Mendalian genetics and Hardy Weinberg Equilibrium law

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Let us look on some of the terms which may not be familiar for some of our colleagues.

- Genes–The fundamental physical and functional unit of heredity, which carries information from one generation to the next.

- Genetics–(1) The study of genes through their variation. (2) The study of inheritance.

- Allele–Alternative form of a gene. One of the different forms of a gene that can exist at a single locus.

- Chromosomes–The rod shaped structure that are found in living cells and contain the genes (= chemical patterns) which control what an animal or plant is like.

- Diploid cell– A cell having two chromosome sets.

- Meiosis–The nuclear and cell division process in diploid eukaryotes that results in four haploid gametes

- Gamete–A germ cell having a haploid chromosome complement. Gametes from parents of opposite sexes fuse to form zygotes.

- Genotype– The genes that an organism possesses.

- Phenotype–The detectable outward manifestations of a specific genotype. The observable attributes of an organism.

- Dominant–An allele that determines phenotype even when heterozygous. Also the trait controlled by that allele.

- Recessive–An allele that is not expressed in the heterozygous condition. Expressed only when the determining gene is in the homozygous condition, recessive traits.

John Mendal's main conclusions are

1. The two members of genes pair segregate from each other during meiosis, and gamete has an equal probability of obtaining either member of the gene pair.

2. Law of independent assortment, unliked or distantly linked segregation gene pairs assort independently at meiosis.

In a population of individuals of a sexually producing species, a single gene is passed from generation to generation following mendalian inheritance.

Each diploid individual has two copies (allele) of each gene.

Example

Gene A may have two alleles in a population A and a. If an individual has

- two copies of A, then the genotype of the individual is AA and it is homozygous.
- with Aa genotype is heterozygous.
- with aa genotype is the other homozygous.

Mendalian segregation implies that for alleles having dominant inheritance, the phenotypic segregation ratio is 3:1 in F_2 progeny.

	parent			
	Aa		Aa	
gamete	a	A	a	A
	aa	$2Aa$		AA

If A is dominant then the ratio is $3:1$. If parents

- Aa and AA then the offspring will have $2aA$ and $2AA$. No segregation in backcross if one of the parent is AA.

- Aa and aa then the offspring will have $2Aa$ and $2aa$. Segregation ratio is 1:1 in backcross if one of the parents have aa.

Mendalian law of independent assortment

Two seed's characters

- Let A and a denote the alleles for round and wrinkled seed.
- Let B and b denote the alleles for yellow and green.

	AA	Aa	aa	Total
BB	38	60	28	126
Bb	65	138	68	271
bb	35	67	30	131
Total	138	265	126	529

Hardy Weinberg

A population is in equilibrium if the gene and genotypic frequencies are constant from generation to generation.
Mating two individuals that are heterozygous i.e., Aa for a trait gives

- 25% of their offspring are homozygous for the dominant allele AA.

- 50% are heterozygous like their parents Aa

- 25% are homozygous for the recession aa.

This is what Mendal found.

- Meiosis separates the two alleles of each heterozygous parent- 50% of the gametes will carry one allele and 50% the other.

- When gametes are brought together at random, each A(or a) carrying egg will have 50% chance of being fertilized by a sperm carrying A(or a).

Result of random union of the two gametes produced by two individual, each heterozygous.

	$0.5A$	$0.5a$
$0.5A$	$0.25AA$	$0.25Aa$
$0.5a$	$0.25aA$	$0.25aa$

$$0.25 + .50 + .25 = 1$$

But the frequency of the two alleles in an entire population of organism is unlikely to be exactly the same.

Example Consider an hypothetical population of Hamster in which

- 80% of all gametes in the entire population carry a dominant allele for black coat A.

- 20% carry the recessive allele for grey coat a.

- Result of random union of the gametes produced by an entire population :

	$0.8A$	$0.2a$
$0.8A$	$0.64AA$	$0.16Aa$
$0.2a$	$0.16Aa$	$0.04aa$

- So 96% of this generation will have black coats $(0.64 + 0.16 + 0.16 = 0.96)$ and 4% gray coat.

- Question:
  Will gray hamster eventually disappear?

- Answer:
  No.

- All gametes formed by AA will contain allele A as well.

- One half the gametes formed by heterozygous Aa hamster.

- So, 80% $(0.64 + .5 \times 0.32)$ of the pool of gametes formed by this generation will contain A.

- All the gametes of the gray aa hamster 4% will contain a.

- One half of the gametes of the heterozygous hamster will contain a as well.

- So, 20% $(0.04 + 0.5 \times 0.32)$ of the gametes will contain a.

- Duplicated the initial condition exactly. The proportion of allele a in the population has remained the same.

- Algebraic analysis of the same problem using expression of the binomial $(p+q)^2$.

$$(p+q)^2 = p^2 + 2pq + q^2$$

- The total number of genes in a gene population is its gene pool.

- Let p_A represent the frequency of one gene in the pool and p_a is the frequency of its single allele. So $p_a + p_A = 1$.

- <u>Estimation of p_a and p_A</u>
  Let in a sample of n individuals one scored for a locus with two alleles A,a and found n_{AA} AA, n_{Aa} Aa and n_{aa} aa. The estimate for p_A :

$$\bar{p}_A = \frac{n_{AA}}{n} + \frac{n_{Aa}}{2n}$$

- Example:
  Suppose that 40 individuals are scored for a locus with two alleles B, b and 25 BB, 13 Bb, 2 bb individuals are found.

a.) Estimate the frequency, p_B, p_b.

b.) Test the sample for Hardy-Weinberg equilibrium with a chi-square test.

- Solution

$$\begin{aligned} p_B &= \tfrac{25}{40} + \tfrac{13}{80} &= 0.7875 \\ p_b &= 1 - p_B &= 0.2125. \end{aligned}$$

- Set the null hypothesis H_0 : data follows HWE. Using Hardy Weinberg

$$p_B^2 + 2p_Bp_b + p_b^2 = 1$$

Genotype	BB	Bb	bb
o_i	25	13	2
p_i	0.62	0.335	0.045
e_i	24.8	13.4	1.81

- Chi-squared test for given probabilities

- data: c(25, 13, 2) $\chi^2 = 0.0358$, df = 2, p-value = 0.9823.

- test $< -$chisq.test($c(25, 15), p = c(.62, .38)$).

- data: c(25, 15) $\chi^2 = 0.0042$, df = 1, p-value = 0.948.

- Do not reject H_0.

Hardy Weinberg Law

Gene frequencies and genotype ratios in a randomly breeding population remain constant from generation to generation.

Following are the circumstances in which the Hardy Weinberg Law may fail to apply

- Mutation.
- gene migration
- genetic drift
- non-random mating
- natural selection.

- <u>Example</u>

  Following is the Mendel's data on cotyledon color from 10 plants:

	1	2	3	4	5	6	7	8	9	10
Y	25	32	14	70	24	20	32	44	50	44
G	18	14	9	13	6	13	27	5	7	11

a). If the 10 samples are homogenous, each has the same proportion of Yellow cotyledon. Estimate the proportion of yellow cotyledon.

b). Perform a chi-square goodness of fit test of hypothesis that yellow and green cotyledon occur in ratio 3:1.

c). What would be expected frequencies if some one like to test that yellow and green cotyledon occur in ratio 1:1?

- Solution

1. Compute the total counts for yellow cotyledon, (o_y) and green cotyledon, (o_g) (observed counts).

2. Estimate of proportion for yellow cotyledon is:

$$\widehat{p}_y = \frac{o_y}{o_y + o_g}$$

- Set the null hypothesis
  $H_0 : p_y = 3/4,\ p_g = 1/4.$

- Assuming H_0 is true the expected counts $e_y = \frac{3}{4} \times (o_y + o_g)$ and $e_g = (o_y + o_g) - e_y$.

	color		Total
counts	Y	G	
o_i	355	123	478
e_i	358.5	119.5	478
$(o_i - e_i)^2$	12.25	12.25	
$\frac{(o_i - e_i)^2}{e_i}$	0.034	0.102	0.136

- test $< -$chisq.test$(c(355, 123), p = c(.75, .25))$.
  Chi-squared test for given probabilities.

- data: c(355, 123) $\chi^2 = 0.1367$,
  df = 1, p-value = 0.7116

- Do not reject H_0.