A-, D- and E-optimal designs for quadratic and cubic growth curve models with correlated errors

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SUMMARY

In this paper polynomial growth curve models with correlated errors are considered. We study A-, D- and E-optimal designs for quadratic and cubic growth curve models with three and four time points on the time interval $[0,2]$. Optimal designs for four correlation structures of errors are compared: nearest-neighbor, autoregression, moving average and unstructured antedependence.

Key words: growth curve model; information matrix; covariance structure; optimal design

1. Introduction

When planning a longitudinal experiment, the researcher must decide on the number and allocation of time points. In such experiments, where some individuals are observed repeatedly, growth curve models are often used. Experiments of this type have broad application, especially in the life sciences and social sciences. For example, most clinical trials of new pharmaceutical drugs and many agronomical investigations are characterized by repeated sampling over time.

In this paper we propose to discuss the optimality aspects of correlated models for quadratic and cubic growth. For example, quadratic growth curve models were used to model the lung volumes of fetuses (Chang et al., 2003), and cubic growth models were used to fit the body mass of beetle larvae (Greenberg and Ar, 1996).

Recently, some results on optimality of designs in polynomial growth curve models have been published. Abt et al. (1997, 1998) studied optimality aspects of linear and quadratic growth curve models with correlated errors. In both papers it is mainly models with autoregressive correlation structures of errors which are analyzed, and it is assumed that the time points are equally spaced in the symmetric interval $[-k,k]$. Optimal designs for linear, quadratic and cubic growth models with autocorrelated errors and with four or fewer time points from the interval $[0,2]$ are given in Moerbeek (2005). Optimal allocation of time points in a growth curve model of higher order with uncorrelated errors is considered in Chang and Lay (2002).

In this paper optimality results with respect to the three most often used criteria, A-, D- and E- optimality, are considered. We assume that observations of the same treatment at different time points are correlated. The purpose of this paper is to extend the optimality results of Moerbeek (2005) to four, most typical correlation structures. Further, we study the efficiency of optimal designs under a model with uncorrelated errors in models with four considered dependence stuctures. We show that for the most values of correlation coefficient those design are highly efficient.

We study models with the nearest neighbor covariance structure NN(1) proposed by Cheng (1988), and with correlation structures of errors presented by Zimmerman and Núñez-Antón (2001) as the structures connected with growth curve models: the first-order autoregression AR(1), the second-order moving average structure MA(2), and the first-order unstructured antedependence observations UAD(1). Observe that the model with uncorrelated errors is a special case of the model with any of the above correlation structures for zero correlation coefficients. The optimality results on models with uncorrelated errors and with errors correlated according to AR(1) are given, for example, in Moerbeek (2005). Since we compare optimality results in models with correlated errors relatively to the type of dependence, following Moerbeek (2005) we assume that the time interval is $[0,2]$. Moreover, since designing a longitudinal study often requires fixing of the first and last time point, we consider designs where the first time point is 0 and the last time point 2.

In our considerations we assume that the number of time points, q, is equal to the number of regression coefficients ($p+1$) in the polynomial growth curve models (cf. Garza, 1954, Pukelsheim, 1993, Mandal, 2002). Moreover, Moerbeek (2005) showed that the efficiency of a design decreases when the number of time points increases.

In this paper we study the efficiency of designs which are optimal in a model with uncorrelated errors relative to the values of correlation coefficient and the type of dependence. The efficiency factors in models with errors correlated according to AR(1) were studied in Moerbeek (2005), but this concerned efficiency with respect to the incorrect number of time points, order of polynomial, value of correlation coefficients and with respect to other optimality criteria.

The optimal designs and the efficiency factors were derived numerically using *Mathematica* 5.0. In the analysis we calculated efficiencies for nonnegative values of the correlation coefficients, which are integer multiplicity of 0.01.

We organize the paper as follows. In Section 2 we present a polynomial growth curve model, the information matrix for estimating unknown regression coefficients, and we formulate criteria for A-, D- and E-optimality of design. In Section 3 we give the forms of the considered correlation structures of errors NN(1), AR(1), MA(2) and UAD(1), and we formulate restrictions for correlation coefficients in each of these structures. In the last section we give some optimality results. We show that the allocation of time points in a D-optimal design does not depend on the correlation structure of errors, and the division of the time interval in D-optimal design does not depend on the ends of time interval. We compare A- and E-optimal designs relatively to the type of dependence. For the considered correlation structures, we study A- and E-efficiency of a design which is optimal in a model with uncorrelated errors.

2. Growth curve model

Consider an experiment where r individuals are assigned to N units. Suppose that the same characteristic is measured at q time points in the time interval $[a,b]$, which are denoted by t_j, $j=1,2,...,q$. Assume that each individual in the unit is observed once at each time point, and all individuals are measured at the same time points. By a design d we mean an allocation of time points in the experiment. Thus, by $\mathcal{D}$ we denote the class of designs with fixed number of individuals and units.

By p we denote a degree of polynomial describing an individual's responses at time points on each unit; in every unit the polynomial coefficients are allowed to be different.

The polynomial growth curve model of such an experiment has the form

$$\mathbf{Y} = \mathbf{A}\mathbf{B}\mathbf{X}_d' + \mathbf{E}, \tag{1}$$

where $\mathbf{Y}$ is an $N \times q$ matrix of observations, the $N \times r$ matrix $\mathbf{A}$ is the design matrix of individuals, the $r \times (p+1)$ matrix $\mathbf{B}$ is the matrix of unknown parameters (regression coefficients), the $q \times (p+1)$ matrix $\mathbf{X}_d$ is the design matrix of time points, and $\mathbf{E}$ is an $N \times q$ matrix of random errors with zero mean. We assume that the observations of individuals on the different units measured at the same time points are uncorrelated, while the correlation between observations of individuals at different time points is described by the matrix $\mathbf{V}$. Hence, the dispersion matrix of errors has the form $\mathrm{D}(\mathrm{vec}(\mathbf{E})) = \sigma^2 \mathbf{V} \otimes \mathbf{I}_N$, where $\mathrm{vec}(\mathbf{E})$ denotes the Nq-dimensional vector formed by writing the columns of $\mathbf{E}$ one under the other in sequence, $\mathbf{V}$ is a known $q \times q$ positive definite matrix, $\mathbf{I}_N$ is the $N \times N$ identity matrix, and the symbol $\otimes$ denotes the Kronecker product.

In the considered model the design matrix of time points, $\mathbf{X}_d$, is of the form:

$$\mathbf{X}_d = \begin{bmatrix} 1 & t_1 & t_1^{\ 2} & \cdots & t_1^{\ p} \\ 1 & t_2 & t_2^{\ 2} & \cdots & t_2^{\ p} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & t_q & t_q^{\ 2} & \cdots & t_q^{\ p} \end{bmatrix}. \tag{2}$$

Since the assignment of observations on units is fixed, observe that the design matrix $\mathbf{A}$ does not depend on the allocation of time points and therefore it is not indexed by d.

Using the property of the "vec" operator, model (1) can be rewritten in univariate manner as

$$\text{vec}\mathbf{Y} = (\mathbf{X}_d \otimes \mathbf{A})\text{vec}\mathbf{B} + \text{vec}\mathbf{E}. \tag{3}$$

Under the polynomial growth curve model, the least squares estimator of $\mathbf{B}$ and the dispersion matrix of $\hat{\mathbf{B}}$ are:

$$\hat{\mathbf{B}} = (\mathbf{A}'\mathbf{A})^{-1}\mathbf{A}'\mathbf{Y}\mathbf{V}^{-1}\mathbf{X}_d(\mathbf{X}_d'\mathbf{V}^{-1}\mathbf{X}_d)^{-1},$$

$$\text{D}(\hat{\mathbf{B}}) = (\mathbf{X}_d'\mathbf{V}^{-1}\mathbf{X}_d)^{-1} \otimes (\mathbf{A}'\mathbf{A})^{-1}.$$

From the assumption that in the design each individual is measured at least once, the matrix $\mathbf{A}'\mathbf{A}$ is a diagonal matrix with the numbers of replications of each individual on the diagonal. Since each individual is measured at different time points, the matrix $\mathbf{X}_d'\mathbf{X}_d$ is nonsingular.

Denoting the inverse of the dispersion matrix $\text{D}(\hat{\mathbf{B}})$ by $\mathbf{M}_d$, i.e.

$$\mathbf{M}_d = (\mathbf{X}_d'\mathbf{V}^{-1}\mathbf{X}_d) \otimes (\mathbf{A}'\mathbf{A}), \tag{4}$$

we obtain the information matrix of a design d for the estimation of $\mathbf{B}$.

We are interested in the optimality of designs in a polynomial growth curve model. An optimality criterion is a function ϕ from the closed cone of nonnegative definite matrices into the real line, where ϕ is isotonic, concave and positive homogeneous (for more details see Pukelsheim, 1993). We will consider the most often used optimality criteria, such as the following.

An A-optimal design d^* maximizes the inverse of the trace of the inverse of information matrix of d^*, i.e. $(\operatorname{tr}\mathbf{M}_{d^*}^{-1})^{-1}$ is maximal over $d \in \mathcal{D}$. This criterion is equivalent to minimizing the average-variance of $\mathrm{D}(\widehat{\mathbf{B}})$. A D-optimal design maximizes the determinant of the information matrix of d^*, i.e. $\det \mathbf{M}_{d^*}$ is maximal over $d \in \mathcal{D}$. An E-optimal design maximizes the smallest eigenvalue of the information matrix of d_E^*, i.e. $\lambda_{\min}(\mathbf{M}_{d^*})$ is maximal over $d \in \mathcal{D}$.

Let d_A^* and d_E^* be, respectively, A- and E-optimal designs in model with correlated errors. For a design d, A- and E-efficiency factors have the following forms:

$$\mathrm{eff}_A(d) = \frac{(\operatorname{tr}\mathbf{M}_d^{-1})^{-1}}{(\operatorname{tr}\mathbf{M}_{d_A^*}^{-1})^{-1}}$$

and

$$\mathrm{eff}_E(d) = \frac{\lambda_{\min}(\mathbf{M}_d)}{\lambda_{\min}(\mathbf{M}_{d_E^*})}.$$

Observe that the matrix $\mathbf{A}'\mathbf{A}$ in (4) does not depend on the allocation of time points. Hence, to determine optimal design in a growth curve model it is enough to consider optimality criteria for the matrix $\mathbf{X}_d'\mathbf{V}^{-1}\mathbf{X}_d$, which will be denoted by $\mathbf{C}_d$. Observe that the matrix $\mathbf{C}_d$ is the information matrix for the estimation of unknown regression coefficients in a univariate polynomial regression model.

Optimality of design in a situation where the matrix $\mathbf{A}$ depends on the design is considered in Markiewicz and Szczepańska (2005).

3. Correlation structures

The correlation structures in a time experiment are relevant if characteristics are measured at three or more consecutive time points. We assume that the correlation between observations of individuals at several time points is described by the matrix $\mathbf{V} = (v_{rs})_{1 \le r,s \le q}$.

A broad overview of the correlation structures of observations in multivariate regression models for analyzing growth curve data is given in Zimmerman and Núñez-Antón (2001). We consider three covariance structures of observations proposed in that paper, and the nearest neighbor correlation structure proposed for example by Cheng (1988).

Once and for all, we will assume, for obvious technical reasons, that the correlation coefficient between observations from different time points is positive, i.e. belongs to the interval $[0,1)$.

3.1. The nearest-neighbor correlation structure NN(1)

The correlation matrix of the nearest-neighbor model has elements of the form

$$v_{rs} = \begin{cases} 1 & \text{if} \quad r = s \\ \rho & \text{if} \quad |r-s| = 1 \\ 0 & \text{otherwise} \end{cases}$$

(Cheng, 1988). This correlation structure is relevant to the model, in which only observations measured at neighboring time points are correlated. The assumption that $\mathbf{V}$ is a positive definite matrix implies that $\rho \in [0, \frac{\sqrt{2}}{2})$ for the quadratic growth curve models and $\rho \in [0, \frac{\sqrt{5}-1}{2})$ for the cubic growth curve models.

3.2. The first-order autoregression AR(1)

For the first-order autoregressive model, the correlation matrix $\mathbf{V}$ has elements of the form

$$v_{rs} = \rho^{|r-s|},$$

which shows that the dependence between observations at two time points decreases exponentially with the distance between time points (Zimmerman and Núñez-Antón (2001)). Observe that each value of the correlation coefficient $\rho \in [0,1)$ satisfies nonnegative-definiteness of the matrix $\mathbf{V}$ for both quadratic and cubic growth curve models.

3.3. The second-order moving average MA(2)

The response correlations between observations in the second-order moving average model are given by

$$v_{rs} = \begin{cases} 1 & \text{if} \quad r = s \\ \rho_{|r-s|} & \text{if} \quad |r-s| = 1,2 \\ 0 & \text{if} \quad |r-s| \geq 3 \end{cases}$$

(Zimmerman and Núñez-Antón (2001)). Since the matrix $\mathbf{V}$ is positive definite, the correlation coefficients $\rho_i \in [0,1)$, $i = 1,2$, must satisfy the conditions $(1-\rho_2)(1+\rho_2-2\rho_1^2) > 0$ for the quadratic growth curve model, and in addition $\rho_1^4 - \rho_1^2(2\rho_2^2 - 4\rho_2 + 3) + (\rho_2^2 - 1)^2 > 0$ for the cubic. This implies that the values of the correlation coefficients lie within the area shown in Figure 1.

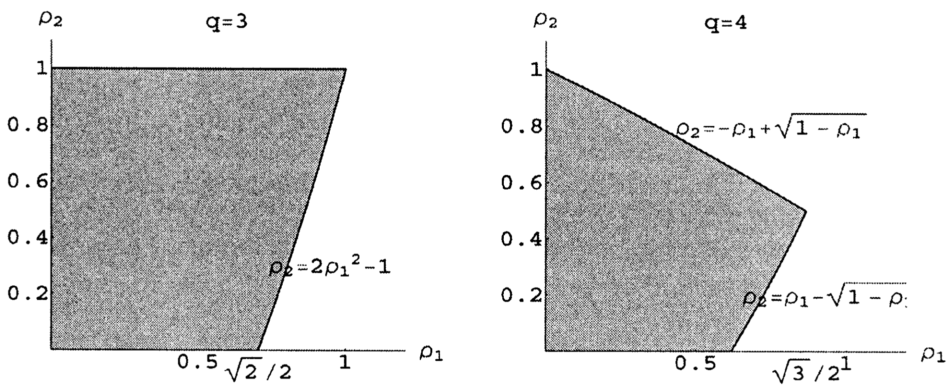

Figure 1. The area of values of the correlation coefficients

3.4. The first-order unstructured antedependence errors UAD(1)

Definition and properties of the first-order unstructured antedependence are given below, following Zimmermann and Núñez-Antón (2001).

The UAD(1) generalizes the stationary AR(1) by allowing the autoregressive coefficients to vary with time. The effect of this is to allow the correlations between responses equidistant in time to vary. This greater generality makes UAD models useful for situations in which measurement times are unequally spaced or there is clear evidence of nonstationarity in the data's correlation structure.

In the first-order unstructured antedependence model, response correlations between observations lagged 1 observation apart are arbitrary, but correlations between observations lagged more than 1 observation apart are completely determined by those corresponding to lags of 1. This implies that the variance-covariance matrix of UAD(1) has elements of the form:

$$v_{rs} = \begin{cases} 1 & \text{if} \quad r = s \\ \prod_{k=r}^{s-1} \rho_k & \text{if} \quad r < s \\ \prod_{k=s}^{r-1} \rho_k & \text{if} \quad r > s \end{cases}$$

(Zimmerman and Núñez-Antón, 2001). The correlation coefficients $\rho_i \in (0,1)$, $i = 1,2,3$, satisfy the conditions for positive definiteness of **V**, i.e. $(1-\rho_1^2)(1-\rho_2^2) > 0$ for quadratic growth curve models and in addition $(1-\rho_1^2)(1-\rho_2^2)(1-\rho_3^2) > 0$ for cubic.

4. Results

In this section we give A-, D- and E-optimal designs under growth curve models with correlated errors. We assume that in quadratic growth we observe characteristics at three time points, while in cubic growth, they are observed, at four (for more details see e.g. Garza, 1954, Pukelsheim, 1993, or Mandal, 2002).

For D-optimal designs we show that the allocation of time points does not depend on the correlation structure of errors. Moreover, we determine D-optimal time points in an arbitrary time interval $[a,b]$. Since designing a longitudinal study often requires fixing the first and the last time point, we consider designs with the first time point a and the last time point b.

Since we want to compare A- and E-optimality results on models with correlated errors relative to the type of dependence (including uncorrelated errors), following Moerbeek (2005) we assume that the time interval is $[0,2]$.

4.1. D-optimal designs

First we show that D-optimal designs do not depend on the correlation structure of errors. From the properties of the determinant we can write the D-criterion as

$$\max_{d\in\mathcal{D}} \det \mathbf{C}_d = \max_{d\in\mathcal{D}} \det(\mathbf{X}'_d \mathbf{V}^{-1}\mathbf{X}_d) = \frac{1}{\det \mathbf{V}} \max_{d\in\mathcal{D}} (\det \mathbf{X}_d)^2 \tag{5}$$

and hence D-optimal designs do not depend on the type of correlation. Following Moerbeek (2005), for growth curve models with uncorrelated errors, D-optimal time points are equal respectively to 0 and 2 for linear growth, 0, 1 and 2 for quadratic growth, and 0, 0.553, 1.447 and 2 for cubic growth.

Moreover, D-optimal designs do not depend on the chosen time interval $[a,b]$. Observe that the matrix $\mathbf{X}_d$ defined in (2) for $q = p+1$ is a Vandermonde matrix, for which

$$\det \mathbf{X}_d = \prod_{\substack{i,j=1 \\ i>j}}^{q} (t_i - t_j)$$

(Horn and Johnson, 1985). From this formula it is easy to see that this determinant does not change if the experimental domain is $[a+\alpha_1, b+\alpha_1]$. For the interval $[\alpha_2 a, \alpha_2 b]$ we obtain the determinant $\alpha^q \det \mathbf{X}_d$, which does not change the time points for which the maximum in (5) is obtained. Hence, D-optimal time points from the interval $[a,b]$ and from $[\alpha_2 a+\alpha_1, \alpha_2 b+\alpha_1]$ determine the same division of the respective time interval.

For quadratic and cubic growth curve models with correlated errors, the D-optimal time points from the interval $[a,b]$ are:

$$a, \frac{a+b}{2}, b \quad \text{for quadratic growth, and}$$

$$a, \frac{5(a+b)+\sqrt{5}(a-b)}{10}, \frac{5(a+b)-\sqrt{5}(a-b)}{10}, b \quad \text{for cubic growth.}$$

4.2. A- and E-optimal designs

In this section we present A- and E-optimal allocation of time points in models with different correlation structures relative to the type of dependence. For the considered correlation structures, we study A- and E-efficiency of the designs d_A^0 and d_E^0, which are, respectively, A- and E-optimal in growth curve models with uncorrelated errors. A- and E-optimal optimal time points for growth curve models with uncorrelated errors are presented in Table 1 (Moerbeek, 2005).

Table 1

	d_A^0	d_E^0
quadratic growth	0, 1.057, 2	0, 1.069, 2
cubic growth	0, 0.528, 1.572, 2	0, 0.526, 1.582, 2

Figure 2 and Figure 4 present optimal allocations of time points in, respectively, quadratic and cubic growth models with NN(1) and AR(1) correlation structure, as a function of the correlation coefficient ρ. Figure 3 and Figure 5 show the optimal allocation of time points in these models relative to the type of dependence. Figure 6 and Figure 7 present the optimal allocation of time points as a function of ρ_1 and ρ_2, in a quadratic growth curve model with MA(2) and UAD(1) correlation structures, respectively.

From Figure 2 it can be seen that in quadratic growth curve models with small correlation coefficient, A- and E-optimal designs are similar in both NN(1) and AR(1) models. Moreover, these optimal allocations of time points tend to the optimal allocation of time points in a model with uncorrelated observations. This implies that efficiency factors should be very high. Computation shows that the A- and E-efficiency factors of the designs d_A^0 and d_E^0 are very high (>0.9) for all values of the correlation coefficient. Moreover, for $\rho \le 0.5$, the A- and E-efficiency factors are very close to 1 (>0.99), except for the E-efficiency factor of the model with NN(1), which is, however, at least 0.977.

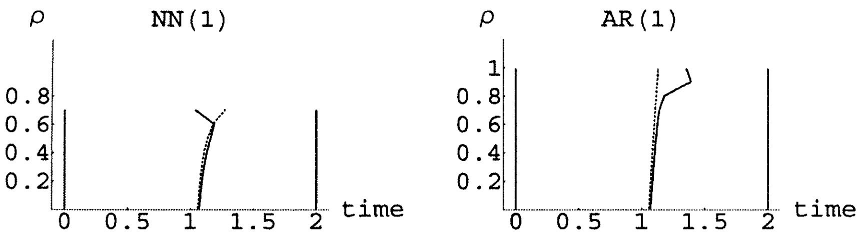

Figure 2. $q = 3$; Dotted lines: A-optimal design; Solid lines: E-optimal design

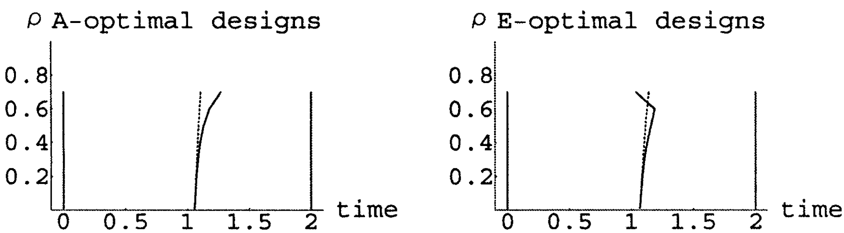

Figure 3. $q = 3$; Dotted lines: AR(1); Solid lines: NN(1)

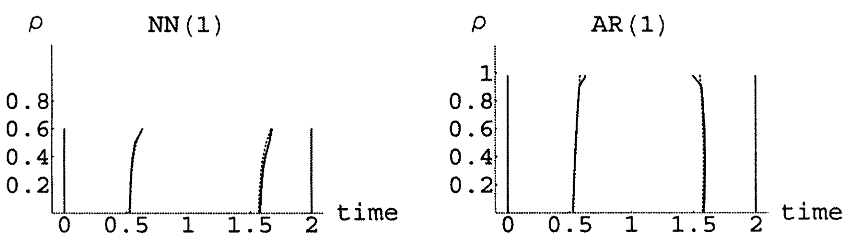

Figure 4. $q = 4$; Dotted lines: A-optimal design; Solid lines: E-optimal design

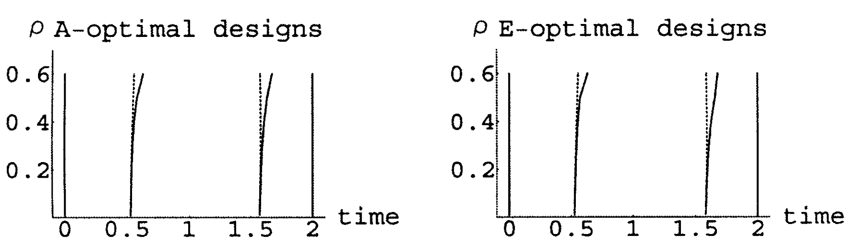

Figure 5. $q = 4$; Dotted lines: AR(1); Solid lines: NN(1)

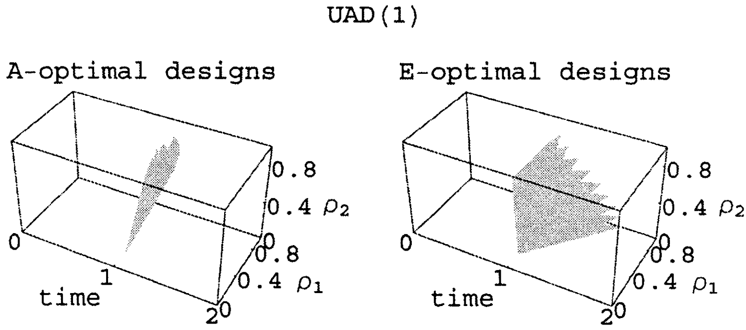

Figure 6. $q=3$

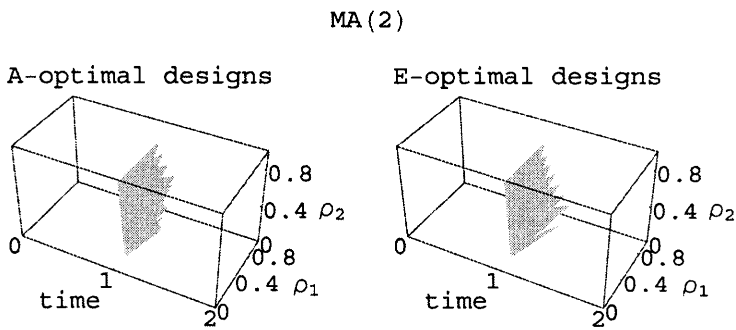

Figure 7. $q=3$

From Figure 4 it can be seen that in the cubic growth models with NN(1) or AR(1), the A- and E-optimal designs are almost the same for all values of the correlation coefficient. If the correlation coefficient ρ increases, then the optimal allocation of time points in models with NN(1) and AR(1) differs widely from the optimal allocation of time points in a model with uncorrelated observations. Moreover, for large ρ, the optimal time points in a model with NN(1) change more rapidly than the optimal time points in a model with AR(1). By calculation it is formed that the A- and E-efficiency factors in a model with NN(1) are at least 0.9 for $\rho \le 0.54$ and $\rho \le 0.51$ respectively. For higher values of ρ, the efficiency factors decrease rapidly. In a model with AR(1), both A- and E-efficiency factors are close to 1 (>0.977) for all values of the correlation coefficient.

Since in models with UAD(1) and MA(2) we have two correlation coefficients (and three in the cubic growth curve model with UAD(1)), it is difficult to compare A- and E-optimal designs. Therefore in these cases we study the efficiency of designs d_A^0 and d_E^0.

For the quadratic growth curve model with UAD(1), if the difference between ρ_1 and ρ_2 increases, then the values of the A- and E-optimal time points decrease. Nevertheless, the majority of efficiencies is higher than 0.9. From Figure 8 it can be observed that efficiencies decrease if the correlation coefficients lie at the end of the area of values of the correlation coefficients.

In the quadratic growth curve model with MA(2), if $\rho_1 < \rho_2$, the values of optimal time points are smaller than the values of optimal time points in a model with uncorrelated errors in the majority of cases. Comparing the A- and E-optimal designs, we can observe that these optimal allocations of time points are similar. From the analysis of efficiency it can be observed that both A- and E-efficiency factors are at least 0.89 for all values of the correlation coefficients. Moreover, the majority of efficiency factors are at least 0.95.

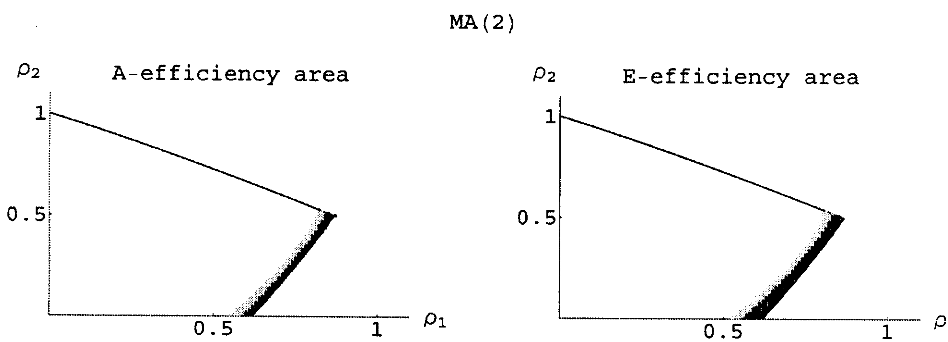

Figure 8. The efficiency factors for a quadratic growth: $\text{eff}(d^0) \geq 0.9$ - white, $0.8 \leq \text{eff}(d^0) < 0.9$ - gray, $\text{eff}(d^0) < 0.8$ - black

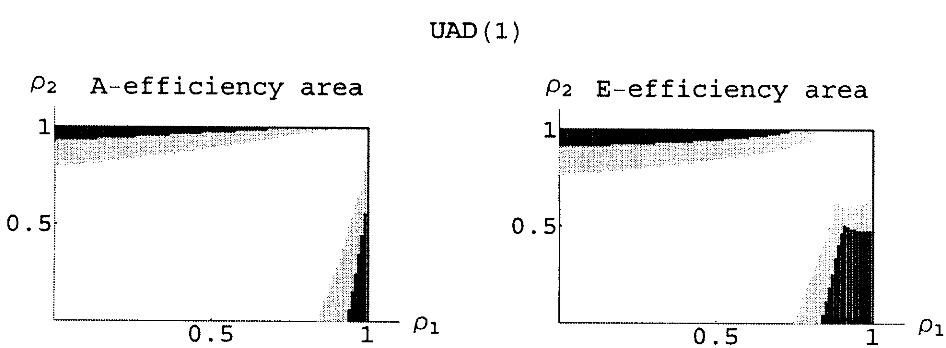

Figure 9. The efficiency factors for a cubic growth: $\text{eff}(d^0) \geq 0.9$ - white, $0.8 \leq \text{eff}(d^0) < 0.9$ - gray, $\text{eff}(d^0) < 0.8$ - black

It can be seen that, for large ρ_2, the values of both A- and E-optimal time points in a model with UAD(1) are higher than in a model with MA(2).

From the analysis of the efficiency of d_A^0 and d_E^0 in the cubic growth curve model with UAD(1), it follows that both efficiencies are very diversified.

In the cubic growth curve model with MA(2), from the analysis of the efficiency of d_A^0 and d_E^0 it follows that in the majority of cases both A- and E-efficiency factors are at least 0.91. From Figure 9 it can be seen that the efficiency decreases for such correlation coefficients, that lie at the end of the area of values of the correlation coefficients.

By calculation it follows that the E-efficiency factors are smaller than the A-efficiency factors. For example, the minimal efficiencies are $\text{eff}_A(d_A^0) = 0.421$ (if $\rho_1 = 0.86$ and $\rho_2 = 0.49$) and $\text{eff}_E(d_E^0) = 0.319$ (if $\rho_1 = 0.83$ and $\rho_2 = 0.43$).

From the results presented it follows that there exist differences between growth curve models with different correlation structures mainly for large values of the correlation coefficients. It has been shown that, for small or relatively small values of the correlation coefficients, the optimal designs in a model with uncorrelated errors are highly efficient in models with correlated errors. In such situations, these designs can be recommended in practice.

If the correlation coefficients are large, the efficiency of designs which are optimal for $\rho = 0$ decreases. In these cases, the experimenter should consider an alternative choice of time points.

The results presented in this paper imply that optimality of a design depends on the values of correlation coefficients as well as on the correlation structure. Since in growth curve models with NN(1), AR(1) and MA(2) the efficiency of designs which are optimal in a model with uncorrelated errors is very high, these designs are recommended for use in practice. Observe however that, since in the model with UAD(1) the efficiency is more diversified, an experimenter should not ignore this dependence and should use time points which are optimal in that model.

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