Genetic parameter estimation. A general-purpose maximum likelihood program: J. ROSTRON (*North East London Polytechnic*)

This program, written in SNOBOL and implemented on an ICL 1900 computer, was described. It takes as input firstly formulae for various phenotypic classes, then the frequencies for each class. After supplying a plausible starting value it estimates the parameters in the formulae using maximum likelihood methods and the Newton–Raphson iteration. The parameters are given, with sampling errors, as are any secondary parameters derivable from them.

Ascertainment when the trait has a variable age of onset: S. P. SIMPSON (*University of Sheffield*)

We are often interested in studying rare genetic traits. In order to do so individuals are ascertained and their families brought into the study. These sets of related individuals rarely constitute a random sample. It is possible to ascertain individuals or probands at random and include their sibs and parents in the study. The occurrence of affecteds is often so sparse as to render this method practically useless. Sibships may be brought into the study via the ascertainment of affected probands only. Each sibship contains at least one affected individual and sibships have unequal probabilities of ascertainment. Biases, so caused, can be removed from the likelihood by Weinberg's proband method, for example, but the most satisfactory approach is to condition the likelihood upon the ascertainment event, the presence of at least one affected ascertained individual (Morton (1959), Thompson and Cannings (1979)). This is readily done for sibships of fixed size.

In order to study more complex genetic models pedigrees, or extended families, may be ascertained via an affected individual using some ill-defined sequential sampling rule. The removal of biases due to ascertainment now becomes extremely difficult since the structure of the ascertained pedigree must be taken into account. This problem is avoided if a suitable sequential sampling rule is employed. If the choice of individuals to be included in the pedigree is based only on the observations of individuals already in the pedigree, it is sufficient to condition on the affected status of the proband (Cannings and Thompson (1977)). For example, we may choose to include those individuals who are expected to be the most informative, i.e. those who maximise

$$E(\text{information}) = P(\text{affected})(\text{information} \mid \text{affected}) + P(\text{not affected})(\text{information} \mid \text{not affected}).$$

Many traits of interest have a late or variable age of onset. There will be individuals in the population who have the potential to become affected but are indistinguishable from normal individuals, and individuals who have the potential and are affected. Pedigrees may be ascertained using the method described above. Older individuals in the population will generally be more informative. If they have the potential to become affected they are more likely to express the affected phenotype. There will thus be a bias towards selecting older pedigrees and if the age of onset depends on the genotype there may be a bias towards certain genotypes. This is because P(affected) depends on the ages of the individuals to be included. This source of bias is avoided if we ignore the