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DETECTION OF THE FIXATION COEFFICIENT *F* FROM MNS BLOOD GROUP DATA

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SUMMARY

Since the MNS blood group system does not exhaust the total degrees of freedom under the Wright's equilibrium law, it was felt that the peculiar problems facing the detection of *F* (the fixation coefficient of Wright's model) from ABO blood group data may not be totally relevant to the MNS system. To verify this, a short discussion on the detection of *F* from MNS blood group data is given here.

INTRODUCTION

The ABO blood group system exhausts all the degrees of freedom under the Wright's equilibrium law, since the number of independent parameters (two gene frequencies and one fixation coefficient, *F*) is equal to the total degrees of freedom (3). The recent controversial problem of estimating *F* when it is very small (Yasuda 1966 and 1970, Schull and Ito 1969 and 1970, Yee and Morton 1970) was tackled by Ward and Sing (1970) and Chakraborty and Rao (1972) as a problem of detecting *F* through a consideration of the power function of noncentral chi-square distribution. The latter studies suggested that to detect very small values of *F* from ABO data, one needs very large sample sizes. For example, to detect $F = 0.05$ with reasonable accuracy one needs a sample size of 5,376 (Chakraborty and Rao 1972). It is clear that in practice almost none goes for such large sample sizes. Hence, unless one knows on *a priori* grounds that *F* is very high, it is not possible to estimate it with reasonable accuracy from samples of sizes we have up to date.

Are such large sample sizes necessary for MNS blood group data also? The answer appears to be mostly yes, for the peculiar problems in the detection of *F* arise only when it is very small. However, since the MNS system under Wright's model does not exhaust the total degrees of freedom, it is felt necessary to investigate this problem further. It should, nevertheless, be noted that the resulting degrees of freedom do not appear to have any direct effect on the required sample sizes.

* Most of the work was carried out when the author was a research scholar at the Indian Statistical Institute, Calcutta.

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DETECTION OF F

Let

m = M-gene frequency
n = N-gene frequency $= 1 - m$
m_s = Ms-chromosome frequency
m_S = MS-chromosome frequency $= m - m_s$
n_s = Ns-chromosome frequency
n_S = NS-chromosome frequency $= n - n_s$

out of which only three are independent parameters (say, m, m_s, and n_s).

Consider a random sample of size G tested for MNS system with three antisera (anti-M, anti-N and anti-S). The six phenotypes and their expected frequencies under Wright's model are as given in Table I below.

TABLE I
PHENOTYPIC FREQUENCIES FOR MNS SYSTEM UNDER WRIGHT'S MODEL

Phenotype	Frequency
M	$E_1^* = m_s^2 (1-F) + Fm_s$
MS	$E_2^* = m_S^2 (1-F) + Fm_S + 2(1-F)m_s m_S$
MN	$E_3^* = 2 (1-F)m_s n_s$
MNS	$E_4^* = 2 (1-F) (mn-m_s n_s)$
N	$E_5^* = n_s^2 (1-F) + Fn_s$
NS	$E_6^* = n_S^2 (1-F) + Fn_S + 2 (1-F) n_s n_S$

Let us denote the phenotypic frequencies under random mating by $E_1, E_2, \ldots, E_6$. We get E_i from E_i^* of Table I by putting $F = 0$. Thus, from Table I one can write

$$E_i^* = E_i + \frac{c_i}{\sqrt{G}} \quad : i = 1, 2, \ldots, 6,$$

where c_i's are known functions of the parameters and the sample size G. For example, $c_1 = \sqrt{G}\, F\, m_s(1 - m_s)$. To detect any deviation from random mating, one employs a noncentral χ^2 test whose noncentrality parameter for this problem is given by (see Chapman 1968)

$$\lambda(\alpha,\beta) = \sum_{i=1}^{6} c_i^2/E_i$$
$$= GF^2 \left[(1 - m_s)^2 + 2mn + (1 - n_s)^2 + \frac{m_S(n - m_s)^2}{m + m_s} + \frac{n_S(m - n_s)^2}{n + n_s} \right],$$

where α and β are the level and the power of the noncentral χ^2 test, respectively.

The degrees of freedom for the limiting noncentral χ^2 distribution are equal to $5 - 3$ (total degrees of freedom less the number of independent parameters estimated) $= 2$. Owen (1962) tabulated the probability points for such a distribution with 2 *df*. Thus, for fixed values of α and β, one can directly read the value of $\lambda(\alpha, \beta)$ from Owen's tables corresponding to 2 *df*. On the other hand, once we know the estimates of the parameters (gene and chromosome frequencies), the right side of the above expression for $\lambda(\alpha, \beta)$ reduces to a function of G and F only. Thus, for given values of F one can obtain G, the required (minimum) sample sizes to detect (or to estimate) such given magnitudes of F. For example, let us take $\alpha = 0.05$ and $\beta = 0.5$. Thus, from Owen's tables we get $\lambda(\alpha, \beta) = 4.96$. Further, let the estimates of the parameters be

$$\hat{m} = 0.55, \quad \hat{m}_s = 0.45, \quad \text{and} \quad \hat{n}_s = 0.40.$$

Then the equation for $\lambda(\alpha, \beta)$ reduces to

$$4.96 = GF^2(1.158824) \text{ or, } G = (4.280201)/F^2,$$

from which one can compute G for given values of F. A few values are given below.

F	0.2	0.1	0.05	0.04	0.03	0.02	0.01
G	107	428	1,712	2,675	4,756	10,700	42,802

It is clear that in human populations several forces (like subdivision, etc.) apart from inbreeding contribute to F. Thus, the actual values of F may be well over 0.05. This means that we do not need very high sample sizes to detect the magnitudes of F that occur in human populations through MNS blood group data. On the other hand, as reported by Chakraborty and Rao (1972), one needs very large sample sizes to detect such magnitudes of F through ABO blood group data. At least from the example discussed above and from the example discussed by Chakraborty and Rao (1972), it appears that to detect a given value of F the required sample size for ABO data is roughly three times that for MNS data. It appears that similar relation holds good in general as well, in which case it is wise to estimate F from MNS data rather than ABO data.

ILLUSTRATION

The following are the phenotypic frequencies in a sample of 805 individuals as reported by Lester (1961):

M : 145	MS: 80	MN: 240
MNS: 144	N : 135	NS : 61

Under Wright's model (Table I) maximum likelihood estimates of the parameters are obtained by the well-known iterative scoring method (Rao 1965), which are reported in Table II. In particular,

$$\hat{F} = 0.0528 \quad \text{and} \quad SE = 0.0336.$$

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The standard error of $\hat{F}$ seems to be rather high, which may be partly justified as follows. Using the estimates of gene and chromosome frequencies of Table II, the equation for $\lambda(\alpha, \beta)$ becomes, for $\alpha = 0.05$ and $\beta = 0.5$,

$$G = (4.0533)/F^2$$

or, to detect a value of $F = 0.0528$, we need a sample of size $G = 1{,}454$. Since the sample size in our example is smaller than this (805) we might have got a higher standard error for the estimate of F.

TABLE II

MAXIMUM LIKELIHOOD ESTIMATES OF CHROMOSOME FREQUENCIES AND FIXATION COEFFICIENT FROM MNS BLOOD GROUP DATA

Parameter	Estimate	*SE*
m_S	0.1114	0.0022
m_s	0.4066	0.0096
n_S	0.0902	0.0037
n_s	0.3918	0.0091
F	0.0528	0.0336

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RIASSUNTO

Poiché il sistema dei gruppi sanguigni MNS non esaurisce tutti i gradi di libertà nella legge di equilibrio di Wright, si è pensato che i particolari problemi che s'incontrano nella determinazione di F (il coefficiente di fissazione del modello di Wright) a partire dai gruppi del sistema ABO non fossero di totale rilievo nel caso del sistema MNS. Per verificare tale ipotesi viene effettuata una breve discussione sulla determinazione di F a partire dai gruppi del sistema MNS.

RÉSUMÉ

Étant donné que le système de groupes sanguins MNS n'épuise pas tous les degrés de liberté dans les conditions de la loi d'équilibre de Wright, l'on a pensé que les problèmes spéciaux qui se posent pour la détermination de F (le coefficient de fixation du modèle de Wright) partant des données du système ABO ne se posent pas totalement dans le cas du système MNS. Afin de vérifier cette hypothèse une brève discussion est effectuée sur la détermination de F partant des données du système MNS.

ZUSAMMENFASSUNG

Da das MNS-Blutgruppensystem nicht alle Freiheitsgrade im Gleichgewichtsgesetz nach Wright erfüllt, dachte man daran, dass die besonderen Probleme bei der Bestimmung von F (Fixierungskoeffizient des Wright'schen Modells) von den Blutgruppen des Systems ABO ab, beim MNS-System nicht so wesentlich seien. Um diese Ansicht zu prüfen, folgt eine kurze Erörterung über die Bestimmung von F von den Blutgruppen des MNS-Systems ab.

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