Experimental designs for radiation dosimetry calibration

Jesús López-Fidalgo
fidalgo@unav.es
joint work with
Mariano Amo-Salas

Outline

Outline

1. Motivation.

Outline

1. Motivation.
2. Optimal experimental design.

Outline

1. Motivation.
2. Optimal experimental design.
3. Inverse function theorem.

Outline

1. Motivation.
2. Optimal experimental design.
3. Inverse function theorem.
4. Optimal designs.

Outline

1. Motivation.
2. Optimal experimental design.
3. Inverse function theorem.
4. Optimal designs.
5. Optimal dose–calibration designs.

Motivation

A real case

Calibration model in dosimetry.

A real case

Calibration model in dosimetry.
Ramos-García L.I. and Pérez-Azorín J.F. (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).

A real case

Calibration model in dosimetry.
Ramos-García L.I. and Pérez-Azorín J.F. (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).

$$\eta^{-1}(D,\theta) \quad = \quad \mu(netOD,\theta) = \alpha \; netOD + \beta \; netOD^{\gamma},$$

A real case

Calibration model in dosimetry.
Ramos-García L.I. and Pérez-Azorín J.F. (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).

$$
\begin{aligned}
\eta^{-1}(D,\theta) &= \mu(netOD,\theta) = \alpha\ netOD + \beta\ netOD^{\gamma}, \\
D \in [0,B] & \quad \text{Dose,}
\end{aligned}
$$

Calibration model in dosimetry.
Ramos-García L.I. and Pérez-Azorín J.F. (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).

$$\begin{aligned} \eta^{-1}(D,\theta) &= \mu(netOD,\theta) = \alpha \; netOD + \beta \; netOD^{\gamma}, \\ D \in [0,B] & \quad \text{Dose}, \\ netOD & \quad \text{Observed value} \end{aligned}$$

A real case

Calibration model in dosimetry.
Ramos-García L.I. and Pérez-Azorín J.F. (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).

$$\begin{aligned} \eta^{-1}(D,\theta) &= \mu(netOD,\theta) = \alpha \; netOD + \beta \; netOD^{\gamma}, \\ D \in [0,B] & \quad \text{Dose,} \\ netOD & \quad \text{Observed value} \\ \theta &= (\alpha,\ \beta,\ \gamma)^T \text{ to be estimated using the OLS.} \end{aligned}$$

Optimal experimental design (OED)

Ordinary OED

Ordinary OED

$$y = \eta(x, \theta) + \varepsilon, \quad \varepsilon \equiv N(0, \sigma = 1), \quad x \varepsilon \chi$$

Ordinary OED

$$y = \eta(x,\theta) + \varepsilon, \quad \varepsilon \equiv N(0, \sigma = 1), \quad x \varepsilon \chi$$

Approximate design: Probability measure on the design space,

$$\xi = \begin{Bmatrix} x_1 & x_2 & \dots & x_k \\ p_1 & p_2 & \dots & p_k \end{Bmatrix},$$

Ordinary OED

$$y = \eta(x,\theta) + \varepsilon, \quad \varepsilon \equiv N(0,\sigma = 1), \quad x \varepsilon \chi$$

Approximate design: Probability measure on the design space,

$$\xi = \begin{Bmatrix} x_1 & x_2 & \dots & x_k \\ p_1 & p_2 & \dots & p_k \end{Bmatrix},$$

Fisher Information Matrix (FIM) for the exponential family,

$$M(\xi,\theta) = \sum_{x \varepsilon \chi} I(x,\theta)\xi(x),$$

where $I(x,\theta) = \frac{\partial \eta(x,\theta)}{\partial \theta} \frac{\partial \eta(x,\theta)}{\partial \theta}^T$ is the FIM at x.

Ordinary OED

$$y = \eta(x,\theta) + \varepsilon, \quad \varepsilon \equiv N(0, \sigma = 1), \quad x \varepsilon \chi$$

Approximate design: Probability measure on the design space,

$$\xi = \begin{Bmatrix} x_1 & x_2 & \dots & x_k \\ p_1 & p_2 & \dots & p_k \end{Bmatrix},$$

Fisher Information Matrix (FIM) for the exponential family,

$$M(\xi,\theta) = \sum_{x\varepsilon\chi} I(x,\theta)\xi(x),$$

where $I(x,\theta) = \frac{\partial\eta(x,\theta)}{\partial\theta}\frac{\partial\eta(x,\theta)}{\partial\theta}^T$ is the FIM at x.
Inverse asymptotically proportional to the covariance matrix.

Ordinary OED

Optimality criterion.

Ordinary OED

Optimality criterion.
Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.

Ordinary OED

Optimality criterion.
Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.
Equivalence theorem.

Ordinary OED

Optimality criterion.
Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.
Equivalence theorem.
Efficiency,

$$\text{eff}_{\Phi}(\xi) = \frac{\Phi[M(\xi^*, \theta)]}{\Phi[M(\xi, \theta)]}.$$

Ordinary OED

Optimality criterion.

Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.

Equivalence theorem.

Efficiency,

$$\text{eff}_\Phi(\xi) = \frac{\Phi[M(\xi^*, \theta)]}{\Phi[M(\xi, \theta)]}.$$

$D-$optimality, $\Phi_D[M(\xi, \theta)] = \det M^{-1/m}(\xi, \theta)$.

Ordinary OED

Optimality criterion.

Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.

Equivalence theorem.

Efficiency,

$$\text{eff}_{\Phi}(\xi) = \frac{\Phi[M(\xi^*, \theta)]}{\Phi[M(\xi, \theta)]}.$$

$D-$optimality, $\Phi_D[M(\xi, \theta)] = \det M^{-1/m}(\xi, \theta)$.
$c-$optimality, $\Phi_c[M(\xi, \theta)] = c^T M^{-}(\xi, \theta) c$.

Ordinary OED

Optimality criterion.
Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.
Equivalence theorem.
Efficiency,

$$\text{eff}_{\Phi}(\xi) = \frac{\Phi[M(\xi^*, \theta)]}{\Phi[M(\xi, \theta)]}.$$

$D-$optimality, $\Phi_D[M(\xi, \theta)] = \det M^{-1/m}(\xi, \theta)$.
$c-$optimality, $\Phi_c[M(\xi, \theta)] = c^T M^{-}(\xi, \theta) c$.
$G-$optimality, $\Phi_G[M(\xi, \theta)] = \max_{x \in \chi} \frac{\partial \eta(x, \theta)}{\partial \theta^T} M^{-1}(\xi, \theta) \frac{\partial \eta(x, \theta)}{\partial \theta}$.

Ordinary OED

Optimality criterion.
Convex and non-increasing: A $\Phi-$optimal design minimizes Φ.
Equivalence theorem.
Efficiency,

$$\text{eff}_\Phi(\xi) = \frac{\Phi[M(\xi^*, \theta)]}{\Phi[M(\xi, \theta)]}.$$

$D-$optimality, $\Phi_D[M(\xi,\theta)] = \det M^{-1/m}(\xi,\theta)$.
$c-$optimality, $\Phi_c[M(\xi,\theta)] = c^T M^-(\xi,\theta)c$.
$G-$optimality, $\Phi_G[M(\xi,\theta)] = \max_{x\in\chi} \frac{\partial\eta(x,\theta)}{\partial\theta^T} M^{-1}(\xi,\theta)\frac{\partial\eta(x,\theta)}{\partial\theta}$.
$V-$optimality, $\Phi_V[M(\xi,\theta)] = \int \frac{\partial\eta(x,\theta)}{\partial\theta^T} M^{-1}(\xi,\theta)\frac{\partial\eta(x,\theta)}{\partial\theta} dx$.

Inverse function theorem

Inverse function theorem for computing FIM

$\eta(x,\theta)$ unknown but $\mu(y,\theta) = \eta^{-1}(x,\theta)$ known.

Inverse function theorem for computing FIM

$\eta(x,\theta)$ unknown but $\mu(y,\theta) = \eta^{-1}(x,\theta)$ known.
Differentiating

$$x = \mu(y,\theta) = \mu(\eta(x,\theta),\theta),$$

$$0 = \left(\frac{\partial \mu(y,\theta)}{\partial y}\right)_{y=\eta(x,\theta)} \frac{\partial \eta(x,\theta)}{\partial \theta} + \left(\frac{\partial \mu(y,\theta)}{\partial \theta}\right)_{y=\eta(x,\theta)}.$$

Inverse function theorem for computing FIM

$\eta(x,\theta)$ unknown but $\mu(y,\theta) = \eta^{-1}(x,\theta)$ known.
Differentiating

$$x = \mu(y,\theta) = \mu(\eta(x,\theta),\theta),$$

$$0 = \left(\frac{\partial \mu(y,\theta)}{\partial y}\right)_{y=\eta(x,\theta)} \frac{\partial \eta(x,\theta)}{\partial \theta} + \left(\frac{\partial \mu(y,\theta)}{\partial \theta}\right)_{y=\eta(x,\theta)}.$$

$$\frac{\partial \eta(x,\theta)}{\partial \theta} = -\left(\frac{\partial \mu(y,\theta)}{\partial y}\right)^{-1}_{y=\eta(x,\theta)} \left(\frac{\partial \mu(y,\theta)}{\partial \theta}\right)_{y=\eta(x,\theta)}.$$

D–, c– & sub–optimal designs

Case study

Case study

Computing the design on $netOD \in \chi_{netOD} = [0, 0.6]$ and transforming it, $D = 690netOD + 1550netOD^2 \in \chi = [0, 972]$,

$$\xi_D = \left\{ \begin{array}{ccc} 75.6 & 427.8 & 972 \\ 1/3 & 1/3 & 1/3 \end{array} \right\},$$

Case study

Computing the design on $netOD \in \chi_{netOD} = [0, 0.6]$ and transforming it, $D = 690netOD + 1550netOD^2 \in \chi = [0, 972]$,

$$\xi_D = \left\{ \begin{array}{ccc} 75.6 & 427.8 & 972 \\ 1/3 & 1/3 & 1/3 \end{array} \right\},$$

and the $c-$optimal,

$$\xi_\gamma = \left\{ \begin{array}{ccc} 46.25 & 439.36 & 972 \\ 0.476 & 0.359 & 0.165 \end{array} \right\}, \quad \xi_\alpha = \left\{ \begin{array}{ccc} 46.25 & 439.36 & 972 \\ 0.742 & 0.186 & 0.0717 \end{array} \right\},$$

$$\xi_\beta = \left\{ \begin{array}{cc} 170.7 & 972 \\ 0.622 & 0.378 \end{array} \right\}.$$

Computing the design on $netOD \in \chi_{netOD} = [0, 0.6]$ and transforming it, $D = 690netOD + 1550netOD^2 \in \chi = [0, 972]$,

$$\xi_D = \left\{ \begin{array}{ccc} 75.6 & 427.8 & 972 \\ 1/3 & 1/3 & 1/3 \end{array} \right\},$$

and the $c-$optimal,

$$\xi_\gamma = \left\{ \begin{array}{ccc} 46.25 & 439.36 & 972 \\ 0.476 & 0.359 & 0.165 \end{array} \right\}, \quad \xi_\alpha = \left\{ \begin{array}{ccc} 46.25 & 439.36 & 972 \\ 0.742 & 0.186 & 0.0717 \end{array} \right\},$$

$$\xi_\beta = \left\{ \begin{array}{cc} 170.7 & 972 \\ 0.622 & 0.378 \end{array} \right\}.$$

c_γ–efficiency	0.567,	c_α–efficiency	0.424
	c_β–efficiency	0.652	

Suboptimal designs with more 10 points

Suboptimal designs with more 10 points

- Arithmetic sequences on *netOD* and *D*.
- Geometric sequences on *netOD* and *D*.
- Uniform sequences on *netOD* and *D*.

Suboptimal designs with more 10 points

- Arithmetic sequences on *netOD* and *D*.
- Geometric sequences on *netOD* and *D*.
- Uniform sequences on *netOD* and *D*.

	Design points									D–Eff
ξ^A_{netOD}	49.0	107.3	176.6	257.1	348.5	451.1	564.7	689.4	825.1	78.1 %
ξ^A_D	57.2	158.8	260.5	362.1	463.7	565.4	667.	768.7	870.3	75.5%
ξ^G_{netOD}	55.6	73.3	97.2	130.2	176.3	241.4	334.9	471.	671.8	76.9%
ξ^G_D	55.6	73.3	97.2	130.2	176.3	241.4	334.9	471.	671.8	77.8%
ξ^E_{netOD}	0	52.8	119.5	200	294.2	402.2	524	659.5	808.8	71.1%
ξ^E_D	0	108	216	324	432	540	648	756	864	64.9%

Last point omitted

Dose–calibration designs

Aim: Calibration

Aim: Calibration

- For calibration models, the main goal is the precise prediction (calibration) of the explanatory variable.

Aim: Calibration

- For calibration models, the main goal is the precise prediction (calibration) of the explanatory variable.
- "Inverse" of G- and V-optimality need to be adapted for "inverse" prediction.

Aim: Calibration

- For calibration models, the main goal is the precise prediction (calibration) of the explanatory variable.
- "Inverse" of G- and V-optimality need to be adapted for "inverse" prediction.
- The Fedorov-Wynn algortihm is adapted for computing the optimal designs.

Criteria for calibration

Criteria for calibration

The variance of the prediction of D given a value of the target $netOD$ is

$$Var(\hat{D}) = \left(\frac{\partial\mu(netOD,\theta)}{\partial\theta}\right)^T M^{-1}(\xi_D,\theta)\left(\frac{\partial\mu(netOD,\theta)}{\partial\theta}\right).$$

Criteria for calibration

The variance of the prediction of D given a value of the target *netOD* is

$$Var(\hat{D}) = \left(\frac{\partial\mu(netOD,\theta)}{\partial\theta}\right)^T M^{-1}(\xi_D,\theta)\left(\frac{\partial\mu(netOD,\theta)}{\partial\theta}\right).$$

Criteria for predictions,

$$\begin{aligned}\Phi_{G_I}(\xi) &= \max_{netOD\in\chi_{netOD}} Var(\hat{D})\\ \Phi_{V_I}(\xi) &= \frac{1}{\triangle_{netOD}}\int Var(\hat{D})dZ,\end{aligned}$$

where χ_{netOD} contains possible targets and
$\triangle_{netOD}$ = length of χ_{netOD}.
Optimized for *netOD* and transformed to the optimal design in D.

Algorithms for G_I- and V_I-optimality

Algorithms for G_I- and V_I-optimality

G_I-optimal design,

$$\xi_{G_I} = \left\{ \begin{array}{ccc} 123.6 & 541.5 & 972 \\ 0.11 & 0.34 & 0.55 \end{array} \right\}.$$

V_I-optimal design,

$$\xi_{V_I} = \left\{ \begin{array}{ccc} 89.5 & 469.3 & 972 \\ 0.23 & 0.47 & 0.30 \end{array} \right\}.$$

Thank you for your attention

- Biedermann, Bissantz, Dette, Jones (2011) Optimal designs for indirect regression. *Inverse Problems* 27(10), 1-21.
- Kitsos (1992). Quasi-Sequential Procedures for the Calibration Problem. *Metrika*, **59**, 235 – 244.
- Kitsos and Muller Ch.H. (1995). Robust linear calibration. *Statistics* 27(1-2), 93–106.
- López-Fidalgo, Rodríguez Díaz (2004). Elfving's method for m−dimensional models. *Metrika*, **59**.
- Ramos-García, Pérez-Azorín (2013). Improving the calibration of radiochromic films. *Medical Physics*, 40(7).