

LD Scans for Ongoing Selective Sweeps

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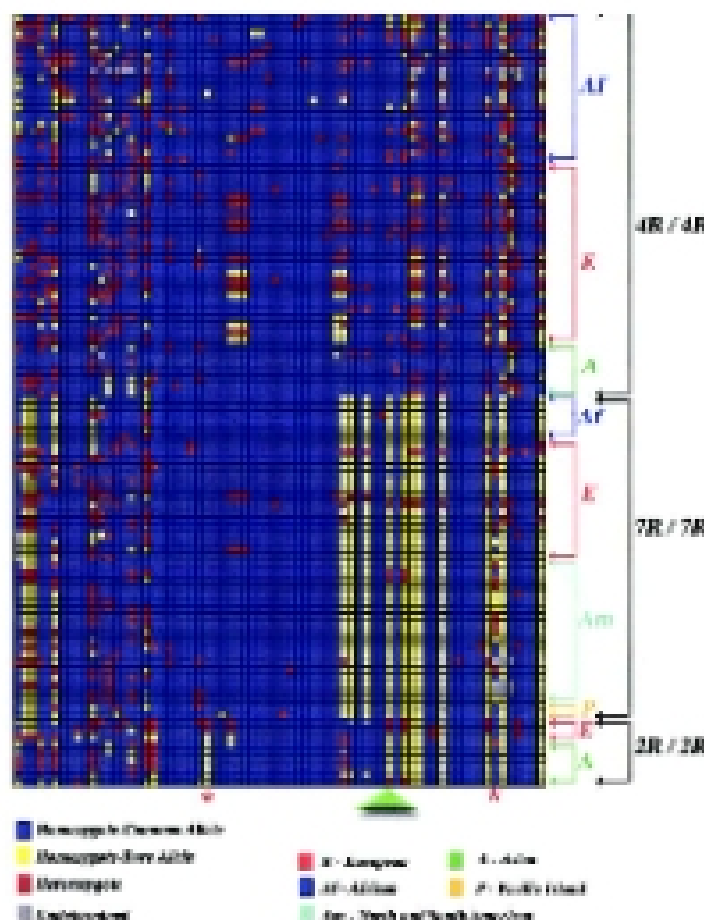
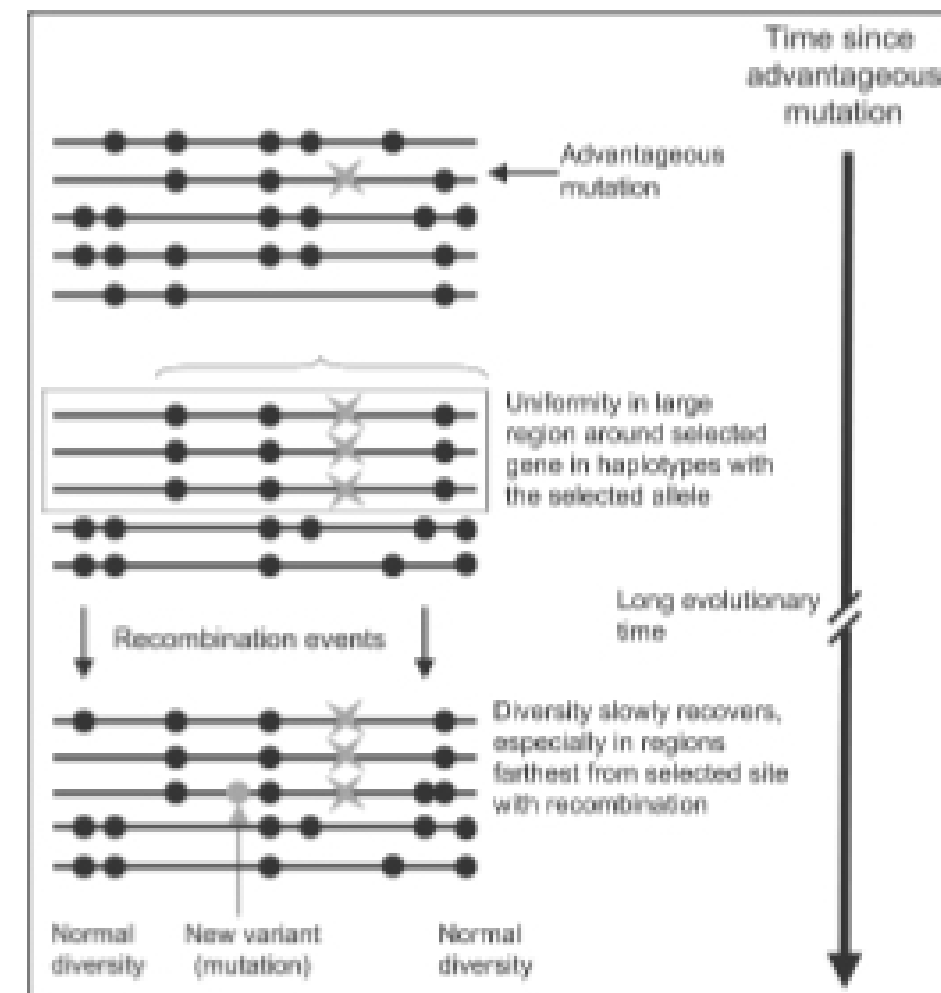
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Outline

- Questions
 - Have humans evolved rapidly or slowly during the past 40 kyr?
 - What functional categories of gene have evolved most?
- Selection and recombination
- Data
- Results

Are we still evolving?

- Since split with chimps, there has been rapid evolution in proteins expressed in brain and in sperm.
- Recent selection at various loci: lactase, DRD4, etc
- How common are such loci in the human genome?
- How can we tell?



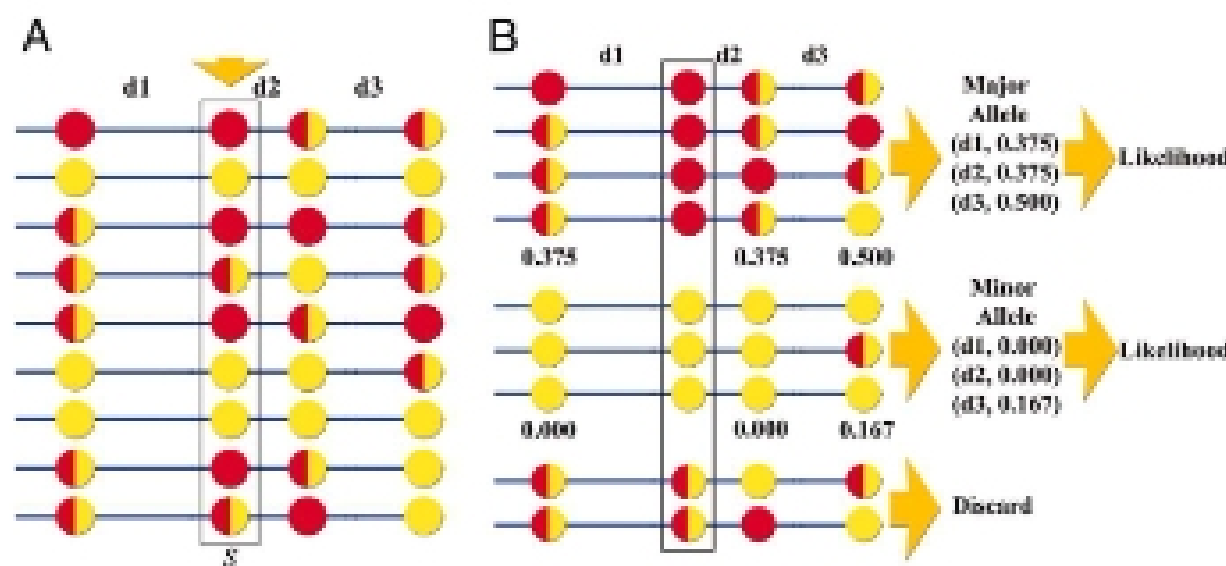
Signature of an ongoing selective sweep at DRD4

- Sweeping allele is
 - common
 - has low diversity over large region
- High LD over large region

Two methods for finding sweeping alleles

- Frequency of recombinant chromosomes (FRC): Wang et al 2006
- Extended haplotype homozygosity (EHH): Voigt et al 2006

Fraction of Recombinant Chromosomes (FRC)



At a given site

- FRC increases with time.
- Rate of increase depends on recombination rate.

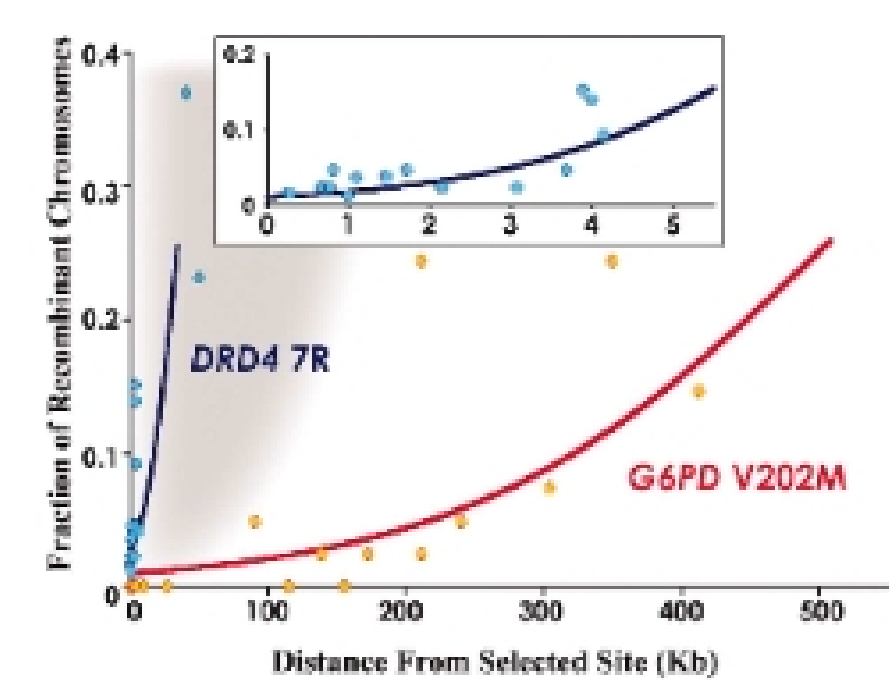
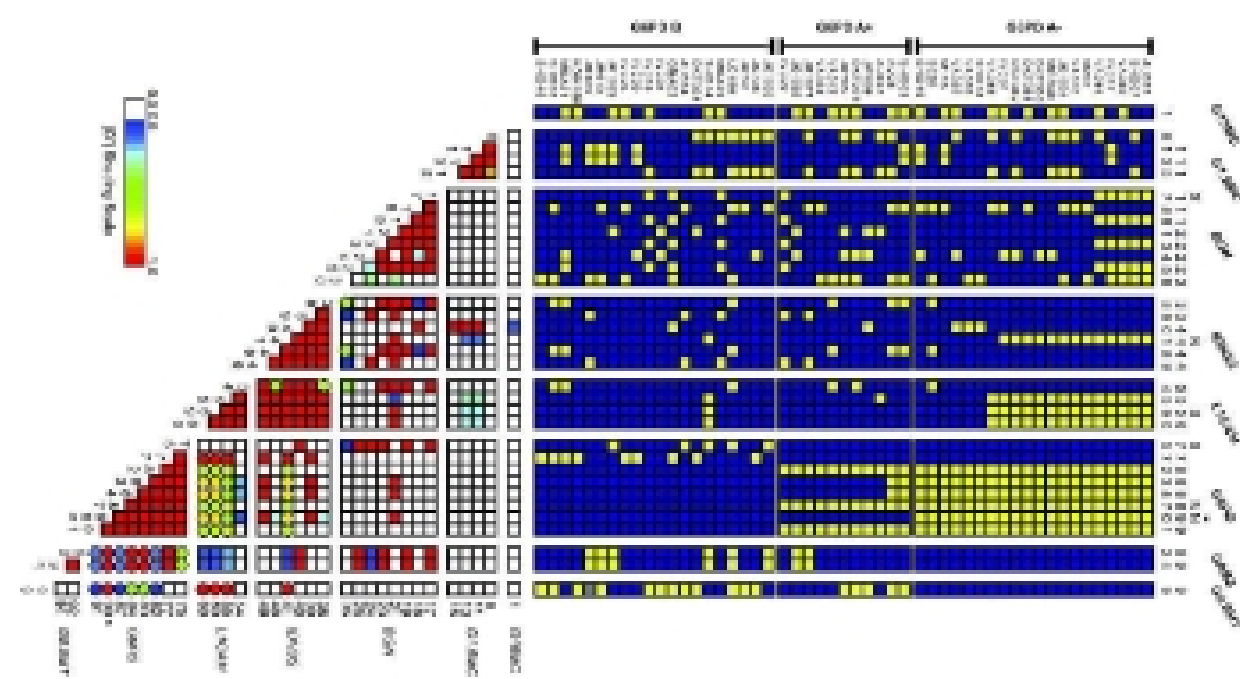
At a given time

- FRC increases with distance along the chromosome.
- Rate of increase is fast near neutral sites.
(Neutral $\Rightarrow$ old $\Rightarrow$ lots of recombination.)
- Rate is slow near ongoing selective sweeps.
(Selected $\Rightarrow$ young $\Rightarrow$ little recombination.)

Recipe
Look for regions where FRC is low in big sections of chromosome.

Linkage disequilibrium at G6PD

Left: LD plot; right: haplotype plot



- fraction recombinants increases with distance
- G6PD: recent selection
- DRD4: older, or in a region with more recombination

Results for G6PD

- Favored allele is about 100 generations old.
- Selective advantage: $s \approx 0.1$.

Study of Wang et al (2006)

- ▶ 1.6 million polymorphic nucleotide sites from throughout the genome
- ▶ most typed in worldwide sample of 71 people

Vertical lines: selected loci (Wang et al 2006)



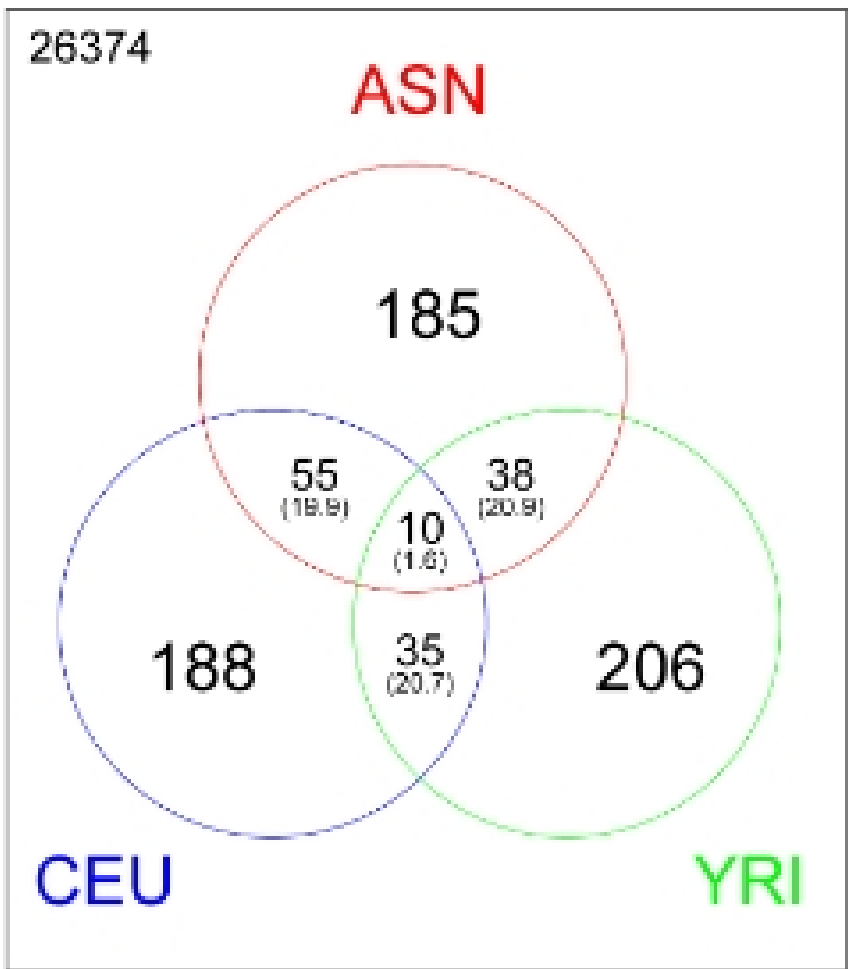
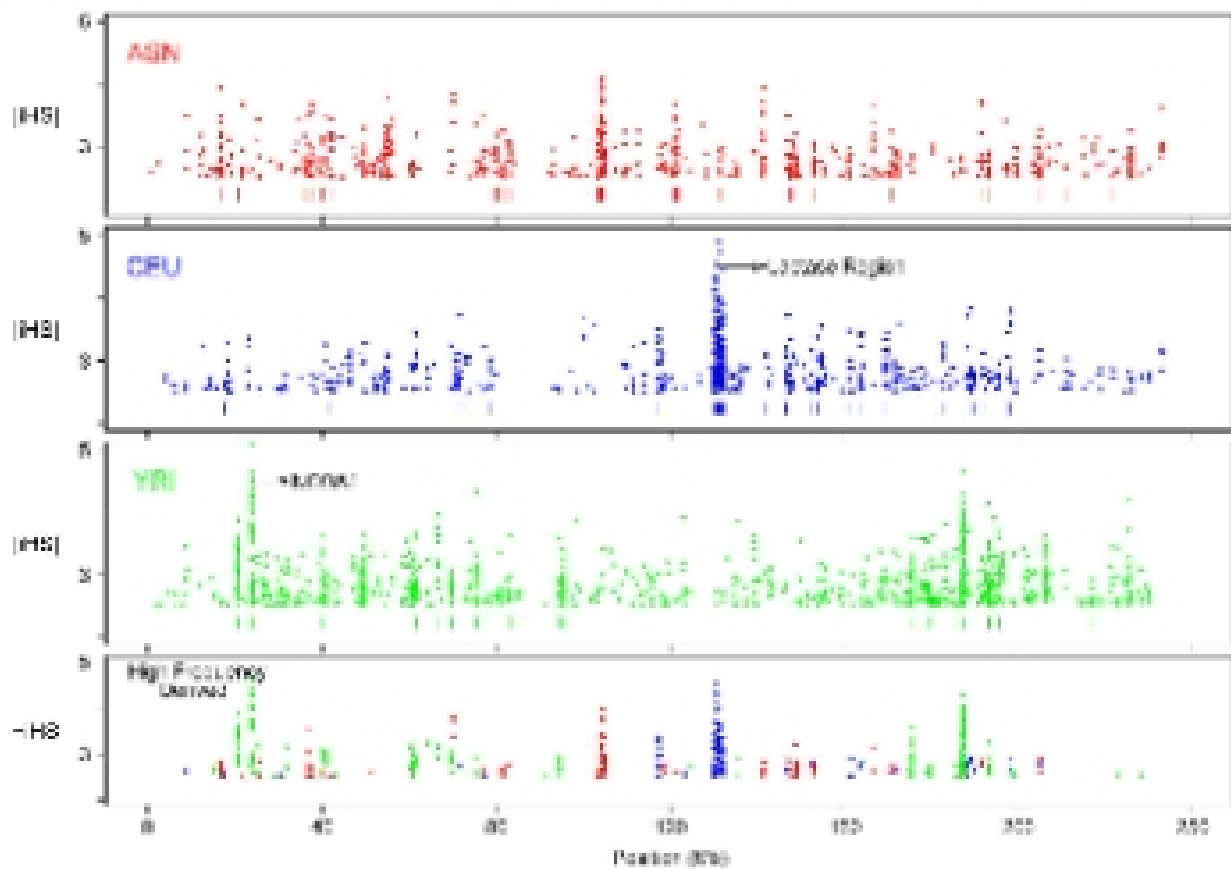
Entire genome (Wang et al 2006)



Study of Voigt et al (2006)

- ▶ 800,000 SNPs in 309 people
- ▶ 431 sweeping loci
- ▶ Most sweeps started w/i past 10,000 years

LD on human chromosome 2 (Voigt et al 2006)



Voight et al (2006):
431 sweeping loci.

ASN: Asia
YRI: Africa
CEU: Europe.

Most are sweeping w/i
only one continent.
Also true of Wang et al
data.