MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **13**, Number **1**, February **2016**

doi:10.3934/mbe.2016.13.67

pp. **67–82**

KL-OPTIMAL EXPERIMENTAL DESIGN FOR DISCRIMINATING BETWEEN TWO GROWTH MODELS APPLIED TO A BEEF FARM

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(Communicated by Yang Kuang)

Abstract. The body mass growth of organisms is usually represented in terms of what is known as ontogenetic growth models, which represent the relation of dependence between the mass of the body and time. The paper is concerned with a problem of finding an optimal experimental design for discriminating between two competing mass growth models applied to a beef farm. T-optimality was first introduced for discrimination between models but in this paper, KL-optimality based on the Kullback-Leibler distance is used to deal with correlated obsevations since, in this case, observations on a particular animal are not independent.

1. **Introduction.** The technology involved in breeding livestock has undergone a significant development, resulting in the high productivity rates of farms. In order to optimize the efficiency of beef production systems, it is of great importance to know the behaviour of weight gain in cattle throughout time. The growth of beef specialized breeds is characterized by models based on non-linear sigmoid curves. The most popular are the well-known [10], [41], [7], [35] (generalized logistic) and [21]. The shape and characteristics of these curves can vary depending on factors such as the environment, production system, type of breed and so on.

This study has been carried out in a beef farm called *Navalázaro*, located in the northwest of the region of Córdoba, Spain, and concerns a specific beef cattle breed called Limousine. The farm abides by both the European and the Spanish law related to good practices when treating animals (*Council Regulation, EC, No. 1/2005 of 22th of December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation, EC, No 1255/97 (OJ L 3 of 5.1.2005) and Spanish Royal Decree No. 692/2010 of 20th of May 2010*). Furthermore, the farm is aware of the fact that animal welfare is not only affected by veterinarian cares but also by implementing an ethical code by which animals are going to feel in a comfortable environment.

Just after weaning, which happens around six months after birth, calves are sent from the farm to the growing facility, where they remain for approximately 12 months before being sent to the abattoir. During this period the animal's weight

2010 *Mathematics Subject Classification.* 62k05.
Key words and phrases. Discrimination between models, Growth models, KL-optimality, T-optimality.

must be kept under control. This permits to make the best choice regarding the type and amount of fodder to give, based on its developmental stage and, in turn, will influence the quality and quantity of the meat.

The weight control is adjusted by using growth models such as the above mentioned. This paper considers the problem of constructing optimal experimental designs to discriminate between Brody and Richards models. These two models are nested (the extended model reduces to the simpler model for a specic choice of a subset of the parameters) and appear frequently in livestock researches ([49], [22], [24], [14]).

Several studies have compared growth models for cattle ([11], [28], [25], [20]) whereas [16] and [6] compared Brody and Richards curves. The Brody equation has been the most used in beef cattle studies because of its ease of computation and its goodness of fit ([44], [36], [26]), though in some studies Richards model was reported to fit data better than Brody ([16], [6], [28]).

Although the article is focused on discriminating between these two models, a decision-making problem with more than two models may be considered in further research.

Optimal design theory has been applied to growth models can be found in the literature (e.g. [17], [29]), but in these cases, optimal designs have been calculated for uncorrelated observations. There is also an extensive literature on optimal design of experiments for correlated observations. [43] accomplished the study for regression models from a theoretical point of view, while [34] worked on the framework of spatial statistics. An example of a numerical method for the construction of optimal designs for time-dependent models in the presence of correlation is shown in [47]. [50] introduced a new design methodology for constructing asymptotic optimal designs for correlated data, and recently, [18] made some progress providing explicit results on optimal designs for linear regression models with correlated observations which are not restricted to the location scale model. However, the literature does not address optimal design of experiments for a growth model with correlated observations.

Next, basic concepts of the general theory of T-optimality are briefly introduced as well as the KL-optimality criterion. Section 3 explains how the design has been constructed for discriminating between two models and following that, in Section 4, robustness issues are discussed with respect to the choice of the nominal values of the parameters and with respect to the specification of the dependence structure.

2. **Optimal design theory.**

Design of Experiments is used to help us determine how to change the inputs of processes in order to identify the factors associated with changes in the response y, which is usually expressed as follows,

$$y = \eta(t, \theta) \ + \ \varepsilon \quad t \in \chi,$$

where $\eta(t, \theta)$ is the expected value of y, θ represents the r-dimensional vector of unknown parameters and t represents the time-points at which the response is observed. These times vary in a compact design space χ. The error ε follows a Gaussian process with zero mean and a covariance structure of y depending on the period of time between measurements (isotropic),

$$\text{Cov}\left(y(t_i), y(t_j)\right) = c(|t_i - t_j|, \beta), \tag{1}$$

where $c(\cdot, \beta)$ is called the *covariance function*.

An *exact experimental design* of size n consists of a collection of n points (experimental conditions) $\xi = (t_1, \ldots, t_n)'$, in a given compact space χ. After realizing the experiment at those values, n responses will be available. Some of the experimental conditions in the design may be repeated but, in this paper, designs will consist of a list of n distinct times since replicates of measurements at the same time on the same calf do not make sense from a practical point of view. Optimal Design of Experiments theory allows us to find the *best* design in the sense of obtaining an optimal estimator of the parameters of the model by minimizing a function of the variance-covariance matrix of $\hat{\theta}$ through what it is defined as *criterion* Φ [38]. The *best* design over all the designs on χ following the criterion Φ is called a Φ-optimal design.

A feature common to all non-linear models is that the optimal design will depend upon the value of the parameter θ. Since the purpose of the design is to estimate θ, the dependence of the design on the value of the parameter is unfortunate, but unavoidable for optimal designs with non-linear models. For that reason, it is necessary to use a prior estimator $\theta^{(0)}$, called *nominal value*, which usually represents the best guess for the parameter θ at the beginning of the experiment, and then to consider designs which minimizes the criterion function. The resulting design is called *locally optimal design* [12]. A sensitivity analysis is then convenient to evaluate the impact in guessing wrongly the nominal values of the parameters.

2.1. **T-optimality and KL-optimality criteria.** In order to determine an optimal design for discriminating between two rival models $\eta_1(t, \theta_1)$ and $\eta_2(t, \theta_2)$, [5] proposed to fix one of them, say $\eta(t, \theta) = \eta_1(t, \theta_1)$ (more precisely its corresponding parameters θ_1), considering it as the "*true*" model, and then to determine the design which maximizes

$$T_{21}(\xi) = \min_{\theta_2 \in \Omega_2} \int [\eta(t) - \eta_2(t, \theta_2)]^2 \, \xi(\mathrm{d}t),$$

where $\eta(t) = \eta_1(t, \theta_1^{(0)})$ is completely determined using some nominal values of $\theta_1 \in \Omega_1$, i.e. $\theta_1 = \theta_1^{(0)}$. This criterion has been studied by numerous authors ([40], [19] or [30] among others). In particular, [48] considered multiple response, that is, different outcomes from the same experiment. However, there was independence between different experiments and the correlation was just between the responses for "the same" unit (experiment). Thus, they could still use approximate designs and T–optimality is applicable as a direct extension. In this paper we consider a different problem since there is correlation between different experiments. Then, approximate designs can not be used, the general equivalence theorem is not valid anymore and the sample size has to be fixed in advance.

T-optimality is essentially a maximin problem. The minimization is carried out since we first assume the worst-case scenario, that is, when $\eta_2(t, \theta_2)$ is as close as possible to the "true" model. Then, we maximize $T_{21}(\xi)$ to find the best among those worst possible situations. Except for very simple models, T-optimal discriminating designs are not easy to find and even their numerical determination is a very challenging task. As mentioned above, an important drawback of this approach consists of the fact that the criterion and, as a consequence, the corresponding optimal discriminating designs depend sensitively on the parameters of one of the competing models. In contrast to other optimality criteria this dependence appears even for linear models. Therefore, T-optimal designs are locally optimal since they can only be implemented if some prior information regarding these parameters is available.

For the correlated case, the definition of $T_{21}(\xi)$ can be given as follows ([2]),

$$T_{21}(\xi) = \min_{\theta_2 \in \Omega_2} \left(\eta(t) - \eta_2(t,\theta_2)\right)' \Sigma^{-1}(\eta(t) - \eta_2(t,\theta_2)), \tag{2}$$

where Σ is the covariance matrix whose generic (i,j) entry is defined as in (1). It is a natural generalization of the T-optimality criterion function for correlated observations when the covariance structures of the rival models are exactly the same. Optimal exact designs are computed by maximizing this criterion. Actually, this criterion is again a particular case of KL-optimality and therefore it maximizes the test power for discrimination.

Let $f_1(y,t,\theta_1)$ and $f_2(y,t,\theta_2)$ be two rival density functions, where $f_1(y,t,\theta_1^{(0)})$ is assumed to be the true model. With this notation, the KL distance between the true model and $f_2(y,t,\theta_2)$ is defined as

$$\mathcal{I}(f_1,f_2,t,\theta_2) = \int f_1(y,t,\theta_1^{(0)}) \log\left[\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right] \mathrm{d}y, \quad t \in \mathcal{X},$$

where the integral is computed over the sample space of the possible observations. [27] developed this quantity, motivated by considerations of *information theory*. They used the notation $\mathcal{I}(f_1, f_2, \ldots)$ as a measure of the loss of *information* when f_2 is fitted to approximate f_1. Therefore, the KL-optimality criterion is defined as follows ([30]),

$$\mathcal{I}_{12}(\xi) = \min_{\theta_2 \in \Omega_2} \int_{\mathcal{X}} \mathcal{I}(f_1,f_2,t,\theta_2)\, \xi(\mathrm{d}t). \tag{3}$$

A design which maximizes $\mathcal{I}_{12}(\xi)$ is called KL-optimal design.

Theorem 2.1. *Given two competing Gaussian processes with means $\eta_1(t,\theta_1^{(0)})$ and $\eta_2(t,\theta_2)$, and covariance structures Σ_1 and Σ_2, respectively, the KL-optimality criterion leads to the expression,*

$$\begin{aligned} 2\mathcal{I}(f_1,f_2,t,\theta_2) = & -\log\frac{|\Sigma_1|}{|\Sigma_2|} - n + tr(\Sigma_2^{-1}\Sigma_1) + \\ & \left(\eta_1(t,\theta_1^{(0)}) - \eta_2(t,\theta_2)\right)' \Sigma_2^{-1}(\eta_1(t,\theta_1^{(0)}) - \eta_2(t,\theta_2). \end{aligned}$$

Proof.

$$\begin{aligned} \mathcal{I}(f_1,f_2,t,\theta_2) &= \int f_1(y,t,\theta_1^{(0)}) \log\left[\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right] \mathrm{d}y \\ &= \mathrm{E}_1\left[\log\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right]. \end{aligned}$$

As $f_1(y,t,\theta_1^{(0)})$ and $f_2(y,t,\theta_2)$ follow a Gaussian distribution,

$$\begin{aligned} \mathrm{E}_1\left[\log\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right] &= \mathrm{E}_1\left[\log f_1(y,t,\theta_1^{(0)}) - \log f_2(y,t,\theta_2)\right] \\ &= -\frac{1}{2}\mathrm{E}_1\left[\log\frac{|\Sigma_1|}{|\Sigma_2|}\right] \\ &\quad -\frac{1}{2}\mathrm{E}_1\left[(y - \eta_1(t,\theta_1^{(0)}))'\Sigma_1^{-1}(y - \eta_1(t,\theta_1^{(0)}))\right] \end{aligned}$$

$$+\frac{1}{2}\mathrm{E}_1\left[(y-\eta_2(t,\theta_2))'\Sigma_2^{-1}(y-\eta_2(t,\theta_2))\right]$$

For simplicity, let denote $\eta_1(t,\theta_1^{(0)})$ and $\eta_2(t,\theta_2)$ as η_1 and η_2, respectively. The second term of the expectation E_1 is,

$$\begin{aligned}\mathrm{E}_1\left[(y-\eta_1)'\Sigma_1^{-1}(y-\eta_1)\right] &= tr\left(\Sigma_1^{-1}\mathrm{E}_1\left[(y-\eta_1)'(y-\eta_1)\right]\right)\\ &= tr\left(\Sigma_1^{-1}\Sigma_1\right) = n.\end{aligned}$$

And the third,

$$\mathrm{E}_1\left[(y-\eta_2)'\Sigma_2^{-1}(y-\eta_2)\right] = \mathrm{E}_1\left[\left[(y-\eta_1)+(\eta_1-\eta_2)\right]'\Sigma_2^{-1}\left[(y-\eta_1)+(\eta_1-\eta_2)\right]\right]$$

$$= tr\left(\Sigma_2^{-1}\Sigma_1\right) + 2\mathrm{E}_1\left[(y-\eta_1)'\Sigma_2^{-1}(\eta_1-\eta_2)\right] + \mathrm{E}_1\left[(\eta_1-\eta_2)'\Sigma_2^{-1}(\eta_1-\eta_2)\right]$$

$$= tr\left(\Sigma_2^{-1}\Sigma_1\right) + 2\Sigma_2^{-1}(\eta_1-\eta_2)\mathrm{E}_1[y-\eta_1]$$

$$+(\eta_1-\eta_2)'\Sigma_2^{-1}(\eta_1-\eta_2) = tr\left(\Sigma_2^{-1}\Sigma_1\right) + 0 + (\eta_1-\eta_2)'\Sigma_2^{-1}(\eta_1-\eta_2).$$

Therefore,

$$\mathcal{I}(f_1,f_2,t,\theta_2) = -\frac{1}{2}\log\frac{|\Sigma_1|}{|\Sigma_2|} - \frac{1}{2}n + \frac{1}{2}tr\left(\Sigma_2^{-1}\Sigma_1\right) + \frac{1}{2}(\eta_1-\eta_2)'\Sigma_2^{-1}(\eta_1-\eta_2).$$

□

Remark 1. For $\Sigma_1 = \Sigma_2 = \Sigma$,

$$\mathcal{I}(f_1,f_2,t,\theta_2) = \frac{1}{2}(\eta_1-\eta_2)'\Sigma^{-1}(\eta_1-\eta_2),$$

which is the criterion (2). Therefore, the criterion defined in (3) is an extension of the extended T-optimality criterion for correlated observations when the covariance matrix is assumed equal for the rival models.

3. **Experimental designs to compare Richards and Brody models.** As mentioned above, these two models have already been compared for cattle, though in none of them this comparison have been carried out by using optimal designs. They are general models for ontogenetic growth in organisms based on principles for the allocation of metabolic energy between the maintenance of existing tissue and the production of new ones [37]. Richards model provides the mass of the organism at any time t:

$$\eta(t,\theta) = M\left(1 - B\exp\{-kt\}\right)^A$$

where t is the age, M represents the asymptotic maximum body mass (asymptotic mature weight) , B is a time scale parameter and k and A being the rate of approach to mature weight and a shape parameter that allows for a variable inflection point, respectively. Brody model is nested within Richards since it is a particular case of it when $A = 1$.

The presence of correlation has been considered because the observations on a single calf may not be independent. The fact of carrying out a measurement at the same time on the same animal has no utility from a practical point of view.

Therefore, we will introduce a so-called nugget effect in the covariance structure in order to avoid collapsing of design points. This effect produces a shift in these points which leads to an optimal design without replicated points. The conception of the nugget term was first introduced in Geostatistics by [32]. It is also widely used in Gaussian processes [39] and Spatial Statistics [13, 42]. For an isotropic correlation structure the variance-covariance matrix for two observations tends to a singular form when the distance tends to zero. This behavior is due to the lack of microvariation allowed for by the assumed covariance function. Then optimal designs tend to avoid collapsing points. If the nugget effect is introduced in the covariance structure more meaningful and practically relevant designs arise. In particular, sometimes it may be proved that the distance between the points of a two-point D-optimal design is an increasing function of the nugget effect [45]. These correlation functions are typically used in the literature [13]. [1] provided a general result to obtain a large class of feasible models for a covariance structure. We will define the covariance structure by using a function which exponentially decays with increasing time-distance between the measurements,

$$\mathrm{Cov}(y_{t_i}, y_{t_j}) = \begin{cases} \sigma^2\,\rho\,\exp\{-\beta\,|t_i - t_j|\} & \text{for} \quad t_i \neq t_j, \\ \sigma^2\,(1-\rho) & \text{for} \quad t_i = t_j, \end{cases} \tag{4}$$

where ρ is the nugget term [45].

3.1. **Hypothesis test for discrimination.** Let consider two competing Gaussian processes with means $\eta_1(t,\theta_1)$ and $\eta_2(t,\theta_2)$ given by Richards and Brody functions, respectively,

$$\begin{aligned} \eta_1(t,\theta_1) &= M_1\left(1 - B_1 \exp\{-k_1 t\}\right)^{A_1} \\ \eta_2(t,\theta_2) &= M_2\left(1 - B_2 \exp\{-k_2 t\}\right), \end{aligned}$$

with correlation structures defined by (4). In this situation, the density functions associated to these two processes are

$$f_k(y,t,\theta_k) = \frac{1}{(2\pi)^{n/2}|\Sigma_k|^{1/2}} \exp\{(y - \eta_k(t,\theta_k))'\Sigma_k^{-1}(y - \eta_k(t,\theta_k))\} \quad k = 1,2$$

where Σ_k is the variance-covariance matrix whose generic (i,j) entry is defined as in (4).

To discriminate between Richards and Brody models, the following hypotheses test may be considered:

$$\left.\begin{array}{l} H_0 : f_2(y,t,\theta_2) \\ H_1 : f_1(y,t,\theta_1^{(0)}) \end{array}\right\}$$

where $\theta_1^{(0)}$ are nominal values of the parameter θ_1. In this test the alternative hypothesis is assumed to be "true" (this means Richards model is assumed to be "true") since we want to maximize the test power. The likelihood ratio for an observation y at time t will be

$$L = \frac{f_2(y,t,\theta_2)}{f_1(y,t,\theta_1^{(0)})},$$

and a common statistical test is that based on the statistic

$$R = -2\log(L) = 2\log\left\{\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right\},$$

in such a way that the hypothesis H_0 will be rejected for large values of R. The expectation of this statistic for one design point, under H_1, is

$$\mathrm{E}_{H_1}(R) = 2\int f_1(y,t,\theta_1^{(0)}) \log\left[\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right] \mathrm{d}y = 2\,\mathcal{I}(f_1,f_2,t,\theta_2). \tag{5}$$

The larger $\mathrm{E}_{H_1}(R)$ and $\mathcal{I}(f_1,f_2,t,\theta_2)$ are, the larger the power function of R is. This is because hypothesis H_0 is rejected when this statistic is greater than a critical value. Using equation (5) for an exact design and the corresponding observations, we obtain,

$$\mathcal{I}_{12}(\xi) = \min_{\theta_2\in\Omega_2}\left\{\int_\chi \int f_1(y,t,\theta_1^{(0)}) \log\left[\frac{f_1(y,t,\theta_1^{(0)})}{f_2(y,t,\theta_2)}\right] \mathrm{d}y\,\xi(\mathrm{d}t)\right\} \propto \min_{\theta_2\in\Omega_2}\{\mathrm{E}_{H_1}(R)\}.$$

Therefore, the KL-optimal design maximizes the power function in the worst case [30].

3.2. **Algorithm to calculate the KL-optimal design.** In order to compute optimal designs, the numerical algorithm developed by [9] is adapted to KL-optimality. It is an exchange-type algorithm that starts from an arbitrary initial n-points design. In case of exact designs, this number of points is fixed by the practitioner and none of them are repeated. At each iteration one support point is deleted from the current design and a new point is included in its place to maximize the value of the criterion function. Next, the algorithm is detailed:

Step 1. Select an initial design $\xi_n^{(0)} = \{t_1^{(0)},\dots,t_n^{(0)}\}$ such that, $t_i^{(0)} \neq t_j^{(0)}$, $i,j\in I = \{1,2,\dots,n\}$ and $i\neq j$.

Step 2. Compute

$$\widetilde{\theta}_2^{(0)} = \arg\min_{\theta_2\in\Omega_2} \mathcal{I}(f_1,f_2,t,\theta_2) \quad \text{and} \quad \Delta(\xi_n^{(0)}) = \mathcal{I}(f_1,f_2,t,\theta_2^{(0)})$$

Step 3. Determine

$$(i^*,t^*) = \arg\max_{(i,t)\in I\times\chi} \Delta(\xi^{(0)}_{n,t_i\rightleftharpoons t}),$$

where $\Delta(\xi^{(0)}_{n,t_i\rightleftharpoons t})$ means that the support point t_i in the design $\xi_n^{(0)}$ is exchanged by $t\in\chi$. If

$$\frac{\Delta(\xi^{(0)}_{n,t_{i^*}\rightleftharpoons t^*}) - \Delta(\xi_n^{(0)})}{\Delta(\xi_n^{(0)})} < \delta,$$

where δ is the given tolerance, then STOP. Otherwise,

$$\xi_n^{(1)} = \{t_1^{(0)},\dots,t_{i^*}^*,\dots,t_n^{(0)}\},$$

and we go to step 1, taking $\xi_n^{(1)}$ as initial design.

Before calculating the value of $\widetilde{\theta}_2^{(0)}$ we must know the nominal value of θ_1, $\theta_1^{(0)}$. This nominal value has been obtained by using the Maximum-Likelihood Estimation from historical data,

$$\theta_1^{(0)} = \arg\max_{\theta_1} \log\frac{1}{(2\pi)^{n/2}|\Sigma_1|^{1/2}} \exp\{(y-\eta_1(t,\theta_1))'\Sigma_1^{-1}(y-\eta_1(t,\theta_1))\},$$

The values of $y = (y_1,\dots,y_n)$ correspond to the weight of a single calf at eight different ages (see Appendix) and they were provided by Naválázaro farm. Once the Maximum-Likelihood method has been carried out,

$$\theta_1^{(0)} = (M_1^{(0)},\ B_1^{(0)},\ k_1^{(0)},\ A_1^{(0)},\ \beta_1^{(0)},\ \rho_1^{(0)}) = (796, 0.66, 0.0044, 3.89, 0.04, 0.95). \tag{6}$$

These values of $\theta_1^{(0)}$ are used as nominal values for computing a locally optimal design.

3.3. **Calculation of KL-optimal design.** As mentioned at the introduction, calves are sent to the growing facility just after their weaning, all of them being weighed upon their arrival. Accordingly, one cannot determine a priori exactly the age at which the animals will be weighed for the first time. As the distribution of birth can be considered uniform over time, this design specifies that the first measure after weaning will be taken at time $t_1 \sim \mathcal{U}(170, 190)$, since approximately every 20 days a group of animals are sent to the growing facility. Around eighteen months after birth (540 days), the yearlings are sent to the abattoir where they will be killed for consumption as food. Therefore, the first measurement will be made as soon as possible after weaning, that is, $t_1 \sim \mathcal{U}(170, 190)$ and the last one when they are about 540 days old, that is, $t_8 = t_1 + 540 - 180 = t_1 + 360$. The design ξ will consist then of measuring at times

$$\{t_1,\, t_2,\, t_3,\, t_4,\, t_5,\, t_6,\, t_7,\, t_8\},$$

where $t_1 \sim \mathcal{U}(170, 190)$, $t_8 = t_1 + 360$ and for the rest of the times,

$$t_i = t_1 + \sum_{j=2}^{i} h_j \quad i = 2, \ldots, 7, \quad \sum_{j=2}^{7} h_j \leq 540 - 180 = 360. \tag{7}$$

The values of $h_2,\, h_3,\, h_4,\, h_5,\, h_6,\, h_7 > 0$ have to be optimized by using the algorithm. Since t_1 is a random time, we cannot control a priori the exact age at which the calf will be weighed. Thus, we will optimize the periods of time between measurements. Once this minimization has been carried out, we have the locally KL-optimal design,

$$\xi^* = \{t_1, t_1 + 30, t_1 + 60, t_1 + 80, t_1 + 90, t_1 + 110, t_1 + 240, t_1 + 360\}.$$

The *relative efficiency* of any design ξ compared with another ζ is computed by dividing the values of the KL-optimality criterion. We compare the values

$$\mathrm{eff}_{\xi,\zeta} = \frac{\mathcal{I}_{12}(\xi)}{\mathcal{I}_{12}(\zeta)}\cdot$$

The efficiency can sometimes be multiplied by 100 and be reported in percentage terms. If this efficiency is higher than 1 then the power test for discrimination between the two models is higher with the design ξ than with the design ζ. We intend to compare the relative efficiency of ξ with respect to the measurements taken at the growing facility (see Appendix), which from now on will be expressed as ξ_f:

$$\xi_f = \{t_1, t_1 + 50, t_1 + 100, t_1 + 150, t_1 + 205, t_1 + 255, t_1 + 310, t_1 + 360\},$$

where $t_1 \sim \mathcal{U}(170, 190)$. This design consists of eight points representing the age at which the calves were weighed at the growing facility. Through the efficiency we measure how much better ξ^* is compared to ξ_f,

$$\mathrm{eff}_{\xi_f,\xi^*} = \frac{\mathcal{I}_{12}(\xi_f)}{\mathcal{I}_{12}(\xi^*)} = 66\,\%\cdot$$

4. **Robustness analysis.**

4.1. **Sensitivity analysis versus the choice of the nominal values.** In this section it will be checked how the quality of the optimal design would be affected by a wrong choice of the nominal value. Let us call θ^* as any possible true value of the parameters and $\theta^{(0)}$ being the nominal values used for the computation of the KL-optimal design $\xi^*_{\theta^{(0)}}$. The efficiency

$$\text{eff}_{\xi^*_{\theta(0)},\xi^*_{\theta^*}} = \frac{\mathcal{I}_{12}(\xi^*_{\theta(0)})}{\mathcal{I}_{12}(\xi^*_{\theta^*})},$$

measures the goodness of the design $\xi^*_{\theta(0)}$ obtained under the nominal values, where $\xi^*_{\theta^*}$ is the actual optimal design. Table 1 illustrates the robustness of the KL-optimal design ξ^* with respect to the choice of the parameters M_1, B_1, k_1 and A_1. Shifting around 10% the parameters k_1, A_1 and B_1 keeps the efficiency over 70%, even when the variations of the parameter M_1 is large (from 756 to 835 kg). On the other hand, Figure (1) shows the robustness of ξ^* with respect to the choice of the parameters ρ and β. The higher the value of ρ is, the greater the decrease in the value of efficiency will be.

		$k_1 = 0.0039$			$k_1 = 0.0044$			$k_1 = 0.0048$		
		756	**796**	**835**	**756**	**796**	**835**	**756**	**796**	**835**
A_1=3.5	**0,59**	63	68	69	65	69	71	67	71	72
	0.66	71	74	74	72	76	76	74	78	77
	0.73	71	73	72	72	74	73	74	76	74
		756	**796**	**835**	**756**	**796**	**835**	**756**	**796**	**835**
A_1=3.89	**0.59**	92	96	96	92	96	95	93	96	95
	0.66	98	99	98	98	**100**	98	98	99	98
	0.73	95	96	93	95	96	92	95	96	92
		756	**796**	**835**	**756**	**796**	**835**	**756**	**796**	**835**
A_1=4.28	**0.59**	75	76	74	73	74	72	71	72	70
	0.66	77	78	74	76	76	72	74	74	71
	0.73	72	71	67	71	70	65	69	68	63

TABLE 1. Relative efficiencies (in %) of the design ξ^* for different values of the parameters; $M_1 = 756, 796, 835$; $B_1 = 0.59, 0.66, 0.73$

4.2. **Sensitivity analysis versus the choice of the correlation structure.** We have considered a well known and widely used model for the trend of the growing of the weight of animals. We claim a correlation structure has to be considered when there are repeated measurements. This is convenient from both the practical and the statistical points of view, resulting in information gain and cost reductions. A novelty that this paper introduces is the choice of such a correlation structure. The one used here is rather usual within this framework, but other may also be suitable.

We compare the efficiency of the locally optimal designs obtained with respect to the choice of these three typical covariance structures:

(a) Dagum function,

$$\text{Cov}(y_{t_i}, y_{t_j}) = \begin{cases} \sigma^2 \left[\rho \left(1 - \dfrac{(t_i - t_j)^\beta}{1 + (t_i - t_j)^\beta} \right)^\gamma \right] & \text{for} \quad t_i \neq t_j \\ \sigma^2\,(1-\rho) & \text{for} \quad t_i = t_j. \end{cases} \tag{8}$$

(b) Cauchy function,

$$\text{Cov}(y_{t_i}, y_{t_j}) = \begin{cases} \sigma^2\,\rho\,\left(1 + (t_i - t_j)^\beta\right)^{-\gamma} & \text{for} \quad t_i \neq t_j \\ \sigma^2\,(1-\rho) & \text{for} \quad t_i = t_j. \end{cases} \tag{9}$$

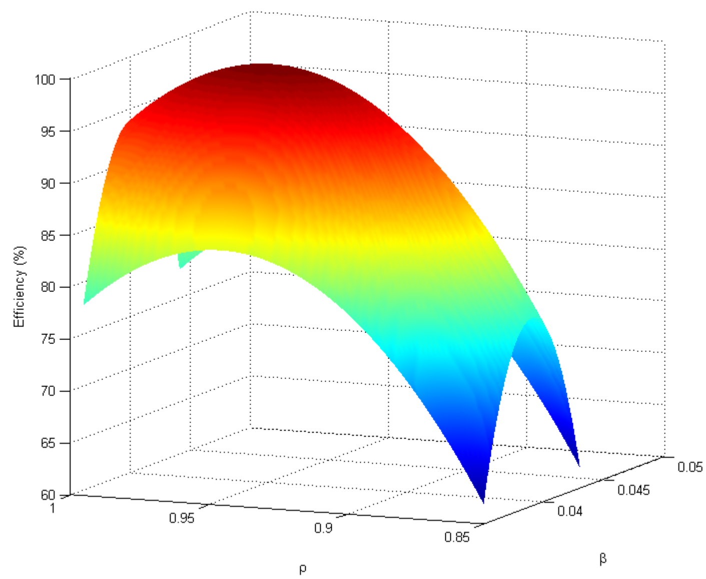

FIGURE 1. Relative efficiencies of the design ξ^* for different values of the correlation and nugget parameters

(c) Gaussian model,

$$\mathrm{Cov}(y_{t_i}, y_{t_j}) = \begin{cases} \sigma^2\,\rho\,\exp\{-\beta^2\,(t_i - t_j)^2\} & \text{for} \quad t_i \neq t_j \\ \sigma^2\,(1-\rho) & \text{for} \quad t_i = t_j. \end{cases} \tag{10}$$

Table 2 shows the efficiencies of the locally optimal design ξ^* with respect to the designs ξ^*_{dag}, ξ^*_{ca} and ξ^*_{ga}, which have been calculated assuming covariance structures (8), (9) and (10), respectively. The similar behavior of the correlation structures (Figure 2) allows us to compare the designs obtained with them. The efficiency is not substantially affected by the choice of these three correlation structures (always over 75%).

	KL-optimal design	eff(ξ^*)
ξ_{dag}	$\{t_1, t_1+145, t_1+155, t_1+170, t_1+180, t_1+250, t_1+300, t_1+360\}$	87 %
ξ_{ca}	$\{t_1, t_1+50, t_1+60, t_1+70, t_1+210, t_1+260, t_1+330, t_1+360\}$	75 %
ξ_{ga}	$\{t_1, t_1+30, t_1+60, t_1+80, t_1+90, t_1+110, t_1+240, t_1+360\}$	77 %

TABLE 2. Designs based on covariance structures (8), (9) and (10) and their corresponding efficiencies with respect to ξ^*.

5. **Discussion.** In this paper we have computed a restricted optimal design for discrimination between two well-known and widely used models for the trend of the growing weights of animals. The criterion used in Section 2 generalizes the T-optimality criterion for correlated observations.

On the other hand, it is important to point out that the results obtained cannot be extended to other areas of Spain or Europe; not even to other Limousine farms

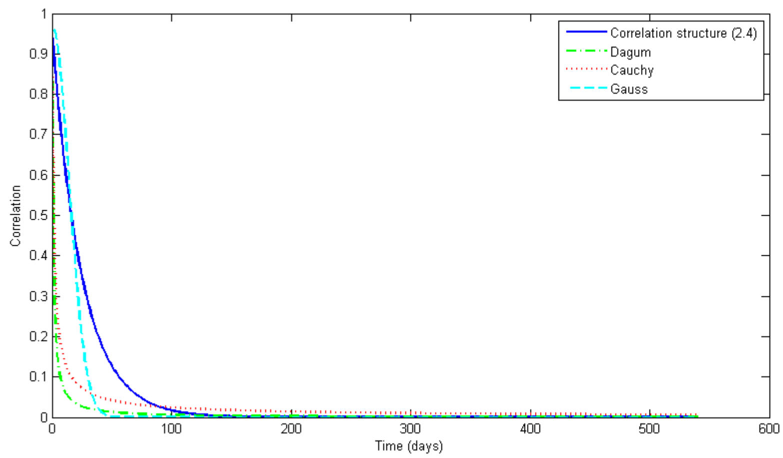

FIGURE 2. Plot of the correlation structures (4), (8), (9) and (10).

due to the wide variability of this breed. Furthermore, the design depends on the prior values of the parameters of the model assumed to be the true one. This means a local fitting has to be performed and used for each individual farm, but the procedures apply straightforward. Moreover, in Navalázaro farm the calves are sent to the abattoir when they are 18 months old but not every beef farm operates on the same way since despite at this age the quality of the meat is high, it is also more expensive and more difficult to place this product in the market. Therefore, we should not extrapolate from these particular outcomes to other farms.

The introduction of the nugget effect avoids the collapsing of some optimal design points. The efficiency of the design used in practice with respect to the computed design is around 66%, which is substantially low. Thus, the restricted optimal design computed implies an important gain with respect to the traditional one. Therefore, the choice of a robust correlation structure is an important contribution of this paper since there is not much literature on optimal design for discrimination between models in the context of correlated observations and this work provides a methodology that can be used for any correlation structure. Apart from the fact that there are not many results regarding practical determination of optimal design for discrimination between models in the context of correlated observations.

Figure 2 shows that the correlation between two observations in less than 10 days is greater than 0.75, but for a difference of 50 days it decreases to about 0.3 and after 5 months the correlation is quite low. The exponential correlation used here is one of the most usual within this framework, but others may be suitable. Besides, the introduction of the nugget effect has produced a shift in the optimal points which has led to an optimal design without replications. We have performed a robustness analysis in order to show the importance of a right choice of the structure of correlation.

The example considered in this paper (in which constant variance is assumed) agrees with the usual treatment of the problem by [3] and [4]. Nevertheless, a non–constant variance may be considered breaking the property of isotropy or doing it in a similar way as the introduction of the nugget effect. This has been considered recently by [8], where the efficiency for repeated measurements will be much better under the presence of heteroscedastic variance.

Another way of dealing with the correlation of the observations would be through mixed models with random coefficients. As a matter of fact, there is an increasing interest in finding optimal designs for regression models with random effects, see e.g. [46] for a recent work. In a different context, [23] considered models with random effects, but they always tried to find the covariance structure behind (e.g. in pages 155 or 270). Sometimes the distinction between fixed and random effects is not clear (e.g. [31], examples in Chapter 1). Furthermore, [15] devotes Chapter 4 to a growth model analyzing different cases for the covariance matrix showing that our approach is rather usual in this context. In any case, the mixed models are gaining in popularity and deserve further research in optimal experimental design.

The design computed here is mainly for discrimination between two rival models. Several issues arise at this respect:

(a) Optimality criteria to estimate the parameters of doing predictions may be considered using compound criteria for both purposes (May and Tommasi, 2014).

(b) If the choice has to be made among more than two rival models, different criteria derived from KL-optimality may be used. The authors are currently working on this topic.

(c) The designs computed or mentioned here are for statistical inference purposes. In practical terms the farmer would like to know what are the best times for an optimal control of the weight. This is not exactly the same topic although there is very much related.

(d) From a statistical point of view, it seems as if eighteen moths is too little a period of time to reach weight saturation and that calves' lives schould be prolonged in order to reach optimal weight. It is clear that weights at longer periods would help fit the models in a more efficient way, but the farm decides at which age the calves must sent to the slaughterhouse based on economic considerations. When calves are around eighteen months old, the carcass efficiency is optimal and the organoleptic properties are ideal for consumption. At this stage, the meat is tender and has a good red color since the animals have a greater movement capacity, implying that the hemoglobin already reaches the tissues completely. Some people prefer to eat meat from younger calves (around twelve months) but this meat is not very red and for most customers it is too tender. Besides, it is sold for a higher price, since at this age the carcass perfomance is not optimal. After eighteen months, the carcass efficiency decreases so the economic loss is higher for the farm. Furthermore, the meat becomes increasingly less red and harder.

Finally, we would like to remark that the realization of the design would comply both the Spanish and the European regulations and would not affect to the animals welfare since this implementation only implies to weigh the heifers at different points in time from those carried out at the growing facility.

Appendix. The following data were provided by Navalázaro farm. Each row corresponds to the weight of a single calf at its corresponding age. The first column refers to the weight of the calf upon arrival at the growing facility, with the last column referring to its weight before being sent to the abattoir.

	day	**kg**	**day**	**kg**	**day**	**kg**	**day**	**kg**	**day**	**kg**	**day**	**kg**	**day**	**kg**	**day**	**kg**
calf 1	170	215	236	291	277	337	333	402	389	478	434	539	493	617	537	677
calf 2	170	160	238	266	285	333	344	414	386	459	436	502	494	537	534	565
calf 3	170	184	229	298	276	366	338	465	383	517	443	596	493	652	541	720
calf 4	170	161	228	228	287	299	340	367	386	423	440	491	496	555	531	588
calf 5	171	209	226	307	288	422	324	477	394	579	441	631	488	684	541	731
calf 6	171	196	233	276	286	344	338	417	393	500	444	560	493	619	541	655
calf 7	171	187	224	261	286	327	330	374	393	434	429	469	498	524	540	543
calf 8	171	245	227	301	288	374	338	443	378	502	429	607	480	710	530	838
calf 9	171	149	224	252	276	348	328	430	382	505	433	560	482	619	535	654
calf 10	171	225	240	329	285	396	328	452	383	537	429	583	483	667	535	719
calf 11	172	163	224	253	286	358	334	429	379	495	437	583	481	646	531	718
calf 12	172	240	224	308	276	394	336	488	387	567	428	625	497	717	544	768
calf 13	172	168	225	284	274	371	334	458	379	512	445	568	480	597	530	631
calf 14	172	206	229	303	278	385	338	468	381	518	445	574	495	612	537	640
calf 15	173	174	229	288	289	394	340	483	376	536	435	647	489	713	538	784
calf 16	173	218	238	312	285	384	331	453	379	511	435	576	488	634	532	663
calf 17	173	180	224	251	286	345	326	404	386	490	437	556	495	636	539	678
calf 18	173	259	229	324	275	375	324	453	394	557	433	627	484	706	536	803
calf 19	173	199	228	259	273	322	334	403	382	491	430	579	482	677	548	806
calf 20	173	243	236	338	290	412	331	466	389	535	433	585	489	650	546	714
calf 21	173	160	222	305	287	440	331	517	388	597	434	666	491	739	530	785
calf 22	174	204	239	321	275	367	340	463	386	512	445	560	480	567	538	598
calf 23	174	214	237	296	290	370	342	428	386	473	439	508	481	544	547	581
calf 24	175	186	222	274	274	358	340	428	389	452	433	474	497	489	530	497
calf 25	175	180	237	302	281	382	342	472	379	531	432	584	481	620	532	657
calf 26	175	133	226	234	281	339	328	408	391	513	445	566	480	613	540	671
calf 27	176	230	233	297	276	354	339	460	380	538	445	672	483	759	545	925
calf 28	176	230	227	332	287	442	324	492	376	564	440	620	490	648	540	664
calf 29	176	180	240	328	275	406	338	519	388	570	443	608	486	634	544	648
calf 30	177	228	238	298	284	346	335	401	394	469	432	510	493	567	545	594
calf 31	177	202	225	290	282	382	331	459	394	539	445	615	480	645	544	732
calf 32	177	194	228	298	286	391	336	450	391	491	434	524	482	543	531	554
calf 33	178	194	239	281	288	346	343	411	388	468	427	506	495	592	548	637
calf 34	178	187	222	249	277	328	326	404	379	484	431	570	486	636	530	685
calf 35	178	207	223	270	284	353	333	418	389	486	441	559	491	620	530	673
calf 36	178	215	234	313	275	374	342	450	379	490	432	519	494	544	539	559
calf 37	178	258	230	338	275	409	324	495	381	589	433	674	491	770	549	849
calf 38	179	240	230	292	281	356	330	416	385	489	437	576	494	665	545	742
calf 39	179	241	237	327	287	397	342	477	393	561	433	617	492	708	533	777
calf 40	179	186	228	290	288	394	339	463	389	540	429	595	478	653	541	734
calf 41	180	187	223	258	289	371	340	447	390	517	430	573	491	624	540	667
calf 42	180	213	227	286	274	366	336	475	391	569	435	650	480	715	535	805
calf 43	180	268	235	346	283	402	344	472	380	505	429	552	480	599	531	641
calf 44	180	195	239	272	290	344	336	400	378	456	431	533	482	594	530	641
calf 45	180	230	231	304	290	394	331	463	384	550	444	666	478	729	549	834
calf 46	181	206	230	288	273	358	331	464	378	544	443	646	484	697	540	756
calf 47	181	197	234	331	273	407	336	511	382	573	428	642	488	704	533	756
calf 48	181	193	227	256	275	332	328	397	393	481	428	530	483	604	531	659
calf 49	181	207	227	267	276	325	336	402	395	456	430	491	483	527	537	567
calf 50	181	191	234	310	273	369	331	458	384	511	431	569	492	625	547	684
calf 51	182	221	236	297	285	375	333	454	386	539	433	596	493	692	533	738
calf 52	182	204	233	286	277	353	330	428	385	492	431	551	495	601	533	627
calf 53	182	219	240	288	277	334	337	396	381	427	440	474	492	501	531	508
calf 54	182	225	229	292	290	375	324	415	384	494	435	563	487	614	545	662
calf 55	182	250	235	328	285	407	343	503	379	563	441	649	483	716	532	775
calf 56	182	228	223	263	280	307	325	357	385	436	435	509	498	612	546	704
calf 57	183	230	229	293	280	357	344	428	376	449	444	504	496	521	545	549
calf 58	183	232	232	311	286	399	337	473	379	523	429	586	498	659	533	699

calf 59	183	245	231	348	283	459	333	549	378	610	436	670	495	732	547	742
calf 60	183	226	224	286	287	387	326	445	378	541	439	655	485	739	543	830
calf 61	183	220	230	299	277	386	326	465	392	584	430	631	481	698	543	747
calf 62	183	209	225	281	285	376	325	442	383	517	440	574	497	610	546	640
calf 63	184	222	236	302	278	377	337	473	388	564	430	619	480	692	539	765
calf 64	184	213	240	273	279	316	343	393	382	440	444	513	487	555	538	633
calf 65	185	196	229	258	277	330	332	405	377	464	429	503	497	555	549	586
calf 66	185	209	224	272	290	384	344	473	386	536	444	606	490	664	533	699
calf 67	185	213	228	287	285	381	339	454	377	505	429	566	489	639	539	683
calf 68	185	206	223	293	278	391	329	475	386	555	428	591	486	647	532	682
calf 69	185	164	232	239	281	322	329	403	390	512	431	592	480	669	545	796
calf 70	185	206	238	312	282	399	336	479	394	576	436	638	478	694	547	781
calf 71	185	193	229	239	282	311	338	394	395	476	433	533	495	638	544	711
calf 72	186	208	239	289	275	339	342	451	388	518	429	564	484	633	540	674
calf 73	186	321	232	393	276	455	329	520	393	574	427	611	488	635	533	655
calf 74	186	240	241	315	287	381	331	431	387	506	429	555	496	631	547	690
calf 75	186	243	238	314	277	378	336	458	387	528	437	602	495	683	535	743
calf 76	186	202	230	274	290	380	332	452	391	540	435	619	494	711	545	803
calf 77	186	246	236	323	275	377	334	466	382	515	438	570	486	591	538	634
calf 78	187	228	240	301	283	369	327	422	378	482	432	539	495	600	535	626
calf 79	188	234	240	319	281	374	326	437	380	515	435	590	490	665	535	726
calf 80	188	200	236	293	273	367	331	462	389	539	441	604	483	636	535	669
calf 81	188	187	237	293	278	351	335	424	395	480	441	522	495	558	538	586
calf 82	188	221	232	280	287	353	335	420	376	472	436	563	491	652	540	730
calf 83	189	258	228	309	278	370	325	429	381	487	428	524	488	568	545	626
calf 84	189	200	236	283	279	352	337	430	380	482	433	541	492	597	540	631

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Received March 02, 2015; Accepted June 16, 2015.

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