

Inbreeding depression for litter size in a mice population divergently selected for environmental variability of birth weight

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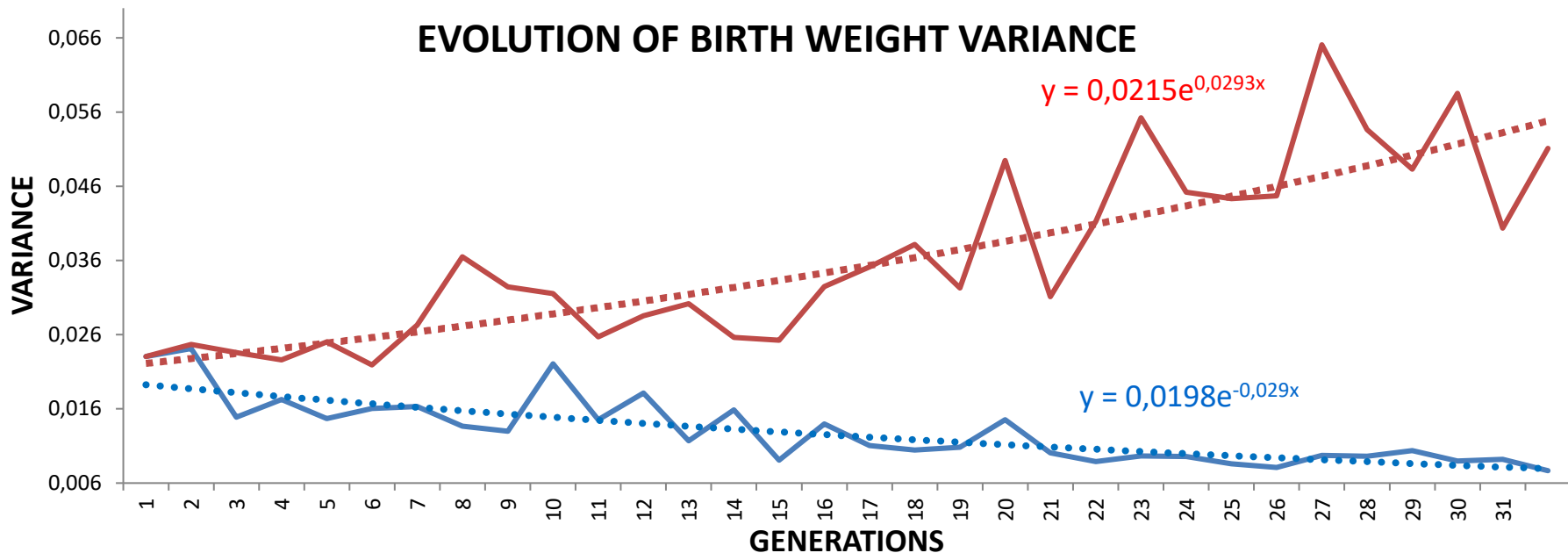
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INTRODUCTION

EVOLUTION OF BIRTH WEIGHT VARIANCE



HIGH VARIABILITY LINE (H-LINE)

LOW VARIABILITY LINE (L-LINE)

Low-LINE > High-LINE

- Heritability
- Feed restriction
- Longevity
- Fertility
- Robustness

The aim of this study was to estimate **inbreeding depression** in the first birth **litter size** in the two mice lines divergently selected using pedigree and genomic information to assess if there was a **differential influence of inbreeding between the lines**



Phenotypes (Litter Size) and **genotypes**
from 25 generations of selection :

- 648 females from the H-Line
- 732 females from the L-Line



Affimetrix Mouse Genotyping Array

545,656 SNPs



Missing genotypes $\geq 3\%$
Sex chromosomes

Pedigree 26 selection generations and 5 previous generations ,5054 individuals

Reference population (RP): 70 females, 1st selection generation

• PEDIGREE

(Wright, 1922)

F_{PED}

• ROH $F_{ROH_i} = \frac{\sum L_{ROH}}{L_{AUTO}}$ (McQuillan et al, 2008)

✓ F_{ROH} based on ROH lengths

✓ F_{ROH} per chromosome (F_{ROH_chr})

F_{ROH1-2}	1-≤2 Mb
F_{ROH2-4}	2-≤4 Mb
F_{ROH4-8}	4- ≤ 8 Mb
$F_{ROH8-12}$	8- ≤ 12 Mb
$F_{ROH12-16}$	12- ≤ 16 Mb
$F_{ROH16-20}$	16 - ≤ 20 Mb
$F_{ROH20-26}$	20- ≤ 26 Mb
$F_{ROH26-32}$	26- ≤ 32 Mb
F_{ROH32}	> 32 Mb

• HBD

(Druet et al, 2017)

✓ $F_{HBD} = F_{HBD2} + \dots + F_{HBD512}$

✓ F_{HBD} based on age related clases

F_{HBD2}	F_{HBD64}
F_{HBD4}	F_{HBD128}
F_{HBD8}	F_{HBD256}
F_{HBD16}	F_{HBD512}
F_{HBD32}	

ADJUSTMENT OF INBREEDING COEFFICIENTS

$$F_{X0} = \frac{F_X - \overline{F_{XRP}}}{1 - \overline{F_{XRP}}}$$

Inbreeding Depression analysis

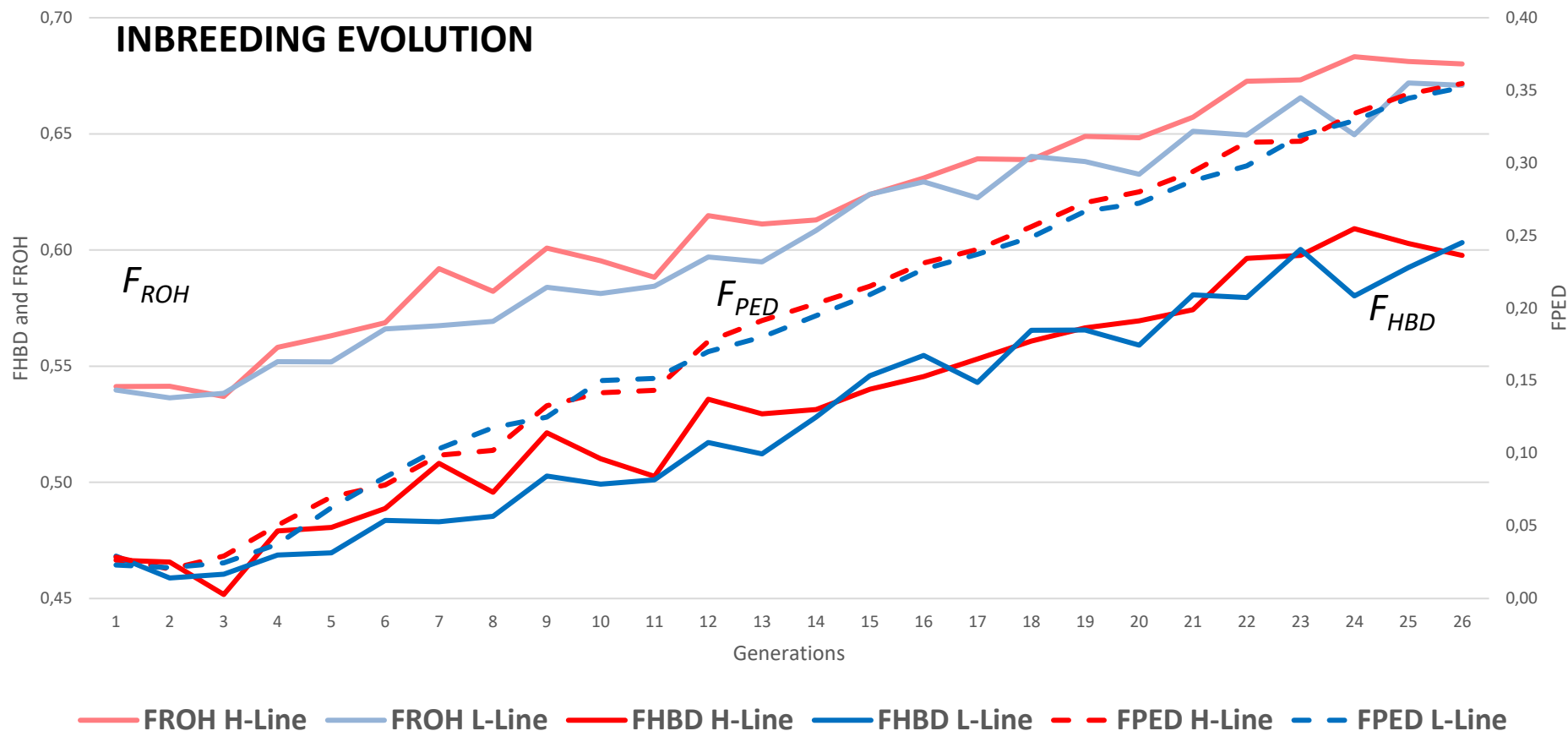
Linear regression

$$\text{Litter size} = \text{Female Age} + b * F_{x0}$$

Restrictive Bonferroni correction

$p < 0.05/\text{number of tests}$

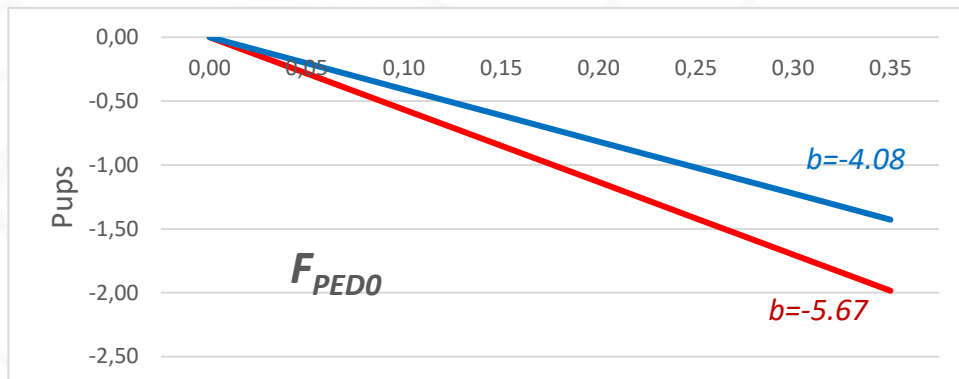
Analysis	Software
ROH	<i>PLINK v 1.9</i>
HBD	<i>RZooRoH R package</i>
F _{PED}	<i>ENDOG V 4.8</i>
Linear regression	<i>lm function of R environment</i>



RESULTS

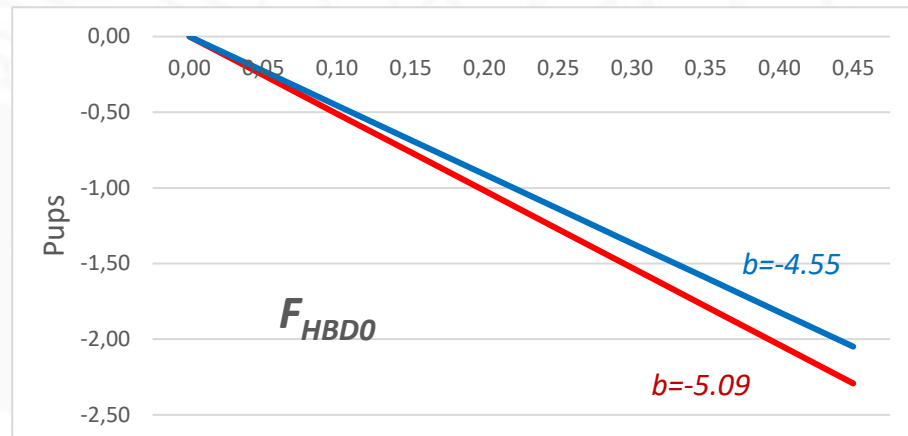
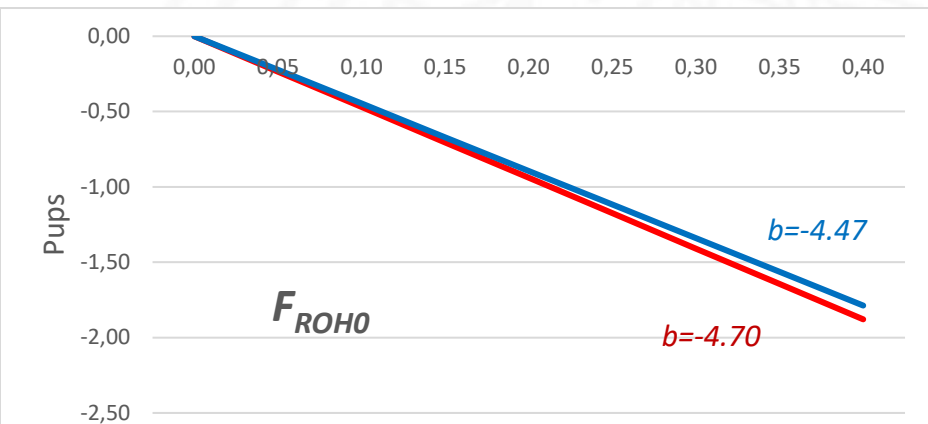
Inbreeding Depression

High-Line
Low-Line



- All were significant after Bonferroni correction

- Inbreeding Depression was higher in H-Line only significant in FPEDO



Inbreeding Depression on Litter Size

F_{ROH0} per chromosome

*: sinificant after Bonferroni correction

^a, ^b: signicant differences between lines

	High-Line	Low-Line
F_{ROH0_1}	-1.35	-2.14*
F_{ROH0_2}	-0.57	-0.15
F_{ROH0_3}	-1.64	-1.10
F_{ROH0_4}	-1.60	-0.91
F_{ROH0_5}	-1.55	-0.77
F_{ROH0_6}	-1.17	-0.91
F_{ROH0_7}	-1.18	-1.08
F_{ROH0_8}	-0.89	-0.38
F_{ROH0_9}	-0.63^a	-1.63*^b
F_{ROH0_10}	-0.93^a	-1.22^b
F_{ROH0_11}	-0.80	-1.39*
F_{ROH0_12}	-1.09	-0.58
F_{ROH0_13}	-1.37*	-0.61
F_{ROH0_14}	-0.90	-0.25
F_{ROH0_15}	-0.08	-0.26
F_{ROH0_16}	-1.17	-0.61
F_{ROH0_17}	-0.84	-1.17
F_{ROH0_18}	-0.96	-0.35
F_{ROH0_19}	-0.82	-0.80

RESULTS

Inbreeding Depression on Litter Size
 F_{ROH0} based on ROH lengths

*: sinificant after Bonferroni correction

^a, ^b: signicant differences between lines

	High-Line	Low-Line
$F_{ROH \geq 32 Mb0}$	-8.12	-7.27*
$F_{ROH26-32 Mb0}$	-15.77	-8.08
$F_{ROH20-26 Mb0}$	-8.11	-9.03
$F_{ROH16-20 Mb0}$	-12.65	-15.55
$F_{ROH16-12 Mb0}$	-4.59	-5.14
$F_{ROH8-12 Mb0}$	1.08^a	-13.92^b
$F_{ROH4-8 Mb0}$	2.92^a	17.37*^b
$F_{ROH2-4 Mb0}$	21.32	23.03
$F_{ROH1-2 Mb0}$	59.40*	44.46*
Total F_{ROH0}	-4.70	-4.47

Inbreeding Depression on Litter Size
 F_{HBD0} based on *HBD* age related classes

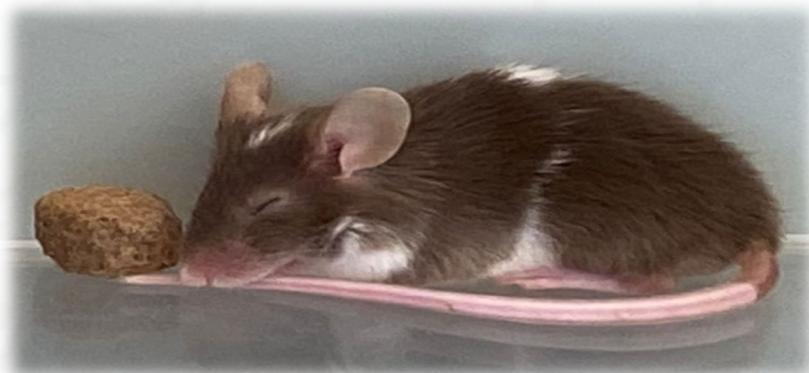
*: sinificant after Bonferroni correction

^a, ^b: sinificant differences between lines

	High-Line	Low-Line
F_{HBD0_2}	-6.24	-4.76
F_{HBD0_4}	-5.10^a	-0.35^b
F_{HBD0_8}	-0.38^a	-3.08*^b
F_{HBD0_16}	-1.93^a	0.18^b
F_{HBD0_32}	1.71	0.08
F_{HBD0_64}	2.74	2.07
F_{HBD0_128}	-8.05	-6.58
F_{HBD0_256}	5.69^a	21.80*^b
F_{HBD0_512}	32.42	15.02
Total F_{HBD0}	-5.09	-4.55

- Significant negative effects of global inbreeding coefficients on the litter size were detected in both lines being more negative in the **High-line**.
- Differences were detected in the inbreeding depression of chromosomal F_{ROH0} between lines. Chromosomes 1, 9, 11 and 13 were candidates of future gene search.
- More recent F_{ROH0} and F_{HBD0} showed negative effects on litter size and older F_{ROH0} and F_{HBD0} showed positive effects on litter size in both lines.
- Divergent selection for homogeneity resulted in different inbreeding effect in a fitness trait such as litter size.

THANK YOU FOR YOUR ATTENTION



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	Cr 1	Cr 2	Cr 3	Cr 4	Cr 5	Cr 6	Cr 7	Cr 8	Cr 9	Cr 10	Cr 11	Cr 12	Cr 13	Cr 14	Cr 15	Cr 16	Cr 17	Cr 18	Cr 19
Cr 1	1.00	0.16	0.26	0.13	0.27	0.11	0.19	0.14	0.20	0.17	0.20	0.14	0.18	0.18	0.08	0.20	0.19	0.16	0.19
Cr 2	0.16	1.00	0.23	0.17	0.22	0.08	0.14	0.11	0.13	0.15	0.14	0.15	0.23	0.15	-0.05	0.18	0.18	0.18	0.15
Cr 3	0.26	0.23	1.00	0.09	0.28	-0.04	0.19	0.10	0.22	0.23	0.14	0.17	0.20	0.14	-0.07	0.22	0.26	0.22	0.16
Cr 4	0.13	0.17	0.09	1.00	0.17	0.25	0.17	0.17	0.04	0.14	0.18	0.03	0.08	0.17	0.10	0.14	0.14	0.16	0.15
Cr 5	0.27	0.22	0.28	0.17	1.00	0.16	0.24	0.19	0.20	0.20	0.22	0.19	0.16	0.26	0.07	0.25	0.19	0.23	0.18
Cr 6	0.11	0.08	-0.04	0.25	0.16	1.00	0.16	0.26	0.02	0.15	0.27	-0.01	0.08	0.27	0.32	0.14	0.11	0.10	0.27
Cr 7	0.19	0.14	0.19	0.17	0.24	0.16	1.00	0.13	0.20	0.18	0.18	0.14	0.15	0.15	0.06	0.22	0.21	0.13	0.19
Cr 8	0.14	0.11	0.10	0.17	0.19	0.26	0.13	1.00	0.08	0.14	0.13	0.03	0.10	0.21	0.16	0.16	0.13	0.13	0.18
Cr 9	0.20	0.13	0.22	0.04	0.20	0.02	0.20	0.08	1.00	0.17	0.17	0.15	0.14	0.09	-0.01	0.16	0.19	0.15	0.16
Cr 10	0.17	0.15	0.23	0.14	0.20	0.15	0.18	0.14	0.17	1.00	0.22	0.13	0.10	0.20	0.06	0.15	0.20	0.15	0.23
Cr 11	0.20	0.14	0.14	0.18	0.22	0.27	0.18	0.13	0.17	0.22	1.00	0.12	0.14	0.29	0.12	0.15	0.20	0.14	0.19
Cr 12	0.14	0.15	0.17	0.03	0.19	-0.01	0.14	0.03	0.15	0.13	0.12	1.00	0.15	0.12	0.07	0.14	0.17	0.16	0.13
Cr 13	0.18	0.23	0.20	0.08	0.16	0.08	0.15	0.10	0.14	0.10	0.14	0.15	1.00	0.13	0.02	0.15	0.24	0.18	0.19
Cr 14	0.18	0.15	0.14	0.17	0.26	0.27	0.15	0.21	0.09	0.20	0.29	0.12	0.13	1.00	0.17	0.17	0.12	0.18	0.23
Cr 15	0.08	-0.05	-0.07	0.10	0.07	0.32	0.06	0.16	-0.01	0.06	0.12	0.07	0.02	0.17	1.00	0.01	0.05	0.04	0.16
Cr 16	0.20	0.18	0.22	0.14	0.25	0.14	0.22	0.16	0.16	0.15	0.15	0.14	0.15	0.17	0.01	1.00	0.14	0.19	0.14
Cr 17	0.19	0.18	0.26	0.14	0.19	0.11	0.21	0.13	0.19	0.20	0.20	0.17	0.24	0.12	0.05	0.14	1.00	0.17	0.17
Cr 18	0.16	0.18	0.22	0.16	0.23	0.10	0.13	0.13	0.15	0.15	0.14	0.16	0.18	0.18	0.04	0.19	0.17	1.00	0.16
Cr 19	0.19	0.15	0.16	0.15	0.18	0.27	0.19	0.18	0.16	0.23	0.19	0.13	0.19	0.23	0.16	0.14	0.17	0.16	1.00

