The computation of four AREs

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University of Chinese Academy of Sciences— July 29, 2018

1 Introduction

1.1 Notation

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

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

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

1.2 Algorithm

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

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

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

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

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

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

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

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

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

$$\begin{aligned} \tilde{e}_C(Z_{MERT}, Z_{\theta^{(0)}}) &= \frac{\tilde{Q}_{Z_{MERT}}}{\tilde{Q}_{Z_{\theta^{(0)}}}} \\ \tilde{Q}_{Z_{\theta^{(0)}}} &= 2\left(1 - \Phi\left(\frac{\mu^{(1)}(\lambda_0, \theta^{(0)})}{2\sigma(\theta^{(0)})}\right)\right) \\ \tilde{Q}_{Z_{MERT}} &= 2\left(1 - \Phi\left(\left[\frac{\mu^{(1)}(\lambda_0, \theta_i)}{2\sigma(\theta_i)} + \frac{\mu^{(1)}(\lambda_0, \theta_j)}{2\sigma(\theta_j)}\right] / \sqrt{8(1 + \rho_{\theta_i, \theta_j})}\right)\right) \\ \lambda_0 &= 1 \end{aligned}$$

step 9 Compute

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

step 10 Compute

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

Table 1: The Four AREs of Z_{MERT} and $Z_{\theta^{(0)}}$

		$\lambda = 1.1$				$\lambda = 1.3$				$\lambda = 1.5$			
MAF	$\theta^{(0)}$	e_P	e_C	e_{HL}	e_B	e_P	e_C	e_{HL}	e_B	e_P	e_C	e_{HL}	e_B
0.15	0												
	1/4												
	1/2												
	1												
0.30	0												
	1/4												
	1/2												
	1												
0.45	0												
	1/4												
	1/2												
	1												

1.3 simulation

Let p be the minor allele frequency (MAF) of the marker of interest in the population. we consider case-control data with $r = 500$ cases and $s = 500$ controls. and $\lambda \in \{1.1, 1.2, 1.3\}$ and $p \in \{0.15, 0.30, 0.45\}$, and the true $\theta^{(0)} \in \{0, 1/4, 1/2, 1\}$. . we generate $Nrep = 1000$ datasets. and we compute the mean and variance of the four AREs to Z_{MERT} and $Z_{\theta^{(0)}}$