

## Chapter 4

# Genetic Linkage

### 4.1 Linkage and recombination: genetic distance

Contrary to Mendel's second law (Mendel, 1866), there is dependence in the inheritance of genes at syntenic loci (that is, loci on the same chromosome pair). Such loci are said to be *linked*. Where the data are affected by the alleles at more than one locus on a chromosome pair, it is no longer sufficient to consider the inheritance of genes at each locus separately.

Recall the meiosis indicators of (equation (1.2)):

$$\begin{aligned} S_{i,j} &= 0 && \text{if copied gene at meiosis } i \text{ locus } j \text{ is parent's maternal gene} \\ &= 1 && \text{if copied gene at meiosis } i \text{ locus } j \text{ is parent's paternal gene.} \end{aligned}$$

Here  $i = 1, \dots, m$  indexes the meioses of the pedigree, and  $j = 1, \dots, L$  indexes the genetic loci. The marginal distribution of each  $S_{i,j}$  is as before (section 1.2):

$$\Pr(S_{i,j} = 0) = \Pr(S_{i,j} = 1) = \frac{1}{2}.$$

For different meioses  $i$ , the  $S_{i,j}$  are independent.

We say that, in a given meiosis, *recombination* has occurred between two loci  $j$  and  $l$ , if the genes segregating to the gamete at these two loci are from different parental chromosomes. That is, they derive from different grandparents. For two loci, we do not need a full model for the vector  $S_{i,\bullet}$  (equation 1.3). The pairwise distribution of  $(S_{i,j}, S_{i,l})$  is determined by the *recombination frequency*, which is a measure of the dependence in inheritance between the two loci. For two given loci ( $l$  and  $j$ ) the recombination frequency  $\rho$  between them is

$$(4.1) \quad \rho = \Pr(S_{i,l} \neq S_{i,j}) \quad \text{for each } i, \quad 0 \leq \rho \leq \frac{1}{2}.$$

For loci that are close together on a chromosome,  $\rho$  is close to 0. For independently segregating loci,  $\rho = \frac{1}{2}$ . Note that, although  $\theta$  is the notation often used for the