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FACULTY OF ENGINEERING & TECHNOLOGY DEPARTMENT OF BIOTECHNOLOGY

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Maps



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Genetic Maps

Order and location of markers assigned to chromosome on the basis of linkage analysis

Distance measured in Morgans (M)



Physical Maps

Actual structure of genetic material At highest level DNA sequence Distance measured in 10⁶bp (Mbp)

Genetic and physical maps are usually 'linked' together



Example of a map

Cattle chromosomes 1-5, from Cattle Genome Database hosted at the Queensland Biosciences Precinct: http://www.cgd.csiro.au





Genetic maps

Map distance is determined from the number of observed recombination events

1cM = 1 recombination event per 100 meiosis (simple mapping function)



Map distance versus r

- Only odd number of crossover events are observed
 - r = probability of an odd-number of cross-over events
 - 1-r = probability of an even number of cross-over events, including zero



Mapping functions

- Mapping functions predict the number of crossover events from observed recombination events
- Also account for interference (where a recombination) event in one region affects the likelihood of a recombination event in a closely aligned region)



Different Mapping functions

Haldane

- assumes no interference (crossovers occur randomly and independently over the entire chromosome)
- M = -(ln(1-2r))/2
- Kosambi
 - assumes moderate interference (i.e. some crossover interference at adjacent sites)
 - $M = \frac{1}{4} \ln (1 + \frac{2r}{1 2r})$
- Simple
 - assumes complete interference
 - r = M



Comparison of mapping functions





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Construction of linkage maps

Simple example is 3 point testcross (see lecture notes)



Construction of linkage maps

- In practice genetic maps are often constructed from complex pedigrees
 - First need to determine parental phase, such that gametes can be classed as recombinant or nonrecombinant
 - Typically use a maximum likelihood approach



Construction of linkage maps

- Identification of recombinant gametes is easier if
 - linkage phase of parents is known
 - Sire AaBb x Dam AABB → 9 AABB, 1 AaBB, 1 AABb, 9 AaBb
 - Sire thus gave gametes in frequency 0.45 AB, 0.05 aB, 0.05 Ab, 0.45ab
 - Most likely phase is AB ab
 - haplotype of gametes transmitted from parents to offspring is known
 - AaBb x AABB \rightarrow AaBb, sire gave ab dam gave AB
 - AaBb x AaBb \rightarrow AaBb, cannot determine transmitted haplotypes



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Physical maps

- Cytogenetic maps
 - banding pattern observed under light microscopy of stained chromosomes
 - low resolution (only estimates of the number of bp)





Talking glossary of genetics, 2008



Human Karyotype



Talking glossary of genetics, 2008



Physical maps

- Radiation hybrid
 - Use breaks induced by radiation to determine the distance between two markers



Physical maps continued

- Sequence tag sites (STS)
 - STS are short, unique DNA sequences with known location
- Sequence maps
 - 'the ultimate'
 - now available for a number of livestock species



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Relationship between genetic and physical distance

No universal relationship

- Comparison of human genetic and sequence based physical maps, Yu et al. "Recombination rates varied greatly along each chromosome, from 0 to at least 9 centiMorgans per megabase"
- Various depending on
 - species
 - chromosomal region: crossovers often suppressed at centromeres, telomeres
 - Sex: female mammals usually have greater map distances than males, no crossover in male Drosophila



Australian Sheep Gene Mapping Website

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		Predicted Human Positions and Microsatellites for Sheep BAC Ends 28th January 2005					
		Locus Assignments for GenBank Sheep EST and RNA sequences 22nd April 2004					
		Latest Sheep versus Human Comparisons 17th December 2003					
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http://rubens.its.unimelb.edu.au/~jillm/jill.htm

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Extract from Australian Sheep Map

Sheep Best Positions Linkage Map Version 4.4

Chromosome	Sex Av cl	/I Female cl	M Male cM	Locus Code	Marker
1	0.0	0.0	0.0	\RM309	<u>RM309A</u>
1	14.2	6.6	22.5	\BMS2833	BMS2833
1	16.7	10.1	24.4	\TGLA127	<u>TGLA127</u>
1	16.7	10.1	24.4	\INRA197	<u>INRA197</u>
1	16.7	10.1	24.4	\MCM46	<u>MCM46</u>
1	19.0	12.5	26.6	<u>PPT1</u>	<u>PPT</u>
1	24.3	19.6	30.9	\EPCDV022	EPCDV22



http://rubens.its.unimelb.edu.au/~jillm/jill.htm

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