Asymptotic Relative Efficiencies of the Score and Robust Tests in Genetic Association Studies

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1 Introduction

1.1 notation

The null hypothesis is $H_0 : \lambda = 1$. The likeliood and log-likelihood function:
likelihood function: $L_n(\lambda_1, \lambda_2, \eta)$
log-likelihood function $l_n(\lambda, \eta, \theta)$
we work with $l_n(\lambda, 1 - \theta - +\theta\lambda, \eta)$, where θ is explicitly epressed.

$$\begin{aligned}
x_1 =& \lambda \\
x_2 =& 1 - \theta - \theta\lambda \\
x_3 =& \eta
\end{aligned}$$

Denote

$$\begin{aligned}
l_{n,\mu} =& \partial l_n / \partial x_\mu \quad \text{for} \quad \mu = 1, 2, 3 \\
l_{n,\mu\nu} =& \partial^2 l_n / \partial x_\mu \partial x_\nu \quad \text{for} \mu = 1, 2, \nu = 1, 2, 3 \\
l_{n,33} =& \partial^2 l_n / \partial x_3 \partial x_3 \\
l_{n,\mu\nu} =& l_{n,\nu\mu} \quad \text{for} \mu, \nu = 1, 2 \\
l_{n,\mu\nu} =& l^T_{n,\nu\mu} \quad \text{for} \mu = 1, 2, \nu = 3 \\
L_{\mu\nu}(\eta) =& E_{H_0}(l_{1,\mu\nu}(1, 1, \eta)) \quad \text{for} \mu = 1, 2, 3, \nu = 1, 2, 3
\end{aligned}$$

$$s(\theta, \eta) = l_{1,1}(1, 1, \eta) + \theta l_{1,2}(1, 1, \eta) - (L^T_{13}(\eta) + \theta L^T_{23}(\eta))L^{-1}_{33}(\eta) l_{1,3}(1, 1, \eta)$$
$$\mu(\lambda, \theta) = E_{H_1,\eta_0}(s(\theta, \eta_\theta))$$

$$\begin{aligned}
\sigma(\theta) =& (I_{\lambda\lambda})^{-1} = A_{\eta_0}\theta^2 + 2B_{\eta_0}\theta + C_{\eta_0} \\
A_\eta =& L_{23}(\eta)L^{-1}_{33}(\eta)L_{32} - L_{22}(\eta) \\
B_\eta =& L_{13}(\eta)L^{-1}_{33}(\eta)L_{31}(\eta) - L_{12}(\eta) \\
C_\eta =& L_{13}(\eta)L^{-1}_{33}(\eta)L_{31}(\theta) - L_{11}(\eta)
\end{aligned}$$

$$\sigma(\eta, \theta_i, \theta_j) = A_\eta \theta_i \theta_j + B_\eta(\theta_i + \theta_j) + C_\eta$$

when $\theta = \theta^{(0)}$ is the true value $Z(\theta^{(0)})$ is the asymptotically most powerful (optimal). Let $\hat{\eta}_n$ satisfy $\partial l_n / \partial \eta|_{H_0,\hat{\eta}_n} = l_{n,3}(1, 1, 1, \hat{\eta}_n) = 0$. Let η_0 be the true value (unknown) of η under either H_0 or H_1, Let $\hat{\eta}_{0,n}$ be the MLE of η under H_0, and $(\hat{\eta}_{1,n}, \hat{\lambda}_n)$ be that of (η, λ) under H_1.

1.2 Pitman ARE

$$e_P(Z_{MERT}, Z(\theta^{(0)})) = \frac{(\rho_{\theta_i,\theta^{(0)}} + \rho_{\theta_j,\theta^{(0)}})^2}{2(1+\rho_{\theta_i,\theta_j})}$$

$$\rho_{\theta_i,\theta_j} = \frac{\sigma(\eta_0,\theta_i,\theta_j)}{\sigma(\eta_0,\theta_i,\theta_i)\sigma(\eta_0,\theta_i,\theta_j)^{1/2}}$$

1.3 Chernoff ARE

$$\tilde{e}_C(Z_{MERT}, Z_{\theta^{(0)}}) = \frac{\tilde{Q}_{Z_{MERT}}}{\tilde{Q}_{Z_{\theta^{(0)}}}}$$

$$\tilde{Q}_{Z_{\theta^{(0)}}} = 2\left(1 - \Phi\left(\frac{\mu^{(1)}(\lambda_0, \theta^{(0)})}{2\sigma(\theta^{(0)})}\right)\right)$$

$$\tilde{Q}_{Z_{MERT}} = 2\left(1 - \Phi\left(\left[\frac{\mu^{(1)}(\lambda_0,\theta_i)}{2\sigma(\theta_i)} + \frac{\mu^{(1)}(\lambda_0,\theta_j)}{2\sigma(\theta_j)}\right] / \sqrt{8(1+\rho_{\theta_i,\theta_j})}\right)\right)$$

$$\mu^{(1)}(\lambda,\theta) = \partial\mu(\lambda,\theta)/\partial\lambda$$

λ_0 be the null hypothesis , $H_0 : \lambda_0 \in \Lambda_0$

1.4 Hodges-Ledmann ARE

$$e_{HL}(Z_{MERT}, Z_\theta) = \frac{d_{Z_{MERT}}(\lambda)}{d_{Z_\theta(\lambda)}}$$

$$d_{Z_\theta}(\lambda) = \frac{\mu^2(\lambda,\theta)}{\sigma^2(\theta)}$$

$$d_{Z_{MERT}}(\lambda) = \mu^2_{MERT}(\lambda) = [\mu(\lambda,\theta_i)/\sigma(\theta_i) + \mu(\lambda,\theta_j)/\sigma(\theta_j)]/\sqrt{2(1+\rho_{\theta_i,\theta_j})}$$

1.5 Bahadur ARE

$$e_B(Z_{MERT}, Z_\theta) = e_{HL}(Z_{MERT}, Z_\theta)$$

$$\tilde{e}_B(Z_{MERT}, Z_\theta) = \frac{\tilde{c}_{Z_{MERT}}}{\tilde{c}_{Z_\theta}}$$

$$\tilde{c}_{Z_{MERT}} = 1 - \Phi(\mu^{(1)}_{MERT}(1))$$

$$\tilde{c}_{Z_\theta} = 1 - \Phi(\mu^{-1}(1,\theta_0)/\sigma(\theta_0))$$

$$\mu(1,\theta_0) = 0$$

1.6 Algorithm

likelihood function

$$L_n(\lambda_1, \lambda_2, \eta) = \frac{\lambda_1^{r_1}\lambda_2^{r2} exp(r\eta)}{\{1+exp(\eta)\}^{n_0}\{1+\lambda_1 exp(\eta)\}^{n_1}\{1+\lambda_2 exp(\eta)\}^{n_2}} \tag{1}$$

log-likelihood function $l_n(\lambda,\eta,\theta)$
we work with $l_n(\lambda, 1-\theta-+\theta\lambda, \eta)$, where θ is explicitly epressed.

$$\begin{aligned} x_1 =& \lambda \\ x_2 =& 1-\theta-\theta\lambda \\ x_3 =& \eta \end{aligned}$$

Denote

$$
\begin{aligned}
l_{n,\mu} =& \partial l_n/\partial x_\mu \quad \text{for} \quad \mu = 1,2,3 \\
l_{n,\mu\nu} =& \partial^2 l_n/\partial x_\mu \partial x_\nu \quad \text{for} \quad \mu = 1,2, \nu = 1,2,3 \\
l_{n,33} =& \partial^2 l_n/\partial x_3 \partial x_3 \\
l_{n,\mu\nu} =& l_{n,\nu\mu} \quad \text{for} \quad \mu,\nu = 1,2 \\
l_{n,\mu\nu} =& l^T_{n,\nu\mu} \quad \text{for} \quad \mu = 1,2, \nu = 3 \\
L_{\mu\nu}(\eta) =& E_{H_0}(l_{1,\mu\nu}(1,1,\eta)) \quad \text{for} \quad \mu = 1,2,3, \nu = 1,2,3
\end{aligned}
$$

- input: Y, G, $\theta^{(0)}$, θ_i, θ_j
- output: $e_P(Z_{MERT}, Z_{\theta^{(0)}})$, $\tilde{e}_C(Z_{MERT}, Z_{\theta^{(0)}})$, $e_{HL}(Z_{MERT}, Z_{\theta^{(0)}})$, $e_B(Z_{MERT}, Z_{\theta^{(0)}})$

step 1 Estimate $\hat{\eta}$. where $\hat{\eta}$ satisfy $\partial l_n/\partial \eta|_{H_0,\hat{\eta}_n} = l_{n,3}(1,1,\hat{\eta}_n) = 0$.

step 2 Compute $l_n(1,1,\hat{\eta})$; $l_{n,\mu}(1,1,\hat{\eta})$, for $\mu = 1,2,3$; $l_{n,\mu\nu}(1,1,\hat{\eta})$ for $\mu = 1,2,3$, $\nu = 1,2,3$.

step 3 Compute $L_{\mu\nu}(\hat{\eta}) = E_{H_0}(l_{1,\mu\nu}) = \frac{1}{n} l_{n,\mu\nu}(1,1,\hat{\eta})$

step 4 Compute $\sigma(\theta^{(0)})$, $\sigma(\theta_i)$, $\sigma(\theta_j), \sigma(\theta^{(0)},\theta_i), \sigma(\theta^{(0)},\theta_j), \sigma(\theta_i,\theta_j)$, where

$$\sigma(\theta_i,\theta_j) = A_{\hat{\eta}}\theta_i\theta_j + B_{\hat{\eta}}(\theta_i+\theta_j) + C_{\hat{\eta}}$$

$$
\begin{aligned}
A_\eta =& L_{23}(\eta)L_{33}^{-1}(\eta)L_{32} - L_{22}(\eta) \\
B_\eta =& L_{13}(\eta)L_{33}^{-1}(\eta)L_{31}(\eta) - L_{12}(\eta) \\
C_\eta =& L_{13}(\eta)L_{33}^{-1}(\eta)L_{31}(\eta) - L_{11}(\eta)
\end{aligned}
$$

step 5 Compute $\mu(\lambda,\theta^{(0)}), \mu(\lambda,\theta_i), \mu(\lambda,\theta_j)$,

$$\mu(\lambda,\theta) = E_{H_1,\eta_0}(s(\theta,\eta_\theta)) = \frac{1}{n}(l_{n,1}(n,1,\hat{\eta}) + \theta l_{n,2}(n,1,\hat{\eta}) - (L_{13}^T(\eta) + \theta L_{23}^T(\eta))L_{33}^{-1}(\eta)l_{n,3}(1,1,\eta))$$

step 6 Compute $\mu^{(1)}(\lambda,\theta^{(0)}), \mu^{(1)}(\lambda,\theta_i), \mu^{(1)}(\lambda,\theta_j)$,

$$\mu(\lambda,\theta) = E_{H_1,\eta_0}(s(\theta,\eta_\theta)) = \frac{1}{n}(l_{n,11}(n,1,\hat{\eta}) + \theta l_{n,21}(n,1,\hat{\eta}) - (L_{13}^T(\hat{\eta}) + \theta L_{23}^T(\hat{\eta}))L_{33}^{-1}(\hat{\eta})l_{n,31}(1,1,\hat{\eta}))$$

$$
\begin{aligned}
\mu(\lambda,\theta) = E_{H_1,\eta_0}(s(\theta,\eta_\theta)) =& \frac{1}{n}(l_{n,11}(n,1,\hat{\eta}) + \theta l_{n,21}(n,1,\hat{\eta}) - (L_{13}^T(\hat{\eta}) + \theta L_{23}^T(\hat{\eta}))L_{33}^{-1}(\hat{\eta})l_{n,31}(1,1,\eta)) \\
=& L_{11}(\hat{\eta}) + \theta L_{21}(\hat{\eta}) - (L_{13}^T(\hat{\eta}) + \theta L_{23}^T(\hat{\eta}))L_{33}^{-1}(\hat{\eta})L_{31}(\hat{\eta}))
\end{aligned}
$$

step 7 Compute $e_P(Z_{MERT}, Z(\theta^{(0)}))$.

$$e_P(Z_{MERT}, Z(\theta^{(0)})) = \frac{(\rho_{\theta_i,\theta^{(0)}} + \rho_{\theta_j,\theta^{(0)}})^2}{2(1+\rho_{\theta_i,\theta_j})}$$

$$\rho_{\theta_i,\theta_j} = \frac{\sigma(\hat{\eta},\theta_i,\theta_j)}{\sigma(\hat{\eta},\theta_i,\theta_i)\sigma(\hat{\eta},\theta_i,\theta_j)^{1/2}}$$

step 8 Compute

$$\tilde{e}_C(Z_{MERT}, Z_{\theta^{(0)}}) = \frac{\tilde{Q}_{Z_{MERT}}}{\tilde{Q}_{Z_{\theta^{(0)}}}}$$

$$\tilde{Q}_{Z_{\theta^{(0)}}} = 2\left(1 - \Phi\left(\frac{\mu^{(1)}(\lambda_0,\theta^{(0)})}{2\sigma(\theta^{(0)})}\right)\right)$$

$$\tilde{Q}_{Z_{MERT}} = 2\left(1 - \Phi\left(\left[\frac{\mu^{(1)}(\lambda_0,\theta_i)}{2\sigma(\theta_i)} + \frac{\mu^{(1)}(\lambda_0,\theta_j)}{2\sigma(\theta_j)}\right] / \sqrt{8(1+\rho_{\theta_i,\theta_j})}\right)\right)$$

$$\lambda_0 = 1$$

step 9 Compute

$$
\begin{aligned}
e_{HL}(Z_{MERT}, Z_\theta) &= \frac{d_{Z_{MERT}}(\lambda)}{d_{Z_\theta(\lambda)}} \\
d_{Z_\theta}(\lambda) &= \frac{\mu^2(\lambda, \theta)}{\sigma^2(\theta)} \\
d_{Z_{MERT}}(\lambda) = \mu^2_{MERT}(\lambda) &= [\mu(\lambda, \theta_i)/\sigma(\theta_i) + \mu(\lambda, \theta_j)/\sigma(\theta_j)]/\sqrt{2(1 + \rho_{\theta_i, \theta_j})}
\end{aligned}
$$

step 10 Compute

$$
\begin{aligned}
e_B(Z_{MERT}, Z_\theta) &= e_{HL}(Z_{MERT}, Z_\theta) \\
\tilde{e}_B(Z_{MERT}, Z_\theta) &= \frac{\tilde{c}_{Z_{MERT}}}{\tilde{c}_{Z_\theta}} \\
\tilde{c}_{Z_{MERT}} &= 1 - \Phi(\mu^{(1)}_{MERT}(1)) \\
\tilde{c}_{Z_\theta} &= 1 - \Phi(\mu^{-1}(1, \theta^{(0)})/\sigma(\theta^{(0)}))
\end{aligned}
$$