Exercise 2.2

QTL analysis and Interval mapping

Problem 1

Aim

Determine QTL-marker association of 4 marker loci, make inferences about effect and location of QTL, and determine whether the markers in this example can be used in a selection program.

Case study

A dairy bull is genotyped for 10 markers, and he was found to be heterozygous for 4 markers (A,B,C and D). In 100 of his 150 female offspring it was possible to determine which of the two marker alleles was obtained from the sire. Each of these female offspring produces a lactation record on milk production. The population average for milk production per lactation (corrected to a 305 days lactation period) is equal to 5000 Kg. The means for each group of offspring for the following paternal marker alleles was:

A1-	**5025**	**C1-**	**4850**
A2-	4975	C2-	5150
B1-	5200	D1-	5060
B2-	4800	D2-	4940

Based on linkage analysis, we know that marker A is located on chromosome 1, markers B and C are located on chromosome 4 and marker D is located on chromosome 19. The genetic distance between markers B and C has previously been estimated at 30cM with marker B at about 20 cM from the telomeric end.

Assume the group size of offspring for each marker allele was equal to 50. Also assume that the mean given are corrected for differences due to herd, age and season of calving etc. The within half-sib family standard deviation of milk production (for one lactation) is equal to 500kg.

- Test for each of the marker alleles whether there is a significant difference between the marker-haplotype groups.
  You can use a t-test, assuming that the variance of the difference between two progeny group means is equal to $2\sigma^2/n$, where σ is equal to the within half sib family standard deviation, and n is the number of individuals in one marker-allele group.

- What does a significant group difference tell you about the existence of a putative QTL.

- Is it possible based on the information given to estimate the allele substitution effects of the QTL?
- Try to work out an expression where the difference between the marker-allele progeny groups is a function of the allele substitution effect and the recombination rate of QTL and marker.
- Can you give an indication of which marker haplotype is associated with the positive QTL-allele?
- What can you say about the location of the QTL?
- Describe how the current information could help in selection decisions in the breeding program, based on marker genotype information.

Problem 2

Consider two markers that are 40 cM apart. The alleles are M1/m1 at locus 1 and M2/m2 at locus 2.

- Calculate the recombination frequency between the markers, assuming Haldane's mapping function
- Calculate the recombination frequency, assuming Kosambi's mapping function

From now on we will use Haldane's mapping function.

Now assume there is a QTL effect at 10 cM from the first marker locus. The QTL has two alleles (Q/q). Consider a bull that has received a M1QM2 gamete from the sire and a m1qm1 gamete from the mother.

- What are the expected paternal marker haplotype frequencies in the offspring from this bull?
- What are the recombination frequencies between the marker loci and the QTL.
- How many paternal haplotypes for the three loci (M1-Q-M2) can be found in the offspring from this bull? What are their expected frequencies?
- Calculate conditional probabilities for carrying the Q-allele for each paternal marker haplotype.
- Calculate expected phenotypic means for each group of progeny of a particular paternal marker haplotype, given the genotypic means of QQ, Qq and qq genotypes are 9, 10 and 11, respectively. Assume that the dams of the progeny contribute q alleles only.