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Identifiability of parameters in - and equivalence of animal and sire models for Gaussian and threshold characters, traits following a Poisson mixed model, and survival traits

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Abstract In this paper we give necessary and sufficient conditions for identifiability of parameters in animal and sire models of Gaussian traits, for binary and ordered categorical threshold characters, for traits following a Poisson mixed model and in frailty models for survival data. For survival data we consider Weibull and Cox log normal frailty models with time-independent covariates. Furthermore, we consider Cox frailty models with time-independent covariates, extended with either an extra random effect, time-dependent covariates with associated fixed effects, or time-dependent covariates with associated random effects. We show that sire models are consistent with the additive genetic infinitesimal model if and only if a normally distributed error term is included and the sire variance is less than one third of the variance of the normally distributed error term.

Key words: categorical trait, Cox log normal frailty models, equivalence of animal and sire models, Gaussian trait, identifiability, infinitesimal model, Poisson mixed model, survival trait, time-dependent covariates with associated fixed effects, time-dependent covariates with associated random effects, Weibull log normal frailty model.

1 Introduction

The purpose of animal breeding is to select the best animals to breed from. Animals are selected based on their estimated (predicted) breeding potential with the objective of increasing the mean genetic value - of the trait being selected for - in future generations. For normally distributed traits (e.g. milk, fat or protein yield in cattle) then the theory is well established. This is not the case for some other traits, for example traits following Poisson mixed models (e.g. litter size in pigs) or survival traits (e.g. longevity, that is length of life, measured from birth (or another starting date) until culling). A lot of countries are selecting for, or are going to select bulls based on their breeding potential for longevity, based on a so-called 'sire' models for survival data. However, in this paper we prove that these models are inconsistent with (postulated) assumptions of the additive genetic infinitesimal model. Furthermore we define sire models for survival data, which are consistent with the additive genetic infinitesimal model.

The additive genetic value of an animal is a measure of the breeding potential of the animal, and the name 'animal model' refer to models including additive genetic values for all animals in the data. If data consist of groups of halfsibs, where a group is determined by a common sire (father), then it is computationally much easier to use a sire model equivalent to the animal model. Sometimes a sire model is used in order to handle larger data sets (often millions of records), at the expense of ignoring part of the relationships between animals (part of the correlations between random effects associated with additive genetic values). In the (simplest) sire model it is implicitly assumed that all offspring have different dams (mothers), and it is assumed that all of the sires and dams are unrelated (additive genetic values of all the sires and dams are mutually independent).

The log normal frailty model where the logarithm of individual frailties are normally distributed is attractive from a genetic point of view. This is because, by assumptions of the additive genetic infinitesimal model, then it can be argued by the central limit theorem that the random effects associated with additive genetic values of animals follow a multivariate normal distribution, with common mean and variance covariance matrix $\mathbf{A}\sigma_a^2$, where **A** is a known matrix. In the (simplest) animal mixed model (Korsgaard et al., 1998) for survival data, it is assumed that the hazard function of animal i, conditional on log frailty, $a_i + e_i$, is given by $\lambda_i (t | a_i + e_i) = \lambda_0 (t) \exp \{x_i \beta + a_i + e_i\}$, where x_i is the design vector associated with fixed effects of animal i, $(a_i)_{i=1,\dots,n}$ is a vector of random additive genetic values and $(e_i)_{i=1,...,n}$ is a vector of independent and normally distributed residuals in log frailty (independent of the vector of additive genetic values). Ducrocq and Casella (1996) considered Weibull animal frailty models for survival data without the residual term in log frailty, the same did Gauderman and Thomas (1994), the latter using the name polygenic effect for the additive genetic value.

In the (simplest) size frailty models for survival data described in this paper, it is assumed that the hazard function of animal i, conditional on log frailty,

 $s_{g(i)} + e_i$, is given by $\lambda_i (t|s_{g(i)} + e_i) = \lambda_0 (t) \exp \{x_i\beta + s_{g(i)} + e_i\}$, where g(i) is the sire of animal i. In animal breeding a sire often has large progeny groups and $s_{g(i)}$ is a random effect common to all progeny of that sire, in the simplest sire models then the random vector of sire effects, \mathbf{s} , is normally distributed with $\mathbf{s} \sim N_G (\mathbf{0}, \mathbf{I}_G \sigma_s^2)$. The initial model for routine breeding value evaluation for longevity of dairy cows implemented in France was a (complicated) Weibull 'sire' frailty model (Ducrocq and Sölkner, 1998) without the error term in log frailty - this model is inconsistent with assumptions of the additive genetic infinitesimal model.

In Gaussian linear mixed models it is well known that for the sire model to be consistent with assumptions of the additive genetic infinitesimal model, then the sire variance, σ_s^2 , must be less than one third of the variance of the normally distributed error term. Among geneticists/animal breeders it has been discussed whether it makes sense to include an error term in log frailty. This is indicated by different papers concerning the definition of heritability of survival traits (e.g. Ducrocq (1999), Korsgaard et al. (1999, 2000) and Yazdi et al. (2000)). In this paper we prove that it makes sense to include the error term in log frailty - the error variance can be identified - and we prove that the error term is absolutely necessary in sire models for these to be consistent with assumptions of the additive genetic infinitesimal model. In this paper we are concerned in general - for models frequently used in animal breeding - with conditions under which sire models are consistent with assumptions of the additive genetic infinitesimal model. All of the models we consider are mixed models, where the joint distribution of mixing distributions (or the joint distribution of log mixing distributions) is multivariate normal, namely models for threshold characters, Poisson mixed models and survival models. First, and for each of the models, we give necessary and sufficient conditions for identifiability of parameters in animal and sire models.

The structure of the paper is as follows: In section 2, a summary is given of the genetic theory required in this paper. Next follows, in section 3, a summary of results on identifiability of parameters in Gaussian animal and sire models; and for parameterised (parameters identifiable) sire models the condition is given for existence of an equivalent animal model. In section 4, 5 and 6 we consider identifiability of parameters in animal and sire models of threshold characters, traits following Poisson mixed models and for survival traits, respectively. In the same series of models we give the condition under which the sire model is consistent with the animal model (i.e. with assumptions of the additive genetic infinitesimal model). For threshold characters we consider separately binary threshold characters and ordered categorical traits with three or more categories. For survival models we consider Weibull and Cox log normal frailty models. For Weibull frailty models only models with time-independent covariates are considered. For Cox frailty models we consider models with i) time-independent covariates, ii) an extra random effect, iii) timedependent (piecewise constant) covariates with associated fixed effects and iv) time-dependent (piecewise constant) covariates with associated random effects. In ii), iii) and iv) time-independent covariates may also be included. The paper ends with a discussion and conclusion.

2 Genetic theory and notation

In this paper, we will work under the assumptions of a genetic model of i) a large (strictly infinite) random mating population in Hardy Weinberg and linkage equilibrium; i.e. no selection, migration, mutation or inbreeding; and ii) traits of concern are controlled by a large (strictly infinite) number of additive loci, i.e. changes of gene frequency is of no concern and under the assumption of no dominance or epistatic effects. These assumptions are given as basis of much of the methodology used in animal breeding (e.g. Kennedy, 1995) and will be used here as well. By assumptions of the additive genetic infinitesimal model, then it can be argued by the central limit theorem that the random effects associated with additive genetic values of animals follow a multivariate normal distribution (e.g. Bulmer, 1980), with common mean and variance covariance matrix $\mathbf{A}\sigma_a^2$, where **A** is a known matrix, namely the numerator relationship matrix. The ij'th off-diagonal element of A is the numerator of Wright's (1922) coefficient of relationship between animals i and j and the i'th diagonal element is $1 + f_i$, where f_i is Wright's (1922) coefficient of inbreeding for animal *i* (Quass, 1976). In this paper, we work under the assumption of no inbreeding; i.e. $f_i = 0$ for all i.

Example 1 Consider three half sibs, C1, C2 and C3, with a common father and three different mothers. It is implicitly assumed that the father and the three different mothers are mutually unrelated. In this example the matrix \mathbf{A} (associated with C1, C2 and C3) is:

$$\mathbf{A} = \left(\begin{array}{ccc} 1 & \frac{1}{4} & \frac{1}{4} \\ \frac{1}{4} & 1 & \frac{1}{4} \\ \frac{1}{4} & \frac{1}{4} & 1 \end{array}\right)$$

Without inbreeding then **A** is a correlation matrix. The correlation between additive genetic values of any two halfsibs is $\frac{1}{4}$, reflecting the fact that (on average) they share one quarter of their genes.

Notation 2 Usually Y_i is used as notation for a random variable and y_i as notation for a specific value of that random variable. In this paper we will sometimes use e.g. a_i (e_i) for a random variable and sometimes for a specific value of the random variable. The interpretation should be clear from the context.

3 Linear mixed model

3.1 Animal model

For normally distributed traits (e.g. milk, fat or protein yield in cattle) then the animal model used for genetic evaluations could be given by

$$Y_i = x_i\beta + a_i + e_i$$

for i = 1, ..., n, with $\mathbf{a} \sim N_n (\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_e^2)$; furthermore \mathbf{a} and \mathbf{e} are assumed to be independent. In this model we know that the parameters $(\beta, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the design matrix \mathbf{X} (with rows x_i) has full column rank, and at least one A_{ij} , for $i \neq j$ satisfy $0 < A_{ij}$ (at least two different animals are related, i.e. the additive genetic values of these two animals are correlated).

3.2 Sire model

Next consider the sire model given by

$$\widetilde{Y}_i = x_i \widetilde{\beta} + s_{g(i)} + \widetilde{e}_i \tag{1}$$

for i = 1, ..., n and with $g(i) \in \{1, ..., G\}$, where $\mathbf{s} \sim N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$ and $\mathbf{\tilde{e}} \sim N_n(\mathbf{0}, \mathbf{I}_n \sigma_{\tilde{e}}^2)$; furthermore \mathbf{s} and $\mathbf{\tilde{e}}$ are assumed to be independent. For all sire models considered in this paper, we will assume the following: For all $j \in \{1, ..., G\}$ there exist at least one animal $i \in \{1, ..., n\}$ with g(i) = j. In this model we know that the parameters $(\tilde{\beta}, \sigma_s^2, \sigma_{\tilde{e}}^2)$, where $0 < \sigma_s^2, \sigma_{\tilde{e}}^2 < \infty$, are identifiable if and only if the design matrix \mathbf{X} (with rows x_i) has full column rank and G < n (i.e. at least one sire has more than one offspring).

3.3 Equivalence of sire and animal models

We also know that for a parameterised (parameters identifiable) size model given by (1) there exists an equivalent animal model (where **A** is a block diagonal matrix. Each block of **A** relates to animals of a given size, and has diagonal elements equal to 1, and off diagonal elements equal to 1/4) if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$. The equivalent animal model is determined by $\beta = \tilde{\beta}$, $(\sigma_a^2 + \sigma_e^2) =$ $(\sigma_s^2 + \sigma_{\tilde{e}}^2)$ and $\sigma_a^2 = 4\sigma_s^2$.

4 Threshold models

4.1 Binary trait

4.1.1 Animal model

Now consider the animal model, for a binary threshold character given by

$$Y_i = \begin{cases} 1 & if \ U_i > \tau \\ 0 & if \ U_i \le \tau \end{cases}$$
(2)

where $U_i = x_i\beta + a_i + e_i$, for i = 1, ..., n; $\mathbf{a} \sim N_n (\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_e^2)$; **a** and **e** are assumed to be independent. Let **X** denote the design matrix associated with fixed effects on the underlying scale, the U-scale (or the liability scale). For reasons of identifiability and provided that the vector of ones, 1, belongs to span of the columns of **X**, then without loss of generality we can assume that $\tau = 0$ and $\sigma_a^2 + \sigma_e^2 = 1$ (or instead of a restriction on $\sigma_a^2 + \sigma_e^2$ we could have put a restriction on only σ_a^2 or σ_e^2).

Theorem 3 In the model specified by (2) (and with above mentioned restrictions imposed), the parameters (β, σ_a^2) , where $0 < \sigma_a^2 < 1$, are identifiable if and only if

A1) The design matrix \mathbf{X} (with rows x_i) has full rank.

A2) At least one A_{ij} , for $i \neq j$, satisfy $0 < A_{ij}$. I.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2; $M_{(i,j),1} = A_{ij}$ and $M_{(i,j)2} = 1$ {i = j}.

Proof: Conditions A1 and A2 are sufficient for identification of parameters (β, σ_a^2) : From $P(Y_i = 1) = \Phi(x_i\beta)$, it follows, that condition A1 is sufficient for identification of β . Next let $\eta_i = a_i + e_i$; having identified β , then for two related animals, $i \neq j$, consider the joint probability $P(Y_i = 0, Y_j = 0)$ as a function of σ_a^2 . Notice that $P(Y_i = 0, Y_j = 0) = \int_{-\infty}^{-x_i\beta} P(\eta_j < -x_j\beta|\eta_i) \varphi(\eta_i) d\eta_i = \int_{-\infty}^{-x_i\beta} \Phi\left(\frac{-x_j\beta - A_{ij}\sigma_a^2\eta_i}{\sqrt{1 - A_{ij}^2\sigma_a^4}}\right) \varphi(\eta_i) d\eta_i$ (because $\eta_j|\eta_i \sim N\left(A_{ij}\sigma_a^2\eta_i, 1 - A_{ij}^2\sigma_a^4\right)$).

If $x_j\beta \ge 0$ and $x_i\beta \ge A_{ij}x_j\beta$, then the joint probability $P(Y_i = 0, Y_j = 0)$ is a strictly increasing function of σ_a^2 . Similarly, by interchanging the roles of *i* and *j*, then $P(Y_i = 0, Y_j = 0)$ is a strictly increasing function of σ_a^2 for $x_i\beta \ge 0$ and $x_j\beta \ge A_{ij}x_i\beta$. If $x_j\beta \le 0$ and $x_j\beta \le A_{ij}x_i\beta$, then the joint probability $P(Y_i = 1, Y_j = 1) = \int_{-x_j\beta}^{\infty} \Phi\left(\frac{x_i\beta + A_{ij}\sigma_a^2\eta_j}{\sqrt{1 - A_{ij}^2\sigma_a^4}}\right)\varphi(\eta_j) d\eta_j$ is a strictly increasing function of σ_a^2 . And by symmetry, then $P(Y_i = 1, Y_j = 1)$ is also a strictly increasing function of σ_a^2 , for $x_i\beta \le 0$ and $x_i\beta \le A_{ij}x_j\beta$.

Conditions A1 and A2 are necessary for identification of parameters (β, σ_a^2) : Assume that condition A1 is not fulfilled, then there exist a vector $\alpha \neq (0, ..., 0)$ with $x_i \alpha = 0$ for all *i*. This implies that (at least) two different sets of parameters, (β, σ_a^2) and $(\beta + \alpha, \sigma_a^2)$, give equivalent models; i.e. nonidentifiability of parameters. Next, assume that condition A2 is not fulfilled, then $A_{ij} = 0$ for all $i \neq j$. Next take $\sigma_a^2 \neq \sigma_a^2$, with $0 < \sigma_a^2 < 1$. It follows that (at least) two different sets of parameter, (β, σ_a^2) and (β, σ_a^2) , give equivalent models. Q.E.D.

4.1.2 Sire model

Next consider the sire model, for a binary threshold character, given by

$$\widetilde{Y}_i = \begin{cases} 1 & if \ \widetilde{U}_i > \widetilde{\tau} \\ 0 & if \ \widetilde{U}_i \le \widetilde{\tau} \end{cases}$$
(3)

where $\widetilde{U}_i = x_i \widetilde{\beta} + s_{g(i)} + \widetilde{e}_i$, for i = 1, ..., n and with $g(i) \in \{1, ..., G\}$; $\mathbf{s} \sim N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$, $\widetilde{\mathbf{e}} \sim N_n(\mathbf{0}, \mathbf{I}_n \sigma_{\widetilde{e}}^2)$; furthermore \mathbf{s} and $\widetilde{\mathbf{e}}$ are assumed to be independent. Again, for reasons of identifiability and provided that the vector of

ones, **1**, belongs to span of the columns of **X**, then without loss of generality we can assume that $\tilde{\tau} = 0$ and $\sigma_s^2 + \sigma_{\tilde{e}}^2 = 1$ (or instead of a restriction on $\sigma_s^2 + \sigma_{\tilde{e}}^2$ we could have put a restriction on only σ_s^2 or $\sigma_{\tilde{e}}^2$).

Theorem 4 In the model specified by (3) (and with above mentioned restrictions imposed), the parameters $(\tilde{\beta}, \sigma_s^2)$, where $0 < \sigma_s^2 < 1$, are identifiable if and only if

A1) The design matrix \mathbf{X} (with rows x_i) has full rank.

A2) G < n (at least one sire has more than one offspring), i.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and $k = 1, 2; M_{(i,j),1} = 1 \{g(i) = g(j)\}$ and $M_{(i,j),2} = 1 \{i = j\}$.

Proof: The proof is similar to the proof of Theorem 3.

4.1.3 Equivalence of sire and animal models

We have the following result concerning conditions under which the sire model is consistent with the animal model:

Theorem 5 For a parameterised sire model, for a binary threshold character specified by (3) (and with above mentioned restrictions imposed), there exists an equivalent parameterised animal model (with above mentioned restrictions imposed and with **A** a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\overline{e}}^2$ (i.e. $\sigma_s^2 < \frac{1}{4}$).

The equivalent animal model is determined by $\beta = \tilde{\beta}$ and $\sigma_a^2 = 4\sigma_s^2$.

Proof: Existence of an equivalent animal model implies $\sigma_s^2 < \frac{1}{4}$: Now assume that an equivalent animal model exists. From $P(Y_i = 1) = P(\widetilde{Y}_i = 1)$ it follows that $\beta = \widetilde{\beta}$. Furthermore, if $x_j\beta \ge 0$ and $x_i\beta \ge A_{ij}x_j\beta$, then for two halfsibs, i and j, we consider $P(Y_i = 0, Y_j = 0) = P(\widetilde{Y}_i = 0, \widetilde{Y}_j = 0)$, i.e.

$$\int_{-\infty}^{-x_i\beta} \Phi\left(\frac{-x_j\beta - \frac{1}{4}\sigma_a^2\eta_i}{\sqrt{1 - \left(\frac{1}{4}\right)^2\sigma_a^4}}\right)\varphi\left(\eta_i\right)d\eta_i = \int_{-\infty}^{-x_i\beta} \Phi\left(\frac{-x_j\beta - \sigma_s^2\widetilde{\eta}_i}{\sqrt{1 - \sigma_s^4}}\right)\varphi\left(\widetilde{\eta}_i\right)d\widetilde{\eta}_i$$

The left side is a strictly increasing function of $\frac{1}{4}\sigma_a^2$ and the right side is the same function of σ_s^2 . This implies that $\frac{1}{4}\sigma_a^2 = \sigma_s^2$, and further that $\sigma_s^2 < \frac{1}{4}$. (We consider either $P(Y_i = 0, Y_j = 0) = P\left(\tilde{Y}_i = 0, \tilde{Y}_j = 0\right)$ or $P(Y_i = 1, Y_j = 1) = P\left(\tilde{Y}_i = 1, \tilde{Y}_j = 1\right)$ depending on the position of $(x_i\beta, x_j\beta)$, and according to the proof of Theorem 3).

 $\begin{aligned} \sigma_s^2 &< \frac{1}{4} \text{ implies existence of an animal model equivalent to the sire model:} \\ \text{Let } \beta &= \widetilde{\beta} \text{ and } \sigma_a^2 = 4\sigma_s^2 \text{, then } (x_i\beta + a_i + e_i)_{i=1,\dots,n} \text{ and} \\ \left(x_i\widetilde{\beta} + s_{g(i)} + \widetilde{e}_i\right)_{i=1,\dots,n} \text{ are identically and normally distributed and therefore} \\ \text{also } (Y_i)_{i=1,\dots,n} \text{ and } \left(\widetilde{Y}_i\right)_{i=1,\dots,n} \text{ are identically distributed. Q.E.D.} \end{aligned}$

4.2 Categorical trait with more than two categories

4.2.1 Animal model

The animal model, for an ordered categorical threshold character with $K \geq 3$ categories, is given by

$$Y_{i} = \begin{cases} 1 & if - \infty < U_{i} \le \tau_{1} \\ 2 & if & \tau_{1} < U_{i} \le \tau_{2} \\ \vdots \\ K - 1 & if & \tau_{K-2} < U_{i} \le \tau_{K-1} \\ K & if & \tau_{K-1} < U_{i} < \infty \end{cases}$$
(4)

where $-\infty < \tau_1 < \tau_2 < \cdots < \tau_{K-1} < \infty$, $U_i = x_i\beta + a_i + e_i$, for i = 1, ..., n and $\mathbf{a} \sim N_n (\mathbf{0}, \mathbf{A}\sigma_a^2)$, $\mathbf{e} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_e^2)$, \mathbf{a} and \mathbf{e} are assumed to be independent. Let \mathbf{X} denote the design matrix associated with fixed effects on the underlying scale, the *U*-scale (or the liability scale). Then again, as for binary traits, for reasons of identifiability and provided that the vector of ones, $\mathbf{1}$, belongs to span of the columns of \mathbf{X} , then without loss of generality we can assume that $\tau_1 = 0$ and $\sigma_a^2 + \sigma_e^2 = 1$ (or instead of a restriction on $\sigma_a^2 + \sigma_e^2$ we could have put a restriction on only σ_a^2 or σ_e^2 or one of the thresholds, $\tau_2, ..., \tau_{K-1}$).

Theorem 6 In the model specified by (4) (and with above mentioned restrictions imposed), the parameters $(\beta, \tau_2, ..., \tau_{K-1}, \sigma_a^2)$, where $0 < \sigma_a^2 < 1$, are identifiable if and only if

A1) The design matrix \mathbf{X} (with rows x_i) has full rank.

A2) At least one A_{ij} , for $i \neq j$, satisfy $0 < A_{ij}$.

Proof: Conditions A1 and A2 are sufficient for identification of parameters $(\beta, \tau_2, ..., \tau_{K-1}, \sigma_a^2)$: From $P(Y_i \ge 2) = \Phi(x_i\beta)$, it follows, that condition A1 is sufficient for identification of β . Having identified β , then $\tau_k, k = 2, ..., K-1$ can be identified from $P(Y_i = k) = \Phi(\tau_k - x_i\beta) - \Phi(\tau_{k-1} - x_i\beta)$. Identifiability of σ_a^2 is established by considering joint probabilities $P(Y_i = 1, Y_j = 1)$ and $P(Y_i > 1, Y_j > 1)$ for two related animals $i \ne j$ (see proof of Theorem 3).

Conditions A1 and A2 are necessary for identification of parameters (β , τ_2 , ..., τ_{K-1} , σ_a^2): Straightforward from the proof of Theorem 3. Q.E.D.

4.2.2 Sire model

The sire model, for an ordered categorical threshold character, with $K \geq 3$ categories, is given by

$$\widetilde{Y}_{i} = \begin{cases} 1 & if - \infty < \widetilde{U}_{i} \le \widetilde{\tau}_{1} \\ 2 & if & \widetilde{\tau}_{1} < \widetilde{U}_{i} \le \widetilde{\tau}_{2} \\ \vdots \\ K - 1 & if & \widetilde{\tau}_{K-2} < \widetilde{U}_{i} \le \widetilde{\tau}_{K-1} \\ K & if & \widetilde{\tau}_{K-1} < \widetilde{U}_{i} < \infty \end{cases}$$
(5)

where $-\infty < \tilde{\tau}_1 < \tilde{\tau}_2 < \cdots < \tilde{\tau}_{K-1} < \infty$, $\tilde{U}_i = x_i \tilde{\beta} + s_{g(i)} + \tilde{e}_i$, for i = 1, ..., n, $g(i) \in \{1, ..., G\}$ and $\mathbf{s} \sim N_G (\mathbf{0}, \mathbf{I}_G \sigma_s^2)$, $\tilde{\mathbf{e}} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_{\tilde{e}}^2)$; furthermore \mathbf{s} and $\tilde{\mathbf{e}}$ are assumed to be independent. Again, for reasons of identifiability and provided that the vector of ones, $\mathbf{1}$, belongs to span of the columns of \mathbf{X} , then without loss of generality we can assume that $\tilde{\tau}_1 = 0$ and $\sigma_s^2 + \sigma_{\tilde{e}}^2 = 1$ (or instead of a restriction on $\sigma_s^2 + \sigma_{\tilde{e}}^2$ we could have put a restriction on only σ_s^2 or $\sigma_{\tilde{e}}^2$ or one of the thresholds, $\tilde{\tau}_2, ..., \tilde{\tau}_{K-1}$).

Theorem 7 In the model specified by (5) (and with above mentioned restrictions imposed), the parameters $(\tilde{\beta}, \tilde{\tau}_2, ..., \tilde{\tau}_{K-1}, \sigma_s^2)$, where $0 < \sigma_s^2 < 1$, are identifiable if and only if

A1) The design matrix \mathbf{X} (with rows x_i) has full rank. A2) G < n.

Proof: The proof is similar to the proof of Theorem 6.

4.2.3 Equivalence of sire and animal model

We have the following result concerning conditions under which the sire model is consistent with the animal model:

Theorem 8 For a parameterised size model for an ordered categorical trait with more than two categories, specified by (5), (and with above mentioned restrictions imposed), there exists an equivalent parameterised animal model (with above mentioned restrictions imposed and with **A** a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$ (i.e. $\sigma_s^2 < \frac{1}{4}$).

The equivalent animal model is determined by $\beta = \tilde{\beta}$, $\sigma_a^2 = 4\sigma_s^2$ and $(\tau_2, ..., \tau_{K-1}) = (\tilde{\tau}_2, ..., \tilde{\tau}_{K-1})$.

Proof: Existence of an equivalent animal model implies $\sigma_s^2 < \frac{1}{4}$: Now assume that an equivalent animal model exists. From $P(Y_i = 1) = P\left(\tilde{Y}_i = 1\right)$ it follows that $\beta = \tilde{\beta}$. And from $P(Y_i = k) = P\left(\tilde{Y}_i = k\right)$ we obtain $\tau_k = \tilde{\tau}_k$, for k = 2, ..., K - 1. Next, proceeding as for binary traits (now considering either $P(Y_i = 1, Y_j = 1) = P\left(\tilde{Y}_i = 1, \tilde{Y}_j = 1\right)$ or $P(Y_i > 1, Y_j > 1) = P\left(\tilde{Y}_i > 1, \tilde{Y}_j > 1\right)$ depending on the position of $(x_i\beta, x_j\beta)$) we obtain $\frac{1}{4}\sigma_a^2 = \sigma_s^2$. This implies $\sigma_s^2 < \frac{1}{4}$.

 $\sigma_s^2 < \frac{1}{4} \text{ implies existence of an animal model equivalent to the sire model:} \\ \text{Let } \beta = \widetilde{\beta} \text{ and } \sigma_a^2 = 4\sigma_s^2 \text{, then } (x_i\beta + a_i + e_i)_{i=1,...,n} \text{ and} \\ \left(x_i\widetilde{\beta} + s_{g(i)} + \widetilde{e}_i\right)_{i=1,...,n} \text{ are identically and normally distributed. Therefore,} \\ \text{with } (\tau_2, ..., \tau_{K-1}) = (\widetilde{\tau}_2, ..., \widetilde{\tau}_{K-1}), \text{ then also } (Y_i)_{i=1,...,n} \text{ and } \left(\widetilde{Y}_i\right)_{i=1,...,n} \text{ are identically distributed. Q.E.D.} \\ \end{array}$

5 Poisson mixed model

Both of the animal and sire models for traits following a Poisson mixed model are special cases of the multivariate Poisson - log normal distribution described by Aitchinson and Ho (1989).

5.1 Animal model

The Poisson animal model will be defined by $Y_i | \eta_i \sim Po(\lambda_i)$, where $\lambda_i = \exp(\eta_i)$ with η_i given by

$$\eta_i = \log\left(\lambda_i\right) = x_i\beta + a_i + e_i \tag{6}$$

for i = 1, ..., n, where $\mathbf{a} \sim N_n (\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_e^2)$, furthermore \mathbf{a} and \mathbf{e} are assumed to be independent, and conditional on η (the vector of $\eta'_i s$) then all of the $Y'_i s$ are assumed to be independent. In the Poisson animal model the conditional mean and variance of Y_i given η_i are given by

$$E(Y_i|\eta_i) = Var(Y_i|\eta_i) = \lambda_i = \exp(\eta_i)$$

The expected values of Y_i , $Y_i(Y_i - 1)$ and Y_iY_j (for $i \neq j$) are given by

$$E(Y_i) = \exp\left\{x_i\beta + \frac{1}{2}\left(\sigma_a^2 + \sigma_e^2\right)\right\}$$

$$E(Y_i(Y_i - 1)) = \exp\left\{2x_i\beta + 2\left(\sigma_a^2 + \sigma_e^2\right)\right\}$$

$$E(Y_iY_j) = \exp\left\{x_i\beta + x_j\beta + \left(\sigma_a^2 + \sigma_e^2\right) + A_{ij}\sigma_a^2\right\}$$

$$(7)$$

Theorem 9 In the Poisson animal model specified by (6), the parameters (β , σ_a^2 , σ_e^2), where $0 < \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if

- A1) The design matrix \mathbf{X} (with rows x_i) has full rank.
- A2) At least one A_{ij} , for $i \neq j$, satisfy $0 < A_{ij}$.

Proof: From (7) it follows that for $0 < \sigma_a^2, \sigma_e^2 < \infty$, then the parameters $(\beta, \sigma_a^2, \sigma_e^2)$ are identifiable if conditions A1 and A2 are satisfied. If condition A1 is relaxed, then there exist a vector $\alpha \neq (0, ..., 0)$ with $x_i \alpha = 0$ for all *i*. This implies that (at least) two different sets of parameters, $(\beta, \sigma_a^2, \sigma_e^2)$ and $(\beta + \alpha, \sigma_a^2, \sigma_e^2)$, give equivalent models; i.e. nonidentifiability of parameters. If condition A2 is relaxed, then $A_{ij} = 0$ for all $i \neq j$, and then we can take $\sigma_a^2 \neq \sigma_a^2$, with $\sigma_a^2 + \sigma_e^2 = \sigma_a^2 + \sigma_e^2$. It follows that the two different sets of parameters, $(\beta, \sigma_a^2, \sigma_e^2)$ and $(\beta, \sigma_a^2, \sigma_e^2)$, give equivalent models. Q.E.D.

5.2 Sire model

The Poisson sire model will be defined by $\widetilde{Y}_i | \widetilde{\eta}_i \sim Po\left(\widetilde{\lambda}_i\right)$, where $\widetilde{\lambda}_i = \exp\left(\widetilde{\eta}_i\right)$ with $\widetilde{\eta}_i$ given by

$$\widetilde{\eta}_i = \log\left(\widetilde{\lambda}_i\right) = x_i \widetilde{\beta} + s_{g(i)} + \widetilde{e}_i \tag{8}$$

for $i = 1, ..., n, g(i) \in \{1, ..., G\}$, where $\mathbf{s} \sim N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$ and $\widetilde{\mathbf{e}} \sim N_n(\mathbf{0}, \mathbf{I}_n \sigma_{\widetilde{e}}^2)$, furthermore s and $\tilde{\mathbf{e}}$ are assumed to be independent, and conditional on $\tilde{\eta}$ (the vector of $\widetilde{\eta}_i's$) then all of the $Y_i's$ are assumed to be independent. In the Poisson sire model the conditional mean and variance of \tilde{Y}_i given $\tilde{\eta}_i$ are given by

$$E\left(\widetilde{Y}_{i}|\widetilde{\eta}_{i}\right) = Var\left(\widetilde{Y}_{i}|\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{i} = \exp\left(\widetilde{\eta}_{i}\right)$$

The expected values of $\widetilde{Y}_i, \widetilde{Y}_i(\widetilde{Y}_i-1)$ and $\widetilde{Y}_i\widetilde{Y}_j$ (for $i \neq j$) are given by

$$E\left(\widetilde{Y}_{i}\right) = \exp\left\{x_{i}\widetilde{\beta} + \frac{1}{2}\left(\sigma_{s}^{2} + \sigma_{\overline{e}}^{2}\right)\right\}$$
$$E\left(\widetilde{Y}_{i}\left(\widetilde{Y}_{i} - 1\right)\right) = \exp\left\{2x_{i}\widetilde{\beta} + 2\left(\sigma_{s}^{2} + \sigma_{\overline{e}}^{2}\right)\right\}$$
$$E\left(\widetilde{Y}_{i}\widetilde{Y}_{j}\right) = \exp\left\{x_{i}\widetilde{\beta} + x_{j}\widetilde{\beta} + \left(\sigma_{s}^{2} + \sigma_{\overline{e}}^{2}\right) + \sigma_{s}^{2}\right\}$$

Theorem 10 In the Poisson sire model specified by (8), the parameters $(\tilde{\beta}, \sigma_s^2)$ $\sigma_{\tilde{e}}^2$), where $0 < \sigma_s^2, \sigma_{\tilde{e}}^2 < \infty$, are identifiable if and only if

A1) The design matrix \mathbf{X} (with rows x_i) has full rank. A2) G < n.

Proof: The proof is similar to the one given for identifiability of parameters in the Poisson animal model.

5.3Equivalence of sire and animal model

For the model specified by: $\widetilde{Y}_i | \widetilde{\eta}_i \sim Po\left(\widetilde{\lambda}_i\right)$, where $\widetilde{\lambda}_i = \exp\left(\widetilde{\eta}_i\right)$ with $\widetilde{\eta}_i$ given by $\widetilde{\eta}_i = \log\left(\widetilde{\lambda}_i\right) = x_i\widetilde{\beta} + s_{g(i)}, \text{ for } i = 1, ..., n, g(i) \in \{1, ..., G\}; \mathbf{s} \sim \mathbb{C}$ $N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$ with $\sigma_s^2 > 0$, there does not exist an equivalent animal model. Or identically, the model (8) without an error term in $\tilde{\eta}_i$ is not consistent with assumptions of the additive genetic infinitesimal model. This follows from:

Theorem 11 For a parameterised Poisson sire model given by (8), there exists an equivalent parameterised Poisson animal model (with \mathbf{A} a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$.

The equivalent animal model is determined by $\beta = \tilde{\beta}, \sigma_a^2 + \sigma_e^2 = \sigma_s^2 + \sigma_{\tilde{e}}^2$ and $\sigma_a^2 = 4\sigma_s^2.$

Proof: Existence of an equivalent animal model implies $\sigma_s^2 < \frac{1}{3}\sigma_{\widetilde{e}}^2$: Now assume that an equivalent animal model exists. Then $E(Y_i) = E(\widetilde{Y}_i)$,

 $E(Y_i(Y_i-1)) = E\left(\widetilde{Y}_i\left(\widetilde{Y}_i-1\right)\right)$ and $E(Y_iY_j) = E\left(\widetilde{Y}_i\widetilde{Y}_j\right)$. These equations

can only be solved if $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$. $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$ implies existence of an animal model equivalent to the sire model: Let $\beta = \tilde{\beta}, \ \sigma_a^2 = 4\sigma_s^2$ and $\sigma_a^2 + \sigma_e^2 = \sigma_s^2 + \sigma_{\tilde{e}}^2$, then $(x_i\beta + a_i + e_i)_{i=1,...,n}$ and

 $\left(x_i\widetilde{\beta} + s_{g(i)} + \widetilde{e}_i\right)_{i=1,...,n}$ are identically and normally distributed, and therefore also $(Y_i)_{i=1,...,n}$ and $\left(\widetilde{Y}_i\right)_{i=1,...,n}$ are identically distributed. Q.E.D.

6 Survival models

6.1 Weibull frailty model

6.1.1 Animal model

Now consider the Weibull, log normal animal frailty model, for survival times $(T_i)_{i=1,...,n}$, where the hazard function for T_i , conditional on η_i , is given by

$$\lambda_i \left(t | \eta_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i \beta + \eta_i \right\}$$
(9)

where $\lambda_0(t) = p\gamma(\gamma t)^{p-1}$, and where $\eta_i = a_i + e_i$ with $\mathbf{a} \sim N_n(\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N_n(\mathbf{0}, \mathbf{I}_n \sigma_e^2)$; \mathbf{a} and \mathbf{e} are assumed to be independent, and conditional on η (the vector of $\eta'_i s$), then all of the $T'_i s$ are assumed to be independent. The model is a log linear model for T_i (see Appendix) given by

$$Y_i = \log \left(T_i\right) = -\log \left(\gamma\right) - \frac{1}{p}x_i\beta - \frac{1}{p}a_i - \frac{1}{p}e_i + \frac{1}{p}\varepsilon_i$$

where ε_i follows an extreme value distribution, with $E(\varepsilon_i) = -\gamma_E$, where γ_E is Euler's constant, and $Var(\varepsilon_i) = \pi^2/6$; all of the $\varepsilon'_i s$ are independent and independent of **a** and **e**. The expected value and the variance of Y_i , the expected value of $(Y_i - E(Y_i))^3$ and the covariance between Y_i and Y_j (for $i \neq j$) are given by

$$E(Y_i) = -\log(\gamma) - \frac{1}{p} x_i \beta - \frac{1}{p} \gamma_E$$

$$Var(Y_i) = \frac{1}{p^2} \left(\sigma_a^2 + \sigma_e^2 + \frac{\pi^2}{6} \right)$$

$$E\left((Y_i - E(Y_i))^3 \right) = \frac{1}{p^3} \psi^{(2)}(1)$$

$$Cov(Y_i, Y_j) = \frac{1}{p^2} A_{ij} \sigma_a^2$$
(10)

where $\psi(\cdot)$ is the digamma function.

Theorem 12 In the Weibull log normal animal frailty model specified by (9), the parameters $(p, \gamma, \beta, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full column rank.

A2) At least one A_{ij} , for $i \neq j$, satisfy $0 < A_{ij}$. I.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2; $M_{(i,j),1} = A_{ij}$ and $M_{(i,j)2} = 1$ {i = j}.

Remark 13 Condition A1, namely that C has full rank is equivalent to: $(\mathbf{X}, \mathbf{1}_{n \times 1})$ has full rank, where $(\mathbf{X}, \mathbf{1}_{n \times 1})$ is the design matrix \mathbf{X} (with rows x_i) supplied with a column of ones.

Proof: Conditions A1 and A2 are sufficient for identification of parameters: From (10) it follows, under conditions A1 and A2, that the parameters $(p, \gamma, \beta, \sigma_a^2, \sigma_e^2)$ are identifiable.

Conditions A1 and A2 are necessary for identification of parameters:

Condition A1: Assume that condition A1 is not fulfilled, then there exists a vector $\alpha = (\alpha_1, ..., \alpha_p) \neq (0, ..., 0)$ with $(x_i - x_j) \alpha = 0$ for i, j = 1, ..., n, so that (for fixed j):

$$\lambda_{i} (t|\eta_{i}) = p\gamma (\gamma t)^{p-1} \exp \{x_{i}\beta + \eta_{i}\}$$

= $p\gamma (\gamma t)^{p-1} \exp \{-x_{j}\alpha\} \exp \{x_{i} (\beta + \alpha) + \eta_{i}\}$

This implies that (at least) two different sets of parameters, $(p, \gamma, \beta, \sigma_a^2, \sigma_e^2)$ and $(p, \gamma \exp\left\{-\frac{1}{p}x_j\alpha\right\}, (\beta + \alpha), \sigma_a^2, \sigma_e^2)$ give equivalent models, i.e. nonidentifiability of parameters.

Condition A2: Now assume that $rank(\mathbf{M}) = 1$, then $A_{ij} = 1$ $\{i = j\}$. Next take $(\sigma_a^2, \sigma_e^2) \neq (\sigma_a^2, \sigma_e^2)$, with $\sigma_a^2 + \sigma_e^2 = \sigma_a^2 + \sigma_e^2$. It follows that (at least) two different sets of parameters, $(p, \gamma, \beta, \sigma_a^2, \sigma_e^2)$ and $(p, \gamma, \beta, \sigma_a^2, \sigma_e^2)$, give equivalent models. Q.E.D.

6.1.2 Sire model

Next consider the Weibull, log normal sire frailty model for survival times $\left(\widetilde{T}_{i}\right)_{i=1,\ldots,n}$, where the hazard function for \widetilde{T}_{i} , conditional on $\widetilde{\eta}_{i}$ is given by

$$\widetilde{\lambda}_{i}\left(t|\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{0}\left(t\right)\exp\left\{x_{i}\widetilde{\beta} + \widetilde{\eta}_{i}\right\}$$
(11)

where $\widetilde{\lambda}_0(t) = \widetilde{p\gamma} (\widetilde{\gamma}t)^{\widetilde{p}-1}$, and where $\widetilde{\eta}_i = s_{g(i)} + \widetilde{e}_i, g(i) \in \{1, ..., G\}$, with $\mathbf{s} \sim N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$ and $\widetilde{\mathbf{e}} \sim N_n(\mathbf{0}, \mathbf{I}_n \sigma_{\widetilde{e}}^2)$; \mathbf{s} and $\widetilde{\mathbf{e}}$ are assumed to be independent, and conditional on $\widetilde{\eta}$, then all of the $\widetilde{T}'_i s$ are assumed to be independent. This model is a log linear model for \widetilde{T}_i given by

$$\widetilde{Y}_i = \log\left(\widetilde{T}_i\right) = -\log\left(\widetilde{\gamma}\right) - \frac{1}{\widetilde{p}}x_i\widetilde{\beta} - \frac{1}{\widetilde{p}}s_{g(i)} - \frac{1}{\widetilde{p}}\widetilde{e}_i + \frac{1}{\widetilde{p}}\widetilde{e}_i$$

where $\tilde{\varepsilon}_i$ follows an extreme value distribution; all of the $\tilde{\varepsilon}'_i s$ are independent and independent of **s** and $\tilde{\mathbf{e}}$. The expected value and the variance of \tilde{Y}_i , the expected value of $\left(\tilde{Y}_i - E\left(\tilde{Y}_i\right)\right)^3$ and the covariance between \tilde{Y}_i and \tilde{Y}_j (for $i \neq j$) are given by

$$E\left(\widetilde{Y}_{i}\right) = -\log\left(\widetilde{\gamma}\right) - \frac{1}{\widetilde{p}}x_{i}\widetilde{\beta} - \frac{1}{\widetilde{p}}\gamma_{E}$$

$$Var\left(\widetilde{Y}_{i}\right) = \frac{1}{\widetilde{p}^{2}}\left(\sigma_{s}^{2} + \sigma_{\widetilde{e}}^{2} + \frac{\pi^{2}}{6}\right)$$

$$E\left(\left(\widetilde{Y}_{i} - E\left(\widetilde{Y}_{i}\right)\right)^{3}\right) = \frac{1}{\widetilde{p}^{3}}\psi^{(2)}\left(1\right)$$

$$Cov(\widetilde{Y}_{i},\widetilde{Y}_{j}) = \frac{1}{\widetilde{p}^{2}}\sigma_{s}^{2}$$

Theorem 14 In the Weibull, log normal sire fraitly model specified by (11), the parameters $(\tilde{p}, \tilde{\gamma}, \tilde{\beta}, \sigma_s^2, \sigma_{\tilde{e}}^2)$, where $0 < \sigma_s^2, \sigma_{\tilde{e}}^2 < \infty$, are identifiable if and only if

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) G < n (at least one sire has more than one offspring), i.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and $k = 1, 2; M_{(i,j),1} = 1 \{g(i) = g(j)\}$ and $M_{(i,j),2} = 1 \{i = j\}$.

Proof: The proof is similar to the one given for identifiability of parameters in the Weibull, log normal animal frailty model.

6.1.3 Equivalence of sire and animal models

For the model specified by $\lambda_i(t|\tilde{\eta}_i) = \lambda_0(t) \exp\left\{x_i \tilde{\beta} + \tilde{\eta}_i\right\}$ for i = 1, ..., n, where $\lambda_0(t) = \tilde{p}\tilde{\gamma}(\tilde{\gamma}t)^{\tilde{p}-1}$, and where $\tilde{\eta}_i = s_{g(i)}, g(i) \in \{1, ..., G\}$, with $\mathbf{s} \sim N_G(\mathbf{0}, \mathbf{I}_G \sigma_s^2)$, there does not exist an equivalent animal model. Or identically the 'sire' model without an error term in log frailty is not consistent with assumptions of the additive genetic infinitesimal model. This follows from:

Theorem 15 For a parameterised Weibull, log normal sire frailty model given by (11), there exists an equivalent parameterised animal model (with **A** a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$.

The equivalent animal model is determined by $p = \tilde{p}$, $\gamma = \tilde{\gamma}$, $\beta = \tilde{\beta}$, $(\sigma_a^2 + \sigma_e^2) = (\sigma_s^2 + \sigma_{\tilde{e}}^2)$ and $\sigma_a^2 = 4\sigma_s^2$.

Proof: Existence of an equivalent animal model implies $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$: Now assume that an equivalent animal model exists. Then $E(Y_i) = E(\widetilde{Y}_i)$, $Var(Y_i) = Var(\widetilde{Y}_i)$, $E((Y_i - E(Y_i))^3) = E((\widetilde{Y}_i - E(\widetilde{Y}_i))^3)$ and $Cov(Y_i, Y_j) = Cov(\widetilde{Y}_i, \widetilde{Y}_j)$. These equations can only be solved if $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$.

 $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$ implies existence of an animal model equivalent to the Weibull, log normal sire fraitly model: Let $p = \tilde{p}$, $\gamma = \tilde{\gamma}$, $\beta = \tilde{\beta}$, $\sigma_a^2 = 4\sigma_s^2$ and $(\sigma_a^2 + \sigma_e^2) = (\sigma_s^2 + \sigma_{\tilde{e}}^2)$, then $(a_i + e_i)_{i=1,...,n}$ and $(s_{g(i)} + \tilde{e}_i)_{i=1,...,n}$ are identically and normally distributed and furthermore $(Y_i)_{i=1,...,n}$ and $(\tilde{Y}_i)_{i=1,...,n}$ are identically distributed. Q.E.D.

6.2 Cox frailty model

6.2.1 Animal model

Consider the Cox, log normal animal frailty model for survival times $(T_i)_{i=1,...,n}$, where the hazard function for T_i , conditional on η_i , is given by

$$\lambda_i \left(t | \eta_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i \beta + \eta_i \right\}$$
(12)

where $\eta_i = a_i + e_i$, with $\mathbf{a} \sim N_n (\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N_n (\mathbf{0}, \mathbf{I}_n \sigma_e^2)$; \mathbf{a} and \mathbf{e} are assumed to be independent, and conditional on η , then all of the $T'_i s$ are assumed to be independent. The baseline hazard, $\lambda_0 : [0, \infty) \rightarrow [0, \infty)$ is assumed to satisfy $\Lambda_0(t) < \infty$ for all $t \in [0, \infty)$, with $\lim_{t\to\infty} \Lambda_0(t) = \infty$, where $\Lambda_0(t) = \int_0^t \lambda_0(s) \, ds$ is the integrated baseline hazard function. Besides this, $\lambda_0(\cdot)$ is completely arbitrary.

Theorem 16 In the model specified by (12), the parameters $(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) At least one A_{ij} , for $i \neq j$ satisfy $0 < A_{ij}$. I.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2; $M_{(i,j),1} = A_{ij}$ and $M_{(i,j)2} = 1$ {i = j}.

Proof: The Theorem is proved for $rank(\mathbf{C}) \ge 1$ and $rank(\mathbf{C}) = 0$, separately. First for $rank(\mathbf{C}) \ge 1$:

Conditions A1 and A2 are sufficient for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2)$: The proof is by constructive identification, and inspired by Kortram et al. (1995). In the model specified by (12), we have that the integrated hazard function of animal *i*, conditional on η_i , is $\Lambda_i(t|\eta_i) = \exp\{x_i\beta + \eta_i\}\Lambda_0(t)$; the conditional survival function of T_i , given η_i , is $S_i(t|\eta_i) = \exp\{-\Lambda_i(t|\eta_i)\}$ and the marginal survival function of T_i is

$$S_{i}(t) = \int_{-\infty}^{\infty} S_{i}(t|\eta_{i}) p(\eta_{i}) d\eta_{i} = E \left[\exp \left\{ -\exp \left\{ x_{i}\beta + \eta_{i} \right\} \Lambda_{0}(t) \right\} \right]$$
$$= L_{e^{\eta_{i}}} \left(\exp \left\{ x_{i}\beta \right\} \Lambda_{0}(t) \right)$$

where $p(\cdot)$ is the density of η_i , and $L_{e^{\eta_i}}$ is the Laplace transform of $\exp{\{\eta_i\}}$. For notational convenience we let $L = L_{e^{\eta_i}}$ and notice that L only depends on $\sigma_{\eta}^2 =$ $\begin{aligned} &\sigma_a^2 + \sigma_e^2. \text{ Remember that } L: [0,\infty) \to (0,1] \text{ is a strictly decreasing function} \\ &\text{with } L(0) = 1 \text{ (and } L^{-1}: (0,1] \to [0,\infty) \text{ is a strictly decreasing function with } \\ &L^{-1}(1) = 0 \text{), and note that the right first and second order derivatives } L'(0) \\ &\text{and } L''(0) \text{ exists with } L'(0) = -\exp\left\{\frac{1}{2}\sigma_\eta^2\right\} \text{ and } L''(0) = \exp\left\{2\sigma_\eta^2\right\}. \end{aligned}$

Identifiability of β : Using a first order Taylor series expansion of $L(\cdot)$ around zero, it follows that

$$1 - S_i(t) = 1 - L(\exp\{x_i\beta\}\Lambda_0(t))$$

= $-L'(0)\exp\{x_i\beta\}\Lambda_0(t) + o(\exp\{x_i\beta\}\Lambda_0(t))$
= $\exp\{\frac{1}{2}\sigma_\eta^2\}\exp\{x_i\beta\}\Lambda_0(t) + o(\Lambda_0(t))$

so that

$$\frac{1-S_i(t)}{1-S_j(t)} \to \frac{\exp\left\{x_i\beta\right\}}{\exp\left\{x_j\beta\right\}} = \exp\left\{\left(x_i - x_j\right)\beta\right\} \text{ for } t \downarrow \inf\left\{u : \Lambda_0(u) > 0\right\}$$

where $\inf \{u : \Lambda_0(u) > 0\} = \inf \{u : S_k(u) < 1\}$ for k = 1, ..., n. It follows that condition A1 is sufficient for identification of β .

Intermediate step that leads to identification of $\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}(x)$: Now let S_{i}^{-1} be a generalised inverse of S_{i} , i.e. $S_{i}\left(S_{i}^{-1}(x)\right) = x$ for $x \in (0,1]$, then $\Lambda_{0}^{-1}:[0,\infty) \to [0,\infty)$ defined by $\Lambda_{0}^{-1}(t) = S_{i}^{-1}(L(\exp\left\{x_{i}\beta\right\}t))$ for $t \in [0,\infty)$ is a generalised inverse of $\Lambda_{0}(\cdot)$, because

$$\Lambda_0 \left(\Lambda_0^{-1} \left(t \right) \right) = \Lambda_0 \left(S_i^{-1} \left(L \left(\exp \left\{ x_i \beta \right\} t \right) \right) \right)$$

= $\exp \left\{ -x_i \beta \right\} L^{-1} \left(L \left(\exp \left\{ x_i \beta \right\} \Lambda_0 \left(S_i^{-1} \left(L \left(\exp \left\{ x_i \beta \right\} t \right) \right) \right) \right) \right)$
= $\exp \left\{ -x_i \beta \right\} L^{-1} \left(S_i \left(S_i^{-1} \left(L \left(\exp \left\{ x_i \beta \right\} t \right) \right) \right) \right)$
= t

and $S_i^{-1}(x) = \Lambda_0^{-1} \left(\exp \left\{ -x_i \beta \right\} L^{-1}(x) \right)$ is a generalised inverse of $S_i(\cdot)$. Having identified β , then we consider $S_i S_j^{-1}$ for two animals i and j with $\exp \left\{ (x_j - x_i) \beta \right\} > 1$. Let $c = \exp \left\{ (x_j - x_i) \beta \right\}$, it follows that

$$S_i(S_j^{-1}(x)) = L(\exp\{x_i\beta\}\Lambda_0(\Lambda_0^{-1}(\exp\{-x_j\beta\}L^{-1}(x)))) = L(c^{-1}L^{-1}(x))$$

and $(S_i S_j^{-1})^n (x) = L(c^{-n}L^{-1}(x))$ where $(S_i S_j^{-1})^n (x)$ is the n-fold composition of $S_i S_j^{-1}$. Using a first order Taylor series expansion of $L(\cdot)$ around zero, it follows that

$$1 - (S_i S_j^{-1})^n (x) = 1 - L (c^{-n} L^{-1} (x))$$

= $-L' (0) (c^{-n} L^{-1} (x) - 0) + o (c^{-n} L^{-1} (x))$
= $\exp\left\{\frac{1}{2}\sigma_\eta^2\right\} c^{-n} L^{-1} (x) + o (c^{-n}) \text{ for } n \to \infty$

and therefore (dividing by c^{-n} on both sides) that

$$\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}\left(x\right) = \lim_{n \to \infty} c^{n}\left(1 - \left(S_{i}S_{j}^{-1}\right)^{n}\left(x\right)\right)$$

for $x \in (0, 1]$. So now the product $\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}(x)$ is identified. Note: Here $rank(\mathbf{C}) \geq 1$ is used in order to identify $\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}(x)$ - otherwise we could not find two animals, i and j, with $\exp\left\{(x_{j} - x_{i})\beta\right\} > 1$. *Identifiability of* σ_{η}^{2} and L: Differentiating $\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}(x)$ twice w.r.t.

Identifiability of σ_{η}^2 and L: Differentiating $\exp\left\{\frac{1}{2}\sigma_{\eta}^2\right\}L^{-1}(x)$ twice w.r.t. x gives $\exp\left\{\frac{1}{2}\sigma_{\eta}^2\right\}\left(\frac{-L''(L^{-1}(x))}{(L'(L^{-1}(x)))^3}\right)$, which evaluated for x = 1 gives $\exp\left\{\sigma_{\eta}^2\right\}$. Hereby $\exp\left\{\sigma_{\eta}^2\right\}$ is identified and therefore also the Laplace transform L, which only depends on σ_{η}^2 .

Identifiability of $\Lambda_0(\cdot)$: This follows because $\Lambda_0(t) = \exp\{-x_i\beta\}L^{-1}(S_i(t))$

Identifiability of σ_a^2 and σ_e^2 : With $\Lambda_0(t)$ known, then the model specified in (12) is equivalent to a linear model for $Y_i = \log(\Lambda_0(T_i))$ (see Appendix). The model for Y_i is given by

$$Y_i = \log \left(\Lambda_0 \left(T_i \right) \right) = -x_i \beta - a_i - e_i + \varepsilon_i$$

where ε_i follows an extreme value distribution; all of the $\varepsilon'_i s$ are independent and independent of **a** and **e**. Thus, under assumption A2, σ_a^2 and σ_e^2 can be identified.

Conditions A1 and A2 are necessary for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2)$:

Condition A1: Assume that condition A1 is not fulfilled, then (using Remark 13) there exists a vector $(\alpha, \gamma) = (\alpha_1, ..., \alpha_p, \gamma) \neq (0, ..., 0)$ with $x_i \alpha + \gamma = 0$ for i = 1, ..., n, so that

$$\lambda_{i}(t|\eta_{i}) = \lambda_{0}(t) \exp \{x_{i}\beta + \eta_{i}\} = \lambda_{0}(t) \exp \{\gamma\} \exp \{x_{i}(\beta + \alpha) + \eta_{i}\}$$

This implies that (at least) two different sets of parameters, $(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2)$ and $(\Lambda_0(\cdot) \exp{\{\gamma\}}, (\beta + \alpha), \sigma_a^2, \sigma_e^2)$ give equivalent models, i.e. nonidentifiability of parameters.

Condition A2: Now assume that $rank(\mathbf{M}) = 1$, then $A_{ij} = 1$ $\{i = j\}$. Next take $(\sigma_{\overline{a}}^2, \sigma_{\overline{e}}^2) \neq (\sigma_a^2, \sigma_e^2)$, with $\sigma_{\overline{a}}^2 + \sigma_{\overline{e}}^2 = \sigma_a^2 + \sigma_e^2$. It follows that (at least) two different sets of parameters, $(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2)$ and $(\Lambda_0(\cdot), \beta, \sigma_{\overline{a}}^2, \sigma_{\overline{e}}^2)$, give equivalent models.

Second for $rank(\mathbf{C}) = 0$:

Condition A2 is sufficient for identification of parameters $(\Lambda_0(\cdot), \sigma_a^2, \sigma_e^2)$: The proof is by contradiction: Assume that two different sets of parameters $(\Lambda_0(\cdot), \sigma_a^2, \sigma_e^2) \neq (\overline{\Lambda}_0(\cdot), \sigma_a^2, \sigma_e^2)$ lead to equivalent models. Then $S_i(t) = L(\Lambda_0(t)) = \overline{L}(\overline{\Lambda}_0(t))$, where $L(\overline{L})$ is the Laplace transform of exp $\{\eta_i\}$

(exp { $\overline{\eta}_i$ }). This implies $\overline{\Lambda}_0(t) = \overline{L}^{-1}L(\Lambda_0(t))$. Note that $L(\overline{L})$ only depends on $\sigma_{\eta}^2(\sigma_{\overline{\eta}}^2)$. Next, for $i \neq j$, we have $S_{i,j}(s,t) = \overline{S}_{i,j}(s,t)$, where

$$S_{i,j}(s,t) = L_{\exp\{\eta_i\},\exp\{\eta_j\}}(\Lambda_0(s),\Lambda_0(t))$$

 and

$$\begin{split} \overline{S}_{i,j}\left(s,t\right) &= L_{\exp\{\overline{\eta}_{i}\},\exp\{\overline{\eta}_{j}\}}\left(\overline{\Lambda}_{0}\left(s\right),\overline{\Lambda}_{0}\left(t\right)\right) \\ &= L_{\exp\{\overline{\eta}_{i}\},\exp\{\overline{\eta}_{j}\}}\left(\overline{L}^{-1}L\left(\Lambda_{0}\left(s\right)\right),\overline{L}^{-1}L\left(\Lambda_{0}\left(t\right)\right)\right) \end{split}$$

Differentiation of both expressions for $S_{i,j}(t,t)$ twice with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$ gives

$$2 \exp \left\{ 2\sigma_{\eta}^{2} \right\} + 2 \exp \left\{ \sigma_{\eta}^{2} + A_{ij}\sigma_{a}^{2} \right\}$$
(13)
$$2 \exp \left\{ \sigma_{\eta}^{2} + A_{ij}\sigma_{a}^{2} \right\} + 2 \exp \left\{ 2\sigma_{\eta}^{2} \right\}$$

and differentiation of both expressions for $S_{i,j}(t,t)$ three times with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$ gives

=

$$-2 \exp\left\{\frac{9}{2}\sigma_{\eta}^{2}\right\} - 6 \exp\left\{\frac{5}{2}\sigma_{\eta}^{2} + 2A_{ij}\sigma_{a}^{2}\right\}$$
(14)
$$= -6 \exp\left\{\frac{3}{2}\sigma_{\eta}^{2} + \sigma_{\overline{\eta}}^{2} + 2A_{ij}\sigma_{\overline{a}}^{2}\right\} + 6 \exp\left\{\frac{3}{2}\sigma_{\eta}^{2} + \sigma_{\overline{\eta}}^{2} + A_{ij}\sigma_{\overline{a}}^{2}\right\}$$
$$-6 \exp\left\{\frac{5}{2}\sigma_{\eta}^{2} + A_{ij}\sigma_{\overline{a}}^{2}\right\} - 2 \exp\left\{\frac{9}{2}\sigma_{\eta}^{2}\right\}$$

From the equations in (13) and (14) it follows that $\sigma_a^2 = \sigma_a^2$, $\sigma_{\overline{\eta}}^2 = \sigma_{\eta}^2$ and further that $\overline{\Lambda}_0(\cdot) = \Lambda_0(\cdot)$, which gives a contradiction.

Condition A2 is necessary for identification of parameters $(\Lambda_0(\cdot), \sigma_a^2, \sigma_e^2)$: Necessity of condition A2 is established (with obvious modifications) as for rank (C) ≥ 1 . Q.E.D.

6.2.2 Sire model

Consider the Cox, log normal sire frailty model for survival times $\left(\widetilde{T}_{i}\right)_{i=1,...,n}$, where the hazard function for \widetilde{T}_{i} , conditional on $\widetilde{\eta}_{i}$, is given by

$$\widetilde{\lambda}_{i}\left(t|\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{0}\left(t\right)\exp\left\{x_{i}\widetilde{\beta} + \widetilde{\eta}_{i}\right\}$$
(15)

for i = 1, ..., n; where $\tilde{\eta}_i = s_{g(i)} + \tilde{e}_i$, with $\mathbf{s} \sim N_G \left(\mathbf{0}, \mathbf{I}_G \sigma_s^2 \right)$ and $\tilde{\mathbf{e}} \sim N_n \left(\mathbf{0}, \mathbf{I}_n \sigma_{\tilde{e}}^2 \right)$; s and $\tilde{\mathbf{e}}$ are assumed to be independent, and conditional on $\tilde{\eta}$, then all of the $\tilde{T}'_i s$ are assumed to be independent. The baseline hazard, $\tilde{\lambda}_0 : [0, \infty) \to [0, \infty)$ is assumed to satisfy $\tilde{\Lambda}_0 (t) < \infty$ for all $t \in [0, \infty)$, with $\lim_{t\to\infty} \tilde{\Lambda}_0 (t) = \infty$, where $\tilde{\Lambda}_0 (t) = \int_0^t \tilde{\lambda}_0 (s) \, ds$ is the integrated baseline hazard function. Besides this, $\tilde{\lambda}_0 (\cdot)$ is completely arbitrary.

Theorem 17 In the Cox, log normal sire frailty model, the parameters $(\widetilde{\Lambda}_0(\cdot), \widetilde{\beta}, \sigma_s^2, \sigma_{\widetilde{e}}^2)$, where $0 < \sigma_s^2, \sigma_{\widetilde{e}}^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) G < n (at least one sire has more than one offspring), i.e. the matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and $k = 1, 2; M_{(i,j),1} = 1 \{g(i) = g(j)\}$ and $M_{(i,j),2} = 1 \{i = j\}$.

Proof: The proof is similar to the proof of Theorem 16.

6.2.3 Equivalence of sire and animal models

Next we have the following result concerning conditions under which the Cox log normal sire frailty model is consistent with assumptions of the additive genetic infinitesimal model.

Theorem 18 For a parameterised Cox, log normal sire frailty model given by (15), there exists an equivalent parameterised animal model (with A a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$.

The equivalent animal model is determined by $\beta = \tilde{\beta}$, $\sigma_a^2 + \sigma_e^2 = \sigma_s^2 + \sigma_{\tilde{e}}^2$, $\sigma_a^2 = 4\sigma_s^2$ and $\Lambda_0(\cdot) = \tilde{\Lambda}_0(\cdot)$.

Proof: The Theorem is proved for $rank(\mathbf{C}) \geq 1$ and $rank(\mathbf{C}) = 0$, separately. First for $rank(\mathbf{C}) \geq 1$:

Existence of an equivalent animal model implies $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$: In the sire model $\widetilde{S}_i(t|\widetilde{\eta}_i) = \exp\left\{-\widetilde{\Lambda}_i(t|\widetilde{\eta}_i)\right\}$ and in the equivalent animal model $S_i(t|\eta_i) = \exp\left\{-\Lambda_i(t|\eta_i)\right\}$. Let $\widetilde{L} = L_{e^{\widetilde{\eta}_i}}$ and $L = L_{e^{\eta_i}}$ (and remember that \widetilde{L} only depends on $\sigma_{\widetilde{\eta}}^2 = \sigma_s^2 + \sigma_{\widetilde{e}}^2$, and L only on $\sigma_{\eta}^2 = \sigma_a^2 + \sigma_e^2$), then

$$\widetilde{S}_{i}(t) = \widetilde{L}\left(\exp\left\{x_{i}\widetilde{\beta}\right\}\widetilde{\Lambda}_{0}(t)\right) = L\left(\exp\left\{x_{i}\beta\right\}\Lambda_{0}(t)\right) = S_{i}(t)$$

and we want to show that this implies $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$. First relationships between parameters $\left(\widetilde{\Lambda}_0(\cdot), \widetilde{\beta}, \sigma_s^2, \sigma_{\tilde{e}}^2\right)$ of the sire model and parameters $\left(\Lambda_0(\cdot), \beta, \sigma_a^2, \sigma_e^2\right)$ of the animal model are established:

 $\beta = \beta$: From

$$\frac{1-S_{i}\left(t\right)}{1-\widetilde{S}_{j}\left(t\right)} \to \exp\left\{\left(x_{i}-x_{j}\right)\widetilde{\beta}\right\} \text{ for } t\downarrow \inf\left\{u:\widetilde{S}_{k}\left(u\right)<1\right\}$$

and

$$\frac{1-S_i(t)}{1-S_j(t)} \to \exp\left\{\left(x_i - x_j\right)\beta\right\} \text{ for } t \downarrow \inf\left\{u : S_k(u) < 1\right\}$$

it follows that $\beta = \tilde{\beta}$, because $\tilde{S}_k(u) = S_k(u)$ for k = 1, ..., n.

 $\sigma_{\eta}^2 = \sigma_{\tilde{\eta}}^2$: Consider two animals, *i* and *j*, with $c = \exp\{(x_j - x_i)\beta\} = \exp\{(x_j - x_i)\tilde{\beta}\} > 1$, then we have

$$\lim_{n \to \infty} c^n \left(1 - \left(\widetilde{S}_i \widetilde{S}_j^{-1} \right)^n (x) \right) = \exp\left\{ \frac{1}{2} \sigma_{\widetilde{\eta}}^2 \right\} \widetilde{L}^{-1} (x)$$

and

$$\lim_{n \to \infty} c^n \left(1 - \left(S_i S_j^{-1} \right)^n (x) \right) = \exp\left\{ \frac{1}{2} \sigma_\eta^2 \right\} L^{-1} (x)$$

and because $c^n \left(1 - \left(\widetilde{S}_i \widetilde{S}_j^{-1}\right)^n (x)\right) = c^n \left(1 - \left(S_i S_j^{-1}\right)^n (x)\right)$, this implies that $\sigma_\eta^2 = \sigma_{\widetilde{\eta}}^2$ and $L = \widetilde{L}$.

 $\Lambda_0(\cdot) = \widetilde{\Lambda}_0(\cdot)$: It follows, because $\beta = \widetilde{\beta}$, $L = \widetilde{L}$ and $S_i = \widetilde{S}_i$, that

$$\begin{array}{ll} {}_{0}\left(t\right) & = & \exp\left\{-x_{i}\beta\right\}L^{-1}\left(S_{i}\left(t\right)\right) \\ & = & \exp\left\{-x_{i}\widetilde{\beta}\right\}\widetilde{L}^{-1}\left(\widetilde{S}_{i}\left(t\right)\right) = \widetilde{\Lambda}_{0}\left(t\right) \end{array}$$

$$\begin{split} \sigma_a^2 &= 4\sigma_s^2: \text{ With } \Lambda_0\left(\cdot\right) = \widetilde{\Lambda}_0\left(\cdot\right) \text{ and } \beta = \widetilde{\beta}, \text{ then } \widetilde{Y}_i \text{ and } Y_i \text{ are identically distributed, where } \widetilde{Y}_i &= \log\left(\widetilde{\Lambda}_0\left(T_i\right)\right) = -x_i\beta - s_{g(i)} - \widetilde{e}_i + \widetilde{\varepsilon}_i \text{ and } Y_i = \log\left(\Lambda_0\left(T_i\right)\right) \\ &= -x_i\beta - a_i - e_i + \varepsilon_i. \text{ This implies:} \end{split}$$

$$Var\left(\widetilde{Y}_{i}\right) = \sigma_{s}^{2} + \sigma_{\widetilde{e}}^{2} + \frac{\pi^{2}}{6}$$

$$= Var\left(Y_{i}\right) = \sigma_{a}^{2} + \sigma_{e}^{2} + \frac{\pi^{2}}{6}$$
(16)

and for two halfsibs, i and j:

Λ

$$Cov\left(\widetilde{Y}_{i},\widetilde{Y}_{j}\right) = \sigma_{s}^{2}$$

$$= Cov\left(Y_{i},Y_{j}\right) = A_{ij}\sigma_{a}^{2} = \frac{1}{4}\sigma_{a}^{2}$$

$$(17)$$

Given parameters $(\sigma_s^2, \sigma_{\tilde{e}}^2)$ of the sire model, then the equations (in parameters σ_a^2 and σ_e^2) given by (16) and (17), can only be solved if $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$. $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$ implies existence of an animal model equivalent to the Cox,

 $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$ implies existence of an animal model equivalent to the Cox, log normal sire fraitly model: Let $\Lambda_0(\cdot) = \tilde{\Lambda}_0(\cdot)$, $\beta = \tilde{\beta}$, $\sigma_a^2 = 4\sigma_s^2$ and $(\sigma_a^2 + \sigma_e^2) = (\sigma_s^2 + \sigma_{\tilde{e}}^2)$, then $(a_i + e_i)_{i=1,...,n}$ and $(s_{g(i)} + \tilde{e}_i)_{i=1,...,n}$ are identically and normally distributed and furthermore $(T_i)_{i=1,...,n}$ and $(\tilde{T}_i)_{i=1,...,n}$ are identically distributed.

Second for $rank(\mathbf{C}) = 0$:

In the sire model $\widetilde{S}_i(t) = \widetilde{L}\left(\widetilde{\Lambda}_0(t)\right)$ and in the equivalent animal model $S_i(t) = L(\Lambda_0(t))$, it follows that $\widetilde{\Lambda}_0(t) = \widetilde{L}^{-1}L(\Lambda_0(t))$. Differentiating

$$\widetilde{S}_{i,j}(t,t) = L_{\exp\{\widetilde{\eta}_i\},\exp\{\widetilde{\eta}_j\}} \left(\widetilde{\Lambda}_0(t), \widetilde{\Lambda}_0(t) \right)$$

$$S_{i,j}(t,t) = L_{\exp\{\eta_i\},\exp\{\eta_j\}}(\Lambda_0(t),\Lambda_0(t)) (=\widetilde{S}_{i,j}(t,t))$$

twice with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$; and by differentiating $\tilde{S}_{i,j}(t,t)$ and $S_{i,j}(t,t)$ three times with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$, then we obtain a set of equations - the result follows by reasoning from these equations. Q.E.D.

6.3 Cox frailty model - extra random effect

6.3.1 Animal model

Next consider the Cox, log normal animal frailty model for survival times $(T_i)_{i=1,...,n}$, where the hazard function for T_i , conditional on $u_{l(i)}$ and η_i is given by

$$\lambda_i \left(t | u_{l(i)}, \eta_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i \beta + u_{l(i)} + \eta_i \right\}$$
(18)

for $l(i) \in \{1, ..., q\}$. $\lambda_0(t)$, η_i , **a** and **e** are as before and **u** ~ $N_q(\mathbf{0}, \mathbf{I}_q \sigma_u^2)$. Furthermore **u**, **a** and **e** are assumed to be independent, and conditional on $(u_{l(i)} + \eta_i)_{i=1,...,n}$, then all of the T'_is are assumed to be independent.

Theorem 19 In the model specified by (18), the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_u^2, \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) The matrix **M** has rank 3, where **M** is the $n^2 \times 3$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2, 3; $M_{(i,j),1} = 1 \{l(i) = l(j)\}, M_{(i,j),2} = A_{ij}$ and $M_{(i,j),3} = 1 \{i = j\}.$

Proof: The Theorem is proved for $rank(\mathbf{C}) \ge 1$ and $rank(\mathbf{C}) = 0$, separately. First for $rank(\mathbf{C}) \ge 1$:

Conditions A1 and A2 are sufficient for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$: In the model specified by (18), we have that $S_i(t) = L_{\exp\{u_{l(i)} + a_i + e_i\}}(\exp\{x_i\beta\}\Lambda_0(t))$, where $L_{\exp\{u_{l(i)} + a_i + e_i\}}$, the Laplace transform of $\exp\{u_{l(i)} + a_i + e_i\}$, only depends on $\sigma_u^2 + \sigma_a^2 + \sigma_e^2$. It follows that β , $\sigma_u^2 + \sigma_a^2 + \sigma_e^2$ and $\Lambda_0(\cdot)$ can be identified using exactly the same idea as for Cox frailty models (without an extra random effect). With $\Lambda_0(t)$ known, then the model specified in (18) is equivalent to a linear model for $Y_i = \log(\Lambda_0(T_i))$. The model for Y_i is given by

$$Y_{i} = \log \left(\Lambda_{0} \left(T_{i} \right) \right) = -x_{i}\beta - u_{l(i)} - a_{i} - e_{i} + \varepsilon_{i}$$

where ε_i follows an extreme value distribution; all of the $\varepsilon'_i s$ are independent and independent of **u**, **a** and **e**. Thus, under assumption A2, it follows that σ_u^2 , σ_a^2 and σ_e^2 can be identified.

Conditions A1 and A2 are necessary for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$:

and

Condition A1: For Cox frailty models, specified by (18), necessity of condition A1 can be established proceeding as for Cox frailty models without an extra random effect.

Conditions A2: Assume that $rank(\mathbf{M}) < 3$, then there exist a vector $(\alpha_1, \alpha_2, \alpha_3) \neq (0, 0, 0)$ such that

$$1 \{ l(i) = l(j) \} \alpha_1 + A_{ij}\alpha_2 + 1 \{ i = j \} \alpha_3 = 0 \ \forall i, j$$

Next define $(\sigma_u^2, \sigma_a^2, \sigma_e^2) = (\sigma_u^2, \sigma_a^2, \sigma_e^2) + \frac{1}{k} (\alpha_1, \alpha_2, \alpha_3)$, where the constant $k \neq 0$ is chosen so that $\sigma_u^2 > 0$, $\sigma_a^2 > 0$ and $\sigma_e^2 > 0$, and consider the model specified by:

$$\overline{\lambda}_{i}\left(t|\overline{u}_{l(i)},\overline{\eta}_{i}\right) = \lambda_{0}\left(t\right)\exp\left\{x_{i}\beta + \overline{u}_{l(i)} + \overline{\eta}_{i}\right\}$$
(19)

for i = 1, ..., n, where $\overline{\mathbf{u}} \sim N_q \left(\mathbf{0}, \mathbf{I}_q \sigma_{\overline{u}}^2 \right), \overline{\eta}_i = \overline{a}_i + \overline{e}_i$ with $\overline{\mathbf{a}} \sim N_n \left(\mathbf{0}, \mathbf{A} \sigma_{\overline{a}}^2 \right)$ and $\overline{\mathbf{e}} \sim N_n \left(\mathbf{0}, \mathbf{I}_n \sigma_{\overline{e}}^2 \right)$; $\overline{\mathbf{u}}$, $\overline{\mathbf{a}}$ and $\overline{\mathbf{e}}$ are assumed to be independent. Equivalence of the models specified by (18) and (19), follows from

$$Cov (u_{l(i)} + \eta_i, u_{l(j)} + \eta_j)$$

$$= 1 \{l (i) = l (j)\} \sigma_u^2 + A_{ij}\sigma_a^2 + 1 \{i = j\} \sigma_e^2$$

$$= 1 \{l (i) = l (j)\} \sigma_u^2 + A_{ij}\sigma_a^2 + 1 \{i = j\} \sigma_e^2$$

$$+ \frac{1}{k} (1 \{l (i) = l (j)\} \alpha_1 + A_{ij}\alpha_2 + 1 \{i = j\} \alpha_3)$$

$$= Cov (\overline{u}_{l(i)} + \overline{\eta}_i, \overline{u}_{l(j)} + \overline{\eta}_j) \forall i, j$$

Second for $rank(\mathbf{C}) = 0$:

Condition A2 is sufficient for identification of the parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2)$: The proof is by contradiction and proceed as for Cox frailty models (without the extra random effect): Assume that two different sets of parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2) \neq (\overline{\Lambda}_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2)$ lead to equivalent models. Then $S_i(t) = L(\Lambda_0(t)) = \overline{L}(\overline{\Lambda}_0(t))$, where $L(\overline{L})$ is the Laplace transform of $\exp\{u_{l(i)} + a_i + e_i\}$ ($\exp\{\overline{u}_{l(i)} + \overline{a}_i + \overline{e}_i\}$). This implies $\overline{\Lambda}_0(t) = \overline{L}^{-1}L(\Lambda_0(t))$. Note that $L(\overline{L})$ only depends on $\sigma_u^2 + \sigma_a^2 + \sigma_e^2(\sigma_u^2 + \sigma_a^2 + \sigma_e^2)$. Next for $i \neq j$ consider

$$\begin{split} S_{i,j}\left(s,t\right) &= L_{\exp\left\{u_{l\left(i\right)}+a_{i}+e_{i}\right\},\exp\left\{u_{l\left(j\right)}+a_{j}+e_{j}\right\}}\left(\Lambda_{0}\left(s\right),\Lambda_{0}\left(t\right)\right) \\ &= L_{\exp\left\{\overline{u}_{l\left(i\right)}+\overline{a}_{i}+\overline{e}_{i}\right\},\exp\left\{\overline{u}_{l\left(j\right)}+\overline{a}_{j}+\overline{e}_{j}\right\}}\left(\overline{\Lambda}_{0}\left(s\right),\overline{\Lambda}_{0}\left(t\right)\right) \end{split}$$

Differentiation of both expressions for $S_{i,j}(t,t)$ twice with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$; and differentiation of both expressions for $S_{i,j}(t,t)$ three times with respect to $\Lambda_0(t)$, equating and evaluating for $\Lambda_0(t) = 0$ gives a set of equations From these equations, and under condition A2, it follows that $\sigma_u^2 = \sigma_u^2$, $\sigma_a^2 = \sigma_a^2$, $\sigma_e^2 = \sigma_e^2$ and further that $\overline{\Lambda}_0(\cdot) = \Lambda_0(\cdot)$, which gives a contradiction.

Condition A2 is necessary for identification of parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2)$: Necessity of condition A2 is established (with obvious modifications) as for rank (C) ≥ 1 . Q.E.D. **Example 20** Consider three animals, 1, 2 and 3. 1 and 2 are halfsibs and 3 is unrelated to 1 and 2. In this case $(\sigma_u^2, \sigma_a^2, \sigma_e^2)$ can be identified if **M** is equal to either

| (| 1 | 1 | 1 | | $\begin{pmatrix} 1 \end{pmatrix}$ | 1 | 1 | Ϊ |
|---|---|---------------|-----|----|-----------------------------------|---------------|---|---|
| | 0 | $\frac{1}{4}$ | 0 | | 0 | $\frac{1}{4}$ | 0 | |
| | 1 | Ō | 0 | | 0 | Ō | 0 | |
| | 0 | $\frac{1}{4}$ | 0 | | 0 | $\frac{1}{4}$ | 0 | |
| | 1 | 1 | 1 | or | 1 | ĺ | 1 | |
| | 0 | 0 | 0 | | 1 | 0 | 0 | |
| | 1 | 0 | 0 | | 0 | 0 | 0 | |
| | 0 | 0 | 0 | | 1 | 0 | 0 | |
| L | 1 | 1 | 1 / | | 1 | 1 | 1 |] |

(The rows corresponds to (i, j) equal to (1, 1), (1, 2), (1, 3), (2, 1), (2, 2), (2, 3), (3, 1), (3, 2) and (3, 3) respectively). In both cases the two half sibs, 1 and 2, are in different herds (if **u** is a vector of herd effects), and animal 3 is in the same herd as either animal 1 or 2.

6.3.2 Sire model

Consider the Cox, log normal sire frailty model for survival times $(\widetilde{T}_i)_{i=1,...,n}$, where the hazard function for \widetilde{T}_i , conditional on $\widetilde{u}_{l(i)}$ and $\widetilde{\eta}_i$ is given by

$$\widetilde{\lambda}_{i}\left(t|\widetilde{u}_{l(i)},\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{0}\left(t\right)\exp\left\{x_{i}\widetilde{\beta} + \widetilde{u}_{l(i)} + \widetilde{\eta}_{i}\right\}$$
(20)

for $l(i) \in \{1, ..., q\}$. $\tilde{\lambda}_0(t)$, $\tilde{\eta}_i$, $\tilde{\mathbf{s}}$ and $\tilde{\mathbf{e}}$ are as before (as for Cox, log normal sire frailty models specified by (15)) and $\tilde{\mathbf{u}} \sim N_q \left(\mathbf{0}, \mathbf{I}_q \sigma_{\tilde{u}}^2\right)$. Furthermore $\tilde{\mathbf{u}}, \tilde{\mathbf{s}}$ and $\tilde{\mathbf{e}}$ are assumed to be independent, and conditional on $(\tilde{u}_{l(i)} + \tilde{\eta}_i)_{i=1,...,n}$, then all of the $\tilde{T}'_i s$ are assumed to be independent.

Theorem 21 In the model specified by (20), the parameters $(\widetilde{\Lambda}_0(\cdot), \widetilde{\beta}, \sigma_{\widetilde{u}}^2, \sigma_{\widetilde{a}}^2, \sigma_{\widetilde{e}}^2)$, where $0 < \sigma_{\widetilde{u}}^2, \sigma_{\widetilde{e}}^2, \sigma_{\widetilde{e}}^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) The matrix **M** has rank 3, where **M** is the $n^2 \times 3$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2, 3; $M_{(i,j),1} = 1 \{l(i) = l(j)\}, M_{(i,j),2} = 1 \{g(i) = g(j)\}$ and $M_{(i,j),3} = 1 \{i = j\}.$

Proof: The proof is similar to the proof of Theorem 19.

6.3.3 Equivalence of sire and animal models

Next we have the following result concerning conditions under which the Cox log normal sire frailty model is consistent with assumptions of the additive genetic infinitesimal model.

Theorem 22 For a parameterised Cox, log normal sire frailty model given by (20), there exists an equivalent parameterised animal model (with A a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{c}}^2$.

The equivalent animal model is determined by $\beta = \tilde{\beta}$, $\sigma_u^2 + \sigma_a^2 + \sigma_e^2 = \sigma_{\tilde{u}}^2 + \sigma_s^2 + \sigma_{\tilde{e}}^2$, $\sigma_u^2 = \sigma_{\tilde{u}}^2$, $\sigma_a^2 = 4\sigma_s^2$ and $\Lambda_0(\cdot) = \tilde{\Lambda}_0(\cdot)$.

Proof: Having in mind the proofs of Theorem 19 and Theorem 18, then the proof is straightforward. Q.E.D.

6.4 Time-dependent covariates - fixed effects

6.4.1 Animal model

Now consider the Cox, log normal animal frailty model with time-dependent covariates. The effects associated with the time-dependent covariates are assumed to be fixed, and the time-dependent covariates to be left continuous and piecewise constant. The hazard function for survival time T_i is, conditional on random effect η_i , given by

$$\lambda_i \left(t | \eta_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_{i1} \beta + x_{i2} \left(t \right) \gamma + \eta_i \right\}$$
(21)

for i = 1, ..., n; where $\lambda_0(t)$, the baseline hazard function, and $\eta_i = a_i + e_i$ are given as before, and conditional on η , then all of the T'_is are assumed to be independent. The dimension of β is p and the dimension of γ is q. We will assume that $q \ge 1$, otherwise the model is dealt with earlier.

Notation 23 We introduce the following partitioning of R_+ defined by jumps in the covariate processes $(x_{i2}(\cdot))_{i=1,...,n}$: $R_+ = \bigcup_{m_0=1}^{P_0} (l_{m_0}, r_{m_0}]$, with $1 \leq P_0 \leq \infty$; the subsets are disjoint (but not necessarily ordered in the sense that $r_{m_0} = l_{m_0+1}$ for $m_0 = 1, ..., P_0 - 1$). Next we consider the set of those intervals (in the above mentioned partitioning of R_+) with $S_i(l_{m_0}) - S_i(r_{m_0}) > 0$. If $S_i(l_{m_0}) - S_i(r_{m_0}) > 0$ for some $i \in \{1, ..., n\}$ then $S_i(l_{m_0}) - S_i(r_{m_0}) > 0$ for all $i \in \{1, ..., n\}$. We let

$$\bigcup_{m=1}^{P} (l_m, r_m] = \{ (l_{m_0}, r_{m_0}], m_0 = 1, \dots, P_0 : S_i (l_{m_0}) - S_i (r_{m_0}) > 0 \}$$

where $1 \leq P \leq P_0$.

Theorem 24 In the model specified by (21), the parameters $(\Lambda_0(\cdot), \beta, \gamma, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The matrix \mathbf{C} with rows

$$(x_{i1} - x_{j1}, x_{i2} (r_m) - x_{j2} (r_m))$$

i, j = 1, ..., n, m = 1, ..., P, has full rank.

A2) The matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2; $M_{(i,j),1} = A_{ij}$ and $M_{(i,j)2} = 1$ {i = j }.

Proof: Conditions A1 and A2 are sufficient for identification of the parameters $(\Lambda_0(.), \beta, \gamma, \sigma_a^2, \sigma_e^2)$: In the model specified by (21), we have

$$\Lambda_{i}(t|\eta_{i}) = \exp\left\{x_{i1}\beta + \eta_{i}\right\} \int_{0}^{t} \lambda_{0}(s) \exp\left\{x_{i2}(s)\gamma\right\} ds$$

 $S_i(t|\eta_i) = \exp\left\{-\Lambda_i(t|\eta_i)\right\}$ and

$$S_{i}(t) = L\left(\exp\left\{x_{i1}\beta\right\}\int_{0}^{t}\lambda_{0}(s)\exp\left\{x_{i2}(s)\gamma\right\}ds\right)$$

where $L = L_{e^{\eta_i}}$ is the Laplace transform of exp $\{\eta_i\}$. Therefore, for $t \in (l_m, r_m]$, the conditional survival function of T_i given the random effect, η_i , and $T_i > l_m$, is:

$$S_{i}(t|\eta_{i}, T_{i} > l_{m}) = \exp\{-\exp\{x_{i1}\beta + x_{i2}(r_{m})\gamma + \eta_{i}\}(\Lambda_{0}(t) - \Lambda_{0}(l_{m}))\}$$

m = 1, ..., P. The conditional survival function of T_i given $T_i > l_m$, is for $t \in (l_m, r_m]$:

$$S_{i}(t|T_{i} > l_{m}) = \int_{-\infty}^{\infty} S_{i}(t|\eta_{i}, T_{i} > l_{m}) p(\eta_{i}) d\eta_{i}$$
(22)
= $L(\exp\{x_{i1}\beta + x_{i2}(r_{m})\gamma\}(\Lambda_{0}(t) - \Lambda_{0}(l_{m})))$

Identifiability of (β, γ) : For $t \in (l_m, r_m]$ (all of the covariate processes of the different animals are constant in this interval), we find, using a first order Taylor series expansion of $L(\cdot)$ around zero, that

$$1 - S_{i} (t|T_{i} > l_{m})$$

$$= 1 - L (\exp \{x_{i1}\beta + x_{i2} (r_{m})\gamma\} (\Lambda_{0} (t) - \Lambda_{0} (l_{m})))$$

$$= -L' (0) \exp \{x_{i1}\beta + x_{i2} (r_{m})\gamma\} (\Lambda_{0} (t) - \Lambda_{0} (l_{m}))$$

$$+ o (\exp \{x_{i1}\beta + x_{i2} (r_{m})\gamma\} (\Lambda_{0} (t) - \Lambda_{0} (l_{m})))$$

$$= \exp \{\frac{1}{2}\sigma_{\eta}^{2}\} \exp \{x_{i1}\beta + x_{i2} (r_{m})\gamma\} (\Lambda_{0} (t) - \Lambda_{0} (l_{m}))$$

$$+ o ((\Lambda_{0} (t) - \Lambda_{0} (l_{m})))$$

so that

$$\frac{1 - S_i(t|T_i > l_m)}{1 - S_j(t|T_j > l_m)} \to \exp\{(x_{i1} - x_{j1})\beta + (x_{i2}(r_m) - x_{j2}(r_m))\gamma\}$$

for $t \downarrow \inf\{u : \Lambda_0(t) - \Lambda_0(l_m) > 0\}$

where $\inf \{u : \Lambda_0(t) - \Lambda_0(l_m) > 0\} = \inf \{u : S_i(u|T_k > l_m) < 1\}$ for k = 1, ..., n. Under assumption A1, it follows that (β, γ) is identified.

Intermediate step that leads to identification of $\exp\left\{\frac{1}{2}\sigma_{\eta}^{2}\right\}L^{-1}(x)$: For notational convenience and for $t \in [l_{m}, \infty)$, we let $S_{i}^{m}(t) = S_{i}(t|T_{i} > l_{m})$. Having

identified (β, γ) , then we consider an interval $(l_m, r_m]$, where for two animals, i and j, we have

$$x = \exp \left\{ (x_{j1} - x_{i1}) \beta + (x_{j2} (r_m) - x_{i2} (r_m)) \gamma \right\} > 1$$

C

For $x \in (S_i^m(r_m), S_i^m(l_m)] = (S_i^m(r_m), 1]$ we let $(S_i^m)^{-1}(x)$ be a generalised inverse of $S_i^m(t)$. Now define $\Lambda_0^m(t) = \Lambda_0(t) - \Lambda_0(l_m)$, then for $t \in (l_m, r_m]$ we have

$$S_{i}^{m}(t) = L\left(\exp\left\{x_{i1}\beta + x_{i2}(r_{m})\gamma\right\}\Lambda_{0}^{m}(t)\right)$$

and $(\Lambda_0^m)^{-1}(t)$ defined by $(S_i^m)^{-1}(L(\exp\{x_{i1}\beta + x_{i2}(r_m)\gamma\}t))$ is a generalised inverse of $\Lambda_0^m(\cdot)$ for $t \in [0, \exp\{-(x_{i1}\beta + x_{i2}(r_m)\gamma)\}L^{-1}S_i^m(r_m))$ and $(S_i^m)^{-1}(x) = (\Lambda_0^m)^{-1}(\exp\{-\{x_{i1}\beta + x_{i2}(r_m)\gamma\}\}L^{-1}(x))$. Next, for $x \in (S_i^m(r_m), 1]$, consider $1 - (S_i^m(S_j^m)^{-1})^n(x) = 1 - L(c^{-n}L^{-1}(x))$ and identify $\exp\{\frac{1}{2}\sigma_\eta^2\}L^{-1}(x)$ (using exactly the same procedure as for Cox frailty models).

Identifiability of σ_{η}^2 and L: Differentiating $\exp\left\{\frac{1}{2}\sigma_{\eta}^2\right\}L^{-1}(x)$ twice w.r.t. x and evaluating for x = 1 gives $\exp\left\{\sigma_{\eta}^2\right\}$. Hereby $\exp\left\{\sigma_{\eta}^2\right\}$ is identified and therefore also L, which only depends on σ_{η}^2 .

Identifiability of $\Lambda_0(t) - \Lambda_0(l_m)$ for $t \in (l_m, r_m]$, m = 1, ..., P: For $t \in (l_m, r_m]$, it follows from (22) that

$$\Lambda_0(t) - \Lambda_0(l_m) = \exp\{-[x_{i1}\beta + x_{i2}(r_m)\gamma]\}L^{-1}(S_i^m(t))$$

Identifiability of σ_a^2 and σ_e^2 : With $\Lambda_0(t)$ and γ known, then the model specified in (21) is equivalent to a linear model for $Y_i = \log(h_i(T_i))$ (on the $\log h_i(\cdot)$ -scale), where $h_i(t) = \int_0^t \lambda_0(s) \exp\{x_{i2}(s)\gamma\} ds$. Note that the scale is specific for each animal (or for groups of animals with the same time-dependent covariates). The model for Y_i is given by

$$Y_{i} = \log \left(h_{i}\left(T_{i}\right)\right) = -x_{i1}\beta - a_{i} - e_{i} + \varepsilon_{i}$$

where ε_i follows an extreme value distribution; all of the $\varepsilon'_i s$ are independent and independent of **a** and **e**. Thus, under assumption A2, σ_a^2 and σ_e^2 can be identified.

Conditions A1 and A2 are necessary for identification of the parameters $(\Lambda_0(\cdot), \beta, \gamma, \sigma_a^2, \sigma_e^2)$: Condition A1: Assume that condition A1 is not fulfilled, then there exist a vector $(\alpha'_1, \alpha'_2) = (\alpha_{11}, ..., \alpha_{1p}, \alpha_{21}, ..., \alpha_{2q}) \neq (0, ..., 0)$ with $(x_{i1} - x_{j1}) \alpha_1 + (x_{i2} (r_m) - x_{j2} (r_m)) \alpha_2 = 0$ for all i, j = 1, ..., n, m = 1, ..., P, so that for fixed j:

$$\begin{aligned} \lambda_{i} (t|\eta_{i}) &= \lambda_{0} (t) \exp \{ x_{i1}\beta + x_{i2} (t) \gamma + \eta_{i} \} \\ &= \lambda_{0} (t) \exp \{ -x_{j1}\alpha_{1} - x_{j2} (t) \alpha_{2} \} \\ &\times \exp \{ x_{i1} (\beta + \alpha_{1}) + x_{i2} (t) (\gamma + \alpha_{2}) + \eta_{i} \} \end{aligned}$$

This implies that (at least) two different sets of parameters, $(\Lambda_0(\cdot), \beta, \gamma, \sigma_a^2, \sigma_e^2)$ and $(\overline{\Lambda}_0(\cdot), (\beta + \alpha_1), (\gamma + \alpha_2), \sigma_a^2, \sigma_e^2)$, with

$$\overline{\Lambda}_{0}(\cdot) = \int_{0}^{t} \lambda_{0}(s) \exp\left\{-x_{j1}\alpha_{1} - x_{j2}(s)\alpha_{2}\right\} ds$$

give equivalent models, i.e. nonidentifiability of parameters.

Condition A2: Necessity of condition A2 can be established proceeding as for Cox frailty models. Q.E.D.

6.4.2 Sire model

In the Cox log normal size frailty model with time-dependent covariates - with associated fixed effects, the hazard function of survival time \tilde{T}_i is, conditional on random effect, $\tilde{\eta}_i$, given by

$$\widetilde{\lambda}_{i}\left(t|\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{0}\left(t\right)\exp\left\{x_{i1}\widetilde{\beta} + x_{i2}\left(t\right)\widetilde{\gamma} + \widetilde{\eta}_{i}\right\}$$
(23)

for i = 1, ..., n. $\tilde{\lambda}_0$ (·), the baseline hazard function and $\tilde{\eta}_i = s_{g(i)} + \tilde{e}_i$ are given as described earlier, and conditional on $\tilde{\eta}$, then all of the $\tilde{T}'_i s$ are assumed to be independent. The dimension of $\tilde{\beta}$ is p and the dimension of $\tilde{\gamma}$ is q.

Theorem 25 In the model specified by (23), the parameters $(\widetilde{\Lambda}_0(\cdot), \widetilde{\beta}, \widetilde{\gamma}, \sigma_s^2, \sigma_{\tilde{e}}^2)$, where $0 < \sigma_s^2, \sigma_{\tilde{e}}^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The matrix \mathbf{C} with rows

$$(x_{i1} - x_{j1}, x_{i2} (r_m) - x_{j2} (r_m)),$$

i, j = 1, ..., n, m = 1, ..., P, has full rank.

A2) The matrix **M** has rank 2, where **M** is the $n^2 \times 2$ dimensional matrix with entries $M_{(i,j),k}$, i, j = 1, ..., n and k = 1, 2; $M_{(i,j),1} = 1 \{g(i) = g(j)\}$ and $M_{(i,j),2} = 1 \{i = j\}$.

Proof: The proof is similar to the proof of Theorem 24.

6.4.3 Equivalence of sire and animal models

Furthermore, we have the following result about equivalence of sire and animal models:

Theorem 26 For a parameterised Cox, log normal sire frailty model given by (23), there exists an equivalent parameterised animal model (with A a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\sigma_{\tilde{e}}^2$.

The equivalent animal model is determined by $\beta = \tilde{\beta}$, $\gamma = \tilde{\gamma}$, $\sigma_a^2 + \sigma_e^2 = \sigma_s^2 + \sigma_{\tilde{\epsilon}}^2$, $\sigma_a^2 = 4\sigma_s^2$ and $\Lambda_0(\cdot) = \tilde{\Lambda}_0(\cdot)$.

Proof: Having in mind the proof of identifiability of parameters in the Cox log normal animal frailty model, with time-dependent covariates (with associated fixed effects) (Theorem 24) and the proof of Theorem 18, then the proof of this Theorem is straightforward.

6.5 Time-dependent covariates - random effects

6.5.1 Animal model

Now consider the Cox log normal animal frailty model with time-dependent covariates. This time the effects, \mathbf{u} , associated with the time-dependent covariates are assumed to be random. The hazard function for survival time T_i is, conditional on random effects, \mathbf{u} and η_i , given by

$$\lambda_i \left(t | \mathbf{u}, \eta_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i \beta + z_i \left(t \right) \mathbf{u} + \eta_i \right\}$$
(24)

i = 1, ..., n; where $\lambda_0(t)$ is the baseline hazard function, and $\mathbf{u} \sim N_q(\mathbf{0}, \mathbf{I}_q \sigma_u^2)$; **a** and **e** are given as before. Furthermore \mathbf{u} , **a** and **e** are assumed to be independent, and conditional on η , then all of the T'_i s are assumed to be independent. The time-dependent covariate, $z_i(t)$, is assumed to be left continuous and piecewise constant, and is, for $t \in [0, \infty)$, assumed to be a vector with exactly one element $z_{il'}(t) = 1$, and $z_{il}(t) = 0$ for $l \neq l'$. In this model

$$\Lambda_{i}\left(t|\mathbf{u},\eta_{i}\right) = \exp\left\{x_{i}\beta + \eta_{i}\right\} \int_{0}^{t} \lambda_{0}\left(s\right) \exp\left\{z_{i}\left(s\right)\mathbf{u}\right\} ds$$

and

$$S_{i}(t) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \cdots \int_{-\infty}^{\infty} \exp\left\{-\Lambda_{i}(t|\mathbf{u},\eta_{i})\right\} p(\mathbf{u}) p(\eta_{i}) d\mathbf{u} d\eta_{i}$$

Notation 27 This time we consider disjoint subsets of R_+ defined and indexed exactly as in the previous section, except that now the partitioning is defined by jumps in the covariate processes $(z_i(\cdot))_{i=1,...,n}$.

Theorem 28 In the model specified by (24), the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$, where $0 < \sigma_u^2, \sigma_a^2, \sigma_e^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) The matrix **M** with rows $(z_i (r_{m_1}) z_j (r_{m_2})', A_{ij}, 1 \{i = j\}), m_1, m_2 = 1, ..., P, i, j = 1, ..., n, has rank 3.$

Proof: The Theorem is proved for $rank(\mathbf{C}) \ge 1$ and $rank(\mathbf{C}) = 0$, separately. First for $rank(\mathbf{C}) \ge 1$:

Conditions A1 and A2 are sufficient for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$: In the model specified by (24), we have for $t \in (l_m, r_m]$:

$$\Lambda_{i}(t|\mathbf{u},\eta_{i}) = \exp \{x_{i}\beta + \eta_{i}\} \sum_{\substack{m_{1}=1\\m_{1}:r_{m_{1}} \leq t}}^{P} \exp \{z_{i}(r_{m_{1}})\,\mathbf{u}\} (\Lambda_{0}(r_{m_{1}}) - \Lambda_{0}(l_{m_{1}})) + \exp \{x_{i}\beta + \eta_{i}\} \exp \{z_{i}(r_{m})\,\mathbf{u}\} (\Lambda_{0}(t) - \Lambda_{0}(l_{m}))$$

and

$$S_{i}\left(t|\mathbf{u},\eta_{i},T_{i}>l_{m}\right)=\exp\left\{-\exp\left\{x_{i}\beta+z_{i}\left(r_{m}\right)\mathbf{u}+\eta_{i}\right\}\left(\Lambda_{0}\left(t\right)-\Lambda_{0}\left(l_{m}\right)\right)\right\}$$

so that

$$S_{i}(t|T_{i} > l_{m}) = L_{\exp\{z_{i}(r_{m})\mathbf{u}+\eta_{i}\}}\left(\exp\left\{x_{i}\beta\right\}\left(\Lambda_{0}(t) - \Lambda_{0}(l_{m})\right)\right)$$

For notational convenience we let $L = L_{\exp\{z_i(r_m)\mathbf{u}+\eta_i\}}$ and notice that L only depends on $\sigma_u^2 + \sigma_\eta^2$. Furthermore, we let $S_i^m(t) = S_i(t|T_i > l_m)$.

Identifiability of β : For $t \in (l_m, r_m]$ we find, (because exp $\{z_i(r_m) \mathbf{u} + \eta_i\}$, i = 1, ..., n are identically distributed and using exactly the same procedure as in the proof of Theorem 24) that

$$\frac{1 - S_i^m(t)}{1 - S_i^m(t)} \to \frac{\exp\left\{x_i\beta\right\}}{\exp\left\{x_j\beta\right\}} = \exp\left\{\left(x_i - x_j\right)\beta\right\}$$

for $t \downarrow \inf \{u : \Lambda_0(u) - \Lambda_0(l_m) > 0\}$, where $\inf \{u : \Lambda_0(u) - \Lambda_0(l_m) > 0\} = \inf \{u : S_k^m(u) < 1\}$ for k = 1, ..., n. Under assumption A1, it follows (as before) that β is identifiable.

Identifiability of $\sigma_u^2 + \sigma_\eta^2$, L and $\Lambda_0(t) - \Lambda_0(l_m)$ for $t \in (l_m, r_m]$, m = 1, ..., P: Next it follows that $\exp\left\{\frac{1}{2}\left(\sigma_u^2 + \sigma_\eta^2\right)\right\}L^{-1}(x)$ can be identified for $x \in (S_i^m(r_m), 1]$. Differentiating $\exp\left\{\frac{1}{2}\left(\sigma_u^2 + \sigma_\eta^2\right)\right\}L^{-1}(x)$ twice w.r.t. x and evaluating for x = 1 gives $\exp\left\{\frac{1}{2}\left(\sigma_u^2 + \sigma_\eta^2\right)\right\}$. Hereby $\sigma_u^2 + \sigma_\eta^2$ is identified and therefore also L, which only depends on $\sigma_u^2 + \sigma_\eta^2$. It follows that $\Lambda_0(t) - \Lambda_0(l_m) = \exp\left\{-x_i\beta\right\}L^{-1}(S_i^m(t))$ for $t \in (l_m, r_m]$.

 $\begin{array}{l} \exp\left\{-x_{i}\beta\right\}L^{-1}\left(S_{i}^{m}\left(t\right)\right) \text{ for } t \in \left(l_{m}, r_{m}\right]. \\ Identifiability \text{ of } \sigma_{u}^{2}, \sigma_{a}^{2} \text{ and } \sigma_{e}^{2} \text{ : The joint survival function of } \left(T_{i}, T_{j}\right) \text{ conditional on } \left(\mathbf{u}, \eta_{i}, \eta_{j}\right) \text{ and on } \left(T_{i} > l_{m_{1}}, T_{j} > l_{m_{2}}\right) \text{ is for } (s, t) \in \left(l_{m_{1}}, r_{m_{1}}\right] \times \left(l_{m_{2}}, r_{m_{2}}\right] \text{ given by} \end{array}$

$$S_{i,j} (s, t | \mathbf{u}, \eta_i, \eta_j, T_i > l_{m_1}, T_j > l_{m_2})$$

= exp { - exp { $x_i\beta + z_i (r_{m_1}) \mathbf{u} + \eta_i$ } ($\Lambda_0 (s) - \Lambda_0 (l_{m_1})$)}
× exp { - exp { $x_j\beta + z_j (r_{m_2}) \mathbf{u} + \eta_j$ } ($\Lambda_0 (t) - \Lambda_0 (l_{m_2})$)}

It follows that

$$S_{i,j} (s, t | T_i > l_{m_1}, T_j > l_{m_2})$$

= $L (\exp \{x_i\beta\} (\Lambda_0 (s) - \Lambda_0 (l_{m_1})), \exp \{x_j\beta\} (\Lambda_0 (t) - \Lambda_0 (l_{m_2})))$

where L is the bivariate Laplace transform of

$$\left(\exp\left\{z_{i}\left(r_{m_{1}}\right)\mathbf{u}+\eta_{i}\right\},\exp\left\{z_{j}\left(r_{m_{2}}\right)\mathbf{u}+\eta_{j}\right\}\right)$$

Let $\tilde{s} = \exp \{x_i\beta\}$ $(\Lambda_0(s) - \Lambda_0(l_{m_1}))$ and $\tilde{t} = \exp \{x_j\beta\}$ $(\Lambda_0(t) - \Lambda_0(l_{m_2}))$. By differentiation of $L(\tilde{s}, \tilde{t})$ with respect to \tilde{s}, \tilde{t} and both of \tilde{s} and \tilde{t} , evaluating for $(\tilde{s}, \tilde{t}) = (0, 0)$, and using that

$$\frac{\frac{\partial^2 L(0,0)}{\partial \tilde{t} \partial \tilde{s}}}{\frac{\partial L(0,0)}{\partial \tilde{s}} \frac{\partial L(0,0)}{\partial \tilde{t}}} = \exp\left\{Cov\left(z_i\left(r_{m_1}\right)\mathbf{u} + \eta_i, z_j\left(r_{m_2}\right)\mathbf{u} + \eta_j\right)\right\}$$

then we get

$$\frac{\frac{\partial^2 L(0,0)}{\partial t\partial \tilde{s}}}{\frac{\partial L(0,0)}{\partial \tilde{s}}} = \exp\left\{z_i\left(r_{m_1}\right)z_j\left(r_{m_2}\right)'\sigma_u^2 + A_{ij}\sigma_a^2 + 1\left\{i=j\right\}\sigma_e^2\right\}$$

It follows that $(\sigma_u^2, \sigma_a^2, \sigma_e^2)$ are identifiable, provided that assumption A2 is satisfied.

Conditions A1 and A2 are necessary for identification of the parameters $(\Lambda_0(\cdot), \beta, \sigma_u^2, \sigma_a^2, \sigma_e^2)$:

Condition A1: Necessity of condition A1 can be established proceeding as for Cox frailty models specified by (12).

Condition A2: Assume that $rank(\mathbf{M}) < 3$, then there exist a vector $(\alpha_1, \alpha_2, \alpha_3) \neq (0, 0, 0)$ such that

$$(z_i (r_{m_1}) z_j (r_{m_2})') \alpha_1 + A_{ij} \alpha_2 + 1 \{i = j\} \alpha_3 = 0$$

for $i, j = 1, ..., n, m_1, m_2 = 1, ..., P$. Next define $\left(\sigma_u^2, \sigma_a^2, \sigma_e^2\right) = \left(\sigma_u^2, \sigma_a^2, \sigma_e^2\right) + \frac{1}{k}\left(\alpha_1, \alpha_2, \alpha_3\right)$, where the constant $k \neq 0$ is chosen so that $\sigma_u^2 > 0, \sigma_a^2 > 0$ and $\sigma_e^2 > 0$, and consider the model specified by:

$$\overline{\lambda}_i \left(t | \overline{\mathbf{u}}, \overline{\eta}_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i \beta + z_i \left(t \right) \overline{\mathbf{u}} + \overline{\eta}_i \right\}$$
(25)

for i = 1, ..., n, where $\overline{\mathbf{u}} \sim N_q \left(\mathbf{0}, \mathbf{I}_q \sigma_{\overline{u}}^2 \right), \overline{\eta}_i = \overline{a}_i + \overline{e}_i$ with $\overline{\mathbf{a}} \sim N_n \left(\mathbf{0}, \mathbf{A} \sigma_{\overline{a}}^2 \right)$ and $\overline{\mathbf{e}} \sim N_n \left(\mathbf{0}, \mathbf{I}_n \sigma_{\overline{e}}^2 \right)$; $\overline{\mathbf{u}}$, $\overline{\mathbf{a}}$ and $\overline{\mathbf{e}}$ are assumed to be independent. Equivalence of the models specified by (24) and (25), follows from

$$Cov (z_i (t) \mathbf{u} + \eta_i, z_j (t) \mathbf{u} + \eta_j)$$

$$= z_i (t) z_j (t)' \sigma_u^2 + A_{ij} \sigma_a^2 + 1 \{i = j\} \sigma_e^2$$

$$= z_i (t) z_j (t)' \sigma_u^2 + A_{ij} \sigma_a^2 + 1 \{i = j\} \sigma_e^2$$

$$+ \frac{1}{k} (z_i (t) z_j (t)' \alpha_1 + A_{ij} \alpha_2 + 1 \{i = j\} \alpha_3)$$

$$= Cov (z_i (t) \overline{\mathbf{u}} + \overline{\eta}_i, z_j (t) \overline{\mathbf{u}} + \overline{\eta}_j) \quad \forall i, j$$

- and a contradiction is established.

Second for $rank(\mathbf{C}) = 0$:

Condition A2 is sufficient for identification of the parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2)$: The proof is by contradiction: Assume that two different sets of parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2) \neq (\overline{\Lambda_0}(\cdot), \sigma_{\overline{u}}^2, \sigma_{\overline{e}}^2, \sigma_{\overline{e}}^2)$ lead to equivalent models. Then, for $t \in (l_m, r_m], S_i^m(t) = L(\Lambda_0(t) - \Lambda_0(l_m)) = \overline{L}(\overline{\Lambda_0}(t) - \overline{\Lambda_0}(l_m))$, where $L(\overline{L})$ is the Laplace transform of exp $\{z_i(r_m)\mathbf{u} + a_i + e_i\}$ (exp $\{z_i(r_m)\overline{\mathbf{u}} + \overline{a}_i + \overline{e}_i\}$). This implies $\overline{\Lambda_0}(t) - \overline{\Lambda_0}(l_m) = \overline{L}^{-1}L(\Lambda_0(t) - \Lambda_0(l_m))$ for $t \in (l_m, r_m]$. Note that $L(\overline{L})$ only depends on $\sigma_u^2 + \sigma_a^2 + \sigma_e^2(\sigma_{\overline{u}}^2 + \sigma_{\overline{a}}^2 + \sigma_{\overline{e}}^2)$. Next for $i \neq j$ and for $s, t \in (l_m, r_m]$ consider

$$S_{i,i}(s,t|T_i > l_m, T_i > l_m$$

$$= L_{\exp\{z_{i}(r_{m})\mathbf{u}+a_{i}+e_{i}\},\exp\{z_{j}(r_{m})\mathbf{u}+a_{j}+e_{j}\}} (\Lambda_{0}(s) - \Lambda_{0}(l_{m}), \Lambda_{0}(t) - \Lambda_{0}(l_{m}))$$

 $= L_{\exp\{z_i(r_m)\overline{\mathbf{u}}+\overline{a}_i+\overline{e}_i\},\exp\{z_j(r_m)\overline{\mathbf{u}}+\overline{a}_j+\overline{e}_j\}} \left(\overline{\Lambda}_0(s) - \overline{\Lambda}_0(l_m), \overline{\Lambda}_0(t) - \overline{\Lambda}_0(l_m)\right)$

Differentiation of both expressions for $S_{i,j}(t,t|T_i > l_m, T_j > l_m)$ twice with respect to $\Lambda_0(t) - \Lambda_0(l_m)$, equating and evaluating for $\Lambda_0(t) - \Lambda_0(l_m) = 0$; and differentiation of both expressions for $S_{i,j}(t,t|T_i > l_m, T_j > l_m)$ three times with respect to $\Lambda_0(t) - \Lambda_0(l_m)$, equating and evaluating for $\Lambda_0(t) - \Lambda_0(l_m) = 0$ we obtain a set of equations. Solving these equations, then we obtain, under condition A2, that $\sigma_{\overline{u}}^2 = \sigma_u^2$, $\sigma_{\overline{e}}^2 = \sigma_e^2$ and further that $\overline{\Lambda_0}(\cdot) = \Lambda_0(\cdot)$. And a contradiction is established.

Condition A2 is necessary for identification of parameters $(\Lambda_0(\cdot), \sigma_u^2, \sigma_a^2, \sigma_e^2)$: Necessity of condition A2 is established (with obvious modifications) as for rank (C) ≥ 1 . Q.E.D.

Example 29 Consider 2 animals, 1 and 2, that are halfsibs. Animal 2 is born one year later than animal 1 and time is measured in days. Both animals are in the same herd. Besides time-independent fixed effects, the model has a timedependent covariate with associated random effects (e.g. a period-effect), with $z_1(t)$ and $z_2(t)$ given by

$$z_1(t) = \begin{cases} (1,0) \text{ for } t \in (0,730] \\ (0,1) \text{ for } t \in (730,\infty] \end{cases}$$

and

$$z_2(t) = \begin{cases} (1,0) \text{ for } t \in (0,365] \\ (0,1) \text{ for } t \in (365,\infty) \end{cases}$$

respectively. We will assume that $\Lambda_0(\cdot)$ is strictly increasing. Let $l_1 = 0$, $r_1 = l_2 = 365$, $r_2 = l_3 = 730$ and $r_3 = \infty$, then P = 3 and the matrix **M** in Theorem 28 is then $(9 \times 4) \times 3$ dimensional matrix given by

$$\mathbf{M} = \begin{pmatrix} \mathbf{M}^{11} \\ \mathbf{M}^{12} \\ \mathbf{M}^{13} \\ \mathbf{M}^{21} \\ \mathbf{M}^{22} \\ \mathbf{M}^{23} \\ \mathbf{M}^{31} \\ \mathbf{M}^{32} \\ \mathbf{M}^{33} \end{pmatrix}$$

where

$$\begin{split} \mathbf{M}^{11} &= \mathbf{M}^{33} = \begin{pmatrix} 1 & 1 & 1 & 1 \\ 1 & \frac{1}{4} & 0 \\ 1 & \frac{1}{4} & 0 \\ 1 & 1 & 1 \end{pmatrix}, \ \mathbf{M}^{12} = \begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & \frac{1}{4} & 0 \\ 0 & 1 & 1 \end{pmatrix}, \\ \mathbf{M}^{13} &= \mathbf{M}^{31} = \begin{pmatrix} 0 & 1 & 1 \\ 0 & \frac{1}{4} & 0 \\ 0 & 1 & 1 \end{pmatrix}, \ \mathbf{M}^{21} = \begin{pmatrix} 1 & 1 & 1 & 1 \\ 1 & \frac{1}{4} & 0 \\ 0 & \frac{1}{4} & 0 \\ 0 & 1 & 1 \end{pmatrix}, \\ \mathbf{M}^{22} &= \begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & \frac{1}{4} & 0 \\ 0 & \frac{1}{4} & 0 \\ 1 & 1 & 1 \end{pmatrix}, \ \mathbf{M}^{23} = \begin{pmatrix} 0 & 1 & 1 \\ 0 & \frac{1}{4} & 0 \\ 1 & \frac{1}{4} & 0 \\ 1 & 1 & 1 \end{pmatrix} and \ \mathbf{M}^{32} = \begin{pmatrix} 0 & 1 & 1 \\ 1 & \frac{1}{4} & 0 \\ 0 & \frac{1}{4} & 0 \\ 1 & 1 & 1 \end{pmatrix} \end{split}$$

6.5.2 Sire model

In the Cox log normal size frailty model with time-dependent covariates - with associated random effects, $\tilde{\mathbf{u}}$, the hazard function for survival time \tilde{T}_i is, conditional on $\tilde{\mathbf{u}}$ and $\tilde{\eta}_i$ given by

$$\widetilde{\lambda}_{i}\left(t|\widetilde{\mathbf{u}},\widetilde{\eta}_{i}\right) = \widetilde{\lambda}_{0}\left(t\right)\exp\left\{x_{i}\widetilde{\beta} + z_{i}\left(t\right)\widetilde{\mathbf{u}} + \widetilde{\eta}_{i}\right\}$$
(26)

for i = 1, ..., n; where $\tilde{\lambda}_0(t)$, the baseline hazard function, and $\tilde{\eta}_i = s_{g(i)} + \tilde{e}_i$ are given as described earlier; $\tilde{\mathbf{u}} \sim N_q(\mathbf{0}, \mathbf{I}_q \sigma_{\tilde{u}}^2)$. Furthermore $\tilde{\mathbf{u}}$, \mathbf{s} and $\tilde{\mathbf{e}}$ are assumed to be independent, and conditional on $(\tilde{\mathbf{u}}, \tilde{\eta})$, then all of the $\tilde{T}'_i s$ are assumed to be independent. The time-dependent covariate, $z_i(t)$, is given as described in section 6.5.1.

Theorem 30 In the model specified by (26), the parameters $(\widetilde{\Lambda}_0(\cdot), \widetilde{\beta}, \sigma_{\widetilde{u}}^2, \sigma_s^2, \sigma_{\widetilde{e}}^2)$, where $0 < \widetilde{\sigma}_u^2, \sigma_s^2, \sigma_{\widetilde{e}}^2 < \infty$, are identifiable if and only if the following conditions are satisfied:

A1) The $n^2 \times p$ dimensional matrix $\mathbf{C} = (x_i - x_j)_{i,j=1,...,n}$ (with rows $(x_i - x_j)$) has full rank.

A2) The matrix \mathbf{M} with rows

$$(z_i(r_{m_1}) z_j(r_{m_2})', 1 \{g(i) = g(j)\}, 1 \{i = j\}),$$

 $m_1, m_2 = 1, ..., P, i, j = 1, ..., n, has rank 3.$

Proof: The proof is similar to the proof of Theorem 28.

6.5.3 Equivalence of sire and animal models

Furthermore we have the following result about equivalence of sire and animal models:

Theorem 31 For a parameterised Cox, log normal sire frailty model given by (26), there exists an equivalent animal model (with **A** a block diagonal matrix given exactly as for the linear mixed model) - if and only if: $\sigma_s^2 < \frac{1}{3}\tilde{\sigma}_e^2$.

The equivalent animal model is determined by $\beta = \tilde{\beta}$, $\sigma_u^2 + \sigma_a^2 + \sigma_e^2 = \sigma_{\tilde{u}}^2 + \sigma_s^2 + \sigma_{\tilde{e}}^2$, $\sigma_u^2 = \sigma_{\tilde{u}}^2$, $\sigma_a^2 = 4\sigma_s^2$ and $\Lambda_0(\cdot) = \tilde{\Lambda}_0(\cdot)$.

Proof: Having in mind the proof of identifiability of parameters in the Cox log normal animal frailty model, with time-dependent covariates (with associated random effects) (Theorem 28) and the proof of Theorem 22, then the proof of this Theorem is straightforward.

7 Discussion and conclusion

In a series of models, namely the Gaussian mixed linear model, models for binary and ordered categorical traits using a threshold model, Poisson mixed models and survival models - necessary and sufficient conditions for identifiability of parameters has been established in sire and in animal models. All of the models considered are mixed models, where the mixture distribution (or the logarithm of the mixture distribution) is the normal distribution. Only in Gaussian mixed linear models, we have observations on the normally distributed scale. For binary and ordered categorical traits using a threshold model, the observed value is uniquely determined by a grouping on the normally distributed scale, the liability scale. In Poisson mixed models we have conditional on the outcome of the normally distributed random variable, observations from a Poisson distribution. In survival models, and conditional on random effects, then $\log(\Lambda_i(T_i|random effects))$ follows an extreme value distribution with mean $-\gamma_E$ and variance $\pi^2/6$. In the same series of models, it has been established that sire models without an error term at the normally distributed level of the model, are inconsistent with assumptions of the additive genetic infinitesimal model. Under the assumption that the normally distributed sire and error effects are independent, then σ_s^2 must be less than one third of the variance of the normally distributed error term - for the model to be equivalent to an animal model (with the normally distributed animal and error effects independent).

Having obtained these results, then it is relatively easy to see that the results generalise to e.g. sire-dam models and sire-maternal grandsire models, or other models, where only a part of the additive genetic variance is accounted for by the random effects included. Of course the condition for existence of an equivalent animal model is a bit different.

In the sire models considered, it was assumed that sires were unrelated, this assumption can be relaxed with the consequence that the **A**-matrix in the equivalent animal model has another structure.

In the discussion Foulley and Im (1993) suggested to include an error term in models for traits following a Poisson sire model (without a normally distributed error term) in order to fit the fraction (3/4) of the genetic variance that is not

explicitly accounted for in the model. Ducrocq and Casella (1996) noted that the sire model for survival data (without a normally distributed error term in log frailty) does not account for the overdispersion implicitly created by the effect representing three quarters of the total additive genetic variance. Nevertheless, in practice sire models for survival data without the error term in log frailty, have been frequently used - in the belief that they somehow were consistent with assumptions of the additive genetic infinitesimal model.

Elbers and Ridder (1982) showed identifiability of the regression function, the integrated baseline hazard, and the mixing distribution of individual frailties in frailty models with non constant regression functions. They worked under the assumption of mean one of frailty and a differentiable non constant regression function and the proof was by contradiction. Without parametric assumptions on the mixing distribution, nor on the integrated baseline hazard, then Kortram et al. (1995) were able to recover, by constructive identification, the regression function, the integrated baseline hazard and the distribution of the individual frailty term from the observed survival distribution. The assumption of a differentiable regression function was relaxed, but still the regression function was assumed to be non constant, and individual frailties were assumed to have mean one. In this paper, we have assumed multivariate normality of log individual frailties, frailties are correlated and log frailties have mean zero - we do not need the assumption on non constant regression functions.

8 References

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9 Appendix

Let T_i be the random variable representing survival time of animal *i*. In the frailty model, it is assumed that conditional on log frailty, $V_i = v_i$, (or frailty) the hazard function of animal *i*, is given by

$$\lambda_i \left(t | v_i \right) = \lambda_0 \left(t \right) \exp \left\{ x_i' \beta + v_i \right\}$$
(27)

where $\lambda_0(t)$ is a common baseline hazard function, x_i is a vector of timeindependent covariates of animal *i*, and β is the corresponding vector of regression parameters. Furthermore, conditional on $(V_i)_{i=1,...,n}$, then all of the T'_is are assumed to be independent. In the model specified by (27), the conditional integrated hazard function is

$$\Lambda_i \left(t | v_i \right) = \Lambda_0 \left(t \right) \exp \left\{ x_i' \beta + v_i \right\}$$

and the conditional survival function is

$$S_i(t|v_i) = \exp\left\{-\Lambda_i(t|v_i)\right\}$$

Because $S_i(T_i|v_i) = \exp\{-\Lambda_i(T_i|v_i)\}$ is uniformly distributed on the interval (0; 1), the transformed random variable, $Y_i = \Lambda_i(T_i|V_i)$, conditional on $V_i = v_i$, is exponentially distributed with parameter 1. In turn, ε_i , the logarithm of Y_i , given by

$$\varepsilon_i = \log\left(Y_i\right) = \log\left(\Lambda_i\left(T_i|V_i\right)\right) = \log\left(\Lambda_0\left(T_i\right)\right) + x_i'\beta + V_i \tag{28}$$

conditional on $V_i = v_i$, follows an extreme value distribution. By rearranging terms in (28) it follows, that the model in (28), is equivalent to a linear model on the log ($\Lambda_0(\cdot)$) scale:

$$\log\left(\Lambda_0\left(T_i\right)\right) = -x_i^{\prime}\beta - V_i + \varepsilon_i$$

The unconditional mean and variance of log $(\Lambda_0(T_i))$ are $-x'_i\beta - E(V_i) - \gamma_E$ and $Var(V_i) + \frac{\pi^2}{6}$, respectively, where γ_E is Euler's constant.