

# Mapping QTL to a phylogenetic tree

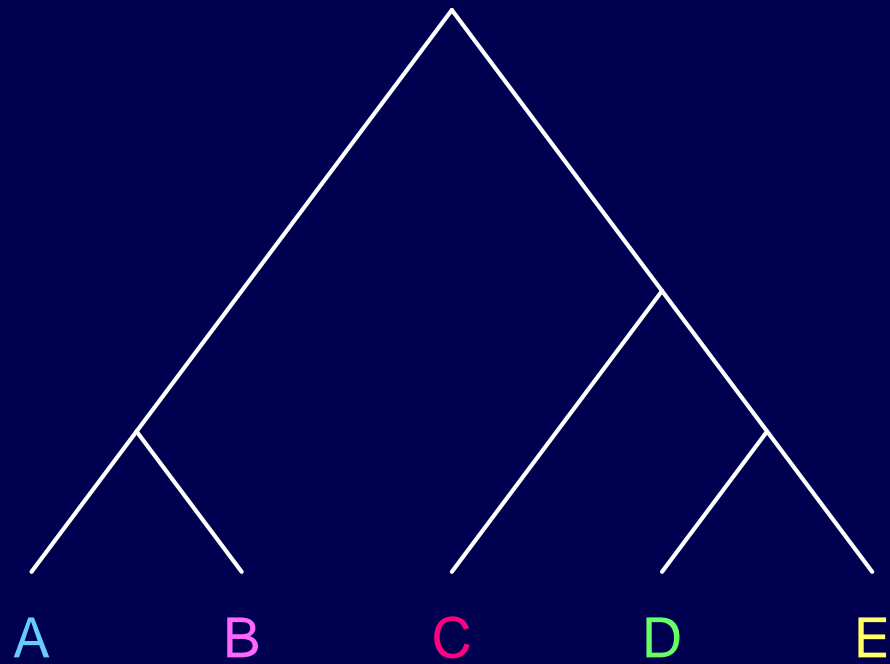
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Karl W Broman

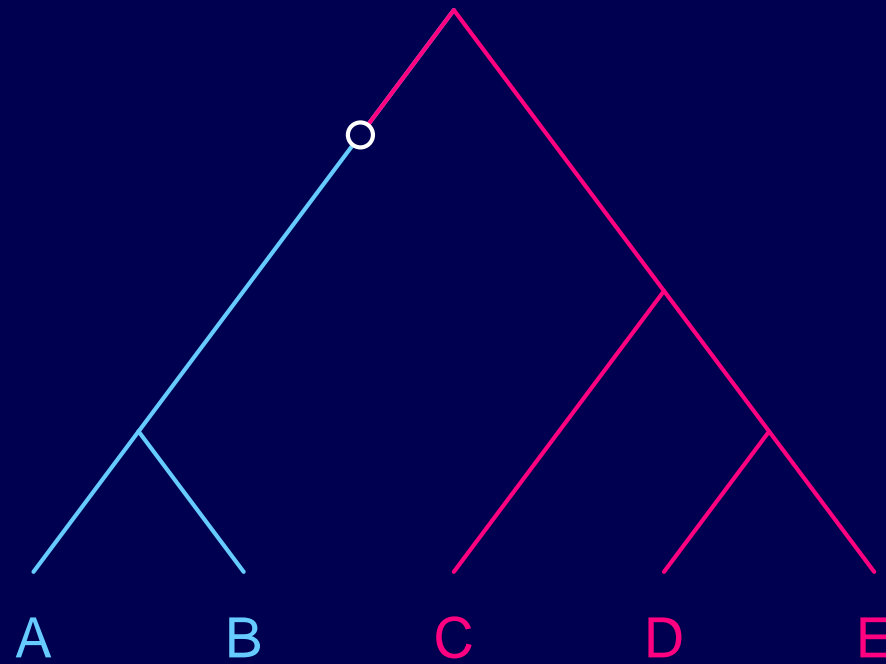
Department of Biostatistics & Medical Informatics  
University of Wisconsin – Madison

[www.biostat.wisc.edu/~kbroman](http://www.biostat.wisc.edu/~kbroman)

# A tree

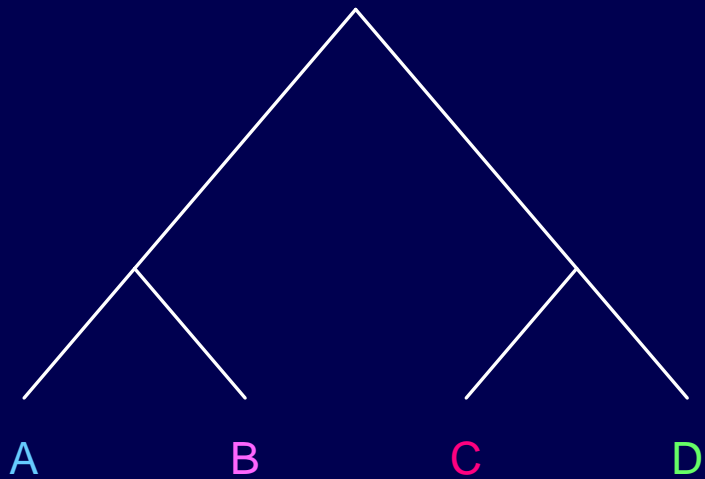


# A QTL on a tree



# QTL on a tree

## Assumptions



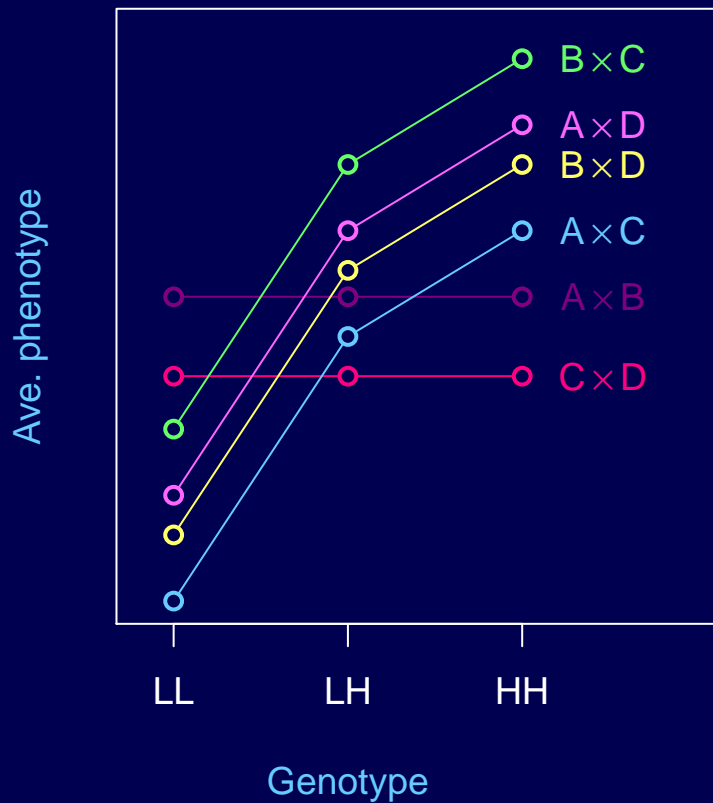
- Single diallelic QTL
- No epistasis or background effects
- No variation in recombination
- Known tree

# QTL on a tree

## Assumptions

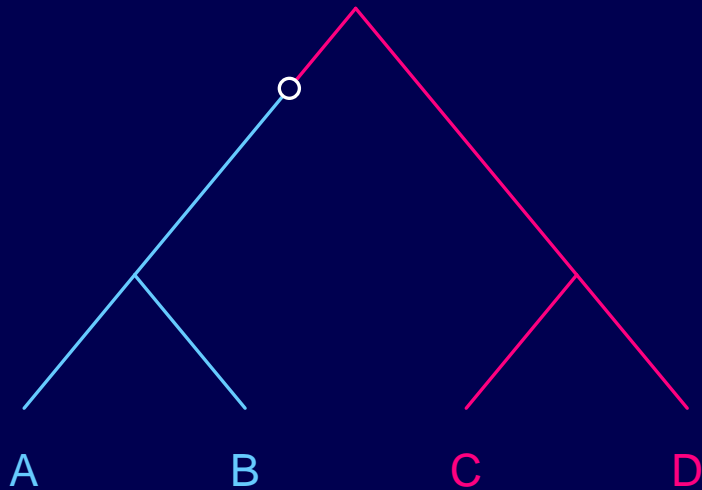
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### No epistasis



# QTL on a tree

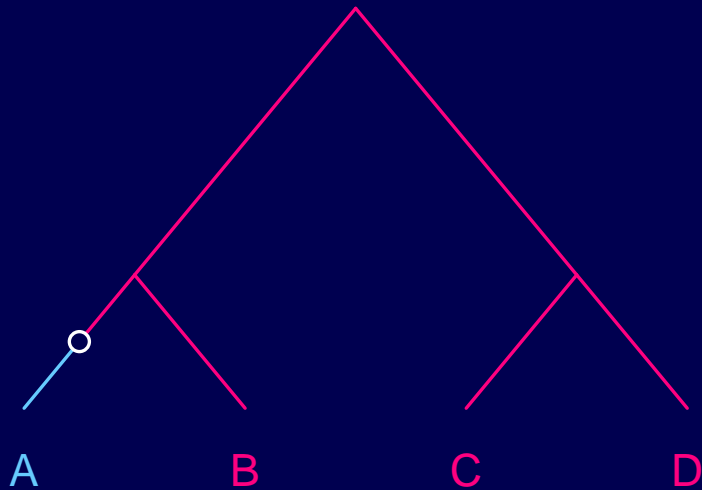
## Assumptions



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- Known tree

# QTL on a tree

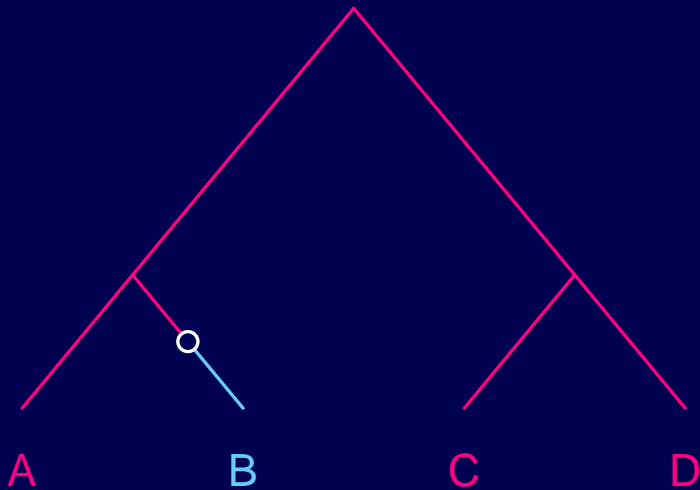
## Assumptions



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# QTL on a tree

## Assumptions

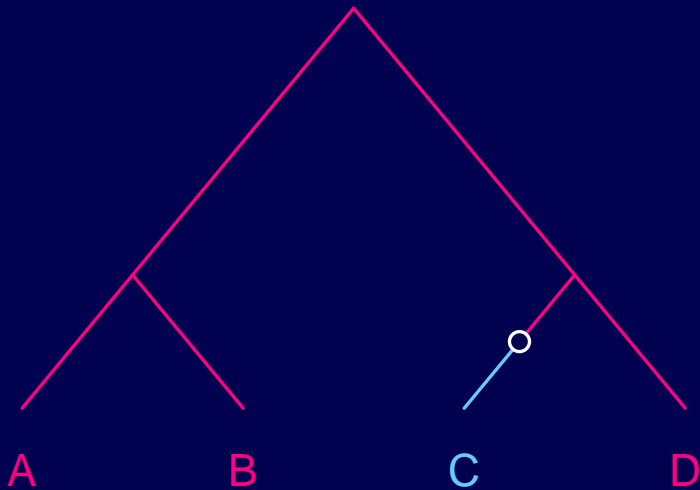


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# QTL on a tree

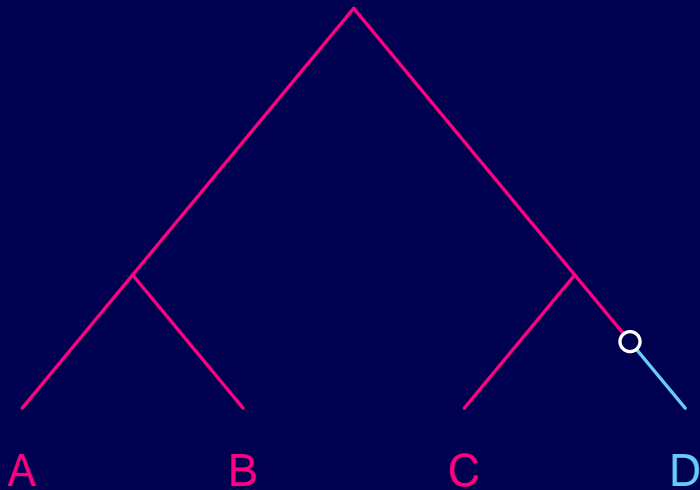
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# QTL on a tree

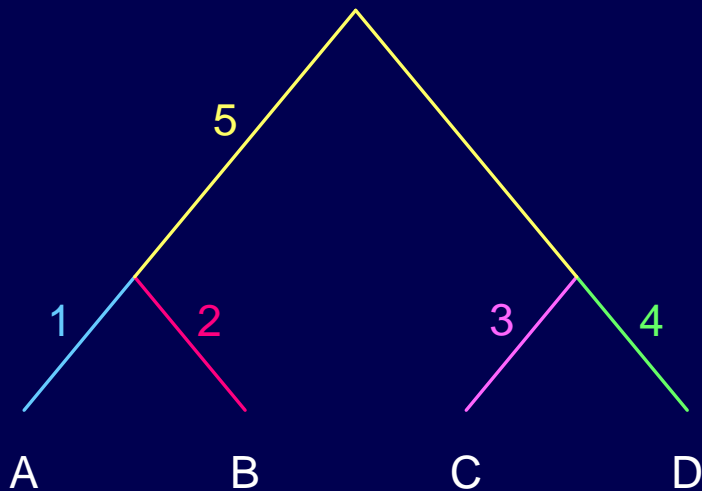
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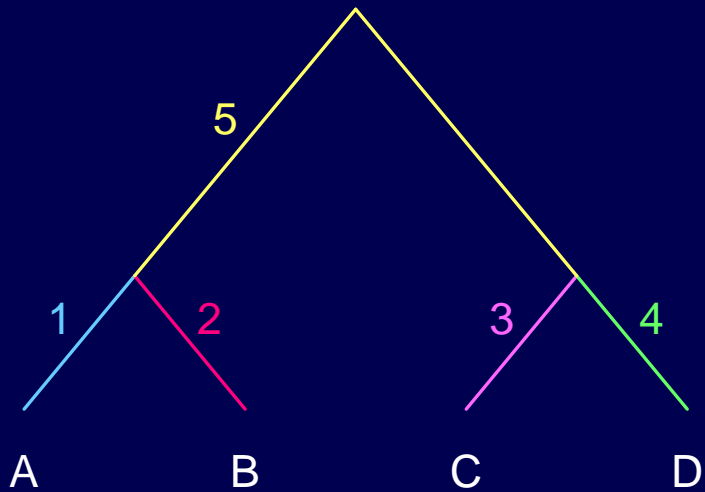
# QTL on a tree

## Assumptions



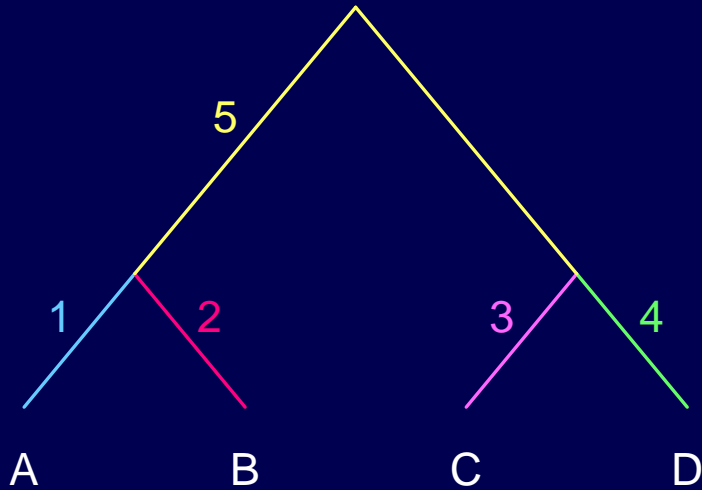
- Single diallelic QTL
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# QTL on a tree



Cross	QTL position (partition of taxa)				
	1 (A BCD)	2 (B ACD)	3 (C ABD)	4 (D ABC)	5 (AB CD)
A × B	✓	✓	×	×	×
A × C	✓	×	✓	×	✓
A × D	✓	×	×	✓	✓
B × C	×	✓	✓	×	✓
B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# QTL on a tree



Cross	QTL position (partition of taxa)				
	1 (A BCD)	2 (B ACD)	3 (C ABD)	4 (D ABC)	5 (AB CD)
A × B	✓	✓	×	×	×
A × C	✓	×	✓	×	✓
A × D	✓	×	×	✓	✓
B × C	×	✓	✓	×	✓
B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# Combining crosses

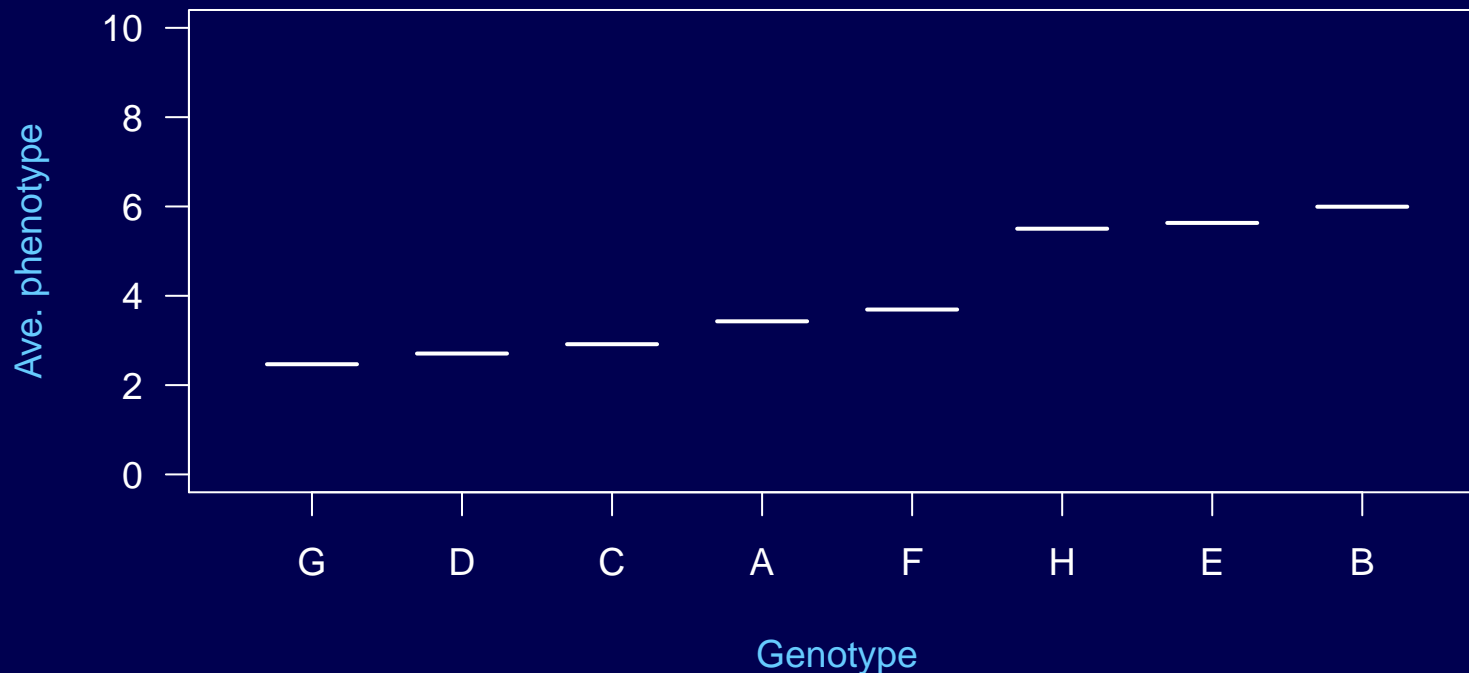
Li et al., Genetics 169:1699–1709, 2005

- Four mouse intercrosses,  $I \times P$ ,  $P \times D$ ,  $D \times C$ ,  $C \times S$
- $I$ ,  $D$ ,  $S$  have low plasma HDL cholesterol
- $P$ ,  $C$  have high plasma HDL cholesterol
- Use results from individual crosses to determine partition
- Recode genotypes in each cross to  $L/H$  and combine (with the goal of increasing mapping precision)

# Diallelic QTL

Macdonald and Long, *Genetics* 176:1261–1281, 2007

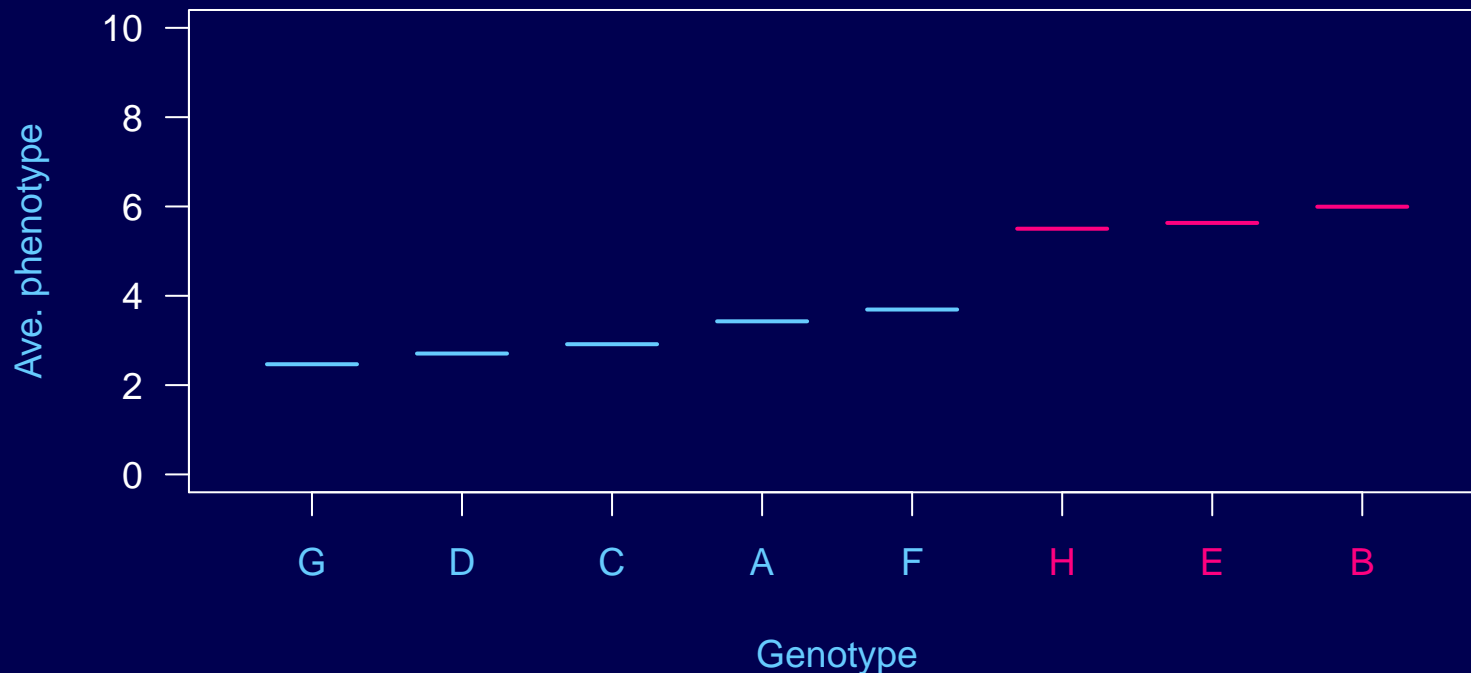
- *Drosophila* recombinant inbred lines (RIL) developed from 8 strains
- Assume an underlying diallelic QTL (that the 8 alleles are of two flavors)
- Approximate method for partitioning the 8 alleles into 2 groups



# Diallelic QTL

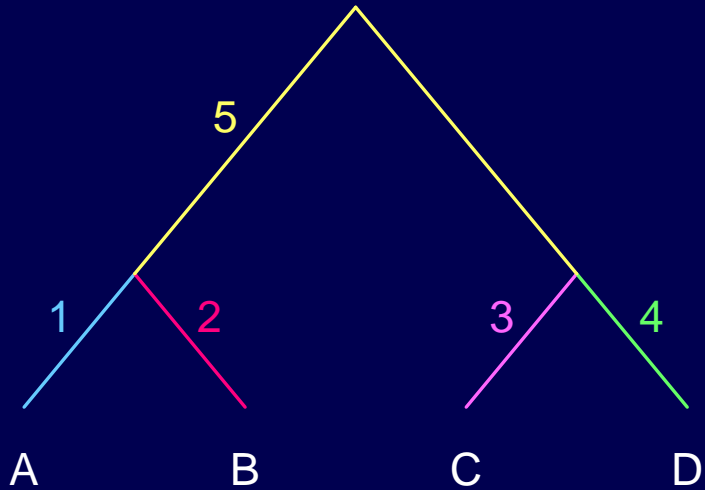
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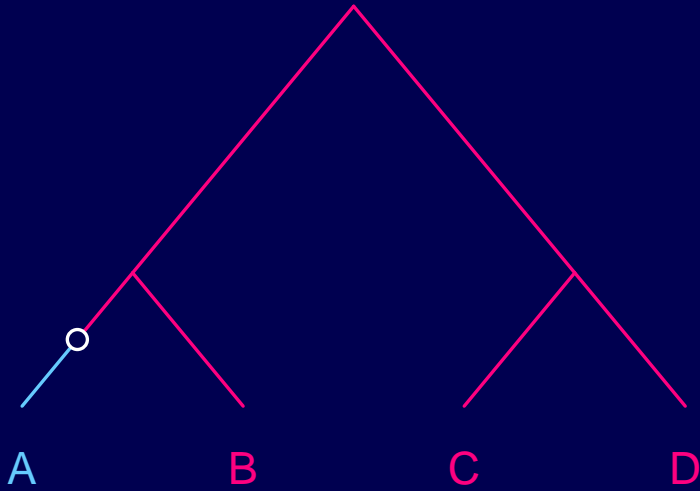


# The basic idea



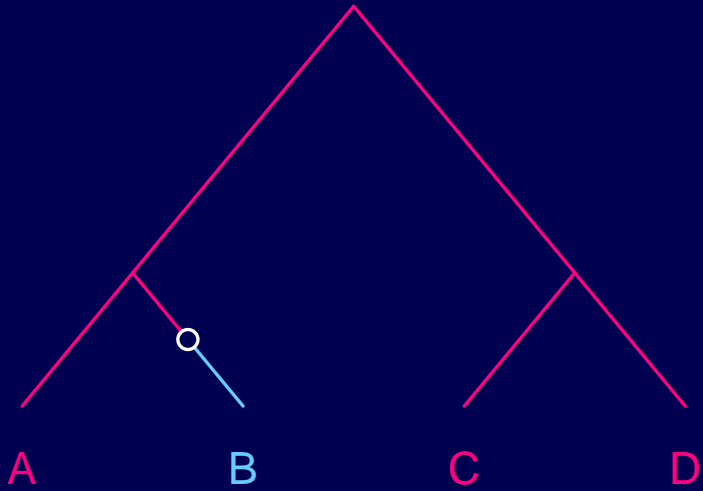
Cross	QTL position (partition of taxa)				
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A × B	✓	✓	×	×	×
A × C	✓	×	✓	×	✓
A × D	✓	×	×	✓	✓
B × C	×	✓	✓	×	✓
B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# The basic idea



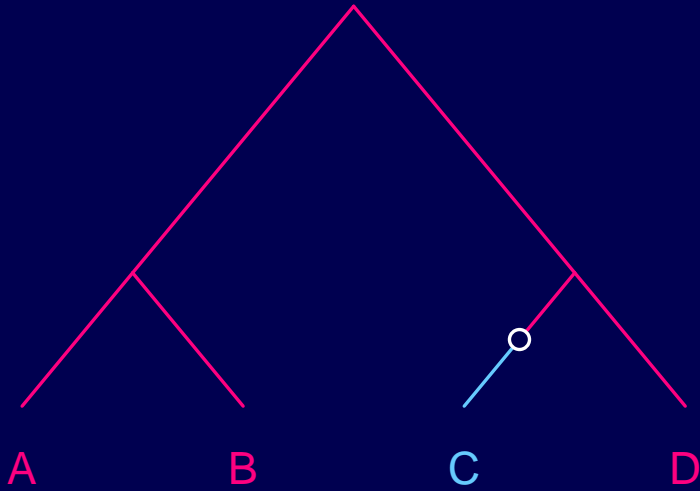
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	1 (A BCD)	2 (B ACD)	3 (C ABD)	4 (D ABC)	5 (AB CD)
A × B	✓	✓	×	×	×
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A × D	✓	×	×	✓	✓
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B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# The basic idea



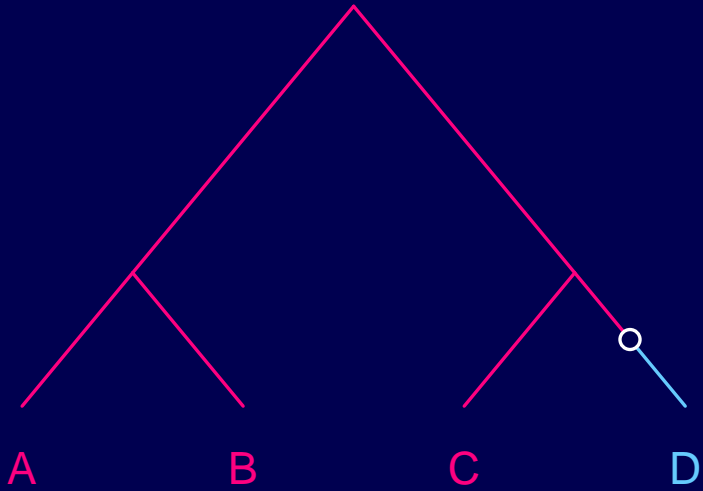
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B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# The basic idea



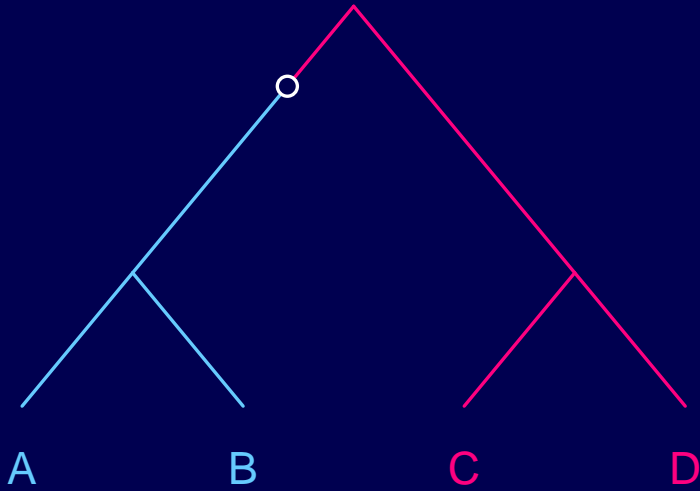
Cross	QTL position (partition of taxa)				
	1 (A BCD)	2 (B ACD)	3 (C ABD)	4 (D ABC)	5 (AB CD)
A × B	✓	✓	✗	✗	✗
A × C	✓	✗	✓	✗	✓
A × D	✓	✗	✗	✓	✓
B × C	✗	✓	✓	✗	✓
B × D	✗	✓	✗	✓	✓
C × D	✗	✗	✓	✓	✗

# The basic idea



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	1 (A BCD)	2 (B ACD)	3 (C ABD)	4 (D ABC)	5 (AB CD)
A × B	✓	✓	×	×	×
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A × D	✓	×	×	✓	✓
B × C	×	✓	✓	×	✓
B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

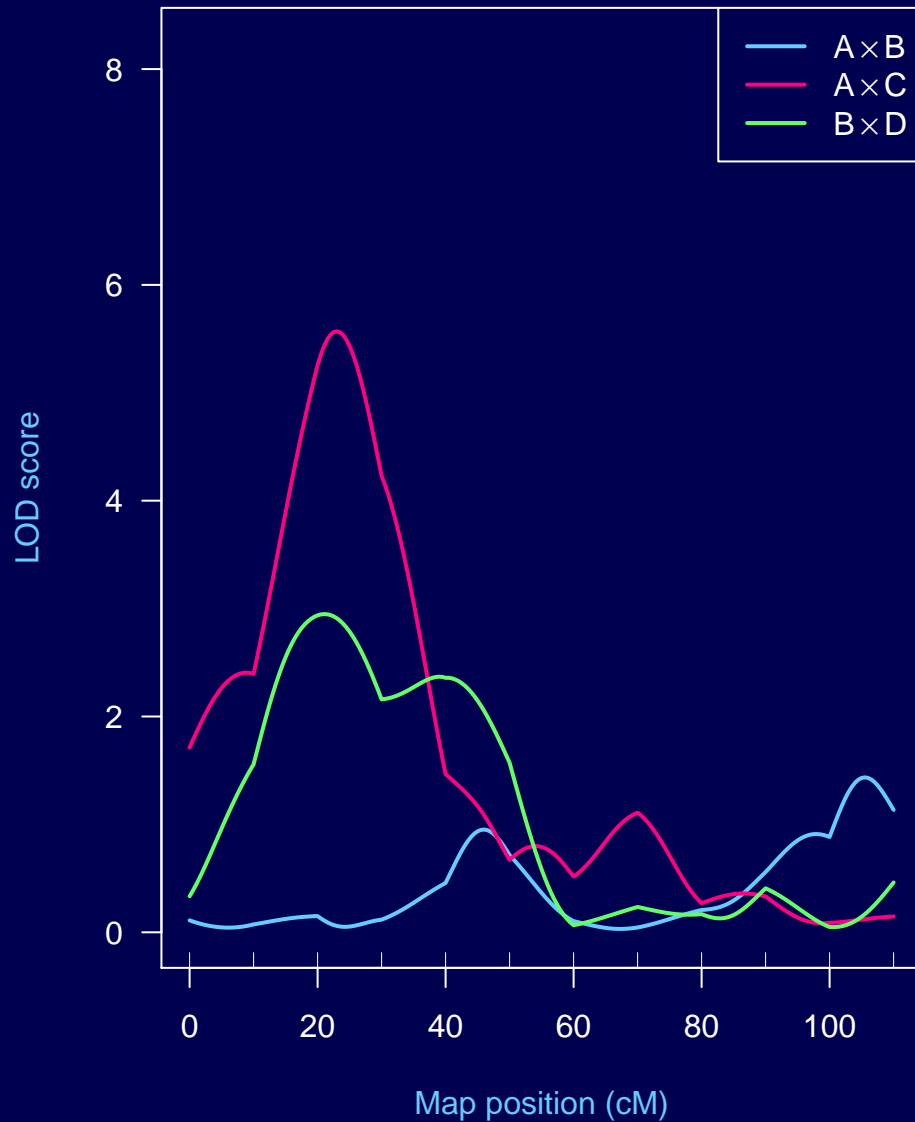
# The basic idea



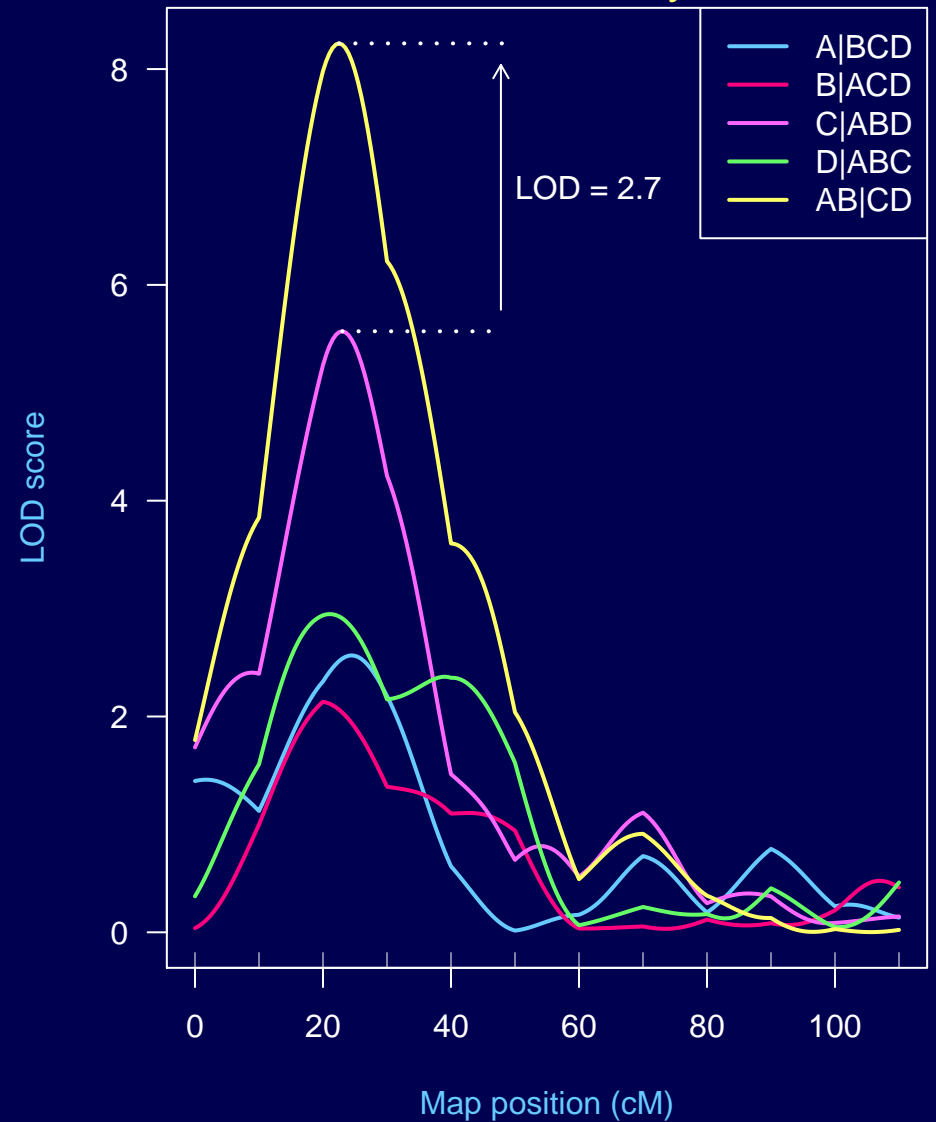
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A × D	✓	×	×	✓	✓
B × C	×	✓	✓	×	✓
B × D	×	✓	×	✓	✓
C × D	×	×	✓	✓	×

# Simulated example

## Individual crosses



## Combined analysis



# Summary

- It works, though power is low
- Experimental design results left unmentioned
- Caveats:
  - Epistasis
  - Multiple linked QTL
  - More than two alleles
- Future work:
  - Sensitivity to departures from assumptions
  - Multiple linked loci
  - Jointly consider multiple unlinked regions



# Acknowledgments

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Cécile Ané     Statistics and Botany, UW–Madison

Sungjin Kim    Statistics, UW–Madison

NIH/NIGMS     R01 GM074244