Optimal design for generalised linear mixed models

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Motivation

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  - Drug with binary response
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- What about subject effect?

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- Numerical investigation showed large discrepancies
- Aim: to develop a more accurate approximation

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- Approximate designs: where weights $w_i \in [0,1]$ sum to 1, represent proportion of experimental effort at each point

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- D-optimality (Smith, 1918; Box and Lucas, 1959): maximise determinant of Fisher information matrix

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- So D-optimal design depends on θ, such designs are *locally* optimal

Logistic regression

- Fixed effects model:

$$\eta_j = \text{logit}\{P(y_j = 1)\} = \log\{p_j/(1 - p_j)\} = x_j\theta$$

so that

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- Fisher information matrix:

$$M_F(\theta, \xi) = X^T W X$$

where

$$W = \mathrm{diag}\{w_j p_j (1-p_j)\}$$

Logistic regression example

- Model (Atkinson & Haines, 1996):

$$\eta = \mathrm{logit}\{p\} = \theta_0 + \theta_1 x_1 + \theta_2 x_2$$

$(x_1, x_2) \in [-1,\, 1] \times [-1,\, 1]$

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- Locally D-optimal design for $\theta = (3, 3, 1)^{\mathrm{T}}$:

$$\xi = \begin{Bmatrix} (-1, -1) & (-1, 1) & (-0.068, -1) \\ \frac{1}{3} & \frac{1}{3} & \frac{1}{3} \end{Bmatrix}$$

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- Parameters: $\psi = (\beta^{\mathrm{T}}, \sigma_1^2, \ldots, \sigma_q^2)^{\mathrm{T}}$

Log-likelihood

$$\ell = \sum_j \log \int \underset{\mathbb{R}^q}{\cdots} \int P_j(b_j)\Phi_q(b_j)\mathrm{d}b_j$$

where

$$\begin{aligned} P_j(b_j) &= \prod_{i=1}^{n_j} \{p_{ij}(b_j)\}^{y_{ij}} \{1 - p_{ij}(b_j)\}^{1-y_{ij}} \\ p_{ij}(b_j) &= \mathrm{logit}^{-1}\{x_{ij}\beta + z_{ij}b_j\} \end{aligned}$$

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- Gaussian quadrature
- Taylor expansion

Taylor approximation to log-likelihood

From Longford (1994),

$$\ell \;\approx\; \sum_{j=1}^{N} \left[\log\{P_j(0)\} + \frac{1}{2} e_j^{\mathrm{T}} H_j e_j - \frac{1}{2} \log |G_j| \right]$$

where

$$\begin{aligned} G_j &= I_q + \Sigma^{1/2} Z_j^{\mathrm{T}} W_j Z_j \Sigma^{1/2}, \quad \text{and} \\ H_j &= W_j Z_j \Sigma^{1/2} G_j^{-1} \Sigma^{1/2} Z_j^{\mathrm{T}} W_j \\ W_j &= \mathrm{diag}\{w_j\}, \quad w_j = (w_{1j}, \ldots, w_{n_j j})^{\mathrm{T}} \\ w_{ij} &= p_{ij}(0)(1 - p_{ij}(0)) \end{aligned}$$

etc.

Approximate information matrix

- Longford (1994) ignores dependence of w_{ij} on on β to give

$$M_F(\psi, \xi_j) \approx \begin{bmatrix} A_j & 0 \\ 0 & B_j \end{bmatrix},$$

where

$$A_j = X_j^{\mathrm{T}} V_j^{-1} X_j,$$

and the (u, v) element of B_j is

$$B_j^{(u,v)} = \frac{1}{2}\mathrm{tr}\left(V_j^{-1} \frac{\partial V_j}{\partial \sigma_u^2} V_j^{-1} \frac{\partial V_j}{\partial \sigma_v^2} \right)$$

where $V_j = W_j^{-1} + Z_j \Sigma Z_j^{\mathrm{T}}$

Less approximate information matrix?

- What if we acknowledge the dependence of w_{ij} on on β?

Less approximate information matrix?

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- $M_F(\psi, \xi_j) \approx$ 10 pages of LaTeX

Brute force numerical methods

- Recall $M_F(\psi, \xi) = -\mathrm{E}\left[\frac{\partial^2 \ell(\psi;y)}{\partial\psi\partial\psi^{\mathrm{T}}}\right]$

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  where the derivatives are evaluated numerically
- ℓ may be evaluated
  - by Gaussian quadrature, or
  - Taylor approximation

Summary of methods

	Derivatives	Log-likelihood	w_{ij} depends on β?
Nick [Longford]	Analytic	Approx.	No
Tim [me]	Analytic	Approx.	Yes
Brute force 1	Numerical	Approx.	N/A
Brute force 2	Numerical	Quadrature	N/A

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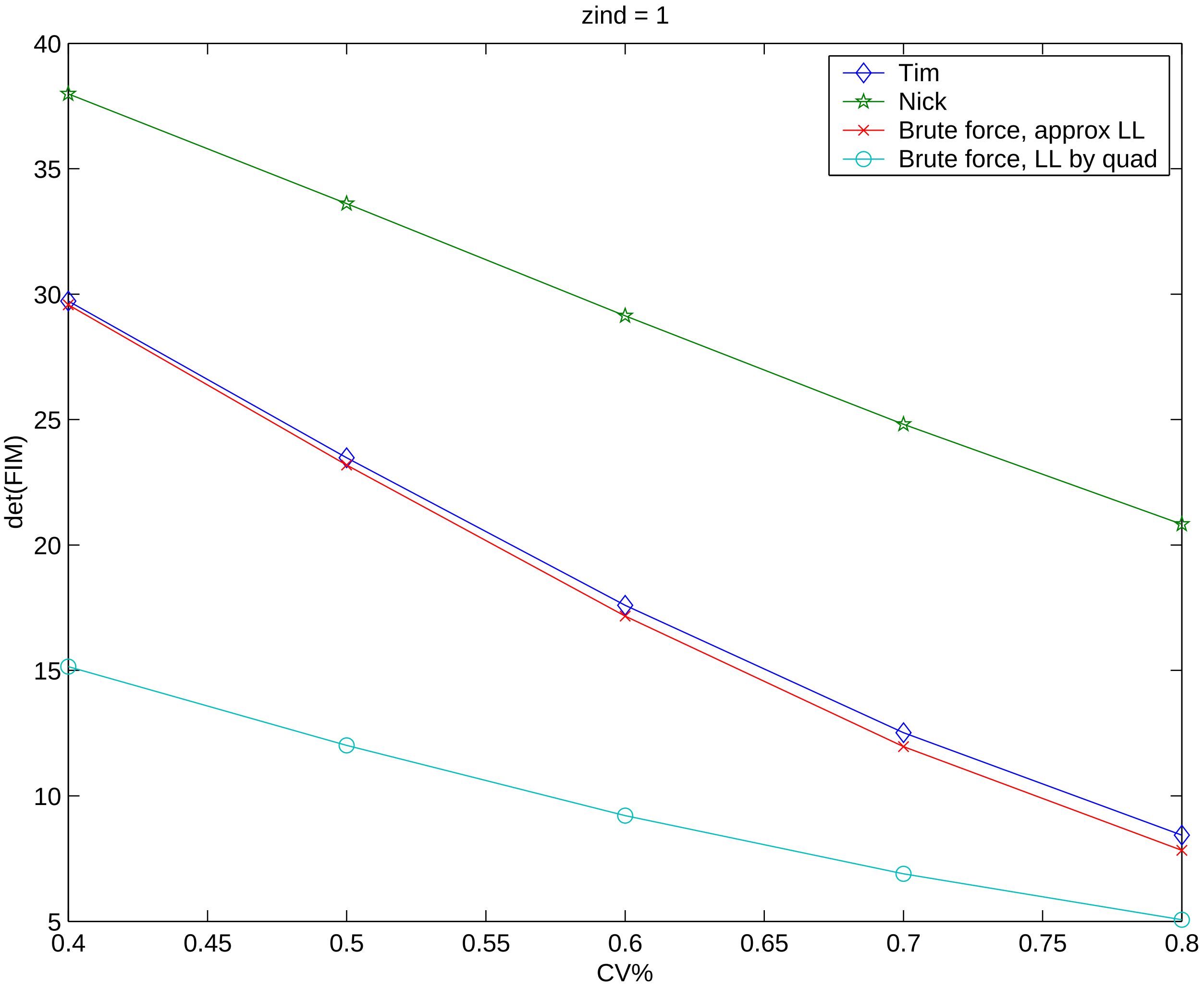

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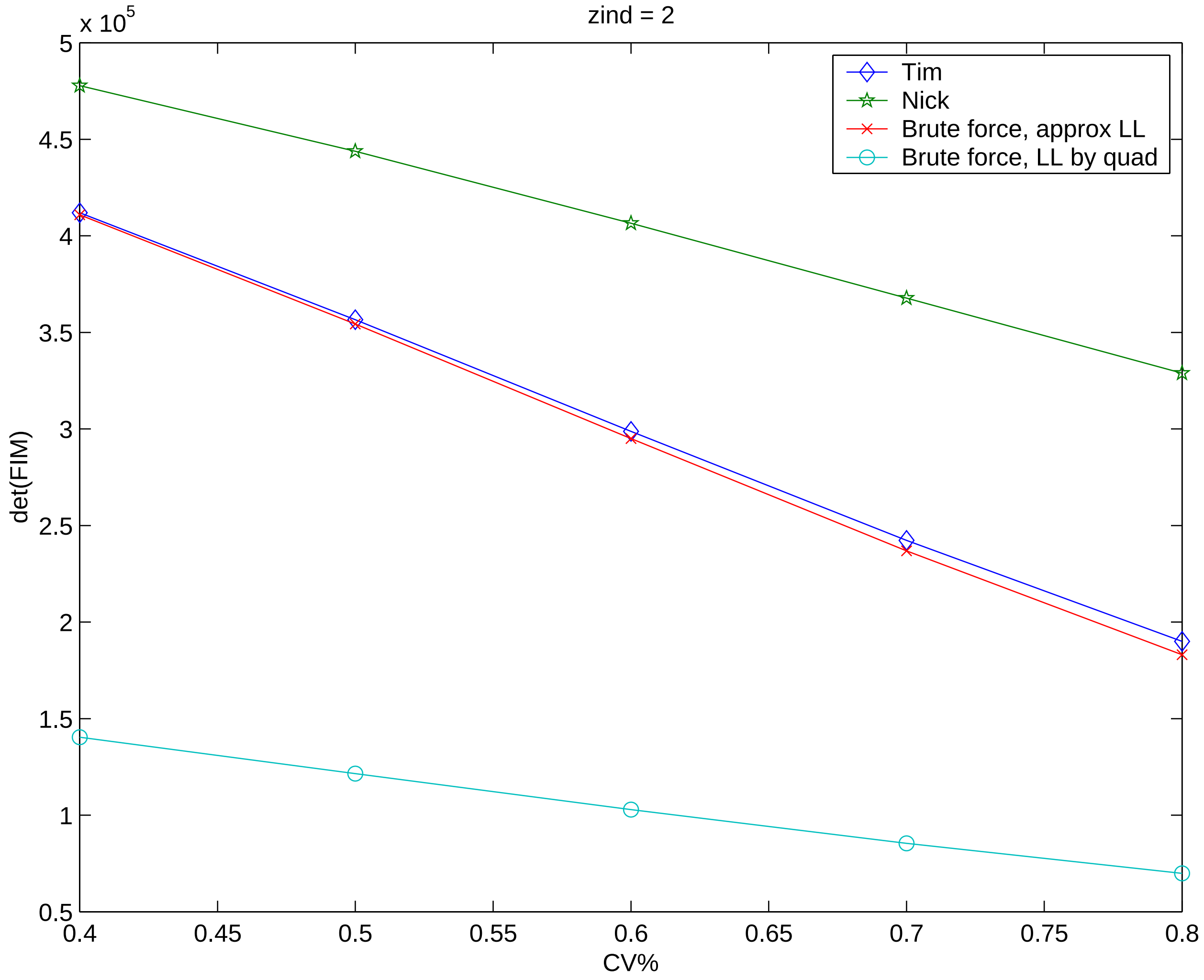
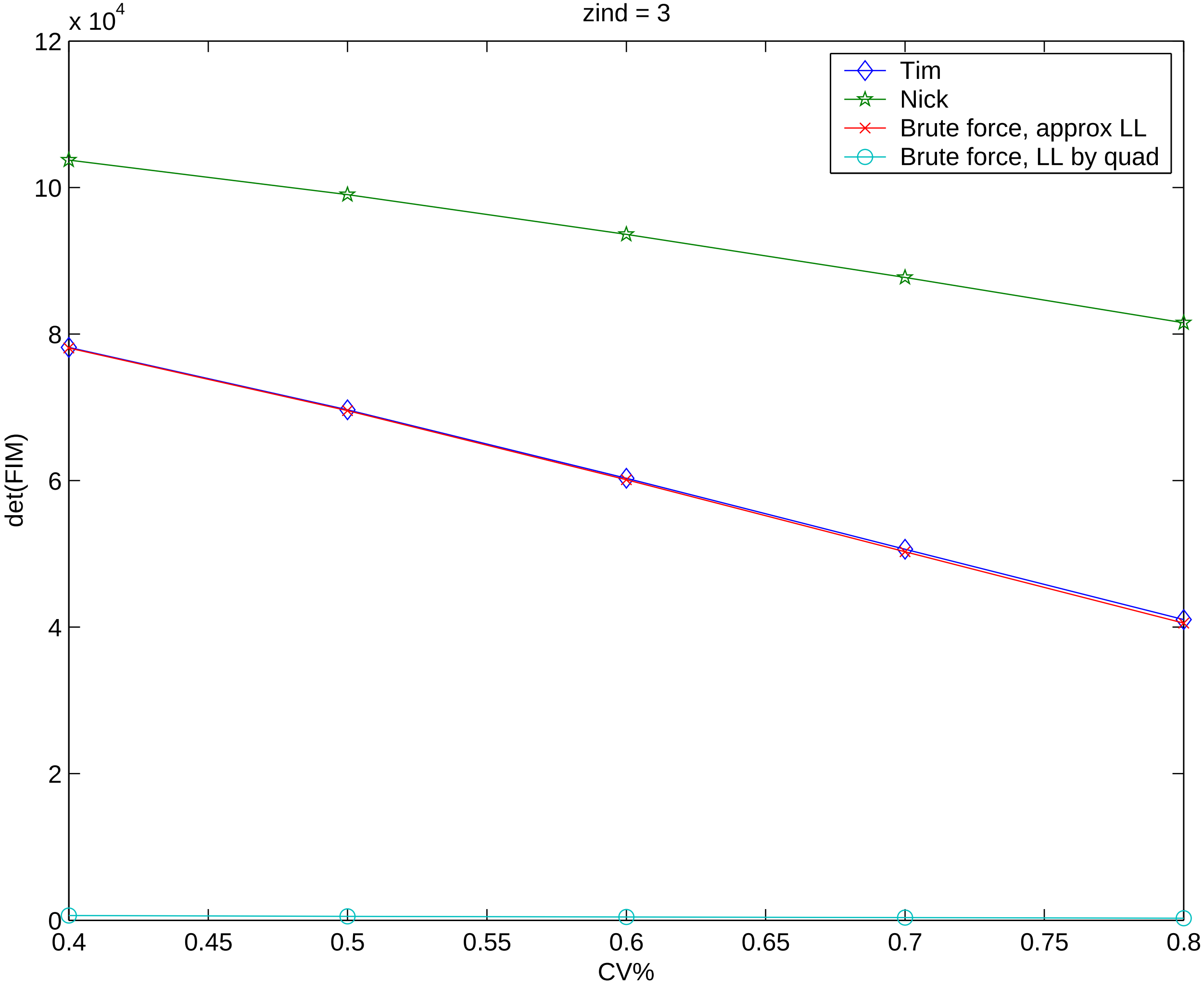


Testing. . .

$$\text{logit}\{p_j\} = \beta_0 + \beta_1 x_1 + (\beta_2 + b_j) x_2$$



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- Higher order Taylor expansion would make algebra even more unmanageable
- Next step: optimal design!