

**Chapter 6**

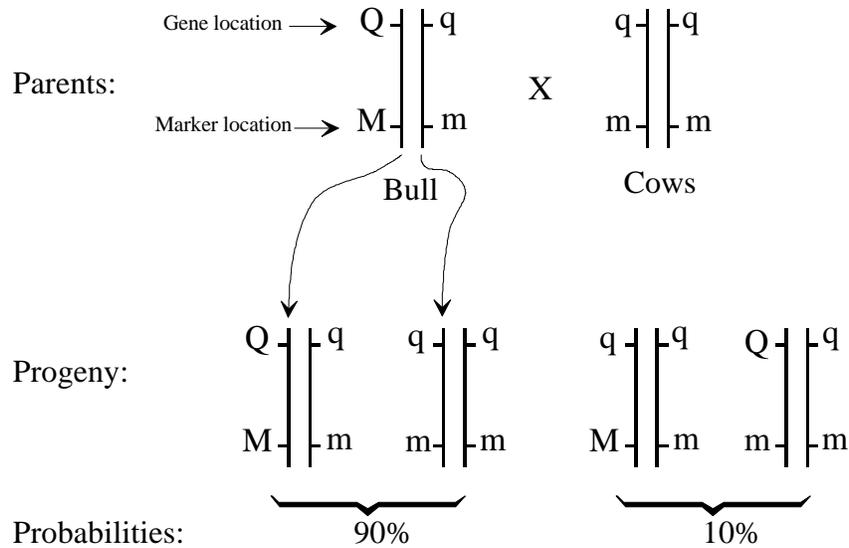
**Determining associations between genetic markers  
and QTL with single markers**

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Detecting QTL segregation in a sire family .....56  
    The need to treat each sire family separately .....57  
    Expected progeny means.....57  
    Interpreting results .....57  
    The effect of QTL status in dams .....58  
More powerful approaches .....59

### Detecting QTL segregation in a sire family

Consider a sire that is heterozygous for both genetic marker ( $M, m$ ) and QTL ( $Q, q$ ). We can actually determine his marker genotype from a DNA test, but his QTL genotype can only be postulated. Consider only 'informative progeny' that is, progeny from whom we know which of the marker alleles they obtained from their sire. This is true in the following diagram where all dams are recessive  $mm$ :



The next table shows what kind of progeny will be in the group, with their frequencies.

What is important here are

- The *recombination rate* between marker allele and QTL allele (taken as 10% above). This is indicated by the symbol  $r$ .
- The difference between progeny receiving  $Q$  vs. progeny receiving  $q$  from their sire. This is equal to the allele-substitution effect with the symbol  $\alpha$ .

| Parental genotype: |     | $M$            | $Q$ |                    |
|--------------------|-----|----------------|-----|--------------------|
|                    |     | $m$            | $q$ |                    |
| Possible gametes   |     | recombination? |     | gamete probability |
| $M$                | $Q$ | no             |     | $(1-r)/2$          |
| $m$                | $Q$ | yes            |     | $r/2$              |
| $M$                | $q$ | yes            |     | $r/2$              |
| $m$                | $q$ | no             |     | $(1-r)/2$          |

### ***The need to treat each sire family separately***

Note that, using this simple approach, these probabilities hold only within the progeny group of a given sire. In another family, the sire may have another QTL-allele associated with the M-allele.

### ***Expected progeny means***

For the given QTL effect we can now work out the expected progeny means of each marker group within the sire's progeny group:

| Marker allele<br>mean obtained from<br>sire group | QTL allele<br>obtained from sire | frequency | Expected<br>of progeny |
|---|----------------------------------|-----------|------------------------|
| M   | Q                                | $(1-r)/2$ | $\mu + \alpha$         |
| M   | q                                | $r/2$     | $\mu$                  |
| m   | Q                                | $r/2$     | $\mu + \alpha$         |
| m   | q                                | $(1-r)/2$ | $\mu$                  |

From the previous table we can work out the expected difference between the M-group and the m-group:

|                  |   |                      |
|------------------|---|----------------------|
| Mean of M-group: | $((1-r)(\mu + \alpha)/2 + r.\mu/2) / 0.5 =$ | $\mu + (1-r) \alpha$ |
| Mean of m-group: | $(r.(\mu + \alpha)/2 + (1-r).\mu/2)/0.5 =$  | $\mu + r \alpha$     |
| Difference (D)   |   | $(1-2r)\alpha$       |

### ***Interpreting results***

If there is no difference between the M-group and the m-group of progeny, then we have no evidence of a QTL. It could be that there is a QTL that is linked to the marker, but its recombination rate with the marker must be close to 0.5 (= unlinked), and/or its effect is small.

If we do find a progeny group difference (within the sire), it means that there is an association. However, we can't distinguish between a large QTL effect that is loosely linked ( $\alpha$  high and  $r$  high) or a smaller effect that is tightly linked ( $\alpha$  low and  $r$  low), as  $\alpha$  and  $r$  cannot be untangled in  $(1-2r)\alpha$ .

The following Table shows some possible combinations of recombination rate ( $r$ ) and QTL effect ( $\alpha$ ) giving rise to the same difference ( $D$ ) between marker genotype groups within the sire's progeny.

| Recombination rate M-Q ( $=r$ ) | QTL-effect (Q-q substitution $=\alpha$ ) | Mean of progeny <sup>1</sup> receiving M-allele | Mean of progeny <sup>1</sup> receiving m-allele | Marker allele contrast ( $D$ ) |
|---------------------------------|--|---|---|--------------------------------|
| 0                               | 50                                       | 50  | 0   | 50                             |
| 0.1                             | 62.5                                     | 56.25   | 6.25  | 50                             |
| 0.2                             | 83                                       | 67  | 17  | 50                             |
| 0.3                             | 125                                      | 87.5  | 37.5  | 50                             |
| 0.4                             | 250                                      | 150   | 100   | 50                             |
| 0.5                             | 1000                                     | 500   | 500   | 0                              |

<sup>1</sup> Mean is relative to the progeny receiving a q-allele from the sire.

### ***The effect of QTL status in dams***

Note that until now we have not worried what kind of alleles progeny would receive from their dam. In a way, this is not relevant for determining a marker-QTL association, as long as the dams are randomly distributed over the two marker groups of progeny (it is hard to be non-random here!). The dam population is relevant if we want to interpret the allele substitution effect ( $\alpha$ ). The possibilities are:

| Dam population contributes                     | The allele substitution effect ( $\alpha$ ) represents           |
|--|--|
| Only q-alleles                                 | Difference between Qq and qq genotypes:<br>$\mu_{qQ} - \mu_{qq}$ |
| Only Q-alleles                                 | Difference between QQ and Qq genotypes:<br>$\mu_{QQ} - \mu_{qQ}$ |
| Q in frequency $p$ ,<br>q in frequency $(1-p)$ | $p(\mu_{QQ} - \mu_{qQ}) + (1-p)(\mu_{Qq} - \mu_{qq})$            |

As in Falconer's book, we can define the following symbols for the means of the three possible genotype:

$$\begin{array}{ll} \mu_{QQ} & +a \\ \mu_{qQ} & d \\ \mu_{qq} & -a \end{array}$$

Where  $d$  is 'dominance' is the deviation of the heterozygote from the homozygote mean. In general, the Q-allele substitution effect can then be written as  $\alpha = a + (q-p)d$ . This shows that the QTL effect found in the sire's progeny is likely to be different when the sire is mated to another dam population (another breed), as the  $p$  ( $=\text{freq}(Q)$ ) is likely to be different in this other population.

**More powerful approaches**

If we take account of the whole pedigree then we have some power to infer not just  $\alpha$  under current conditions, but also  $a$  and  $d$ . This requires genotype information on sufficient animals (ideally on all animals) and use of statistical methods that we will cover later in the course.