11-2015-10-28-gail-trying-to-match-the-table-for-09-kernelPvals092415

I began by following gitboxes/b-blueb/trunk/docum/2015/grits/b-2015-05-11-tracking-down-independent-independent/19-NL-and-GBPvals051715.pdf. Now I am following 38-NL&GBPvals062415.pdf and 38-NL&GBPvals062415Tbl1.pdf

After moving to "/Users/ggong/aaa-ebony/43-gritsr2/gritsr2/gails-stuff/b-examples/02-v-9010/a-docum" I am following /Volumes/2015a-stanford/aaa/gitboxes/b-blueb/trunk/docum/2015/grits/e-2015-10-13-grits-competitor/03-kernelPvals091815.pdf

/Users/ggong/aaa-ebony/43-gritsr2/gritsr2/gails-stuff/b-examples/02-v-9010/a-docum

Created "2015-10-28 07:34:24 PDT"

saved and latexed: 2015-10-28 07:34:36

1 `davies_fn`

Given the J dimensional random vector (of functions of genotypes) $Z \sim N\Big(\mu_Z, V_Z\Big)$ and the matrix A, the p-value for the statistic $Q = Z^T AZ$ can be gotten from `davies_fn(zzz, mu_z, V_z, AAA)`

This function performs the following calculations

$\tilde{Z} = V_Z^{-1/2} Z \sim N\Big(\mu_{\tilde{Z}} = V_Z^{-1/2}\mu_Z, I\Big)$.

$Q = Z^T AZ = Z^T V^{-1/2} V^{1/2} AV^{1/2} V^{-1/2} Z = \tilde{Z}^T \tilde{A}\tilde{Z}$

$\tilde{A} = V^{1/2} AV^{1/2}$

$\tilde{A} = U^T \Lambda U$. The spectral decomposition of $\tilde{A}$, so Λ is a diagonal matrix containing the eigenvalues of $\tilde{A}$, and $U^T U = UU^T = I$.

$Q = \tilde{Z}^T \tilde{A}\tilde{Z} = \tilde{Z}^T U^T \Lambda U\tilde{Z} = X^T \Lambda X$

$X = U\tilde{Z} \sim N\Big(\mu_X = U\mu_{\tilde{Z}}, UIU^T = I)$

$Q = X^T \Lambda X = \sum_{j=1}^J \lambda_j X_j^2$ is a sum of independent χ^2 random variables with noncentrality parameters μ_X^2.

The R package `CompQuadForm` provides the function `davies` which computes $P(Q > q)$ where $Q = \sum_{j=1}^J \lambda_j X_j + \sigma X_0$ where X_j are independent randomvariables having a non-central χ^2 distribution with n_j degrees of freedom and noncentrality parameter δ_j^2, and X_0 having a standard normal distribution.

In our case, the degrees of freedom is $n_j = 1$, and the noncentrality parameter is $\delta_j^2 = \mu_X^2$.

2 The genotype matrix

G is the genotype matrix.

$E\Big(G_{nm}\Big) = 2\pi_m$

$\Gamma = \text{cov}(G_n)$, a covariance matrix of dimension $M \times M$. I can calculate the empirical covariance matrix by `cov(genotype)`.

Ψ is 2 times the kinship matrix. $\Psi_{n_1\,n_2} = \text{Cor}\Big(G_{n_1\,m}, G_{n_2\,m}\Big)$ while holding m equal to any number in $1, \cdots, M$.

$\text{Cov}\Big(G_{n_1 m_1}, G_{n_2 m_2}\Big) = \Gamma_{m_1 m_2}\Psi_{n_1 n_2}$

$W = W_{M\times M}$ is the diagonal matrix of weights.

3 Y_1, Y_2, $N_{\textbf{cases}}$ and e

Y_1 is a vector of dimension N, the n-th element being the indicator for disease of the n-th person.

N_{cases} is the number of cases.

Y_2 is a vector of outcome predictors. By design, each element of this vector is equal to N_{cases}/N.

$e = Y_1 - Y_2$ is the vector of residuals.

4 Couch everything in terms if $Z = Z^{(2)}$

$$Z = \begin{pmatrix} Z_1 \\ Z_2 \end{pmatrix} = \begin{pmatrix} WGy \\ WGp \end{pmatrix}$$

5 Lines 1, 2, and 5 of Alice's Table 1

$$
\begin{aligned}
Z^{(1)} &= Z_1 - Z_2 \\
A^{(1)}_{\text{burden}} &= J_M \\
A^{(1)}_{\text{skat}} &= I_M \\
A^{(1)}_{\text{lee}} &= (1-\rho)A^{(1)}_{\text{burden}} + \rho A^{(1)}_{\text{skat}} = (1-\rho)J_M + \rho I_M
\end{aligned}
$$

6 Lines 3, 4, and 6 of Alice's Table 1

$$
\begin{aligned}
Z^{(2)} &= Z \\
A^{(2)}_{\text{burden}} &= \begin{pmatrix} J_M & 0 \\ 0 & -J_M \end{pmatrix} = \Delta\Big(J_M, -J_M\Big) \\
A^{(2)}_{\text{skat}} &= \begin{pmatrix} I_M & 0 \\ 0 & -I_M \end{pmatrix} = \Delta\Big(I_M, -I_M\Big) \\
A^{(2)}_{\text{lee}} &= (1-\rho)A^{(2)}_{\text{burden}} + \rho A^{(2)}_{\text{skat}} = (1-\rho)\Delta\Big(J_M, -J_M\Big) + \rho\Delta\Big(I_M, -I_M\Big)
\end{aligned}
$$

7 Lines 7, 8, and 9 of Alice's Table 1

$$
\begin{aligned}
Z^{(3)} &= \begin{pmatrix} Z_1 - Z_2 \\ Z_1 \\ Z_2 \end{pmatrix} \\
A^{(3)}_{\text{burden}} &= \begin{pmatrix} \Big(1-\tau_b\Big)A^{(1)}_{\text{burden}} & 0 \\ 0 & \tau_b A^{(2)}_{\text{burden}} \end{pmatrix} = \Delta\Big\{(1-\tau_b)J_M, \tau_b\Delta\Big(J_M, -J_M\Big)\Big\} \\
A^{(3)}_{\text{skat}} &= \begin{pmatrix} \Big(1-\tau_s\Big)A^{(1)}_{\text{skat}} & 0 \\ 0 & \tau_s A^{(2)}_{\text{skat}} \end{pmatrix} = \Delta\Big\{(1-\tau_s)I_M, \tau_s\Delta\Big(I_M, -I_M\Big)\Big\} \\
A^{(3)}_{\text{lee}} &= (1-\rho)A^{(3)}_{\text{burden}} + \rho A^{(3)}_{\text{skat}} \\
&= \Delta\Big\{(1-\rho)(1-\tau_b)J_M + \rho(1-\tau_s)I_M, (1-\rho)\tau_b\Delta\Big(J_M, -J_M\Big) + \rho\tau_s\Delta\Big(I_M, -I_M\Big)\Big\} \\
&= \Delta\Big\{\beta_1 J_M + \beta_2 I_M, \beta_3\Delta\Big(J_M, -J_M\Big) + \beta_4\Big(I_M, -I_M\Big)\Big\}
\end{aligned}
$$

Another way to generalize is like this

$$
\begin{aligned}
A^{(3)}_{\text{another}} &= \begin{pmatrix} (1-\tau)A^{(1)}_{\text{lee}}(\rho^{(1)}) & 0 \\ 0 & \tau A^{(2)}_{\text{lee}}(\rho^{(2)}) \end{pmatrix} = \Delta\Big\{(1-\tau)A^{(1)}_{\text{lee}}(\rho^{(1)}), \tau A^{(2)}_{\text{lee}}(\rho^{(2)})\Big\} \\
&= \Delta\Big\{(1-\tau)(1-\rho^{(1)})J_M + (1-\tau)\rho^{(1)}I_M, \tau(1-\rho^{(2)})\Delta\Big(J_M, -J_M\Big) + \tau\rho^{(2)}\Delta\Big(I_M, -I_M\Big)\Big\} \\
&= \Delta\Big\{\beta_1 J_M + \beta_2 I_M, \beta_3\Delta\Big(J_M, -J_M\Big) + \beta_4\Big(I_M, -I_M\Big)\Big\}
\end{aligned}
$$

Record the following in case I need it

$$
\begin{aligned}
A^{(3)}_{\text{lee}} &= \Delta\Big\{A^{(3)}_1, A^{(3)}_2, A^{(3)}_3\Big\} \\
A^{(3)}_1 &= (1-\rho)(1-\tau_b)J_M + \rho(1-\tau_s)I_M \\
A^{(3)}_2 &= (1-\rho)\tau_b J_M + \rho\tau_s I_M \\
A^{(3)}_3 &= -A^{(3)}_2
\end{aligned}
$$

$$
\begin{aligned}
A^{(3)}_{\text{another}} &= \Delta\Big\{A^{(4)}_1, A^{(4)}_2, A^{(4)}_3\Big\} \\
A^{(4)}_1 &= (1-\tau)(1-\rho^{(1)})J_M + (1-\tau)\rho^{(1)} I_M \\
A^{(4)}_2 &= \tau(1-\rho^{(2)})J_M + \tau\rho^{(2)} I_M \\
A^{(4)}_3 &= -A^{(4)}_2
\end{aligned}
$$

8 To get the distribution of $Q = Z^T AZ$.

For lines 7, 8, and 9 of Alice's Table 1, I note that Z^3 has covariance that is singular, but I can write

$$
\begin{aligned}
Z^{(3)} &= \begin{pmatrix} Z_1 - Z_2 \\ Z_1 \\ Z_2 \end{pmatrix} = BZ \\
B &= \begin{pmatrix} I_M & -I_M \\ I_M & 0 \\ 0 & I_M \end{pmatrix} \\
Q &= Z^{(3)T} A^{(3)} Z^{(3)} = Z^T B^T A^{(3)} BZ = Z^T AZ \\
A &= B^T A^{(3)} B = \begin{pmatrix} A_1 + A_2 & -A_1 \\ -A_1 & A_1 - A_2 \end{pmatrix} \\
A^{(3)} &= \Delta\Big\{A_1, A_2, -A_2\Big\} \\
A_1 &= \beta_1 J_M + \beta_2 I_M \\
A_2 &= \beta_3 J_M + \beta_4 I_M
\end{aligned}
$$