

Skew distribution of founder-specific inbreeding depression effects on the longevity of Landrace sows

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Summary

Inbreeding is a biological phenomenon of special relevance in domestic species in which its influence has been typically associated with reductions in animal fitness. Nevertheless, recent research suggests substantial founder-specific variability in terms of inbreeding depression on some productive traits, although this centred on a very reduced number of founders. This research focuses on the modelling of founder-specific inbreeding depression (FSID) effects from a more general point of view, characterizing the expected distribution of FSID effects on sow longevity. Under a change-point Weibull proportional hazards model solved through Bayesian inference, a skew-normal *a priori* distribution for the FSID effects of 19 founders was assumed. In terms of the deviance information criterion, this model was clearly preferred to other prior distributions for FSID effects as well as to a standard analysis of the overall inbreeding depression effect, although all models were consistent with an overall negative genetic effect of inbreeding on sow longevity. The joint posterior distribution of FSID effects showed a skewed pattern with substantial right-tail overexpression, in which the mean (0.036), mode (0.034), S.D. (0.032) and asymmetry parameter (0.045) reported a higher incidence of positive estimates (85.2%) with an unfavourable effect on sow longevity. The founder with the worst inbreeding depression effect reduced sow longevity by 32 days for 1% or 167 days for 10% partial inbreeding. As a whole, our analyses highlighted substantial variability in FSID effects, with unfavourable, neutral and even favourable influences on sow longevity. This heterogeneity could be related to an uneven distribution of the recessive deleterious genetic load among founder genomes, and also with the different selection pressures applied to each founder line. The implementation of skew-normal priors also proved an appealing way to bypass the strict scenario imposed by the standard symmetric-Gaussian distribution, allowing right- and left-tail overexpression as well as non-zero modal estimates.

1. Introduction

Inbreeding is defined as the identity-by-descent (IBD) probability at any given autosomal locus and results from the mating of related individuals (Wright, 1922; Malécot, 1948). The effects of inbreeding on traits of interest have been associated with substantial changes in phenotypic expectation and genetic variability

(Falconer & Mackay, 1996; Pannell, 2008). More specifically, Mendelian sampling variance decreases with inbreeding, and reductions in fitness would therefore be expected due to the higher phenotypic expression of deleterious recessive genes (Falconer & Mackay, 1996). In domestic species, this fitness impairment has been revealed for multiple traits of interest, including birth weight (Norberg & Sørensen, 2007), growth (Pariacote *et al.*, 1998; Fernández *et al.*, 2002), litter size (Farkas *et al.*, 2007; Norberg & Sørensen, 2007), milk production (Miglior *et al.*, 1995; Mc Parland *et al.*, 2007) and longevity (Sewalem *et al.*, 2006).

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Some researchers have proposed an alternative way to account for inbreeding depression by modelling founder-specific partial inbreeding coefficients instead of analysing the overall inbreeding of each individual (Rodrig  n  z *et al.*, 1998; Gulisija *et al.*, 2006). This approach allows substantial heterogeneity of inbreeding depression effects in inbred descendants. This founder-related heterogeneity revealed a wide range of neutral and negative (and even positive) effects on litter size in swine (Rodrig  n  z *et al.*, 1998), milk yield in dairy cattle (Gulisija *et al.*, 2006) and birth weight in meat-type sheep (Casellas *et al.*, 2009). Nevertheless, this research was focused on a few well-characterized founders with a large number of inbred descendants, with estimates being circumscribed to a relatively unrepresentative scenario that does not allow accurate extrapolations to entire populations.

Among the substantial profit of founder-specific inbreeding depression (FSID) estimates, inferences based on their expected distribution provide a more robust analysis and allow direct characterization of the inbreeding depression pattern and its biological relevance to the analysed population. Moreover, modelling FSID under the assumption of a given parametric distribution would increase model robustness and permit unbiased estimates even for founders with few data (Robinson, 1991). Note that this phenomenon cannot be easily modelled given the skew pattern of FSID (Rodrig  n  z *et al.*, 1998; Gulisija *et al.*, 2006; Casellas *et al.*, 2009), where a standard symmetrical-Gaussian prior could originate abnormal model fits. Recent developments focused on the implementation of skew distributions in biological data analysis (Zhang *et al.*, 2005; Varona *et al.*, 2006, 2008) have opened a very appealing way to model asymmetry within the context of mixed models. More specifically, the skew patterns implemented by Sahu *et al.* (2003) in the Gaussian distribution, allow left- or right-tail overexpressions with the only inclusion of just one additional parameter.

Sow longevity is a trait of major relevance for the swine industry (Serenius & Stalder, 2004; Serenius *et al.*, 2006; Tarr  s *et al.*, 2006), with relevant implications on both economic and welfare grounds. Although most of the genetic and environmental sources of variation in this trait have been extensively analysed in recent years, the effect of inbreeding on sow longevity remains unknown. Inbreeding depression has previously been related to longevity traits in dairy cattle (Sewalem *et al.*, 2006), deer (Sternicki *et al.*, 2003), beetles (Fox *et al.*, 2006) and *Drosophila* (Vermeulen & Bijlsma, 2004; Swindell & Bouzat, 2006), among others, but we lack available results for swine. Moreover, the effect of FSID on the longevity of domestic species has never been evaluated. The recent implementation of change-point

baselines in survival analysis (Tarr  s *et al.*, 2005, 2006) and the inclusion of the change points as unknown parameters in the model (Casellas, 2007) allow a direct and straightforward characterization of the aging process of the analysed population within a parametric framework. Indeed, this approach reduced model parameterization when compared with semi-parametric methodologies (Cox, 1972) and provides a vast increase in terms of model flexibility to address longevity data. In the present study, we assumed the methodology developed by Casellas (2007) given its reasonable flexibility to fit longevity data as well as the integrated estimation of the change points. Although previous analyses with the Casellas (2007) model were focused on systematic and additive genetic effects, this hierarchical approach can be easily expanded to account for additional sources of variation such as inbreeding-related effects governed by a set of different prior distributions.

Within this context, the aim of the present study was to analyse sow longevity and the impact of the effect of FSID on a Landrace population, with special emphasis on the characterization of the distribution pattern of FSID and its implications for sow longevity and breeding programmes.

2. Materials and methods

(i) Sow longevity data source

Longevity data for 4226 hyperprolific Landrace sows (mean \pm S.D., 13.3 ± 7.2 piglets per litter) were recorded between 1988 and 2006 at a breeding farm (COPAGA S.C.C.L., Solsona, Spain). These sows were kept in standard farm facilities under standard management conditions, and all relevant reproductive and productive data were appropriately recorded (including date of mating, parturition and weaning, total number of piglets born, numbers of live and still births and weaned piglets, among others). Sow longevity was measured as the time interval (in days) between the first mating and culling or death (complete records), whereas records for sows that were still alive at the end of the data collection period were considered censored (Cox, 1972). Except for the first few years when voluntary culling was minimized to increase population size (Table 1), the culling criteria remained the same throughout the period of data collection. As expected, average longevity was abnormally high for first cohorts of sows because old sows were retained in order to increase the population size (1604 days for sows firstly mated between years 1988 and 1990), whereas in subsequent years this average quickly decreased to reach average longevities ranging between 438 days (1995) and 691 days (1998). This heterogeneity falls within the range of previous studies in sows (Brandt *et al.*, 1999; Yazdi *et al.*, 2000;

Table 1. Number of longevity records (n), percentage of censoring, and average longevity (\pm S.E.) according to years of first mating

Year of first mating	N	Percentage of censoring	Average longevity ^a (days)
1988–1990	104	0	1604 \pm 31
1991	147	0	1181 \pm 21
1992	258	0	888 \pm 14
1993	162	0	587 \pm 19
1994	102	0	604 \pm 33
1995	375	0	438 \pm 19
1996	327	0	518 \pm 24
1997	435	0	550 \pm 22
1998	178	0	691 \pm 34
1999	228	0	650 \pm 30
2000	281	0	668 \pm 23
2001	253	0	577 \pm 23
2002	261	0	598 \pm 22
2003	299	0.7	469 \pm 19
2004	349	31.5	340 \pm 15
2005 and 2006	467	66.8	42 \pm 4
Overall	4226	7.6	602 \pm 7

^a Censored records were not considered.

Tarrés *et al.*, 2006). Sows were mainly culled when either (i) their biological status did not allow any additional reproductive cycles (i.e. insufficient body condition, illness, severe deficiencies in leg or teat condition) or (ii) their reproductive performance was unsatisfactory (i.e. sows that failed to become pregnant after successive inseminations, that produced small litters or that performed poorly at weaning). Indeed, this population has undergone a selection experiment for prolificacy (Noguera *et al.*, 2002*a, b*) between 1993 and 1998 across three successive generations, although culling criteria did not change during this period. Nevertheless, the genetic trend obtained for the number of piglets born alive (\approx 0.5 piglets per litter) could have modulated the effect of the number of weaned piglets included in our analysis (see below). The overall survival probability for this Landrace population was characterized by the non-parametric Kaplan–Meier method (Kaplan & Meier, 1958).

Full pedigree included 6355 individuals with 458 boars and 5897 sows, 1082 of which were considered founders without known ancestors (177 boars and 905 sows). This population was founded from the acquisition of sows and boars from two different origins plus an additional incorporation of foreign individuals during the mid-1990s. After founder generation, pedigree data were accurately registered and parents are known for all boars and sows born in this population. Only 346 boars had progeny with registered longevity, with an average of 12.1 ± 16.0

daughters per boar (mean \pm S.D.). This value ranged from 1 to 166 daughters per boar. Although mating between close relatives was avoided whenever possible, inbreeding occurred in successive generations. Moreover, separate breeding lines were generated (see Noguera *et al.*, 2002*b*) and partially fused at the end of the selection experiment for hyperprolific sows. This population had overlapped generations, pedigree extending over 9–14 generations for gilts born in 2006. Table 1 shows the number of records and average longevity according to the year of first mating and also the percentage of censored data.

(ii) Inbreeding and partial inbreeding coefficients

Following Wright (1922) and Malécot (1948), the inbreeding coefficient for the i th non-founder individual (F_i) can be defined as the IBD probability at any given neutral locus, and is easily calculated as half the relationship coefficient between i 's parents. Although F_i has been widely used in the animal breeding literature, it does not provide detailed information about the contribution of each founder to the IBD probability. If founder-specific inbreeding coefficients are considered, F_i can be partitioned as $F_i = \sum_{j=1}^f F_{ij}$, where F_{ij} is the IBD probability due to the j th founder on the i th individual and f is the number of founders contributing to i (Lacy *et al.*, 1996; Rodríguez *et al.*, 1998). These F_{ij} can be easily calculated following Gulisija *et al.* (2006) via partial coancestry matrices.

In our data set, 35 founders contributed inbred descendants although only 22 of them contributed more than 150 inbred sows with longevity data. These 22 founders were distributed among the three origins of foreign individuals and all of them had first-generation descendants with longevity data. Of these 22 founders, four couples of founders were fused into 4 virtual founders because each couple only contributed one offspring to the pedigree. FSID was evaluated on 14 founders and 4 virtual founders in order to assess the effects of FSID on sow longevity, with an extra level grouping the remaining 13 less-represented founders that contributed inbred descendants. Note that these 13 underrepresented founders originated inbreeding at a very low level and they were grouped to avoid model instability, mainly when a vague flat prior was assumed for inbreeding-related effects. To evaluate potential collinearity between F_{ij} , pairwise correlation coefficients between F_{ij} coefficients were estimated using the SAS Correlation procedure (v.9.1; Statistical Analysis Systems (SAS) Institute, Cary, NC, USA).

The analysed Landrace herd showed an average inbreeding percentage of $0.52 \pm 0.01\%$, although only 1198 of the sows with phenotypic data (28.4%) were inbred ($F_i > 0$; inbreeding coefficients ranged between 0.09 and 25%). Figures 1*a* and 1*b* show the average

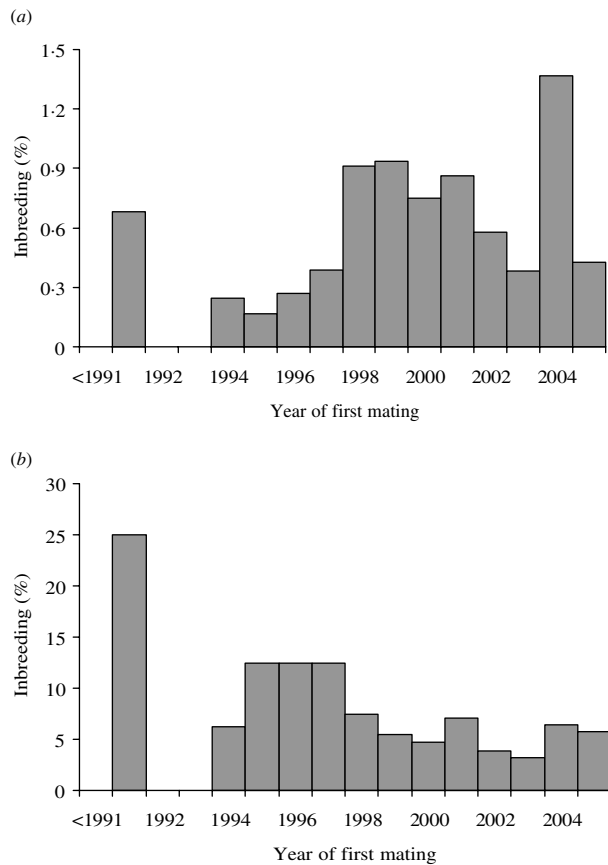


Fig. 1. Average (a) and maximum (b) inbreeding of Landrace sows by years of first mating.

and maximum levels of inbreeding for Landrace sows per year at first mating. It can be observed that inbreeding appeared early in this population (sows born in 1991 or at the end of 1990) and showed an irregular increase from 1994 onwards. Within-year average inbreeding was less than 1%, with the exception of the sows firstly mated in 2004 for which the average value was 1.37% (Fig. 1a). Maximum inbreeding fluctuated between 2.86 and 12.33% during the period 1994–2005, although the highest value (25%) was reached in 1991 (Fig. 1b). These values agreed with those reported by Rathje (2000) for other commercial and selected pig populations. Note that these irregular patterns could be due to the selection experiment carried out during the 1990s with two separate breeding lines fused in the year 1998, at the end of the experimental selection procedure (Noguera *et al.*, 2002b).

(iii) Statistical analyses

(a) Proportional hazards model

Within the context of the change point models introduced by Nguyen *et al.* (1984) and Noura & Read (1990) for survival analysis, sow longevity data were

analysed under a change-point Weibull proportional hazards model with unknown change points (Casellas, 2007). The applied methodology was a Bayesian implementation of the change-point models adopted by Tarrés *et al.* (2005) and previously suggested by Yazdi *et al.* (2002), assuming a common shape parameter throughout the parametric space, whereas the scale parameter could change at each predefined time-dependent period. This change-point characterization must be viewed as a simplified version of the Tarrés *et al.* (2006) model where all the parameters of the Weibull baseline change at a given change point. Moreover, omitting the different treatment of the change points in the models described by Tarrés *et al.* (2006) and Casellas (2007), Tarrés *et al.* (2006) is more parameterized and thus advantages in model flexibility would be lost due to a greater penalization for overparameterization. Casellas (2007) methodology was preferred given that it is based on a well known and long used extension of a regular Weibull model where an extra time-dependent effect is included to increase flexibility (Ducrocq *et al.*, 1988; Yazdi *et al.*, 2002; Tarrés *et al.*, 2005; Casellas *et al.*, 2006). Following the standard survival model described by Cox (1972), the hazard ($h_i(t; \mathbf{x}_i, \mathbf{z}_i)$) function at time t for a given sow i influenced by a set of systematic (\mathbf{b}_1 and \mathbf{b}_2), permanent environmental (\mathbf{p}), inbreeding depression (\mathbf{d}) and additive genetic (\mathbf{a}) effects can be written as:

$$h_i(t; \mathbf{x}_{1i}, \mathbf{x}_{2i}(t), \mathbf{z}_{1i}(t), \mathbf{z}_{2i}, \mathbf{z}_{3i}) = h_0(t) \exp(\mathbf{x}'_{1i}\mathbf{b}_1 + \mathbf{x}'_{2i}(t)\mathbf{b}_2 + \mathbf{z}'_{1i}(t)\mathbf{p} + \mathbf{z}'_{2i}\mathbf{d} + \mathbf{z}'_{3i}\mathbf{a}), \quad (1)$$

where \mathbf{x}_{1i} , \mathbf{z}_{2i} and \mathbf{z}_{3i} ($\mathbf{x}_{2i}(t)$ and $\mathbf{z}_{1i}(t)$) are appropriate column vectors of incidences linking \mathbf{b}_1 , \mathbf{d} and \mathbf{a} time-independent effects (\mathbf{b}_2 and \mathbf{p} time-dependent effects), respectively. Following Casellas (2007), $h_0(t)$ is the baseline hazard function with the form $h_0(t) = \lambda\rho(\lambda t)^\rho - 1 \xi_k$ for $\tau_k < t \leq \tau_{k+1}$ and $k \in 1, \dots, m$. Note that y_i is the longevity record of sow i , λ and ρ are the parameters of a Weibull distribution, ξ_k is the time-dependent effect between change points τ_k and τ_{k+1} , m is the number of change points, and τ_{m+1} is the longest observed lifetime in the data set.

More specifically, \mathbf{b}_1 accounted for the time-independent effect of year at first mating with 16 levels (the years 1988–1990 and 2005–2006 were grouped; see Table 1) and \mathbf{b}_2 accounted for the time-dependent effect of the number of weaned piglets with 8 levels (gilts, 1–6 piglets, 7 piglets, 8 piglets, 9 piglets, 10 piglets, 11 piglets and more than 11 piglets) following Tarrés *et al.* (2006). Note that \mathbf{b}_2 was a time-dependent effect that was changed (if required) at each weaning date. In addition, \mathbf{p} was a random time-dependent year–season effect with 71 levels. Year at first mating and year–season effects were required to account for involuntary heterogeneity in culling

decisions during the analysed period, as well as for the voluntarily relaxed culling criteria during the first few years (Table 1).

(b) Likelihood and prior specifications

Five different models were analysed depending on the structure of vector \mathbf{d} and its prior distribution. The most standard approach assumed \mathbf{d} as a scalar element (improper uniform prior) accounting for the overall effect of inbreeding depression on sow longevity (model U_1). Alternatively, \mathbf{d} was a 19×1 column vector containing the founder-specific (14 founders, 4 virtual founders and 1 extra category for the less-contributing founders) estimates of inbreeding depression under five different *a priori* distributions: improper uniform distribution (model U_{19}), symmetric normal distribution with mean fixed at zero (model $SN0_{19}$), symmetric normal distribution with mean μ ($SN\mu_{19}$), asymmetric normal distribution with mean fixed at 0 (model $AN0_{19}$) and asymmetric normal distribution with mean μ as an additional unknown in the model (model $AN\mu_{19}$).

Taking model $AN\mu_{19}$ as a starting point, the joint posterior distribution of all the parameters conditional to the data was proportional to the likelihood multiplied by the prior distribution of the parameters,

$$\begin{aligned}
 & p(\mathbf{b}_1, \mathbf{b}_2, \mathbf{p}, \mathbf{d}, \mathbf{a}, \lambda, \rho, \xi, \boldsymbol{\tau}, \sigma_p^2, \sigma_d^2, \sigma_a^2, \alpha | \mathbf{y}) \\
 & \propto p(\mathbf{y} | \mathbf{b}_1, \mathbf{b}_2, \mathbf{p}, \mathbf{d}, \mathbf{a}, \lambda, \rho, \xi, \boldsymbol{\tau}, \sigma_p^2, \sigma_d^2, \sigma_a^2, \alpha) p(\mathbf{b}_1) \\
 & \quad \times p(\mathbf{b}_2) p(\mathbf{p} | \sigma_p^2) p(\sigma_p^2) p(\mathbf{d} | \sigma_d^2, \alpha, \mu) p(\sigma_d^2) p(\alpha) \\
 & \quad \times p(\mu) p(\mathbf{a} | \mathbf{A}, \sigma_a^2) p(\sigma_a^2) p(\lambda) p(\rho) p(\xi) p(\boldsymbol{\tau}),
 \end{aligned}
 \tag{2}$$

where ξ and $\boldsymbol{\tau}$ are the column vectors of baseline-related time-dependent effects and change points, respectively; σ_p^2 , σ_d^2 and σ_a^2 are the permanent environmental, inbreeding depression and additive genetic variance components, respectively; \mathbf{A} is the numerator relationship matrix, and α is the asymmetry parameter related to \mathbf{d} (see below). Under the assumption that censoring was independent and non-informative, the likelihood was stated as described by Allison (1995) and Casellas (2007).

The recent development of skew-elliptical distributions (Sahu *et al.*, 2003; Sahu & Chai, 2005) has allowed the implementation of a skew-Gaussian prior distribution for \mathbf{d} ,

$$\begin{aligned}
 & p(\mathbf{d} | \sigma_d^2, \alpha, \mu) \propto \prod_{q=1}^{19} \frac{2}{\sqrt{\sigma_d^2 + \alpha^2}} \phi\left(\frac{d_q - \mu}{\sqrt{\sigma_d^2 + \alpha^2}}\right) \\
 & \quad \times \Phi\left(\frac{\alpha(d_q - \mu)}{\sigma_d \sqrt{\sigma_d^2 + \alpha^2}}\right),
 \end{aligned}
 \tag{3}$$

where d_q is the q th element in \mathbf{d} , α is the degree of asymmetry defined in real space, and $\phi(\cdot)$ and $\Phi(\cdot)$,

respectively, denote the density function and cumulative density function of a standard normal distribution with arguments as defined in parentheses. This assumption is of special relevance to this particular research because it allows a straightforward characterization of the posterior distribution of \mathbf{d} in terms of symmetric ($\alpha=0$) patterns, or right-tail (left-tail) overexpressions when $\alpha > 0$ ($\alpha < 0$). Note that the first and second moments of the posterior distribution of \mathbf{d} can be directly calculated from $E(\mathbf{d}) = \mu + \alpha\sqrt{2/\pi}$ and $\text{Var}(\mathbf{d}) = \sigma_d^2 + \alpha^2[1 - (2/\pi)]$, respectively (Sahu *et al.*, 2003). *A priori* distributions for \mathbf{p} and \mathbf{a} vectors were stated as $p(\mathbf{p} | \sigma_p^2) \propto N(\mathbf{0}, \mathbf{I}_p \sigma_p^2)$ and $p(\mathbf{a} | \mathbf{A}, \sigma_a^2) \propto N(\mathbf{0}, \mathbf{A} \sigma_a^2)$, where \mathbf{I}_p is an identity matrix with dimensions equal to the number of elements in \mathbf{p} . Note that relationship matrix \mathbf{A} was constructed following Westell *et al.* (1988) to account for the different origins of the founder individuals. As previously reported by Damgaard & Korsgaard (2006), Casellas (2007) and Varona *et al.* (2008), *a priori* model parameters ρ , λ , ξ , σ_p^2 , σ_d^2 , σ_a^2 , α and the elements of \mathbf{b}_1 and \mathbf{b}_2 were assumed to be mutually independent with improper flat priors. The prior distribution for $\boldsymbol{\tau}$ assumed that change points were distributed as order statistics from a uniform distribution on the interval $[0, \tau_{m+1}]$, where $\tau_1 = 0 < \tau_2 < \dots < \tau_m < \tau_{m+1}$ (Casellas, 2007). The prior distribution of μ was assumed to be improper flat. This model was reduced to $AN0_{19}$ by fitting $\mu = 0$. In this case, the *a priori* probability of \mathbf{d} was conditioned to σ_d^2 and α . All the remaining *a priori* distributions were stated as for model $AN\mu_{19}$ (see above for a detailed description of these priors).

For model $SN0_{19}$, the posterior distribution was identical to the posterior distribution of model $AN0_{19}$ after the arbitrarily fit $\alpha = 0$. In a similar way, the posterior distribution for model $SN\mu_{19}$ fitted $\alpha = 0$ and assumed $p(\mathbf{d} | \sigma_d^2, \mu) \propto N(\mu, \mathbf{I}_d \sigma_d^2)$, where \mathbf{I}_d is a 19×19 identity matrix, and an improper flat prior for $p(\mu)$. The posterior distribution for models U_1 and U_{19} were assumed as in the previous model, with the exception of $p(\mathbf{d})$, which had an improper flat distribution.

(c) Markov chain Monte Carlo sampling and model comparison

Preliminarily, each model (U_1 , U_{19} , $SN0_{19}$, $SN\mu_{19}$, $AN0_{19}$ and $AN\mu_{19}$) was analysed six times, from no change points to 5 change points, and the appropriate number of change points was established by comparing model performance in terms of the deviance information criterion (DIC; Spiegelhalter *et al.*, 2002). Models with smaller DIC were favoured as this indicates a better fit and lower degree of model complexity (Spiegelhalter *et al.*, 2002). In general, differences larger than 3–5 DIC units are typically assumed as relevant (Spiegelhalter *et al.*, 2002, 2003).

In all cases, DIC reached its smaller value for models with 3 change points, it being 4.1–7.4 DIC units smaller than the second best model (4 change points; results not shown). Within this context, further analyses were focused on the basis of models with 3 change points, and alternative prior specifications for \mathbf{d} were compared with DIC.

Five independent chains of 1 000 000 rounds were launched for each model and the first 50 000 iterations were discarded as burn-in (Raftery & Lewis, 1992). Metropolis–Hastings sampling (Metropolis *et al.*, 1953; Hastings, 1970) and Gibbs sampling (Gelfand & Smith, 1990) procedures were used to sample from the marginal posterior distribution of all the unknowns in the models. A uniform proposal distribution with mathematical expectation at the current value of each parameter was used for Metropolis–Hastings sampling. The range of the proposed distribution for each parameter was determined in a preliminary analysis, with an acceptance rate of greater than 20% for all parameters. Given the high autocorrelation between successive samples related to the Metropolis–Hastings method, a total of 19 000 samples of model parameters were saved from each chain with a lag interval of 50 iterations.

3. Results and discussion

(i) Partial inbreeding coefficients in the analysed Landrace population

As described above, partial inbreeding coefficients were estimated for 14 founders, 4 virtual founders (couples of founders considered together) and an extra level corresponding to the remaining 13 founders, which contributed a few inbred descendants. Each founder (or group of founders) contributed between 160 and 1162 inbred descendants with an average partial inbreeding coefficient of 0.003 and 0.11%, even though (within-founder) maximum values oscillated between 0.39 and 25% (results not shown in the tables). This variability indicated that the breeding strategies applied to this herd resulted in unequal contribution of founder genomes to overall inbreeding, as previously described in other species (Gulisija *et al.*, 2006; Casellas *et al.*, 2009). Correlations for partial inbreeding coefficients between pairs of founders ranged from -0.01 ($P=0.672$) to 0.25 ($P=0.048$), suggesting a small or null incidence of potential biases due to collinearity.

(ii) Empirical assessment of Landrace sow longevity

Figure 2 shows the empirical Kaplan–Meier (Kaplan & Meier, 1958) survival function for the analysed Landrace population. The Kaplan–Meier survival function showed a pseudo-cyclic pattern with peaks

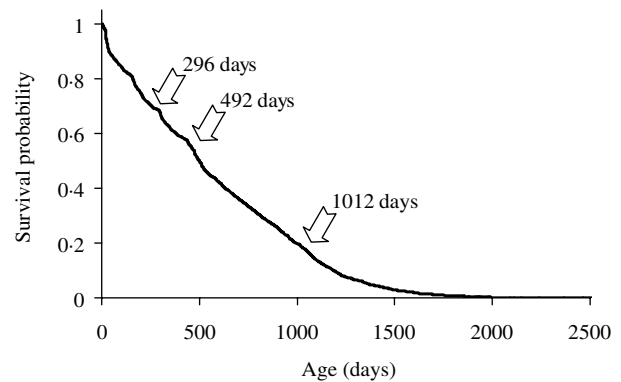


Fig. 2. The Kaplan–Meier (Kaplan & Meier, 1958) survival function for the analysed Landrace population.

each ~ 140 days during the first 500 days of productive life. These falls started at day 20 (3 weeks after the first mating), and could have been related to a substantial culling of gilts that failed to become pregnant during their first heats. After that, the observed reduction in the cycle every ~ 140 days may have matched the end of each reproductive cycle (gestation ~ 114 days; weaning period ~ 25 days), as previously reported by Serenius *et al.* (2006), Tarrés *et al.* (2006) and Fernández de Sevilla *et al.* (2008). After day 500, survival probability showed a smooth trend with a long tail extending for longevities of greater than 2000 days. The average length of the productive life of sows was then 524 days (1 year and 5 months) with an annual replacement rate of 69.7%. Note that this average longevity (replacement rate) was substantially shorter (greater) than those reported in other populations such as Landrace sows (Yazdi *et al.*, 2000; 617 days), Large White \times Landrace crossbred sows (Le Cozler *et al.*, 1998; ~ 1000 days), Large White sows (Tarrés *et al.*, 2006; 602 days) and crossbred sows (Brandt *et al.*, 1999; 880 days).

(iii) Model comparison, change-point baseline function and genetic background

The DIC statistic allowed straightforward comparison across models (Table 2). Model AN₀₁₉ was preferred on account of its smaller DIC values, although differences with AN _{μ} ₁₉ were small and almost negligible. Within this context, the small advantage showed by model AN₀₁₉ in front of model AN _{μ} ₁₉ was not conclusive, although the reduction in model parameterization proposes AN₀₁₉ as a more parsimonious choice. This small difference in terms of model performance could be due to the small estimate obtained for μ under model AN _{μ} ₁₉ (mode = 0.003). DICs suggested that model AN₀₁₉ achieved a better fit to sow longevity data when compared with models

Table 2. Model comparison in terms of mean (empirical S.E.) of the DIC (Spiegelhalter *et al.*, 2002). All models addressed three additional change points in the baseline function

Model	DIC
U ₁	55 079.2 (1.0)
U ₁₉	55 077.9 (0.8)
SN0 ₁₉	55 068.1 (1.0)
SNμ ₁₉	55 066.9 (0.8)
AN0 ₁₉	55 063.2 (0.9)
ANμ ₁₉	55 064.0 (0.0)

U₁, U₁₉, SN0₁₉ and SNμ₁₉. The small empirical S.E. obtained for average DIC estimates (~1 DIC unit) corroborated the relevance of these differences, ranging between 3.7 DIC units (AN0₁₉ against SNμ₁₉) and 16.0 DIC units (AN0₁₉ against U₁). Note that these magnitudes fell within the range of statistically relevant differences suggested by Spiegelhalter *et al.* (2002, 2003). Within this context, using partial inbreeding coefficients seems the best way to model inbreeding depression in domestic species, as previously suggested by Casellas *et al.* (2009). Furthermore, DIC differences between models U₁₉, SN0₁₉, SNμ₁₉, AN0₁₉ and ANμ₁₉ (Table 2) suggested that the restrictions imposed by the skew-normal prior on inbreeding depression effects were preferable to the symmetric pattern and were probably more robust than analysis with the improper flat prior. In a similar way, models SNμ₁₉, AN0₁₉ and ANμ₁₉ allowed for non-null centrality parameters for FSID effects, this increased flexibility being also preferred in terms of DIC (Table 2). In conclusion, model AN0₁₉ was preferred given that it was less parameterized than model ANμ₁₉ and clearly reached a smaller DIC than the remaining models.

Baseline parameters for model AN0₁₉ are shown in Table 3. The Weibull pattern showed a ρ value of 0.93, close to an exponential form, whereas λ was small (8 × 10⁻⁵; models U₁, U₁₉, SN0₁₉, SNμ₁₉ and ANμ₁₉ converged at approximately the same values). Modal estimates (and the highest posterior density region at 95% (HPD95)) for change points in the model AN0₁₉ were located at 296 days (289–300 days), 492 days (477–499 days) and 1012 days (1088–1017 days), and the hazard ratio significantly increased with the age of the sow (Table 3). More interestingly, the additive genetic variance for sow longevity was close to 0.31, suggesting a moderate to low genetic background for this trait (h² = 0.16). Our heritability estimate agreed with those cited by López-Serrano *et al.* (2000) and Yazdi *et al.* (2000) and suggested that sow longevity could be effectively improved in this population through genetic selection.

Table 3. Baseline parameter estimates for each analysis of model AN0₁₉ (0–5 change points in the model): mode (HPD95) of the posterior distribution

Parameter ^a	Mode	HPD95
ρ	0.93	0.88–0.97
λ (× 100)	0.008	0.006–0.011
τ ₂	296	289–300
ξ ₂	1.93	1.69–2.17
τ ₃	492	477–499
ξ ₃	3.60	3.15–4.06
τ ₄	1.01	1.01 to 1.02
ξ ₄	14.93	12.62–17.33
σ _a ²	0.31	0.25–0.38
h ²	0.16	0.13–0.19
σ _d ² (× 10 000)	4.94	0.74–9.25
α (× 100)	4.49	0.77–13.81

^a The variables ρ and λ are the parameters of the Weibull distribution; ξ_k is the time-dependent effect between change points τ_k and τ_{k+1}; σ_a² and σ_d² are the additive genetic and inbreeding depression variance components, respectively; heritability (h²) was calculated as h² = σ_a² / [σ_a² + (π²/6)]; α is the asymmetry parameter for inbreeding depression effects.

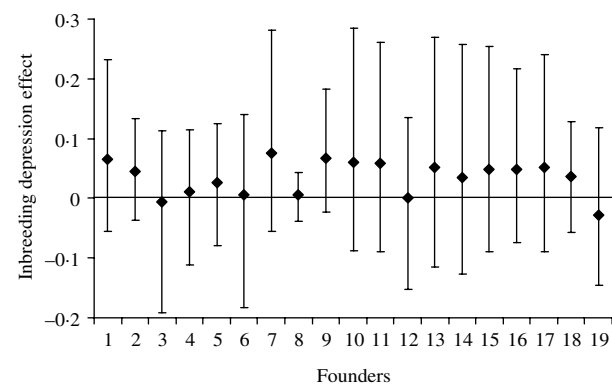


Fig. 3. FSID effects on sow longevity obtained through model AN0₁₉ (the point represents the modal estimate; the whiskers show the range of the HPD95).

(iv) Inbreeding depression effects and distribution pattern

Assuming partial inbreeding coefficients in terms of percentage, model AN0₁₉ suggested substantial heterogeneity for **d** effects (Fig. 3). The 19 founder elements contributing to inbreed descendants showed positive modal estimates for the posterior distribution of the regression coefficients in vector **d**, except for two elements that showed negative modes (Fig. 3). Given the form of eqns (1) and (2), positive estimates reduced sow longevity, whereas negative estimates implied an increase in the length of productive life (Allison, 1995). More specifically, the greatest effect in **d** reached a mode of 0.076 for each 1% increase in inbreeding, which suggested that the hazard

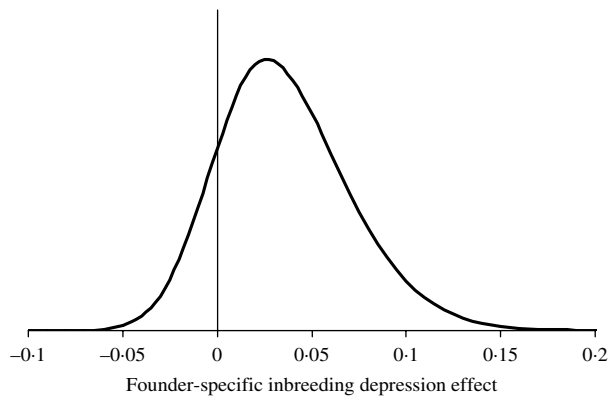


Fig. 4. Predicted distribution of the FSID effects under model AN₀₁₉.

probabilities were respectively 1.08 and 2.14 times greater for 1% and 10% inbred individuals (founder-specific partial inbreeding coefficient) in comparison with outbred sows. In our case, these increases in hazard probabilities are equal to a reduction in sow longevity of 32 and 167 days, respectively. The majority of modal values for **d** elements were grouped around 0.03, the same value as that obtained by the U₁ model for the modal estimate of overall inbreeding depression on sow longevity (0.032; HPD95 ranged between -0.002 and 0.065) and close to the modal estimate obtained for μ in model SN μ_{19} (0.027; HPD95 ranged between -0.011 and 0.053). As expected, estimates of **d** suffered from low precision and provided wide HPD95 due to the limited amount of available information with which to estimate each parameter. Given the selection experiment on sow prolificacy carried out in this population during three generations, an uncontrolled contribution of the selection scheme on **d** estimates cannot be completely discarded. Note that sow prolificacy may also be influenced by inbreeding and, consequently, longevity of inbred animals may have been genetically modified by involuntary selection and not only by loss of fitness. This uncontrolled contribution must be ruled by a substantial genetic correlation between sow longevity and prolificacy traits (Tholen *et al.*, 1996; Serenius & Stalder, 2004).

The most relevant result from this research was the general pattern described by the joint posterior distribution of elements in **d** under model AN₀₁₉ with 3 change points. This posterior distribution was straightforwardly characterized by σ_d^2 and α parameters, with both being positive and significantly different from zero (Table 3). Considering modal estimates, the joint posterior distribution of **d** describes a right-sided overexpressed distribution with its mode located at 0.034 (Fig. 4), agreeing with the dispersion of the **d** elements that is roughly shown in Fig. 3, as well as with the modal estimate obtained

under model U₁. This distribution (model AN₀₁₉) had a mean of 0.036, an S.D. of 0.032 (see equations in section 2) and an asymmetry parameter of 0.045, and reported 85.2% of positive estimates (with a negative effect on sow longevity) for the elements in **d**. Posterior asymmetry under model AN₀₁₉ is clearly characterized in Fig. 4, with 59.3% of probability placed on the right-hand side of the modal estimate. Note that Sahu's approach (Sahu *et al.*, 2003), which is shown in eqn (3), substantially increased the flexibility of the standard-Gaussian prior typically assumed for random effects in mixed models, allowing for asymmetry and also for non-zero modal estimates, as previously reported by Varona *et al.* (2008).

The results obtained in this study also highlight that heterogeneity in inbreeding depression effects is an important phenomenon with a relevant impact on sow longevity, and therefore also on the economics of the swine industry. Heterogeneity in inbreeding depression effects has previously been reported in the productive and reproductive traits of sows (Rodrig  nez *et al.*, 1998), dairy cows (Gulisija *et al.*, 2006) and ewes (Casellas *et al.*, 2009), although their impact and expected distribution pattern had never been studied in relation to the longevity of domestic breeds. The overall effect of inbreeding depression on animal life span has been typically reported as negative in experimental species (Vermeulen & Bijlsma, 2004; Fox *et al.*, 2006; Swindell & Bouzat, 2006), wild species (Sternicki *et al.*, 2003) and domestic species (Sewalem *et al.*, 2006), and this trend was confirmed in the present paper. Beyond this overall trend, this research has also shown a wide range of negative, neutral and even positive effects of inbreeding on sow longevity. These must be more carefully considered in further analyses and genetic evaluations in order to eliminate bias from mixed model solutions (Gulisija *et al.*, 2006). Negative and neutral effects can be easily related to the unevenly distribution of the deleterious recessive genetic load among the founder genomes or to the differential selection intensity applied to the different founder lines (Gulisija *et al.*, 2006), which partially supports the traditional assumption that inbreeding must be avoided in domestic livestock. Indeed, the founders acquired at different years could support the hypothesis of differential selection intensity applied to the different founder genomes. Within the context of dominance (recessive) effects, the positive effect may be associated with the fixation of favourable alleles and the purging of deleterious alleles from previous generations (MacKinnon, 2003), although this hypothesis needs to be confirmed by further studies. Indeed, positive effects of inbreeding have been previously reported in *Drosophila melanogaster* (S  nchez *et al.*, 1999; pupa size). Similarly, Weiner *et al.* (1992) reported an increase in lamb birth weight, and Galal *et al.* (1981) observed an increase in

lamb survival, although both results were obtained under high values of inbreeding.

As a whole, our results allow a more accurate description of the effects of inbreeding depression phenomena and the expected distribution within a founder-specific framework. Beyond the particular estimation of inbreeding depression effects related to each founder, the assumption of an *a priori* skew-normal distribution for \mathbf{d} allows a detailed characterization of the expected dispersion pattern of FSID effects, and also of their biological relevance for sow longevity.

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