Integrability and Bayesian *D*-optimality

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Outline

- Bayesian design and approximations
- Parameter singularities and non-integrability
- Suggestions for addressing non-integrability
- Illustration: how badly things can go wrong

Motivation

In recent years, there have been many developments in optimal experimental designs for more sophisticated models

- generalized linear mixed models
- nonlinear mixed effects models

For these models, D-optimal designs etc. depend on the values of the parameters

Approaches

- locally optimal 'best guess'
- Bayesian design
- maximin designs
- response-adaptive/sequential design

Bayesian design

(Chaloner & Verdinelli, 1995)

Notation

- $\mathbf{y} \in \mathcal{Y}$ responses
- $\boldsymbol{\theta} \in \Theta$ parameter vector
- prior knowledge summarized by $f(\boldsymbol{\theta})$
- ξ finitely-supported approximate design

Idea: choose ξ to maximize the expected 'distance' / information gain

$$f(\boldsymbol{\theta}) \text{ prior } \rightarrow f(\boldsymbol{\theta}|\xi, \mathbf{y}) \text{ posterior}$$

'Distance' measured via Kullback-Leibler divergence / Shannon information gain

$$\psi_{KL}(\xi) = \int_{\mathcal{Y}} \int_{\Theta} \log \frac{f(\boldsymbol{\theta}|\xi, \mathbf{y})}{f(\boldsymbol{\theta})} f(\mathbf{y}, \boldsymbol{\theta}|\xi) d\boldsymbol{\theta} d\mathbf{y}$$

In practice, optimization of expected information gain is usually too hard

Instead we typically optimize a surrogate objective function

$$\phi(\xi) = \mathrm{E}_{\boldsymbol{\theta}} \log |nM(\xi, \boldsymbol{\theta})| \tag{1}$$

$$\phi_2(\xi) = \mathrm{E}_{\boldsymbol{\theta}} \log |nM(\xi, \boldsymbol{\theta}) + R| \tag{2}$$

- $M(\xi, \boldsymbol{\theta})$ is the Fisher information matrix, $\mathrm{E}_{\mathbf{y}} \left[-\frac{\partial^2 \log f(\mathbf{y}|\xi, \boldsymbol{\theta})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\theta}^\top} \right]$
- $R = \frac{\partial^2 \log f(\boldsymbol{\theta})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\theta}^\top}$, or $R = \mathrm{var}(\boldsymbol{\theta})^{-1}$

Objective function (1) is the most common

Also sometimes used when a Bayesian analysis will not be conducted (pseudo-Bayesian design)

Focus of the talk - sometimes the approximation ϕ can fail badly

Singularities

Intuitive definition

A parameter singularity is a combination of parameter values where all designs are 'uninformative'

Formal definition

$\boldsymbol{\theta}_0$ is a parameter singularity if, for any ξ, $|M(\xi, \boldsymbol{\theta}_0)| = 0$

Example

Exponential regression model

$$y_i \sim N[\eta(x_i), \sigma^2]$$
$$\eta(x) = e^{-x/\theta}$$

parameterized by lifetime $\theta > 0$

Parameter singularities $\{0, \infty\}$

Singularities

Intuitive definition

A parameter singularity is a combination of parameter values where all designs are 'uninformative'

Formal definition

$\boldsymbol{\theta}_0$ is a parameter singularity if, for any fixed ξ, $|M(\xi, \boldsymbol{\theta})| \to 0$ as $\boldsymbol{\theta} \to \boldsymbol{\theta}_0$

Example

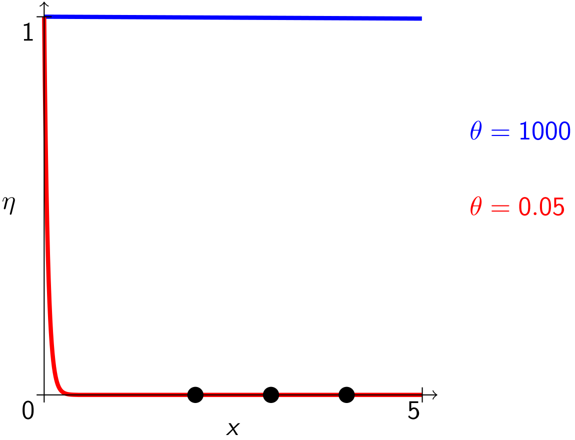
Exponential regression model

$$y_i \sim N[\eta(x_i), \sigma^2]$$
$$\eta(x) = e^{-x/\theta}$$

parameterized by lifetime $\theta > 0$

Parameter singularities $\{0, \infty\}$

Why are there parameter singularities at 0 and ∞?



Example II

Logistic regression

Binary response (0/1) - event occurs or does not occur. Controllable variable, x, is usually a (log)-dose

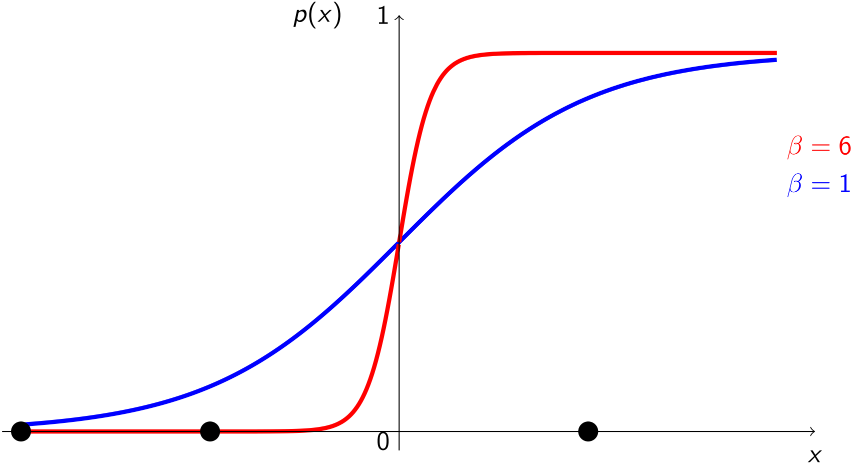
$$y_i \sim \text{Bernoulli}(p_i)$$
$$p_i = \frac{1}{1 + \exp\{-\beta(x_i - \mu)\}}$$

- μ is the dose at which there is a 50% chance of the event occuring
- Chaloner & Larntz (1989) studied Bayesian design for this model

Parameter singularities at $\beta = 0$, $\beta = \infty$

Why? When $\beta = 0$, μ is not identifiable

Parameter singularity at $\beta = \infty$



The punchline

Reconsider

$$\phi(\xi) = \int_{\Theta} \log |M(\xi, \boldsymbol{\theta})| f(\boldsymbol{\theta}) d\boldsymbol{\theta}$$

- near parameter singularities, $|M(\xi, \boldsymbol{\theta})| \to 0$

- the integrand above $\to -\infty$ in parts of the domain of integration

So the integral

- may not exist (Riemann)
- may equal $-\infty$ (Lebesgue)

(in the same sense that $\int_{[0,1]} \frac{-1}{x^2} dx$ either doesn't exist or is $-\infty$)

Chaloner & Verdinelli (1995) discussed integrability, but only highlighted the issue where the prior has unbounded support

Tsutakawa (1972) gave a problem where the integral is $-\infty$

The issue is not restricted to unbounded supports

What can be done?

1. Use a different approximation

- not ϕ, instead e.g. ϕ_2, or a more sophisticated computational approximation

2. Use a different design selection criterion

- if Bayesian analysis will not be used, the principled justification of Shannon information gain breaks down

3. Use a different prior

4. Density designs?

Alternative criteria

Efficiency distribution

Consider the D-efficiency function

$$\text{eff}(\xi|\boldsymbol{\theta}) = \left\{ \frac{|M(\xi, \boldsymbol{\theta})|}{\sup_{\xi'} |M(\xi', \boldsymbol{\theta})|} \right\}^{1/p}$$

- prior on $\boldsymbol{\theta}$ induces a distribution on $\text{eff}(\xi|\boldsymbol{\theta})$
- Woods et al. (2006) used efficiency function & distribution to assess designs

From pseudo-Bayesian viewpoint, optimization of e.g. ϕ is a device to obtain satisfactory efficiency distribution

If analysis non-Bayesian, and ϕ is degenerate, makes sense to use a criterion which is well-behaved

Mean local efficiency

One approach is to maximize

$$\Psi(\xi) = \mathsf{E}_{\boldsymbol{\theta}}\,\mathsf{eff}(\xi|\boldsymbol{\theta})$$

- has an interpretation as minimizing an expected *cost regret*
- (amount of overspend due to inefficiency, when compared with other equally informative designs)

Density designs

One suggestion is, instead of finitely-supported designs,

$$\left\{ \begin{array}{ccc} \mathbf{x}_1 & \ldots & \mathbf{x}_k \\ w_1 & \ldots & w_k \end{array} \right\}$$

define a design using a probability density function, $g(\mathbf{x})$, on $\mathcal{X}$

In some sense such designs 'get everywhere' in $\mathcal{X}$, and are infinitely-supported

Have been considered, e.g. by Wiens (1992) in context of model robustness

Information matrix formed as

$$M(\xi, \boldsymbol{\theta}) = \int_{\mathcal{X}} M(x, \boldsymbol{\theta}) g(\mathbf{x}) d\mathbf{x}$$

Detailed example

Exponential regression

$$y_i \sim N[\eta(x_i), \sigma^2]$$
$$\eta(x) = e^{-x/\theta}$$

Assume a priori that

$$\theta \sim U(0, a)$$

Parameter singularities $\{0, \infty\}$, but for $\theta > 0$ only singular *design* is $x = 0$

- for fixed $\theta > 0$, $|M(\xi, \theta)| = 0$ only when ξ puts unit mass on $x = 0$

Lemma all single-point designs have $\phi(\xi) = -\infty$

Theorem all finitely-supported designs have $\phi(\xi) = -\infty$

Conclusion: here ϕ is useless in helping us make a choice between designs

- despite the fact the prior support is bounded
- numerical methods - spurious comparisons

To prove the Lemma, consider

$$\log |M(x,\theta)| = -\frac{2x}{\theta} - 4\log\theta + 2\log x$$

To prove the Theorem, make use of the following inequality. For $x > 0$, $y \geq 0$

$$\log(x+y) \leq \log(x) + y/x$$

Can be used to show that

$$\log |M(\xi,\theta)| \leq \log w_1 + \log M(x_1,\theta) + T(\theta)$$

WLOG $x_1 \leq x_2 \leq \ldots x_n$, in which case it is true that $0 \leq T(\theta) \leq 1$

$$\mathrm{E}\log |M(\xi,\theta)| \leq \log w_1 + \mathrm{E}\log M(x_1,\theta) + \mathrm{E}\, T(\theta) = -\infty$$

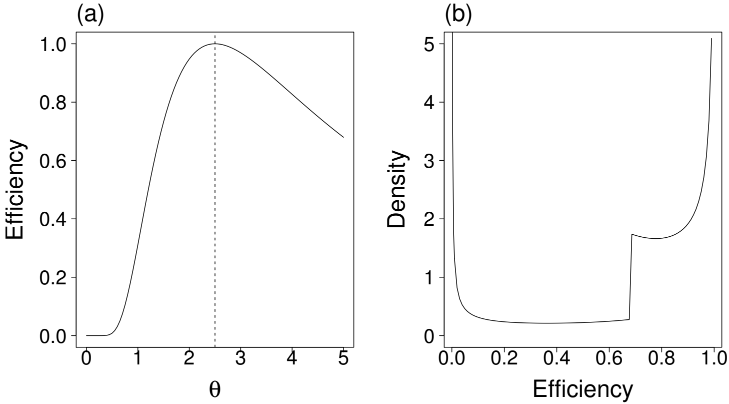
Locally optimal and maximum mean efficiency designs can be computed analytically

Proposition the locally D-optimal design at θ is the single-point design $x = \theta$

Proposition the design which maximizes the mean local efficiency under $\theta \sim U(0, a)$ is the single-point design $x = a/2$

- the mean local efficiency of this design is 67%, regardless of a

Properties of the Ψ-optimal design



Density designs

Consider the design ξ_U defined by a uniform probability density on $(0, a)$

$$g(x) = a^{-1}\mathbf{1}(0 < x < a)$$

Recall that the information matrix is

$$M(\xi_U, \theta) = \frac{1}{a}\int_0^a M(x, \theta)\, dx$$

It can be shown that

$$\phi(\xi_U) = \mathrm{E}\log|M(\xi_U, \theta)| > -\infty$$

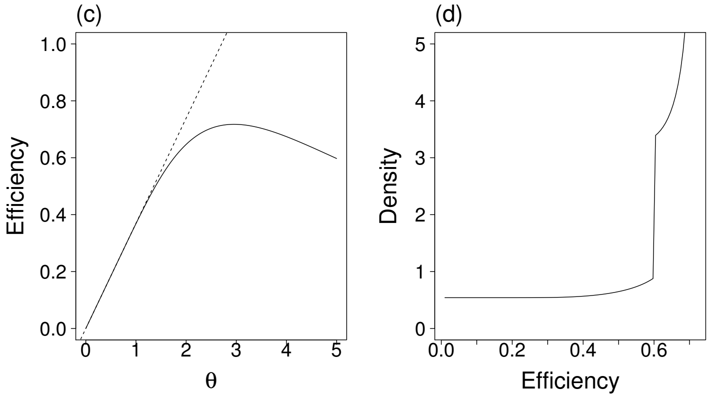
so the uniform design is not degenerate with respect to ϕ

Can also compute the *D*-efficiency

$$\mathrm{eff}(\xi_U|\theta) = \left\{\frac{|M(\xi_U, \theta)|}{\sup_{\xi'}|M(\xi', \theta)|}\right\}^{1/p}$$

and the efficiency distribution

Properties of the uniform density design



Interpretation of density designs

Density designs cannot be used directly in practice.
How about finite (random) samples from the distribution?

Let $X_n = (x_1, \ldots, x_n)$ be such a sample.

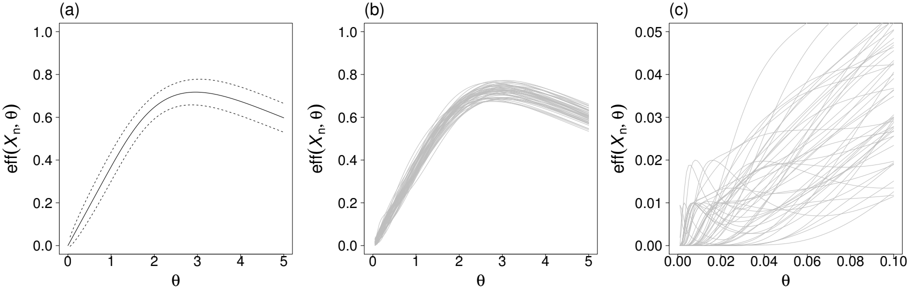
Proposition

As $n \to \infty$,

$$\text{eff}(X_n|\theta) \to \text{eff}(\xi_U|\theta) \quad \text{almost surely}$$

Moreover we can produce '95% performance limits'

Sampling properties of uniform design, $n = 100$



For any θ, we have a positive probability of obtaining a reasonably efficient design

This must be traded off with the probability of obtaining a design which is inefficient for most values of θ

Moreover, the sampled design will have $\phi(X_n) = -\infty$

Conclusions

- when producing Bayesian designs, be cautious about integrability
- if parameter singularities can't be avoided, consider alternative approximations/criteria

Future work

- development of further explicitly pseudo-Bayesian criteria
- other situations where random designs may be helpful

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