RESEMBLANCE BETWEEN RELATIVES

❑Objective:

Develop mathematical models that quantify/model resemblance between relatives for phenotypes of a quantitative trait :

- based on **pedigree**
- based on **markers**

- based on pedigree ←→ based on markers
- average across the genome ←→ at individual loci

Outlines:

- ✓ **Causal model for covariances between relatives**
- ✓ **Genetic covariances between relatives**
- ✓ **Deriving a causal model for covariances among relatives**
- ✓ **Identity By Descent, Coefficients of coancestry and additive and dominance relationships**
- ✓ **Causes of non-genetic covariances between relatives**
- ✓ **Variance of the average phenotype of a group of relatives**
- ✓ **Use of marker data to estimate resemblance at a linked locus using linkage and linkage disequilibrium information**

Why?

- **Resemblance between relatives can be used to estimate trait population parameters**
  - **estimate** genetic variances, heritabilities, etc.
  - **predict** breeding values using phenotypic data on relatives
  - detect, evaluate, and incorporate **QTL**

OBSERVATIONAL model

(STATISTICAL)

Degree of resemblance can be estimated from data by statistics

- **Correlation between phenotype of parent and offspring**
- **Regression of offspring on parent phenotype**
- **Covariance/correlation between sibs**
- **Analysis of variance**
- **Maximum likelihood**

CAUSAL model

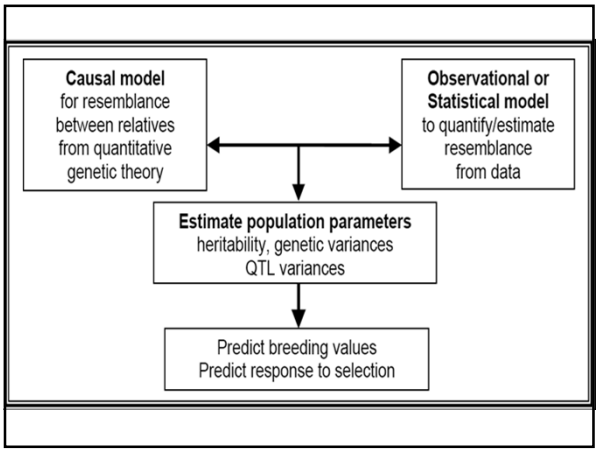
- ***Degree of (genetic) resemblance of relatives depends on:***

- genetic relationship between relatives

✓ proportion of alleles related individuals share / have in common/identical by descent

✓ coefficient of coancestry, genetic relationship

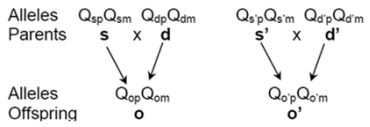
- variance components (additive, dominance, environmental)



A CAUSAL MODEL FOR GENETIC RESEMBLANCE BETWEEN RELATIVES

Consider two individuals, o and o'
with parents s, d and s', d'
and alleles at a locus **Q** denoted as:

Q_{ip} = **p**aternal allele for individual I = allele received from sire
Q_{im} = **m**aternal allele for individual I = allele received from dam



If **o** and **o'** are related and the trait has a genetic basis, **o** and **o'** will share alleles and have similar phenotype, i.e. a non-zero covariance: $cov(P_o,P_{o'})>0$.

Deriving a causal model for $cov(P_o,P_{o'})$

Phenotypes of individuals can resemble each other
because:
- **genetics, genetically related –**

and/or because:
- ***environment (e.g. lambs raised by the same dam or in the same pen):***

$$Cov(P_o,P_{o'}) = Cov(G_o+E_o,G_{o'}+E_{o'}) = Cov(G_o,G_{o'}) + Cov(E_o,E_{o'})$$

Model for GENETIC resemblance

First using single locus theory
(results apply to **QTs** under multi-loci)

Assume a phenotype by a single gene, along with environment

o carries alleles Q_{op} and Q_{om} (abbreviated by alleles op and om)

o' carries alleles $Q_{o'p}$ and $Q_{o'm}$ (abbreviated by alleles o'p and o'm)

α_{ip} = average effect of the paternal allele of individual i (= additive effect)

α_{im} = average effect of the maternal allele of individual i (= additive effect)

δ_{ipm} = dominance deviation for individual i

The model for genotypic values is: $G_o = \alpha_{op} + \alpha_{om} + \delta_{opm}$

$G_{o'} = \alpha_{o'p} + \alpha_{o'm} + \delta_{o'pm}$

$$Cov(G_o,G_{o'}) = Cov(\alpha_{op},\alpha_{o'p}) + Cov(\alpha_{op},\alpha_{o'm}) + Cov(\alpha_{om},\alpha_{o'p}) + Cov(\alpha_{om},\alpha_{o'p}) + Cov(\delta_{opm},\delta_{o'pm})$$

Are two alleles the same?

Identity By State (IBS) ***versus*** *Identity By Descent (IBD)*

IBS: *if we can genotype individuals* ***o*** *and* ***o'*** *for this locus (QTL), then we can directly determine whether the alleles the two individuals carry are indeed the same*

if they are the same, this is referred to as the alleles being ***IBS***

Are two alleles the same?

Identity By State (IBS) ***versus*** *Identity By Descent (IBD)*

IBD: *if cannot genotype, then cannot determine IBS directly but, if* ***o*** *and* ***o'*** *have a common ancestor => can determine the probability that the two alleles are identical*

- Prob(op is IBD to o'p) = P(op Ξ o'p)
  = probability that alleles op and o'p originated from the same allele of the common ancestor

Example IBD probabilities, coefficients of coancestry and additive and dominance coefficients

	IBD probabilities for pairs of alleles				Coancestry coefficient	Additive relationship coefficient	Dominance relationship coefficient
Individual o – o'	op–o'p	om–o'm	op–o'm	om–o'p	$f_{oo'}$	$r_{oo'}$	$u_{oo'}$
Sire(o) – Offspring(o')	½	0	0	½	¼	½	0
Dam – Offspring	0	½	½	0	¼	½	0
Paternal half-sibs	½	0	0	0	$^1/_8$	¼	0
Full sibs	½	½	0	0	¼	½	¼
Identical twins	1	1	0	0	½	1	1

Some side notes:

Coefficient of coancestry (also coeff. of kinship or consanguinity) between **o** and **o'**

= $f_{oo'}$ = probability that an allele drawn at random from **o** is IBD to an allele drawn random from **o'**
= average of the 4 possible IBD probabilities between alleles at o and o'

$r_{oo'} = 2f_{oo'}$ = **coefficient of relationship = additive genetic relationship coefficient**

NOTE: $f_{oo'}$ is also equal to the **coefficient of inbreeding** of a progeny produced by **o** and **o'**
= probability that an individual's alleles are IBD

Covariance between the average effect of allele ***p*** from **o** and allele ***p*** from **o'**:

$Cov(\alpha_{op},\alpha_{o'p}) = E(\alpha_{op}\,\alpha_{o'p}) - E(\alpha_{op})E(\alpha_{o'p})$ Note: $E(\alpha_{op})=E(\alpha_{o'p})=0$

2 possibilities: **op** and **o'p** are IBD or they are not IBD

$= E(\alpha_{op}\,\alpha_{o'p} \mid op \equiv o'p)\,Pr(op \equiv o'p) + E(\alpha_{op}\,\alpha_{o'p} \mid op \not\equiv o'p)\,Pr(op \not\equiv o'p)$

If IBD then: op = o'p and $\alpha_{op} = \alpha_{o'p}$

$= E(\alpha_{op}\,\alpha_{op})\,Pr(op \equiv o'p) = E(\alpha_{op}^2)\,Pr(op \equiv o'p)$

$= Pr(op \equiv o'p)Var(\alpha_p)$ Note: $Var(\alpha_p) = E(\alpha_p^2) - E(\alpha_p)^2$ but $E(\alpha_p)=0$

$= Pr(op \equiv o'p)\,\frac{1}{2}V_A$ Note that $Var(\alpha_p) = \frac{1}{2}V_A$

The same holds for the other pairs of alleles:

$Cov(\alpha_{om},\alpha_{o'm}) = Pr(om \equiv o'm)\,\frac{1}{2}V_A$

$Cov(\alpha_{op},\alpha_{o'm}) = Pr(op \equiv o'm)\,\frac{1}{2}V_A$

$Cov(\alpha_{om},\alpha_{o'p}) = Pr(om \equiv o'p)\,\frac{1}{2}V_A$

$Cov(G_o,G_{o'}) = Cov(\alpha_{op},\alpha_{o'p}) + Cov(\alpha_{op},\alpha_{o'm}) + Cov(\alpha_{om},\alpha_{o'p}) + Cov(\alpha_{om},\alpha_{o'p}) + Cov(\delta_{opm},\delta_{o'pm})$

$= \{ Pr(op \equiv o'p) + Pr(op \equiv o'm) + Pr(om \equiv o'p) + Pr(om \equiv o'm)\}\,\frac{1}{2}V_A + Cov(\delta_{opm},\delta_{o'pm})$

$= 2f_{oo'}V_A + Cov(\delta_{opm},\delta_{o'pm})$

$= r_{oo'}V_A + Cov(\delta_{opm},\delta_{o'pm})$

$Cov(\delta_{opm},\delta_{o'pm}) \neq 0$ only if:

(op $\equiv$ o'p ***and*** om $\equiv$ o'm) occurs with prob = Pr(op $\equiv$ o'p)*Pr(om $\equiv$ o'm)

OR (op $\equiv$ o'm ***and*** om $\equiv$ o'p) occurs with prob = Pr(op $\equiv$ o'm)*Pr(om $\equiv$ o'p)

Dominance relationship coeff. = $u_{oo'}$ = Pr(op $\equiv$ o'p)*Pr(om $\equiv$ o'm) + Pr(op $\equiv$ o'm)*Pr(om $\equiv$ o'p)

→ $Cov(\delta_{opm},\delta_{o'pm}) = E(\delta_{opm},\delta_{o'pm}) - E(\delta_{opm})E(\delta_{o'pm})$ $E(\delta_{opm})=E(\delta_{o'pm})=0$

$= E(\delta_{opm}^2)\, u_{oo'}$

$= Var(\delta_{ij})\, u_{oo'} = u_{oo'}V_D$ $Var(\delta_{ij}) = V_D$

→ $Cov(\delta_{opm},\delta_{o'pm}) = E(\delta_{opm},\delta_{o'pm}) - E(\delta_{opm})E(\delta_{o'pm})$ $E(\delta_{opm})=E(\delta_{o'pm})=0$

$= E(\delta_{opm}^2)\, u_{oo'}$

$= Var(\delta_{ij})\, u_{oo'} = u_{oo'}V_D$ $Var(\delta_{ij}) = V_D$

Thus: $\boxed{\mathbf{Cov(G_o,G_{o'}) = r_{oo'}V_A + u_{oo'}V_D}}$

Summing variances over loci ($\mathbf{V_A = \Sigma V_{Ai}}$), this equation also applies to multiple loci

Some example applications or coefficients of relationships:

Offspring-parent regression: how does offspring phenotype relate to parent phenotype?

$E(P_o|P_s) = \mu + b_{P_o,P_s}(P_s-\mu)$

$b_{P_o,P_s} = Cov(P_o,P_s)/Var(P_s)$

$= Cov(G_o,G_s)/Var(P_s) = (r_{os}V_A + u_{os}V_D)/V_P = \frac{1}{2}V_A/V_P = \frac{1}{2}h^2$

(Assume $Cov(E_o,E_s) = 0$)

Regression of offspring phenotype on parental average phenotype (mid-parent):

$\bar{P} = \frac{1}{2}(P_s+P_d)$

$b_{P_O\bar{P}} = \mathrm{Cov}(P_O,\bar{P})/\mathrm{Var}(\bar{P})$

$\mathrm{Cov}(P_O,\bar{P}) = \mathrm{Cov}[P_o,\frac{1}{2}(P_s+P_d)] = \frac{1}{2}\mathrm{Cov}(P_o,P_s) + \frac{1}{2}\mathrm{Cov}(P_o,P_d) =$

$= \frac{1}{2}\frac{1}{2}V_A + \frac{1}{2}\frac{1}{2}V_A = \frac{1}{2}V_A$

$\mathrm{Var}(\bar{P}) = \mathrm{Var}(\frac{1}{2}P_s+\frac{1}{2}P_d)) = \frac{1}{4}\mathrm{Var}(P_s) + \frac{1}{4}\mathrm{Var}(P_d) + \frac{1}{2}\mathrm{Cov}(P_s,P_d) = \frac{1}{2}V_P$

$b_{P_O\bar{P}} = \frac{1}{2}V_A/\frac{1}{2}V_P = V_A/V_P = h^2$

Correlation between half-sibs = *intra-class correlation*:

$t_{(HS)} = \mathrm{Cov}(P_o,P_{o'})/\sqrt{\mathrm{Var}(P_O)\mathrm{Var}(P_{O'})}$

$= \frac{1}{4}V_A/V_P = \frac{1}{4}h^2$

Correlation between full-sibs:

$t_{(FS)} = \mathrm{Cov}(P_o,P_{o'})/\sqrt{\mathrm{Var}(P_O)\mathrm{Var}(P_{O'})}$

$= (\frac{1}{2}V_A+\frac{1}{4}V_D)/V_P = \frac{1}{2}h^2 + \frac{1}{4}V_D/V_P$

Correlation between monozygotic twins:

$t_{(MZ)} = \mathrm{Cov}(P_o,P_{o'})/\sqrt{\mathrm{Var}(P_O)\mathrm{Var}(P_{O'})}$

$= V_G/V_P = H^2$ = broad sense heritability

Extension of causal model to include epistatic interactions

$\mathrm{Cov}(G_o,G_{o'}) = r V_A + uV_D + r^2V_{AA} + ruV_{AD} + u^2V_{DD} + r^3V_{AAA} + r^2uV_{AAD} + ru^2V_{ADD} + u^3V_{DDD} \ldots .$

Causal components to covariances of relatives

Relatives		V_A	V_D	V_{AA}	V_{AD}	V_{DD}
Offspring - Parent	Cov_{OP} =	½	-	¼	-	-
Half sibs	$\mathrm{Cov}_{(HS)}$ =	¼	-	$^1/_{16}$	-	-
Full sibs	$\mathrm{Cov}_{(HS)}$ =	½	¼	¼	$^1/_8$	$^1/_{16}$
General	Cov =	r	u	r^2	ru	u^2

ALTERNATIVE DERIVATION OF ADDITIVE COVARIANCES

based on *quantitative genetics algebra*

Model of phenotype: $P = A + E$ E includes D, I, environment

Offspring phenotype: $P_o = A_o + E_o = \frac{1}{2}A_s + \frac{1}{2}A_d + RA_s + RA_d + E_o$

$\frac{1}{2}$ * breeding value of parents

- Breeding value = $2*E(P_O)$
- Includes some dominance and epistatic effects

RA_s , RA_d = random assortment / Mendelian sampling terms
- sampling of 1 of 2 parent alleles at each locus during meiosis
- by definition independent from other terms: $Cov(A_s,RA_s) = 0$

Without inbreeding: $Var(RA_s) = \frac{1}{4}V_A$ $Var(RA_d) = \frac{1}{4}V_A$ (see derivation below)

With inbreeding: $Var(RA_s) = \frac{1}{4}(1-F_s)V_A$ $Var(RA_d) = \frac{1}{4}(1-F_d)V_A$

Thus: $Var(A_o) = Var(\frac{1}{2}A_s + \frac{1}{2}A_d + RA_s + RA_d) =$

$= \frac{1}{4}V_A + \frac{1}{4}V_A + \frac{1}{4}V_A + \frac{1}{4}V_A = V_A$ (no inbreeding or selection)

Single locus derivation of Var(RA)

Parent Geno-type	Fre-quen-cy	Genotypic value of parent [α=a+(q-p)d]		Offspring mean phenotype = ½*breeding value parent	Trans-mitted allele	Fre-quen-cy	Offspring mean phenotype	Mendelian sampling term (RA)
A_1A_1	p^2	a	$2q(\alpha-qd)$	$q\alpha$	A_1	1	$q\alpha$	0
A_1A_2	$2pq$	d	$(q-p)\alpha+2qd$	$\frac{1}{2}(q-p)\alpha$	A_1	½	$q\alpha$	$\frac{1}{2}\alpha$
					A_2	½	$-p\alpha$	$-\frac{1}{2}\alpha$
A_2A_2	q^2	$-a$	$-2p(\alpha+pd)$	$-p\alpha$	A_2	1	$-p\alpha$	0

$E(RA_s) = p^2(0) + 2pq\frac{1}{2}(\frac{1}{2}\alpha) + 2pq\frac{1}{2}(-\frac{1}{2}\alpha) + q^2(0) = 0$

Without inbreeding: $Var(RA_s) = p^2(0)^2 + 2pq\frac{1}{2}(\frac{1}{2}\alpha)^2 + 2pq\frac{1}{2}(-\frac{1}{2}\alpha)^2 + q^2(0)^2$

$= \frac{1}{2}pq\alpha^2 = \frac{1}{4}V_A$ $(V_A = 2pq\alpha^2)$

With inbreeding: F_s = Pr(two alleles in s are ibd) → $RA_s = 0$

$1-F_s$ = Pr(two alleles in s not ibd) → RA_s = as in Table above

$Var(RA_s) = F_s(0) + (1-F_s)\frac{1}{4}V_A = \frac{1}{4}(1-F_s)V_A$

Examples of application (considering additive effects/breeding values only):

Offspring-parent:

$Cov(P_o,P_s) = Cov(\frac{1}{2}A_s + \frac{1}{2}A_d + RA_s + RA_d + E_o , A_s + E_s)$
$= Cov(\frac{1}{2}A_s,A_s)$ *(assuming unrelated dam, no common environment)*
$= \frac{1}{2}V_A$

Offspring-mid-parent:

$Cov(P_o,\bar{P}) = Cov(P_o, \frac{1}{2}P_s+\frac{1}{2}P_d) = \frac{1}{2}Cov(P_o,P_s) + \frac{1}{2}Cov(P_o,P_d) = \frac{1}{2}V_A+\frac{1}{2}V_A = V_A$

Half sibs:

$Cov(P_o,P_{o'}) = Cov(\frac{1}{2}A_s + \frac{1}{2}A_d + RA_{s,o} + RA_{d,o} + E_o , \frac{1}{2}A_s + \frac{1}{2}A_{d'} + RA_{s,o'} + RA_{d',o'} + E_{o'})$
$= Cov(\frac{1}{2}A_s,\frac{1}{2}A_s)$ *(unrelated dams, no common environment)*
$= \frac{1}{4}V_A$

Full sibs:

$Cov(P_o,P_{o'}) = Cov(\frac{1}{2}A_s + \frac{1}{2}A_d + RA_{s,o} + RA_{d,o} + E_o , \frac{1}{2}A_s + \frac{1}{2}A_d + RA_{s,o'} + RA_{d',o'} + E_{o'})$
$= Cov(\frac{1}{2}A_s,\frac{1}{2}A_s) + Cov(\frac{1}{2}A_d,\frac{1}{2}A_d)$ *(no common environment)*
$= \frac{1}{4}V_A + \frac{1}{4}V_A$
$= \frac{1}{2}V_A$

PHENOTYPIC RESEMBLANCE BETWEEN RELATIVES

$Cov(P_o,P_{o'}) = Cov(A_o+E_o,A_{o'}+E_{o'}) = Cov(A_o,A_{o'}) + Cov(E_o,E_{o'})$ *(assume no dominance)*

Environmental covariance $Cov(E_o,E_{o'}) \neq 0$ if relatives are exposed to the same environment (and this is not accounted for in model)

- family members reared together
- maternal effects (mothering ability)
- can be negative – competition, aggression

New model: $P_o = A_o + Ec + Ew_o$ Ec = Environment effect common to family members
$P_{o'} = A_{o'} + Ec + Ew_{o'}$ Ew = individual environment effect (independent among family members)

$Var(P_o) = Var(P_{o'}) = V_P = V_A + V_{Ec} + V_{Ew}$

If o, o' full sibs exposed to common environment: $Cov(P_o,P_{o'}) = \frac{1}{2}V_A + V_{Ec}$

intraclass correlation = $t_{(FS)} = Corr(P_o,P_{o'}) = (\frac{1}{2}V_A+V_{Ec})/V_P = \frac{1}{2}h^2+V_{Ec}/V_P$
$= \frac{1}{2}h^2 + c^2$ with $c^2 = V_{Ec}/V_P$

GENETIC RESEMBLANCE AT A QTL WITH MARKER DATA

Measures of genetic resemblance derived above are based on average relationships.

But for a given locus, two
halfsibs either have received the same or a different allele from their sire

From before, based on pedigree only:

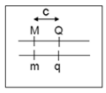
$Cov(A_o,A_{o'}) = \{ Pr(op \equiv o'p) + Pr(op \equiv o'm) + Pr(om \equiv o'p) + Pr(om \equiv o'm)\} \frac{1}{2}V_A = \mathbf{r_{oo'}V_A}$

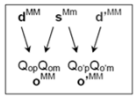
For halfsibs, when using average relationships: $Pr(op \equiv o'p) = {}^1/_4$ and all other IBD probs are 0

covariance between additive genetic values at a QTL (A_Q) between o and o' is:

$Cov(A_{Qo},A_{Qo'}|\text{halfsibs}) = \frac{1}{4}V_Q$ with V_Q = variance explained by the QTL = $2pq\alpha_Q^2$

When marker data is available, genetic resemblance at a linked QTL can be estimated more precisely by using information on whether the marker alleles inherited by **o** and **o'** are IBD:





Q_{ip} = QTL allele received by *i* from it's sire (paternal)
Q_{im} = QTL allele received by *i* from it's dam (maternal)

In this example, marker alleles received by **o** and **o'** from **s** are IBD (both M).

probability that the QTL alleles o and o' received from **s** are IBD:

$Pr(Q_{op} \equiv Q_{o'p} \mid \text{marker alleles received from } \mathbf{s} \text{ by o and o' } \mathbf{are} \text{ IBD}) = (1-c)^2 + c^2$

$(1-c)^2$: Both o and o' received non-recombinant marker-QTL segments from **s**
c^2: recombinant

$Pr(Q_{om} \equiv Q_{o'm} |$ o and o' both received M from their dam) = 0 if d and d' are unrelated and marker-QTL **LE** across population

→ $Cov\left(A_{Qo},A_{Qo'} \middle| \begin{array}{l}\text{paternal marker alleles are IBD} \\ \text{maternal marker alleles not IBD}\end{array}\right) = [(1-c)^2+c^2]\cdot[\frac{1}{2}V_Q] + 0\cdot[\frac{1}{2}V_Q] = \frac{1}{2}[(1-c)^2+c^2]V_Q$

for paternal alleles; maternal

Note that if c=½ (i.e. marker and QTL unlinked), then this covariance reduces to the covariance based on average relationships (¼ for halfsibs and ½ for fullsibs)

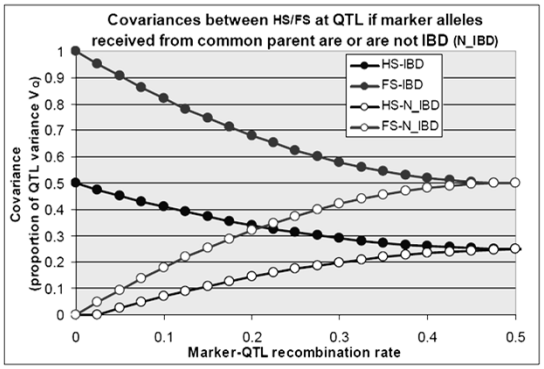
If o and o' received paternal marker alleles that are NOT IBD, then one of the paternal gametes must be a marker-QTL recombinant for the paternal QTL alleles to be IBD:

$\Pr(Q_{op} \equiv Q_{o'p} \mid \text{marker alleles received from s by o and o' not IBD}) = 2c(1-c)$

$\rightarrow \mathrm{Cov}\left[A_{Qo}, A_{Qo'} \mid \begin{matrix}\text{paternal marker alleles not IBD} \\ \text{maternal marker alleles not IBD}\end{matrix}\right] = [2c(1-c)]\cdot[\tfrac{1}{2}V_Q] + 0\cdot[\tfrac{1}{2}V_Q] = [c(1-c)]V_Q$

for paternal alleles; maternal

Example of genetic resemblance at a QTL for paternal half-sibs and for full-sibs based on genotypes at a marker that is linked to a QTL with recombination rate c.



These concepts can be expanded to capture:

- information from multiple markers around the QTL
- uncertainty of marker inheritance - by adding IBD probabilities at the marker – these were assumed 0/1 above
- see Lynch and Walsh.

Marker-based Covariances based on Linkage Disequilibrium

The above assumes **Linkage Equilibrium** between the marker and QTL across the population

only used linkage information or LD **within** a family

When markers and QTL are closely linked, LD across the population

non-zero IBD probabilities to be quantified even between seemingly unrelated by utilizing observed IBS at markers.

Meuwissen & Goddard (2001 GSE)

Meuwissen & Goddard (2001 GSE)

They derived general analytical equations to obtain such IBD probabilities, conditional on assumptions about population history:

- Historical effective population size
- Number of generations when the mutation that created variation at the QTL occurred

	SNP haplotypes around ●	# markers IBS to	
Haplotype 1:	01111●11001	left of ●	right of ●
Haplotype 2:	01111●11011	5	3
Haplotype 3:	00101●11011	1	3

Pr(1 and 2 are IBD at ●)
is greater than
Pr(1 and 3 are IBD at ●)

An example

Ne = 100

6 markers in 10 cM, putative QTL position in centre:
M_M_M_Q_M_M_M

– Sample 4 haplotypes from population:
001001, 001001, 011001, 111011

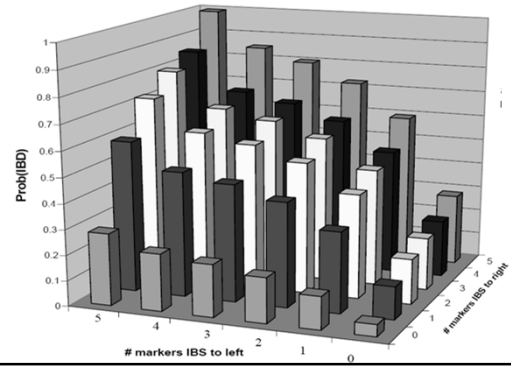
– IBD matrix is:

	001001	001001	011001	111011
001001	1			
001001	0.82	1		
011001	0.63	0.63	1	
111011	0.49	0.49	0.56	1

This is an LD based IBD matrix

Covariance between one individual with haplotype 112112 and one individual with haplotype 122112 : $0.63*\sigma_v^2$
if this segment contains a QTL with variance 2 σ_v^2

IBD probabilities of haplotype pairs at locus *A*.
The haplotypes consist of 10 bi- allelic markers that had allele frequencies equal to 0.5 in the base population (1 cM apart). Locus A is at the middle of this haplotype.

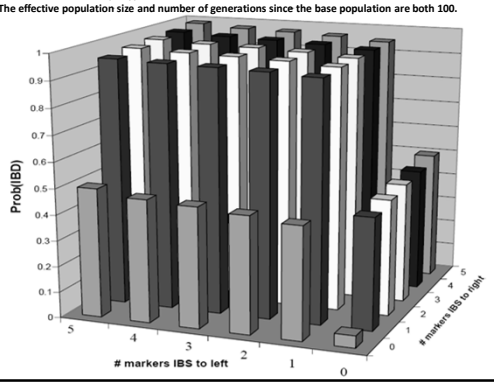


Combine covariances from linkage and LD (combined LDLA analysis)

IBD probabilities of haplotype pairs at locus *A*.

The haplotypes consist of 10 markers that had founder alleles in the base population(1 cM apart). Locus A is at the middle of this haplotype.

The effective population size and number of generations since the base population are both 100.



Genetic resemblance at QTL based on combined linkage disequilibrium and linkage / cosegregation

Linkage IBD matrices assume QTL alleles in founders are not IBD

LD IBD matrices capture IBD between founder QTL alleles

combine these two approaches LD-LA analysis

consider again the dense marker haplotypes:

Sire 0100 / 0101
Dam 0111 / 0100
Progeny 0100 / 0111

LA

The linkage based IBD matrix:

		Sire		Dam		Progeny	
		Pat	Mat	Pat	Mat	Pat	Mat
Sire	Pat	1					
	Mat	0	1				
Dam	Pat	0	0	1			
	Mat	0	0	0	1		
Progeny	Pat	1	0	0	0	1	
	Mat	0	0	1	0	0	1

consider again the dense marker haplotypes:

Sire 0100 / 0101
Dam 0111 / 0100
Progeny 0100 / 0111

LD

The LD-based IBD matrix of founder haplotypes, *e.g.*:

		Sire		Dam	
		Pat	Mat	Pat	Mat
Sire	Pat	1			
	Mat	0.8	1		
Dam	Pat	0.5	0.5	1	
	Mat	0.9	0.5	0.5	1

consider again the dense marker haplotypes:

Sire 0100 / 0101
Dam 0111 / 0100
Progeny 0100 / 0111

LDLA

Combining these gives: :

		Sire		Dam		Progeny	
		Pat	Mat	Pat	Mat	Pat	Mat
Sire	Pat	1					
	Mat	0.8	1				
Dam	Pat	0.5	0.5	1			
	Mat	0.9	0.5	0.5	1		
Progeny	Pat	1	0.8	0.5	0.9	1	
	Mat	0.5	0.5	1	0.5	0.8	1