Suppose we observe p values $\pi_1, ..., \pi_n$ coming from Z scores $Z_1, ..., Z_n$ such that $\pi_i = 2\Phi(-|Z_i|)$ and $Z = [Z_1, ..., Z_n]^T \sim MVN(0, \Sigma)$ under the null where $\Phi$ is the CDF of N(0,1). For notation we use $I\{A\} = 1$ if $A$ occurs 0 otherwise (i.e. indicator). Let $S(t) = \sum_k I\{|Z_k| \geq t\}$.

In the grant we have a band of $h_i$ and we reject the global null if $\pi_{(i)} \leq h_i$ for any $i$ . The $h_i$ are chosen such that $\alpha = P[X \leq h_i]$ where $X \sim Beta(i, n+1-i)$. I suggesting observing that

$$\begin{aligned}
P_0\left[\pi_{(i)} \leq h_i\right] &= P_0\left[|Z|_{(d+1-i)} \geq -\Phi^{-1}(h_i/2)\right] \\
&= P_0\left[\left(\sum_k I\left\{|Z_k| \geq -\Phi^{-1}(h_i/2)\right\}\right) \geq i\right] \\
&= P_0\left[S\left(-\Phi^{-1}(h_i/2)\right) \geq i\right]
\end{aligned}$$

When $\Sigma \neq I$, $S(t)$ has the null distribution of an over or under-dispersed binomial. [1] and [2] approximate the distribution of $S(t)$ with the Extended Beta Binomial distribution $EBB(\lambda, \gamma)$ where they choose $\lambda$ and $\gamma$ to match the mean and variance of $S(t)$. Let $f(x; t)$ be its PMF.

We choose a new adjusted $\hat{h}_i$ such that

$$\begin{aligned}
\alpha &= P_0\left[S\left(-\Phi^{-1}\left(\hat{h}_i/2\right)\right) \geq i\right] \\
&\approx 1 - \sum_{k=1}^{i-1} f\left(k\ ;\ -\Phi^{-1}\left(\hat{h}_i/2\right)\right)
\end{aligned}$$

$P(S(t) \geq x)$ should be decreasing in $t$ for any $x$. And $-\Phi^{-1}(x/2)$ should be decreasing in $x$. Thus in practice given an $\alpha$ we can reject the global null if for any $i$

$$\begin{aligned}
\alpha &\geq 1 - \sum_{k=1}^{i-1} f\left(k\ ;\ -\Phi^{-1}(\pi_{(i)}/2)\right) \\
&= 1 - \sum_{k=1}^{i-1} f\left(k\ ;\ |Z|_{(d+1-i)}\right)
\end{aligned}$$

References


1. Sun, Lin 2017. Set-Based Tests for Genetic Association Using the Generalized Berk-Jones Statistic

2. Barnett et al 2017. The Generalized Higher Criticism for Testing SNP-Set Effects in Genetic Association Studies