Bioinformation

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3.1 The linear step-up procedure

Let $P_{1:m} \leq P_{2:m} \leq \cdots \leq P_{m:m}$ be the order statistics of the P values, and let $\pi_0 = m_0/m$. Assuming that the P values corresponding to the true null hypotheses are independent, Benjamini and Hochberg (1995) prove that for any specified $q^* \in (0, 1)$, rejecting all the null hypotheses corresponding to $P_{1:m}, \ldots, P_{k^*:m}$ with $k^* = \max\{k : P_{k:m} / (k/m) \leq q^*\}$ controls the FDR at the level $\pi_0 q^*$, i.e., $FDR_{\Theta}(\hat{\Theta}(P_{k^*:m})) \leq \pi_0 q^* \leq q^*$ in the notation given in Section 2. [6] Note this procedure is equivalent to applying the data-driven threshold $\alpha = P_{k^*:m}$ to all P values in (3), i.e., $HT(P_{k^*:m})$.

3.2 Adaptive FDR control

Recognizing the potential of constructing less conservative FDR control by the above procedure, Benjamini and Hochberg (2000) propose an estimator of m_0 , \hat{m}_0 , (hence an estimator of π_0 , $\hat{\pi}_0 = \hat{m}_0 / m$), and replace k / m by k / \hat{m}_0 in determining k^* . [10] They call this procedure adaptive FDR control. The estimator $\hat{\pi}_0 = \hat{m}_0 / m$ will be discussed in Section 4. A recent development of adaptive FDR control can be found in Benjamini *et al.* (2006). [18]

3.3 Another adaptive FDR control

Storey (2002) [7] considers the FDR estimator **FDR** (α) := $\frac{\hat{\pi}_0(\lambda)\alpha}{\max\{R(\alpha),l\}/m}$ for a P value cut-off α , where $\hat{\pi}_0(\lambda)$ is an

estimator of π_0 (See Section 4.1) and $R(\alpha)$ is the number of P values less than or equal to α . FDR control can be performed by "inverting" this estimator: for a given FDR level q^* , find the largest possible $\hat{\alpha}$ such that **FDR** ($\hat{\alpha}$) $\leq q^*$, and reject all the null hypotheses with $P \leq \hat{\alpha}$. This operation can be represented in a "q-value style". Let $q_i := \inf_{j \geq i} \{ \text{FDR}(P_{j:m}) \}$, i = 1, ...,m; then reject all the null hypotheses for which $q_i \leq q^*$. Storey *et al.* (2004) [8] show that using a slightly modified version of **FDR** (\cdot) this procedure guarantees to control the FDR under q^* if the P values corresponding to the true null hypotheses are independent.

3.4 Dependent Tests

Storey *et al.* (2004) [8] show that if the P values are weakly dependent in the sense of being dependent in general but satisfying certain ergodicity conditions as $m \to \infty$, then the procedure is conservative in the limit in the sense that

 $\lim_{m\to\infty} \hat{\alpha} < \lim_{m\to\infty} \alpha^* \text{ where } \alpha^* \text{ is the largest possible } \alpha \text{ such that the actual } FDR(\alpha) \le q^*.$

Yekutieli and Benjamini (1999) **[19]** develop a resampling-based approach to FDR control for correlated tests. Qiu *et al.* (2005) **[20]** also describe the use of resampling to assess the stability of gene selection in microarray analysis. Benjamini and Yekutieli (2001) **[13]** show that the Benjamini and Hochberg (1995) **[6]** procedure controls the FDR if the test statistics satisfy the "positive regression dependence" condition. They also introduce a very conservative, but universal procedure that guarantees the FDR control for arbitrary P values (dependent or independent, discrete or continuous): control the FDR at the level $q^{**} = \left(\sum_{i=1}^{m} (1/i)\right)^{-1} q^*$ with the Benjamini and Hochberg (1995) **[6]** procedure guarantees to control the FDR at level q^* regardless dependence and/or discreteness of the P values.

In a series of papers, van der Laan and colleagues **[21, 22]** and Dutdoit and colleagues **[23]** developed procedures to control the gFWER for arbitrarily dependent tests.