

## APPENDIX

### The derivation process of $E(U|T)$ and $Var(U|T)$

Since  $E(U|T) = \frac{2}{n-1} \sum_{i=1}^n \bar{F}_i E[\sum_{l=1}^m \log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T]$ , according to the independence of each rare variant locus, it is easy to obtain that

$$E(U|T) = \frac{2}{n-1} \sum_{i=1}^n \bar{F}_i \sum_{l=1}^m E[\log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T],$$

where

$$\begin{aligned} & E[\log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T] \\ &= E[(\log n_{DG_{il}} + \log n_{MG_{il}} + \log n_{OG_{il}}) | T] \\ &= E(\log n_{DG_{il}} | T) + E(\log n_{MG_{il}} | T) + E(\log n_{OG_{il}} | T) \\ &= P(DG_{il} = 0) \log n_{D0} + P(DG_{il} = 1) \log n_{D1} + P(DG_{il} = 2) \log n_{D2} \\ &\quad + P(MG_{il} = 0) \log n_{M0} + P(MG_{il} = 1) \log n_{M1} + P(MG_{il} = 2) \log n_{M2} \\ &\quad + P(OG_{il} = 0) \log n_{O0} + P(OG_{il} = 1) \log n_{O1} + P(OG_{il} = 2) \log n_{O2} \\ &= 3[\log n + 2(1 - p_l)^2 \log(1 - p_l) + 2p_l(1 - p_l) \log 2p_l(1 - p_l) + 2p_l^2 \log p_l] \\ &= 3[\log n + 2(1 - p_l) \log(1 - p_l) + 2p_l \log p_l + 2p_l(1 - p_l) \log 2]. \end{aligned}$$

Besides, the genetic data of each family are independent, therefore

$$\begin{aligned} Var(U|T) &= Var\left[\frac{2}{n-1} \sum_{l=1}^m \sum_{i=1}^n \bar{F}_i \log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T\right] \\ &= \left(\frac{2}{n-1}\right)^2 \sum_{i=1}^n \bar{F}_i \bar{F}_i^T Var\left[\sum_{l=1}^m \log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T\right] \\ &= \left(\frac{2}{n-1}\right)^2 \sum_{i=1}^n \bar{F}_i \bar{F}_i^T \sum_{l=1}^m Var[\log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T], \end{aligned}$$

where

$$\begin{aligned} & Var[\log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T] \\ &= E[\log^2(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T] - \{E[\log(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T]\}^2, \end{aligned}$$

and

$$\begin{aligned} & E[\log^2(n_{DG_{il}} n_{MG_{il}} n_{OG_{il}}) | T] \\ &= E[(\log n_{DG_{il}} + \log n_{MG_{il}} + \log n_{OG_{il}})^2 | T] \\ &= E[(\log^2 n_{DG_{il}} + \log^2 n_{MG_{il}} + \log^2 n_{OG_{il}} + 2 \log n_{DG_{il}} \log n_{MG_{il}} \\ &\quad + 2 \log n_{DG_{il}} \log n_{OG_{il}} + 2 \log n_{MG_{il}} \log n_{OG_{il}}) | T] \\ &= E(\log^2 n_{DG_{il}} | T) + E(\log^2 n_{MG_{il}} | T) + E(\log^2 n_{OG_{il}} | T) \\ &\quad + 2E(\log n_{DG_{il}} \log n_{MG_{il}}) + 2E[\log n_{OG_{il}} (\log n_{DG_{il}} + \log n_{MG_{il}})] \\ &= E(\log^2 n_{DG_{il}} | T) + E(\log^2 n_{MG_{il}} | T) + E(\log^2 n_{OG_{il}} | T) \\ &\quad + 2E(\log n_{DG_{il}} | T) E(\log n_{MG_{il}} | T) + 2E[\log n_{OG_{il}} (\log n_{DG_{il}} n_{MG_{il}}) | T], \end{aligned}$$

where

$$\begin{aligned}
& E[\log n_{OG_{il}}(\log n_{DG_{il}}n_{MG_{il}})|T] \\
&= P(DG_{il} = 0)P(MG_{il} = 0) \log n_{O0} \log n_{D0}n_{M0} \\
&\quad + \frac{1}{2}P(DG_{il} = 0)P(MG_{il} = 1) \log n_{O0} \log n_{D0}n_{M1} \\
&\quad + \frac{1}{2}P(DG_{il} = 1)P(MG_{il} = 0) \log n_{O0} \log n_{D1}n_{M0} \\
&\quad + \frac{1}{2}P(DG_{il} = 0)P(MG_{il} = 1) \log n_{O1} \log n_{D0}n_{M1} \\
&\quad + \frac{1}{2}P(DG_{il} = 1)P(MG_{il} = 0) \log n_{O1} \log n_{D1}n_{M0} \\
&\quad + P(DG_{il} = 0)P(MG_{il} = 2) \log n_{O1} \log n_{D0}n_{M2} \\
&\quad + P(DG_{il} = 2)P(MG_{il} = 0) \log n_{O1} \log n_{D2}n_{M0} \\
&\quad + \frac{1}{4}P(DG_{il} = 1)P(MG_{il} = 1) \log n_{O0} \log n_{D1}n_{M1} \\
&\quad + \frac{1}{2}P(DG_{il} = 1)P(MG_{il} = 1) \log n_{O1} \log n_{D1}n_{M1} \\
&\quad + \frac{1}{2}P(DG_{il} = 1)P(MG_{il} = 1) \log n_{O2} \log n_{D1}n_{M1} \\
&\quad + \frac{1}{4}P(DG_{il} = 1)P(MG_{il} = 2) \log n_{O1} \log n_{D1}n_{M2} \\
&\quad + \frac{1}{2}P(DG_{il} = 2)P(MG_{il} = 1) \log n_{O1} \log n_{D2}n_{M1} \\
&\quad + \frac{1}{2}P(DG_{il} = 1)P(MG_{il} = 2) \log n_{O2} \log n_{D1}n_{M2} \\
&\quad + \frac{1}{2}P(DG_{il} = 2)P(MG_{il} = 1) \log n_{O2} \log n_{D2}n_{M1} \\
&\quad + P(DG_{il} = 2)P(MG_{il} = 2) \log n_{O2} \log n_{D2}n_{M2} \\
&= 2\log^2 n[(1 - p_l)^4 + 4p_l(1 - p_l)^3 + 6p_l^2(1 - p_l)^2 + 4p_l^3(1 - p_l) + p_l^4] \\
&\quad + 8(1 - p_l)^2 \log n \log(1 - p_l) + 8(1 - p_l)^3 \log^2(1 - p_l) + 8p_l(1 - p_l) \log n \\
&\quad \log 2p_l(1 - p_l) + 8p_l(1 - p_l)^2 \log(1 - p_l) \log 2p_l(1 - p_l) + 2p_l(1 - p_l) \\
&\quad \log^2 2p_l(1 - p_l) + 8p_l^2 \log n \log p_l + 8p_l^2(1 - p_l) \log p_l \log 2p_l(1 - p_l) \\
&\quad + 8p_l^3 \log^2 p_l.
\end{aligned}$$

Based on the above derivation, we have

$$\begin{aligned}
& Var[\log(n_{DG_{il}}n_{MG_{il}}n_{OG_{il}})|T] \\
&= E[\log^2(n_{DG_{il}}n_{MG_{il}}n_{OG_{il}})|T] - E[\log(n_{DG_{il}}n_{MG_{il}}n_{OG_{il}})|T]^2 \\
&= 3\log^2 n\{1 + 2[(1 - p_l)^4 + 4p_l(1 - p_l)^3 + 6p_l^2(1 - p_l)^2 + 4p_l^3(1 - p_l) + p_l^4]\} \\
&\quad + 36(1 - p_l)^2 \log n \log(1 - p_l) + 4(1 - p_l)^2(2p_l^2 - 8p_l + 9)\log^2(1 - p_l) \\
&\quad + 36p_l(1 - p_l) \log n \log 2p_l(1 - p_l) + 2p_l(1 - p_l)(5 + 4p_l(1 - p_l))\log^2 2p_l(1 - p_l) \\
&\quad + 36p_l^2 \log n \log p_l + 4p_l^2(3 + 4p_l + 2p_l^2)\log^2 p_l \\
&\quad + 16p_l(2 - p_l)(1 - p_l)^2 \log(1 - p_l) \log 2p_l(1 - p_l) \\
&\quad + 16p_l^2(1 - p_l)(1 + p_l) \log p_l \log 2p_l(1 - p_l) + 16p_l^2(1 - p_l)^2 \log p_l \log(1 - p_l) \\
&\quad - 9\{\log^2 n + 4(1 - p_l)^4 \log^2(1 - p_l) + 4p_l^2(1 - p_l)^2 \log^2 2p_l(1 - p_l) + 4p_l^4 \log^2 p_l \\
&\quad + 4(1 - p_l)^2 \log n \log(1 - p_l) + 4p_l(1 - p_l) \log n \log 2p_l(1 - p_l) + 4p_l^2 \log n \log p_l \\
&\quad + 8p_l(1 - p_l)^3 \log(1 - p_l) \log 2p_l(1 - p_l) + 8p_l^2(1 - p_l)^2 \log p_l \log(1 - p_l) \\
&\quad + 8p_l^3(1 - p_l) \log p_l \log 2p_l(1 - p_l)\} \\
&= 4p_l(1 - p_l)^2(10 - 7p_l)\log^2(1 - p_l) + 2p_l(1 - p_l)(14p_l^2 - 14p_l + 5)\log^2 2p_l(1 - p_l) \\
&\quad + 4p_l^2(1 - p_l)(7p_l + 3)\log^2 p_l + 8p_l(1 - p_l)^2(7p_l - 5) \log(1 - p_l) \log 2p_l(1 - p_l) \\
&\quad + 8p_l^2(1 - p_l)(2 - 7p_l) \log p_l \log 2p_l(1 - p_l) - 56p_l^2(1 - p_l)^2 \log p_l \log(1 - p_l).
\end{aligned}$$