Optimal Designs in Random Intercept Model with Heteroscedastic Errors

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Abstract
This paper considers optimal designs based on the D-, G-, A-, I- and Ds-optimality criteria for a random intercept model with heteroscedastic errors. It is shown that the search of optimal approximate designs can be confined at extreme settings of the design region if heteroscedastic structure satisfies specified conditions. Closed expressions for the optimal proportions are given.
Keywords Optimal design, Random intercept model, Heteroscedastic errors, Identical design

1 Introduction

Random coefficient models have been widely used for the researching in the area of biosciences, psychology and population pharmacokinetics, where repeated measurements are available from different individuals. These models have been introduced by Longford[1], for recent researching we refer to Pena and Yohai[2] and Yu[3]. In recent years, the problem of optimal designs for random coefficient models has attracted growing interest. Schmelter[4-5] showed that optimal designs in the linear mixed models could be restricted to the class of group-wise identical designs, and optimal designs in the class of single-group designs were also optimal designs in the larger class of more group designs when the design criteria satisfied some assumptions. Schwabe and Schmelter[6], Schmelter et al[7] and Luoma et al[8] . investigated optimal designs in random intercept model, random slope model and random coefficient cubic regression model, respectively. Entholzner et al[9] obtained optimal and efficient designs in mixed models. Debusho and Haines[10] provided V-optimal and D-optimal designs with longitudinal data in linear regression models with a random intercept.

There are many other results of optimal designs are obtained, such as Wang et al[11], Yu[12] and Wen et al[13]. In this article, we investigate the problem of optimal designs based on some common optimality criteria for a random intercept model with heteroscedastic errors. In Section 2, we introduce the model with necessary notations. Section 3 provides a lemma which makes it sure that we can confine the search of optimal designs at extreme settings of the design region if the optimality criteria satisfy an assumption. Simple expressions of these optimal designs are given in this section. Section 4 introduces some examples. Proof of Lemma 1 is given in Appendix.

2 The Random Intercept Model with Heteroscedastic Errors

We investigate a linear regression model on the unit interval with a random intercept and heteroscedastic errors. It is assumed that there are individuals with observations each, and the jth observation of ith individual is described by

$$y_{ij} = \mu_i + x_{ij}\beta + e(x_{ij}), \quad i = 1, ..., n; \quad j = 1, ..., m_i. \tag{1}$$

Where, $x_{ij} \in [0, 1]$ is the experimental setting; μ_i denotes the ith individual effect with unknown mean μ and known variance σ_μ^2; β is the unknown slope parameter; observational errors $e(x_{ij})$ are assumed to be heteroscedastic with zero mean and variance $\sigma^2/\lambda(x_{ij})$, here σ^2 is known and $\lambda(x_{ij})$ is a positive real-valued continuous function defined on [0,1]. We assume that

$$\begin{cases} COV(\mu_i, \mu_{i'}) = 0, \quad i \neq i' \\ COV(\mu_i, e(x_{i'j})) = 0, \quad \forall i, i'; \\ COV(e(x_{ij}), e(x_{i'j'})) = 0, \quad (i, j) \neq (i', j'). \end{cases}$$

For the ith individual, denote

$$Y_i = \begin{pmatrix} y_{i1} \\ \vdots \\ y_{im_i} \end{pmatrix}, \quad X_i = \begin{pmatrix} x_{i1} \\ \vdots \\ x_{im_i} \end{pmatrix}, \quad e(x_i) = \begin{pmatrix} e(x_{i1}) \\ \vdots \\ e(x_{im_i}) \end{pmatrix}, \quad F_i = (1_{m_i}, X_i)$$

Here 1_{m_i} is a vector of length m_i with all entries equal one. Then the model (1) can be expressed by

$$Y_i = F_i \begin{pmatrix} \mu \\ \beta \end{pmatrix} + 1_{m_i}(\mu_i - \mu) + e(x_i) \triangleq F_i\theta + 1_{m_i}(\mu_i - \mu) + e(x_i), \quad i = 1, \ldots, n.$$

By the assumptions we have $(\mu_i - \mu) \sim (0, \sigma_\mu^2)$ and

$$V_i \triangleq COV(Y_i) = \sigma^2 diag\{1/\lambda(x_{i1}), \ldots 1/\lambda(x_{im_i})\} + \sigma_\mu^2 1_{m_i} 1_{m_i}^T \triangleq \sigma^2(D_i + d 1_{m_i} 1_{m_i}^T).$$

Here $D_i = diag\{1/\lambda(x_{i1}), \ldots 1/\lambda(x_{im_i})\}$ and $d = \sigma_\mu^2/\sigma^2$. For all n individuals, the vector of all observations can be expressed by

$$Y = \begin{pmatrix} Y_1 \\ \vdots \\ Y_n \end{pmatrix} = \begin{pmatrix} F_1 \\ \vdots \\ F_n \end{pmatrix} \theta + \begin{pmatrix} 1_{m_1} & & 0 \\ & \ddots & \\ 0 & & 1_{m_n} \end{pmatrix} \begin{pmatrix} \mu_1 - \mu \\ \vdots \\ \mu_n - \mu \end{pmatrix} + \begin{pmatrix} e(x_1) \\ \vdots \\ e(x_n) \end{pmatrix} \tag{2}$$

The design matrix for random intercepts is block diagonal, e.g.,

$$\begin{pmatrix} 1_{m_1} & & 0 \\ & \ddots & \\ 0 & & 1_{m_n} \end{pmatrix}.$$

Consequently, the covariance matrix of Y is $COV(Y) = diag\{V_1, \ldots, V_n\}$. The best linear unbiased estimate of θ is given by

$$\hat{\theta} = \left(\sum_{i=1}^{n} F_i^T V_i^{-1} F_i\right)^{-1} \sum_{i=1}^{n} F_i^T V_i^{-1} Y_i. \tag{3}$$

And we can get

$$COV(\hat{\theta}) = \left(\sum_{i=1}^{n} F_i^T V_i^{-1} F_i\right)^{-1}.$$

3 Optimal Designs

In this section, we investigate the optimal designs based on D-, G-, A-, I- and Ds-optimality criteria for the models described in previous section. The D-optimal design minimizes the generalized variance of parameter estimates, the G-optimal design minimizes the maximum variance of the predicted value of the response over the design region, the A-optimal design minimizes the total variance of the parameter estimates, the I-optimal design minimizes the integrated mean squared error and the interest of Ds-optimal design is in estimating the slope.

In some practical situations like human or animal pharmaceutics studies or medical diagnostics there are often restrictions, e.g., technical implementations, which force the experiment to be performed with identical regimes for all individuals. This means that for each individual the number m_i of repeated measurements equals m and experimental settings $x_{ij} = x_j$ are identical across all the individuals. So we only consider identical designs in the following, i.e., $m_i = m$, $x_i = x_1$ and hence, $F_i = F_1$, $V_i = V$ for all i. Then the best linear unbiased estimate of θ can be written as

$$\hat{\theta} = \left(nF_1^T V_1^{-1} F_1\right)^{-1} F_1^T V_1^{-1} \sum_{i=1}^{n} Y_i.$$

Here

$$\begin{aligned} V_1^{-1} &= \frac{1}{\sigma^2}\left(D_1 + d1_m 1_m^T\right)^{-1} \\ &= \frac{1}{\sigma^2}\left(D_1^{-1} - \frac{dD_1^{-1}1_m 1_m^T D_1^{-1}}{1 + d1_m^T D_1^{-1} 1_m}\right) \\ &= \frac{1}{\sigma^2}\left(diag\{\lambda(x_j)\} - \frac{dD_1^{-1}1_m 1_m^T D_1^{-1}}{1 + d\sum_{j=1}^{n} \lambda(x_j)}\right). \end{aligned}$$

Without loss of generality, we assume $\sigma^2 = 1$ in the followings. Furthermore, we will consider approximate designs. For any approximate design ξ of the following form

$$\xi = \begin{pmatrix} x_1, & \dots, & x_p \\ \omega_1, & \dots, & \omega_p \end{pmatrix}, \quad 2 < p < m, \quad \sum_{j=1}^{p} \omega_j = 1. \tag{4}$$

Denote

$$\nu_k = \int_0^1 x_k \lambda(x) d\xi(x) = \sum_{j=1}^{p} \omega_j x_j^k \lambda(x_j), \quad k = 0, 1, 2.$$

Then the information matrix corresponding to the design ξ of the form (4) can be expressed by

$$M(\xi) = \frac{mn}{1 + \gamma\nu_0} \begin{pmatrix} \nu_0 & \nu_1 \\ \nu_1 & \nu_2 + \gamma(\nu_0\nu_2 - \nu_1^2) \end{pmatrix}. \tag{5}$$

Here we note $\gamma = md$.

For regression model without any random effects, optimal designs are obtained at extreme settings of the design region and Schwabe et al[6] discussed optimal designs of random intercept models. We can't use the conclusions in Schwabe et al[6] directly in the random intercept model with heteroscedastic errors, but we have the following lemma.

Lemma 1 *In the model (2), assume that* $m_i = m, (i = 1, \dots, n)$ *and* $\lambda(x)$ *satisfies the following condition*

$$\frac{1}{\lambda(x)} \geq \frac{1 - x}{\lambda_0} + \frac{x}{\lambda(1)}, x \in [0, 1]. \tag{6}$$

Where $\lambda_0 = \lambda(0)$ *and* $\lambda_1 = \lambda(1)$. *Then for any approximate design* ξ *of the form (4), there exists an approximate design of the form*

$$\xi^* = \begin{pmatrix} 0, & 1 \\ 1 - \omega, & \omega \end{pmatrix}, \quad 0 < \omega < 1.$$

Such that $M(\xi^*) \geq M(\xi)$.

The proof of Lemma 1 can be found in the Appendix.

The criteria, $\Phi(\cdot)$, considered in this paper are functions of the information matrices which are required to satisfy the following assumptions:

A1 $\Phi(\cdot)$, is a real-valued function defined on the whole set $\mathcal{M}$ of 2×2 symmetric non-negative definite matrices, $\Phi : M \to (-\infty, \infty]$;

A2 $\Phi(\cdot)$ is monotone (the Loewner order (e.g., Pukelsheim[14], p.101)) on $\mathcal{M}$ in the sense that $M_1, M_2 \in \mathcal{M}, \mathcal{M}_\infty \geq \mathcal{M}_\in \Rightarrow \oplus(\mathcal{M}_\infty) \leq \oplus(\mathcal{M}_\in)$.

These assumptions are satisfied for most of the common criteria including the D-, G-, A-, I- and Ds-optimality. So, by majorization we can confine the search of optimal designs at extreme settings $x = 0$ and $x = 1$ if $\lambda(x)$ satisfies the condition (6) in Lemma 1. Therefore, in what follows we only consider approximate designs ξ of the form

$$\xi = \begin{pmatrix} 0 & 1 \\ 1-\omega & \omega \end{pmatrix}. \tag{7}$$

For approximate designs of the form (7), we have

$$\nu_0 = \lambda_1\omega + \lambda_0(1-\omega), \quad \nu_1 = \nu_2 = \lambda_1\omega.$$

First, we consider the D-optimality $\Phi(M(\xi)) = \left|M^{-1}(\xi)\right|$. Note that

$$|M(\xi)| \triangleq |M(\omega)| = \frac{(mn)^2\lambda_0\lambda_1\omega(1-\omega)}{1+\gamma[\omega\lambda_1+(1-\omega)\lambda_0]}.$$

It is easy to verify that $|M(\omega)|$ is maximized at $\omega = \sqrt{1+\gamma\lambda_0}/(\sqrt{1+\gamma\lambda_0}+\sqrt{1+\gamma\lambda_1})$ and hence $\left|M^{-1}(\omega)\right|$ is minimized. Therefore we have

Theorem 1 *For the model (2) with $m_i = m$ $(i = 1,\ldots,n)$ and $\lambda(x)$ satisfying (6) the D-optimal design is*

$$\xi_D^* = \begin{pmatrix} 0, & 1 \\ 1-\omega_D, & \omega_D \end{pmatrix}, \quad \omega_D = \frac{\sqrt{1+\gamma\lambda_0}}{\sqrt{1+\gamma\lambda_0}+\sqrt{1+\gamma\lambda_1}}$$

For the Ds-optimality, note that the covariance matrix of $\hat{\theta}$ can be calculated by

$$\begin{aligned} M^{-1}(\omega) &= \frac{1}{mn(\nu_0-\nu_2)}\begin{pmatrix} 1+\gamma(\nu_0-\nu_1) & -1 \\ -1 & \frac{\nu_0}{\nu_1} \end{pmatrix} \\ &= \frac{1}{mn}\begin{pmatrix} \frac{1}{\lambda_0(1-\omega)}+\gamma & -\frac{1}{\lambda_0(1-\omega)} \\ -\frac{1}{\lambda_0(1-\omega)} & \frac{1}{\lambda_0(1-\omega)}+\frac{1}{\lambda_1(\omega)} \end{pmatrix} \end{aligned}$$

The variance of the estimate for β is given by

$$COV(\hat{\beta}) = [M^{-1}(\omega)]_{22} = \frac{1}{mn}[\frac{1}{\lambda_0(1-\omega)}+\frac{1}{\lambda_1\omega}].$$

The variance of $\hat{\beta}$ is minimized at $\omega = \sqrt{\lambda_0}/(\sqrt{\lambda_0}+\sqrt{\lambda_1})$. Therefore we have

Theorem 2 *For the model (2) with $m_i = m$ $(i = 1,\ldots,n)$, and $\lambda(x)$ satisfying (6) the Ds-optimal design is*

$$\xi_{D_s}^* = \begin{pmatrix} 0, & 1 \\ 1-\omega_{D_s}, & \omega_{D_s} \end{pmatrix}, \quad \omega_{D_s} = \frac{\sqrt{\lambda_0}}{\sqrt{\lambda_0}+\sqrt{\lambda_1}}.$$

Consider the G-optimality, then $\Phi(M(\omega)) = \max_{x\in[0,1]} d(\omega, x)$. Here $d(\omega, x)$ is the variance of the predicted value of the response, which is given by

$$\begin{aligned} d(x,\omega) &= \begin{pmatrix} 1 & x \end{pmatrix} M^{-1}(\omega) \begin{pmatrix} 1 \\ x \end{pmatrix} \\ &= \frac{1}{mn}\Big\{\Big[\frac{1}{\lambda_0(1-\omega)} + \frac{1}{\lambda_1\omega}\Big]x^2 - \frac{2x}{\lambda_0(1-\omega)} + \frac{1}{\lambda_0(1-\omega)} + \gamma\Big\}. \end{aligned}$$

As $d(\omega, x)$ is a polynomial of degree 2 with positive leading term, its maximum is attained either $x = 0$ or $x = 1$ or both, i.e., $max\ d(\omega, x) = \max_{x\in[0,1]}\{d(0, \omega), d(1, \omega)\}$. Note that

$$d(0,\omega) = \frac{1}{mn}\Big\{\frac{1}{\lambda_0(1-\omega)} + \gamma\Big\} \quad \text{is strictly increasing in } \omega,$$

$$d(1,\omega) = \frac{1}{mn}\Big\{\frac{1}{\lambda_1(\omega)} + \gamma\Big\} \quad \text{is strictly decreasing in } \omega.$$

Thus $\min_{\omega\in[0,1]} \max_{x\in[0,1]} d(x, \omega)$ is attained when $d(0, \omega) = d(1, \omega)$, i.e.,

$$\frac{1}{\lambda_0(1-\omega)} = \frac{1}{\lambda_1(\omega)}.$$

So we have

Theorem 3 *For the model (2) with $m_i = m$ $(i = 1, \dots, n)$, and $\lambda(x)$ satisfying (6) the G-optimal design is*

$$\xi_G{}^* = \begin{pmatrix} 0, & 1 \\ 1-\omega_G, & \omega_G \end{pmatrix}, \quad \omega_G = \frac{\lambda_0}{\lambda_0 + \lambda_1}.$$

For the I-optimality,

$$\Phi(M(\omega)) = \int_0^1 d(x,\omega)dx = \frac{1}{mn}\Big[\gamma + \frac{1}{3\lambda_0(1-\omega)} + \frac{1}{3\lambda_1\omega}\Big].$$

Which is minimized at $\omega = \sqrt{\lambda_0}/(\sqrt{\lambda_0} + \sqrt{\lambda_1}) = \omega_{D_s}$. So we have

Theorem 4 *For the model (2) with $m_i = m$ $(i = 1, \dots, n)$, and $\lambda(x)$ satisfying (6) the I-optimal design is*

$$\xi_I^* = \begin{pmatrix} 0, & 1 \\ 1-\omega_I, & \omega_I \end{pmatrix}, \quad \omega_I = \frac{\sqrt{\lambda_0}}{\sqrt{\lambda_0} + \sqrt{\lambda_1}}.$$

For the A-optimality

$$\Phi(M(\omega)) = tr\big(M^{-1}(\omega)\big) = \frac{1}{mn}\Big[\frac{1}{\lambda_1\omega} + \frac{2}{\lambda_0(1-\omega)} + \gamma\Big].$$

It is easy to verify that $tr\big(M^{-1}(\omega)\big)$ is minimized at $\omega = \frac{\sqrt{\lambda_0}}{\sqrt{\lambda_0}+\sqrt{2\lambda_1}}$ .Therefore we have

Theorem 5 *For the model (2) with $m_i = m$ $(i = 1, \dots, n)$, and $\lambda(x)$ satisfying (6) the A-optimal design is*

$$\xi_A{}^* = \left(\begin{array}{cc} 0, & 1 \\ 1-\omega_A, & \omega_A \end{array}\right), \quad \omega_I = \frac{\sqrt{\lambda_0}}{\sqrt{\lambda_0}+\sqrt{2\lambda_1}}.$$

From above discussion, we observe that the G-, Ds-, I- and A-optimal designs only depend on the variances at extreme settings; the D-optimal design depends repeated times m and variance proportion d and error variances at the extreme settings. Note that the particular shape of $\lambda(x)$ is immaterial for the results, but only its values at 0 and 1, as long as condition (6) is satisfied.

Specially, when heteroscedastic structure satisfies $\lambda_0 = \lambda_1 = \max_{x\in[0,1]} \lambda(x)$, the optimal designs discussed above are independent of the variance ratio d. These optimal designs are the same as the corresponding optimal designs in the linear regression model without any random effects, i.e.,

$$\omega_D = \omega_G = \omega_I = \omega_{D_s} = \frac{1}{2}, \quad \omega_A = \sqrt{2} - 1.$$

4 Examples

In this section, we consider three random intercept models with the following heteroscedastic errors

$$\lambda(x) = x^2 + 1, \quad \lambda(x) = \frac{1}{1+x}, \quad \lambda(x) = \frac{x^4+1}{x^2+1}.$$

It is easy to verify that these three $\lambda(x)$ satisfy the condition (6). These heteroscedastic structures are also considered in Chang[15] for D-optimal designs in weighted polynomial regression models.

We will give the optimal designs for the three models in terms for the results given in Section 3. We also compare the D- and G-optimal designs for the three models with the equireplicated design $\omega_0 = 0.5$ which is simultaneously D- and G-optimal for the fixed effects only model ($d = 0$) in terms of the D- and G-efficiency which are defined as following

$$Eff_D(\omega_0) = \left(\frac{|M(\omega_0)|}{|M(\omega)|}\right)^{\frac{1}{2}}, \quad Eff_D(\omega_0) = \frac{\max_{x\in[0,1]} d(x,\omega_G)}{\max_{x\in[0,1]} d(x,\omega_0)} \tag{8}$$

Example 1 *For the model (2) with* $m_i = m(i = 1, \ldots, n)$*, and* $\lambda(x) = x^2 + 1$ *, from the theorems in Section 3, we obtain the D-, G-, A-, I- and Ds-optimal proportions as follows:*

$$\omega_D = \frac{\sqrt{1+\gamma}}{\sqrt{1+\gamma} + \sqrt{1+2\gamma}}, \quad \omega_G = \omega_A = \frac{1}{3}, \quad \omega_I = \omega_{D_s} = \sqrt{2} - 1.$$

The D- and G-efficiencies defined by (8) of the equireplicated design $\omega_0 = 0.5$ *are as follows:*

$$Eff_D(\omega_0) = \frac{\sqrt{1+2\gamma} + \sqrt{1+\gamma}}{\sqrt{4+6\gamma}}, \quad Eff_D(\omega_0) = \frac{\gamma + 1.5}{\gamma + 2}.$$

It is clear that $Eff_D(\omega_0)$ decreases strictly in γ and ultimately tends to $(\sqrt{2} + 1)/\sqrt{6}$, and $Eff_D(\omega_0)$ increases strictly in γ and ultimately tends to one. Fig.1 shows the plots of these two efficiencies.

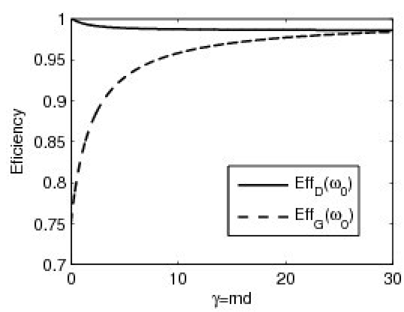

Fig.1 The efficiencies of $Eff_D(\omega_0)$ and $Eff_G(\omega_0)$ with different λ

Example 2 *For the model (2) with* $m_i = m(i = 1, \ldots, n)$*,and* $\lambda(x) = \frac{1}{1+x}$*, the D-, G-, A-, I- and Ds-optimal proportions as follows:*

$$\omega_D = \frac{\sqrt{2+2\gamma}}{\sqrt{+\gamma} + \sqrt{2+2\gamma}}, \quad \omega_G = \frac{2}{3}, \quad \omega_A = \frac{1}{2}, \quad \omega_I = \omega_{D_s} = 2 - \sqrt{2}.$$

The D- and G-efficiencies defined by (8) of the equireplicated design $\omega_0 = 0.5$ *are as follows:*

$$Eff_D(\omega_0) = \frac{\sqrt{2+2\gamma} + \sqrt{2+\gamma}}{\sqrt{8+6\gamma}}, \quad Eff_D(\omega_0) = \frac{\gamma + 3}{\gamma + 4}.$$

It is clear that $Eff_D(\omega_0)$ *decreases strictly in* γ *and ultimately tends to* $(\sqrt{2} + 1)/\sqrt{6} = 0.9856$*, and* $Eff_D(\omega_0)$ *increases strictly in* γ *and ultimately tends to one. Fig.2 shows the plots of these two efficiencies.*

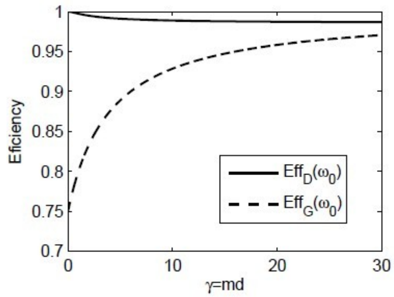

Fig.2 The efficiencies of $Eff_D(\omega_0)$ and $Eff_G(\omega_0)$ with different λ

Example 3 *For the model (2) with* $m_i = m$ $(i = 1, \ldots, n)$, *and* $\lambda(x) = \frac{x^4+1}{x^2+1}$, *the D-, G-, A-, I- and Ds-optimal proportions as follows:*

$$\omega_D = \omega_G = \omega_I = \omega_{D_s} = \frac{1}{2}, \quad \omega_A = \sqrt{2} - 1.$$

That is, the D-, G-, I- and Ds-optimal designs are all the equireplicated designs.

Appendix

Proof of Lemma 1 *From Liski et al[16], we get*

$$M^{-1}(\xi) = M_0^{-1}(\xi) + \begin{pmatrix} \frac{d}{n} & 0 \\ 0 & 0 \end{pmatrix}$$

Here $M_0(\xi)$ *is the corresponding generalized information matrix when there are no individual intercepts, i.e.,*

$$M_0(\xi) = mn \begin{pmatrix} \nu_0 & \nu_1 \\ \nu_1 & \nu_2 \end{pmatrix}.$$

Let the proportion ω *in* ξ^* *be of the form* $\omega = \nu_1/\lambda_1$. *It follows that*

$$M_0(\xi^*) = mn \begin{pmatrix} \nu_0^* & \nu_1^* \\ \nu_1^* & \nu_2^* \end{pmatrix},$$

and

$$M_0(\xi^*) - M_0(\xi) = mn \begin{pmatrix} \nu_0^* - \nu_0 & 0 \\ 0 & \nu_2^* - \nu_2 \end{pmatrix}.$$

Here $\nu_0^* = \lambda_1\omega + \lambda_0(1-\omega)$ *and* $\nu_2^* = \nu_1^* = \lambda_1\omega$. *Since*

$$\frac{1}{\lambda(x)} \geq \frac{1-x}{\lambda_0} + \frac{x}{\lambda_1} \geq \frac{x}{\lambda_1},$$

so $\lambda_1 \geq x\lambda(x)$. *It implies* $0 < \omega < 1$.

$$\begin{aligned}\Big[M_0(\xi^*) - M_0(\xi)\Big]_{11} &= mn\Big[\lambda_1\omega + \lambda_0(1-\omega) - \sum_{j=1}^{p}\omega_j\lambda(x_j)\Big] \\ &= mn\sum_{j=1}^{p}\omega_j\Big[\lambda(x_j)x_j(\lambda_1-\lambda_0) - \lambda_1\lambda(x_j) + \lambda_1\lambda_0\Big]\end{aligned}$$

Condition (6) implies

$$\lambda(x)x(\lambda_1-\lambda_0) - \lambda_1\lambda(x) + \lambda_1\lambda_0 \geq 0.$$

So we obtain

$$\Big[M_0(\xi^*) - M_0(\xi)\Big]_{11} \geq 0$$

By $\nu_2^* = \nu_1^* = \nu_1 \geq \nu_2$ *, we have*

$$\Big[M_0(\xi^*) - M_0(\xi)\Big]_{22} \geq 0$$

So we get $M_0(\xi^*) \geq M_0(\xi)$ *and hence* $M(\xi^*) \geq M_0(\xi)$.

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