A POWERFUL STRATEGY FOR DETECTING DIFFERENTIALLY EXPRESSED GENES

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The search for differentially expressed genes aims to detect biologically relevant signals amidst a multitude of unpromising material. Standard test procedures focus on the null of no differential expression to avoid a flood of type I errors. These methods rank genes in the same order as classical p-values even though statistical significance does not imply biological relevance and important findings may be missed. Driven by a concern to detect important alternatives, we complement the traditional p-value (p_0) with an alternative p-value (p_1, a measure of impotence) which summarizes evidence against a target alternative. We build a formal decision criterion in terms of p_0 and p_1 by balancing gene-specific type I and type II errors to optimize an expected gain. This leads to an intuitive measure of relative evidence based on which genes are ranked and selected. We show the impact of this strategy on the detection of differentially expressed genes in hereditary breast cancer. Different genes now yield powerful signals and line up in a substantially different order. We derive experimentwise error rates for this procedure from the perspectives of the null and the alternative. We find that the standard selection procedure accumulates more null genes before reaching a similar number of truly promising genes.