Gene expression

Exchangeable random variables

Phillip Good

Contact: drgood@statcourse.com

In his seminal text, *Testing Statistical Hypotheses,* first set down in the late 1950s, the late and sorely missed Eric Lehmann wrote, '… one may prefer to try to obtain an exact level-α unbiased test (valid for all [probability distributions] f) by replacing the original normal model with the nonparametric model for which the joint density of the variables is

$$f(x_1)\cdots f(x_m)f(y_1-\Delta)\cdots f(y_n-\Delta) \qquad (1)$$

where f is a member of the family of probability densities that are continuous almost everywhere.'

A permutation test $\varphi(x_1,\ldots,x_m,y_1,\ldots y_n)$ for testing $\Delta=0$ against $\Delta>0$ is obtained by choosing a set of rearrangements S of the $n+m$ observations, such that

$$\frac{(n+m)!}{m!\,(n)!}\sum_{z'\in S}\varphi(z')=\alpha \qquad a.e.$$

If Equation (1) be satisfied, then all sets S are equally likely under the null hypothesis. To obtain a permutation test that is both unbiased and most powerful, one need only select the set S so that its probability under the alternative $\Delta>0$ is a maximum. This is accomplished in most cases by rejecting the hypothesis for all values of the test statistic that lie in the upper tail of the permutation distribution.

As research during the intervening half century has amply demonstrated, permutation tests should be used to do *all* of the following:

(1) Make a multivariate comparison of population means.

(2) Analyze the one-way layout.

(3) Compare variances.

(4) Analyze cross-over designs.

(5) Analyze contingency tables.

(See, for example, *Resampling Methods*, Good, Birkhauser, 3rd edn, 2005).

But permutation tests are applicable *only if* the observations are exchangeable, that is, if under the null hypothesis, the joint distribution in Equation (1) remains invariant under all rearrangements of the subscripts. [See, for example, Good, P. (2002) Extensions of the concept of exchangeability and their applications. *J. Modern Appl. Statist. Methods*, **1**, 243–247.]

Thus the belated rediscovery by Yifan Huang, Haiyan Xu, Violeta Calian, and Jason C. Hsu writing in *Bioinformatics* 2006, **22**, 2244–2248 that 'for such tests, if the two distributions are not identical (as for example when they have unequal variances, correlations or skewness), then a permutation test for equality of means based on difference of sample means can have an inflated Type I error rate even when the means are equal' comes as a surprise only to those authors and to their article's reviewers.

Conflict of Interest: none declared.