Construction Of Maxi-Min Efficiency Designs

Tommasi, C.[1], Rodríguez-Díaz J.M.[2], López-Fidalgo J.[3]

[1] University of Milano
[2] University of Salamanca
[3] University of Navarre

mODa 13, July 14 2023 Southampton

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1 : ODE for model discrimination
- Example 2 : ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Outline

- Introduction
- Optimal Design of Experiments
- Maximin efficiency and pseudo-Bayesian-criteria
- Equivalence theorem
- Example 1: ODE for model discrimination
- Example 2: ODE for parameter estimation
- Conclusions

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior, which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior, which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior, which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior, which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Introduction

- Aim: solve a multi-objective optimization problem that consists in the maximization of a minimum design-efficiency
- Different approaches can be classified as maxi-min efficiency criteria (e.g. the standardized max-min criterion)
- Reversely, examples of maxi-min efficiency criteria that can be interpreted as multi-objective problems (e.g. SMV-criterion, or the extensions of T- and KL-criteria). Another might be obtaining an optimal design for model identification, precise parameter estimation and accurate predictions.
- The maxi-min approach arises naturally when protecting against the worst case scenario; however optimal designs are difficult to compute because this criterion is not differentiable
- Main contribution: prove the equivalence between maxi-min efficiency and Bayesian criterion for a specific prior, which is differentiable. Hence, the latter can be used to check for the minimum efficiency optimality

Optimal Design of Experiments

- $f(y, x, \theta)$ model, Y response, $x \in \mathcal{X}$, $\theta \in \Theta \subseteq \mathbb{R}^p$ parameter vector
- Approximate design: probability measure on $\mathcal{X}$ with finite support,

$$\xi = \left\{ \begin{array}{cccc} x_1 & x_2 & \cdots & x_r \\ \xi(x_1) & \xi(x_2) & \cdots & \xi(x_r) \end{array} \right\},$$

  where $\xi(x_i) \approx n_i/n$.
- Aim: find a design ξ_θ^* maximizing (minimizing) a concave (convex) optimality criterion function $\Phi(\xi; \theta)$
- An optimal design ξ_θ^* may be found according to several criteria reflecting different inferential goals: parameter estimation, prediction or model discrimination

Optimal Design of Experiments

- $f(y, x, \theta)$ model, Y response, $x \in \mathcal{X}$, $\theta \in \Theta \subseteq \mathbb{R}^p$ parameter vector
- Approximate design: probability measure on $\mathcal{X}$ with finite support,

$$\xi = \left\{ \begin{array}{cccc} x_1 & x_2 & \cdots & x_r \\ \xi(x_1) & \xi(x_2) & \cdots & \xi(x_r) \end{array} \right\},$$

  where $\xi(x_i) \approx n_i/n$,
- Aim: find a design ξ_θ^* maximizing (minimizing) a concave (convex) optimality criterion function $\Phi(\xi; \theta)$
- An optimal design ξ_θ^* may be found according to several criteria reflecting different inferential goals: parameter estimation, prediction or model discrimination.

Optimal Design of Experiments

- $f(y, x, \theta)$ model, Y response, $x \in \mathcal{X}$, $\theta \in \Theta \subseteq \mathbb{R}^p$ parameter vector
- Approximate design: probability measure on $\mathcal{X}$ with finite support,

$$\xi = \left\{ \begin{array}{cccc} x_1 & x_2 & \cdots & x_r \\ \xi(x_1) & \xi(x_2) & \cdots & \xi(x_r) \end{array} \right\},$$

  where $\xi(x_i) \approx n_i/n$,
- Aim: find a design ξ^*_θ maximizing (minimizing) a concave (convex) optimality criterion function $\Phi(\xi; \theta)$
- An optimal design ξ^*_θ may be found according to several criteria reflecting different inferential goals: parameter estimation, prediction or model discrimination.

Optimal Design of Experiments

- $f(y, x, \theta)$ model, Y response, $x \in \mathcal{X}$, $\theta \in \Theta \subseteq \mathbb{R}^p$ parameter vector
- Approximate design: probability measure on $\mathcal{X}$ with finite support,

$$\xi = \left\{ \begin{array}{cccc} x_1 & x_2 & \cdots & x_r \\ \xi(x_1) & \xi(x_2) & \cdots & \xi(x_r) \end{array} \right\},$$

  where $\xi(x_i) \approx n_i/n$,
- Aim: find a design ξ_θ^* maximizing (minimizing) a concave (convex) optimality criterion function $\Phi(\xi; \theta)$
- An optimal design ξ_θ^* may be found according to several criteria reflecting different inferential goals: parameter estimation, prediction or model discrimination.

Optimal Design of Experiments

- $f(y, x, \theta)$ model, Y response, $x \in \mathcal{X}$, $\theta \in \Theta \subseteq \mathbb{R}^p$ parameter vector
- Approximate design: probability measure on $\mathcal{X}$ with finite support,

$$\xi = \left\{ \begin{array}{cccc} x_1 & x_2 & \cdots & x_r \\ \xi(x_1) & \xi(x_2) & \cdots & \xi(x_r) \end{array} \right\},$$

  where $\xi(x_i) \approx n_i/n$,
- Aim: find a design ξ^*_θ maximizing (minimizing) a concave (convex) optimality criterion function $\Phi(\xi; \theta)$
- An optimal design ξ^*_θ may be found according to several criteria reflecting different inferential goals: parameter estimation, prediction or model discrimination.

- Many optimality criteria are concave (or convex) functions of the information matrix of a design $\xi \in \Xi$,

$$M(\xi, \theta) = \int_{\mathcal{X}} \mathrm{E}_Y \left\{ \frac{\partial \log f(y, x, \theta)}{\partial \theta} \frac{\partial \log f(y, x, \theta)}{\partial \theta^T} \right\} d\xi(x).$$

- For $\Phi(\xi; \theta)$ is a non-negative homogeneous concave function, the efficiency function

$$0 \leq \mathrm{Eff}(\xi, \theta) = \frac{\Phi(\xi, \theta)}{\Phi(\xi_\theta^*, \theta)} \leq 1.$$

is a measure of the goodness of the design ξ with respect to the optimal design ξ_θ^* (the ratio should be reversed for convex criteria).

Optimal Design of Experiments

- Many optimality criteria are concave (or convex) functions of the information matrix of a design $\xi \in \Xi$,

$$M(\xi, \theta) = \int_{\mathcal{X}} \mathrm{E}_Y \left\{ \frac{\partial \log f(y, x, \theta)}{\partial \theta} \frac{\partial \log f(y, x, \theta)}{\partial \theta^T} \right\} d\xi(x).$$

- For $\Phi(\xi; \theta)$ is a non-negative homogeneous concave function, the efficiency function

$$0 \leq \mathrm{Eff}(\xi, \theta) = \frac{\Phi(\xi, \theta)}{\Phi(\xi^*_\theta, \theta)} \leq 1.$$

is a measure of the goodness of the design ξ with respect to the optimal design ξ^*_θ (the ratio should be reversed for convex criteria).

Optimal Design of Experiments

- Many optimality criteria are concave (or convex) functions of the information matrix of a design $\xi \in \Xi$,

$$M(\xi, \theta) = \int_{\mathcal{X}} \mathrm{E}_Y \left\{ \frac{\partial \log f(y, x, \theta)}{\partial \theta} \frac{\partial \log f(y, x, \theta)}{\partial \theta^T} \right\} d\xi(x).$$

- For $\Phi(\xi; \theta)$ is a non-negative homogeneous concave function, the efficiency function

$$0 \leq \mathrm{Eff}(\xi, \theta) = \frac{\Phi(\xi, \theta)}{\Phi(\xi_\theta^*, \theta)} \leq 1.$$

  is a measure of the goodness of the design ξ with respect to the optimal design ξ_θ^* (the ratio should be reversed for convex criteria).

Pseudo Bayesian-criteria

- $\Phi_i(\xi)$, $i = 1, \ldots, k$ concave optimality criteria
- Standardized criteria (Dette, 1997): $\mathrm{Eff}_i(\xi) = \Phi_i(\xi)/\Phi_i(\xi_i^*)$, $i = 1, \ldots, k$
- When interested in a compromise design 'good' for all the criteria, we have to combine them. An easy way is through a linear combination. A Bayesian optimum design maximizes

$$\Phi_B(\xi;\pi) = \sum_{i=1}^{k} \pi_i \cdot \mathrm{Eff}_i(\xi), \quad 0 \leq \pi_i \leq 1, \ \sum_{i=1}^{k} \pi_i = 1,$$

where $\pi^T = (\pi_1, \ldots, \pi_k)$ is a prior probability on the set $\{1, \ldots, k\}$

- A design ξ_π^* is Bayesian optimal if and only if

$$\sum_{i=1}^{k} \pi_i \frac{\partial \Phi_i(\xi_\pi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \quad x \in \mathcal{X}.$$

Pseudo Bayesian-criteria

- $\Phi_i(\xi)$, $i = 1, \ldots, k$ concave optimality criteria
- Standardized criteria (Dette, 1997): $\mathrm{Eff}_i(\xi) = \Phi_i(\xi)/\Phi_i(\xi_i^*)$, $i = 1, \ldots, k$
- When interested in a compromise design 'good' for all the criteria, we have to combine them. An easy way is through a linear combination. A Bayesian optimum design maximizes

$$\Phi_B(\xi;\pi) = \sum_{i=1}^{k} \pi_i \cdot \mathrm{Eff}_i(\xi), \quad 0 \le \pi_i \le 1, \ \sum_{i=1}^{k} \pi_i = 1,$$

  where $\pi^T = (\pi_1, \ldots, \pi_k)$ is a prior probability on the set $\{1, \ldots, k\}$
- A design ξ_π^* is Bayesian optimal if and only if

$$\sum_{i=1}^{k} \pi_i \frac{\partial \Phi_i(\xi_\pi^*, \xi_x)}{\Phi_i(\xi_i^*)} \le 0, \qquad x \in \mathcal{X},$$

Pseudo Bayesian-criteria

- $\Phi_i(\xi)$, $i = 1, \ldots, k$ concave optimality criteria
- Standardized criteria (Dette, 1997): $\text{Eff}_i(\xi) = \Phi_i(\xi)/\Phi_i(\xi_i^*)$, $i = 1, \ldots, k$
- When interested in a compromise design 'good' for all the criteria, we have to combine them. An easy way is through a linear combination. A Bayesian optimum design maximizes

$$\Phi_B(\xi;\pi)=\sum_{i=1}^{k}\pi_i \cdot \text{Eff}_i(\xi), \quad 0 \le \pi_i \le 1, \ \sum_{i=1}^{k}\pi_i = 1,$$

where $\pi^T = (\pi_1, \ldots, \pi_k)$ is a prior probability on the set $\{1, \ldots, k\}$

- A design ξ_π^* is Bayesian optimal if and only if

$$\sum_{i=1}^{k}\pi_i \frac{\partial \Phi_i(\xi_\pi^*, \xi_x)}{\Phi_i(\xi_i^*)} \le 0, \qquad x \in \mathcal{X},$$

Pseudo Bayesian-criteria

- $\Phi_i(\xi)$, $i = 1, \ldots, k$ concave optimality criteria
- Standardized criteria (Dette, 1997): $\mathrm{Eff}_i(\xi) = \Phi_i(\xi)/\Phi_i(\xi_i^*)$, $i = 1, \ldots, k$
- When interested in a compromise design 'good' for all the criteria, we have to combine them. An easy way is through a linear combination. A Bayesian optimum design maximizes

$$\Phi_B(\xi;\pi) = \sum_{i=1}^{k} \pi_i \cdot \mathrm{Eff}_i(\xi), \quad 0 \leq \pi_i \leq 1, \ \sum_{i=1}^{k} \pi_i = 1,$$

where $\pi^T = (\pi_1, \ldots, \pi_k)$ is a prior probability on the set $\{1, \ldots, k\}$

- A design ξ_π^* is Bayesian optimal if and only if

$$\sum_{i=1}^{k} \pi_i \frac{\partial \Phi_i(\xi_\pi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X},$$

Pseudo Bayesian-criteria

- $\Phi_i(\xi)$, $i = 1, \ldots, k$ concave optimality criteria
- Standardized criteria (Dette, 1997): $\text{Eff}_i(\xi) = \Phi_i(\xi)/\Phi_i(\xi_i^*)$, $i = 1, \ldots, k$
- When interested in a compromise design 'good' for all the criteria, we have to combine them. An easy way is through a linear combination. A Bayesian optimum design maximizes

$$\Phi_B(\xi;\pi) = \sum_{i=1}^{k} \pi_i \cdot \text{Eff}_i(\xi), \quad 0 \leq \pi_i \leq 1, \ \sum_{i=1}^{k} \pi_i = 1,$$

  where $\pi^T = (\pi_1, \ldots, \pi_k)$ is a prior probability on the set $\{1, \ldots, k\}$
- A design ξ_π^* is Bayesian optimal if and only if

$$\sum_{i=1}^{k} \pi_i \frac{\partial \Phi_i(\xi_\pi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X},$$

Maximin efficiency

- Another possibility is the minimum efficiency criterion

$$\Phi(\xi) = \min_{i \in \{1,\ldots,k\}} \mathrm{Eff}_i(\xi) = \left[\max_{i \in \{1,\ldots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)} \right]^{-1}.$$

- This criterion is not differentiable, and thus the computation of Φ-optimal designs is not straightforward at all
- A design ξ^* is a *maxi-min efficient* if minimizes the convex criterion

$$\Phi^{-1}(\xi) = \max_{i \in \{1,\ldots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)}.$$

- Connection between both already explored in literature, but always center on specific problems and/or optimality criteria

Maximin efficiency

- Another possibility is the minimum efficiency criterion

$$\Phi(\xi) = \min_{i\in\{1,\dots,k\}} \text{Eff}_i(\xi) = \left[\max_{i\in\{1,\dots,k\}} \frac{1}{\text{Eff}_i(\xi)}\right]^{-1}.$$

- This criterion is not differentiable, and thus the computation of Φ-optimal designs is not straightforward at all
- A design ξ^* is a *maxi-min efficient* if minimizes the convex criterion

$$\Phi^{-1}(\xi) = \max_{i\in\{1,\dots,k\}} \frac{1}{\text{Eff}_i(\xi)}.$$

- Connection between both already explored in literature, but always center on specific problems and/or optimality criteria.

Maximin efficiency

- Another possibility is the minimum efficiency criterion

$$\Phi(\xi) = \min_{i\in\{1,\ldots,k\}} \text{Eff}_i(\xi) = \left[\max_{i\in\{1,\ldots,k\}} \frac{1}{\text{Eff}_i(\xi)} \right]^{-1}.$$

- This criterion is not differentiable, and thus the computation of Φ-optimal designs is not straightforward at all
- A design ξ^* is a *maxi-min efficient* if minimizes the convex criterion

$$\Phi^{-1}(\xi) = \max_{i\in\{1,\ldots,k\}} \frac{1}{\text{Eff}_i(\xi)}.$$

- Connection between both already explored in literature, but always center on specific problems and/or optimality criteria.

Maximin efficiency

- Another possibility is the minimum efficiency criterion

$$\Phi(\xi) = \min_{i \in \{1,\dots,k\}} \mathrm{Eff}_i(\xi) = \left[\max_{i \in \{1,\dots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)} \right]^{-1}.$$

- This criterion is not differentiable, and thus the computation of Φ-optimal designs is not straightforward at all
- A design ξ^* is a *maxi-min efficient* if minimizes the convex criterion

$$\Phi^{-1}(\xi) = \max_{i \in \{1,\dots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)}.$$

- Connection between both already explored in literature, but always center on specific problems and/or optimality criteria.

Maximin efficiency

- Another possibility is the minimum efficiency criterion

$$\Phi(\xi) = \min_{i\in\{1,\dots,k\}} \mathrm{Eff}_i(\xi) = \left[\max_{i\in\{1,\dots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)}\right]^{-1}.$$

- This criterion is not differentiable, and thus the computation of Φ-optimal designs is not straightforward at all
- A design ξ^* is a *maxi-min efficient* if minimizes the convex criterion

$$\Phi^{-1}(\xi) = \max_{i\in\{1,\dots,k\}} \frac{1}{\mathrm{Eff}_i(\xi)}.$$

- Connection between both already explored in literature, but always center on specific problems and/or optimality criteria.

Analytical results

Proposition

The directional derivative of $\Phi^{-1}(\xi)$ at ξ in the direction of $\bar{\xi} - \xi$ is

$$\partial\Phi^{-1}(\xi;\bar{\xi}) = \max_{e_i \in \mathcal{C}(\xi)} \int_{\mathcal{X}} \psi(x, e_i, \xi)\bar{\xi}(dx),$$

where e_i denotes the canonical vector of the Euclidean space,

$$\mathcal{C}(\xi) = \left\{ e_i : \; i = \arg \max_{j \in \{1,\dots k\}} \frac{1}{\mathrm{Eff}_j(\xi)} \right\} = \left\{ e_i : \; i = \arg \min_{j \in \{1,\dots k\}} \mathrm{Eff}_j(\xi) \right\},$$

and $\psi(x, e_i, \xi) = -\Phi_i(\xi_i^*) \dfrac{\partial \Phi_i(\xi, \xi_x)}{\Phi_i^2(\xi)}$.

Analytical results

Proposition

The directional derivative of $\Phi^{-1}(\xi)$ *at* ξ *in the direction of* $\bar{\xi} - \xi$ *is*

$$\partial\Phi^{-1}(\xi;\bar{\xi}) = \max_{e_i \in \mathcal{C}(\xi)} \int_{\mathcal{X}} \psi(x, e_i, \xi)\bar{\xi}(dx),$$

where e_i *denotes the canonical vector of the Euclidean space,*

$$\mathcal{C}(\xi) = \left\{ e_i : \; i = \arg \max_{j \in \{1,\ldots k\}} \frac{1}{\mathrm{Eff}_j(\xi)} \right\} = \left\{ e_i : \; i = \arg \min_{j \in \{1,\ldots k\}} \mathrm{Eff}_j(\xi) \right\},$$

and $\psi(x, e_i, \xi) = -\Phi_i(\xi_i^*) \dfrac{\partial\Phi_i(\xi, \xi_x)}{\Phi_i^2(\xi)}$.

Equivalence theorem

Theorem (Equivalence Theorem)

A design ξ^* is a maxi-min efficiency design if and only if there exists a probability distribution π^* on the index set

$$\mathcal{I}(\xi^*) = \left\{ i : \; i = \arg \min_{j \in \{1,\dots,k\}} \mathrm{Eff}_j(\xi^*) \right\},$$

such that ξ^* is a Bayesian optimum design for the prior distribution π^*, that is, if and only if ξ^* fulfils the following inequality,

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial \Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

Furthermore, the quantity $\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial \Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)}$ attains its maximum value of zero at every support point of ξ^*.

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*,\overline{\xi}) \geq 0, \forall\overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*)\overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\,\eta(de_i)\,\overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\,\eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_x \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\,\overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\,\overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial\Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi^*)} \leq 0, \qquad x \in \mathcal{X},$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i)\, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_x \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial\Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i)\, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial \Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i)\, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_x \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial\Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i)\, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_x \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial \Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*) \, \eta(de_i) \, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*) \, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*) \, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*) \, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial \Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Sketch of the proof

ξ^* is maximin optimum design iff $\partial\Phi^{-1}(\xi^*, \overline{\xi}) \geq 0, \forall \overline{\xi}$, that is

- $\min_{\overline{\xi}} \max_{e_i \in \mathcal{C}(\xi^*)} \int_{\mathcal{X}} \psi(x, e_i, \xi^*) \overline{\xi}(dx) \geq 0$
- $\min_{\overline{\xi}} \max_{\eta} \int_{\mathcal{X}} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i)\, \overline{\xi}(dx) \geq 0$ (η in $\mathcal{C}(\xi^*)$)
- $\max_{\eta} \min_{x} \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \eta(de_i) \geq 0$
- Thus, there exists a measure $\overline{\eta}$ in $\mathcal{C}(\xi^*)$ satisfying $\min_x \int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0$
- That is, $\int_{\mathcal{C}(\xi^*)} \psi(x, e_i, \xi^*)\, \overline{\eta}(de_i) \geq 0, x \in \mathcal{X}$ $(NoMaxMin)$
- Using Proposition and some algebra it can be expressed as

$$\sum_{i \in \mathcal{I}(\xi^*)} \pi_i^* \frac{\partial\Phi_i(\xi^*, \xi_x)}{\Phi_i(\xi_i^*)} \leq 0, \qquad x \in \mathcal{X}.$$

which is the condition of Bayesian optimality

Example 1: Max-min OD for model discrimination

Discriminating designs in toxicology studies (Dette et al., 2010)

- Rival models

$$
\begin{aligned}
\eta_1(x,\theta) &= ae^{-bx}; \quad \theta=(a,b)^T, a>0, b>0,\\
\eta_2(x,\theta) &= ae^{-bx^d}; \quad \theta=(a,b,d)^T, a>0, b>0, d\geq 1,\\
\eta_3(x,\theta) &= a\left[c-(c-1)e^{-bx}\right]; \quad \theta=(a,b,c)^T, a>0, b>0, c\in[0,1],\\
\eta_4(x,\theta) &= a\left[c-(c-1)e^{-bx^d}\right]; \quad \theta=(a,b,c,d)^T, a>0, b>0, c\in[0,1],
\end{aligned}
$$

- Criterion for discriminating between pairs of models:

$$\min_{i\in\{1,2,3,4\}} \mathrm{Eff}_i(\xi) = \min\left\{\mathrm{Eff}^{2-1}(\xi), \mathrm{Eff}^{3-1}(\xi), \mathrm{Eff}^{4-2}(\xi), \mathrm{Eff}^{4-3}(\xi)\right\}$$

(comparisons 1 to 4 respectively)

- For an initial value θ_0, $\mathrm{Eff}_i(\xi) = \frac{\min_\xi \mathbf{e}_i^T \mathbf{M}_i^{-1}(\xi,\theta_0)\mathbf{e}_i}{\mathbf{e}_i^T \mathbf{M}_i^{-1}(\xi,\theta_0)\mathbf{e}_i}$, with

$$\mathbf{e}_i = \begin{cases} e_3 \in \mathbb{R}^3 & \text{for } i=1,2\\ e_3 \in \mathbb{R}^4 & \text{for } i=3\\ e_4 \in \mathbb{R}^4 & \text{for } i=4 \end{cases}; \mathbf{M}_i(\xi,\theta_0) = \begin{cases} M_2(\xi,\theta_0) & \text{for } i=1\\ M_3(\xi,\theta_0) & \text{for } i=2\\ M_4(\xi,\theta_0) & \text{for } i=3,4 \end{cases}$$

Example 1: Max-min OD for model discrimination

Discriminating designs in toxicology studies (Dette et al., 2010)

- Rival models

$$\begin{aligned}
\eta_1(x,\theta) &= ae^{-bx}; \quad \theta=(a,b)^T, a>0, b>0,\\
\eta_2(x,\theta) &= ae^{-bx^{d}}; \quad \theta=(a,b,d)^T, a>0, b>0, d\geq 1,\\
\eta_3(x,\theta) &= a\left[c-(c-1)e^{-bx}\right]; \quad \theta=(a,b,c)^T, a>0, b>0, c\in[0,1],\\
\eta_4(x,\theta) &= a\left[c-(c-1)e^{-bx^{d}}\right]; \quad \theta=(a,b,c,d)^T, a>0, b>0, c\in[0,1],
\end{aligned}$$

- Criterion for discriminating between pairs of models:

$$\min_{i\in\{1,2,3,4\}} \mathrm{Eff}_i(\xi) = \min\left\{\mathrm{Eff}^{2-1}(\xi), \mathrm{Eff}^{3-1}(\xi), \mathrm{Eff}^{4-2}(\xi), \mathrm{Eff}^{4-3}(\xi)\right\}$$

(comparisons 1 to 4 respectively)

- For an initial value θ_0, $\mathrm{Eff}_i(\xi) = \frac{\min_\xi \mathbf{e}_i^T \mathbf{M}_i^-(\xi,\theta_0)\mathbf{e}_i}{\mathbf{e}_i^T \mathbf{M}_i^{-1}(\xi,\theta_0)\mathbf{e}_i}$, with

$$\mathbf{e}_i = \begin{cases} e_3 \in \mathrm{I\!R}^3 & \text{for } i=1,2\\ e_3 \in \mathrm{I\!R}^4 & \text{for } i=3\\ e_4 \in \mathrm{I\!R}^4 & \text{for } i=4 \end{cases}; \mathbf{M}_i(\xi,\theta_0) = \begin{cases} M_2(\xi,\theta_0) & \text{for } i=1\\ M_3(\xi,\theta_0) & \text{for } i=2\\ M_4(\xi,\theta_0) & \text{for } i=3,4 \end{cases}$$

Example 1: Max-min OD for model discrimination

Discriminating designs in toxicology studies (Dette et al., 2010)

- Rival models

$$
\begin{aligned}
\eta_1(x,\theta) &= ae^{-bx}; \quad \theta=(a,b)^T, a>0, b>0,\\
\eta_2(x,\theta) &= ae^{-bx^{d}}; \quad \theta=(a,b,d)^T, a>0, b>0, d\geq 1,\\
\eta_3(x,\theta) &= a\left[c-(c-1)e^{-bx}\right]; \quad \theta=(a,b,c)^T, a>0, b>0, c\in[0,1],\\
\eta_4(x,\theta) &= a\left[c-(c-1)e^{-bx^{d}}\right]; \quad \theta=(a,b,c,d)^T, a>0, b>0, c\in[0,1],
\end{aligned}
$$

- Criterion for discriminating between pairs of models:

$$\min_{i\in\{1,2,3,4\}} \mathrm{Eff}_i(\xi) = \min\left\{\mathrm{Eff}^{2-1}(\xi), \mathrm{Eff}^{3-1}(\xi), \mathrm{Eff}^{4-2}(\xi), \mathrm{Eff}^{4-3}(\xi)\right\}$$

(comparisons 1 to 4 respectively)

- For an initial value θ_0, $\mathrm{Eff}_i(\xi) = \frac{\min_\xi \mathbf{e}_i^T \mathbf{M}_i^-(\xi,\theta_0)\mathbf{e}_i}{\mathbf{e}_i^T \mathbf{M}_i^{-1}(\xi,\theta_0)\mathbf{e}_i}$, with

$$\mathbf{e}_i = \begin{cases} e_3 \in \mathrm{I\!R}^3 & \text{for } i=1,2 \\ e_3 \in \mathrm{I\!R}^4 & \text{for } i=3 \\ e_4 \in \mathrm{I\!R}^4 & \text{for } i=4 \end{cases}; \mathbf{M}_i(\xi,\theta_0) = \begin{cases} M_2(\xi,\theta_0) & \text{for } i=1 \\ M_3(\xi,\theta_0) & \text{for } i=2 \\ M_4(\xi,\theta_0) & \text{for } i=3,4 \end{cases}$$

Example 1: Max-min OD for model discrimination

Discriminating designs in toxicology studies (Dette et al., 2010)

- Rival models

$$\begin{aligned}
\eta_1(x,\theta) &= ae^{-bx}; \quad \theta=(a,b)^T, a>0, b>0,\\
\eta_2(x,\theta) &= ae^{-bx^{d}}; \quad \theta=(a,b,d)^T, a>0, b>0, d\geq 1,\\
\eta_3(x,\theta) &= a\left[c-(c-1)e^{-bx}\right]; \quad \theta=(a,b,c)^T, a>0, b>0, c\in[0,1],\\
\eta_4(x,\theta) &= a\left[c-(c-1)e^{-bx^{d}}\right]; \quad \theta=(a,b,c,d)^T, a>0, b>0, c\in[0,1],
\end{aligned}$$

- Criterion for discriminating between pairs of models:

$$\min_{i\in\{1,2,3,4\}} \mathrm{Eff}_i(\xi) = \min\left\{\mathrm{Eff}^{2-1}(\xi), \mathrm{Eff}^{3-1}(\xi), \mathrm{Eff}^{4-2}(\xi), \mathrm{Eff}^{4-3}(\xi)\right\}$$

(comparisons 1 to 4 respectively)

- For an initial value θ_0, $\mathrm{Eff}_i(\xi) = \frac{\min_\xi \mathbf{e}_i^T \mathbf{M}_i^-(\xi,\theta_0)\mathbf{e}_i}{\mathbf{e}_i^T \mathbf{M}_i^{-1}(\xi,\theta_0)\mathbf{e}_i}$, with

$$\mathbf{e}_i = \begin{cases} e_3 \in \mathbb{R}^3 & \text{for } i=1,2\\ e_3\in\mathbb{R}^4 & \text{for } i=3\\ e_4\in\mathbb{R}^4 & \text{for } i=4\end{cases}; \mathbf{M}_i(\xi,\theta_0) = \begin{cases} M_2(\xi,\theta_0) & \text{for } i=1\\ M_3(\xi,\theta_0) & \text{for } i=2\\ M_4(\xi,\theta_0) & \text{for } i=3,4\end{cases}$$

Example 1: Max-min OD for model discrimination

Max-min optimal discriminating designs in toxicology studies (Dette et al., 2010)

- The authors use a numerical Nedler-Mead based algorithm. For $\theta_0 = (1, 3, 0, 1)^T$ find the solution

$$\xi_s^* = \left\{ \begin{array}{cccc} 0 & .105 & .44 & 1 \\ .141 & .233 & .199 & .427 \end{array} \right\},$$

$\mathrm{Eff}_1(\xi_s^*) = .705$, $\mathrm{Eff}_2(\xi_s^*) = \mathrm{Eff}_4(\xi_s^*) = .682$, $\mathrm{Eff}_3(\xi_s^*) = .871$

- Thus $C(\xi_s^*) = \{2; 4\}$ and $\pi_1^* = \pi_3^* = 0$. Then for the criteria

$$\Phi_i(\xi) = \begin{cases} [\mathrm{e}_i^T \mathrm{M}_i^-(\xi, \theta_0)\, \mathrm{e}_i]^{-1} & \text{if } \mathrm{e}_i \in \mathrm{Range}[\mathrm{M}_i(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases}, i = 1, \ldots$$

it can be found the prior for which ξ_s^* is the corresponding bayesian optimal design: $\pi_2^* = .574$ and $\pi_4^* = 1 - \pi_2^*$

- The authors use a numerical Nedler-Mead based algorithm. For $\theta_0 = (1,3,0,1)^T$ find the solution

$$\xi_s^* = \left\{ \begin{array}{cccc} 0 & .105 & .44 & 1 \\ .141 & .233 & .199 & .427 \end{array} \right\},$$

$\text{Eff}_1(\xi_s^*) = .705$, $\text{Eff}_2(\xi_s^*) = \text{Eff}_4(\xi_s^*) = .682$, $\text{Eff}_3(\xi_s^*) = .871$

- Thus $\mathcal{C}(\xi_s^*) = \{2;4\}$ and $\pi_1^* = \pi_3^* = 0$. Then for the criteria

$$\Phi_i(\xi) = \left\{ \begin{array}{ll} [\mathbf{e}_i^T \mathbf{M}_i^-(\xi,\theta_0)\,\mathbf{e}_i]^{-1} & \text{if } \mathbf{e}_i \in \text{Range}[\mathbf{M}_i(\xi,\theta_0)] \\ 0 & \text{otherwise} \end{array} \right., i = 1, \ldots$$

it can be found the prior for which ξ_s^* is the corresponding bayesian optimal design: $\pi_2^* = .574$ and $\pi_4^* = 1 - \pi_2^*$

Example 1: Max-min OD for model discrimination

Max-min optimal discriminating designs in toxicology studies (Dette et al., 2010)

- The authors use a numerical Nedler-Mead based algorithm. For $\theta_0 = (1, 3, 0, 1)^T$ find the solution

$$\xi_s^* = \left\{ \begin{array}{cccc} 0 & .105 & .44 & 1 \\ .141 & .233 & .199 & .427 \end{array} \right\},$$

$\mathrm{Eff}_1(\xi_s^*) = .705$, $\mathrm{Eff}_2(\xi_s^*) = \mathrm{Eff}_4(\xi_s^*) = .682$, $\mathrm{Eff}_3(\xi_s^*) = .871$

- Thus $\mathcal{C}(\xi_s^*) = \{2; 4\}$ and $\pi_1^* = \pi_3^* = 0$. Then for the criteria

$$\Phi_i(\xi) = \left\{ \begin{array}{ll} [\mathbf{e}_i^T \mathbf{M}_i^-(\xi, \theta_0)\, \mathbf{e}_i]^{-1} & \text{if } \mathbf{e}_i \in \mathrm{Range}[\mathbf{M}_i(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{array} \right. , i = 1, \ldots$$

it can be found the prior for which ξ_s^* is the corresponding bayesian optimal design: $\pi_2^* = .574$ and $\pi_4^* = 1 - \pi_2^*$

Checking condition

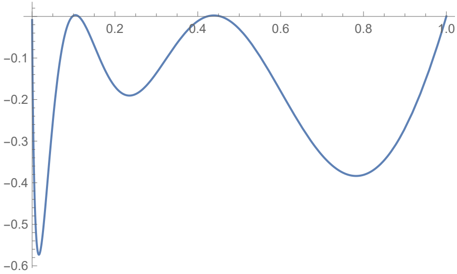

Figure: Sensitivity function

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

- The four-parameter logistic model is the most frequently used model for symmetric immunoassay data
  $y = \theta_1 + \frac{\theta_2 - \theta_1}{1 + (x/\theta_4)^{\theta_3}} + \varepsilon, \quad x \in \mathcal{X} = [0, \infty),$
  where y is the response at the concentration x, $\varepsilon \sim N(0; \sigma^2)$ and $\theta_1 > 0$, $\theta_2 > 0$, $\theta_3 \in \mathbb{R}$, $\theta_4 > 0$ are unknown parameters
- SMV-optimality criterion
  $\Phi_{SMV}(\xi) = \max_{i \in \{1,\ldots,4\}} \frac{e_i^T M^{-1}(\xi, \theta_0)\, e_i}{e_i^T M^{-}(\xi_i^*, \theta_0)\, e_i}$
- It is an example of maximum inefficiency criterion for

$$\Phi_i(\xi) = \begin{cases} [e_i^T M^{-}(\xi, \theta_0)\, e_i]^{-1} & \text{if } e_i \in \text{Range}[M(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases}, i = 1, \ldots$$

- Here $\mathcal{X} = [0, 5]$, $\theta_0 = (1, 2, 1, 1)$ and the gradient is

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

- The four-parameter logistic model is the most frequently used model for symmetric immunoassay data
  $y = \theta_1 + \frac{\theta_2 - \theta_1}{1 + (x/\theta_4)^{\theta_3}} + \varepsilon, \quad x \in \mathcal{X} = [0, \infty),$
  where y is the response at the concentration x, $\varepsilon \sim N(0; \sigma^2)$ and $\theta_1 > 0$, $\theta_2 > 0$, $\theta_3 \in \mathbb{R}$, $\theta_4 > 0$ are unknown parameters
- SMV-optimality criterion
  $\Phi_{SMV}(\xi) = \max_{i \in \{1,\ldots,4\}} \frac{e_i^T M^{-1}(\xi, \theta_0)\, e_i}{e_i^T M^{-}(\xi_i^*, \theta_0)\, e_i}$
- It is an example of maximum inefficiency criterion for

$$\Phi_i(\xi) = \begin{cases} [e_i^T M^{-}(\xi, \theta_0)\, e_i]^{-1} & \text{if } e_i \in \text{Range}[M(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases}, i = 1, \ldots$$

- Here $\mathcal{X} = [0, 5]$, $\theta_0 = (1, 2, 1, 1)$ and the gradient is
  $\frac{\partial \log f(y, x, \theta)}{\partial \theta} = \left(1 - \frac{1}{1+x}, \frac{1}{1+x}, -\frac{x \log[x + 10^{-6}]}{(1+x)^2}, \frac{x}{(1+x)^2}\right)^T$

- The four-parameter logistic model is the most frequently used model for symmetric immunoassay data
  $y = \theta_1 + \frac{\theta_2 - \theta_1}{1 + (x/\theta_4)^{\theta_3}} + \varepsilon, \quad x \in \mathcal{X} = [0, \infty),$
  where y is the response at the concentration x, $\varepsilon \sim N(0; \sigma^2)$ and $\theta_1 > 0$, $\theta_2 > 0$, $\theta_3 \in \mathbb{R}$, $\theta_4 > 0$ are unknown parameters
- SMV-optimality criterion
  $\Phi_{SMV}(\xi) = \max_{i \in \{1,\ldots,4\}} \frac{e_i^T M^{-1}(\xi, \theta_0)\, e_i}{e_i^T M^{-}(\xi_i^*, \theta_0)\, e_i}$
- It is an example of maximum inefficiency criterion for

$$\Phi_i(\xi) = \begin{cases} [e_i^T M^{-}(\xi, \theta_0)\, e_i]^{-1} & \text{if } e_i \in \text{Range}[M(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases}, i = 1, \ldots,$$

- Here $\mathcal{X} = [0, 5]$, $\theta_0 = (1, 2, 1, 1)$ and the gradient is
  $\frac{\partial \log f(y,x,\theta)}{\partial \theta} = \left(1 - \frac{1}{1+x}, \frac{1}{1+x}, -\frac{x \log[x + 10^{-6}]}{(1+x)^2}, \frac{x}{(1+x)^2}\right)^T$

- The four-parameter logistic model is the most frequently used model for symmetric immunoassay data
  $y = \theta_1 + \frac{\theta_2 - \theta_1}{1 + (x/\theta_4)^{\theta_3}} + \varepsilon, \quad x \in \mathcal{X} = [0, \infty),$
  where y is the response at the concentration x, $\varepsilon \sim N(0; \sigma^2)$ and $\theta_1 > 0$, $\theta_2 > 0$, $\theta_3 \in \mathbb{R}$, $\theta_4 > 0$ are unknown parameters
- SMV-optimality criterion
  $\Phi_{SMV}(\xi) = \max_{i \in \{1,\ldots,4\}} \frac{e_i^T M^{-1}(\xi, \theta_0)\, e_i}{e_i^T M^{-}(\xi_i^*, \theta_0)\, e_i}$
- It is an example of maximum inefficiency criterion for

$$\Phi_i(\xi) = \begin{cases} [e_i^T M^{-}(\xi, \theta_0)\, e_i]^{-1} & \text{if } e_i \in \text{Range}[M(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases} \quad , i = 1, \ldots,$$

- Here $\mathcal{X} = [0, 5]$, $\theta_0 = (1, 2, 1, 1)$ and the gradient is
  $\frac{\partial \log f(y,x,\theta)}{\partial \theta} = \left(1 - \frac{1}{1+x}, \frac{1}{1+x}, -\frac{x \log[x + 10^{-6}]}{(1+x)^2}, \frac{x}{(1+x)^2}\right)^T$

- The four-parameter logistic model is the most frequently used model for symmetric immunoassay data
  $y = \theta_1 + \frac{\theta_2 - \theta_1}{1 + (x/\theta_4)^{\theta_3}} + \varepsilon, \quad x \in \mathcal{X} = [0, \infty),$
  where y is the response at the concentration x, $\varepsilon \sim N(0; \sigma^2)$ and $\theta_1 > 0$, $\theta_2 > 0$, $\theta_3 \in \mathbb{R}$, $\theta_4 > 0$ are unknown parameters
- SMV-optimality criterion
  $\Phi_{SMV}(\xi) = \max_{i \in \{1,\ldots,4\}} \frac{e_i^T M^{-1}(\xi, \theta_0)\, e_i}{e_i^T M^{-}(\xi_i^*, \theta_0)\, e_i}$
- It is an example of maximum inefficiency criterion for

$$\Phi_i(\xi) = \begin{cases} [e_i^T M^{-}(\xi, \theta_0)\, e_i]^{-1} & \text{if } e_i \in \text{Range}[M(\xi, \theta_0)] \\ 0 & \text{otherwise} \end{cases} \quad , i = 1, \ldots,$$

- Here $\mathcal{X} = [0, 5]$, $\theta_0 = (1, 2, 1, 1)$ and the gradient is
  $\frac{\partial \log f(y, x, \theta)}{\partial \theta} = \left(1 - \frac{1}{1+x}, \frac{1}{1+x}, -\frac{x \log[x + 10^{-6}]}{(1+x)^2}, \frac{x}{(1+x)^2}\right)^T$

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

Searching for the optimal design

- For every combination of two indexes (i, j), the designs having the same efficency for those criteria are not maximin/bayesian optimal (different reasons)
- The same for every combination of three indexes but $(2, 3, 4)$. For this combination the design

$$\xi^* = \left\{ \begin{array}{cccc} 0 & 0.126 & 1.279 & 5 \\ 0.497 & 0.114 & 0.241 & 0.148 \end{array} \right\},$$

has efficiencies $\{0.5963, 0.4970, 0.4970, 0.4970\}$

- Using the condition of the equivalence theorem for the support points, we get the solution $\pi^* = \{0, 0.493, 0.054, 0.453\}$ with a minimum value of $6.644 \times 10^{-4} \approx 0$
- Thus ξ^* is Bayesian optimal for π^*, and therefore is maximin efficient as well

Searching for the optimal design

- For every combination of two indexes (i, j), the designs having the same efficency for those criteria are not maximin/bayesian optimal (different reasons)
- The same for every combination of three indexes but $(2, 3, 4)$. For this combination the design

$$\xi^* = \left\{ \begin{array}{cccc} 0 & 0.126 & 1.279 & 5 \\ 0.497 & 0.114 & 0.241 & 0.148 \end{array} \right\},$$

  has efficiencies $\{0.5963, 0.4970, 0.4970, 0.4970\}$
- Using the condition of the equivalence theorem for the support points, we get the solution $\pi^* = \{0, 0.493, 0.054, 0.453\}$ with a minimum value of 6.644 x $10^{-4} \approx 0$
- Thus ξ^* is Bayesian optimal for π^*, and therefore is maximin efficient as well

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

Searching for the optimal design

- For every combination of two indexes (i, j), the designs having the same efficency for those criteria are not maximin/bayesian optimal (different reasons)
- The same for every combination of three indexes but $(2, 3, 4)$. For this combination the design

$$\xi^* = \left\{ \begin{array}{cccc} 0 & 0.126 & 1.279 & 5 \\ 0.497 & 0.114 & 0.241 & 0.148 \end{array} \right\},$$

  has efficiencies $\{0.5963, 0.4970, 0.4970, 0.4970\}$
- Using the condition of the equivalence theorem for the support points, we get the solution $\pi^* = \{0, 0.493, 0.054, 0.453\}$ with a minimum value of $6.644 \times 10^{-4} \approx 0$
- Thus ξ^* is Bayesian optimal for π^*, and therefore is maximin efficient as well

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

Searching for the optimal design

- For every combination of two indexes (i, j), the designs having the same efficency for those criteria are not maximin/bayesian optimal (different reasons)
- The same for every combination of three indexes but $(2, 3, 4)$. For this combination the design

$$\xi^* = \left\{ \begin{array}{cccc} 0 & 0.126 & 1.279 & 5 \\ 0.497 & 0.114 & 0.241 & 0.148 \end{array} \right\},$$

  has efficiencies $\{0.5963, 0.4970, 0.4970, 0.4970\}$
- Using the condition of the equivalence theorem for the support points, we get the solution $\pi^* = \{0, 0.493, 0.054, 0.453\}$ with a minimum value of 6.644 x $10^{-4} \approx 0$
- Thus ξ^* is Bayesian optimal for π^*, and therefore is maximin efficient as well

Example 2: ODE for parameter estimation

SMV-optimum designs (Dette, 1997) in biology immunoassays

Searching for the optimal design

- For every combination of two indexes (i, j), the designs having the same efficency for those criteria are not maximin/bayesian optimal (different reasons)
- The same for every combination of three indexes but $(2, 3, 4)$. For this combination the design

$$\xi^* = \left\{ \begin{array}{cccc} 0 & 0.126 & 1.279 & 5 \\ 0.497 & 0.114 & 0.241 & 0.148 \end{array} \right\},$$

  has efficiencies $\{0.5963, 0.4970, 0.4970, 0.4970\}$
- Using the condition of the equivalence theorem for the support points, we get the solution $\pi^* = \{0, 0.493, 0.054, 0.453\}$ with a minimum value of 6.644 x $10^{-4} \approx 0$
- Thus ξ^* is Bayesian optimal for π^*, and therefore is maximin efficient as well

- Maxi-min efficiency criteria take into consideration several tasks expressed by different component-wise criteria Φ_i

  $$\xi^* = \arg\max_\xi \min_{i\in\{1,\ldots,k\}} \mathrm{Eff}_i(\xi)$$

  But they are difficult to manage because of their lack of diff.
- Bayesian optimality is differentiable

  $$\xi^* = \arg\max_\xi \sum_{i=1}^k \pi_i \cdot \mathrm{Eff}_i(\xi), \text{ with } \pi = \{\pi_i\}_i \text{ prior}$$
- A general version of the equivalence theorem, covering any multi-objective problem that can be expressed as a minimum design efficiency (for any component-wise criteria) has been proved.
- Future work: design an efficienta method to determine the prior probability that matches the maxi-min efficiency criterion and the Bayesian optimality, allowing the application of the equivalence theorem.

- Maxi-min efficiency criteria take into consideration several tasks expressed by different component-wise criteria Φ_i
  $$\xi^* = \arg\max_\xi \min_{i\in\{1,\ldots,k\}} \mathrm{Eff}_i(\xi)$$
  But they are difficult to manage because of their lack of diff.
- Bayesian optimality is differentiable
  $$\xi^* = \arg\max_\xi \sum_{i=1}^k \pi_i \cdot \mathrm{Eff}_i(\xi),$$ with $\pi = \{\pi_i\}_i$ prior
- A general version of the equivalence theorem, covering any multi-objective problem that can be expressed as a minimum design efficiency (for any component-wise criteria) has been proved.
- Future work: design an efficienta method to determine the prior probability that matches the maxi-min efficiency criterion and the Bayesian optimality, allowing the application of the equivalence theorem.

- Maxi-min efficiency criteria take into consideration several tasks expressed by different component-wise criteria Φ_i

  $\xi^* = \arg\max_\xi \min_{i\in\{1,\dots,k\}} \text{Eff}_i(\xi)$

  But they are difficult to manage because of their lack of diff.
- Bayesian optimality is differentiable

  $\xi^* = \arg\max_\xi \sum_{i=1}^k \pi_i \cdot \text{Eff}_i(\xi)$, with $\pi = \{\pi_i\}_i$ prior
- A general version of the equivalence theorem, covering any multi-objective problem that can be expressed as a minimum design efficiency (for any component-wise criteria) has been proved.
- Future work: design an efficienta method to determine the prior probability that matches the maxi-min efficiency criterion and the Bayesian optimality, allowing the application of the equivalence theorem.

- Maxi-min efficiency criteria take into consideration several tasks expressed by different component-wise criteria Φ_i

  $\xi^* = \arg\max_\xi \min_{i\in\{1,\dots,k\}} \mathrm{Eff}_i(\xi)$

  But they are difficult to manage because of their lack of diff.
- Bayesian optimality is differentiable

  $\xi^* = \arg\max_\xi \sum_{i=1}^{k} \pi_i \cdot \mathrm{Eff}_i(\xi)$, with $\pi = \{\pi_i\}_i$ prior
- A general version of the equivalence theorem, covering any multi-objective problem that can be expressed as a minimum design efficiency (for any component-wise criteria) has been proved.
- Future work: design an efficienta method to determine the prior probability that matches the maxi-min efficiency criterion and the Bayesian optimality, allowing the application of the equivalence theorem.

- Maxi-min efficiency criteria take into consideration several tasks expressed by different component-wise criteria Φ_i

  $$\xi^* = \arg\max_\xi \min_{i\in\{1,\dots,k\}} \mathrm{Eff}_i(\xi)$$

  But they are difficult to manage because of their lack of diff.

- Bayesian optimality is differentiable

  $\xi^* = \arg\max_\xi \sum_{i=1}^{k} \pi_i \cdot \mathrm{Eff}_i(\xi)$, with $\pi = \{\pi_i\}_i$ prior

- A general version of the equivalence theorem, covering any multi-objective problem that can be expressed as a minimum design efficiency (for any component-wise criteria) has been proved.

- Future work: design an efficienta method to determine the prior probability that matches the maxi-min efficiency criterion and the Bayesian optimality, allowing the application of the equivalence theorem.

References

- Dette H. (1997). Designing experiments with respect to 'standardized' optimality criteria. *Journal of the Royal Statistical Society, Series B*, 59, 97–110
- Dette H., Pepelyshev A., Shpilev P., Wong W.K.(2010). Optimal designs for discriminating between dose-response models in toxicology studies. *Bernoulli* 16(4), 1164–1176
- Tommasi C., Rodríguez-Díaz J.M., López-Fidalgo J. (2023). An equivalence theorem for design optimality with respect to a multi-objective criterion. Statistical Papers (2023) (doi.org/10.1007/s00362-023-01431-2)

Thanks for your attention

Any question?