1 **Inbreeding depression on growth and prolificacy traits in two lines of rabbit**

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Ethical statement

14 Animal Care and Use Committee approval was not obtained for this study because data

15 come from a nucleus farm belonging to IRTA which strictly operates in line with the

16 regulations of the Spanish law on animal protection.

17

Conflict of Interest

19 The authors declare no conflict of interest.

20

Data availability statement

22 Data will be available upon reasonable request.

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37 **Summary**

38

39 Inbreeding depression in closed populations impairs animal fitness, health, and

40 productivity. However, not all inbreeding is expected to be equally damaging. Recent

41 inbreeding is thought to be more harmful than ancient inbreeding because selection

42 decreases the frequency of unfavorable alleles with time. Accordingly, selection

43 efficiency is improved by inbreeding in a process called purging. This research aimed to

44 quantify inbreeding depression on growth and prolificacy traits in two lines of rabbit

45 selected for just one growth (Caldes line) or prolificacy (Prat line) trait, and also to find

46 some evidence of purging of deleterious alleles by selection. Caldes line comprised 51

47 generations and 124,371 animals in the pedigree. Prat line comprised 34 generations

48 and 161,039 animals in the pedigree. The effects of old, intermediate and new

49 inbreeding (Fold, Fint, Fnew), as well as total cumulated classical inbreeding (F) and 3

50 measurements of ancestral inbreeding (AHC, Fa.K and Fa.B) were estimated for

51 average daily gain (ADG), slaughter weight (SW), weaning weight (WW), born alive

52 (BA), the total number of kits (NT) and number of weaned kits (NW). There was a clear

53 inbreeding depression for all growth and prolificacy traits in Caldes line (-7.19 g/d, -

54 0.45 kg, -0.25 kg, -6 kits, -4 kits, and -4 kits per unit of increase in F for ADG, SW,

55 WW, BA, NT and NW, respectively) and also in Prat line (-7.48 g/d, -0.31 kg, -0.11 kg,

56 -4 kits, -5 kits, and -4 kits per unit of increase in F for ADG, SW, WW, BA, NT and

57 NW, respectively). The inbreeding partition appears to be a reliable alternative for

58 assessing inbreeding depression and purging. Thus, for example, in the Caldes line and

59 for ADG the regression coefficients were -7.61, -5.41 and 7.76 g/d per unit of increase

60 in Fnew, Fint and Fold, respectively. In addition, AHC and Fa.B may provide more

61 accurate evidence of purging than Fa.K. This study confirms the existence of inbreeding

62 depression for growth and prolificacy traits in both lines of rabbit and shows evidence

63 of purging of deleterious recessive alleles involved both in growth and prolificacy,

64 independently of the selection criteria established in the line.

65

66 **Keywords:** inbreeding depression, purging, cumulative inbreeding, ancestral

67 inbreeding, selection

Introduction

The adverse consequences of inbreeding on complex traits (i.e., the decrease in the phenotypic mean because of inbreeding) are known as inbreeding depression (Falconer & Mackay, 1996). This phenomenon is probably caused by increased homozygosity of loci carrying partially recessive deleterious alleles, which refers to the partial dominance hypothesis (Charlesworth & Charlesworth, 1999). These unfavorable alleles are maintained at low frequency via mutation-selection balance. However, the alleles of some loci with heterozygote advantage can be maintained at intermediate frequencies by balancing selection and can also lead to inbreeding depression. This denotes the overdominance hypothesis, which is less evident (Leroy, 2014). Traditionally, the degree of inbreeding depression was quantified as the slope of the linear regression of phenotypes on pedigree-based inbreeding coefficients (Doekes et al., 2021).

Initially, it has been suggested stronger inbreeding depression for fitness traits than for morphometric and physiological traits. However, recent analyses do not necessarily support this hypothesis (Doekes et al., 2019). In addition, not all inbreeding is expected to be equally harmful. Recent inbreeding (i.e. inbreeding coming from recent common ancestors) is expected to have a greater impact than ancient inbreeding (i.e. inbreeding arising from more distant common ancestors). This theory is based on the expected decrease in the frequency of deleterious alleles over time because of natural and/or artificial selection (Templeton & Read, 1984; Lacy & Ballou, 1998; Hedrick & Garcia-Dorado, 2016). Because most harmful alleles are recessive, inbreeding improves the efficiency of selection against them by increasing homozygosity, a process known as

5

92   purging, which limitates the degree of inbreeding depression (Gulisija & Crow, 2007;

93   Hinrichs et al., 2007; Parland et al., 2009). The process of purging is more likely to

94   occur when there is strong selection pressure and when inbreeding accumulates slowly

95   over many generations (Boakes & Wang, 2005; Sumreddee et al., 2021). Accordingly,

96   the effectiveness of purging in removing the harmful effects of inbreeding also depends

97   on the environmental conditions and the purging process (nonrandom mating or genetic

98   drift), among others (Sumreddee et al., 2021).

99

100   Rabbit lines used in meat production crossbreeding systems are small, closed

101   populations subjected to generations of within-line selection (Piles et al., 2017).

102   Inbreeding accumulates over generations due to their finite population size and

103   selection, and it is typical to take efforts to control its increase. Prior research assessing

104   the rate of genetic purging in rabbit lines selected for prolificacy traits showed that

105   inbreeding depression was reduced over time and that this reduction was continuous,

106   implying that it depended more on recently generated inbreeding than older,

107   accumulated inbreeding (Ragab et al., 2015). The new inbreeding may account for the

108   effects of new mutations, whereas previous unfavorable alleles may have decreased in

109   frequency or possibly disappeared from the population completely (Ragab et al., 2015).

110

111   This research aimed to quantify inbreeding depression on growth and prolificacy traits

112   in two lines of rabbits selected either for growth (Caldes) or prolificacy (Prat), and also

113   to find some evidence of purging of deleterious alleles, derived from the selection

114   conducted on each one of them.

115

116   **Material and Methods**

117

118   *Data*

119   Two data sets were used in this research corresponding to two rabbit lines, belonging to

120   IRTA, selected for growth and prolificacy traits. The first one corresponds to the Caldes

121   line, founded in 1983 crossing individuals from five New Zealand White lines and a

122   California $\times$ New Zealand synthetic line. It has been selected for litter weight and

123   individual growth rate until 1992, and for growth rate until 2011. From 2011 to 2016 no

124   selection was performed on these animals, and currently is being selected for feed

125   efficiency (see Piles et al., 2017 for more details). Reproductive management was made

126   by avoiding matings between animals with common grandparents. The pedigree

127   comprised 124,371 animals, with 2,948 sires and 8,345 dams, from the foundation of

128   the line (1983) to generation 51. It was complete and only individuals from the base

129   generation had unknown parents. The average number of animals per generation was

130   2,438 with a minimum of 1,285 and a maximum of 3,633 individuals. The average

131   number of does per generation was 164 ranging from 120 to 219 dams. The average

132   number of sires per generation was 58, ranging from 37 to 70 sires. The mean

133   generation interval was 294 d and the 0.05 and 0.95 quartiles of the absolute value of

134   the age difference of dam and sire were 1 and 310 days, respectively.

135

136   The second data set included animals that belong to a rabbit line named Prat and

137   selected for litter size at weaning (Piles et al., 2006). Reproductive management of

138   rabbits was also performed avoiding matings between animals with common

139   grandparents. The pedigree comprised 161,039 animals, with 1,240 sires and 5,924

7

140   dams from generation 1 (in 1992) to generation 34 (in 2012). It was complete and only

141   individuals from the base generation had unknown parents. The average number of

142   animals per generation was 4,715 with a minimum of 1,202 and a maximum of 6,321

143   individuals. The average number of does per generation was 241 ranging from 141 to

144   306 dams. The average number of sires per generation was 60, ranging from 32 to 77

145   sires. The mean generation interval was 280 d and the 0.05 and 0.95 quartiles of the

146   absolute value of the age difference of dam and sire was 1 to 211 days, respectively.

147   For each generation and line, the weighted selection intensity for growth was computed

148   as the standardized selection differential (i.e., the difference between the individual

149   phenotype and the population mean divided by the standard deviation of the population)

150   of ADG (i.e., the selection criterion) weighted by the ratio of the number of offspring of

151   the selected individual to the mean of the total number of offspring. For prolificacy, the

152   EBV of NW was used instead of the phenotype.

153

154   *Inbreeding computation from pedigree*

155

156   Following Ragab et al. (2015), we defined F_u^t as the inbreeding of an animal from

157   generation u considering generation t as the base generation, being $t < u$. For $t = 0$, F_u^0

158   represents the inbreeding accumulated since the foundation of the line, which is divided

159   into several components that account for the inbreeding accumulated during different

160   periods. Thus, for two given generations t_1 and t_2, being $0 < t_1 < t_2 < u$, we defined

161   the inbreeding accumulated until the generation t_1 as $F_{0,t1}^0$, the inbreeding accumulated

162   from generation t_1 to generation t_2 as $F_{t1,t2}^0$ and the inbreeding accumulated from

163   generation t_2 to generation u as $F_{t2,u}^0$. These components are computed from the

164 following formulas derived from the equation for inbreeding in hierarchically structured

165 populations (Wright, 1922):

166

$$1 - F_u^0 = \left(1 - F_{0,ti}^0\right)\left(1 - F_u^{ti}\right) \text{ for } i = 1,2$$

167 Thus,

$$1 - F_u^0 = 1 - F_u^{ti} - F_{0,ti}^0 + F_{0,ti}^0 F_u^{ti}$$

$$F_u^0 = F_u^{ti} + F_{0,ti}^0\left(1 - F_u^{ti}\right)$$

$$F_{0,ti}^0 = \frac{\left(F_u^0 - F_u^{ti}\right)}{\left(1 - F_u^{ti}\right)} \qquad\qquad \{\text{Formula 1}\}$$

168 The part of F_u^0 accumulated between generations t_1 and t_2 corresponds to:

$$F_{t1,t2}^0 = F_{0,t2}^0 - F_{0,t1}^0 \qquad\qquad \{\text{Formula 2}\}$$

169 F_u^0, F_u^{t1} and F_u^{t2} were computed using the program inbupgf90 that implements the

170 algorithm developed by Aguilar & Misztal (2008). $F_{0,t1}^0$ and $F_{0,t2}^0$ were computed from

171 Formula 1 and $F_{t1,t2}^0$ was computed from formula 2. Finally,

$$F_{t1,u}^0 = F_u^0 - F_{0,t1}^0 \text{ and,}$$

$$F_{t2,u}^0 = F_u^0 - F_{0,t2}^0.$$

174 Three periods of 20 generations were considered in the Caldes line, and $t_1 = 20$ and $t_2 =$

175 40. For each individual, the recent pedigree-based inbreeding coefficient (Fnew) is the

176   inbreeding accumulated in the period just before individual birth; the intermediate

177   pedigree-based inbreeding coefficient (Fint) is the inbreeding accumulated during the 20

178   generations period before this, and the ancient pedigree-based inbreeding coefficient

179   (Fold) is the inbreeding accumulated during the first 20 generations period. An animal

180   born before generation 20 has only accumulated Fnew, calculated as F_u^0, whereas Fint

181   and Fold are set to 0. An animal born between generations 20 and 40 has accumulated

182   Fnew, calculated as $F_{20,u}^0 = F_u^0 - F_{0,20}^0$, and Fint, calculated as $F_{0,20}^0$, whereas Fold is set

183   to 0. An individual born after generation 40 has accumulated Fnew calculated as $F_{40,u}^0 =$

184    $F_u^0 - F_{0,40}^0$, Fint calculated as $F_{20,40}^0 = F_{0,40}^0 - F_{0,20}^0$, and Fold calculated as $F_{0,20}^0$. A

185   similar partition was performed for Prat line considering three periods of 12

186   generations, where $t_1 = 12$ and $t_2 = 24$. In addition, the classical (i.e. total cumulated)

187   inbreeding (F) was also calculated both for Caldes and Prat lines.

188

189   The ancestral inbreeding coefficients and the ancestral history coefficient were

190   calculated with the software "Grain" (Baumung et al., 2015) version 2.2 (Doekes et al.,

191   2020). The ancestral inbreeding coefficient defined by Ballou (1997) was also

192   calculated (Fa.B), which represents the probability that an allele in an individual has

193   been at least once identical by descent (IBD) in previous generations. Alternatively, the

194   ancestral inbreeding coefficient according to Kalinowski et al. (2000) (Fa.K) represents

195   the probability that an allele in an individual is currently IBD and has been IBD in

196   previous generations at least once. Finally, we computed the ancestral history

197   coefficient (AHC) defined as the number of times that a random allele in an individual

198   has been IBD in the individual's pedigree. Alleles which have experienced inbreeding

199   more often in the past are less likely to be deleterious than alleles that have undergone

200   IBD less often because those alleles have survived to purging and therefore, it is

201 probably that they have a neutral or even positive effect on the selected traits. Thus,

202 high values of Fa.B or AHC are expected to have a positive effect on the phenotype.

203

204 *Statistical analyses*

205

206 Data were analysed for each line separately using a 3-trait model. The effect of the three

207 components of inbreeding on growth traits at fattening (i.e., ADG: average daily gain in

208 g/d, SW: slaughter weight in kg, and WW: weaning weight in kg) was estimated using

209 the following model for each trait:

210

211 $$y_{ijklmno} = YOB_i + Batch_j + P_k + LS_l + \beta_1 Fold_m + \beta_2 Fint_m + \beta_3 Fnew_m + a_m + c_n + e_{ijklmno}$$

212

213 where $y_{ijklmno}$ is the ADG, SW or WW of an individual m; YOB_i, $Batch_j$, P_k and LS_l

214 are the systematic effects of year of birth i (32 and 22 levels for Caldes and Prat line,

215 respectively), batch j (defined by 3-month periods: 265 and 79 levels for Caldes and Prat

216 line, respectively), parity order k (4 levels: 1st, 2nd, 3rd, 4th and posterior) and litter size l

217 (7 levels: <6, 6, 7, 8, 9, 10, >10 kits), respectively; $Fold_m$, $Fint_m$ and $Fnew_m$ are the

218 three components of F_u^0 for animal m and β_1, β_2 and β_3 the corresponding regression

219 coefficients; a_m is the additive genetic effect; c_n is the litter effect n (19,744 and 20,851

220 levels for Caldes and Prat line, respectively); $e_{ijklmno}$ is the residual. Random effects

221 were assumed to be independent of each other and come from multivariate normal

222 distributions with a mean of zero and variances:

223 $$var\begin{pmatrix} e_{ADG} \\ e_{SW} \\ e_{WW} \end{pmatrix} = I \otimes R_0, \; var\begin{pmatrix} a_{ADG} \\ a_{SW} \\ a_{WW} \end{pmatrix} = A \otimes G_0 \text{ and } var\begin{pmatrix} c_{ADG} \\ c_{SW} \\ c_{WW} \end{pmatrix} = I \otimes C_0$$

224   being $\boldsymbol{R}_0$, $\boldsymbol{G}_0$ *and* $\boldsymbol{C}_0$ 3 x 3 variance-covariance matrices of residual, additive genetic

225   and environmental litter effects; $\boldsymbol{I}$ is the identity matrix and $\boldsymbol{A}$ is the additive genetic

226   relationship matrix. A total of 125,334 and 160,836 records from Caldes and Prat lines,

227   respectively were used for the analysis.

228

229   The model for prolificacy traits (i. e. BA: born alive, NT: total number of kits, and NW:

230   number of weaned kits) was:

231

232      $$y_{ijklmn} = YOB_i + Batch_j + PS_k + \beta_1 Fold_l + \beta_2 Fint_l + \beta_3 Fnew_l + a_l + p_m + e_{ijklmn}$$

233

234   where y_{ijklmn} is the BA, NT or NW of the female m (l in the pedigree file); PS_k is its

235   physiological status k at matting (5 levels: 1, for nulliparous does; 2, and 3 for primiparous

236   does in or not in lactation at mating, respectively; 4 and 5 for multiparous does in or not

237   in lactation at mating); p_m is the permanent effect of female m and all the other terms are

238   as defined above for growth traits. For prolificacy traits, random effects were also

239   assumed to be independent of each other and come from multivariate normal distributions

240   with a mean of zero and variances:

241      $$var \begin{pmatrix} e_{BA} \\ e_{NT} \\ e_{NW} \end{pmatrix} = \boldsymbol{I} \otimes \boldsymbol{R}_0, \; var \begin{pmatrix} a_{BA} \\ a_{NT} \\ a_{NW} \end{pmatrix} = \boldsymbol{A} \otimes \boldsymbol{G}_0 \text{ and } var \begin{pmatrix} p_{BA} \\ p_{NT} \\ p_{NW} \end{pmatrix} = \boldsymbol{I} \otimes \boldsymbol{P}_0$$

242   being $\boldsymbol{R}_0$, $\boldsymbol{G}_0$ *and* $\boldsymbol{P}_0$ 3 x 3 matrices of residual, additive genetic and permanent

243   environmental effects of the female. As for growth traits, values for these matrices were

244   EM-REML estimates. There were 22,796 prolificacy data from 7,379 does, and the

245   pedigree has 8,877 individuals in the Caldes line. For the Prat line, there were 23,128

246   prolificacy data from 6,134 does, and the pedigree has 7,355 individuals. For prolificacy

247   traits, only the inbreeding coefficient of the doe was included in the model.

248

249   The aforementioned models include Fold, Fint and Fnew in the same model. These

250   three inbreeding coefficients were replaced by F, AHC, Fa.K or Fa.B to obtain the

251   corresponding regression coefficients for each inbreeding coefficient, separately. A total

252   of 5 models (Fold+Find+Fnew, F, AHC, Fa.K and Fa.B) were fitted for each trait. A

253   positive regression coefficient significantly different from zero suggests the occurrence

254   of purging of inbreeding depression for the trait under investigation, while a negative

255   regression coefficient statistically different from zero indicates inbreeding depression of

256   the trait (Parland et al., 2009). Analyses were performed using airemlf90 from BLUPf90

257   family programs (Misztal et al., 2002).

258

259   **Results**

260

261   The number of analysed data, the mean and the standard deviation for each of the six

262   evaluated traits in both lines are shown in Table 1. They agree with previously

263   published results in the same populations (Piles et al. 2006; Piles and Tusell, 2012).

264

265   - Table 1 -

266

267 Figure 1 shows the evolution of the inbreeding measurements over the 51 (for Caldes

268 line) or 34 (for Prat line) generations. For both lines, the highest values were observed

269 for the AHC, followed by Fa.B. The lowest values were observed for classical

270 inbreeding (F) and Fa.K.

271

272 - Figure 1 -

273

274 The cumulated inbreeding coefficient was 0.07 on average in the Caldes line (mean in

275 generation 51th = 0.15) which represents an increase of 0.3% per generation and 0.5%

276 per year. Regarding the Prat line, the cumulated inbreeding coefficient was 0.06 on

277 average (mean in generation 34th = 0.12) which represents an increase of 0.4% per

278 generation and 0.6% per year.

279

280 Figure 2 shows the Pearson correlation between all inbreeding measurements calculated

281 in the Caldes line. Close values were obtained for the Prat line (results not shown). It is

282 worth noting that the magnitude of the correlation between the three components of

283 inbreeding (i.e. Fold, Fint and Fnew) is small (equal or lower than 0.3). This indicates

284 that no problems due to colineality are expected in the regression analyses when all

285 three variables are included in the model. All measurements of ancestral inbreeding

286 (i.e., Fa.B, Fa,K and AHC) were highly correlated between them and with F.

287

288   -   Figure 2 -

289

290   Regression coefficients for growth traits in Caldes and Prat lines are shown in Table 2.

291   An increased trend from negative to null in the regression coefficients from Fnew to

292   Fold was observed for all traits in both lines indicating that this partition of inbreeding

293   could provide evidence of the possibility of purging.

294

295   - Table 2 -

296

297   Inbreeding depression was observed for F and Fa.K for all three traits in both lines. For

298   example, inbreeding depression estimates were -7.19 g/d, -0.45 kg, and -0.25 kg per unit

299   of increase in F for ADG, SW and WW, respectively in the Caldes line. Results for

300   growth traits in the Prat line followed the same behaviour as in the Caldes line (-7.48

301   g/d, -0.31 kg, and -0.11 kg per unit of increase of F for ADG, SW and WW,

302   respectively). However, results were not so consistent for Fa.B and AHC. Thus, In the

303   Caldes line there was no effect of Fa.B and AHC except for SW (-0.26 kg per unit of

304   increase in Fa.B) whereas in the Prat line Fa.B had a negative effect on ADG and SW

305   but not on WW, and AHC had a negative effect only on SW.

306

307   Similar results were obtained for prolificacy traits both in Caldes and in Prat Lines

308   (Table 3). Thus, the effect of F and FaK was always negative suggesting the existence

309   of inbreeding depression (in Caldes line: -6 kits, -4 kits, and -4 kits per unit of increase

310   in F for BA, NT and NW, respectively; in Prat line: -4 kits, -5 kits, and -4 kits per unit

311   of increase in F for BA, NT and NW, respectively). On the other hand, Fnew, but not

312   Fint and Fold, had a negative effect on all traits in both lines indicating the possibility of

313   purging of deleterious alleles also for prolificacy traits. Fa.B only affected negatively

314   NW in both lines whereas AHC just impaired NW in the Prat line.

315

316   - Table 3 -

317

318   For all the evaluated traits, evidence of inbreeding depression and purging of deleterious

319   alleles because of selection were found in Caldes and Prat lines It happened for growth

320   and prolificacy traits despite the lines being only selected for growth (in the case of

321   Caldes line) or prolificacy (in the case of Prat line) which suggests that some

322   unperceived selection for prolificacy and growth traits, respectively for Caldes and Prat

323   lines, is being performed (see Figure 3). In fact, the weighted selection intensity was

324   above zero in all evaluated cases, except, as expected, for sires and prolificacy traits.

325   However, selection intensity was higher for growth in the Caldes line than in the Prat

326   line whereas it was higher for prolificacy in the Prat line than in the Caldes line as

327   expected according to their selection criterion.

328

329   - Figure 3 -

330

331   **Discussion**

332

333   The goals of this research were to quantify the inbreeding depression in both growth

334   and prolificacy-related traits and to determine whether new inbreeding is more harmful

16

335 than ancient inbreeding. This idea was supported by the process of purging, which

336 caused a decrease in the frequency of deleterious alleles over time as a result of

337 selection.

338

339 In the two studied rabbit lines, a negative effect of inbreeding was observed on both

340 prolificacy traits (fitness-related traits) and growth-related traits. The idea that fitness

341 traits are more susceptible to inbreeding depression is largely based on findings from

342 wildlife and laboratory populations (Doekes et al., 2021). Theoretically, fitness-related

343 traits should show more inbreeding depression than traits not related to fitness.

344 Directional dominance and/or epistasis cause inbreeding depression. Directional

345 dominance should be less prominent for traits that are less related to fitness and for

346 traits that are under stabilizing selection (Doekes et al., 2021). A combination of

347 production, conformation, growth, reproduction, survival, behavioral, and health traits

348 are often directionally selected in farm populations, in addition to natural selection on

349 fitness traits (Doekes et al., 2021). In fact, selection processes both in Caldes and Prat

350 lines are not so different. Caldes line is being unintentionally selected for prolificacy as

351 well as Prat line is being selected for growth, despite the selection intensity was higher

352 for their corresponding selection criterion (i.e, ADG for the Caldes line and NW for the

353 Prat line).

354

355 Despite the huge research works on pedigree-based inbreeding in farm animals, only a

356 few studies have looked at the impacts of new and ancient inbreeding. Their consistent

357 conclusion was that inbreeding that occurred in recent generations had more negative

358 consequences than inbreeding that occurred in ancient generations (Doekes et al., 2020;

359   Hinrichs et al., 2007). This is in line with the hypothesis that deleterious allele

360   frequencies will decrease over time as a result of selection and purging, both of which

361   influence the extent of inbreeding depression.

362

363   The evolution of positive values for the regression coefficients of old inbreeding to

364   negative values for the equivalent estimations of new inbreeding can be explained by

365   purging deleterious alleles affecting the measured traits, aided by artificial selection

366   (Hinrichs et al., 2007; Ragab et al., 2015). Ragab et al. (2015) observed the same results

367   as those obtained in the present study for prolificacy traits in four lines of rabbits

368   selected for prolificacy. This means that the partition of inbreeding seems a reliable

369   alternative to evaluate inbreeding depression and purging. Accordingly, AHC and Fa.B

370   may provide a better representation of the evidence of purging than Fa.K because the

371   last parameter represents the probability that any allele in an individual is currently IBD

372   and has been IBD in previous generations at least once which could be considered

373   somehow like a mix of recent and old inbreeding. However, in the partition of the

374   inbreeding approach, as a consequence of varied mating systems, pedigree depths, and

375   generation intervals, the number of generations that determined new inbreeding do not

376   allow fair and straight comparisons between studies (Sumreddee et al., 2021). Same

377   happens in the comparison of results of our two lines for a specific trait which are not

378   totally comparable because of the different definition of the periods.

379   Despite this lack of a common base for comparisons, the effectiveness of the purging

380   process may explain some of the heterogeneity in inbreeding depression across studies

381   (Sumreddee et al., 2021). If a large amount of inbreeding depression is attributable to

382   rare and very detrimental recessive mutations present in homozygous form, inbreeding

383 should promptly purge deleterious alleles from a population (Charlesworth & Willis,

384 2009). This means that if the partial dominance theory is a key contributor to inbreeding

385 depression, purging is more likely to eliminate detrimental alleles from a population

386 over time. Additional factors such as the rate of inbreeding (a low rate of inbreeding

387 promotes purging), the genetic architecture of the trait (purging is more effective for

388 large effect alleles), selection pressure (high selection pressure promotes purging), and

389 population size (purging is more likely with small population sizes) could all influence

390 the effectiveness of purging (Wang et al., 1999).

391

392 This study confirms the existence of inbreeding depression for growth and prolificacy

393 traits in two rabbit lines and shows evidence of purging of deleterious recessive alleles

394 involved both in growth and prolificacy, independently of the formally declared

395 selection criteria established in the selected lines. It has to be noted, however, that both

396 populations have been in practice selected for growth.

397

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482

483 **Table 1.** Descriptive statistics (N: number of analysed data, Mean: average phenotypic

484 value, and SD: standard deviation) of the evaluated traits in both rabbit lines (Caldes

485 and Prat). ADG: average daily gain (g/d), SW: slaughter weight (kg), WW: weaning

486 weight (kg), BA: born alive, NT: total number of kits, and NW: number of weaned kits.

487

Line	Parameter	ADG	SW	WW	BA	NT	NW
Caldes	N	125,334	125,334	125,334	22,796	22,796	22,796
	Mean	46.27	2.03	0.75	8.07	8.80	7.42
	SD	8.48	0.33	0.18	3.26	2.99	3.12
Prat	N	160,836	160,836	160,836	23,127	23,127	23,127
	Mean	38.77	1.75	0.67	9.37	9.91	7.88
	SD	7.81	0.28	0.15	3.26	2.99	3.21

488

489

490 **Table 2.** Posterior median [HPD95%] of the regression coefficients for growth traits in

491 Caldes line. ADG: average daily gain (g/d), SW: slaughter weight (kg), and WW:

492 weaning weight (kg). New (Fnew), intermediate (Fint), and old (Fold) inbreeding

493 coefficients, classical (F) inbreeding coefficient, ancestral inbreeding coefficient as

494 defined by Ballou (Fa.B) or Kalinowski et al. (Fa.K), and ancestral history coefficient

495 (AHC). Significant inbreeding depression estimates are in bold. In italics are significant

496 inbreeding depression coefficients indicating purging of deleterious alleles.

Line			Caldes		Prat	
Trait	Inbreeding coefficient	Median	HPD95%	Median	HPD95%
ADG	Fnew	**-7.61**	**[-11.71, -3.73]**	**-17.24**	**[-30.49, -4.15]**
	Fint	-5.34	[-13.43, 2.88]	**-18.49**	**[-32.49, -6.22]**
	Fold	7.76	[-3.60, 19.77]	10.45	[-2.22, 23.86]
	F	**-7.19**	**[-11.01, -3.35]**	**-7.48**	**[-10.72, -4.47]**
	Fa.B	-0.90	[-5.04, 5.34]	**-8.05**	**[-11.63, -2.04]**
	Fa.K	**-10.54**	**[-17.05, -3.83]**	**-15.57**	**[-21.93, -9.80]**
	AHC	-0.21	[-2.06, 2.40]	0.87	[-1.21, 3.78]
SW	Fnew	**-0.48**	**[-0.64, -0.33]**	**-0.83**	**[-1.35, -0.28]**
	Fint	-0.24	[-0.57, 0.11]	**-1.15**	**[-1.65, -0.58]**
	Fold	0.34	[-0.10, 0.77]	*0.79*	*[0.21, 1.31]*
	F	**-0.45**	**[-0.60, -0.30]**	**-0.31**	**[-0.43, -0.18]**
	Fa.B	**-0.26**	**[-0.52, -0.14]**	**-0.49**	**[-0.64, -0.36]**
	Fa.K	**-0.73**	**[-0.98, -0.48]**	**-0.58**	**[-0.85, -0.33]**
	AHC	-0.001	[-0.08, 0.06]	**-0.16**	**[-0.24, -0.10]**
WW	Fnew	**-0.28**	**[-0.37, -0.17]**	**-0.39**	**[-0.65, -0.13]**
	Fint	-0.10	[-0.31, 0.12]	**-0.67**	**[-0.90, -0.42]**
	Fold	0.02	[-0.22, 0.30]	*0.50*	*[0.27, 0.75]*
	F	**-0.25**	**[-0.34, -0.15]**	**-0.11**	**[-0.18, -0.04]**
	Fa.B	-0.04	[-0.11, 0.04]	-0.004	[-0.13, 0.07]
	Fa.K	**-0.42**	**[-0.58, -0.24]**	**-0.17**	**[-0.30, -0.03]**
	AHC	*0.06*	*[0.03, 0.10]*	-0.03	[-0.09, 0.02]

497

498

499 **Table 3.** Posterior median [HPD95%] for prolificacy traits in Caldes line. BA: born

500 alive, NT: total number of kits, and NW: number of weaned kits. New (Fnew),

501 intermediate (Fint), and old (Fold) inbreeding coefficients, classical (F) inbreeding

502 coefficient, ancestral inbreeding coefficient as defined by Ballou (Fa.B) or Kalinowski

503 et al. (Fa.K), and ancestral history coefficient (AHC). Significant inbreeding depression

504 estimates are in bold. In italics are significant inbreeding depression coefficients

505 indicating purging of deleterious alleles.

506

Line			Caldes		Prat
Trait	Inbreeding coefficient	Median	HPD95%	Median	HPD95%
BA	Fnew	**-6.56**	**[-10.30, -2.79]**	**-6.21**	**[-9.37, -2.97]**
	Fint	-2.44	[-9.02, 4.08]	0.91	[-4.55, 6.40]
	Fold	2.52	[-6.93, 11.35]	*15.08*	*[4.94, 24.52]*
	F	**-5.93**	**[-9.70, -2.52]**	**-4.33**	**[-7.26, -1.45]**
	Fa.B	0.46	[-2.47, 3.75]	-2.56	[-5.84, 1.08]
	Fa.K	**-9.05**	**[-15.18, -3.36]**	**-6.94**	**[-12.31, -1.16]**
	AHC	-0.10	[-1.24, 1.08]	-1.44	[-3.08, 0.37]
NT	Fnew	**-4.62**	**[-8.19, -1.19]**	**-6.14**	**[-9.20, -3.10]**
	Fint	-3.19	[-9.35, 2.58]	-1.34	[-6.43, 3.88]
	Fold	5.39	[-2.63, 13.99]	8.14	[-0.35, 17.05]
	F	**-4.46**	**[-7.73, -1.17]**	**-4.94**	**[-7.75, -2.36]**
	Fa.B	3.39	[-0.70, 7.38]	-2.44	[-5.83, 0.67]
	Fa.K	**-5.65**	**[-11.24, -0.15]**	**-9.11**	**[-14.21, -4.13]**
	AHC	*1.43*	*[0.12, 2.75]*	-1.35	[-3.08, 0.13]
NW	Fnew	**-4.07**	**[-7.63, -0.50]**	**-5.92**	**[-8.98, -3.03]**
	Fint	-1.72	[-8.04, 4.71]	1.88	[-3.26, 6.93]
	Fold	5.12	[-4.19, 14.45]	*17.24*	*[8.09, 25.59]*
	F	**-3.79**	**[-7.01, -0.43]**	**-3.89**	**[-6.49, -1.34]**
	Fa.B	**-4.12**	**[-7.01, -0.96]**	**-3.34**	**[-6.48, -0.64]**
	Fa.K	**-7.02**	**[-12.21, -1.55]**	**-5.35**	**[-10.05, -0.43]**
	AHC	-1.09	[-2.09, 0.01]	**-1.71**	**[-3.13, -0.37]**

507

Figure legends

509 **Figure 1.** Measurements of inbreeding in Caldes and Prat lines. AHC: ancestral history

510 coefficient, F: classical inbreeding coefficient, Fa.B: ancestral inbreeding coefficient as

511 defined by Ballou, and Fa.K: ancestral inbreeding coefficient as defined by Kalinowski
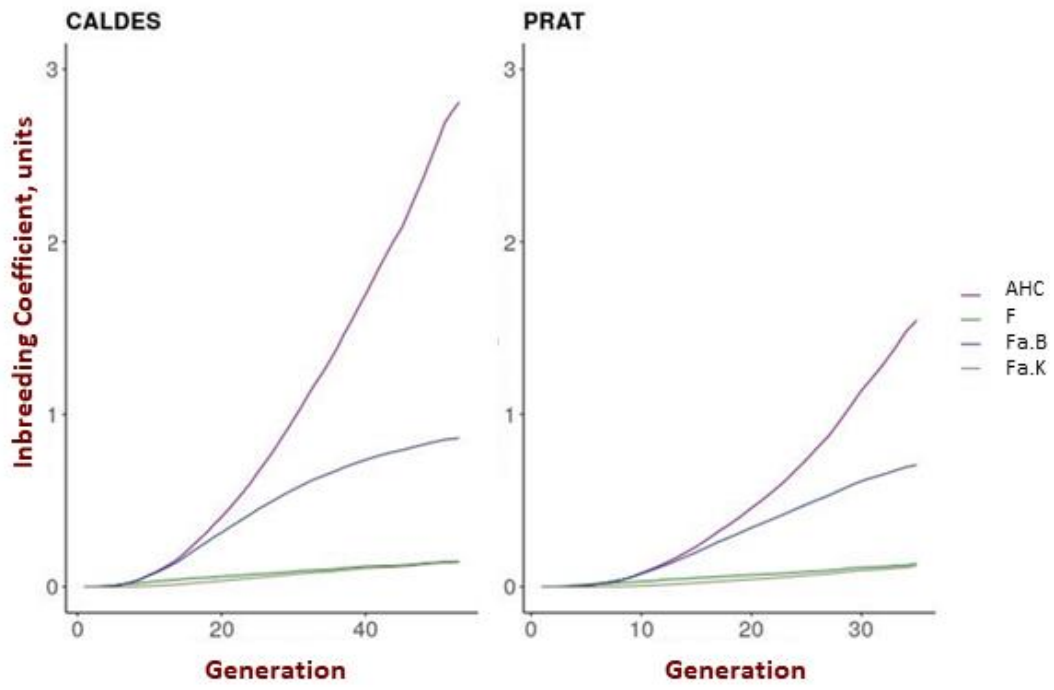
512 et al.

513

514 **Figure 2.** Perason correlations between measurements of inbreeding in Caldes line.

515 AHC: ancestral history coefficient, F: classical inbreeding coefficient, Fa.B: ancestral

516 inbreeding coefficient as defined by Ballou, and Fa.K: ancestral inbreeding coefficient

517 as defined by Kalinowski et al.

518

519 **Figure 3.** Weighted selection intensity in Caldes and Prat lines for growth and
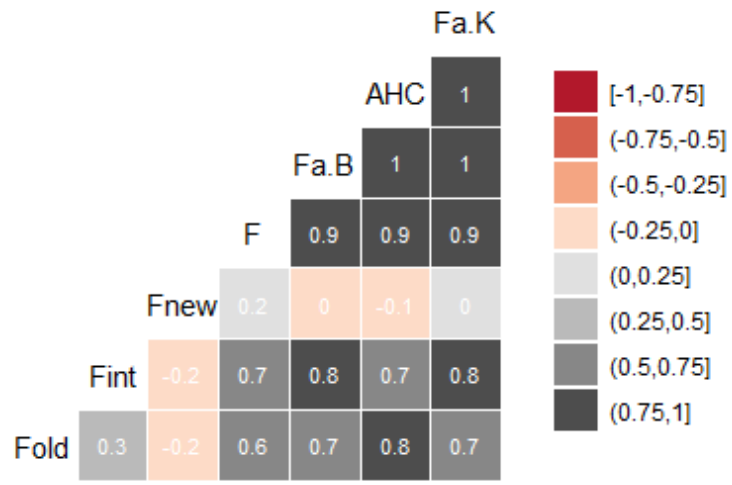
520 prolificacy traits.
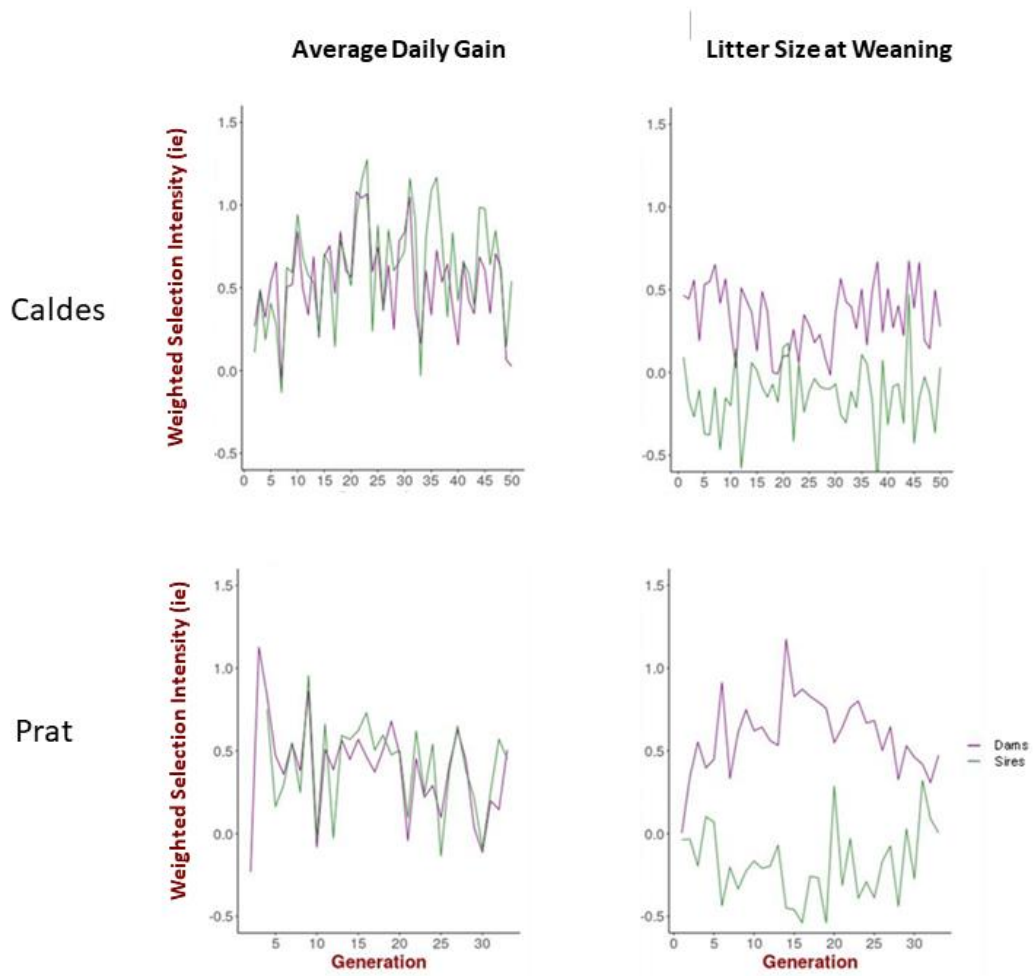
521

522 **Figure 1**

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526   **Figure 2**

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528   **Figure 3**

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