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JOURNAL OF THE INDIAN SOCIETY OF AGRICULTURAL STATISTICS 65(1) 2011 91-98

Optimal Designs for Multi-Response Mixture Experiments

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Received 17 July 2010; Revised 14 January 2011; Accepted 22 January 2011

SUMMARY

Optimal design of multi-response mixture experiments for estimating the parameters of multi-response linear models is an interesting problem which is yet to be discussed in literature. In this paper, we present a formulation of optimal design for multi-response linear models using Semi-Definite Programming (SDP) that can generate D-, A- and E-optimal designs. We generate both approximate and *n*-exact D-optimal designs for multi-response linear models for multi-response mixture experiments. The proposed method has an advantage as using it one can use SDP solver of TOMLAB (Holmstrom 2004) and YALMIP (Löfberg 2005) software within MATLAB environment in order to minimize the amount of computation time needed to generate an optimal design for multi-response models.

Keywords: D-optimal design, Multi-response linear model, Multi-response mixture experiment, Semi-Definite programming.

1. INTRODUCTION

Applications of optimal design of mixture experiments in different fields have been growing continually. The optimal design of mixture experiments has been frequently applied in microbiology (Gallego *et al*. 2008), in medicines and drugs (Gonnissen *et al*. 2008), in food science (Ozdemir and Floros 2008) and in many other areas of science. Draper and Hunter (1966) introduced the techniques of multi-response experiments with their work on the design of experiments for parameter estimation of multi-response model. Roy *et al*. (1971) extended the classical design to a multi-response experimental design. Fedorov (1972) established a theoretical foundation for multi-response experiments and also developed a recursive algorithm for generating multi-response approximate D-optimal designs. Chang (1994) studied the properties of D-optimal designs for multi-response models. Khuri and Cornell (1996) devoted a chapter of their book to multi-response experiments and described Wijesinha's algorithm (Wijesinha 1984) for generating D-optimal designs. Chang (1997) proposed an algorithm which generates nearly D-optimal designs for some special multi-response linear models. So far a lot of work has been done on optimal design for multi-response linear models, but the same work on the literature of mixture experiments has not drawn much and required attention.

In this paper, we propose a formulation for D-, A- and E-optimal designs for multi-response models for multi-response mixture experiments. We generate both approximate and *n*-exact D-optimal designs for multi-response models using FINDMAXIMUM solver of MATHEMATIKA-6.0.

The organization of the rest of this paper is as follows. Section 2 defines multi-response optimal designs for multi-response mixture experiments. In Section 3, we propose the formulation of multi-response optimal designs. For illustrations, we have considered three different models i.e. Scheffé's canonical

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polynomial models (Scheffé 1958, 1963), models with inverse terms (Draper and John 1977a) and K-models for mixture experiments (Draper and Pukelsheim 1998), and have presented the same in Section 4. The advantages of proposed formulation are discussed in Section 5. Section 6 draws some conclusions.

2. MULTI-RESPONSE OPTIMAL DESIGNS FOR MULTI-RESPONSE MIXTURE EXPERIMENTS

In mixture experiments, the measured response is assumed to depend only on the relative proportions of the components present in the mixture. As a result, the factor space reduces to a $(q-1)$ – dimensional simplex S_{q-1}; see Scheffé (1958).

In many practical situations, it may be necessary to measure more than one response for each of the points of S_{q-1}. Such experiments are known as multi-response mixture experiments. The responses are often correlated and thus may not be taken into account separately. In other cases, the cost of experimenting and collecting data using single response mixture experiments makes one to cast the problem as a multi-response mixture experiments.

A multi-response linear model for multi-response mixture experiments can be defined as

$$y_i = \boldsymbol{f}_i'(\boldsymbol{x})\beta_i + \varepsilon_i\,; \qquad i = 1, \ldots, r; \qquad (1)$$

where $\boldsymbol{f}_i(\boldsymbol{x})$ is a vector representing the model form; $\boldsymbol{x} = (x_1, ..., x_q)$ is a design point from S_{q-1}; β_i is a vector of p_i unknown parameters; and ε_i is a random error associated with the ith response and is correlated with ε_j. Assume that the error terms are normally distributed with zero mean and the variance-covariance matrix of the responses are denoted by $\boldsymbol{\Sigma}$.

In optimal design problem, the objective is to find a set of design points so that the function of variance of estimator is minimized. For this purpose we consider approximate design (ξ) and n-exact design (ξ_n); see Atkinson and Donev (1992) and express the variance of estimator as a function of design points and the variance-covariance matrix of random errors. We define the matrix $\mathbf{F}(\boldsymbol{x})$ for each design point $\boldsymbol{x}$ as

$$\mathbf{F}'(\boldsymbol{x}) = \text{Diag}(\boldsymbol{f}_1'(\boldsymbol{x}), \ldots, \boldsymbol{f}_1'(\boldsymbol{x})),$$

denoting a $r \times p$ block-diagonal matrix, where $p = \sum_{i=1}^{r} p_i$. Then, we can write $\text{Var}(\hat{\boldsymbol{\beta}})$ based on n selected observations from S_{q-1} as follows

$$\text{Var}(\hat{\boldsymbol{\beta}}) = \left[\sum_{i=1}^{n} \mathbf{F}(\boldsymbol{x}_i)\boldsymbol{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{x}_i)\right]^{-1}.$$

We assume that $\boldsymbol{\Sigma}$ can be estimated using a consistent estimator like the one suggested by Zellner (1962)

$$\hat{\boldsymbol{\Sigma}} = (\hat{\sigma}_{ij});$$

$$\hat{\sigma}_{ij} = \frac{\boldsymbol{y}_i'[\mathbf{I}_n - \mathbf{X}_i(\mathbf{X}_i'\mathbf{X}_i)^{-1}\mathbf{X}_i'][\mathbf{I}_n - \mathbf{X}_i(\mathbf{X}_i'\mathbf{X}_i)^{-1}\mathbf{X}_i']\boldsymbol{y}_j}{n}; \quad i, j = 1, \ldots, r.$$

One could otherwise assume that the variance-covariance matrix has some known structure such as

$$\begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix}, -1 \le \rho \le 1,$$

for a two response model and similarly for higher dimension.

3. SDP FORMULATION OF MULTI-RESPONSE OPTIMAL DESIGNS

The SDP model has been used in modeling diverse application situations in engineering, statistics, finance and global optimization (Boyd and Vandenberghe 2004, Helmberg 2002). The success of SDP models in various applications has motivated this research to formulate and solve multi-response optimal designs for multi-response mixture experiments as SDP problems.

An n-exact optimal design problem under the conditions specified in Section 2 may be defined as an optimization model as follows

$$\underset{\boldsymbol{x}_i}{\text{Minimize}} \quad \psi\left\{\left[\sum_{i=1}^{n} \mathbf{F}(\boldsymbol{x}_i)\boldsymbol{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{x}_i)\right]^{-1}\right\}$$

$$\text{subject to}: \boldsymbol{x}_i \in S_{q-1},\ i = 1, \ldots, n, \qquad (2)$$

where ψ is a real valued function over the space of positive definite matrices. Given a set of K possible design points denoted by $\gamma_1, ..., \gamma_K \in S_{q-1}$, it is desirable to choose the vector of number of observations $(n_1, ..., n_K)$ to be measured on the design points so that the resulting design ξ_n is maximally informative and $n_1 + ... + n_K = n$. We can write function of general model (2) as follows

$$\left[\sum_{i=1}^{n}\mathbf{F}(\boldsymbol{x_i})\Sigma^{-1}\mathbf{F}'(\boldsymbol{x_i})\right]^{-1} = \left[\sum_{j=1}^{K} n_j\mathbf{F}(\boldsymbol{\gamma_j})\Sigma^{-1}\mathbf{F}'(\boldsymbol{\gamma_j})\right]^{-1}.$$

Therefore, an n-exact optimal design can be defined as the following optimization problem

$$\underset{n_j}{\text{Minimize}} \quad \psi\left\{\left[\sum_{j=1}^{K}\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}$$

subject to : $n_1 + ... + n_K = n,$

$n_j \geq 0$, n_j 's are integers. (3)

We call this problem as multi-response design of multi-response mixture experiment.

Assuming that n_j's are small integers relative to n, a good approximate design can be made by relaxing the integrality constraints. Let $\lambda_j = n_j/n$ be the fraction of the total number of observations to be measured at point $\boldsymbol{\gamma}_j$; we may then express the estimation variance in terms of λ_j as

$$\text{Var}\,(\hat{\boldsymbol{\beta}}) = \frac{1}{n}\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}.$$

The real vector $\boldsymbol{\lambda} \in R^K$ satisfies $\boldsymbol{\lambda} \geq \boldsymbol{0}$, $\boldsymbol{e}'\boldsymbol{\lambda} = 1$, and $\boldsymbol{e}$ represents vector of ones with the appropriate size. Thus, by ignoring the constant factor $1/n$, we have the following model

$$\underset{\lambda_j}{\text{Minimize}} \quad \psi\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}$$

subject to : $\boldsymbol{e}'\boldsymbol{\lambda} = 1$, $\boldsymbol{\lambda} \geq \boldsymbol{0}$. (4)

We call this problem a relaxed multi-response experimental design of mixture experiments and its solution will be an approximate design.

Various real-valued functions (ψ) have been suggested as design criteria (see for example Pukelsheim 1993). Three commonly used criteria are

(1) D-optimality: A design is D-optimal if the determinant of $\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}$ is minimized.

(2) E-optimality: A design is E-optimal if it minimizes the largest eigenvalue of

$$\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}.$$

(3) A-optimality: A design is A-optimal if it minimizes the trace of $\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}$.

We construct the three commonly used optimal design problems by choosing one of the above mentioned forms of ψ as follows

3.1 Multi-response D-optimal Design

Multi-response D-optimal design problem is constructed if ψ is defined to be logarithm of the determinant of the estimation variance-covariance matrix

$$\underset{\lambda_j}{\text{Minimize}} \quad \text{logdet}\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}$$

or equivalently,

$$\underset{\lambda_j}{\text{Maximize}} \quad \text{logdet}\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]\right\}$$

subject to : $\boldsymbol{e}'\boldsymbol{\lambda} = 1$, $\boldsymbol{\lambda} \geq \boldsymbol{0}$. (5)

We have obtained the multi-response D-optimal design using the maximization of the objective function

i.e. $\underset{\lambda_j}{\text{Maximize}} \quad \text{logdet}\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]\right\}$.

3.2 Multi-response E-optimal Design

If ψ is taken as l_2-norm then the multi-response E-optimal design model is constructed as

$$\underset{\lambda_j}{\text{Minimize}}\left\|\left\{\left[\sum_{j=1}^{K}\lambda_j\mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j)\right]^{-1}\right\}\right\|_2$$

subject to: $\boldsymbol{e}'\boldsymbol{\lambda} = 1$, $\boldsymbol{\lambda} \geq \boldsymbol{0}$. (6)

This is a convex optimization problem since the objective function is a convex function of λ. The matrix norm $\left\| \left\{ \left[\sum_{j=1}^{K} \lambda_j \mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j) \right]^{-1} \right\} \right\|_2$ is equivalent to the largest eigenvalue of the matrix, i.e. $\mu_{\max}\left\{ \left[\sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) \right]^{-1} \right\}$. We know that

$$\mu_{\min}(\mathbf{A}) = \frac{1}{\mu_{\max}(\mathbf{A}^{-1})} \text{ and } \mu_{\min}(\mathbf{A}) \geq t \Leftrightarrow \mathbf{A} \succ = t\mathbf{I}$$

(Boyd and Vandenberghe 2004). Then, using these relations the multi-response E-optimal design can be defined in an SDP form as follows

$$\underset{\lambda_j, t}{\text{Maximize}} \quad t$$

$$\text{subject to : } \sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) \succ = t\mathbf{I}$$

$$\boldsymbol{e}'\boldsymbol{\lambda} = 1, \ \boldsymbol{\lambda} \geq \boldsymbol{0}. \tag{7}$$

The sign $\succ =$ indicates Löwner partial order.

3.3 Multi-response A-optimal Design

In multi-response A-optimal design problem we minimize trace of the estimation variance-covariance matrix. Then we can write optimization for A-optimal design as

$$\underset{\lambda_j}{\text{Minimize}} \quad \text{trace}\left[\sum_{j=1}^{K} \lambda_j \mathbf{F}(\gamma_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\gamma_j) \right]^{-1}$$

$$\text{subject to: } \boldsymbol{e}'\boldsymbol{\lambda} = 1, \ \boldsymbol{\lambda} \geq \boldsymbol{0}. \tag{8}$$

This is a convex optimization problem. We can write the model (8) in an SDP form using the Schur complement theorem as explained below.

Let $\mathbf{A} \in S_r^{++}, \mathbf{B} \in Z_q$ and $\mathbf{C} \in M_{r,q}$, S_r^{++} is the set of symmetric positive definite $r \times r$ matrices, Z_q is the set of symmetric $q \times q$ matrices and $M_{r,q}$ is the set of $r \times q$ real matrices. Then

$$\begin{bmatrix} \mathbf{A} & \mathbf{C} \\ \mathbf{C}' & \mathbf{B} \end{bmatrix} \succ = \mathbf{0} \Leftrightarrow \mathbf{B} \succ = \mathbf{C}'\mathbf{A}^{-1}\mathbf{C}.$$

(Helmberg 2002)

According to this theorem and linear algebra, we can write

$$\text{trace}\left[\sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) \right]^{-1} = \sum_{i=1}^{n} \mu_i$$

$$= \text{trace}\,(\text{Diag}(\mu)),$$

$$\begin{bmatrix} \sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) & \mathbf{I} \\ \mathbf{I} & \text{Diag}\,(\mu) \end{bmatrix} \succ = \mathbf{0}$$

$$\Leftrightarrow \quad \text{Diag}\,(\mu) \succ = \mathbf{I}'\left[\sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) \right]^{-1} \mathbf{I}.$$

We can cast model (8) as an SDP model as follows

$$\underset{\lambda_j, \mu}{\text{Minimize}} \ \boldsymbol{e}'\boldsymbol{\mu}$$

$$\text{subject to: } \begin{bmatrix} \sum_{j=1}^{K} \lambda_j \mathbf{F}(\boldsymbol{\gamma}_j)\mathbf{\Sigma}^{-1}\mathbf{F}'(\boldsymbol{\gamma}_j) & \mathbf{I} \\ \mathbf{I} & \text{Diag}\,(\mu) \end{bmatrix} \succ = \mathbf{0},$$

$$\boldsymbol{e}'\boldsymbol{\lambda} = 1, \ \boldsymbol{\lambda} \geq \boldsymbol{0}. \tag{9}$$

We can similarly write the model for n-exact design problems. We obtain optimum λ_j's and n_j's according to approximate and n-exact designs using FINDMAXIMUM solver of MATHEMATIKA-6.0. To obtain optimum λ_j's and n_j's we need to input the following data

(1) The set of all possible design points $\boldsymbol{\gamma}_j$'s.

(2) The variance-covariance matrix Σ which can be estimated as explained in Section 2.

(3) The total number of observations (n) in case of n-exact design.

4. ILLUSTRATIONS

In this section, applicability of the proposed approach is investigated by three different examples. The SDP models have been solved using Mathematika-6.0.

Example 1 : Suppose $q = 2$ and $r = 2$. Let us consider linear and quadratic Scheffé's canonical polynomial models i.e. suppose

$$f_1'(\boldsymbol{x}) = (x_1, x_2)$$

and $$f_2'(\boldsymbol{x}) = (x_1, x_2, x_1x_2).$$

Table 1. Multi-response D-optimal design for Scheffé's canonical polynomial models

x_1	x_2	λ^a	λ^e
1	0	0.375	19
0	1	0.375	19
1/2	1/2	0.25	12
1/4	3/4	1.311e-8	0
3/4	1/4	1.311e-8	0

Let us assume that

$$\Sigma = \begin{bmatrix} 2 & 0.4 \\ 0.4 & 1 \end{bmatrix}$$

and the 5 support points (design points) for the saturated design are (1, 0), (0, 1), (1/2, 1/2), (1/4, 3/4) and (3/4, 1/4). The design measure for an approximate D-optimal design and the number of observations for an n-exact D-optimal design (for $n = 50$) are given as columns λ^a and λ^e respectively in Table 1. The values of the objective function for the two designs are –8.93067 and 6.71634 respectively.

We investigated the sensitivity of the D-optimal design with respect to the variations in $\mathbf{\Sigma}$. In place of

$$\mathbf{\Sigma} = \begin{bmatrix} 2 & 0.4 \\ 0.4 & 1 \end{bmatrix}$$

we consider

$$\mathbf{\Sigma} = \begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix}, \rho \in (-1, 1).$$

By setting $\rho = 0$, $\rho = -0.1$, $\rho = 0.1$, $\rho = -0.4$, $\rho = 0.4$, $\rho = -0.9$ and $\rho = 0.9$, we generate, design measure for approximate D-optimal designs which are given as columns $\lambda^{(1)}, \ldots, \lambda^{(7)}$ in Table 2.

Table 3 gives the variations obtained in the values of objective function in the variance-covariance matrix.

Example 2 : Suppose $q = 2$ and $r = 2$. Let us consider linear and quadratic K-models for mixture experiments i.e.

$$\boldsymbol{f}_1'(\boldsymbol{x}) = (x_1, x_2)$$

Table 2. The results of sensitivity analysis of D-optimal design due to variations in $\mathbf{\Sigma}$ for Scheffé's canonical polynomial models

x_1	x_2	$\lambda^{(1)}$	$\lambda^{(2)}$	$\lambda^{(3)}$	$\lambda^{(4)}$	$\lambda^{(5)}$	$\lambda^{(6)}$	$\lambda^{(7)}$
1	0	0.375	0.375	0.375	0.375	0.375	0.375	0.375
0	1	0.375	0.375	0.375	0.375	0.375	0.375	0.375
1/2	1/2	0.250	0.250	0.25	0.250	0.250	0.250	0.250
1/4	3/4	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8
3/4	1/4	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8	1.311e-8

Table 3. Variations of the objective values with respect to variations in $\mathbf{\Sigma}$

ρ	0	± 0.1	± 0.4	± 0.9
Value of Objective function	–7.79452	–7.76437	–7.27146	–2.81232

Table 4. Multi-response D-optimal design for K-models for mixture experiments

x_1	x_2	λ^a	λ^e
1	0	0.375	19
0	1	0.375	19
1/2	1/2	0.250	12
1/4	3/4	1.56208e-8	0
3/4	1/4	1.56208e-8	0

Table 5. The results of sensitivity analysis of D-optimal design due to variations in Σ for K-models for mixture experiments

x_1	x_2	$\lambda^{(1)}$	$\lambda^{(2)}$	$\lambda^{(3)}$	$\lambda^{(4)}$	$\lambda^{(5)}$	$\lambda^{(6)}$	$\lambda^{(7)}$
1	0	0.375	0.375	0.375	0.375	0.375	0.375	0.375
0	1	0.375	0.375	0.375	0.375	0.375	0.375	0.375
$\frac{1}{2}$	$\frac{1}{2}$	0.250	0.250	0.250	0.250	0.250	0.250	0.250
$\frac{1}{4}$	$\frac{3}{4}$	1.550e-7	1.551e-8	1.551e-8	1.576e-8	1.576e-8	2.271e-8	2.271e-8
$\frac{3}{4}$	$\frac{1}{4}$	1.550e-7	1.551e-8	1.551e-8	1.576e-8	1.576e-8	2.271e-8	2.271e-8

Table 6. Variations of the objective values with respect to variations in Σ

ρ	0	± 0.1	± 0.4	± 0.9
Objective function value	–6.40822	–6.37807	–5.88516	–1.42603

and $$f_2'(\boldsymbol{x}) = \left(x_1^2, x_2^2, 2x_1x_2\right).$$

Using the same design points and variance-covariance matrix as in Example 1, we have the following results for multi-response K-models for mixture experiments as given in Table 4, Table 5 and Table 6.

The values of objective function for approximate D-optimal design and n-exact D-optimal design are -7.54437 and 8.10263 respectively.

Example 3 : Suppose $q = 2$ and $r = 2$. Let us consider linear and quadratic models with inverse terms i.e. suppose

$$f_1'(\boldsymbol{x}) = \left(x_1, x_2, 1/x_1, 1/x_2\right)$$

and $$f_2'(\boldsymbol{x}) = \left(x_1, x_2, x_1x_2, 1/x_1, 1/x_2\right).$$

Assume the same variance-covariance matrix

$$\boldsymbol{\Sigma} = \begin{bmatrix} 2 & 0.4 \\ 0.4 & 1 \end{bmatrix}.$$

We conjecture from Chan and Guan (1994) that the 9 support points for the saturated design can be (0.05, 0.95), (0.95, 0.05), (0.06, 0.94), (0.94, 0.06), (0.07, 0.93), (0.93, 0.07), (0.08, 0.92), (0.92, 0.08), and (0.09, 0.91). The design measure for approximate D-optimal design is given in Table 7. The value of objective function for approximate D-optimal design is –11.4736.

Table 7. Multi-response D-optimal design for models with inverse terms

x_1	x_2	λ^a
0.05	0.95	0.215831
0.95	0.05	0.222216
0.06	0.94	1.49013e-7
0.94	0.06	1.03502e-7
0.07	0.93	0.14255
0.93	0.07	4.65773e-7
0.08	0.92	4.31802e-9
0.92	0.08	0.222205
0.09	0.91	0.197198

The D-optimal design with the same variance-covariance matrix

$$\boldsymbol{\Sigma} = \begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix}, \rho \in (-1, 1),$$

for $\rho = 0$, $\rho = -0.1$, $\rho = 0.1$, $\rho = -0.4$, $\rho = 0.4$, $\rho = -0.9$ and $\rho = 0.9$ have the following results of sensitivity which have been provided in Table 8 and Table 9.

Table 8. The results of sensitivity analysis of D-optimal design due to variations in $\mathbf{\Sigma}$ for models with inverse terms

x_1	x_2	$\lambda^{(1)}$	$\lambda^{(2)}$	$\lambda^{(3)}$	$\lambda^{(4)}$	$\lambda^{(5)}$	$\lambda^{(6)}$	$\lambda^{(7)}$
0.05	0.95	0.215831	0.215831	0.215831	0.215831	0.215831	0.215831	0.215831
0.95	0.05	0.222216	0.222216	0.222216	0.222216	0.222216	0.222216	0.222216
0.06	0.94	1.490e-7	1.490e-7	1.490e-7	1.490e-7	1.490e-7	1.490e-7	1.490e-7
0.94	0.06	1.035e-7	1.035e-7	1.035e-7	1.035e-7	1.035e-7	1.035e-7	1.035e-7
0.07	0.93	0.14255	0.14255	0.14255	0.14255	0.14255	0.14255	0.14255
0.93	0.07	4.657e-7	4.657e-7	4.657e-7	4.657e-7	4.657e-7	4.657e-7	4.657e-7
0.08	0.92	4.318e-9	4.318e-9	4.318e-9	4.318e-9	4.318e-9	4.318e-9	4.318e-9
0.92	0.08	0.222205	0.222205	0.222205	0.222205	0.222205	0.222205	0.222205
0.09	0.91	0.197198	0.197198	0.197198	0.197198	0.197198	0.197198	0.197198

Table 9. Variations of the objective values with respect to variations in $\mathbf{\Sigma}$

ρ	0	± 0.1	± 0.4	± 0.9
Value of objective function	–9.11788	–9.06763	–8.24612	–0.814227

5. DISCUSSION

In this section we have mentioned some of the advantages of the proposed formulation for obtaining multi-response optimal design.

(1) We can perform sensitivity analysis of the optimal design.

(2) The proposed formulation is flexible and comprehensive so that other constraints such as cost may be added to the model. For example, let C is given total budget and cost of measuring observations in each possible design point is given by $c_1,\ldots, c_K$ for $\gamma_1,\ldots,\gamma_K$ respectively. This constraint could be defined and added to the general model as follows

$$n_1c_1 + \ldots + n_Kc_K \leq C.$$

(3) We have used MATHEMATIKA-6.0 to generate multi-response approximate D-optimal design for Examples 1, 2 and 3. We have also generated multi-response n-exact D-optimal design for Examples 1 and 2 only. One can use the SDP solver of TOMLAB (Holmstrom 2004) and YALMIP (Löfberg 2005) software within MATLAB environment to generate multi-response approximate and n-exact D-, A-, E-optimal designs with less computation time.

(4) We assume that the random errors are correlated with each other with variance-covariance matrix which is of heteroscedastic nature. In general, in the literature of mixture experiments it is assumed that the random errors are uncorrelated with variance-covariance matrix which is of homoscedastic nature.

6. CONCLUSIONS

In this paper, we propose a formulation for multi-response D-, E- and A-optimal designs of mixture experiments. Applicability of the proposed methods has been investigated using three different examples. Numerical experiments show that the SDP formulations generate multi-response optimal designs efficiently. The SDP formulation has more flexibility to add some cost and technological constraints within the model.

We have found that using linear and quadratic Scheffé's canonical polynomial models and K-models for mixture experiments we obtain same multi-response n-exact D-optimal design but slightly different approximate D-optimal design using the same design points and variance-covariance matrix. Also we observe that for all the three examples (from Table 3, Table 6, and Table 9), that estimation of the unknown parameters β is improved if the correlation between the responses is large. However, the sign of covariance does not seem to have significant effects on the objective function values.

The SDP formulation enables experimenters to perform sensitivity analysis on the generated optimal designs. Furthermore, it allows experimenters to generate multi-response optimal designs for large scale problems using TOMLAB (Holmstrom 2004) and YALMIP (Löfberg 2005) software within MATLAB environment.

We have considered only linear and quadratic Scheffé's canonical polynomial models, models with inverse terms and K-models for mixture experiments. One can use other models of mixture experiments with more than two response models at a time. Also one can use models of higher degree in place of linear and quadratic.

REFERENCES

Atkinson, A.C. and Donev, A.N. (1992). *Optimum Experimental Designs*. Oxford University Press, Oxford.

Boyd, S. and Vandenberghe, L. (2004). *Convex Optimization*. Cambridge University Press, Cambridge.

Chan, L.Y. and Guan, Y. (1994). Designs in mixtures models with inverse terms for two components. *Proceedings of the 5th Japan-China Symposium on Statistics*, April 1994, Okayama, Japan. University Education Press, 24-27.

Chang, S.I. (1994). Some properties of multi-response D-optimal designs. *J. Math. Anal. Appl*., **184(2)**, 256-262.

Chang, S.I. (1997). An algorithm to generate near D-optimal designs for multi-response surface models. *IIE Trans*, **29,** 1073-1081.

Draper, N.R. and Hunter, W.G. (1966). Designs of experiments for parameter estimation in multi-response situations. *Biometrika*, **53,** 525-533.

Draper, N.R. and John, R.C. St. (1977a). A mixture models with inverse terms. *Technometrics*, **19,** 37-46.

Draper, N.R. and Pukelshiem, F. (1998). Mixtures models based on homogeneous polynomial. *J. Statist. Plann. Inf*., **71,** 303-311.

Fedorov, V.V. (1972). *Theory of Optimal Experiments*. Academic Press. New York.

Gallego, J.B., Lopez, F.N.A., Chiesa, A., Quintana, M.C.D. and Fernandez, A.G. (2008). Use of a D-optimal design with constraints to quantify the effects of the mixture of sodium, potassium, calcium and magnesium chloride salts on the growth parameters of Saccharomyces cerevisiae. *J. Ind. Microbiol. Biotech*., **35(8)**, 889-900.

Gonnissen, Y., Goncalves, S.I.V., Remon, J.P. and Vervaet, C. (2008). Mixture design applied to optimize a directly compressible powder produced via Cospray drying. *Drug. Dev. Ind. Pharm*., **34,** 248-257.

Helmberg, C. (2002). Semidefinite programming (Invited Review). *Eur. J. Oper. Res*., **137,** 461-482.

Holmostrom, K. (2004). TOMLAB version 4.4. Tomlab Optimization, San Diego.

Khuri, A.I. and Cornell, J.A. (1996). *Response Surfaces: Designs and Analysis*, 2nd edn. Marcel Dekker, New York.

Löfberg, J. (2005). YALMIP version 3. Available at http: // control. ee. ethz. ch/ ~joloef /yalmip. php.

Ozdemir, M. and Floros, J.D. (2008). Optimization of edible whey protein films containing preservatives for mechanical and optical properties. *J. Food. Engg*., **84(2),** 116-123.

Pukelsheim, F. (1993). *Optimal Design of Experiments*. Wiley, New York.

Roy, S.N., Gnanadesikan, R. and Srivastava, J.N. (1971). *Analysis and Design of Certain Quantitative Multi-response Experiments*. Pergamon Press, New York.

Scheffé, H. (1958). Experiments with mixtures. *J. Roy. Statist. Soc*., **B20(2),** 344-360.

Scheffé, H. (1963). The simplex-centroid design for experiments with mixtures. *J. Roy. Statist. Soc*., **B25,** 235-263.

Wijesinha, M.M.C. (1984). *Design of experiments for multi-response models*. Unpublished Ph. D. thesis, Department of Statistics, University of Florida, Gainesville.

Zellner, A. (1962). An efficient method of estimating seeming unrelated regressions and tests for aggregation bias. *J. Amer. Statist. Assoc*., **57,** 348-368.