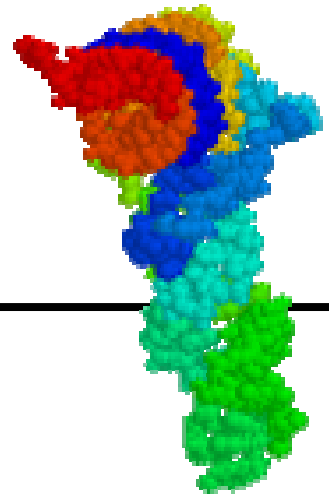
Genomics, Computing, Economics & Society



10 AM Tue 11-Oct 2005
week 4 of 14

MIT-OCW Health Sciences & Technology 508/510

Harvard Biophysics 101

Economics, Public Policy, Business, Health Policy

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Class outline

(1) Topic priorities for homework since last class

(2) Quantitative exercises: **psycho-statistics, combinatorials, random/compression, exponential/logistic, bits, association & multi-hypotheses**

(3) Project level presentation & discussion

(4) Sub-project reports & discussion:

Personalized Medicine & Energy Metabolism

(5) Discuss communication/presentation tools

(6) Topic priorities for homework for next class

Common Disease – Common Variant Theory. How common?

ApoE allele ε4 : Alzheimer's dementia, & hypercholesterolemia
20% in humans, >97% in chimps

HbS 17% & G6PD 40% in a Saudi sample

CCR5Δ32 : resistance to HIV
9% in caucasians

SNPs & Covariance in proteins

e4 20% **ApoE** **e3 80%**

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Ancestral = Arg 112 Thr 61

One form of HIV-1 Resistance

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Association test for CCR-5 & HIV resistance

Alleles	**Obs Neg**	**ObsSeroPos**	total	**ExpecNeg**	**ExpecPos**
CCR-5+	1278	1368	2646	1305	1341
Δ ccr-5	130	78	208	103	105
total	1408	1446	2854		
					P
dof=(r-1)(c-1)=1		ChiSq=sum[(o-e)^2/e]=		**15.6**	0.00008

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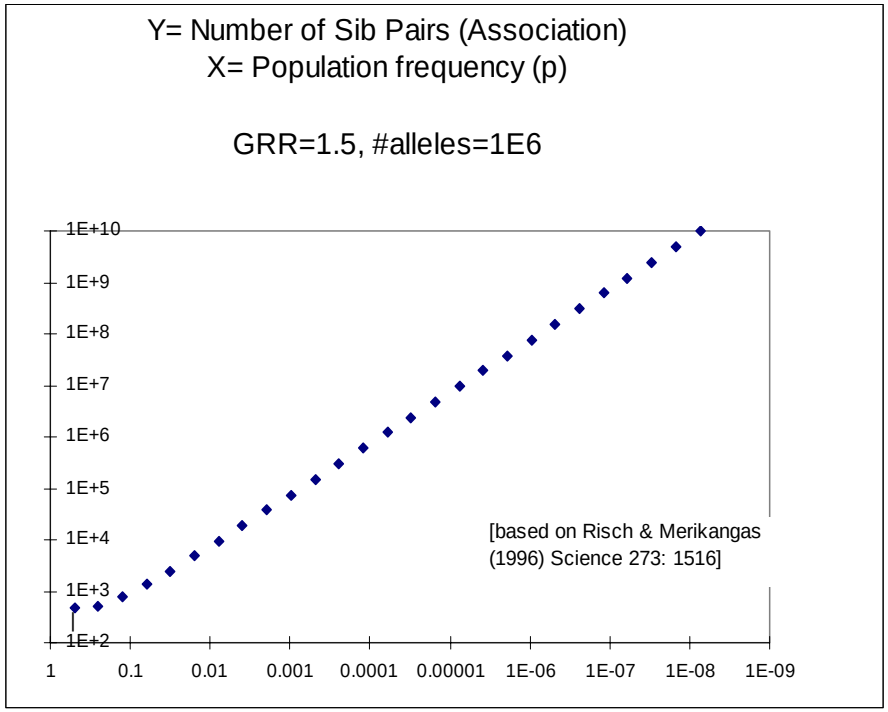
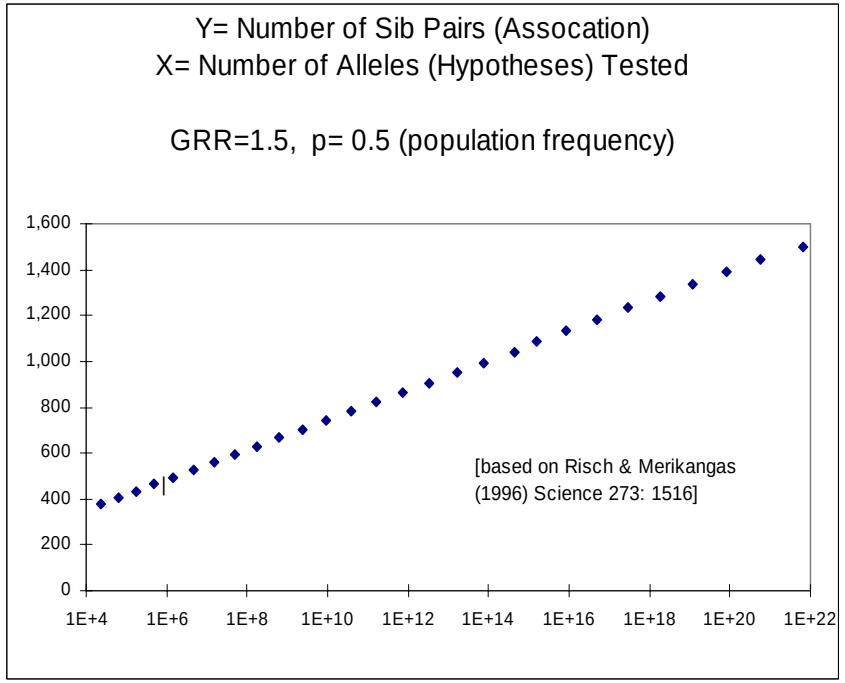
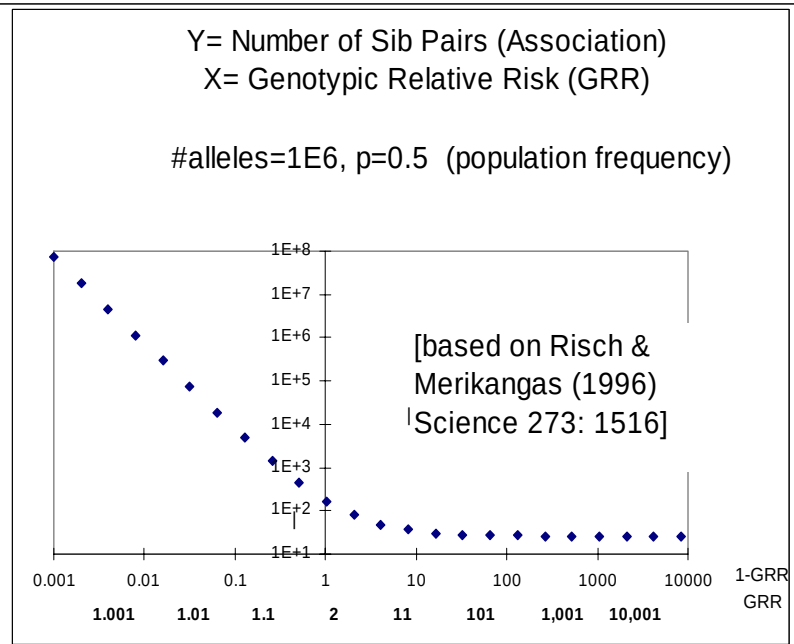
Samson et al. Nature 1996 382:722-5

But what if we test more than one locus?







The future of genetic studies of complex human diseases.
Ref

GRR = Genotypic relative risk

How many "new" mutations?

G= generations of exponential population growth = 5000

N'= population size = 6×10^9 now; N= 10^4 pre-G

m= mutation rate per bp per generation = 10^{-8} to 10^{-9} (ref)

L= diploid genome = 6×10^9 bp

$e^{kG} = N'/N$; so $k = 0.0028$

Av # new mutations per genome $< \sum_{t=1 \text{ to } 5000} Le^{kt}m = 4 \times 10^3$ to 4×10^4

Take home: "High genomic deleterious mutation rates in hominids" accumulate over 5000 generations & confound linkage methods And common (causative) allele assumptions.

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(6) Topic priorities, homework for next class