CS 68: BIOINFORMATICS

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Swarthmore College
Spring 2018

Outline: Mar 21

- Neutral theory of evolution
- Measures of sequence diversity
- Probability distributions and expected value
- The Coalescent

Notes:

- Office hours today are canceled
- Population genetics reading is posted
- Interested in being a ninja? Let me know
- Midterms will be handed back on Friday

Recap last time

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  - *random mating*
  - *the two chromosomes for each individual choose their parents independently*
  - *mutations are* ***neutral*** *(i.e. not selectively advantageous or deleterious)*

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- **Genetic drift**: changes in allele frequencies are due to random chance, not selection

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- The probability of fixation for a new mutation is $1/(2N)$ where N is the population size

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The lower the population size, the greater the chance new mutations will fix, even weakly deleterious ones. This can lead to what would typically be rare traits reaching high frequency.

Brief detour to Hardy-Weinberg

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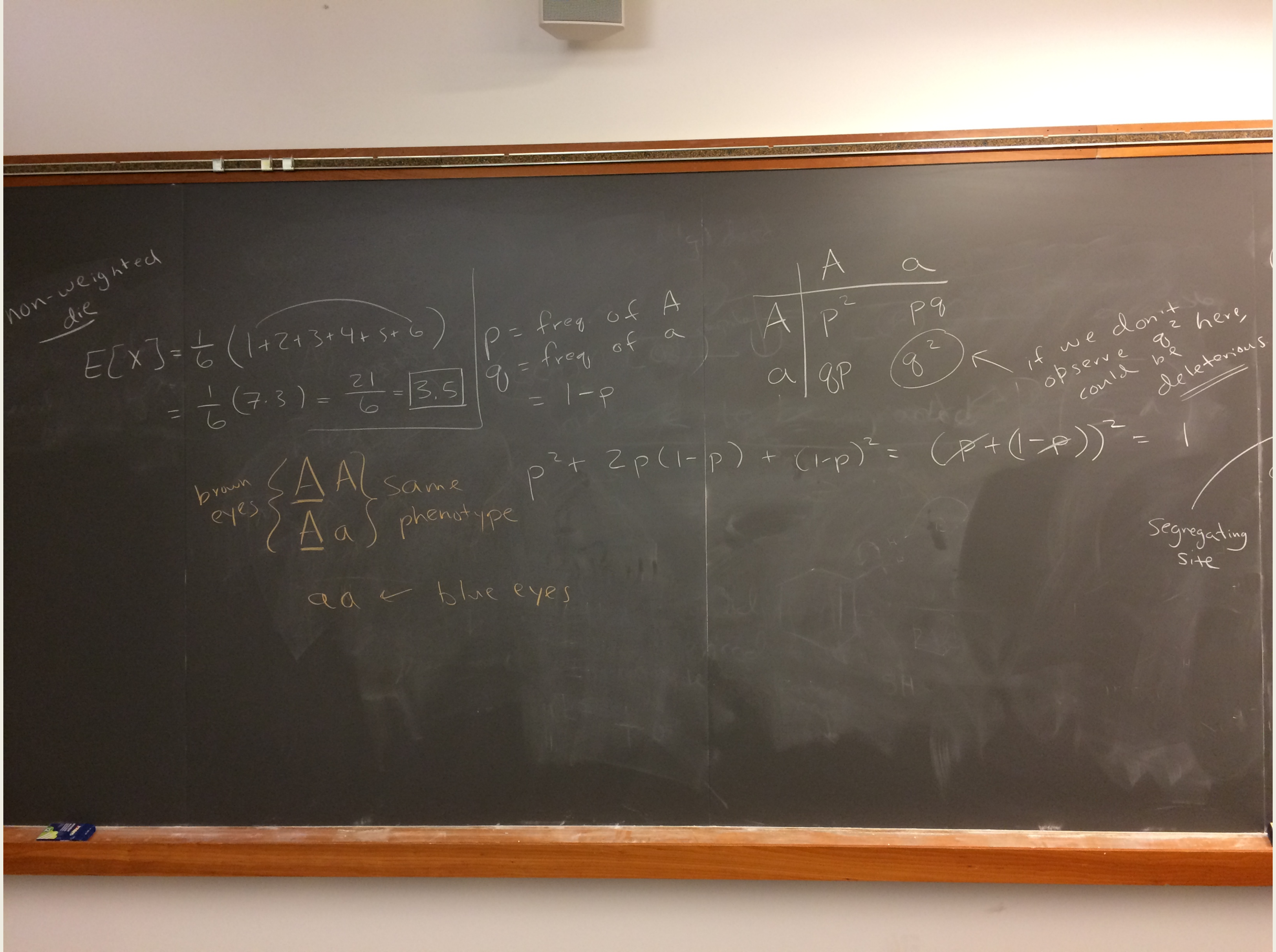
- If most alleles either become fixed or die out, that means eventually everyone will either be aa or AA. This is called the *loss of heterozygosity*



non-weighted die

$$E[X] = \frac{1}{6}(1+2+3+4+5+6)$$

$$= \frac{1}{6}(7 \cdot 3) = \frac{21}{6} = \boxed{3.5}$$

p = freq of A

q = freq of a

= 1-p

	A	a
A	p^2	pq
a	qp	q^2

if we don't observe q^2 here, could be deleterious

$$p^2 + 2p(1-p) + (1-p)^2 = (\cancel{p} + (1-\cancel{p}))^2 = 1$$

brown eyes $\left\{ \begin{array}{l} \underline{A}A \\ \underline{A}a \end{array} \right\}$ same phenotype

aa ← blue eyes

Segregating site

Neutral theory of evolution

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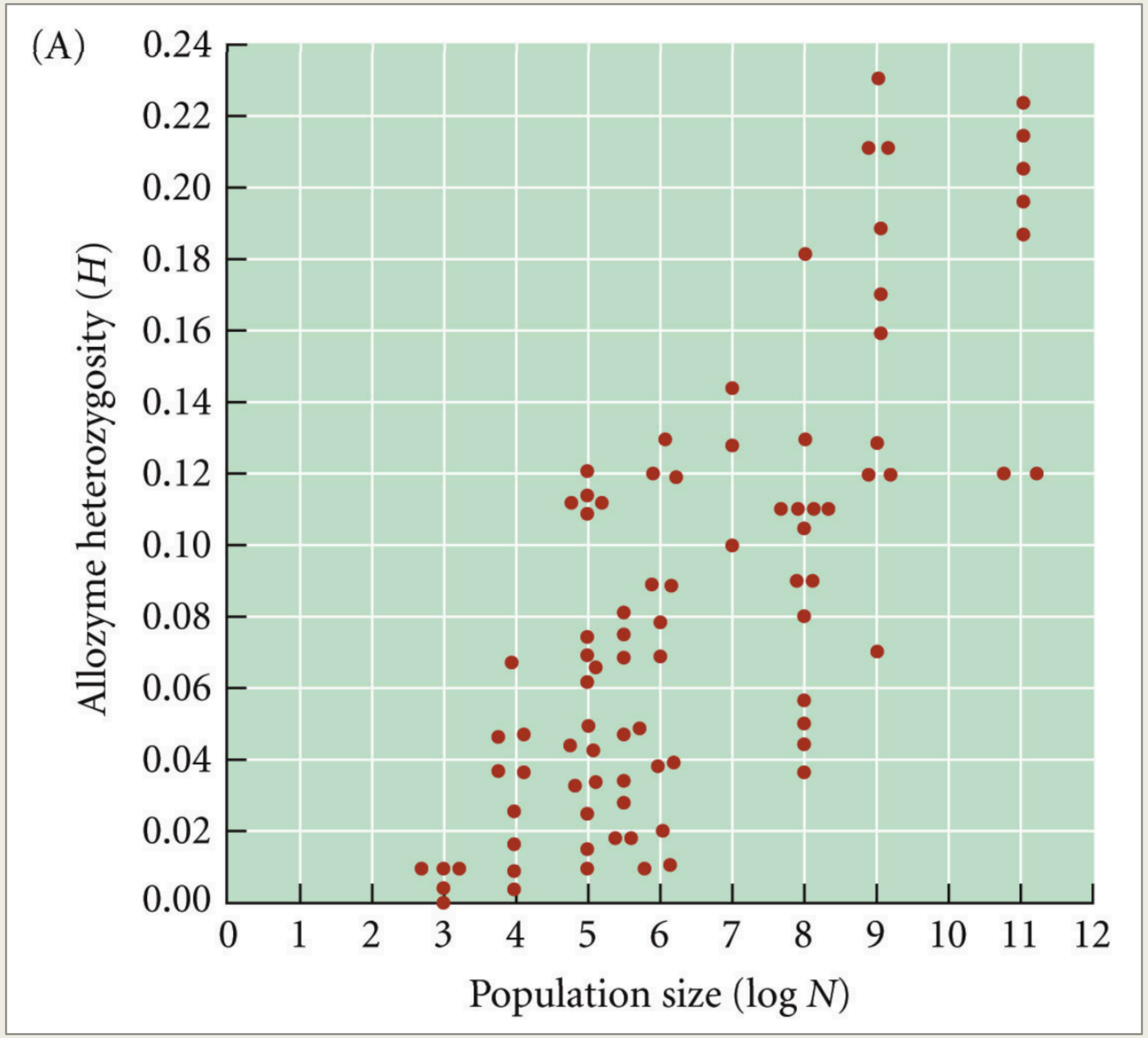
- Kimura 1968

- Claim: most genetic variation is neutral

- Consistent with the idea that population size is responsible for the level of variation in a population

***EVOLUTION 2e*, Figure 10.9 (Part 1)**



From: Graham Coop, https://gcbias.org/2016/09/21/population-genetics-undergrad-class/

Probability distributions and expected value

Discrete probability distribution

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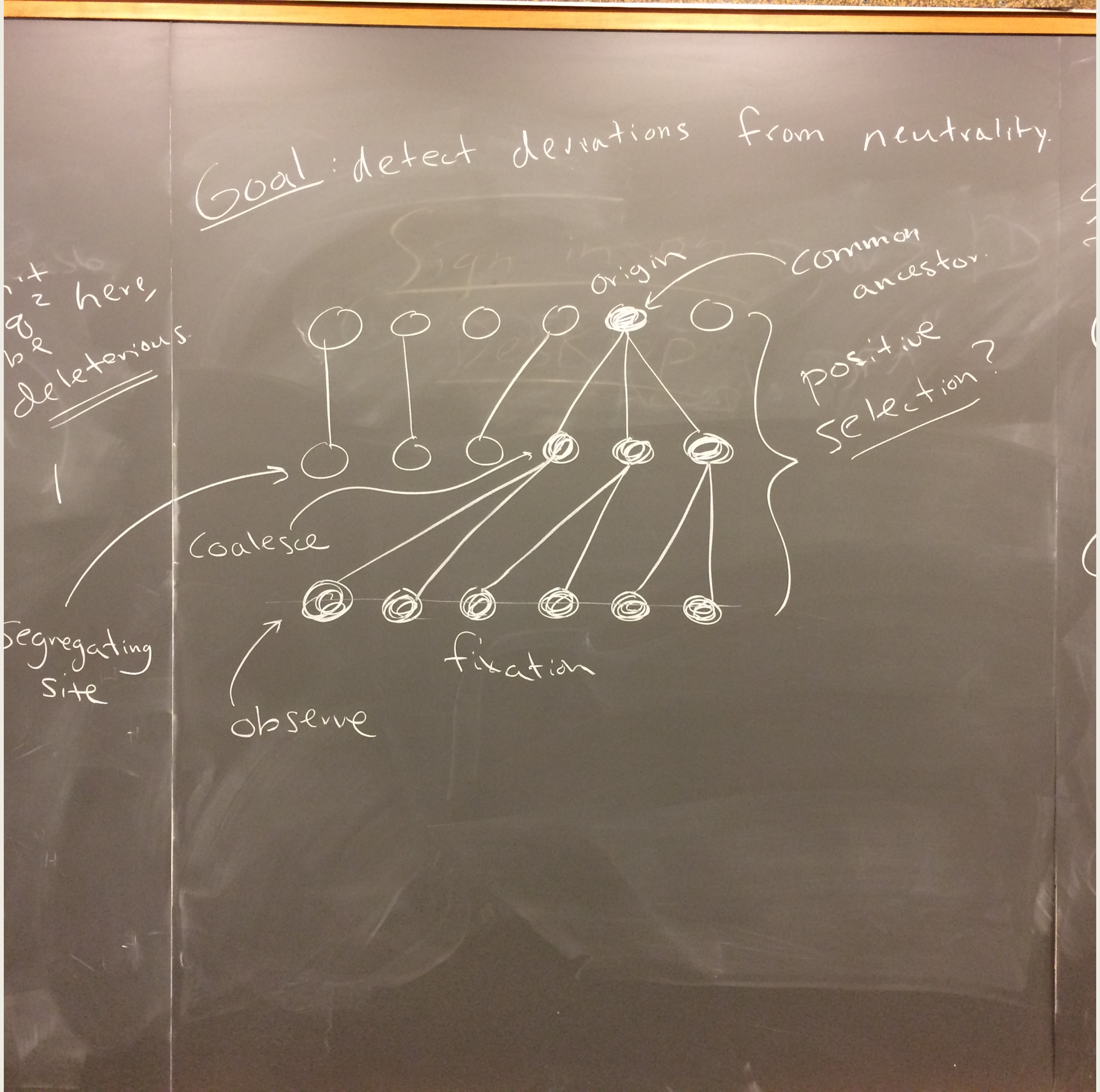
- Compute expectation:

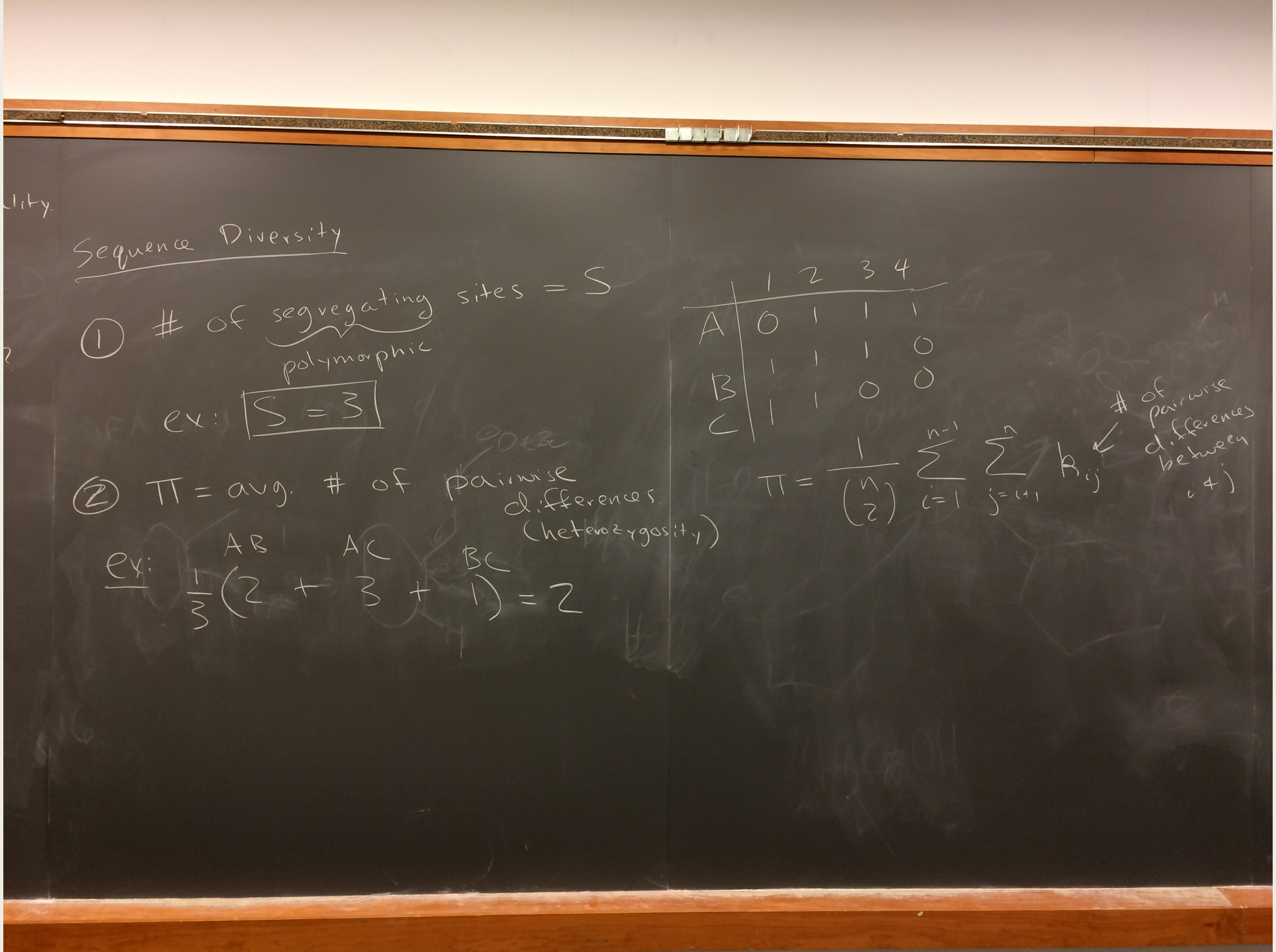
$$E[X] = p_1 x_1 + p_2 x_2 + \cdots + p_k x_k = \sum_{i=1}^{k} p_i x_i$$

$$0 \cdot 1 + \frac{1}{6}(2+3+4+5) + \frac{1}{3} \cdot 6 = 4\frac{1}{3}$$

Measures of sequence diversity



Goal: detect deviations from neutrality.



lity.

Sequence Diversity

① # of $\underbrace{\text{segregating}}_{\text{polymorphic}}$ sites = S

ex: $\boxed{S = 3}$

	1	2	3	4
A	0	1	1	1
B	1	1	1	0
C	1	1	0	0

② π = avg. # of pairwise differences (heterozygosity)

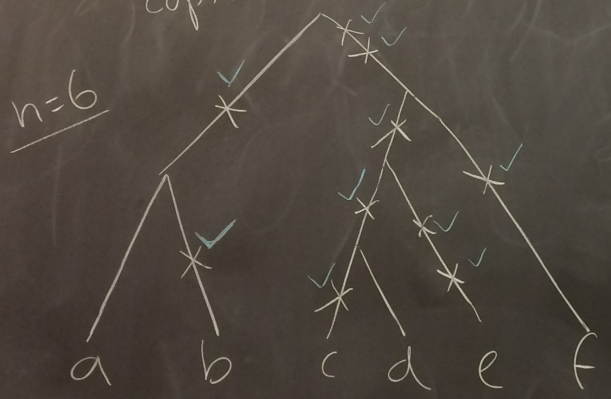
ex: $\frac{1}{3}(\overset{AB}{2} + \overset{AC}{3} + \overset{BC}{1}) = 2$

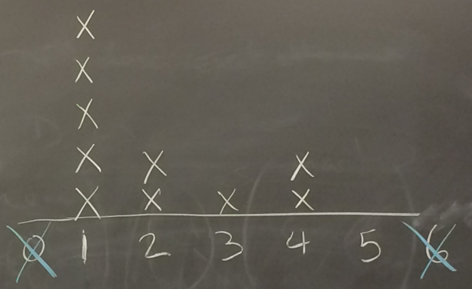
$$\pi = \frac{1}{\binom{n}{2}} \sum_{i=1}^{n-1} \sum_{j=i+1}^{n} k_{ij}$$

k_{ij} ← # of pairwise differences between i + j

③ SFS = site frequency spectrum.

ξ_i = # of sites with $\boxed{i}$ copies of the mutant allele + $\boxed{n-i}$ copies of the ancestral allele

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