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FACULTY OF ENGINEERING &TECHNOLOGY
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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)

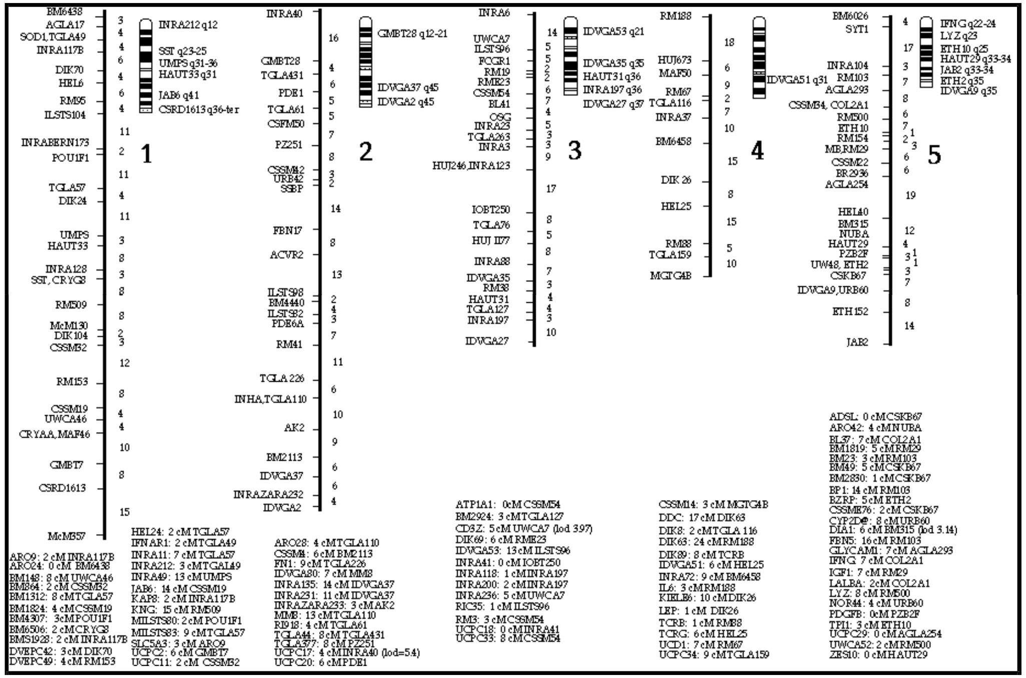
Physical Maps

- Actual structure of genetic material
- At highest level DNA sequence
- Distance measured in 10^6bp (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



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Genetic maps

- Map distance is determined from the number of observed recombination events

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

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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

A B C → A b c

.....a.....b.......c.... → .....a.....B.....C....

.....A.....B.......C.... → .....A.....b.......c.... → .....A......B.......C....

.....a.....b.......c.... → .....a.....B.....C.... → .....a.....b.......c....

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Mapping functions

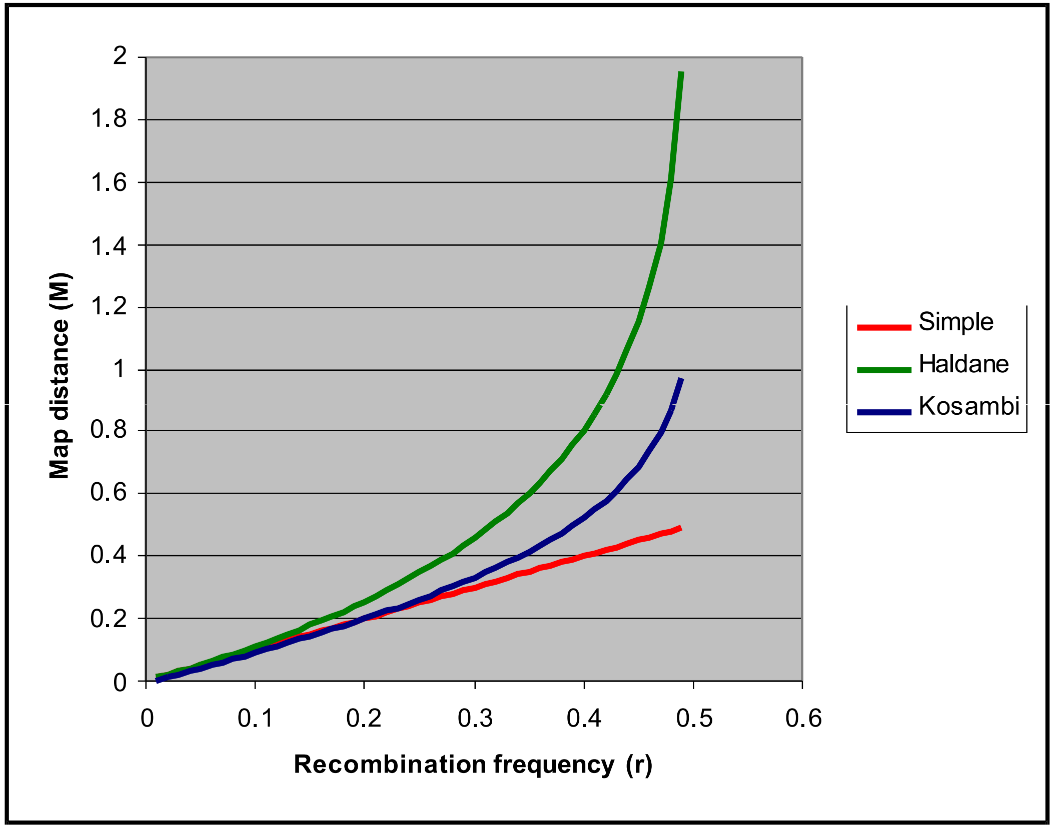
- Mapping functions predict the number of crossover events from observed recombination events

- 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)
  - $M = \frac{1}{4} \ln (1+2r/1-2r)$
- 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 non-recombinant

  – 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 → AaBb, sire gave ab dam gave AB
    - AaBb x AaBb → 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)

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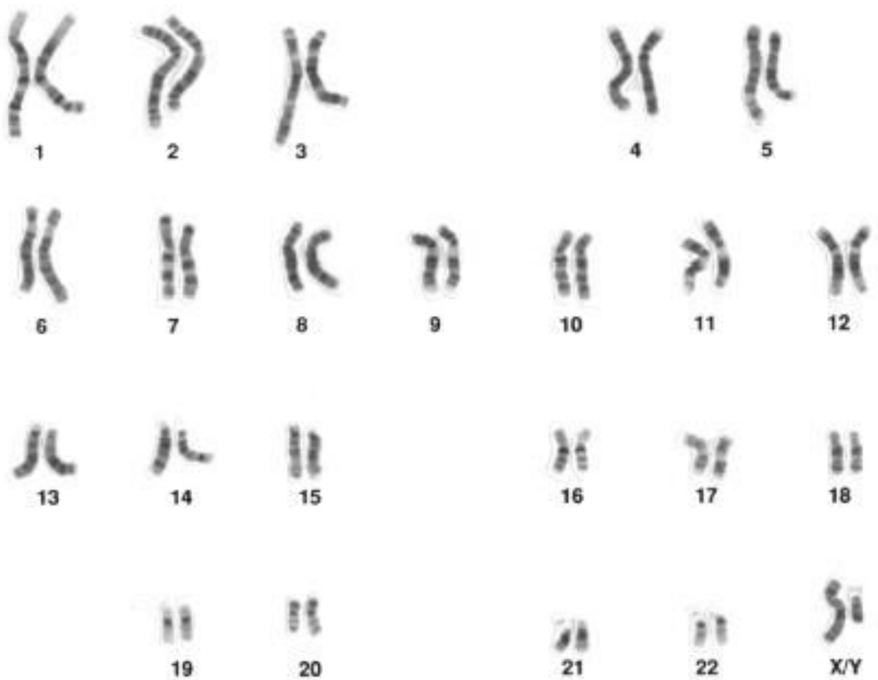
Human Karyotype



Talking glossary of genetics, 2008

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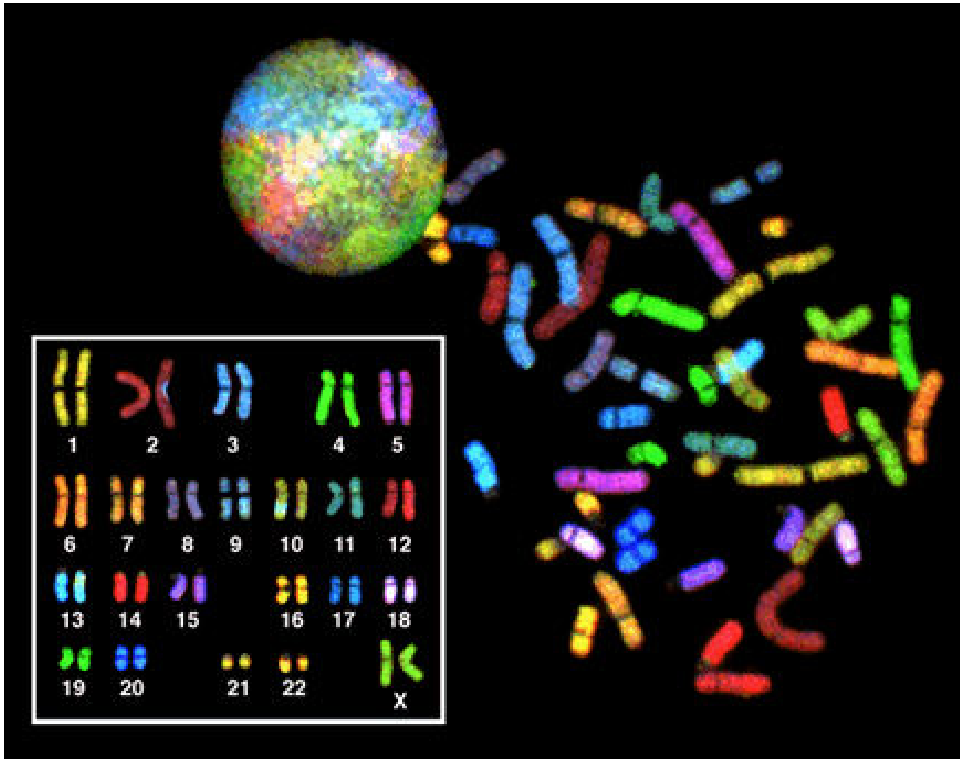
Human Karyotype



Talking glossary of genetics, 2008

Physical maps

– Radiation hybrid

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

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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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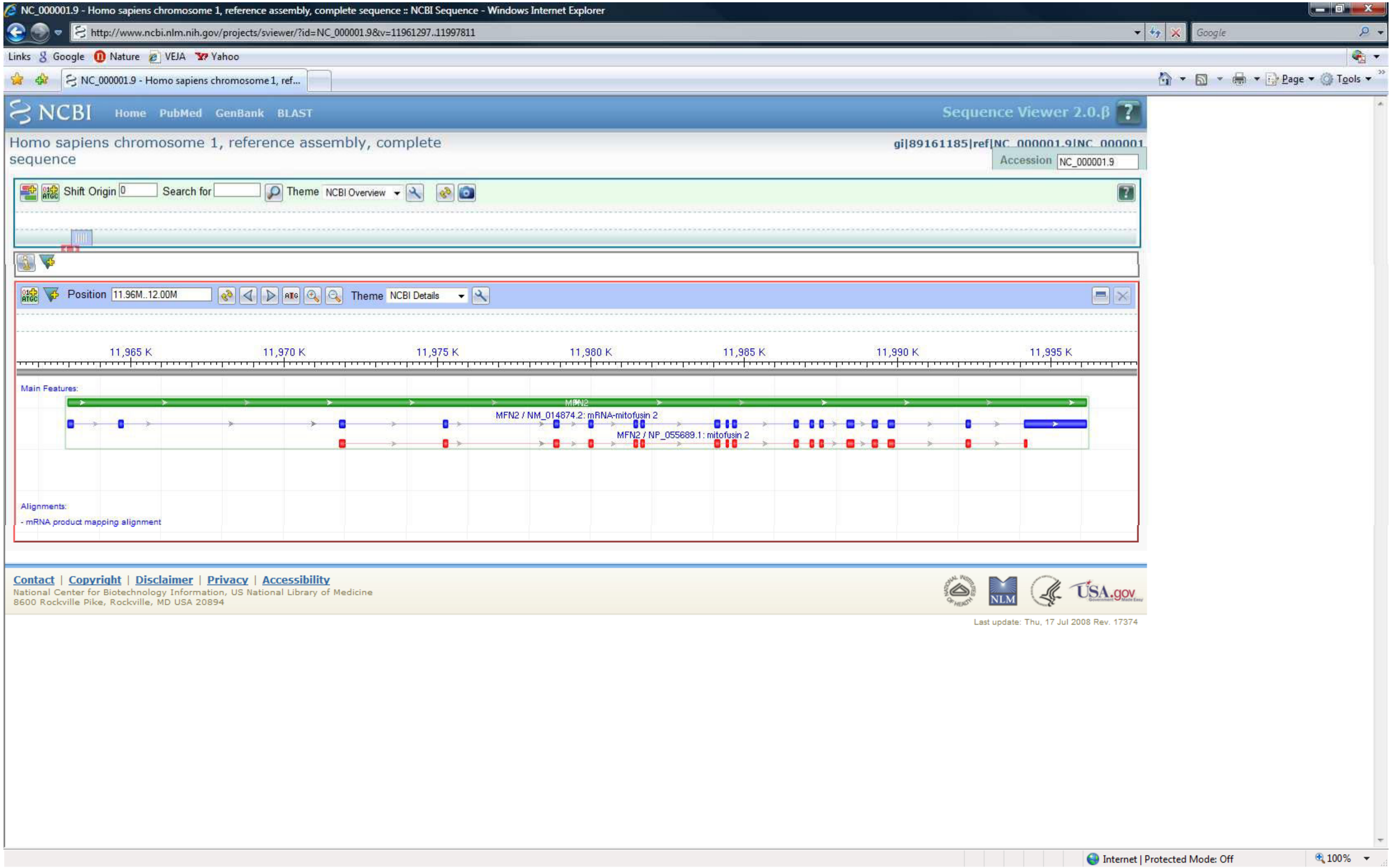
NC_000001.9 - Homo sapiens chromosome 1, reference assembly, complete sequence :: NCBI Sequence - Windows Internet Explorer
http://www.ncbi.nlm.nih.gov/projects/sviewer/?id=NC_000001.9&v=11961297..11997811
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Sequence Viewer 2.0.β
Homo sapiens chromosome 1, reference assembly, complete sequence
gi|89161185|ref|NC_000001.9|NC_000001
Accession NC_000001.9
Shift Origin Search for Theme NCBI Overview
Position 11.96M..12.00M Theme NCBI Details
11,965 K 11,970 K 11,975 K 11,980 K 11,985 K 11,990 K 11,995 K
Main Features:
MFN2
MFN2 / NM_014874.2: mRNA-mitofusin 2
MFN2 / NP_055689.1: mitofusin 2
Alignments:
- mRNA product mapping alignment
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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

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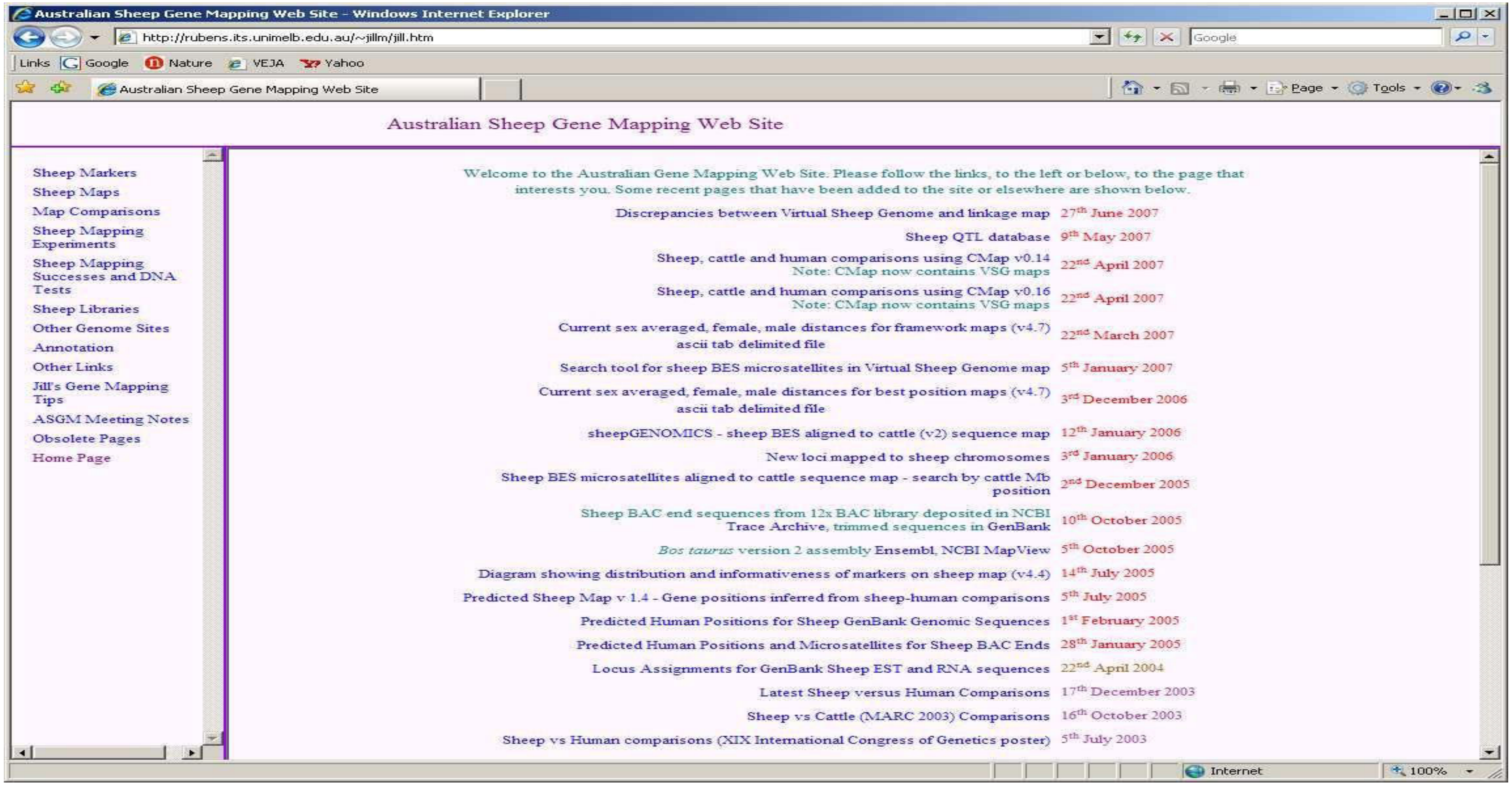
Australian Sheep Gene Mapping Website



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 cM	Female cM	Male cM	Locus Code	Marker
1	0.0	0.0	0.0	\RM309	RM309A
1	14.2	6.6	22.5	\BMS2833	BMS2833
1	16.7	10.1	24.4	\TGLA127	TGLA127
1	16.7	10.1	24.4	\INRA197	INRA197
1	16.7	10.1	24.4	\MCM46	MCM46
1	19.0	12.5	26.6	PPT1	PPT
1	24.3	19.6	30.9	\EPCDV022	EPCDV22

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