

BIS101 F2013 Lecture 6: Population Genetics

Population genetics

What is a population?

a group of individuals of the same species, usually within some geographically delimited area, usually with the possibility of intermating

Evolution:

change in frequency of an allele over time (not the same as natural selection)

Frequency

A_1A_1	A_1A_2	A_2A_2
20	13	17

- what's the *genotype frequency* of A_1A_1 ? 40% (20/50)
- what is the allele frequency of A_2 ? ($p=47\%$ or 0.47 because $34+13/100$)
- what is the frequency of A_1 ? ($1-p=0.53$ b/c has to add to 1)

I come back in 10 years, pop is now A_1A_1 80 A_1A_2 52 and A_2A_2 68

Has evolution occurred ? (not at this locus)

Population genetics is the study of allele frequency change in populations

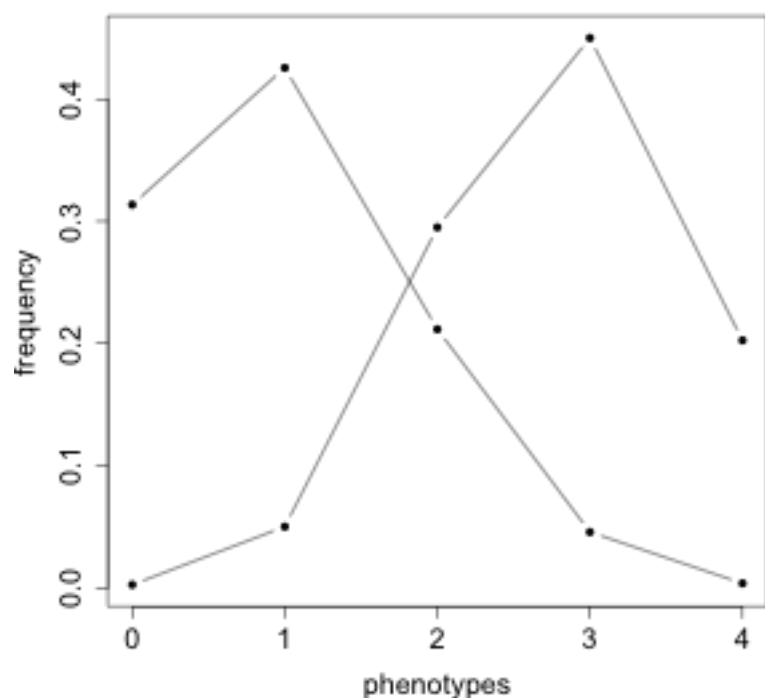
Could argue it is synonymous with evolution

We also care about it because it has effect on phenotypes!

In talking quant gen, we showed phenos for a cross where at each het we have 1:2:1 segregation in F2, but in a population phenotype distribution determined by allele freqs.

So distribution would be freq. of genotype * value, e.g.

Using our model of two loci with each big letter adding 1 to phenotype, @ locus A $p_A = 0.2$ and at locus B $p_B = 0.3$



Mean phenotype in the population = 1 (what's frequency of AA? 0.04, of AABb? 0.20.20.30.3 = 0.0018 and phenotype ??? 4). frequency of aabb ? 0.80.80.70.7 = 0.3136

Now change allele frequencies to $p_A=0.5$ and $p_B=0.9$ and redraw. New mean phenotype = 2.8. So allele frequencies will affect mean phenotype in pop without changing any of the genetics!

Hardy-Weinberg Equilibrium

- We talked about Mendel. HWE **NOT** 1:2:1
- Hardy & Weinberg 1908 (Hardy played crickey w/ Punnet)
- How to solve problem of blending & loss of diversity
- Model (what's a model ?) (what's an equilibrium?)
 - model is a simplified description (mathematical) of a system
 - most of the time oversimplified – “all models are wrong, some models are useful”
 - focus on the important parts of a system (noise in biology)
 - allow predictions of expected outcome & comparison to real data
 - if obs. data do not fit model – biological interesting
 - assumptions wrong, try new model
 - what if data fit model? (my model is that aliens came down from outerspace and put chalk in the room)
 - data consistent w/ model doesn't PROVE model (that's how science works)

HW Model (write on board assumptions)

Assumptions:

- autosomal (which is?)
- locus, 2 alleles, diploid
- mendelian segregation
- random mating
- no other evol. forces (which?)

- no selection
- no migration
- no mutation
- no drift (large. pop size -> inf.)
- equal freq. in both sexes (or all hermaphrodites)
- generations discrete and nonoverlapping (annual plant) (explain)

Define variables (observed outcome of a system), parameters (things that define the model or system)

variables - X, Y, Z obs. freqs of 3 genotypes (A_1A_1 , A_1A_2 , A_2A_2) in our sample

parameter p = freq. A_1 allele, q=freq. A_2 allele = 1-p (why?)

if we have sample (not whole pop) of 18 A_1A_1 and 24 A_1A_2 and 8 A_2A_2

X=0.36, Y=0.48, Z=0.16

$$p = X + \frac{Y}{2} = 0.6 \text{ (60 copies of } A/100 \text{ total copies)}$$

Equations

In next generation:

Gamete Table	prob. A_1 from parent1	prob A_2 from parent1
prob A_1 from parent2	pp	$p(1 - p)$
prob A_2 from parent2	$(1 - p)p$	$(1 - p)(1 - p)$

use prime to denote next generation

$$X' = p^2 \quad Y' = p(1 - p) \\ Z' = (1 - p)^2$$

$$\text{and } p' = X' + Y'/2$$

$$\text{and substituting: } p' = p^2 + 2p(1 - p)/2 = p \text{ <- equilibrium}$$

** In HWE, genetic composition (genotype and allele freqs) predictable w/ one parameter -> p **

Once in HWE, allele freqs. do not change (equilibrium) w/o disturbance

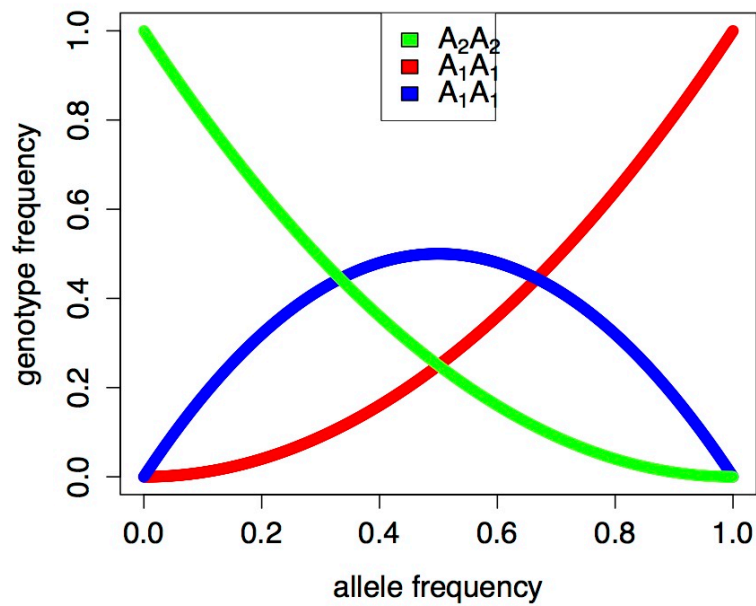
After a single generation of random mating -> HWE

- start with 0.2 A_1A_1 and 0.8 A_2A_2 -> figure out what's p, and what's p' -> HWE after one generation

Conclusions

Single generation of random mating will almost always -> HWE

Rare alleles more common in hets ($p^2 < 2pq$ for whenever $p < q$)



Does dominance change HWE? - no because we haven't said anything about phenotype – just genotype - so will recessive alleles go extinct ?

Surprising # of loci in diff. organisms cannot reject HWE - does this mean no selection, drift, mutation ? why not?

Informative: e.g. red hair. melanocortin 1 receptor MCR1. position 478 in the gene, if you are homozygous for the TT allele instead of the dominant C allele, you are a redhead with freckles.

In the US, the T alleles is at ~8% frequency. So redheads should be at what freq ? = 0.64%. But between 2-6% of the population has red hair. What do conclude?

- assortative mating: maybe redheads mate with other redheads
- selection: maybe redheads are going to take over the world (unlikely)
- gene flow: immigration from countries with lots of redheads (irish, etc.?)
- multiple loci: maybe MCR1 is not only locus involved – in fact we know there are multiple mutations in MCR1 that can cause redhead, so a likely option.

Can use Chi-square to test if loci are in HWE!

- e.g. sample AA= 72 (68.1) Aa = 21 (28.9) aa = 7 (3.1) <- show this for yourself
 - $\chi^2 > 7.28$ so not in HWE (tell them to show for selves)
- e.g. AA= 82 Aa = 38 aa = 5
 - is in high-perfect HWE (test it)

Violate an assumption

Can show effects of violating an assumption (nonequal # of sexes etc.)

Some assumptions have sm. FX

- nonequal sexes, takes longer than 1 gen of random mating to reach HWE but still reach it

- drift or selection -> never reach
- nonrandom mating: include parameter F and can rewrite HWE with inbreeding coefficient

DRIFT

in HWE with $N \rightarrow \infty$ what happens to allele freqs over time (nothing)

in small pops, random chance is imp. (think about freq. heads depends on sample size)

Smaller N -> more drift; Bigger N -> less drift

Draw on board 6 individuals (1 AA 3 Aa 2 aa) (can do χ^2 and show sample does not reject HWE)

- If this is whole pop.: (calculate freqs.) use die roller app to pick mates for next gen.
- Recalculate freqs. (has evolution happened?)
- do a couple more (maybe until fixation?)

Other things associated with drift (define):

- bottleneck
- founder effect

Other deviations from HWE cause drift – separate sexes, etc, uneven offspring production. Humans have as much drift as a theoretical pop of size 10K in spite of being 7Billion of us!

Effective pop size: size of a theoretical population meeting all assumptions that has same allele freq. behavior as your pop.

- because most pops violate assumptions, N_e almost always $\ll N$
- N_e is what matters for drift.
 - Big census size w/ lots of size fluctuation similar drift to smaller pop w/ constant size
- e.g. N_e for Humans is 10K
- for dairy cows 100
- for drosophila 2M

Will skip the math, but:

Drift causes inbreeding: random mating in pop of sample 10, soon you're mating w/ relatives by random!

Chance of fixation = frequency. So most new mutations (at freq. $1/2N$) are lost by to drift!

Differences between species: $2N \cdot \mu$ mutations per gen. * $1/2N$ chance of fixing = μ differences between species per gen. (or between genes, i.e. K_s)

Selection

Natural Selection not same as evolution

- change in frequency of a variant due to its effect on fitness
- multiple components to fitness: viability, mating success, fecundity
- Think in terms of relative fitness: some most fit genotype, and all other genotypes are competing with it
- variant that makes you compete better and make more copies of your genes -> natural selection will

increase freq.

Fitness Table

Genotype | A_1A_1 | A_1A_2 | A_2A_2 | — | — | — | — | Freq. | p^2 | $2p(1-p)$ | $(1-p)^2$ | Fitness | w_{11} | w_{12} | w_{22}

relative fitness of A_1A_1 is w_{11}

- not faster than the bear, faster than the other guy

mean fitness of populations is weighted avg.

$$\{w\} = p^2 w_{11} + 2p(1-p)w_{12} + w_{22}(1-p)^2$$

genotype freq. change depends on rel. fitness, so

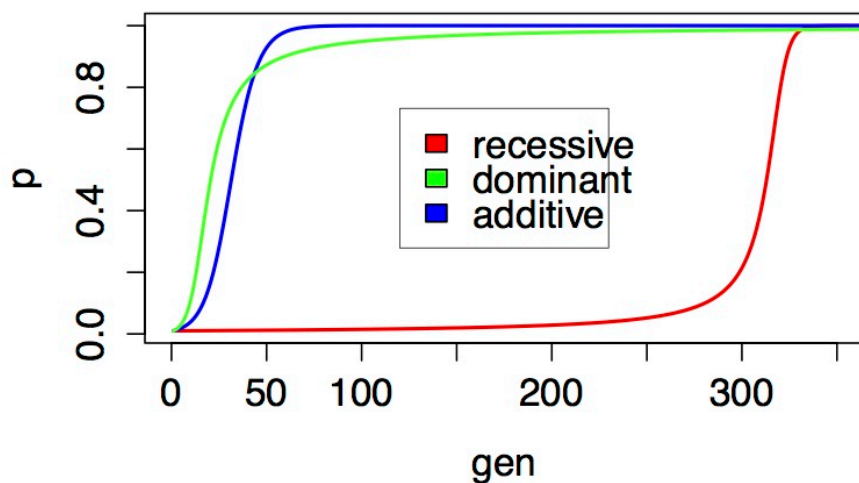
- $X' = \frac{p^2 w_{11}}{\bar{w}}$
- $Y' = \frac{2p(1-p)w_{12}}{\bar{w}}$
- $Z' = \frac{(1-p)^2 w_{22}}{\bar{w}}$

can do some math and show allele freq:

- $p' = \frac{p(pw_{11} + (1-p)w_{12})}{\bar{w}}$

results:

- change in allele freq. depends on difference in fitness b/t heterozygote and homozygote for the allele
- allele freq. (greater change with more middling allele freq)
- stronger s -> faster change in p,
- this general formula allows variation.
 - e.g. $w_{11}=1$ $w_{12}=1-s$ $w_{22}=1-2s$ – when het is intermediate additive or incomplete dominance
 - $w_{11}=1$ $w_{12}=1$ $w_{22}=1-s$ (dominance of A_1)
 - $w_{11}=1$ $w_{12}=1-s$ $w_{22}=1-s$ (recessive A_1)
- draw graph for recessive, dominant, codominant



Other forces

Gene flow: movement of genes from one population to another

- can impact allele frequencies and counteract selection and drift
- different pops should drift independently, but even one migrant/generation enough to prevent extensive divergence

Mutation

- fairly straightforward, increases freq of particular allele

Combos

Mutation-selection balance:

- assuming selection against recessive: $p = \frac{\mu}{s^{0.5}}$
- for a completely recessive mutation, even under lethal selection (s=1) the freq. of A will be μ