EINSTEIN'S equations (1936) yield maximum likelihood estimates of the regional frequency distribution of crossovers in the tetrads from which a given sample of strands was derived, one per tetrad. But clearly, as with all estimates of universe parameters from sample statistics, other values within a certain range cannot be rejected; that range can be ascertained, for each tetrad-rank separately, from the standard error computed by a method also given by WEINSTEIN.

The standard errors of the separate frequencies do not, however, define the range of non-rejectable values of the rank frequencies jointly, where there are more than two ranks. It is with the calculation of the joint range that the present note is concerned.

Only one special case will be considered here: the frequencies of tetrads of rank 0, 1, 2, ⋯, k (or, further on, k + 1) with regard not to the regional location of the crossovers but only to the total number per tetrad, estimated from (k + 1) observed strand-rank frequencies, assuming random recurrence and no sister-strand crossing over.

All possible sets of (k + 1) tetrad frequencies, expressed in decimal fraction, may be thought of as lying within a k-dimensional, unit-edge hypercube, occupying a "corner" of volume $1/k!$. Somewhere within the corner is the point representing Weinstein's maximum likelihood estimate of the universe tetrad-rank frequencies for a given sample.

Now consider any other point within the corner, any other set of universe rank frequencies. Around it lie successive hyperellipsoidal shells (with increasingly flattened areas near the surfaces of the corner), each containing a finite set of points representing equally-likely sets of rank frequencies in samples from the given universe. The likelihood decreases outward from shell to shell. The sum of the likelihoods outside a given shell falls from 1 at the universe point to slightly above 0 at the plane surfaces of the corner (possibly somewhat higher at one of the surfaces).

Suppose next that we locate all points within the corner whose equal-likelihood sample shells passing through the maximum likelihood point have some particular outside likelihood sum, $P$. These points will themselves form a hyperellipsoidal shell, with possibly one or more flattened regions. Our problem is to locate that shell, for $P$ generally somewhere from .01 to .05.

But the complete specifications of such a fiducial limit shell would not be very useful, because incomprehensible in any down-to-earth sense. Obviously then we have to confine our attention to particular points within the shell, to specific sets of

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† Donald R. Charles died before this manuscript reached its final form.
possible universe frequencies: probably, by analogy with the fiducial limits of a single parameter, to some pair of points in opposite directions from the maximum likelihood point, crudely like the two apices of a football.

Several such pairs could be defined, at least where four or more strand ranks are observed. One pair that would seem to be of special interest is that point within the fiducial-limit shell at which the average tetrad-rank is highest, and that point at which it is lowest.

The conditions we have imposed are, altogether, as follows:

1. \[ \sum_{i=0}^{k} T_i = 1 \]
2. \[ \sum_{i=0}^{k} (s_i - \sigma_i)^2 / \sigma_i = G/N \]
3. \[ \frac{\partial}{\partial T_i} i_T = 0 \]

Here \( T_i \) represents a universe frequency of tetrads of rank \( i \); \( \sigma_i \), a universe strand frequency; \( s_i \), an observed strand frequency; \( N \), total strands in a sample; \( k \), the highest observed strand rank; \( G \), the value of \( \chi^2 \) for \( k \) degrees of freedom and some specified fiducial probability, ordinarily .01 to .05.

The relation of the strand frequencies (\( \sigma \)'s) to the tetrad frequencies (\( T \)'s), assuming that there is no crossing over between sister strands but that otherwise association of strands is random, has been given by WEINSTEIN (1936) as follows:

\[
\begin{align*}
\sigma_0 &= T_0 + \frac{1}{2} T_1 + \frac{1}{4} T_2 + \frac{1}{8} T_3 + \frac{1}{16} T_4 + \cdots \\
\sigma_1 &= \frac{1}{2} T_1 + \frac{3}{8} T_2 + \frac{3}{8} T_3 + \frac{1}{16} T_4 + \cdots \\
\sigma_2 &= \frac{1}{4} T_2 + \frac{3}{8} T_3 + \frac{3}{8} T_4 + \cdots \\
\sigma_3 &= \frac{1}{8} T_3 + \frac{1}{4} T_4 + \cdots \\
\vdots & \quad \vdots \\
\sum \sigma_i &= T_0 + T_1 + T_2 + T_3 + T_4 + \cdots = \Sigma T_i = 1 \\
i_T = \Sigma i \sigma_i = \frac{1}{2} T_1 + \frac{3}{8} T_2 + \frac{3}{8} T_3 + \frac{1}{16} T_4 + \cdots = \left( \frac{1}{2} \right) \Sigma i T_i = \frac{1}{2} \Sigma_T
\end{align*}
\]

Since condition 2 has to be given in terms of \( s_i \), and hence \( \sigma_i \), the other two conditions can be imposed more conveniently by bringing them into the same terms:

1. \[ \sum_{i=0}^{k} \sigma_i = 1 \]
2. \[ \frac{\partial}{\partial T_i} i_T = 0 \]

Condition 3' is equivalent to 3 because \( \overline{\sigma} = \overline{i_T}/2 \) for all sets of tetrad-rank frequencies and the strand frequencies calculated from them.

We now express \( \sigma_0 \) and \( \sigma_1 \) in terms of \( \overline{\sigma} \) and \( \sigma_2 \) to \( \sigma_k \) (from condition 1' and the definition of \( \overline{\sigma} \)). We then derive \( \overline{\sigma} \) as a function of \( \sigma_2 \) to \( \sigma_k \) by means of condition 2.

\[
\sigma_0 = 1 - \overline{\sigma} + \sum_{i=2}^{k} (i-1) \sigma_i; \quad \sigma_1 = \overline{\sigma} - \sum_{i=2}^{k} i \sigma_i
\]

\[
\frac{G}{N} + 1 - \sum_{i=2}^{k} \frac{s_i^2}{\sigma_i} = \frac{s_0^2}{1 + \sum_{i=2}^{k} (i-1) \sigma_i - \overline{\sigma}} - \sum_{i=2}^{k} i \sigma_i - \overline{\sigma}
\]
Abbreviating the latter equation we have the following, in which the meanings of $A$, $B$ and $C$ will be obvious by comparison.

$$A = \frac{s_0^2}{B - \delta} - \frac{s_1^2}{C - \delta}$$

$$2\delta = \left[ -\frac{s_0^2}{A} + \frac{s_1^2}{B} + C \right] \pm \left[ \left( \frac{s_0^2}{A} + \frac{s_1^2}{B} + C \right)^2 - \frac{4s_0^2s_1^2}{A^2} \right]^{1/2}$$

Both roots satisfy the equation but if the values $A = \frac{s_0^2}{\sigma_0^2} + \frac{s_1^2}{\sigma_1^2}$, $B = \delta + \sigma_0$, $C = \delta - \sigma_1$ are substituted in the formula for $\delta$, it will be found that it becomes an identity on using the plus sign when $s_0^2 \sigma_1^2 - s_1^2 \sigma_0^2 \geq 0$, and the minus sign when $s_0^2 \sigma_1^2 - s_1^2 \sigma_0^2 < 0$.

$$2 \frac{\partial \delta}{\partial T_i} = \left[ \frac{s_0^2}{A^2} \frac{\partial A}{\partial T_i} + \frac{\partial B}{\partial T_i} + \frac{\partial C}{\partial T_i} \right] - \left[ \left( \frac{s_0^2}{A} + \frac{s_1^2}{B} + C \right)^2 - \frac{4s_0^2s_1^2}{A^2} \right]^{1/2}$$

$$= \left\{ \frac{1}{A^2} \left[ \frac{(s_0^2 - s_1^2)^2}{A} - (B - C)(s_0^2 + s_1^2) \right] \frac{\partial A}{\partial T_i} \right.$$ 

$$+ \left[ \frac{s_0^2 + s_1^2}{A} - B - C \right] \frac{\partial B}{\partial T_i} - \frac{\partial C}{\partial T_i} \right\}$$

Setting this expression equal to 0, for $\delta$, maximal or minimal, and resubstituting for $A$, $B$ and $C$ in terms of $\sigma_0$, $\sigma_1$ and $\delta$, gives, after some simplification:

$$\frac{\partial A}{\partial T_i} + \left( \frac{s_0^2}{\sigma_0} \right)^2 \frac{\partial B}{\partial T_i} - \left( \frac{s_1^2}{\sigma_1} \right)^2 \frac{\partial C}{\partial T_i} = 0 \quad \cdots \cdots (1)$$

The partial derivatives of $A$, $B$ and $C$ with respect to $T_i$ can be obtained on substituting their values in terms of $\sigma_2$ to $\sigma_k$. Thus

$$\frac{\partial A}{\partial T_i} = \sum_{j=2}^{k} \left( \frac{s_j}{\sigma_j} \right)^2 \frac{\partial \sigma_j}{\partial T_i}, \quad \frac{\partial B}{\partial T_i} = \sum_{j=2}^{k} (j - 1) \frac{\partial \sigma_j}{\partial T_i} \quad \frac{\partial C}{\partial T_i} = \sum_{j=2}^{k} j \frac{\partial \sigma_j}{\partial T_i}.$$

It may be seen from Weinstein’s equations that elimination of $\sigma_0$ and $\sigma_1$ automatically eliminates $T_0$ and $T_1$ and that $\frac{\partial \sigma_2}{\partial T_2} = \frac{1}{4}, \frac{\partial \sigma_2}{\partial T_3} = \frac{3}{8}, \frac{\partial \sigma_2}{\partial T_3} = \frac{3}{8}, \text{etc.}$

From the partial derivative of equation (1) with respect to $T_2$ we obtain

$$\left( \frac{s_2}{\sigma_2} \right)^2 = 2 \left( \frac{s_1}{\sigma_1} \right)^2 - \left( \frac{s_0}{\sigma_0} \right)^2 \quad \cdots \cdots (2)$$

Taking the partials with respect to $T_3$, and subtracting (2) multiplied by $\frac{\partial \sigma_2}{\partial T_3}$, gives

$$\left( \frac{s_3}{\sigma_3} \right)^2 = 3 \left( \frac{s_1}{\sigma_1} \right)^2 - 2 \left( \frac{s_0}{\sigma_0} \right)^2 \quad \cdots \cdots (3)$$

So we may proceed, through $T_k$.  

Now, substituting the values of $\sigma_2 \cdots \sigma_k$ from (2), (3), etc. into conditions 1' and 2, we obtain

\[
\left( \frac{\sigma_0}{\sigma_0} \right) \sum_{i=0}^{k} s_i (ix^2 - i + 1)^{-1/2} = 1 \quad \cdots \cdot (4)
\]

\[
\left( \frac{\sigma_0}{\sigma_0} \right) \sum_{i=0}^{k} s_i (ix^2 - i + 1)^{1/2} = \frac{G}{N} + 1 \quad \cdots \cdot (5)
\]

where $x$ represents $s_1 \sigma_0 / s_0 \sigma_1$.

Eliminating $\sigma_0$ between (4) and (5) gives the following, with $x$ as the only unknown.

\[
\sum_{i=0}^{k} s_i (ix^2 - i + 1)^{-1/2} \cdot \sum_{i=0}^{k} s_i (ix^2 - i + 1)^{1/2} = \frac{G}{N} + 1 \quad \cdots \cdot (6)
\]

approximately $[1 \pm (g/NV)^{1/2}]$ where $V$ is the variance of the observed strand ranks. The larger root relates to the lower fiducial limit; the smaller, to the upper. Each can be computed, to any desired degree of accuracy, by some successive approximation method like the Newton-Raphson (WHITTAKER and ROBINSON 1944). The result can be substituted into either (4) or (5) to find $s_0$ which, in turn, with $x$ gives $s_1$. Then $\sigma_2 \cdots \sigma_k$ can be calculated from (2), (3), etc. Finally the two sets of values of $\sigma_0 \cdots \sigma_k$ are put into Weinstein's equations to determine the lower and upper fiducial limits of the tetrad frequencies, as defined above.

The whole process is rather tedious, especially evaluating $x$. A close enough approximation, for most purposes, can be gotten from the first five terms of a Taylor-expansion of (6). Using $\delta$ to represent $(x - 1)$, $T$ for the ratio of third central moment to variance of observed strand ranks, and $F$ for the ratio of fourth central moment to variance,

\[
\delta^2 [1 - [2T + 4t_s - 1] \delta + [3.75F + 3(4t_s - 1)T + 6t_s(2t_s - 1) + 0.25 (1 - 3V)] \delta^2] = G/NV \quad \cdots \cdot (7)
\]

This too has to be handled by successive approximation but seems generally to require much less effort than (6).

An example of the outcome of such fiducial limit calculations is shown in table 1. It will be noticed that upper and lower limits are not equally above and below the observed. The asymmetry is not very large, in the present case, because $N$ is very large; it may, however, be considerable in smaller experiments.

The upper fiducial limits we have obtained are not wholly satisfactory: we have rejected universes with some tetrads of rank higher than any in the observed strands. Judging from the sharp decline in frequency with rank, in the higher strand ranks, we need to worry only about tetrads of one higher rank than the highest observed strands. For these allowance can be readily made, as follows: We calculate, for the sample with which we are concerned, the value of $\sigma_{k+1}$ for which the likelihood of $s_{k+1} = 0$ is some assigned value, generally the same as the fiducial probability corresponding to our chosen value of $G$. (This will usually violate the rule that, in a $x^2$ calculation, no expected class frequency should be less than 5. If it is preferred to adhere to that rule, $\sigma_{k+1}$ may be taken as $5/N$ which is equivalent to choosing a likelihood of .0067 for $s_{k+1} = 0$.) The effects of allowing $\sigma_{k+1} \neq 0$ are: i. to replace $G$ by
TABLE 1

Fiducial limits of strand and tetrad rank-frequencies

<table>
<thead>
<tr>
<th>Rank</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed strand frequency</td>
<td>6607</td>
<td>7555</td>
<td>1913</td>
<td>61</td>
</tr>
<tr>
<td>Lower limit, P = .01, equation 7</td>
<td>6795.6</td>
<td>7463.7</td>
<td>1820.7</td>
<td>56.1</td>
</tr>
<tr>
<td>Lower limit, .05, 7</td>
<td>6762.5</td>
<td>7480.5</td>
<td>1836.2</td>
<td>56.9</td>
</tr>
<tr>
<td>Lower limit, .05, 6</td>
<td>6762.3</td>
<td>7480.6</td>
<td>1836.2</td>
<td>56.9</td>
</tr>
<tr>
<td>Upper limit, .05, 7</td>
<td>6456.1</td>
<td>7619.2</td>
<td>1995.4</td>
<td>65.4</td>
</tr>
<tr>
<td>Upper limit, .01, 7</td>
<td>6425.4</td>
<td>7630.7</td>
<td>2012.9</td>
<td>67.1</td>
</tr>
</tbody>
</table>

Tetrad frequency

<table>
<thead>
<tr>
<th>Rank</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower limit, .01, 7</td>
<td>1096.6</td>
<td>7981.1</td>
<td>6609.8</td>
<td>448.6</td>
</tr>
<tr>
<td>Lower limit, .05, 7</td>
<td>1061.3</td>
<td>7957.6</td>
<td>6662.0</td>
<td>455.1</td>
</tr>
<tr>
<td>Lower limit, .05, 6</td>
<td>1061.0</td>
<td>7957.5</td>
<td>6662.6</td>
<td>454.9</td>
</tr>
<tr>
<td>Maximum likelihood</td>
<td>904</td>
<td>7824</td>
<td>6920</td>
<td>488</td>
</tr>
<tr>
<td>Upper limit, .05, 7</td>
<td>766.8</td>
<td>7649.5</td>
<td>7196.3</td>
<td>523.4</td>
</tr>
<tr>
<td>Upper limit, .01, 7</td>
<td>740.5</td>
<td>7612.4</td>
<td>7246.2</td>
<td>536.9</td>
</tr>
</tbody>
</table>

Drosophila melanogaster X chromosome data of Bridges in Morgan, Bridges and Schultz (1935).

TABLE 2

A comparison of upper fiducial limits of strand and tetrad rank-frequencies calculated in two ways: A, highest tetrad rank same as highest strand; B, highest tetrad rank one higher than highest strand

<table>
<thead>
<tr>
<th>Rank</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>P = .05 A</td>
<td>6456.1</td>
<td>7619.2</td>
<td>1995.4</td>
<td>65.4</td>
</tr>
<tr>
<td>B</td>
<td>6477.5</td>
<td>7607.8</td>
<td>1981.6</td>
<td>65.1</td>
</tr>
<tr>
<td>P = .01 A</td>
<td>6425.4</td>
<td>7630.7</td>
<td>2012.9</td>
<td>67.1</td>
</tr>
<tr>
<td>B</td>
<td>6446.1</td>
<td>7619.8</td>
<td>1999.2</td>
<td>66.2</td>
</tr>
</tbody>
</table>

Data of Bridges, in Morgan, Bridges and Schultz (1935).

The χ² for (k + 1) degrees of freedom, rather than k; ii. to alter the right-hand side of (4), (6) and (7), respectively, to \((1 - \sigma_{k+1}), (G/N + 1) (1 - \sigma_{k+1})\) and \[((G/N + 1) (1 - \sigma_{k+1}) - 1)/V\). Once these changes have been made the procedure in evaluating \(\sigma_0 \cdots \sigma_k\) is exactly as before. An example of the results, with the corresponding values for \(\sigma_{k+1} = 0\), is shown in table 2.

SUMMARY

1. Although Weinstein's equations (1936) give maximum likelihood estimates of the crossover-rank frequencies in the universe of tetrads from which a given sample of strands was derived, just as with every estimate of universe parameters from sample statistics other estimates within a certain range cannot be rejected.
2. Where four or more strand ranks are observed, the limits of the range form a closed shell of three or more dimensions containing, of course, infinite possible sets of tetrad-rank frequencies each of which could be regarded as a fiducial limit of the maximum likelihood estimate.

3. Among these infinite points three seem to be of principal interest:
   (i.) that set of tetrad-rank frequencies for which (a) the $\chi^2$ of the observed strand-rank frequencies would be some specified value, generally corresponding to $P$ between .01 and .05, and (b) the average number of crossovers per tetrad is least;
   (ii.) that set of tetrad-rank frequencies having (a) the same value of $P$ and (b) the highest average number of crossovers per tetrad;
   (iii.) like (ii) but including some tetrads one rank higher than the highest observed strand rank, in a proportion such that absence of strands of the same rank from the given sample would have some specified probability.

4. The lower and two upper fiducial limits, so defined, can be calculated by methods derived and illustrated here.

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To Professor Sewall Wright, of the University of Wisconsin, we express warm gratitude for checking and, in part, amplifying the argument in this manuscript.

K. W. Cooper, University of Rochester.

LITERATURE CITED

