LETTERS TO THE EDITORS

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A Combinatorial Formulation of Multiple Linkage Tests

SEVERAL recent publications[1-4] have suggested that a rational basis for the quantitative analysis of the ideas (interference, coincidence, etc.) arising in the study of genetic recombination will be found in the use of a mapping metric, differing from 'map distance', in that interference phenomena shall now be uniform. Among the forms discussed by Owen, one of great elegance and comparative simplicity gives to intercept lengths of long chromosome arms the distribution of $\chi^2/4$ for four degrees of freedom.

It has recently been shown that in this case the observable frequencies of the recombination classes among any number of marked loci on the same finite arm may be expressed explicitly in terms of the lengths of the segments between the centromere, the marked loci, and the terminus, by the combinatorial permutation of a system of rather simple algebraic functions. If we define :

$$\begin{aligned}
\alpha(x) &= 1 + \frac{1}{4!}x^4 + \frac{1}{8!}x^8 + \quad \ldots, \\
\beta(x) &= x + \frac{1}{5!}x^5 + \frac{1}{9!}x^9 + \quad \ldots, \\
\gamma(x) &= \frac{1}{2!}x^2 + \frac{1}{6!}x^6 + \frac{1}{10!}x^{10} + \quad \ldots, \\
\delta(x) &= \frac{1}{3!}x^3 + \frac{1}{7!}x^7 + \frac{1}{11!}x^{11} + \quad \ldots,
\end{aligned}$$

so that

$$\begin{aligned}
\alpha + \gamma &= \cosh x, \quad & \alpha - \gamma &= \cos x, \\
\beta + \delta &= \sinh x, \quad & \beta - \delta &= \sin x,
\end{aligned}$$

and differentiation with respect to x permutes the symbols in the order $(\delta\gamma\beta\alpha)$, then we may associate residual values (mod 4) of 0 with α, $+1$ with β and -1 with δ. The arguments of the symbols are then to be each twice the metrical value of the corresponding segment. For the frequency of non-recombinants in all segments, we write down all possible successions of the symbols α, β and δ, beginning with α or β for the segment next to the centromere, and ending with α or δ for the terminal segment, such that the sum of the residues of no succession of symbols shall exceed unity in absolute value, while the sum for all shall be zero. Thus for four markers and five segments we have :

$$\begin{array}{llll}
\alpha\alpha\alpha\alpha\alpha & \alpha\alpha\alpha\beta\delta & \beta\alpha\delta\alpha\alpha & \beta\alpha\alpha\alpha\delta \\
\alpha\beta\alpha\delta\alpha & \alpha\alpha\beta\alpha\delta & \beta\alpha\alpha\delta\alpha & \beta\alpha\delta\beta\delta \\
\alpha\alpha\beta\delta\alpha & \alpha\beta\alpha\alpha\delta & \beta\delta\alpha\alpha\alpha & \beta\delta\beta\alpha\delta \\
\alpha\beta\delta\alpha\alpha & \alpha\beta\delta\beta\delta & \beta\delta\beta\delta\alpha & \beta\delta\alpha\beta\delta
\end{array}$$

If recombination occurs in any segment, the symbols of the corresponding column are all permuted according to the permutation $(\alpha\gamma)(\beta\delta)$. If, for example, there is no genetic marker at the centromere, or at the terminus, the distinguishable classes of offspring will have frequencies found by substituting $\alpha + \gamma$ for α and $\beta + \delta$ for β or δ, in the first and fifth segments, giving, in place of the formula above :

$$(\alpha + \gamma) \begin{Bmatrix} \alpha\alpha\alpha \\ \beta\alpha\delta \\ \alpha\beta\delta \\ \beta\delta\alpha \end{Bmatrix} (\alpha + \gamma) \qquad (\beta + \delta) \begin{Bmatrix} \alpha\delta\alpha \\ \alpha\alpha\delta \\ \delta\alpha\alpha \\ \delta\beta\delta \end{Bmatrix} (\alpha + \gamma)$$

$$(\alpha + \gamma) \begin{Bmatrix} \alpha\alpha\beta \\ \alpha\beta\alpha \\ \beta\alpha\alpha \\ \beta\delta\beta \end{Bmatrix} (\beta + \delta) \qquad (\beta + \delta) \begin{Bmatrix} \alpha\alpha\alpha \\ \alpha\delta\beta \\ \delta\beta\alpha \\ \delta\alpha\beta \end{Bmatrix} (\beta + \delta)$$

in which only three columns remain to give by permutation of symbols the eight observable frequencies of a four-point test. However, in the heterogametic sex of many organisms, sex itself acts as a terminal marker for the pairing segment (Z) of the sex-chromosome, while the centromere acts, to some extent, as a marker in tetrad analysis.

By adding all permutations it is easily verified that the sum of all recombination classes is always $\cosh U$, where U is twice the metrical length of the chromosome arm. This is, therefore, a constant divisor for finding absolute frequencies.

The differential coefficient with respect to variation of the metrical length of any single segment will therefore be found by using the permutation $(\delta\gamma\beta\alpha)$ in the appropriate column, and deducting the original value multiplied by $\tanh U$. The frequencies will, of course, be relatively insensitive to variation in the unmarked segments.

The functions employed must have appeared repeatedly in the analysis of diverse problems ; I am not aware that they have any accepted notation. What is remarkable is that, by their aid, the multiplicity of all possible modes of gamete formation, and their functional dependence upon a number of parameters, should be expressible in terms of a single, easily remembered rule.

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[1] Fisher, Lyon and Owen, *Heredity*, **1**, Pt. 3, 355 (1947).
[2] Fisher, R. A., *Biometrics*, **4**, 1 (1948).
[3] Owen, A. R. G., *Proc. Roy. Soc.*, B, **136**, 67 (1949).
[4] Owen, A. R. G., "Advances in Genetics", **3**, 117 (1950).

Vibration Measurement by Interferometry

IN the experimental investigation of the problem of isolating very sensitive measuring instruments from the effects of building vibration, it has been found desirable to measure amplitudes of the order of $0{\cdot}25\,\mu$ (10^{-5} in.). Optical interference methods have been investigated and used by Thomas and Warren[1], Osterberg[2], Cortez[3], Kennedy[4] and other workers. Multiple-beam interference methods, however, have not been applied by these workers. Tolansky and Bardsley[5] have demonstrated the use of multiple-beam methods in studying vibration in quartz crystals. The use of multiple-beam interference techniques in conjunction with stroboscopic techniques offers a method of calibrating the most sensitive vibration detectors in terms of light waves to a high precision.

If the two silvered plates making up the interferometer unit in a multiple-beam Fizeau fringe system are made to vibrate relatively to one another, each bright fringe in the case of a transmission system widens into a broad band. The width of this band in terms of the fringe-spacing determines the displacement of one plate relative to