RT-MAE-8711

ON THE HARDY-WEINBERG EQUILIBRIUM IN GENERALIZED ABO SYSTEMS

Julio M. Singer, Clovis A. Peres
and
Carlos E. Harle

Palavras Chaves: ABO blood groups, Hardy-weinberg models,
(Key words) Wald tests.

Classificação AMS: 62P10
(AMS Classification) 62F03

- Outubro de 1987 -

ON THE HARDY-WEINBERG EQUILIBRIUM IN GENERALIZED ABO SYSTEMS

JULIO M.SINGER, CLOVIS A.PERES AND CARLOS E.HARLE

INSTITUTO DE MATEMÁTICA E ESTATÍSTICA
UNIVERSIDADE DE SÃO PAULO
CAIXA POSTAL 20570 - AGÊNCIA IGUATEMI
01498 - SÃO PAULO, SP - BRAZIL

SUMMARY

We propose a constraint formulation for the Hardy-Weinberg model in generalized ABO-like systems which lends itself to the construction of Wald tests for the corresponding equilibrium hypothesis. We illustrate the testing procedure with practical examples and provide indication for the use of a categorical data computer program (GENCAT) to perform the required calculations. We also demonstrate that as in many other settings, the Wald statistic may have an aberrant behaviour for fixed sample sizes, although it possesses optimal asymptotic properties.

Key words: ABO blood groups, Hardy-Weinberg models, Wald tests.

1. INTRODUCTION

Consider a genetic system with m codominant alleles, $A_1,\ldots,A_m$ and one recessive allele, 0, in a single locus and let q_1, $\ldots,q_m$ and q_o, $\sum_{j=0}^{m} q_j = 1$ denote the corresponding probabilities of occurrence in a given population. Also let the probabilities of ocurrence of the $f = (m^2+m+2)/2$ possible phenotypes be given by:

Phenotype	Genotype	Probability of ocurrence
0	00	p_o
A_1	A_1A_1, A_10	p_1
⋮	⋮	⋮
A_m	A_mA_m, A_m0	p_m
A_1A_2	A_1A_2	p_{12}
⋮	⋮	⋮
$A_{m-1}A_m$	$A_{m-1}A_m$	$p_{m-1,m}$

where $\sum_{i=0}^{m} p_i + \sum_{\substack{i,j=1 \\ j>i}}^{m} p_{ij} = 1$. Genetic systems of this type, of which the well known ABO blood group classification system constitutes a special case (m=2), are important in many practical situations and have been studied by a host of workers, among which we mention Cavalli-Sforza and Bodmer (1971), Elandt-Johnson (1971) and Nam and Gart (1976).

The system is said to follow the Hardy-Weinberg (HW) model (equilibrium) if there exist q_i, $i=0,\ldots,m$ $\sum_{i=0}^{m} q_i = 1$ such that the following relations hold:

$$\text{a) } p_o = q_o^2$$
$$\text{b) } p_i = q_i^2 + 2q_iq_o\,, \quad i = 1,\ldots,m \qquad (1)$$
$$\text{c) } p_{ij} = 2q_iq_j\,, \quad i = 1,\ldots,m,\ j > i$$

A similar model may be considered for situations where there are no recessive alleles; an important special case is the MN blood classification system (m=2), discussed in Elandt-Johnson (1971, ch 14) among other authors. In such cases the relations (1) reduce to:

$$\text{a) } p_i = q_i^2, \quad i = 1,\ldots,m$$
$$\text{b) } p_{ij} = 2q_iq_j, \quad i,j = 1,\ldots,m, \quad j > i. \qquad (2)$$

A problem of general concern to geneticists is to test whether a given population satisfies the HW equilibrium relations [(1) or (2)] based on the evidence provided by a sample of n observational units for which the phenotype frequencies are n_i, $i = 0,\ldots,m$ and n_{ij}, $i,j = 1,\ldots,m$, $j > i$, respectively. $\sum_{i=0}^{m} n_i + \sum_{\substack{i,j=1 \\ j>i}}^{m} n_{ij} = n$. In this paper we address this problem via an alternative formulation of the HW model, based on the restrictions that (1) or (2) impose on the space of the phenotype population proportions $p_o, p_1, \ldots, p_{m-1,m}$. In Section 2 we show the equivalence between the two formulations; in Section 3 we indicate how the constraint formulation may be employed to produce Wald tests for the HW equilibrium hypotheses and consider related computational aspects; finally in Section 4 we discuss statistical properties associated with the proposed tests.

2. A CONSTRAINT FORMULATION FOR THE HARDY-WEINBERG MODEL

Here we show that the ABO-like genetic system described in the previous section is in HW equilibrium if and only if the phenotype parameters, p_i, $i = 0,\ldots,m$, p_{ij}, $i,j = 1,\ldots,m$, $j>i$, $\sum_{i=0}^{m} p_i + \sum_{\substack{i,j=1 \\ j>i}}^{m} p_{ij} = 1$, satisfy the $m(m-1)/2$ relations:

$$p_{ij} = 2(\sqrt{p_i+p_o} - \sqrt{p_o})(\sqrt{p_j+p_o} - \sqrt{p_o}),\ i,j=1,..,m,\ j>i \qquad (3)$$

First suppose that there exist q_i, $i = 0,\ldots,m$, $\sum_{i=0}^{m} q_i = 1$ such that (1) holds. This clearly implies that $\sum_{i=0}^{m} p_i + \sum_{j>i} p_i = 1$. Then, using (1a) and (1b) we may write:

$$q_o = \sqrt{p_o},\quad q_i = \sqrt{p_i+p_o} - \sqrt{p_o},\quad i = 1,\ldots,m \qquad (4)$$

and substituting (4) in (1c) it follows that (3) holds.

Now suppose that the phenotype parameters satisfy (3). Letting q_o, q_i, $i = 1,\ldots,m$ be defined by (4) it follows that (1a) - (1c) hold. It remains to show that $\sum_{i=0}^{m} q_i = 1$. In this direction, let:

$$x = \sum_{i=0}^{m} q_i = \sum_{i=1}^{m} \sqrt{p_i+p_o} - (m-1)\sqrt{p_o} \qquad (5)$$

which implies:

$$(x + (m-1)\sqrt{p_o})^2 = mp_o + \sum_{i=1}^{m} p_i + 2 \sum_{\substack{i=1 \\ j>i}}^{m} \sqrt{(p_i+p_o)(p_j+p_o)} \qquad (6)$$

Now, adding the $m(m-1)/2$ relations (3) memberwise we get:

$$\sum_{\substack{i=1\\ j>i}}^{m} p_{ij} = 2 \sum_{\substack{i=1\\ j>i}}^{m} \sqrt{(p_i+p_o)(p_j+p_o)} - 2(m-1)\sqrt{p_o} \sum_{i=1}^{m} \sqrt{p_i+p_o} + m(m-1)p_o \qquad (7)$$

From (7) and the fact that $\sum_{i=0}^{m} p_i + \sum_{\substack{i,j=1\\ j>i}}^{m} p_{ij} = 1$, it follows that:

$$\sum_{i=1}^{m} p_i + 2 \sum_{\substack{i,j=1\\ j>i}}^{m} \sqrt{(p_i+p_o)(p_j+p_o)} = 1+2(m-1)\sqrt{p_o}\,\{\sum_{i=1}^{m} \sqrt{p_i+p_o} - (m-1)\sqrt{p_o}\} + \\ + (m^2-3m+1)p_o \qquad (8)$$

Substituting (5) into (8) and using (6) we obtain the second degree equation:

$$\{x + (m-1)\sqrt{p_o}\,^2\} = 1 + 2(m-1)\sqrt{p_o}\,x + (m^2-2m+1)p_o$$

which has $x = 1$ as the only positive root and the result follows.

Note that when there are no recessive alleles, the relations (3) reduce to:

$$p_{ij} = 2\sqrt{p_i p_j}, \quad i,j = 1,\ldots,m, \quad j > i \qquad (9)$$

which have been considered in the literature (see Pereira and Rogatko (1984), for example). Also note that the set of parameters $\theta_{ij} = p_{ij}/\{2(\sqrt{p_i+p_o} - \sqrt{p_o})(\sqrt{p_j+p_o} - \sqrt{p_o})\}$, $i,j = 1,\ldots,m$, $j > i$ (or alternatively a set of monotone functions of the θ_{ij}, like $\log \theta_{ij}$) may be employed as a measure of departure from the HW equilibrium; in view of (3), $\theta_{ij} \neq 1$ (or $\log \theta_{ij} \neq 0$) for some (i,j) corresponds to a lack of equilibrium. In the next section we indicate how such ideas may be employed to construct a test of the HW hypothesis.

3. WALD TESTS FOR THE HARDY-WEINBERG EQUILIBRIUM

Let $\underset{\sim}{p} = (p_o,\ldots,p_m,p_{12},\ldots,p_{m-1,m})'$ denote the $(m^2+m+2)/2$ vector of phenotype population proportions and note that the HW equilibrium corresponds to:

$$\underset{\sim}{F}(\underset{\sim}{p}) = \underset{\sim}{0} \qquad (10)$$

where $\underset{\sim}{F}(\cdot)$ is a vector-valued function with elements $F_{ij} = \theta_{ij}-1$ (or $F_{ij} = \log\theta_{ij}$), $i,j = 1,\ldots,m, j > i$. Assume that the vector of observed phenotype frequencies $\underset{\sim}{n} = (n_o,\ldots,n_m,n_{12},\ldots,n_{m-1,m})'$ has a multinomial distribution with parameters n and $\underset{\sim}{p}$; then, if n is sufficiently large, it follows by Central Limit theory that $\hat{\underset{\sim}{p}} = \underset{\sim}{n}/n$ has an asymptotic multinormal distribution with mean vector $\underset{\sim}{p}$ and covariance matrix $\underset{\sim}{V}(\underset{\sim}{p}) = n^{-1}(\underset{\sim}{D}_{\underset{\sim}{p}}-\underset{\sim}{p}\underset{\sim}{p}')$ where $\underset{\sim}{D}_{\underset{\sim}{p}}$ denotes a diagonal matrix with the elements of $\underset{\sim}{p}$ along the main diagonal. As indicated in Bhapkar (1966), a Wald statistic to test (10) is given by:

$$Q = \underset{\sim}{F}(\hat{\underset{\sim}{p}})'(\underset{\sim}{V}_F(\hat{\underset{\sim}{p}}))^{-1}\,\underset{\sim}{F}(\hat{\underset{\sim}{p}}) \qquad (11)$$

where $\underset{\sim}{V}_F(\hat{\underset{\sim}{p}}) = \underset{\sim}{H}(\hat{\underset{\sim}{p}})\underset{\sim}{V}(\hat{\underset{\sim}{p}})\underset{\sim}{H}'(\hat{\underset{\sim}{p}})$ with $\underset{\sim}{V}(\hat{\underset{\sim}{p}}) = n^{-1}(\underset{\sim}{D}_{\hat{\underset{\sim}{p}}}-\hat{\underset{\sim}{p}}\hat{\underset{\sim}{p}})$ and $\underset{\sim}{H}(\hat{\underset{\sim}{p}}) = \left[\dfrac{\partial\underset{\sim}{F}(\underset{\sim}{Z})}{\partial\underset{\sim}{Z}}\cdot\Big|_{\underset{\sim}{Z}=\hat{\underset{\sim}{p}}}\right]$. Under the hypothesis (10), the statistic Q follows an asymptotic chi-squared distribution with $m(m-1)/2$ degrees of freedom. Bhapkar (1966) demonstrated that Q is algebraically identical to Neyman's minimum chi-squared statistic and thus shares the same asymptotic optimality properties of Pearson's chi-squared or Wilks' likelihood ratio criteria.

Letting $F_{ij} = \theta_{ij}-1$, the elements of the matrix of partial derivatives $\underset{\sim}{H}(\hat{p})$ are given by:

$$\frac{\partial F_{ij}}{\partial \hat{p}_o} = \frac{\hat{\theta}_{ij}}{2}\{[\hat{p}_o(\hat{p}_i+\hat{p}_o)]^{-1/2} + [\hat{p}_o(\hat{p}_j+\hat{p}_o)]^{-1/2}\}$$

$$\frac{\partial F_{ij}}{\partial \hat{p}_k} = \begin{cases} -\frac{\hat{\theta}_{ij}}{2}(\sqrt{\hat{p}_i+\hat{p}_o}\sqrt{\hat{p}_j+\hat{p}_o} - \sqrt{\hat{p}_o})^{-1}, & k=i,j \\ 0, & k\neq i,j \end{cases} \qquad (12)$$

$$\frac{\partial F_{ij}}{\partial \hat{p}_{k\ell}} = \begin{cases} \frac{\hat{\theta}_{ij}}{\hat{p}_{ij}}, & (k\ell)=(ij) \\ 0, & (k\ell)\neq(i,j) \end{cases}$$

where $\hat{\theta}_{ij} = \hat{p}_{ij}/2(\sqrt{\hat{p}_i+\hat{p}_o} - \sqrt{\hat{p}_o})(\sqrt{\hat{p}_j+\hat{p}_o} - \sqrt{\hat{p}_o})$. In the case $F_{ij}=\log\theta_{ij}$ the derivatives are obtained by dividing the above expressions by $\hat{\theta}_{ij}$. In general, computation of the Wald statistic (11) must be carried out by appropriate statistical software since it involves the inversion of the matrix $\underset{\sim}{V}_F(\hat{p})$. In this direction, a convenient computer program is GENCAT (Landis et al. (1976)). Among other capabilities related to the analysis of categorical data, it computes Wald statistics for testing that certain classes of functions of the parameters of multinomial distributions are zero. They include functions obtained from compositions of linear, logarithmic and exponential operations along the lines indicated in Forthofer and Koch (1973) or Koch et al. (1977). In particular, For $F_{ij} = \theta_{ij}-1$, the

compound function expression for $\underset{\sim}{F}(\underset{\sim}{p})$ in (10) may be given by $\underset{\sim}{F}(\underset{\sim}{p}) = \exp \underset{\sim}{A}_4 \log \underset{\sim}{A}_3 \exp \underset{\sim}{A}_2 \log \underset{\sim}{A}_1 \underset{\sim}{p} - \underset{\sim}{c}$ where $\log(\cdot)$ and $\exp(\cdot)$ are the elementwise vector logarithmic and exponential operators, respectively (i.e. the i^{th} element of $\log \underset{\sim}{x}$ is $\log x_i$ and that of $\exp \underset{\sim}{x}$ is $\exp x_i$),

$$\underset{\sim}{A}_1 = \underset{(f \times f)}{} \quad \begin{matrix} \overbrace{}^{m+1} & \overbrace{}^{m(m-1)/2} \end{matrix}$$

$$\begin{bmatrix} 1 & 0 & \ldots & 0 & 0 & 0 & \ldots & 0 \\ 1 & 1 & \ldots & 0 & 0 & 0 & \ldots & 0 \\ \vdots & \vdots & & \vdots & \vdots & \vdots & & \vdots \\ 1 & 0 & \ldots & 1 & 0 & 0 & \ldots & 0 \\ 0 & 0 & \ldots & 0 & 1/2 & 0 & \ldots & 0 \\ 0 & 0 & \ldots & 0 & 0 & 1/2 & \ldots & 0 \\ \vdots & \vdots & & \vdots & \vdots & \vdots & & \vdots \\ 0 & 0 & \ldots & 0 & 0 & 0 & \ldots & 1/2 \end{bmatrix}$$

$$\underset{\sim}{A}_2 = \underset{(f \times f)}{} \quad \begin{matrix} \overbrace{}^{m+1} & \overbrace{}^{m(m-1)/2} \end{matrix}$$

$$\begin{bmatrix} 1/2 & 0 & \ldots & 0 & 0 & 0 & \ldots & 0 \\ 0 & 1/2 & \ldots & 0 & 0 & 0 & \ldots & 0 \\ \vdots & & & \vdots & \vdots & \vdots & & \vdots \\ 0 & 0 & \ldots & 1/2 & 0 & 0 & \ldots & 0 \\ 0 & 0 & \ldots & 0 & 1 & 0 & \ldots & 0 \\ 0 & 0 & \ldots & 0 & 0 & 1 & \ldots & 0 \\ \vdots & \vdots & & \vdots & \vdots & \vdots & & \vdots \\ 0 & 0 & \ldots & 0 & 0 & 0 & \ldots & 1 \end{bmatrix}$$

$$\underset{\sim}{A}_3 = \underset{(f-1\times f)}{} \begin{bmatrix} \overbrace{\begin{matrix} -1 & 1 & \dots & 0 \\ \vdots & \vdots & & \vdots \\ -1 & 0 & \dots & 1 \\ 0 & 0 & \dots & 0 \\ 0 & 0 & \dots & 0 \\ \vdots & \vdots & & \vdots \\ 0 & 0 & & 0 \end{matrix}}^{m+1} & \overbrace{\begin{matrix} 0 & 0 & \dots & 0 \\ \vdots & \vdots & & \vdots \\ 0 & 0 & \dots & 0 \\ 1 & 0 & \dots & 0 \\ 0 & 1 & \dots & 0 \\ \vdots & \vdots & & \vdots \\ 0 & 0 & \dots & 1 \end{matrix}}^{m(m-1)/2} \end{bmatrix}$$

$$\underset{\sim}{A}_4 = \underset{\frac{m(m-1)}{2} \times (f-1)}{} \begin{bmatrix} \overbrace{\begin{matrix} -1 & -1 & 0 & \dots & 0 & 0 \\ -1 & 0 & -1 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ -1 & 0 & 0 & \dots & 0 & -1 \\ 0 & -1 & -1 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ 0 & -1 & 0 & \dots & 0 & -1 \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ 0 & 0 & 0 & \dots & -1 & -1 \end{matrix}}^{m} & \overbrace{\begin{matrix} 1 & 0 & \dots & 0 & 0 & \dots & 0 & \dots & 0 \\ 0 & 1 & \dots & 0 & 0 & \dots & 0 & \dots & 0 \\ \vdots & \vdots & & \vdots & \vdots & & \vdots & & \vdots \\ 0 & 0 & \dots & 1 & 0 & \dots & 0 & \dots & 0 \\ 0 & 0 & \dots & 0 & 1 & \dots & 0 & \dots & 0 \\ \vdots & \vdots & & \vdots & \vdots & & \vdots & & \vdots \\ 0 & 0 & \dots & 0 & 0 & \dots & 1 & \dots & 0 \\ \vdots & \vdots & & \vdots & \vdots & & \vdots & & \vdots \\ 0 & 0 & \dots & 0 & 0 & \dots & 0 & \dots & 1 \end{matrix}}^{m(m-1)/2} \end{bmatrix}$$

and $\underset{\sim}{c} = \underset{\sim}{1}_{m(m-1)/2}$, a vector with $m(m-1)/2$ elements equal to 1. For $F_{ij} = \log \theta_{ij}$ we have $\underset{\sim}{F}(\underset{\sim}{p}) = \underset{\sim}{A}_4 \log \underset{\sim}{A}_3 \exp \underset{\sim}{A}_2 \log \underset{\sim}{A}_1 \underset{\sim}{p}$.

We present the details for the two special cases discussed above. First consider the MN blood group classification system. From (9), it follows that the HW equilibrium corresponds to $\theta = p_{MN}/2\sqrt{p_M p_N} = 1$, where p_M, p_N and p_{MN} denote the population proportions of the M, N and MN phenotypes, respectively. Taking $F(\underset{\sim}{p}) = \theta - 1$ we obtain $\underset{\sim}{H}(\hat{\underset{\sim}{p}}) = \frac{\hat{\theta}}{2}(-\hat{p}_M^{-1}, -\hat{p}_N^{-1}, 2\hat{p}_{MN}^{-1})$ and the Wald statistic (11) reduces to:

$$Q = n(1 - \frac{1}{\hat{\theta}})^2(\frac{1}{4\hat{p}_M} + \frac{1}{4\hat{p}_N} + \frac{1}{\hat{p}_{MN}})^{-1} \qquad (13)$$

where $\hat{p}_M$, $\hat{p}_N$ and $\hat{p}_{MN}$ correspond to the observed proportions of the M, N and MN phenotypes, respectively and $\hat{\theta} = \hat{p}_{MN}/2\sqrt{\hat{p}_M\hat{p}_N}$. Alternatively, taking $F(\underset{\sim}{p}) = \log \theta$, we obtain $\underset{\sim}{H}(\hat{\underset{\sim}{p}}) = \frac{1}{2}(-\hat{p}_M^{-1}, -\hat{p}_N^{-1}, 2\hat{p}_{MN}^{-1})$ and the Wald statistic (11) reduces to:

$$Q_L = n \log^2\hat{\theta}\ (\frac{1}{4\hat{p}_M} + \frac{1}{4\hat{p}_N} + \frac{1}{\hat{p}_{MN}})^{-1} \qquad (14)$$

If the system is in HW equilibrium, both (13) and (14) follow asymptotic chi-squared distributions with 1 degree of freedom.

Consider now, the ABO blood group classification system. From (3), it follows that the HW equilibrium corresponds to $\theta = p_{AB}/2(\sqrt{p_A+p_o} - \sqrt{p_o})(\sqrt{p_B+p_o} - \sqrt{p_o}) = 1$, where p_o, p_A, p_B and p_{AB} denote the population proportions of the O, A, B and AB phenotypes, respectively. Taking $F(p) = \theta - 1$, relations (11) and (12) yield, after some algebraic manipulation:

$$Q = n(1 - \frac{1}{\hat{\theta}})^2\ (O^2\hat{p}_o + A^2\,\hat{p}_A + B^2\,\hat{p}_B + \hat{p}_{AB}^{-1})^{-1} \qquad (15)$$

where $O = \{[\hat{p}_o(\hat{p}_A+\hat{p}_o)]^{-1/2} + [\hat{p}_o(\hat{p}_B+\hat{p}_o)]^{-1/2}\}/2$,

$A = -\{2(\hat{p}_A+\hat{p}_o)^{1/2}[(\hat{p}_A+\hat{p}_o)^{1/2} - \hat{p}_o^{1/2}]\}^{-1}$

and $B = -\{2(\hat{p}_B+\hat{p}_o)^{1/2}[(\hat{p}_B+\hat{p}_o)^{1/2} - (\hat{p}_o)^{1/2}]\}^{-1}$. For $F(p) = \log\theta$ the corresponding wald statistic is given by:

$$Q_L = n \log^2\hat{\theta}(O^2\hat{p}_O + A^2\hat{p}_A + B^2\hat{p}_B + \hat{p}_{AB}^{-1})^{-1} \qquad (16)$$

If the HW equilibrium hypothesis holds, both statistics follow asymptotic chi-squared distributions with 1 degree of freedom.

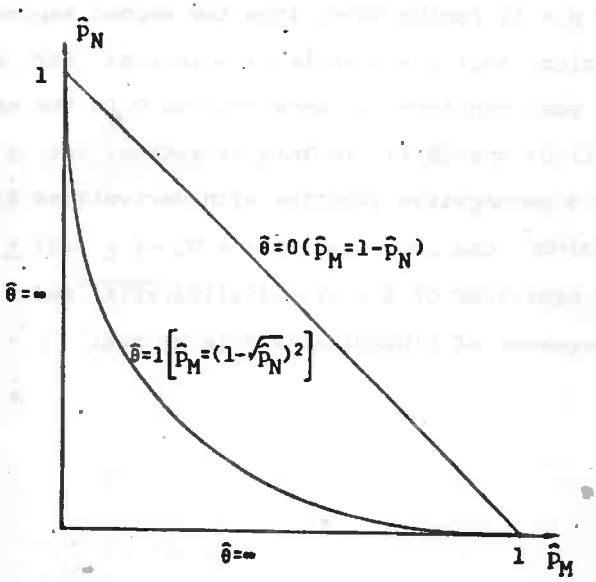
To illustrate the above procedures numerically, we first consider a set of data from the MN blood classification system presented in Crow and Kimura (1970, p.36); the observed phenotype frequencies are $n_M = 362$, $n_N = 282$ and $n_{MN} = 634$ and the Wald statistics obtained from (13) and (14) are $Q = 0.02$ and $Q_L = 0.02$ ($\hat{\theta} = 0.99$); the corresponding Pearson chi-squared statistic is $Q_P = 0.03$. In a second example (Rao (1973), p.402), the observed phenotype frequencies for the O, A, B and AB blood groups are $n_O=121$, $n_A = 120$, $n_B = 79$ and $n_{AB}=33$, respectively. The corresponding Wald statistics, obtained via (15) and (16) are $Q = 0.38$ and $Q_L = 0.44$, respectively ($\hat{\theta} = 1.16$), while the Pearson chi-squared statistic is $Q_P = 0.44$. Finally we consider the data for Esterase variants of Drosophila virilis cited by Yasuda and Kimura (1968, p.415); in this case $m = 3$ and the phenotype observed frequencies are given by $n_o=20$, $n_1 = 1149$, $n_2 = 36$, $n_3 = 17$, $n_{12} = 336$, $n_{13} = 25$ and $n_{23} = 17$. Here we obtain $\hat{\theta}_{12} = 0.88$, $\hat{\theta}_{13} = 1.12$ and $\hat{\theta}_{23} = 1.58$; also from (11) and (12) we get $Q = 11.79$ using $F_{ij} = \theta_{ij} - 1$ and $Q_L = 21.18$ using $F_{ij} = \log \theta_{ij}$ while the corresponding Pearson chi-squared statistic is $Q_P = 26.98$.

4. ON THE BEHAVIOUR OF THE PROPOSED WALD STATISTICS FOR FIXED SAMPLE SIZES.

Although the Wald statistics considered in Section 3 have optimal asymptotic properties, it is of interest to study their statistical behaviour for fixed sample sizes since this is the case in practical applications. Considering one-parameter exponential families, Hauck and Donner (1977) and Væth (1985) have shown that Wald statistics may decrease to zero as the paramter estimate moves away from the null value, indicating an aberrant behaviour. In this section we demonstrate that this is also true for the Wald statistics proposed above, at least in the special case $m = 2$, $p_o = 0$.

Consider, for example, the MN blood group classification system discussed above. Write $\hat{\theta} = (1-\hat{p}_M-\hat{p}_N)/2\sqrt{\hat{p}_M\hat{p}_N}$ and note that the domain of $\hat{\theta}$ as a function of $\hat{p}_M$ and $\hat{p}_N$ corresponds to the region delimited by the triangle in Figure 1.

Figure 1: Domain of the function $\hat{\theta} = \hat{\theta}(\hat{p}_M,\hat{p}_N)$.



Let us first study the behaviour of $\hat{\theta}$ in this domain. Observe that, given $\theta_o \geq 0$, the set of points for which $\hat{\theta} = \theta_o$ corresponds to the curve with equation $\hat{p}_M = (\sqrt{1+(\theta_o^2-1)\hat{p}_N} - \theta_o\sqrt{\hat{p}_N})^2$; in particular for the null value, $\theta_o = 1$, we have $\hat{p}_M = (1-\sqrt{\hat{p}_N})^2$; also, for $\theta_o = 0$, we get $\hat{p}_M = 1 - \hat{p}_N$ and as $\theta_o \to \infty$ we must have either $\hat{p}_M \to 0$ or $\hat{p}_N \to 0$. Therefore we need to be concerned with points on the boundary of the triangular region presented in Figure 1.

For simplicity, let $\hat{p}_M = x$, $\hat{p}_N = y$ and let us examine the behaviour of the statistic (13) which may be written as:

$$Q = n\left(1 - \frac{2\sqrt{xy}}{1-x-y}\right)^2 \left(\frac{1}{4x} + \frac{1}{4y} + \frac{1}{1-x-y}\right)^{-1} =$$

$$= n\left(\frac{1-x-y}{2\sqrt{xy}} - 1\right)^2 \left(\frac{(1-x-y)^2}{16x^2y} + \frac{(1-x-y)^2}{16xy^2} + \frac{(1-x-y)}{4xy}\right)^{-1} \qquad (17)$$

Using the first expression for Q in (17) it is easy to see that $Q \to 0$ as $(x,y) \to (0,p)$ or $(x,y) \to (p,0)$ or $(x,y) \to (p,0)$ or $(x,y) \to (0,0)$ for any $0 < p < 1$; furthermore, from the second expression for Q in (17) it is clear that $Q \to \infty$ as $(x,y) \to (p,1-p)$ for any $0 < p < 1$. Finally, we must consider the behaviour of Q in the neighbourhood of the points (1,0) and (0,1). In this direction, let $y = f(x)$ where $f: [0,1]$ is a nonnegative function with derivatives $\dot{f}(x) = df(x)/dx$ and $\ddot{f}(x) = d^2f(x)/dx^2$ and such that $f(1) = 0$; $-1 \leq \dot{f}(1) \leq 0$ and let us examine the behaviour of $\hat{\theta} = (1-x-f(x))/2\sqrt{xf(x)}$ and Q as $x \to 1$. As a direct consequence of L'Hospital's rule we get:

$$\lim_{x\to 1} \frac{1-x-f(x)}{2\sqrt{xf(x)}} = \begin{cases} 0 & \text{if } \dot{f}(1) \neq 0 \\ [2\ddot{f}(1)]^{-1/2} & \text{if } \dot{f}(1) = 0 \text{ and } \ddot{f}(1) \neq 0 \\ * & \text{if } \dot{f}(1) = 0 \text{ and } \ddot{f}(1) = 0 \end{cases} \tag{18}$$

In particular, note that if $f(x) = (\sqrt{1+(\theta_o^2-1)x} - \theta_o\sqrt{x})^2$, $\theta_o \geq 0$ fixed, so that as $x \to 1$, $(x,y) \to (1,0)$ along the curves corresponding to $\hat{\theta} = \theta_o$, constant, we have $\lim_{x\to 1} \hat{\theta} = \theta_o$. Next write $A(x) = 1-x-f(x)$ and $B(x) = A(x)\{x+f(x)\} + 4xf(x)$ so that:

$$Q = 16n\, x^2 \left\{\frac{1-x-y}{2\sqrt{xy}} - 1\right\}^2 \left\{\frac{f^2(x)}{A(x)B(x)}\right\} \tag{19}$$

Applying L'Hospital's rule to the last term in (19) we obtain:

$$\lim_{x\to 1} \frac{f^2(x)}{A(x)B(x)} = -\frac{\dot{f}^2(1)}{[3\dot{f}(1)-1][\dot{f}(1)+1]} \tag{20}$$

Then, from (17)-(20) we may conclude that:

$$\lim_{x\to 1} Q = \begin{cases} 0 & \text{if } \dot{f}(1) = 0 \text{ and } \ddot{f}(1) \neq 0 \\ \dfrac{16n\,\dot{f}^2(1)}{[3\dot{f}(1)-1][\dot{f}(1)+1]} & \text{if } \dot{f}(1) \neq 0 \\ * & \text{if } \dot{f}(1) = \ddot{f}(1) = 0 \end{cases} \tag{21}$$

Next, consider the statistic (14) which may be expressed as:

$$Q_L = n\{\log(1-x-y) - \log 2 - \tfrac{1}{2}\log x - \tfrac{1}{2}\log y\}^2 \left\{\frac{1}{4x} + \frac{1}{4y} + \frac{1}{1-x-y}\right\}^{-1} \tag{22}$$

An expansion of the squared term in (22) is sufficient to indicate that the limiting behaviour of Q_L is essentially determined by the behaviour of functions of the form $h(x,y) = g(x,y)\{\frac{1}{4x} + \frac{1}{4y} + \frac{1}{1-x-y}\}^{-1}$ where $g(x,y) = \log x$, $g(x,y) = \log^2 x$ or $g(x,y) = \log x \log y$ as $(x,y) \to (0,p)$, $0 \leq p \leq 1$ or $(x,y) \to (p,1-p)$, $0 < p < 1$. Clearly $h(x,y) \to 0$ as $(x,y) \to (p,1-p)$, $0 < p < 1$. Using the fact that for $a > 0$, $x(\log x)^a \to 0$ as $x \to 0$, it is easy to see that $h(x,y) \to 0$ as $(x,y) \to (0,p)$, $0 < p < 1$. Now, using the inequality $0 \leq g(x,y)\{\frac{1}{4x} + \frac{1}{4y} + \frac{1}{1-x-y}\}^{-1} \leq 4xg(x,y)$, it follows that $h(x,y) \to 0$ as $(x,y) \to (0,0)$ or $(x,y) \to (0,1)$ for $g(x,y) = \log x$ or $g(x,y) = \log^2 x$. Finally, note that the case $\log x \log y\{\frac{1}{4x} + \frac{1}{4y} + \frac{1}{1-x-y}\}^{-1} \to 0$ as $(x,y) \to (0,0)$ or $(x,y) \to (0,1)$ is somewhat more ellaborate, but the result may be obtained by writing $x = r\cos\phi$, $y = r\sin\phi$, $0 \leq \phi \leq \pi/2$ and letting $r \to 0$.

From the above discussion we may conclude that both Q and Q_L may converge to zero in situations which clearly violate the equilibrium hypothesis, indicating that such statistics should be used with caution; more specifically, they are not recommended in cases where the observed pehnotype proportions are close to 0 or 1. Although a similar analysis for the general case is mathematically intractable, we believe that the corresponding Wald statistics have the same type of aberrant behaviour.

ACKNOWLEDGEMENTS

Work of the first author was partially supported by a grant from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Brazil.

REFERENCES

Bhapkar, V.P. (1966). A note on the equivalence of two test criteria for hypotheses in categorical data. Journal of the American Statistical Association 61, 228-235.

Cavalli-Sforza, L.L. and Bodmer, W.F. (1971). The Genetics of Human Populations. San Francisco: Freeman.

Crow, J.F. and Kimura, M. (1970). An Introduction to Population Genetics. New York: Harper and Row.

Elandt-Johnson, R.C. (1971). Probability Models and Statistical Methods in Genetics. New York: Wiley.

Forthofer, R.N. and Koch, G.G. (1973). An analysis for compounded functions of categorical data. Biometrics 29, 143-157

Hauck, W.W. and Donner, A. (1977). Wald's test as applied to hypotheses in logit analysis. Journal of the American Statistical Association 72, 851-853. Corrigendum (1980), 75, 482.

Koch, G.G., Landis, J.R., Freeman, J.L., Freeman, D.H.,Jr. and Lehnen, R.G. (1977). A general methodology for the analysis of experiments with repeated measurement of categorical data. Biometrics 33, 133-158.

Landis, J.R., Stanish, W.M., Freeman, J.L. and Koch, G.G. (1976). A computer program for the generalized chi-square analysis of categorical data using weighted least squares (GENCAT). Computer Programs in Biomedicine 6, 196-231.

Nam, J.O. and Gart, J.J. (1976). Bernstein's and gene-counting methods in generalized ABO-like systems. Annals of Human Genetics 39, 361-373.

Pereira, C.A.B. and Rogatko, A. (1984). The Hardy-Weinberg equilibrium under a Bayesian perspective. Revista Brasileira de Genética 7, 689-707.

Rao, C.R. (1973). Linear statistical Inference and its Applications New York: Wiley.

Væth M. (1985). On the use of Wald's test in exponential families. International Statistical Review, 53, 199-214.

Yasuda, N. and Kimura, M.(1968). A gene-counting method of maximum likelihood for estimating gene frequencies in ABO and ABO-like systems. Annals of Human Genetics 31, 409-420.

RELATÓRIO TÉCNICO

DO

DEPARTAMENTO DE ESTATÍSTICA

TÍTULOS PUBLICADOS

7901 - BORGES, W. de S. On the limiting distributios of the failure time of composite material. São Paulo, IME-USP,1979,22p.

7902 - GALVES, A.; LEITE, J.G.; ROUSSIGNOL, M. The invariance principle for the one-dimensional symmetric simple exclusion process. São Paulo, IME-USP, 1979, 9p.

8001 - MENTZ, R.P. et al. Exploratory fitting of autoregressive and moving average models to well-behaved time series data. São Paulo, IME-USP, 1980, 16p.

8002 - MORETTIN, P.A. Walsh spectral analysis. São Paulo, IME-USP , 1980, 27p.

8003 - RODRIGUES, J. Robust estimation and finite population. São Paulo, IME-USP, 1980, 13p.

8004 - BORGES, W. de S. & RODRIGUES, F.W. On the axiomatic theory of multistate coherent structures. São Paulo, IME-USP, 1980, 10p.

8005 - MORETTIN, P.A. A central limit theorem for stationary processes. São Paulo, IME-USP, 1980, 5p.

8101 - DANTAS, C.A.B. & COLUCCI, E. A Simulation program for emergency services-II, São Paulo, IME-USP, 1981, 14p.

8102 - ANDJEL,E.D. Invariant measures for the zero range process. São Paulo, IME-USP, 1981, 55p.

8103 - ANDJEL, E.D. The asymmetric simple exclusion process on Z^d. São Paulo, IME-USP, 1981, 13p.

8104 - MORETTIN, P.A. & TOLOI, C.M.C., Accuracy of forecasting with special reference to the Box-Jenkins and Bayesian Methodologies. São Paulo, IME-USP, 1981, 41p.

8105 - PINO, F.A. & MORETTIN, P.A., Intervention analysis applied to Brazilian coffee and milk time series. São Paulo IME-USP. 1981, 36p.

8106 - BORGES, W.S. & RODRIGUES, J., Testing for new better than used in expectation. São Paulo, IME-USP, 1981, 7p.

8107 - FAHMY, S.; PEREIRA, C.A.B.; PROSCHAN, F., The influence of the sample on the posterior distribution. São Paulo, IME-

8108 - PERES, C.A., Asymptotic efficiency of the likelihood ratio conditional test for multinomial distributions. São Paulo IME-USP, 1981, 29p.

8109 - PERES, C.A., Testing the effect of blocking in a randomized complete block design (RCBD). São Paulo, IME-USP, 1981, 14p.

8110 - BASU, D. & PEREIRA, C.A.B., On the Bayesian analysis fo categorical data: the problem of nonresponse. São Paulo, IME-USP, 1981, 13p.

8201 - BASU, D. & PEREIRA, C.A.B., Conditional independence in statistics, São Paulo, IME-USP, 1982, 37p.

8202 - BASU, D. & PEREIRA, C.A.B., A note on Blackwell sufficiency and a Skibinsky characterization of distributions. São Paulo, IME-USP, 1982, 12p.

8203 - PERES, C.A., On the interpretation of the parameters of the quadratic model for cell survival ofter irradiation. São Paulo, IME-USP, 1982, 22p.

8204 - GALVES, A., et al. Rescaling the stirring process. São Paulo IME-USP, 1982, 23p.

8205 - RODRIGUES, J., On the asymptotic theory for the fixed size confidence ellipsoids. São Paulo, IME-USP, 1982, 14p.

8206 - PEREIRA, C.A.B. & RODRIGUES, J., Robust linear predicition in finite populations. São Paulo, IME-USP, 1982, 14p.

8207 - MORETTIN, P.A., Walsh-Fourier transforms. São Paulo,IME-USP 1982, 15p.

8208 - PERES, C.A. & MORETTIN, P.A., Building bridges between the academic and real wordls-some observations from South America. São Paulo, IME-USP, 1982 16p.

8209 - PEREIRA, C.A.B. & ROGATKO, A., The Hardy-Weinberg equilibrium under a Bayesian perspective. São Paulo, IME-USP , 1982, 16p.

8210 - MORETTIN, P.A., The Levinson algorithm and its applications in time series analysis. São Paulo, IME-USP, 1982, 16p.

8211 - RODRIGUES, J., A Note on Maximized and Conditional Likelihood Functions. São Paulo, IME-USP, 1982, 9p.

8301 - PEREIRA,C.A.B., Stopping rules and conditional inference in 2x2 contigence tables. São Paulo, IME-USP, 1983, 7p.

8302 - BOLFARINE, H., PEREIRA, C.A.B. & RODRIGUES, J., Robust Linear Prediction in Finite Populations: A Bayesian Perspective. São Paulo, IME-USP, 1983, 21p.

8303 - MORETTIN, P.A. et al., Rainfall at Fortaleza, Ceará, Brazil Revisited. São Paulo, IME-USP, 1983, 33p.

8304 - MORETTIN, P.A. & TOLOI, C.M.C., Evaluation of Forecasting Procedures: A Case Study. São Paulo, IME-USP, 1983,30p.

8305 - PERES, C.A., et al., Educating and training undergraduate applied statisticians. São Paulo, IME-USP, 1983, 15p.

8306 - PEREIRA, C.A.B., & LINDLEY, D.V., Examples Questioning the Use of Partial Likelihood. São Paulo, IME-USP, 1983, 10p.

8307 - MORETTIN, P.A. et al., Statistics in South America. São Paulo, IME-USP, 1983, 10p.

8308 - LINDLEY, D.V., Royal Statistical Society 150th Anniversary. São Paulo, IME-USP, 1983, 19p.

8309 - ANDJEL, E.D., Invariant Measures and Long Time Behaviour of the Smoothing Process. São Paulo, IME-USP, 1983, 25p.

8310 - BOLFARINE, H. et al., A General Theory of Prediction in Finite Populations. São Paulo, IME-USP, 1983, 42p.

8401 - BOLFARINE, H. & RODRIGUES, J., Characterization of Alternative Models for Robust Linear Prediction in Finite Populations. São Paulo, IME-USP, 1984, 12p.

8402 - PEREIRA, C.A.B. et al., Inversão de Condicionamento. São Paulo. IME-USP, 1984, 30p.

8403 - BOLFARINE, H. & RODRIGUES, J., On Bayesian Prediction of the Population Variance in Finite Populations. São Paulo, IME-USP, 1984, 21p.

8404 - ZACKS, S., Bayes Sequential Estimation of the Size of a Finite Population. São Paulo, IME-USP, 1984, 23p.

8405 - ROGATKO, A. et al., Bayesian Method for the Estimation of Penetrance: Application to Mandibulofacial and Fronto-Nasal Dysostoses. São Paulo, IME-USP, 1984, 67p.

8406 - SHIBATA, R., Identification and Selection of ARMA models. São Paulo, IME-USP, 1984, 17p.

8407 - MORETTIN, P.A. & MESQUITA, A.R., A Phase Angle Test for Periodic Components in Time Series. São Paulo, IME-USP, 1984, 27p.

8408 - SHIBATA, R., Selection of Regression Variables. São Paulo: IME-USP, 1984, 11p.

8409 - ESTON, V.R. et al., Chthamalus Bissinuatus (Cirripedia) and Brachidontes Solisianus (Bivalvia) Spatial Interactions: A Stochastic Model. São Paulo, IME-USP, 1984, 32p.

8410 - PINO, F.A. & MORETTIN, P.A., Forecasting Linear Combinations of Time Series. São Paulo, IME-USP, 1984, 30p.

8411 - SCHONMANN, R.H., Metastability for the Contact Process. São Paulo, IME-USP, 1984, 29p.

8412 - SCHONMANN, R.H., Central Limit Theorem for the Contact Process. São Paulo, IME-USP, 1984, 10p.

8413 - ANDRADE, D.F. & BOLFARINE, H., Estimation in Covariance Components Models with Unequal Intraclass Variances. São Paulo, IME-USP, 1984, 10p.

8501 - RODRIGUES, J. et al., The EM-Algorithm for Finding the ML-Predictor for Finite Populations in Two-Stage Sampling. São Paulo, IME-USP, 1985, 15p.

8502 - BOLFARINE, H. & RODRIGUES, J., A Missing Value Approach to the Prediction Problem in Finite Populations. São Paulo, IME-USP, 1985, 16p.

8503 - SCHONMANN, R., A New Proof of the Complete Convergence Theorem for Contact Processes in Several Dimensions with Large Infection Parameter. São Paulo, IME-USP, 1985, 11p.

8504 - ZACKS,S. & RODRIGUES, J., A Note on the EM-Algorithm for Maximum Likelihood Estimation in Sampling from a Finite Population with a Multinormal Superpopulation Model. São Paulo, IME-USP, 1985, 5p.

8505 - ANDJEL, E.D., Convergence to a non Extremal Equilibrium Measure in the Exclusion Process. São Paulo, IME-USP, 1985, 15p.

8506 - IRONY, T.Z. & PEREIRA, C.A.B., Exact Tests for Equality of Two Proportions: Fisher x Bayes. São Paulo, IME-USP, 1985, 30p.

8507 - SCHONMANN, R.H. & VARES, M.E., The Survival of the Large Dimensional Basic Contact Process. São Paulo, IME-USP, 1985, 14p.

8508 - ACHCAR, J.A., Modelos de Regressão com Dados Censurados. São Paulo, IME-USP, 1985, 18p.

8509 - ACHCAR, J.A. & BOLFARINE, H., Use of Accurate Approximations for Posterior Densities in Regression Models with Censored data. São Paulo, IME-USP, 1985, 21p.

8510 - SINGER, J.M. & SEN, P.K., M - Methods in Growth Curve Analysis. São Paulo, IME-USP, 1985, 17p.

8511 - BOLFARINE, H. & SANDOVAL, M.C., The Linear Least Squares Prediction Approach to Populations with Trend. São Paulo, IME-USP, 1985, 13p.

8512 - PERES, C.A. & NARULA, S.C., The Quadratic Model for Cell Survival After Irradiation: A New Interpretation of the Parameters. São Paulo, IME-USP, 1985, 15p.

8513 - PERES, C.A. & NARULA, S.C., A New Derivation of the Quadratic Dose-Response Model for Cell Survival in Radiobiological Studies. São Paulo, IME-USP, 1985, 25p.

8514 - PERES, C.A. & NARULA, S.C., A Simple Procedure to Determine the Parameters of a Quadratic Dose-Response Model. São Paulo, IME-USP, 1985, 15p.

8515 - FERRARI, P.A. & GOLDSTEIN, S., Microscopic Stationary States for Stochastic Systems with Particle Flux. São Paulo, IME-USP, 1985, 32p.

8516 - RODRIGUES, J., Some Shrunken Predictors in Finite Populations with a Multinormal Superpopulation Model. São Paulo, IME-USP, 1985, 12p.

8517 - ACHCAR, J.A. & BOLFARINE, H., A Bayesian Analysis of The Log-linear Model with one Covariate and a Generalized / Gamma Distribution for the Error. São Paulo, IME-USP, 1985, 27p.

8518 - SINGER, J.M. et al.; Tests for the Hardy-Weinberg Equilibrium. São Paulo, IME-USP, 1985, 10p.

8519 - BOLFARINE, H., Some Shrinkage Tecniques for Predicting the Population Total in Finite Populations. São Paulo, IME-USP, 1985, 14p.

8520 - BUENO, U.C.; A Model in Negative Dependence Through Stochastic Ordering Using Order Statistics. São Paulo, IME-USP , 1985, 21p.

8521 - PAULINO, C.D.M.; Um Ensaio sobre Identificabilidade de Modelos Estatísticos Paramétricos. São Paulo, IME-USP, 1985, 80p.

8522 - PEREIRA, C.A.B. & PERICCHI, L.R.; Analysis of Diagnosability. São Paulo, IME-USP, 1985, 44p.

8601 - GALVES, A., OLIVIERI, E., VARES, M.E.; Metastability for a Class of Dynamical Systems Subjetc to Small Random Pertur bations. São Paulo, IME-USP, 1986, 15p.

8602 - BOLFARINE, H., ACHCAR, J.A.; Predictive Densities in Survial Analysis with a Generalized Gamma Regression Model, São Paulo, IME-USP, 1986, 22p.

8603 - RODRIQUES, J., BOLFARINE, J.; A Kalman Filter Model for Single and Two-Stage, Repeated Surveys. São Paulo, IME-USP , 22p.

8604 - MORETTIN, P.A., PINO, F.A., MENTZ, R.P.; Modelling and Forecasting Linear Combinations of Time Series, São Paulo, IME -USP, 1986, 49p.

8605 - RODRIGUES, J. & BOLFARINE, H., Some Asymptotic Results on Generalized Regression Predictors in Survey Sampling, São Pau lo, IME-USP, 1986, 23p.

8606 - ACHCAR, J.A., BOLFARINE, H., AND PERICCHI, L,; Transformation of survival data to an extreme value distribution, São Pau-

8607 - RODRIGUES, J.; The Coordinate - Free Prediction in Finite Populations, São Paulo, IME-USP, 1986, 19p.

8608 - BUENO, V. C.; Importance of Components for Multistate Monotone Systems, São Paulo, IME-USP, 1986, 27p.

8609 - RODRIGUES, J., BOLFARINE, H. & J.G. LEITE; Continuous - Time Markov Models for Finite Populations, São Paulo, IME-USP, 1986, 11p.

8610 - LEITE, J.G. & PEREIRA, C.A.B.; An Urn Model for the Capture/Recapture Sequential Sampling Process, São Paulo, IME -USP, 1986, 13p.

8611 - LEITE, J.G., OISHI, J. & PEREIRA, C.A.B.; Exact ML Estimate of a Finite Population Size: Capture/Recapture Sequential Sample Data, São Paulo, IME-USP, 1986, 19p.

8612 - PAULA, G.A. & PERES, C.A.; Medidas de Diagnóstico para Modelos Lineares Generalizados com Restrições nos Parâmetros, São Paulo, IME-USP, 1986, 19p.

8613 - RODRIGUES, J. & BOLFARINE, H.; A Bayesian Shrunken Predictor in Repeated Sampling, São Paulo, IME-USP, 1986, 10p.

8614 - PAULA, G.A.; Resíduos Projetados na Classe dos Modelos Lineares Generalizados, São Paulo, IME-USP, 1986, 30p.

8615 - LEITE, J.G., PEREIRA, C.A.B., ZACKS, S.; Bayes Estimation of a Finite Population Size: Capture/Recapture Sequential Sample Data, IME-USP, 1986, 26p.

8616 - BUENO, V.C.; A Note on the Components Lifetime Estimation of a Multistate Monotone System Through the System Lifetime, IME-USP, 1986, 8p.

8701 - ACHCAR, J.A. & BOLFARINE, H.; Constant Hazard Against a Change-Point Alternative: A Bayesian Approach with Censored Data, São Paulo, IME-USP, 1987, 20p.

8702 - RODRIGUES, J.; Some Results on Restricted Bayes Least Squares Predictors for Finite Populations, São Paulo, IME-USP, 1987, 16p.

8703 - LEITE, J.G., BOLFARINE, H. & RODRIGUES, J.; Exact Expression for the Posterior Mode of a Finite Population Size: Capture-Recapture Sequential Sampling, São Paulo, IME-USP, 1987, 14p.

8704 - RODRIGUES, J., BOLFARINE, H. & LEITE, J.G.; A Bayesian Analysis in Closed Animal Populations from Capture Recapture Experiments with Trap Response, São Paulo, IME-USP, 1987, 21p.

8705 - PAULINO, C.D.M.; Analysis of Categorical Data with Full and Partial Classification: A Survey of the Conditional Maximum Likelihood and Weighted Least Squares Approaches, São Paulo, IME-USP, 1987, 52p.

8706 - CORDEIRO, G.M. & BOLFARINE, H.; Prediction in a Finite Population under a Generalized Linear Model, São Paulo, IME-USP, 1987, 21p.

8707 - RODRIGUES, J. & BOLFARINE, H.; Nonlinear Bayesian Least-Squares Theory and the Inverse Linear Regression, São Paulo, IME-USP, 1987, 15p.

8708 - RODRIGUES, J. & BOLFARINE, H.; A Note on Bayesian Least-Squares Estimators of Time-Varying Regression Coefficients, São Paulo, IME-USP, 1987, 11p.

8709 - ACHCAR, J.A., BOLFARINE, H. & RODRIGUES, J.; Inverse Gaussian Distribution: A Bayesian Approach, São Paulo, IME-USP, 1987, 20p.

87.10 - CORDEIRO, G.M. & PAULA, G.A.; Improved Likelihood Ratio Statistics for Exponential Family Nonlinear Models, São Paulo, IME-USP, 1987, 26p.