

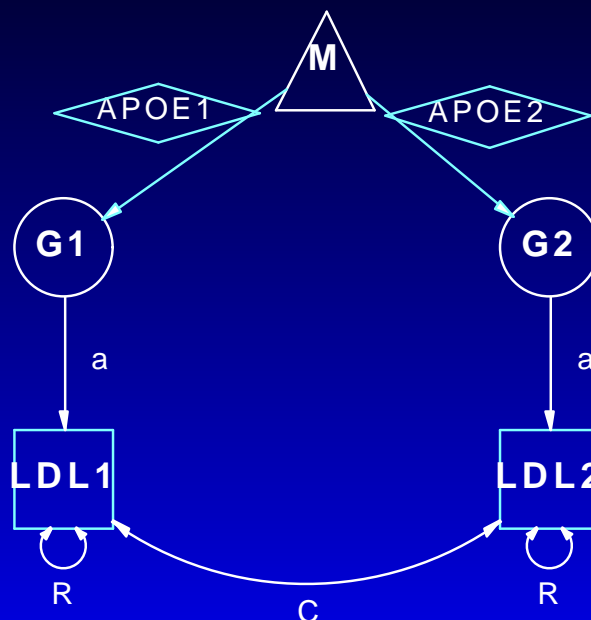
Association Analysis

Using sib pairs to control for stratification

Michael Neale Boulder Workshop 2001

Association Model

Each sib pair i has different MEANS



Features of Association Model

Attractive

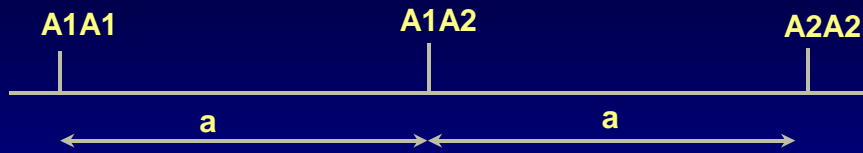
- Residual variances & covariances (R & C)
 - change
 - could use linkage model for joint analysis
- Can be extended to multiple alleles, loci, phenotypes and larger pedigrees
- But assumes no population stratification

Fulker association model

- Separate associated mean differences
 - between sib pairs
 - within sib pairs
- Between = within if genuine allelic effect
- Derive cunning model

Allelic effects

Assuming additivity, unnecessarily



Call contributions to pair sum b 's
Call contributions to pair diffs w 's

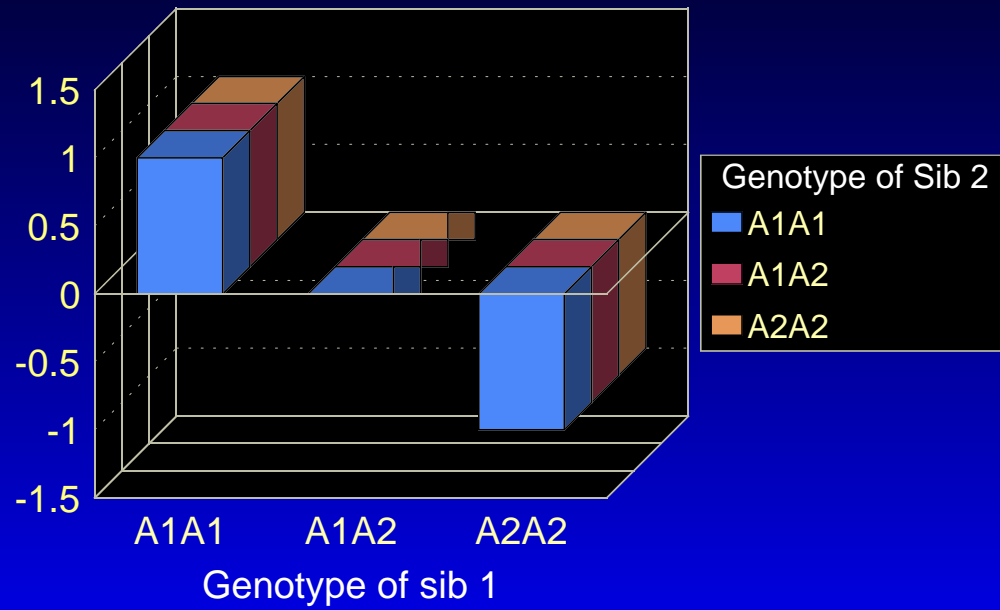
Pair means & differences

G Sib1	G Sib2	Pair Sum/2	Pair Diff/2	Mean Sib1	Mean Sib2
A1A1	A1A1	b	0	b	b
A1A1	A1A2	$b/2$	$w/2$	$b/2+w/2$	$b/2-w/2$
A1A1	A2A2	0	w	w	$-w$
A1A2	A1A1	$b/2$	$-w/2$	$b/2-w/2$	$b/2+w/2$
A1A2	A1A2	0	0	0	0
A1A2	A2A2	$-b/2$	$w/2$	$w/2-b/2$	$-b/2-w/2$
A2A2	A1A1	0	$-w$	$-w$	w
A2A2	A1A2	$-b/2$	$-w/2$	$-b/2-w/2$	$-b/2+w/2$
A2A2	A2A2	$-b$	0	$-b$	$-b$

Within pair distance between homozygote = w ; between pairs it is b

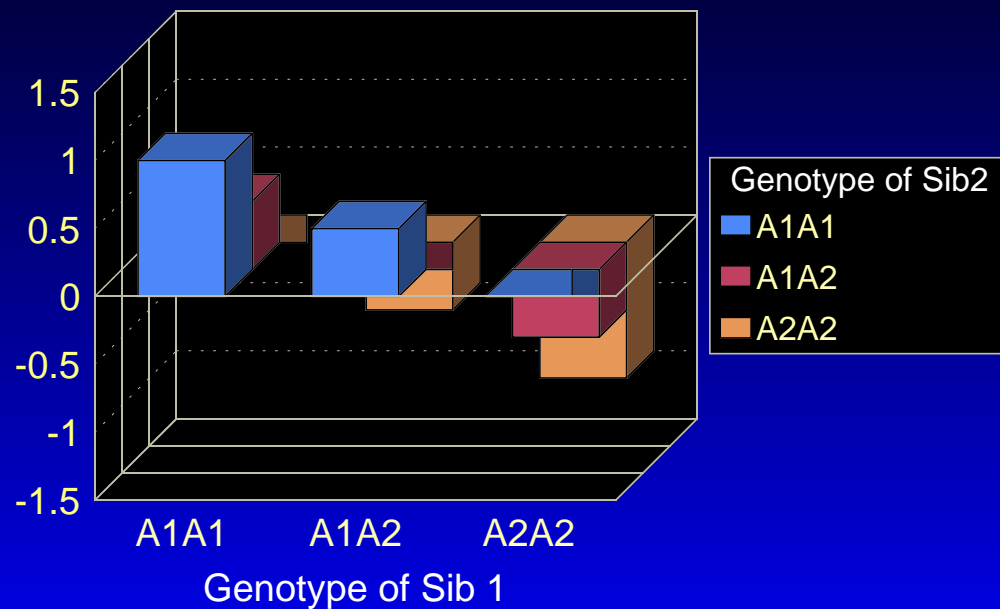
Mean of sib 1

b=w (no stratification)



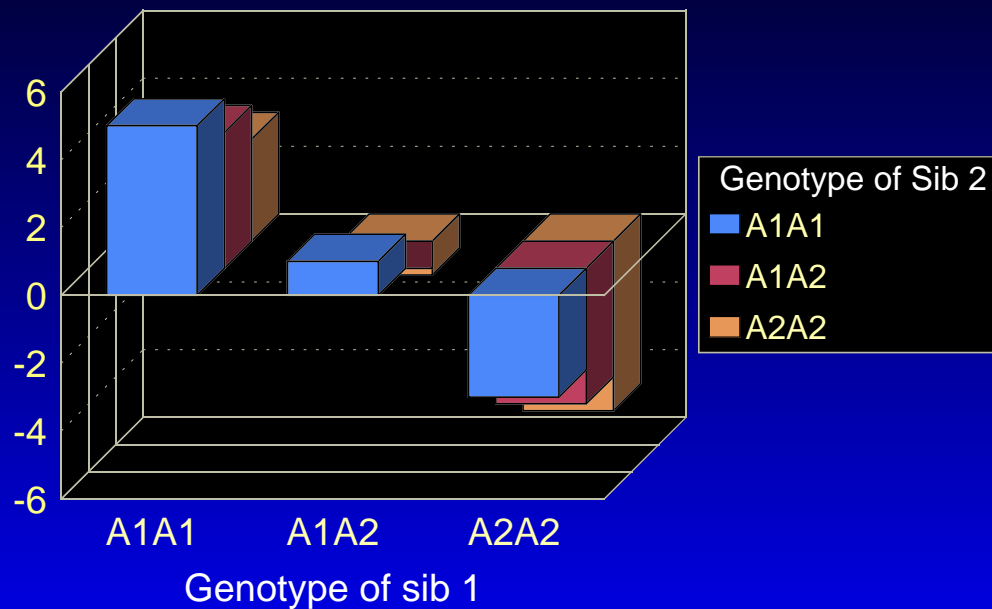
Mean of sib 1

No w (all stratification)



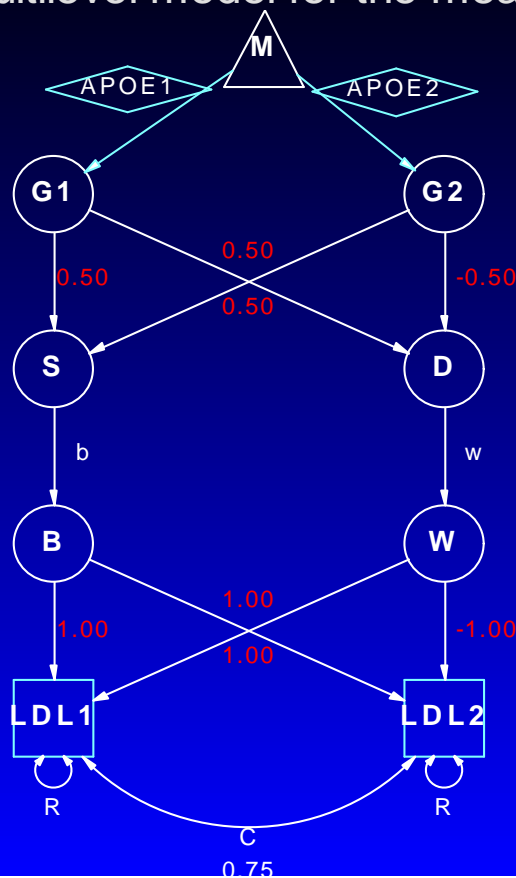
Mean of sib 1

$b=5$ $w=4$ (some of each)



Fulker Association Model

Multilevel model for the means



Conclusion

Association analysis

- Easy method to control for stratification
- Sibling samples are readily available
- Extensions straightforward:
 - Multivariate
 - Multiallelic
 - Multiple sibs