

Statistical Theory and Related Fields

ISSN: 2475-4269 (Print) 2475-4277 (Online) Journal homepage: www.tandfonline.com/journals/tstf20

Locally *D*-optimal designs for a class of generalized functional measurement error models

Min-Jue Zhang & Rong-Xian Yue

To cite this article: Min-Jue Zhang & Rong-Xian Yue (09 Nov 2026): Locally *D*-optimal designs for a class of generalized functional measurement error models, Statistical Theory and Related Fields, DOI: 10.1080/24754269.2026.2755105

To link to this article: https://doi.org/10.1080/24754269.2026.2755105

© 2026 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

Published online: 09 Nov 2026.

Submit your article to this journal

Article views: 39

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=tstf20

STATISTICAL THEORY AND RELATED FIELDS
https://doi.org/10.1080/24754269.2026.2755105

Taylor & Francis
by informa

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Locally *D*-optimal designs for a class of generalized functional measurement error models

Min-Jue Zhang[a] and Rong-Xian Yue [b,c]

[a]Department of Statistics, Jiangsu University of Technology, Changzhou, People's Republic of China; [b]College of Arts and Sciences, Fuyao University of Science and Technology, Fuzhou, People's Republic of China; [c]Department of Mathematics, Shanghai Normal University, Shanghai, People's Republic of China

ABSTRACT

This paper investigates the optimal design problem for a class of generalized functional measurement error models, in which some covariates contain measurement errors. Utilizing the locally *D*-optimality criterion, an equivalence theorem is established to verify the optimality of a given design. Furthermore, it is demonstrated that local *D*-optimal designs for such models can be derived explicitly. Specifically, under certain sufficient conditions, the locally *D*-optimal design for the generalized functional measurement error model can be expressed as the product of the designs for the corresponding measurement error model and the classical regression model. Two examples are provided to illustrate these theoretical results.

ARTICLE HISTORY
Received 1 May 2026
Revised 6 July 2026
Accepted 20 October 2026

KEYWORDS
Generalized functional measurement error models; local *D*-optimality; equivalence theorem; product designs

1. Introduction

In practice, it is common that some predictor variables cannot be directly observed or precisely measured. For example, in cardiovascular disease research, long-term average systolic blood pressure and cholesterol levels are critical factors, yet their measurements frequently contain errors (see Whitlock et al., 2001). Similarly, Röösli et al. (2003) found in a study on lung cancer risk that the inhaled dose of air pollutants is challenging to obtain precisely, typically requiring the use of average pollutant concentrations in a specific area as a proxy indicator, among others. For datasets in which the covariates are subject to measurement errors, the measurement error (ME) model has become a primary approach for modelling and analysis.

To illustrate the key characteristics of this model, we begin with the simple case of a single covariate and consider the following ME model:

$$\begin{aligned} Y &= m(x,\theta) + e, \\ X &= x + u, \end{aligned} \tag{1}$$

where θ is the vector of unknown model parameters, and e and u denote the errors in the response and the covariate, respectively. The observable covariate X is referred to as the manifest variable, while the true covariate x is termed the latent variable. Depending on the error

CONTACT Rong-Xian Yue yue2@shnu.edu.cn College of Arts and Sciences, Fuyao University of Science and Technology, Fuzhou 350109, People's Republic of China; Department of Mathematics, Shanghai Normal University, 100 Guilin Road, Xuhui District, Shanghai 200234, People's Republic of China

© 2026 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

structure, ME models are generally classified into three types. The first two fall under the classical error model, where the ME u is assumed to be independent of the latent variable. Specifically, the model is called a structural model or a functional model when x is treated as a random variable or as an unknown fixed constant, respectively. The third type is the Berkson error model, in which the manifest variable X is fixed and controlled by the experimenter, while the error u arises from the settings of the latent variable values and remains independent of X. The Berkson error model applies when the experimenter prescribes the manifest variable, but the latent variable values actually used in the experiment deviate from the intended ones. For comprehensive reviews of statistical inference for these ME models, see Fuller (1987), Carroll et al. (2006), and Buonaccorsi (2010).

Owing to the broad applicability of ME models, identifying efficient experimental designs for these models is of substantial interest. Recent results on optimal designs for Berkson error models were given in Pronzato (2002) and Donev (2004), and for structural models were investigated in Doví et al. (1993). Compared with Berkson error models and structural models, the functional ME models are more frequently encountered in applications, due to sampling and instrument recording errors. As an early reference, Keeler and Reilly (1992) employed the classical D-optimality criterion to construct sequential designs. More recently, Konstantinou and Dette (2015) developed an approximate optimal design theory based on the local D-optimality criterion for the functional Michaelis-Menten, Emax, and exponential ME models, and later extended this work by proposing a robust design strategy to address parameter misspecification (see Konstantinou & Dette, 2017). Zhang and Yue (2020, 2021) studied the optimal design theory for functional polynomial ME models. However, most existing research on optimal designs for ME models remains limited to scenarios where all covariates are subject to MEs.

The primary objective of this study is to investigate locally D-optimal designs for generalized functional measurement error models (GFMEMs) in which certain covariates are subject to measurement error, with a particular emphasis on both the verification and explicit construction of optimal designs under such error-prone settings. Our contributions are threefold. First, we establish an equivalence theorem for the GFMEM, which furnishes a rigorous and verifiable criterion for assessing the local D-optimality of any given design. Second, under a set of mild sufficient conditions, we derive a closed-form characterization of the locally D-optimal design, thereby facilitating its analytical construction. Third, for more general model specifications that do not satisfy these conditions, we develop a computationally efficient numerical algorithm based on convex optimization (CVX) to reliably obtain the locally D-optimal design, ensuring the practical utility of our approach across a wide range of applications. Taken together, these results provide a comprehensive framework for optimal design in GFMEMs, substantially extending the existing theory beyond the case where all covariates are measured with error. The remainder of this paper is organized as follows. Section 2 briefly introduces local D-optimality and the basic notation of the GFMEM. Section 3 presents the main results on the construction of locally D-optimal designs. Section 4 provides two illustrative examples to demonstrate the theoretical findings. Section 5 offers concluding remarks, and all technical proofs are relegated to the Appendix.

2. Preliminaries

Assume that we observe the triplet $(Y_{ij}, X_{ij}^\top, z_i^\top)$ for each individual $i = 1, \ldots, n$ and each observation $j = 1, \ldots, r_i$, where Y_{ij} is the response variable, X_{ij} (with dimensions $p \times 1$) and

z_i (with dimensions $q \times 1$) are covariate vectors measured with and without error, respectively. Here, X_{ij} denotes the error-prone surrogate for the unobservable true covariate x_i. The vector z_i may include indicator variables, such as gender and treatment received, along with continuous variables like age and weight of the ith individual. The following GFMEM is proposed for $Y_{ij}, X_{ij}^\top$, and $z_i^\top$:

$$\begin{aligned} Y_{ij} &= f^\top(x_i, z_i)\theta + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, r_i, \end{aligned} \tag{2}$$

where $f(x_i, z_i) = (1, f_1^\top(x_i), f_2^\top(z_i))^\top$ is a vector of $1 + m_1 + m_2$ linearly independent regression functions defined on a compact space $\mathcal{X} \subset \mathbb{R}^{p+q}$, with $f_1(x_i) = (f_{11}(x_i), \ldots, f_{1m_1}(x_i))^\top$ and $f_2(z_i) = (f_{21}(z_i), \ldots, f_{2m_2}(z_i))^\top$. The vector $\theta = (\alpha, \beta^\top, \gamma^\top)^\top$ represents a set of unknown model parameters, with n denoting the number of distinct experimental settings and r_i indicating the number of repeated observations collected for the ith setting. We further assume that the vectors of response errors e_{ij} and covariate errors u_{ij}, denoted as $\varepsilon_{ij} = (e_{ij}, u_{ij}^\top)^\top$ for $i = 1, \ldots, n$ and $j = 1, \ldots, r_i$, are independent and identically normally distributed with a mean of zero and a covariance matrix Σ_{eu}, where

$$\Sigma_{eu} = \begin{pmatrix} \sigma_e^2 & \sigma_{e,u_1} & \cdots & \sigma_{e,u_p} \\ \sigma_{u_1,e} & \sigma_{u_1}^2 & \cdots & \sigma_{u_1,u_p} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{u_p,e} & \sigma_{u_p,u_1} & \cdots & \sigma_{u_p}^2 \end{pmatrix}$$

is a nonsingular matrix.

Since the vector of MEs is normally distributed, the ML estimator $\hat{\theta}$ is defined as the value of θ that minimizes

$$\sum_{i=1}^{n} \sum_{j=1}^{r_i} \left(Y_{ij} - f^\top(x_i, z_i)\theta, X_{ij}^\top - x_i^\top\right) \Sigma_{eu}^{-1} \left(Y_{ij} - f^\top(x_i, z_i)\theta, X_{ij}^\top - x_i^\top\right)^\top.$$

It is well known that the ML estimator $\hat{\theta}$ is generally inconsistent in ME models, unlike in classical regression settings. To ensure the consistency of the ML estimator $\hat{\theta}$, we follow Fuller (1987) and impose the following assumptions.

(i) The function $f^\top(x, z)\theta$ is continuous and has continuous first and second order derivatives with respect to both θ and x.

(ii) For every $\zeta > 0$, there exists a constant $\delta_\zeta > 0$ such that

$$\begin{aligned} Q_r(\theta) = \frac{1}{r} \sum_{i=1}^{n} \sum_{j=1}^{r_i} \inf_{Y_{ij} = f^\top(x_i, z_i)\theta} & (Y_{ij} - f^\top(x_i, z_i)\theta, X_{ij}^\top - x_i^\top) \\ & \times \Sigma_{eu}^{-1} (Y_{ij} - f^\top(x_i, z_i)\theta, X_{ij}^\top - x_i^\top)^\top > \delta_\zeta, \end{aligned}$$

for θ satisfying $|\theta - \theta_\star| > \zeta$, where $\theta_\star$ denotes the true value of the model parameter vector.

Remark 2.1: Assumption (ii) is a technical condition, also referred to as the parameter identifiability condition, which is introduced to ensure the consistency of the estimator in the functional ME model within the ML estimation framework. Although the positive definiteness of Σ_{eu} guarantees that $Q_r(\theta)$ is pointwise positive for any fixed $\theta \neq \theta_\star$, this property alone is insufficient to rule out the possibility that the estimator $\hat{\theta}$ diverges to infinity. To ensure the consistency of the estimator $\hat{\theta}$, it is necessary to impose a uniform positive lower bound on $Q_r(\theta)$ over the set $\{\theta : |\theta - \theta_\star| > \zeta\}$, for any fixed $\zeta > 0$. This condition parallels Assumption (3.2.23) in Theorem 3.2.1 of Fuller (1987), and plays a crucial role in deriving the asymptotic properties of the ML estimator in such models.

Let

$$\xi = \begin{Bmatrix} (x_1^\top, z_1^\top)^\top & (x_2^\top, z_2^\top)^\top & \cdots & (x_n^\top, z_n^\top)^\top \\ \omega_1 & \omega_2 & \cdots & \omega_n \end{Bmatrix}, \quad 0 < \omega_i \leq 1, \quad \sum_{i=1}^{n} \omega_i = 1,$$

be an approximate design, where $(x_i^\top, z_i^\top)^\top$ and ω_i are called the support points and weights of the design, respectively. The limiting properties of the ML estimator $\hat{\theta}$ are derived under the allocation condition

$$\lim_{r \to \infty} \frac{r_i}{r} = \omega_i > 0, \quad i = 1, \ldots, n,$$

where $r = \sum_{i=1}^{n} r_i$ is the total number of trials. That is, as the total sample size increases, the proportions of observations at the support points converge to the corresponding design weights.

On account of Theorem 3.2.1 of Fuller (1987), we can obtain the asymptotic properties of the estimator $\hat{\theta}$ for the model parameter θ:

$$\sqrt{r}(\hat{\theta} - \theta_\star) \xrightarrow{L} N(0, M^{-1}(\xi, \theta_\star)),$$

where $\theta_\star$ denotes the true value of the model parameter, $\xrightarrow{L}$ denotes convergence in distribution and the inverse of the asymptotic covariance matrix $M(\xi, \theta_\star)$ is called the information matrix of design ξ. In view of the definition of the regression function $f(x, z)$ in Model (2), it is reasonable to assume that there exists a design ξ for which the information matrix $M(\xi, \theta_\star)$ is positive definite. This positive definiteness guarantees the identifiability of the model parameter vector θ, and constitutes a standard assumption in the optimal design literature (see Fedorov & Leonov, 2014). The information matrix $M(\xi, \theta_\star)$ is given by

$$\begin{aligned} M(\xi, \theta_\star) &= \int_{\mathcal{X}} \frac{1}{\sigma(x, \beta_\star)} f(x, z) f^\top(x, z) \mathrm{d}\xi(x, z) \\ &= \sum_{i=1}^{n} \frac{\omega_i}{\sigma(x_i, \beta_\star)} f(x_i, z_i) f^\top(x_i, z_i), \end{aligned} \tag{3}$$

with

$$\sigma(x_i, \beta_\star) = \left(1, \beta_\star^\top \frac{\partial f_1(x_i)}{\partial x_i^\top}\right) \Sigma_{eu} \left(1, \beta_\star^\top \frac{\partial f_1(x_i)}{\partial x_i^\top}\right)^\top. \tag{4}$$

An optimal approximate design for the ML estimation in Model (2) maximizes an appropriate concave functional, say ψ. There are numerous criteria that can be used to discriminate between competing designs (see Atkinson et al., 2007). Here, we concentrate on the

well-known D-optimality criterion (see Chernoff, 1953):

$$\psi_D(\xi,\theta) = \log\{\det\{M(\xi,\theta)\}\}. \tag{5}$$

A design ξ^* that maximizes (5) is called a locally D-optimal design, which depends on the value of the unknown parameter vector θ for the GFMEM defined in (2) and minimizes the volume of the asymptotic confidence ellipsoid for the parameter vector θ with respect to the choice of the design ξ. These designs require an initial guess of the unknown parameters in the model, and there are numerous situations where such knowledge is available (see Fedorov & Leonov, 2014).

3. Main results

3.1. Theoretical results of locally D-optimal designs for the GFMEM

In the context of ML estimation, the criterion defined in (5) is concave with respect to the design ξ. Hence, the equivalence theorem for checking the local D-optimality of a candidate design for the model described in (2) is given below.

Theorem 3.1: *A design ξ^* on X is locally D-optimal for the GFMEM defined by* (2) *if and only if the inequality*

$$\varphi(x,z,\xi^*,\theta) := \frac{f^\top(x,z)M^{-1}(\xi^*,\theta)f(x,z)}{\sigma(x,\beta)} \le 1 + m_1 + m_2 \tag{6}$$

holds for all $(x^\top, z^\top)^\top \in \mathcal{X}$ with the equality at the support points $(x^{*\top}, z^{*\top})^\top$ of ξ^*.

Note that the information matrix of the design ξ for the GFMEM defined by (2) is associated with both the information matrix of the multivariate linear ME model (7) and that of the classical multivariate linear model (8).

$$\begin{aligned} Y_{ij} &= \alpha + f_1^\top(x_i)\beta + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \quad i = 1,\dots,n, \quad j = 1,\dots,r_i, \end{aligned} \tag{7}$$

and

$$Y_{ij} = \alpha + f_2^\top(z_i)\gamma + e_{ij}, \quad i = 1,\dots,n, \quad j = 1,\dots,r_i. \tag{8}$$

Let $\xi_1 \in \Xi_1$ and $\xi_2 \in \Xi_2$ be the designs for the multivariate linear ME model (7) with covariance Σ_{eu} and for the classical multivariate linear model (8) with variance σ_e^2, respectively. These designs are defined on design spaces $\mathcal{X}_1 \subset \mathbb{R}^p$ and $\mathcal{X}_2 \subset \mathbb{R}^q$. Here, Ξ_k denotes the set of all designs for Model (7) when $k = 1$ and for Model (8) when $k = 2$. The information

matrices of Models (7) and (8) are

$$M_1(\xi_1,\beta)=\begin{pmatrix}\displaystyle\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x) & \displaystyle\int_{\mathcal{X}_1}\frac{f_1^\top(x)}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\\ \displaystyle\int_{\mathcal{X}_1}\frac{f_1(x)}{\sigma(x,\beta)}\mathrm{d}\xi_1(x) & \displaystyle\int_{\mathcal{X}_1}\frac{f_1(x)f_1^\top(x)}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\end{pmatrix}, \tag{9}$$

and

$$M_2(\xi_2)=\begin{pmatrix}1 & \displaystyle\int_{\mathcal{X}_2}f_2^\top(z)\mathrm{d}\xi_2(z)\\ \displaystyle\int_{\mathcal{X}_2}f_2(z)\mathrm{d}\xi_2(z) & \displaystyle\int_{\mathcal{X}_2}f_2(z)f_2^\top(z)\mathrm{d}\xi_2(z)\end{pmatrix}. \tag{10}$$

Next, we focus on constructing the locally D-optimal designs for the GFMEM defined by (2) using product designs. As noted by Schwabe (1996), the concept of product design is one of the most important parts in design analysis for multi-factor experiments. The product design is defined as $\xi=\xi_1\otimes\xi_2$, with the product measure on $\mathcal{X}_1\times\mathcal{X}_2$ given by $\xi(x,z)=\xi_1(x)\xi_2(z)$.

Lemma 3.2: *In the GFMEM defined by* (2)*, we have*

$$(1)\quad \det\{M(\xi_1\otimes\xi_2,\theta)\}=\left(\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\right)^{m_2}\det\{M_1(\xi_1,\beta)\}\det\{M_2(\xi_2)\}, \tag{11}$$

$$(2)\quad \varphi(x,z,\xi_1\otimes\xi_2,\theta)=\frac{(1\,f_1^\top(x))M_1^{-1}(\xi_1,\beta)\binom{1}{f_1(x)}}{\sigma(x,\beta)}+\frac{\widetilde{f}_2^\top(z)J^{-1}\widetilde{f}_2(z)}{\sigma(x,\beta)\displaystyle\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)}, \tag{12}$$

where

$$\widetilde{f}_2(z)=f_2(z)-\int_{\mathcal{X}_2}f_2(z)\mathrm{d}\xi_2(z),$$

and

$$J=\int_{\mathcal{X}_2}f_2(z)f_2^\top(z)\mathrm{d}\xi_2(z)-\int_{\mathcal{X}_2}f_2(z)\mathrm{d}\xi_2(z)\int_{\mathcal{X}_2}f_2^\top(z)\mathrm{d}\xi_2(z).$$

Theorem 3.3: *Let ξ_k^* ($k=1,2$) be the locally D-optimal designs for Models* (7) *and* (8)*, respectively. If the condition*

$$\max_{\xi_1\in\Xi_1}\left\{\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\right\}=\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x) \tag{13}$$

holds, the product design $\xi^*=\xi_1^*\otimes\xi_2^*$ is locally D-optimal for the GFMEM defined by (2)*.*

Corollary 3.4: *Let ξ_k^* ($k=1,2$) be the locally D-optimal designs for Models* (7) *and* (8)*, respectively. If the condition*

$$\max_{x\in\mathcal{X}_1}\left\{\frac{1}{\sigma(x,\beta)}\right\}=\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x),$$

holds, the product design $\xi^*=\xi_1^*\otimes\xi_2^*$ is locally D-optimal for the GFMEM defined by (2)*.*

Remark 3.1: Corollary 3.4 typically applies to the GFMEM in which $\sigma(x,\beta)$ is a nonzero constant on the design space $\mathcal{X}_1$. This includes the case where $f_1(x)$ takes a specific form, e.g., $f_1(x) = x$. Under this setting, the locally D-optimal design for the GFMEM defined by (2) can be obtained as the product of the locally D-optimal design for the multivariate linear ME model (7) and the D-optimal design for the classical multivariate linear model (8).

It is worth mentioning that this work on locally D-optimal criterion can be directly extended to the nonlinear case given by

$$\begin{aligned} Y_{ij} &= \eta(x_i, z_i, \theta) + e_{ij} = \alpha + \eta_1(x_i, \beta) + \eta_2(z_i, \gamma) + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \end{aligned} \tag{14}$$

where $i = 1, \ldots, n$ and $j = 1, \ldots, r_i$. The vectors of response errors and covariate errors, $\varepsilon_{ij} = (e_{ij}, u_{ij}^\top)^\top$, follow the same assumptions as those given in Section 2. The nonlinear function $\eta(x, z, \theta)$ is continuous and has continuous first and second order derivatives with respect to both $\theta = (\alpha, \beta^\top, \gamma^\top)^\top \in \mathbb{R}^{1+m_1+m_2}$ and x. In fact, the information matrices for Model (14) and related models can be written in a form analogous to that presented in (3), (9), and (10). Define

$$\nabla\eta = \left(1, \frac{\partial\eta_1(x,\beta)}{\partial\beta^\top}, \frac{\partial\eta_2(z,\gamma)}{\partial\gamma^\top}\right)^\top,$$

which is the gradient vector of $\eta(x, z, \theta)$. Thus, the conclusions of Theorems 3.1 and 3.3, as well as Lemma 3.2, extend to the nonlinear case by replacing $f(x, z)$ in Model (2) with $\nabla\eta$.

Remark 3.2: The sufficient conditions in Corollary 3.4 impose strong constraints on the design space and the model structure. These conditions are satisfied, for instance, in the case of multivariate linear ME models, as well as for some specific nonlinear settings (e.g., when the design space for x is finite and symmetric, and the covariance matrix is diagonal). However, as demonstrated in the numerical example of Section 4, these conditions generally fail for commonly used nonlinear models, such as the exponential ME model. In such cases, Theorem 3.3 provides the theoretical underpinning for numerically solving locally D-optimal designs for the GFMEM, thereby ensuring that the CVX-based algorithm developed in Section 3.2 has broad applicability.

3.2. CVX-generated locally D-optimal designs

When the data fail to meet the conditions of Corollary 3.4, the locally D-optimal design for the GFMEM defined by (2) must be found numerically via Theorem 3.3. In this section, we focus on the CVX package (see Grant & Boyd, 2013) in MATLAB R2023a, which is specifically designed for disciplined convex programming. In the setting of nonlinear models, CVX-based algorithms are widely recognized as more practical and flexible for solving optimal design problems under convex criteria compared with conventional statistical approaches.

According to Theorem 3.3, the required optimal design ξ_1^* for Model (7) is generally not merely the locally D-optimal design in Model (7), but must also maximize $\int_{\mathcal{X}_1} 1/\sigma(x,\beta)\mathrm{d}\xi_1(x)$. Consequently, it can be obtained by minimizing the following objective

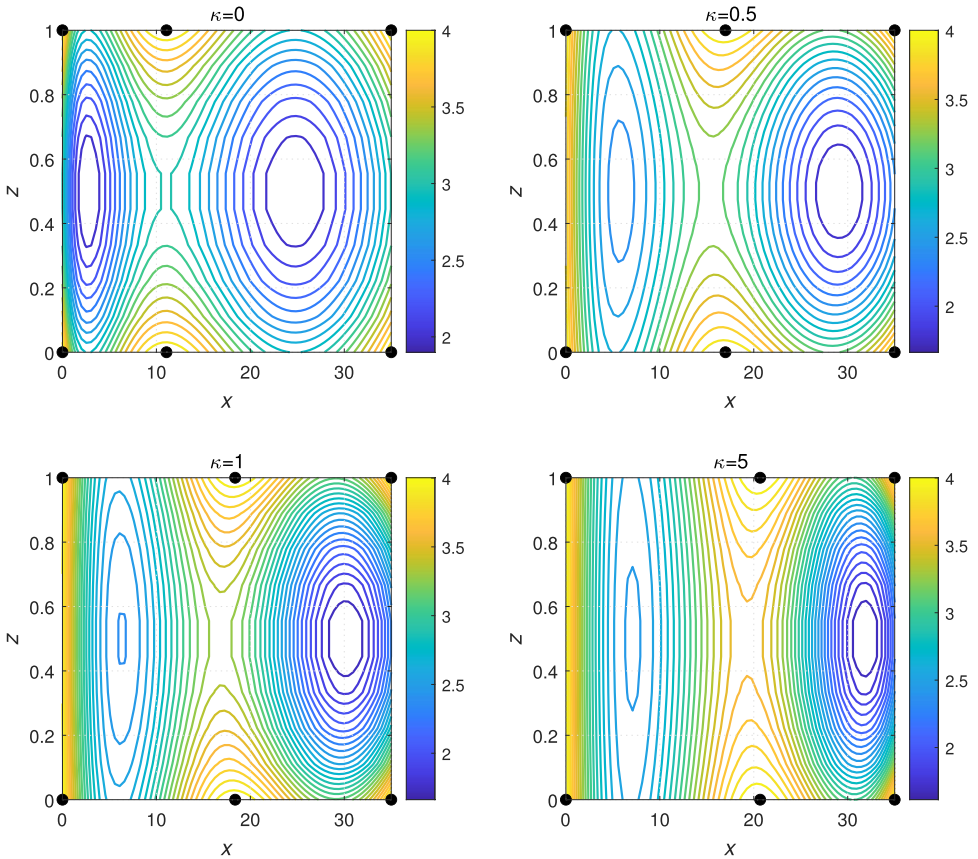


Figure 1. The contour plots of the function $\varphi(x, z, \xi^*, \theta)$ defined by (6) with $\kappa = 0, 0.5, 1, 5$ in Model (19) for fixed $\theta = (1210, 66.07, 0.0696, 1)^\top$.

function:

$$\begin{cases} \min\limits_{\xi_1 \in \Xi_1} \; -\log\left\{\displaystyle\int_{\mathcal{X}_1} \frac{1}{\sigma(x,\beta)}\, \mathrm{d}\xi_1(x)\right\} - \log\{\det\{M_1(\xi_1,\theta)\}\} \\ \text{subject to}: a_i \geq 0, \quad \displaystyle\sum_{i=1}^{n} a_i = 1, \quad i = 1, \ldots, n, \end{cases} \tag{15}$$

where x_i and $a_i, i = 1, \ldots, n$, are called support points and weights of the design ξ_1.

The CVX-based algorithm proposed in Wong and Zhou (2019) can be used to numerically construct the design ξ_1^*. The main steps of this algorithm are as follows.

(1) Specify the parameter value θ and a set of candidate design points $x_1, \ldots, x_N$, where $n = N$ is a sufficiently large integer.
(2) Compute the information matrices $M_1(x_i, \theta)$ for $i = 1, \ldots, N$.
(3) Use CVX to solve the optimization problem in (15) with respect to $a_1, \ldots, a_N$, and denote the solution by $\hat{a}_1, \ldots, \hat{a}_N$.
(4) Check the optimality of $\hat{a}_1, \ldots, \hat{a}_N$ using Equation (6) in Theorem 3.1.

Table 1. The locally D-optimal designs for the models in (19) with $\kappa = 0, 0.5, 1, 5$ on $\mathcal{X} = [0, 35]$ for fixed $\theta = (1210, 66.07, 0.0696, 1)^\top$.

κ	ξ_1^*	$\xi^* = \xi_1^* \otimes \xi_2^*$
0	$\begin{Bmatrix} 0 & 11.011 & 35 \\ 1/3 & 1/3 & 1/3 \end{Bmatrix}$	$\begin{Bmatrix} (0,0) & (0,1) & (11.011,0) & (11.011,1) & (35,0) & (35,1) \\ 1/6 & 1/6 & 1/6 & 1/6 & 1/6 & 1/6 \end{Bmatrix}$
0.5	$\begin{Bmatrix} 0 & 16.953 & 35 \\ 0.26 & 0.32 & 0.42 \end{Bmatrix}$	$\begin{Bmatrix} (0,0) & (0,1) & (16.953,0) & (16.953,1) & (35,0) & (35,1) \\ 0.13 & 0.13 & 0.16 & 0.16 & 0.21 & 0.21 \end{Bmatrix}$
1	$\begin{Bmatrix} 0 & 18.384 & 35 \\ 0.256 & 0.308 & 0.436 \end{Bmatrix}$	$\begin{Bmatrix} (0,0) & (0,1) & (18.384,0) & (18.384,1) & (35,0) & (35,1) \\ 0.128 & 0.128 & 0.154 & 0.154 & 0.218 & 0.218 \end{Bmatrix}$
5	$\begin{Bmatrix} 0 & 20.669 & 35 \\ 0.252 & 0.284 & 0.464 \end{Bmatrix}$	$\begin{Bmatrix} (0,0) & (0,1) & (20.669,0) & (20.669,1) & (35,0) & (35,1) \\ 0.126 & 0.126 & 0.142 & 0.142 & 0.232 & 0.232 \end{Bmatrix}$

4. Illustrative examples

The theoretical results obtained in Section 3 are illustrated via the following examples in this section.

Example 4.1: To assess the performance of the GFMEM, Patriota and Bolfarine (2010) considered the following simple linear formulation:

$$\begin{aligned} Y_{ij} &= \alpha + \beta x_i + \gamma z_i + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, r_i, \end{aligned} \tag{16}$$

where x_i is a covariate in the interval $[1, 10]$, and z_i is a binary treatment indicator, taking the value one if the ith experimental unit receives the treatment and zero otherwise. The covariance matrix of the random errors e_{ij} and u_{ij} is assumed to be

$$\Sigma_{eu} = \begin{pmatrix} \sigma_e^2 & \sigma_{e,u} \\ \sigma_{e,u} & \sigma_u^2 \end{pmatrix}.$$

Furthermore, preliminary experiments provide prior information about the parameters, e.g., $(\alpha, \beta, \gamma) = (1, 1, 2)$.

By applying Corollary 3.4, the D-optimal design ξ^* for this model can be obtained from the D-optimal designs $\xi_i^* (i = 1, 2)$ for the linear ME model (7) and the linear model (8), respectively; that is,

$$\xi^* = \xi_1^* \otimes \xi_2^* = \begin{Bmatrix} (1,0) & (1,1) & (10,0) & (10,1) \\ 1/4 & 1/4 & 1/4 & 1/4 \end{Bmatrix}. \tag{17}$$

We then have

$$\varphi(x, z, \xi^*, \theta) = \frac{4}{81}\left(x - \frac{11}{2}\right)^2 + 4\left(z - \frac{1}{2}\right)^2 + 1.$$

From Theorem 3.1, it is readily verified that this function attains its maximum value of 3 at all support points of ξ^*.

Example 4.2: The second simulation study investigates the locally D-optimal design for the exponential ME model across different populations. The exponential ME model is commonly used to describe the dose-effect relationship between dosage and response, with the

mathematical expression:

$$\begin{aligned} Y_{ij} &= \alpha + \beta_1 \exp(-\beta_2 x_i) + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, r_i, \end{aligned} \tag{18}$$

where $\alpha \geq 0$ denotes the placebo effect (i.e., the baseline effect), $\beta_1 > 0$ represents the slope of the curve, and $\beta_2 \in \{\mathbb{R} \setminus 0\}$ describes the rate of the dose effect. Optimal designs for the exponential ME models have been determined by Konstantinou and Dette (2015).

To account for the influence of different sex populations on dose-response relationships, the exponential ME model is extended by introducing an indicator variable z. Let $z_i = 1$ denote that the ith experimental unit is male, while $z_i = 0$ denotes female. The generalized exponential ME model can then be expressed as

$$\begin{aligned} Y_{ij} &= \alpha + \beta_1 \exp(-\beta_2 x_i) + \gamma z_i + e_{ij}, \\ X_{ij} &= x_i + u_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, r_i. \end{aligned} \tag{19}$$

Assuming prior information regarding the model parameter values is available from preliminary experiments, namely, $(\alpha, \beta_1, \beta_2)^\top = (1210, 66.07, 0.0696)^\top$, the covariance matrix of e_{ij} and u_{ij} is given by $\Sigma_{eu} = \text{diag}\{5.68, 5.68\kappa\}$, where $\kappa = \sigma_u^2/\sigma_e^2 = \sigma_u^2/5.68$ refers to the error-variance ratio (see Konstantinou & Dette, 2015, 2017). Additionally, the design space is assumed to be $\mathcal{X} = [0, 35] \times \{0, 1\}$.

We numerically compute the locally D-optimal designs for Model (19) for different error-variance ratios κ within the design space $\mathcal{X} = [0, 35] \times \{0, 1\}$. The results indicate that the D-optimal designs are influenced by the values of κ, β_1, and β_2, while showing insensitivity to α and γ . Therefore, in what follows, we fix $\alpha = 1210$ and assume $\gamma = 1$.

Based on Formula (15), the optimal design ξ_1^* for various values of κ can be obtained using the CVX-based algorithm, as shown in the second column of Table 1. Meanwhile, ξ_2^* is the D-optimal design for the simple linear regression model, given by

$$\xi_2^* = \begin{Bmatrix} 0 & 1 \\ 1/2 & 1/2 \end{Bmatrix}.$$

The corresponding locally D-optimal designs for $\kappa = 0, 0.5, 1, 5$ are presented in the right part of Table 1. Figure 1 displays the contour plots of the function $\varphi(x, z, \xi^*, \theta)$, illustrating that φ reaches a maximum value of 4 at all support points of ξ^*.

5. Concluding remarks

Within the framework of ML estimation, this paper presents a systematic study of the locally D-optimal design for the GFMEM defined in (2). We establish an equivalence theorem as a fundamental tool for verifying design optimality and, under certain sufficient conditions, derive locally D-optimal designs for the GFMEM using a product design. This product design not only reveals the structural relationship between the GFMEM and its submodels, but also substantially reduces computational complexity when the conditions are satisfied. For more general cases, we develop a CVX-based numerical algorithm to efficiently construct the desired designs, and its effectiveness is corroborated by numerical examples. In summary, our work provides a complete methodological framework for the locally D-optimal design in the GFMEM, including theoretical characterization, analytic construction under tractable

conditions, and numerical implementation in the general setting. Finally, it is worth noting that although our analysis is carried out under the assumption of normally distributed errors, the proposed methodology is sufficiently general to be extended to other error distribution specifications.

Author contributions

CRediT: **Min-Jue Zhang:** Conceptualization, Formal analysis, Investigation, Methodology, Software, Validation, Writing – original draft; **Rong-Xian Yue:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the National Natural Science Foundation of China [grant number 12301319].

ORCID

Rong-Xian Yue http://orcid.org/0000-0001-6899-4636

References

Atkinson, A., Donev, A., & Tobias, R. (2007). *Optimum experimental designs, with SAS* (2nd ed.). Oxford University Press.

Buonaccorsi, J. P. (2010). *Measurement error: Models, methods, and applications*. Chapman and Hall.

Carroll, R., Ruppert, D., & Stefanski, L. (2006). *Measurement error in nonlinear models: A modern perspective* (2nd ed.). Chapman and Hall.

Chernoff, H. (1953). Locally optimal designs for estimating parameters. *The Annals of Mathematical Statistics*, *24*(4), 586–602. https://doi.org/10.1214/aoms/1177728915

Donev, A. N. (2004). Design of experiments in the presence of errors in factor levels. *Journal of Statistical Planning and Inference*, *126*(2), 569–585. https://doi.org/10.1016/j.jspi.2003.09.002

Doví, V. G., Reverberi, A. P., & Maga, L. (1993). Optimal design of sequential experiments for error-in-variables models. *Computers & Chemical Engineering*, *17*(1), 111–115. https://doi.org/10.1016/0098-1354(93)80008-B

Fedorov, V., & Leonov, S. (2014). *Optimal design for nonlinear response models*. Chapman and Hall.

Fuller, W. A. (1987). *Measurement error models*. Wiley.

Grant, M. C., & Boyd, S. P. (2013). *The CVX Users' Guide, Release 2.0 (Beta)* (Tech. Rep.). Stanford, CA: CVX Research Inc.

Keeler, S. E., & Reilly, P. M. (1992). The design of experiments when there are errors in all the variables. *The Canadian Journal of Chemical Engineering*, *70*(4), 774–779. https://doi.org/10.1002/cjce.v70:4

Konstantinou, M., & Dette, H. (2015). Locally optimal designs for errors-in-variables models. *Biometrika*, *102*(4), 951–958. https://doi.org/10.1093/biomet/asv048

Konstantinou, M., & Dette, H. (2017). Bayesian *D*-optimal designs for error-in-variables models. *Applied Stochastic Models in Business and Industry*, *33*(3), 269–281. https://doi.org/10.1002/asmb.v33.3

Patriota, A. G., & Bolfarine, H. (2010). Measurement error models with a general class of error distribution. *Statistics*, *44*(2), 119–127. https://doi.org/10.1080/02331880903023795

Pronzato, L. (2002). Information matrices with random regressors: Application to experimental design. *Journal of Statistical Planning and Inference*, *108*(1–2), 189–200. https://doi.org/10.1016/S0378-3758(02)00278-1

Röösli, M., Künzli, N., Schindler, C., Theis, G., Oglesby, L., Mathys, P., Camenzind, M., & Braun-Fahrländer, C. (2003). Single pollutant versus surrogate measure approaches: Do single pollutant risk assessments underestimate the impact of air pollution on lung cancer risk. *Journal of Occupational and Environmental Medicine*, *45*(7), 715–723. https://doi.org/10.1097/01.jom.0000079082.33909.c2

Schwabe, R. (1996). *Optimum designs for multi-factor models* (Vol. 113). Springer.

Whitlock, G., Clark, T., Vander Hoorn, S., Rodgers, A., Jackson, R., Norton, R., & MacMahon, S. (2001). Random errors in the measurement of 10 cardiovascular risk factors. *European Journal of Epidemiology*, *17*(10), 907–909. https://doi.org/10.1023/A:1016228410194

Wong, W. K., & Zhou, J. (2019). CVX-based algorithms for constructing various optimal regression designs. *The Canadian Journal of Statistics*, *47*(3), 374–391.

Zhang, M. J., & Yue, R. X. (2020). Locally *D*-optimal designs for heteroscedastic polynomial measurement error models. *Metrika*, *83*(6), 643–656. https://doi.org/10.1007/s00184-019-00745-2

Zhang, M. J., & Yue, R. X. (2021). Optimal designs for homoscedastic functional polynomial measurement error models. *AStA Advances in Statistical Analysis*, *105*(3), 485–501. https://doi.org/10.1007/s10182-021-00399-4

Appendix. Proofs

Proof of Theorem 3.1: For the locally *D*-optimal design ξ^* and any design ξ, let $\xi_t = (1-t)\xi^* + t\xi$ with $t \in [0,1]$. The directional derivative of the function $\psi_D(\xi,\theta)$ at ξ^* in the direction of $\xi - \xi^*$ is given by

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\psi_D(\xi_t,\theta)\mid_{t=0} &= \frac{1}{\det\{M(\xi^*,\theta)\}}\frac{\mathrm{d}}{\mathrm{d}t}\det\{M(\xi_t,\theta)\}\Big|_{t=0} \\
&= \mathrm{tr}\{M^{-1}(\xi^*,\theta)\frac{\mathrm{d}}{\mathrm{d}t}\det\{M(\xi_t,\theta)\}\}\Big|_{t=0} \\
&= \mathrm{tr}\{M^{-1}(\xi^*,\theta)(M(\xi,\theta) - M(\xi^*,\theta))\} \\
&= \mathrm{tr}\{M^{-1}(\xi^*,\theta)M(\xi,\theta)\} - (1+m_1+m_2),
\end{aligned}$$

where $\mathrm{tr}(B)$ denotes the trace of the matrix B. Replacing ξ by the Dirac measure $\delta_{(x^\top,z^\top)^\top}$ with mass 1 at the point $(x^\top,z^\top)^\top \in \mathcal{X}$, we have

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\psi_D(\xi_t,\theta)\mid_{t=0} &= \mathrm{tr}\{M^{-1}(\xi^*,\theta)M(x,z,\theta)\} - (1+m_1+m_2) \\
&= \frac{f^\top(x,z)M^{-1}(\xi^*,\beta)f(x,z)}{\sigma(x,\beta)} - (1+m_1+m_2).
\end{aligned}$$

The nonpositivity of the directional derivative at ξ^* is a necessary and sufficient condition for the optimality of ξ^*, considering $\psi_D(\xi,\theta)$ is a concave function of ξ, and then the inequality

$$\varphi(x,z,\xi^*,\theta) := \frac{f^\top(x,z)M^{-1}(\xi^*,\theta)f(x,z)}{\sigma(x,\beta)} \le 1+m_1+m_2$$

follows for all $(x^\top,z^\top)^\top \in \mathcal{X}$.

For the proof of the equality part of Theorem 3.1, let us assume that

$$\varphi(x,z,\xi^*,\theta) < 1+m_1+m_2.$$

Then

$$\int_{\mathcal{X}} \varphi(x,z,\xi^*,\theta)\mathrm{d}\xi(x,z) < \int_{\mathcal{X}} (1+m_1+m_2)\mathrm{d}\xi(x,z) = 1+m_1+m_2.$$

Now for any design ξ, from the expression on the left side of (6), we have

$$\begin{aligned}\int_{\mathcal{X}} \varphi(x,z,\xi,\theta)\mathrm{d}\xi(x,z) &= \int_{\mathcal{X}} \frac{f^{\top}(x,z)M^{-1}(\xi,\theta)f(x,z)}{\sigma(x,\beta)}\mathrm{d}\xi(x,z)\\ &= \int_{\mathcal{X}} \mathrm{tr}\left\{\frac{f^{\top}(x,z)M^{-1}(\xi,\theta)f(x,z)}{\sigma(x,\beta)}\right\}\mathrm{d}\xi(x,z)\\ &= \int_{\mathcal{X}} \mathrm{tr}\left\{M^{-1}(\xi,\theta)\frac{f(x,z)f^{\top}(x,z)}{\sigma(x,\beta)}\right\}\mathrm{d}\xi(x,z)\\ &= \mathrm{tr}\left\{M^{-1}(\xi,\theta)\int_{\mathcal{X}}\frac{f(x,z)f^{\top}(x,z)}{\sigma(x,\beta)}\mathrm{d}\xi(x,z)\right\}\\ &= 1+m_1+m_2,\end{aligned}$$

which contradicts our initial assumption. Hence,

$$\max_{(x^{\top},z^{\top})^{\top}\in\mathcal{X}} \varphi(x,z,\xi^*,\theta) = 1+m_1+m_2$$

which is attained at the support of ξ^*, and this completes the proof. ■

Proof of Lemma 3.2: Let the matrix

$$L = \begin{pmatrix} 1 & 0_{1\times m_1} & 0_{1\times m_2}\\ 0_{m_1\times 1} & I_{m_1\times m_1} & 0_{m_1\times m_2}\\ -\int_{\mathcal{X}_2} f_2(z)\mathrm{d}\xi_2(z) & 0_{m_2\times m_1} & I_{m_2\times m_2}\end{pmatrix}.$$

Then

$$LM(\xi_1\otimes\xi_2,\theta)L^{\top} = \begin{pmatrix} M_1(\xi_1,\beta) & 0_{(1+m_1)\times m_2}\\ 0_{m_2\times(1+m_1)} & \int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)J\end{pmatrix}. \tag{A1}$$

By Lemma 3.2 in Schwabe (1996), we obtain

$$\det\{J\} = \det\{M_2(\xi_2)\}.$$

Furthermore, since L is lower triangular with all diagonal entries equal to 1, it is regular and satisfies $\det\{L\} = 1$. Consequently,

$$\det\{M(\xi_1\otimes\xi_2,\theta)\} = \left(\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\right)^{m_2}\det\{M_1(\xi_1,\beta)\}\det\{M_2(\xi_2)\}.$$

Using Equation (A1), we obtain

$$M^{-1}(\xi_1\otimes\xi_2,\theta) = L^{\top}\begin{pmatrix} M_1^{-1}(\xi_1,\beta) & 0_{(1+m_1)\times m_2}\\ 0_{m_2\times(1+m_1)} & J^{-1}/\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\end{pmatrix}L,$$

and thus

$$\begin{aligned}
&\varphi(x,z,\xi_1\otimes\xi_2,\theta)\\
&\quad=\frac{f^\top(x,z)M^{-1}(\xi_1\otimes\xi_2,\theta)f(x,z)}{\sigma(x,\beta)}\\
&\quad=(1,f_1^\top(x),f_2^\top(z))L^\top\begin{pmatrix}\frac{M_1^{-1}(\xi_1,\beta)}{\sigma(x,\beta)} & \frac{0_{(1+m_1)\times m_2}}{\sigma(x,\beta)}\\ 0_{m_2\times(1+m_1)} & \frac{J^{-1}}{\sigma(x,\beta)\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)}\end{pmatrix}L(1,f_1^\top(x),f_2^\top(z))^\top\\
&\quad=\frac{(1\,f_1^\top(x))M_1^{-1}(\xi_1,\beta)\binom{1}{f_1(x)}}{\sigma(x,\beta)}+\frac{\widetilde{f}_2^\top(z)J^{-1}\widetilde{f}_2(z)}{\sigma(x,\beta)\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)}.
\end{aligned}$$

■

Proof of Theorem 3.3: Suppose the condition (13) holds. Then, for any $\xi_1\in\Xi_1$,

$$\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1(x)\le\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x).$$

Replacing ξ_1 by the Dirac measure δ_x (mass 1 at $x\in\mathcal{X}_1$) shows

$$\frac{1}{\sigma(x,\beta)}\le\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x),\quad\forall x\in\mathcal{X}_1.$$

Multiplying by $\sigma(x,\beta)>0$ yields

$$1\le\sigma(x,\beta)\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x),\quad\forall x\in\mathcal{X}_1.$$

Then, by Formula (12) in Lemma 3.2, we have

$$\begin{aligned}
\varphi(x,z,\xi_1^*\otimes\xi_2^*,\theta)&=\frac{(1\,f_1^\top(x))M_1^{-1}(\xi_1^*,\beta)\binom{1}{f_1(x)}}{\sigma(x,\beta)}+\frac{\widetilde{f}_2^{*\top}(z)J^{*-1}\widetilde{f}_2^*(z)}{\sigma(x,\beta)\int_{\mathcal{X}_1}\frac{1}{\sigma(x,\beta)}\mathrm{d}\xi_1^*(x)}\\
&\le\frac{(1\,f_1^\top(x))M_1^{-1}(\xi_1^*,\beta)\binom{1}{f_1(x)}}{\sigma(x,\beta)}+\widetilde{f}_2^{*\top}(z)J^{*-1}\widetilde{f}_2^*(z)\\
&\le 1+m_1+m_2,
\end{aligned}$$

where

$$\widetilde{f}_2^*(z)=f_2(z)-\int_{\mathcal{X}_2}f_2(z)\mathrm{d}\xi_2^*(z)$$

and

$$J^*=\int_{\mathcal{X}_2}f_2(z)f_2^\top(z)\mathrm{d}\xi_2^*(z)-\int_{\mathcal{X}_2}f_2(z)\mathrm{d}\xi_2^*(z)\int_{\mathcal{X}_2}f_2^\top(z)\mathrm{d}\xi_2^*(z).$$

The final inequality follows from Theorem 3.3 in Schwabe (1996) and Theorem 1 in Zhang and Yue (2021). Combining this with Theorem 3.1 yields that $\xi^*=\xi_1^*\otimes\xi_2^*$ is locally D-optimal for the GFMEM defined by (2). ■

Proof of Corollary 3.4: Under the assumptions of the corollary, for any $\xi_1 \in \Xi_1$,

$$\begin{aligned}\int_{\mathcal{X}_1} \frac{1}{\sigma(x,\beta)} \mathrm{d}\xi_1(x) &\leq \int_{\mathcal{X}_1} \max_{x\in\mathcal{X}_1} \left\{ \frac{1}{\sigma(x,\beta)} \right\} \mathrm{d}\xi_1(x) \\ &= \max_{x\in\mathcal{X}_1} \left\{ \frac{1}{\sigma(x,\beta)} \right\} \\ &= \int_{\mathcal{X}_1} \frac{1}{\sigma(x,\beta)} \mathrm{d}\xi_1^*(x).\end{aligned}$$

Thus, $\xi^* = \xi_1^* \otimes \xi_2^*$ is the locally *D*-optimal design for Model (2), by Theorem 3.3. ■