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Efron's conjecture on vulnerability to bias in a method for balancing sequential trials

BY J. MICHAEL STEELE
Department of Statistics, Stanford University

SUMMARY

Efron (1971) proposed a method for sequential assignment to treatments or control which is in many ways superior to traditional procedures. To analyse the method's susceptibility to accidental bias a criterion concerning the maximum eigenvalue of a fundamental covariance matrix was introduced. On the basis of numerical evidence, Efron conjectured an explicit formula for this eigenvalue. This note gives a proof of that conjecture.

Some key words: Balanced experiment; Biased coin design; Covariance matrix; Maximum eigenvalue; Sequential trial.

Suppose that subjects are to be assigned sequentially to either treatment or control. If at the time of arrival of a new subject there have been D more subjects assigned to treatment than control, then Efron (1971) suggests the following:

if $D > 0$, assign to treatment with probability q and to control with probability p, where $p+q=1$, $p>\frac{1}{2}$;
if $D = 0$, assign to treatment with probability $\frac{1}{2}$ and to control with probability $\frac{1}{2}$;
if $D < 0$, assign to treatment with probability p and to control with probability q.

This biased-coin design has several benefits over some traditional procedures such as Student's sandwich plan, and has attracted considerable practical and theoretical attention (Matts & McHugh, 1978; Pocock, 1979; Pocock & Simon, 1975; Wei, 1977, 1978).

Now suppose that N subjects have been assigned to treatment and let T_k be $+1$ or -1 accordingly as the kth subject is assigned to treatment or control. The vector $\overline{T} = (T_1, \ldots, T_n)$ has mean $E(\overline{T}) = 0$, and its covariance matrix will be denoted by Ω.

Efron argued persuasively that the vulnerability of a balancing design to an accidental bias is sensibly measured by the maximum eigenvalue of the covariance matrix Ω, and he studied this by considering the maximum eigenvalue λ_N of the asymptotic covariance of the vector $(T_{h+1}, \ldots, T_{h+N})$ as $h \to \infty$. As $N \to \infty$, these λ_N increase to a finite limit λ, and on the basis of considerable numerical evidence, Efron conjectured that $\lambda = 1+(p-q)^2$.

To prove this consider the asymptotic covariances and the associated spectral density:

$$\rho_k = \lim_{h\to\infty} E(T_h T_{h+k}), \quad f(\omega) = \sum_{k=-\infty}^{\infty} \rho_k e^{-i\omega k}.$$

Efron observed that $\lambda = \max f(\omega)$; this maximum can now be calculated using a general lemma (Katznelson, 1968, p. 22).

LEMMA. *Suppose that an even sequence* $\{a_n\}$ *of positive real numbers tend to zero and satisfy* $a_{n+1} - 2a_n + a_{n-1} \geqslant 0$ *for all* $n > 0$, *then the series*

$$g(x) = \sum_{n=-\infty}^{\infty} a_n e^{-inx}$$

represents a nonnegative function.

Setting $g(x) = f(\pi) - f(x)$ one expands g in a Fourier series with coefficients $\{a_n\}$. Efron's Theorem 4 shows $f(\pi) = 1-(p-q)^2$, so that by the lemma it remains only to check the positivity and convexity of the $\{a_n\}$.

Setting $r = p/q$, Efron showed that

$$\rho_0 = 1, \quad \rho_1 = -\tfrac{1}{2}(r-1)^2/\{r(r+1)\}, \quad \rho_2 - \rho_1 = \tfrac{1}{2}(r-1)^2/\{r(r+1)^2\},$$

and that for $k \geqslant 1$, $\rho_{k+1} - \rho_k$ is positive and decreasing. This implies that $a_{n+1} - 2a_n + a_{n-1} \geqslant 0$ for $n > 1$. To check the remaining case $n = 0$ one computes

$$\begin{aligned} a_2 - 2a_1 + a_0 &= -\tfrac{1}{2}(r-1)^3/\{r(r+1)^2\} - \tfrac{1}{2}(r-1)^2/\{r(r+1)\} + (r-1)^2/(r+1)^2 \\ &= (r-1)^2/\{r(r+1)^2\} \geqslant 0. \end{aligned}$$

The lemma then shows $g(x) \geqslant 0$ and the conjecture is proved.

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