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

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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 $\bar{T} = (T_1, \ldots, T_n)$ has mean $E(\bar{T}) = 0$, 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* $a_{n+1} - 2a_n + a_{n-1} \geq 0$ *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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