Lecture 12

Experimental strategies for QTL detection

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Molecular Genetic Strategies for QTL Detection

Genome Scan Approach

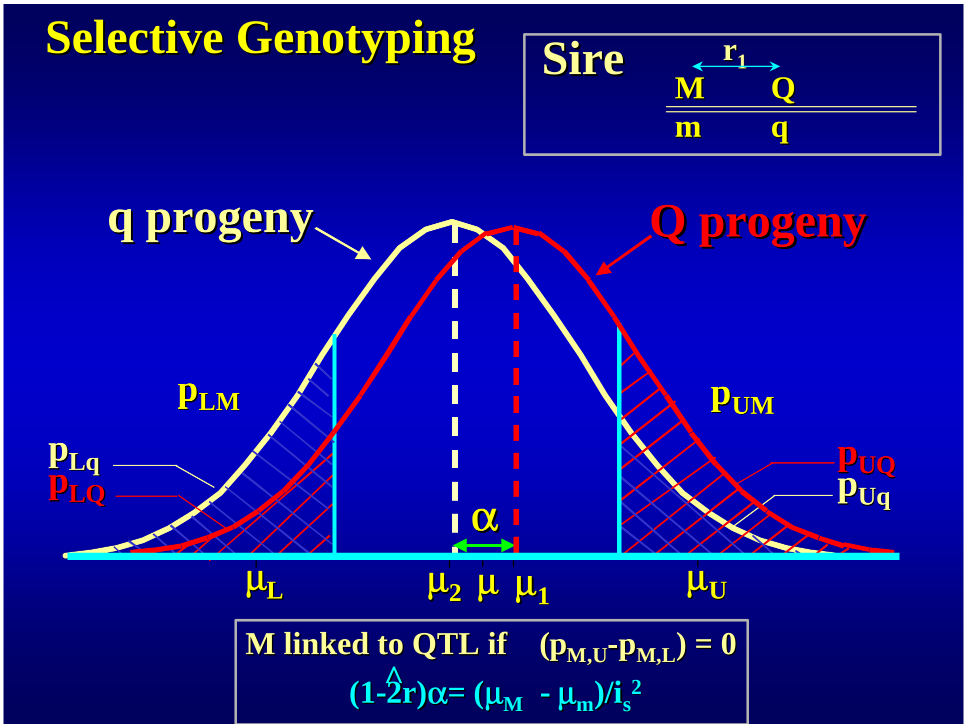
- Anonymous genetic markers placed across genome (every 20 cM)

M_1	M_2	M_3	Q	M_4	M_5	M_6
m_1	m_2	m_3	q	m_4	m_5	m_6

- Look for association of markers with trait phenotype
- Requires populations segregating for QTL and markers
- Requires linkage disequilibrium between markers and QTL
  - marker and QTL (expected to be) in population-wide equilibrium (unless tightly linked)
  - Need specific family/resource population designs that generate sufficient linkage disequilibrium

Populations designs for marker QTL mapping

- Crosses between inbred (preferred) or outbred lines
  - must differ in QTL frequency
  - Back cross
  - F2 cross
  - Advanced intercrosses (F3, etc.)
- Within outbred populations
  - Half sib families
  - Full sib families
  - 3-generation families (e.g. grand daughter design)
  - Selective Genotyping
  - Selective DNA pooling (Bulk segregant analysis)



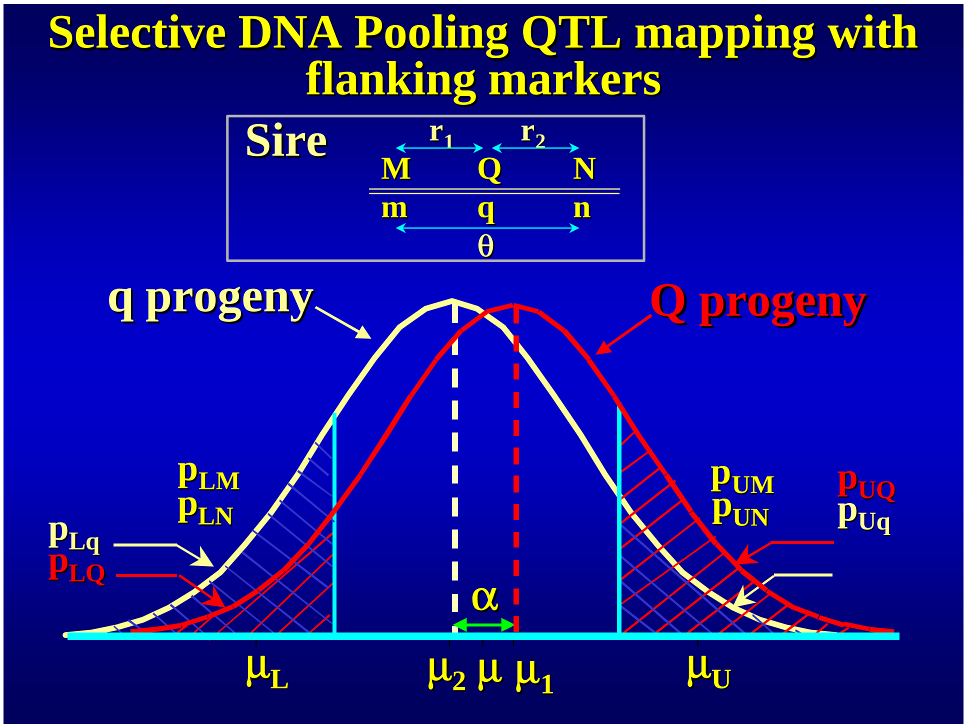
Power of alternative QTL mapping designs

For given number of animals genotyped

Candidate gene > F2 > BC > Fullsib > Halfsib

Strategies to reduce # genotypings

- **3-generation families** (grand-daughter design)
- **Selective genotyping**



Model for frequencies in upper tail

$E(p_{UM}|p_{UQ})$

Non recombinants — Recombinants — Sampling of Marker-QTL recombinants — Random technical error

$$p_{UM} = (1-r_1)p_{UQ} + r_1(1-p_{UQ}) + u_{UM} + e_{UM}$$

$$= r_1 + (1-2r_1)p_{UQ} + u_{UM} + e_{UM}$$

$$E(p_{UM}-p_{LM}) = (1-2r_1)(p_{UQ}-p_{LQ})$$

$$= (1-2r_1)(2p_{UQ}-1)$$

$(p_{UM}-p_{LM})$ *vs* $(p_{UN}-p_{LN})$ provides information on QTL position and effect

$$E(p_{UM}-p_{LM}) = (1-2r_1)(2p_{UQ}-1)$$

$$E(p_{UN}-p_{LN}) = (1-2r_2)(2p_{UQ}-1) = (1-2\theta)(2p_{UQ}-1)/(1-2r_1)$$

$$\hat{r}_1 = \tfrac{1}{2} - \tfrac{1}{2}\sqrt{[(1-2\theta)(p_{UM}-p_{LM})/(p_{UN}-p_{LN})]}$$

$$\hat{p}_{UQ} = \tfrac{1}{2} \pm \tfrac{1}{2}\sqrt{[(1-2\theta)(p_{UM}-p_{LM})(p_{UN}-p_{LN})]}$$

$$\hat{\alpha} = (\mu_M - \mu_m)/i_s^2$$

Selective Genotyping across the Population With linkage disequilibrium between the Marker and QTL