Complex Genetic Architecture of the Chicken Genome
An Example of Growth1 QTL Region
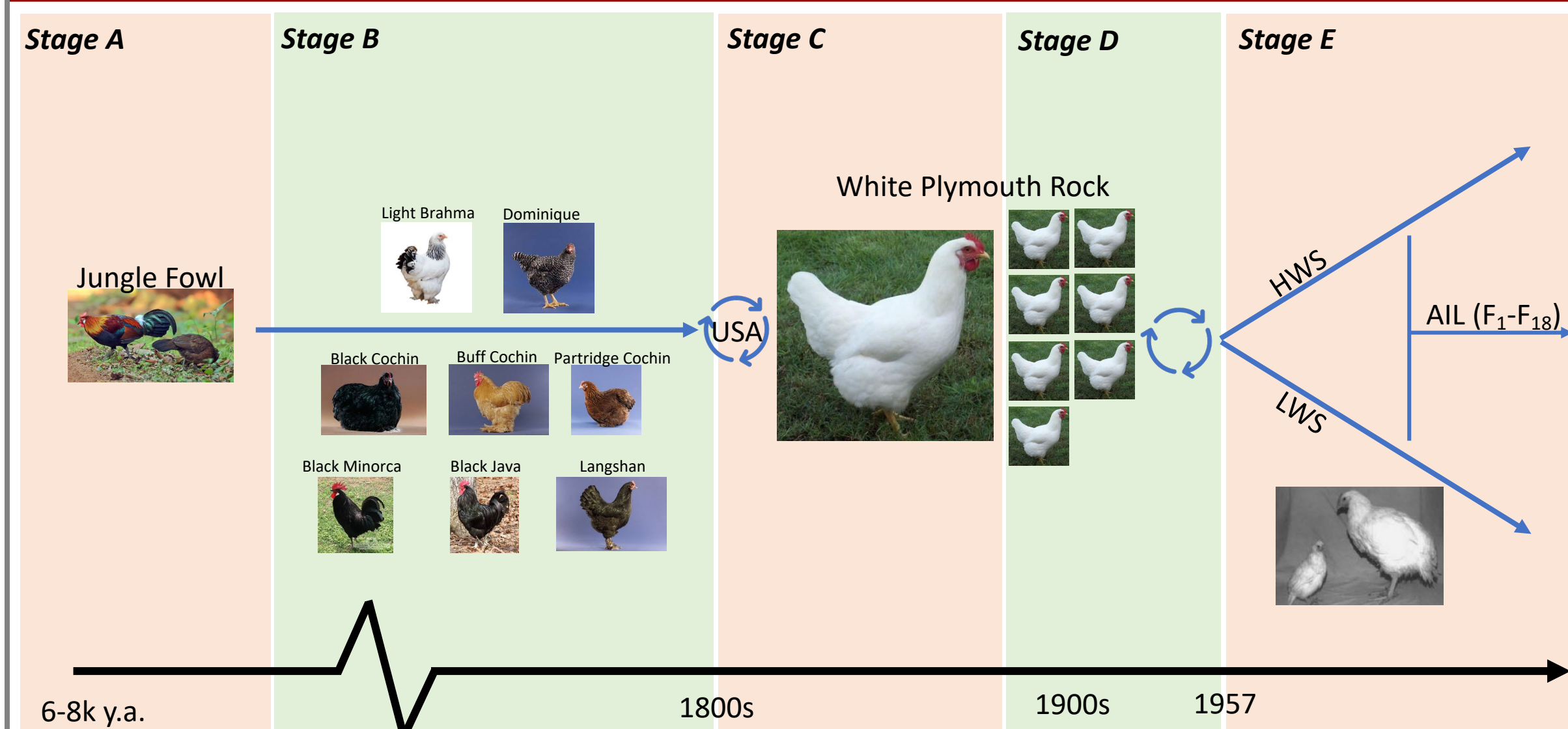
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ABSTRACT

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.
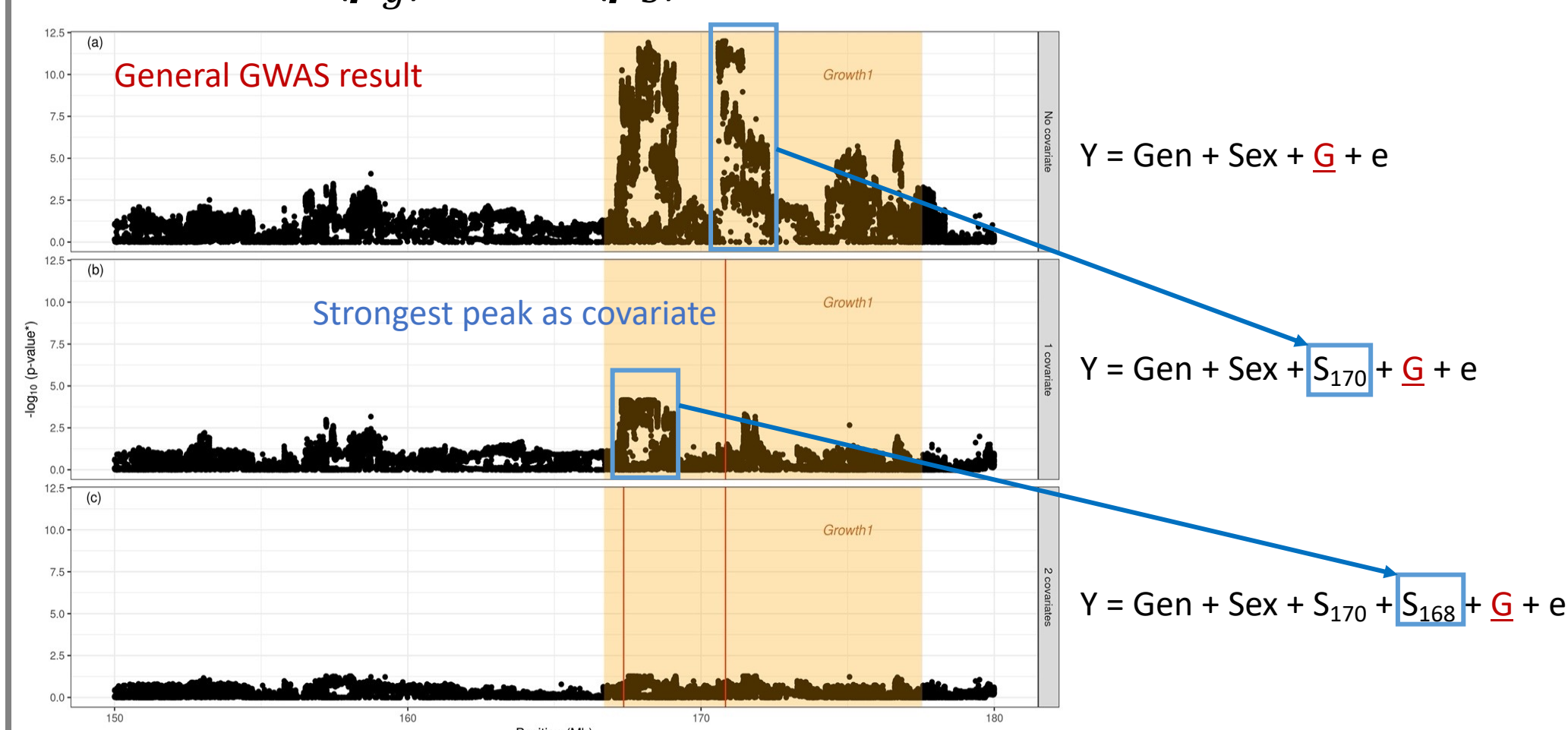
VIRGINIA CHICKEN LINES

Stage A | Stage B | Stage C | Stage D | Stage E

White Plymouth Rock

Jungle Fowl

Light Brahma, Dominique, Black Cochin, Buff Cochin, Partridge Cochin, Black Minorca, Black Java, Langshan

USA

HWS, LWS, AIL (F₁-F₁₈)

6-8k y.a. | 1800s | 1900s | 1957

- **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.
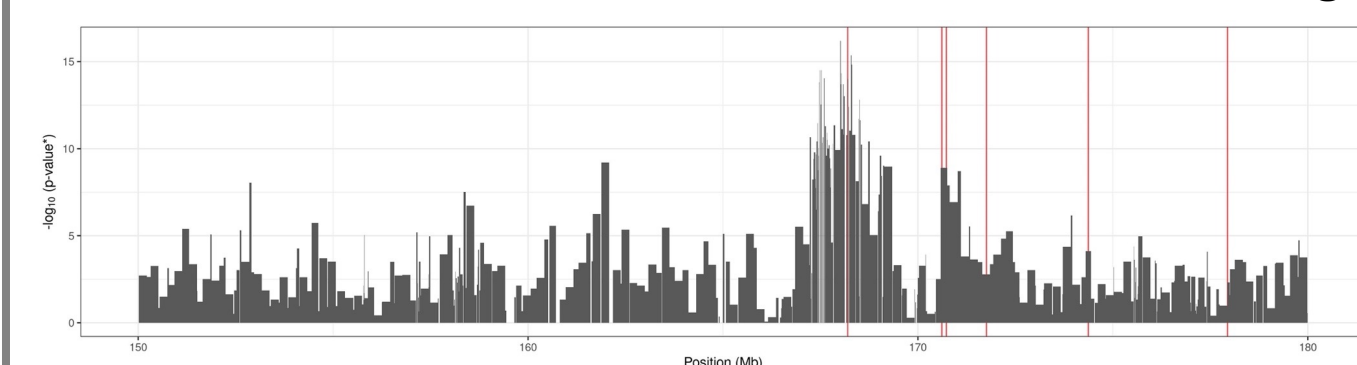
ASSOCIATION STUDIES

SNP Markers (GWAS)

$$y = 1\mu + S\boldsymbol{\beta}_S + g\boldsymbol{\beta}_g + A_j\boldsymbol{a}_j + \boldsymbol{\epsilon}$$

- Single marker association study. Marker effect of SNP j: $\boldsymbol{a}_j$.
- Generation ($\boldsymbol{\beta}_g$) and sex ($\boldsymbol{\beta}_S$) are considered as fixed effect.

General GWAS result — Growth1

Y = Gen + Sex + <u>G</u> + e

Strongest peak as covariate — Growth1

Y = Gen + Sex + S_{170} + <u>G</u> + e

Growth1

Y = Gen + Sex + S_{170} + S_{168} + <u>G</u> + e

Haplotype-based association study

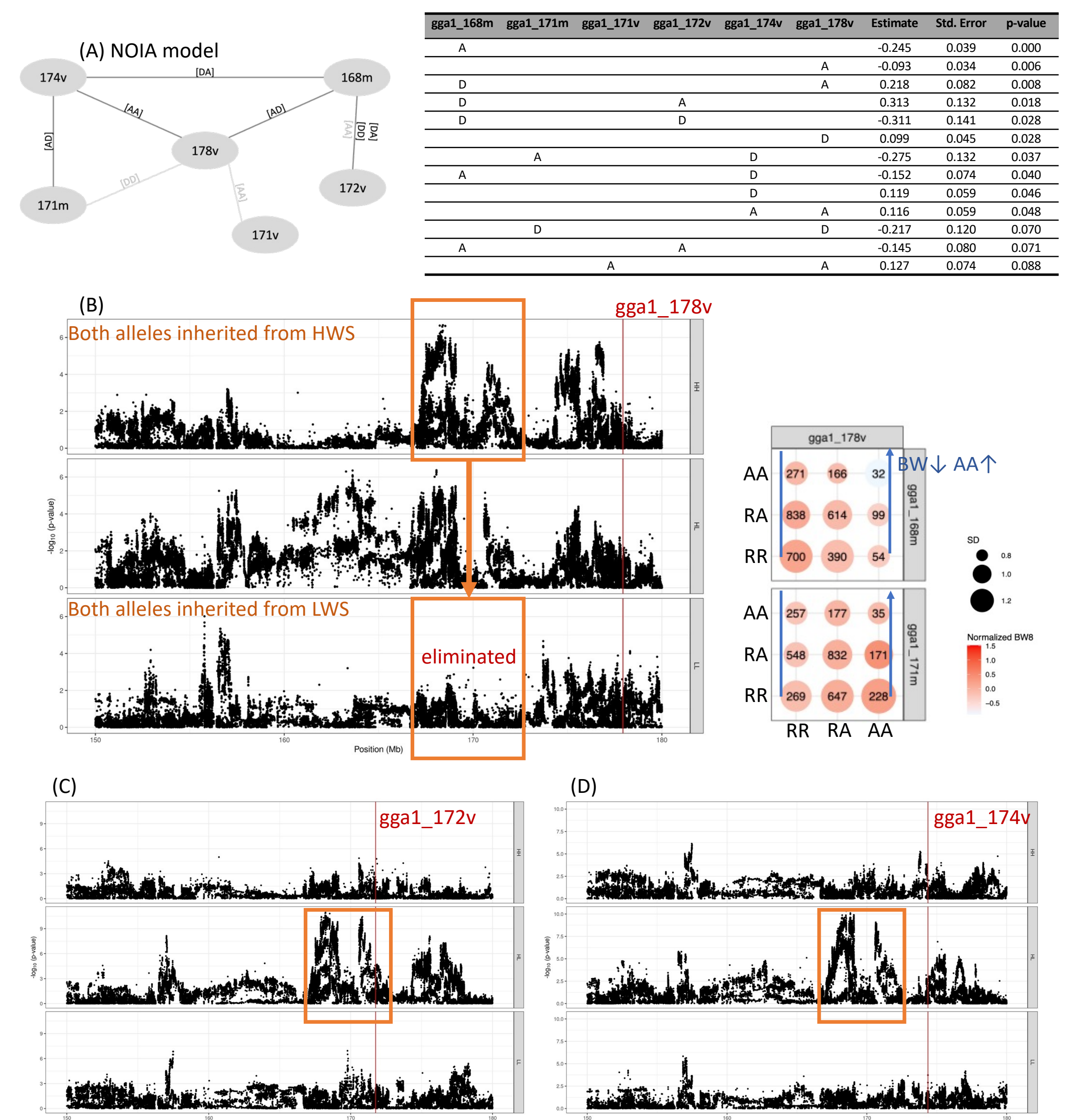$$y = 1\mu + S\boldsymbol{\beta}_S + g\boldsymbol{\beta}_g + H_j\boldsymbol{h}_j + \boldsymbol{\epsilon}$$

Variance-heterogeneity GWAS (vGWAS)

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

EPISTASIS

(A) NOIA model

174v — [DA] — 168m
171m — [AA] — 178v — [DD]/[AD] — 172v
[DD] — 171v
[AD]/[AA] — [DD]/[AD]

gga1_168m	gga1_171m	gga1_171v	gga1_172v	gga1_174v	gga1_178v	Estimate	Std. Error	p-value
A						-0.245	0.039	0.000
					A	-0.093	0.034	0.006
					A	0.218	0.082	0.008
D			A			0.313	0.132	0.018
D			D			-0.311	0.141	0.028
					D	0.099	0.045	0.028
	A			D		-0.275	0.132	0.037
A				D		-0.152	0.074	0.040
				D		0.119	0.059	0.046
			A	A		0.116	0.059	0.048
D				D		-0.217	0.120	0.070
A		A				-0.145	0.080	0.071
	A				A	0.127	0.074	0.088

(B) gga1_178v

Both alleles inherited from HWS

Both alleles inherited from LWS — eliminated

gga1_178v

BW↓ AA↑

	RR	RA	AA
AA	271	166	32
RA	838	614	99
RR	700	390	54

gga1_168m

	RR	RA	AA
AA	257	177	35
RA	548	832	171
RR	269	647	228

gga1_171m

SD: 0.8 / 1.0 / 1.2
Normalized BWB: 1.0 / 0.5 / 0.0 / -0.5

(C) gga1_172v

(D) gga1_174v

A. 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

B. Association study with gga1_178v as a covariate

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