INVESTIGATIONS OF HOMEOSTASIS AND OTHER GENETICAL PROBLEMS
USING VARIANCE COMPONENTS WITH APPLICATION TO HUMAN FAMILY DATA

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This thesis uses statistical models and computer simulations to investigate problems in genetics, in particular, the issue of heterozygote advantage. One of the ways in which it is believed that heterozygote advantage manifests itself is by the reduced effect that environmental changes have on heterozygous individuals, thus rendering their traits less variable than those of homozygotes.

Three data sets have been analysed in this thesis. The first consisted of 414 mother-newborn baby pairs for which nine quantitative traits and the genotypes of several polymorphic loci were available. This set was used in Chapter 3. The second consisted of 43 same-sex twin pairs for which height, IQ and six genotypes had been ascertained. The third data set consisted of 99 pairs of dizygous twins and the variable of interest was lung function. These two sets were used in chapter 4.

The first data set was used to investigate more appropriate statistical methods for analysing variances of several related traits. In particular, interest lay in finding statistical methods which were more appropriate than those used in earlier work on this problem. Methods such as multivariate parametric and nonparametric tests for equality of dispersion matrices were found to be superior to multivariate coefficients of variation and principal components analysis. The appropriateness of the data to the problem of examining heterozygote advantage has also been discussed.

These data were also used to consider an adaptive distances model, an alternative approach suggested in the literature. The problems of fitting this model in practice have been discussed fully in Chapter 3.

In the final part of Chapter 3 a new way of estimating heritability using multivariate analysis of variance (MANOVA) has been suggested. The third data set was also used to estimate heritability by the MANOVA method but was less successful and these results appear in the final part of Chapter 4.

Most of Chapter 4 is concerned with modifying a pedigree model to include components of variance for heterozygotes and homozygotes. The pedigrees used were the twin pairs of the second data set.

Previous research reported in the literature has found that if all the alleles at a locus act additively on a particular trait and if there are several such loci all acting additively then the variance of the trait will decrease with increasing heterozygosity, even though there may be no heterozygote advantage *per se*. Other research has shown that this effect depends on the relative frequencies of different alleles, when there are more than two alleles at each locus. In chapter 2 of this thesis, algebraic calculations and computer simulations have been used to show that these effects change if the assumptions of additivity are relaxed.

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