **Stage A:** Chicken domestication from the wild ancestor, the Red Jungle Fowl.
- **Stage B:** Formation of endogenous and historical breeds independently in Europe and Asia.
- **Stage C:** Migration and admixture events started to create modern chicken breeds for meat and egg production in the USA.
- **Stage D:** The work at Virginia Polytechnic Institute starts to generate the experimental population with multiple inbred lines from the White Plymouth Rock breeds.
- **Stage E:** Siegel and his co-workers started the bidirectional single-trait selection experiment 1957.

ASSOCIATION STUDIES

SNP Markers (GWAS)

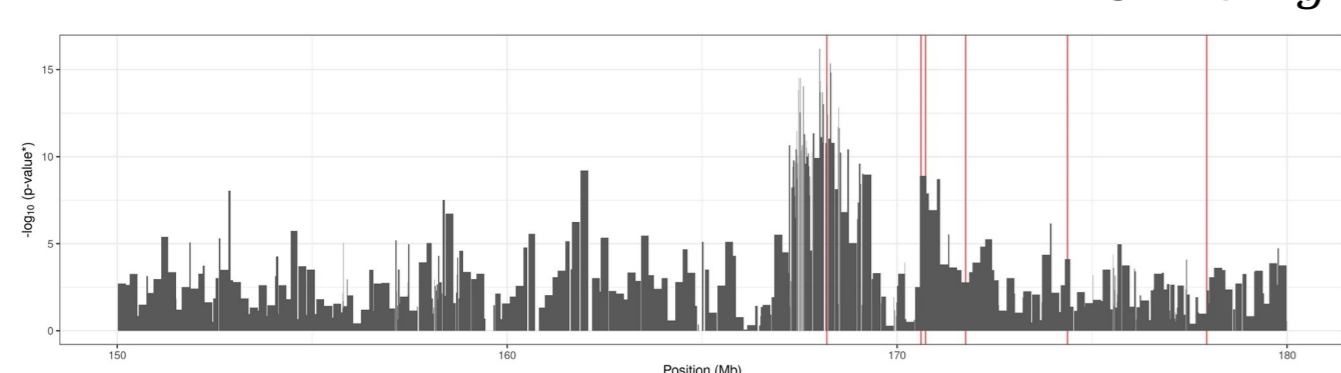
$$y = 1\mu + S\beta_S + g\beta_g + A_j a_j + \epsilon$$

- Single marker association study. Marker effect of SNP j : a_j .
- Generation (β_g) and sex (β_S) are considered as fixed effect.



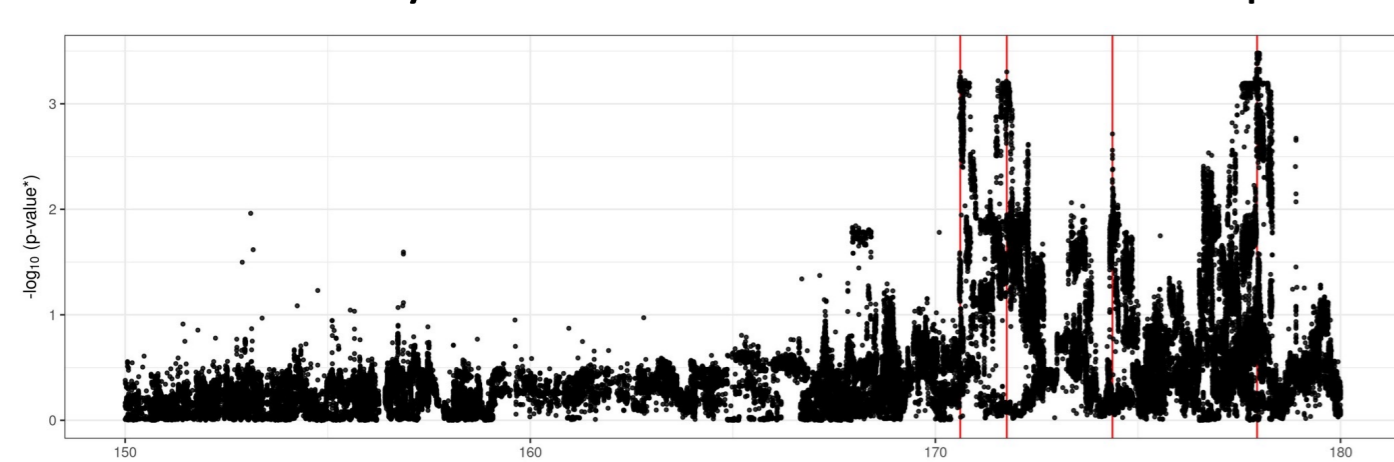
Haplotype-based association study

$$y = 1\mu + S\beta_S + g\beta_g + H_j h_j + \epsilon$$

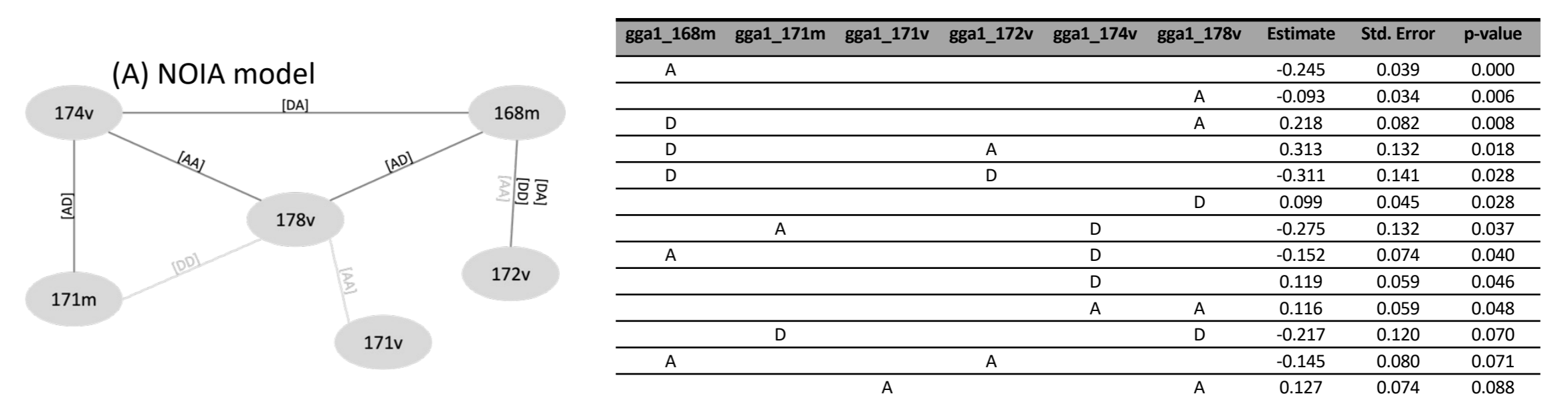


Variance-heterogeneity GWAS (vGWAS)

- Interactions and haplotypes (Forsberg et al. 2015)
- Brown-Forsythe test: ANOVA based on the spread in each group.

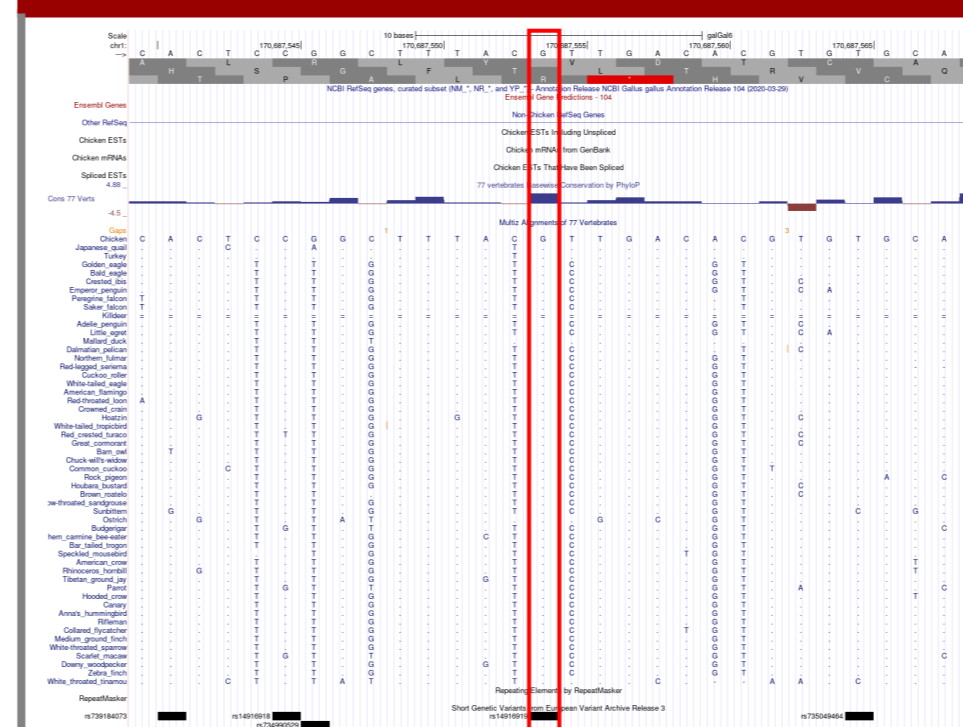


EPISTASIS



- Natural and Orthogonal InterAction (NOIA) model
 - A statistical framework aiming at unifying, extending, and simplifying existing models of genetic effects
 - According to the interaction network, the regulation of body weight via *Growth1* QTL is not solely determined by the independent effects of the loci
- Association studies using samples grouped by the *gga1_178v* genotype. Signals were eliminated in the LL group.
- Association studies with samples grouping by the genotype of *gga1_172v*.
- Association studies with samples grouping by the genotype of *gga1_174v*.

GENE IDENTIFICATION



An example: rs14916919

- $-\log_{10}(p\text{-value}) = 7.55$
- Highly conserved in 77 bird species
- All LWS samples carried reference allele (G)
- All HWS samples carried alternative allele (A)

DISCUSSION

- Extending generation to F₁₈ provides a better resolution for discovering complex genetic architecture by accumulating recombination.
- Haplotype effect + Epistasis network
- Effects were observed in various bird species, but further investigation is required to validate the existence of local interactions.

