GENETICS: PART I

Course Syllabus:

- 1. Genetic Transmissions.
- 2. Mendelian Genetics.
- 3. Transmission and inheritance of chromosomes.
- 4. Linkage and Mapping.
- 5. Mendelien Genetics in Corn (Zea mays). (22/10)Student presentations and open discussion
- 6. Extensions of Mendel's laws.

Objectives:

By doing this course well, you will be able to:

- Differentiate between the different ways of transmission
- Be familiar with common genetic terms and definitions
- Be familiar with the basic principles of Mendelian inheritance
- Apply the principles of inheritance as formulated by Mendel to solve problems.
- Be able to calculate estimated genotypic and phenotypic frequencies resulting from crosses between specific genotypes, for one and two-gene cases.
- Understand the difference between single-gene traits and polygenic (quantitative) traits
- Apply the principles of extensions to Mendelian inheritance
- Analyze genetic data using statistical procedures.
- Understand the concept of linkage. Learn to recognize when two genes are linked.
- Realize how the linkage of two genes results in a different set of gametes than if the two genes were unlinked.
- Understand the nature of crossing over, and how this affects linked alleles.

• Be able to map gene positions on a chromosome, using rates of crossover.

GENETICS TRANSMISSION

Genetics

It is the science that seeks to understand, explain and ultimately exploit the phenomenon of heredity (i.e. transmission of biological characteristics of organisms from one generation to the next from parents to offspring).

Genetic material

The genetic material of a cell can be a gene, a part of a gene, a group of genes, a DNA molecule, a fragment of DNA, a group of DNA molecules, or the entire genome of an organism. They are found in the nucleus, mitochondria and plastids (for plant), which play a fundamental role in determining the structure and nature of cell substances, and capable of self-propagating and variation.

Genetic transmission (genetic transfer, GT) is the study of how genetic information from genes are transmitted from cell to cell and generation to generation (from parent to offspring), how they recombine and segregate, with the goal of explaining the numerical proportions of the progeny in cross. Genetic transmission is almost synonymous with heredity, or from one location in a cell to another, and it should not be confused with chromosomal translocation, which is rearrangement of parts between non-homologous chromosomes.

There are two types of genetic transmission:

1. Vertical gene transmission (VGT) is the transmission of genes from one generation of species (the parental or ancestor generation) to the next generation of the same species (offspring) via sexual or asexual reproduction.

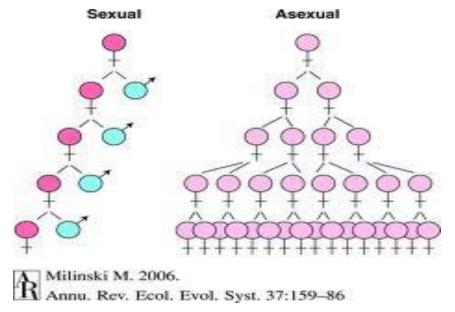
DNA encodes all the information necessary to make an organism. Every organism's DNA is made of the same basic parts, arranged in different orders. DNA is divided into chromosomes, or groups of genes, which code for proteins.

There are two ways for vertical gene transfer:

Sexual reproduction is a biological process by which organisms create descendants that have a combination of genetic material contributed from two (usually) different members of the species using meiosis. Most animals (including humans) and plants reproduce sexually. Sexually reproducing organisms have different sets of genes for every trait (called alleles). Offspring inherit one allele for each trait from each parent, thereby ensuring that offspring have a combination of the parents' genes.

Asexually reproducing organisms reproduce using mitosis. Bacteria divide asexually via binary fission; viruses take control of host cells to produce viruses; Hydras (invertebrates of the order *Hydroidea*) and yeasts are more able reproduce by budding. Other ways of asexual reproduction include parthenogenesis, fragmentation and spore formation.

Both these mechanisms involve duplication of DNA, which then gets passed to offspring. RNA is a key component in the duplication of DNA.

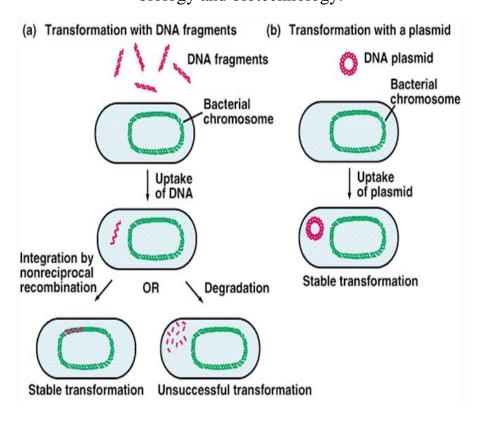


2. Horizontal gene transmission (HGT) refers to the transfer of genes between organisms, from one species to another species, in a manner other than traditional reproduction. It is also termed lateral gene transfer. HGT has been shown to be an important mechanism that drives evolution of many organisms

due to the incorporation of genetic material from an organism to another one without being the offspring of that organism.

There are several mechanisms for horizontal gene transfer:

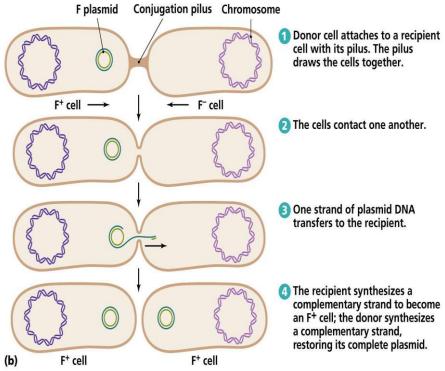
a. Transformation, the genetic alteration of a cell resulting from the introduction, uptake and expression of foreign genetic material (DNA or RNA) either naturally or artificially. This process is relatively common in bacteria.
 Transformation is often used in laboratories to insert novel genes into bacteria for experiments or for industrial or medical applications through molecular biology and biotechnology.



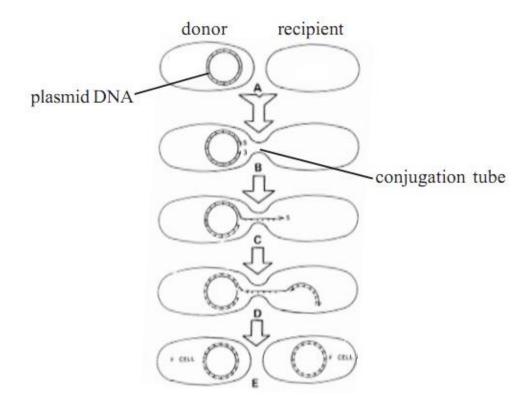
b. Bacterial conjugation, a process in which a bacterial cell transfers genetic material to another cell by cell-to-cell contact or by a bridge-like connection cells. **Bacterial** conjugation between two is often regarded the bacterial equivalent of sexual reproduction or mating since it involves the exchange of genetic material. During conjugation the donor cell provides a conjugative or mobilizable genetic element that is most often

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a <u>plasmid</u> or <u>transposon</u>. Most conjugative plasmids have systems ensuring that the recipient cell does not already contain a similar element. The genetic information transferred is often beneficial to the recipient. Benefits may include antibiotic resistance, xenobiotic tolerance or the ability to use new metabolites.

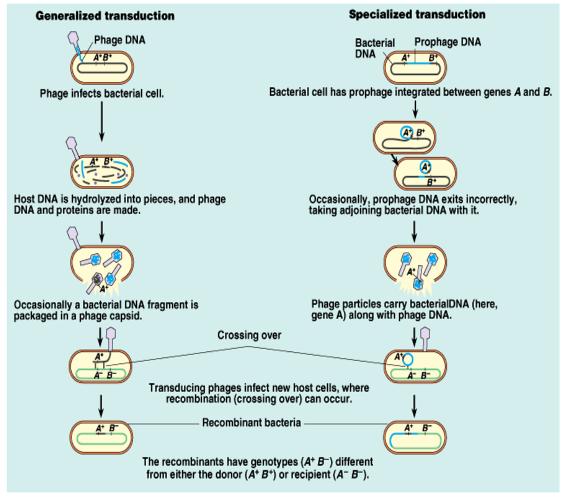


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c. Transduction is a method of transferring genetic materials.

The process in which bacterial DNA is moved from one bacterium to another by a virus (a bacteriophage, or <u>phage</u>) is called **Generalized transduction**, while the process whereby foreign DNA is introduced into another cell <u>via a viral vector</u> (**Specialized transduction**). Transduction does not require physical contact between the cell donating the DNA and the cell receiving the DNA (which occurs in conjugation). Transduction is a common tool used by molecular biologists to stably introduce a foreign gene into a host cell's genome. Transduction is especially important because it explains one mechanism by which antibiotic drugs become ineffective due to the transfer of antibiotic-resistance genes between bacteria.



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Horizontal gene transfer is the primary reason for bacterial antibiotic resistance and plays an important role in the evolution of bacteria that can degrade novel compounds such as human-created pesticides and in the evolution, maintenance, and transmission of virulence.

This horizontal gene transfer often involves temperate bacteriophages and plasmids. Genes that are responsible for antibiotic resistance in one species of bacteria can be transferred to another species of bacteria through various mechanisms, subsequently arming the antibiotic resistant genes' recipient against antibiotics, which is becoming a medical challenge to deal with. This is the most critical reason that antibiotics must not be consumed and administered to patients without appropriate prescription from a medical physician. Artificial horizontal gene transfer is a form of genetic engineering.

Most thinking in genetics has focused upon vertical transfer, but there is a growing awareness that horizontal gene transfer is a highly significant phenomenon and among single-celled organisms perhaps the dominant form of genetic transfer.

GENETIC TERMS

Heredity – the passing on of characteristics from parents to offspring.

Breeding- is the reproduction producing of offspring, usually animals or plants.

Traits – characteristics that are inherited.

Hybrid – offspring of parents that have different traits.

MENDELIAN TERMS

Genetic cross -breeding of two different individuals resulting in offspring that carries a portion of the genetic material of both the parent individuals.

Monohybrid crosses – the two parent plants differ by a single trait (eg. height).

Dihybrid cross – parents differ by two different traits (eg. height and color).

Trihybrid cross- is between two individuals that are heterozygous for three different traits (eg. Shape and color of pea seeds and the shape of the pod)

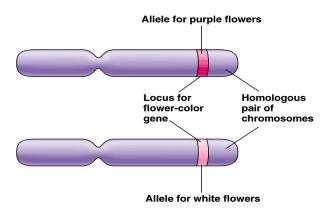
Test cross- is used to determine the unknown genotype of a particular phenotype. If an organism has the dominant phenotype, you can't be sure whether it is homozygous dominant or heterozygous. By crossing it with a homozygous recessive individual (tester), you can infer the genotype by observing the offspring.

 P_1 generation – "parent" - the original true-breeding parents

 F_1 generation – "filial" (or son or daughter) offspring of the parent plants

F₂ **generation** or "second filial generation" (or granddaughter or grandson)

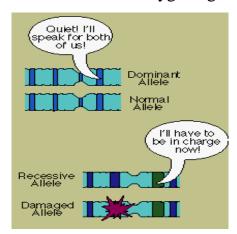
Alleles- alternative form of a single gene passed from generation to generation.



Dominance in genetics is a relationship between alleles of a single gene, in which one allele masks the phenotypic expression of another allele at the same gene locus.

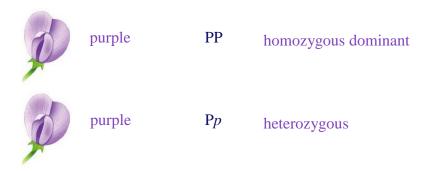
Dominant gene - gene that produces the same phenotype in the organism whether or not its allele identical.

Recessive gene is an allele that causes a phenotype (visible or detectable characteristic) that is only seen in a homozygous genotype (an organism that has two copies of the same allele) and never in a heterozygous genotype

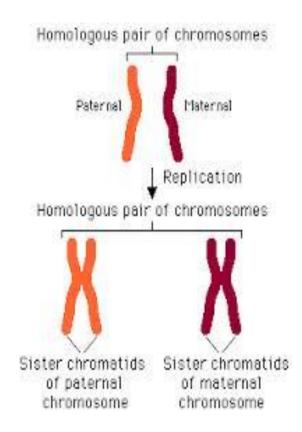


Homozygous – an organisms 2 alleles for a trait are the same (TT, tt)

Heterozygous - an organisms 2 alleles for a trait are different (Tt)



Homologous chromosomes- are chromosome pairs of approximately the same length, centromere position, and staining pattern, with genes for the same characteristics at corresponding loci. One homologous chromosome is inherited from the organism's mother; the other from the organism's father. They are usually not identical, but carry the same type of information i.e. similar but not identical.

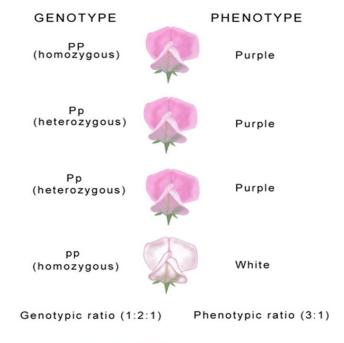


Phenotype – the way an organism looks and behaves (tall or short or color,...)

Phenotypic ratio- a ratio that shows the different outcomes after a cross based on physical appearance alone. For example yellow flowers, round seeds, brown hair, green eyes etc.

Genotype – it is the genetic make-up and can give the information about the gene combination an organism contains either homozygous or heterozygous alleles (TT, Tt, tt)

Genotypic ratio- is the proportion of genotypes found in individuals after a cross. It is the proportion of genotypes found in individuals after a cross.



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Punnett Squares - a shorthand way of finding the expected proportions of possible genotypes in the offspring of a cross invented by an English biologist Reginald Punnett, 1905).

GENETICS TRANSMISSION: HERITAGE FROM MENDEL

The genetic material is found primarily in the nucleus of the cell and that it is organized in the form of chromosomes. We will explore how the genetic material is inherited from generation to generation and the changes in the organization of the genetic material that occur between generations. This subdiscipline of genetics is called Transmission Genetics or Mendelian Genetics after Gregor Mendel who discovered the laws of inheritance with his experiments on garden peas.

The chapter is organized into three major sections: (1) Mendelian Genetics; (2) Transmission and inheritance of chromosomes; and (3) Extensions of Mendel's laws.



MENDELIAN GENETICS

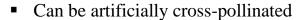
Mendel's Crossing Experiments with Peas

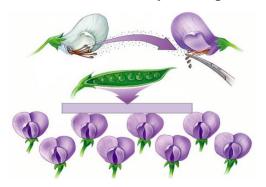
In 1865, the Austrian monk Gregor Mendel began his series of crossing experiments with garden peas. By any standard, Mendel was a very gifted scientist who appreciated the importance of carefully designing and interpreting his experiments. Mendel sought to understand the patterns of inheritance of seven different characters in peas by crossing plants with identifiably different **phenotypes** of a particular character, and then following the presence or absence of the character in successive generations. The traits Mendel studied were morphological attributes of the seed, pod, flower and stem. The types of crosses Mendel made are still widely used in genetics today. Unfortunately, Mendel's discoveries were largely ignored during his lifetime, and it was not until 1900 that his work was rediscovered by three European scientists, Hugo de Vries, Carl Correns, and Erich von Tschermak and its importance finally appreciated. Mendel's findings allowed other scientists to predict the expression of traits on the basis of mathematical probabilities.

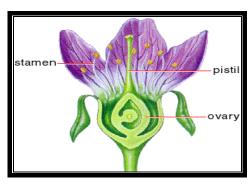
Why peas?

- Can be grown in a small area
- Produce lots of offspring
- Available in many varieties with distinct heritable features with different variations: flower color, seed color, seed shape, etc.

Produce pure plants when allowed to self-pollinate for several generations

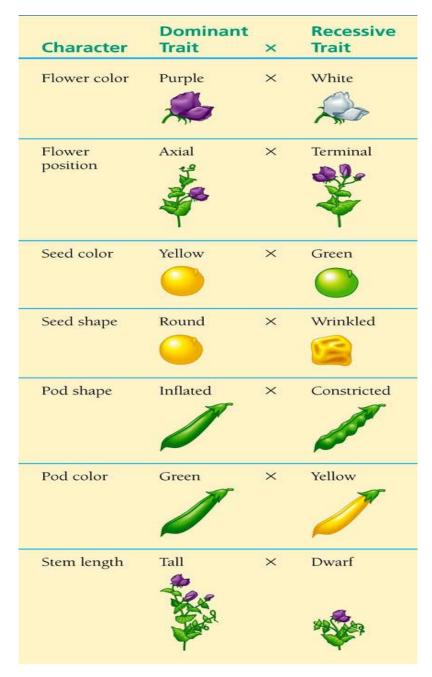






- Mendel had strict control over which plants mated with which:
 - 1. Peas contain both gametes in the same flower
 - 2. Pollen contains sperm produced by the stamen
 - 3. Ovary contains eggs inside the flower
 - 4. Pollen carries sperm to the eggs for fertilization:
 - Self-fertilization can occur in the same flower
 - Cross-fertilization can occur between flowers

Table 2. Pea-Plant characters studied by Mendel



Rule of Dominance

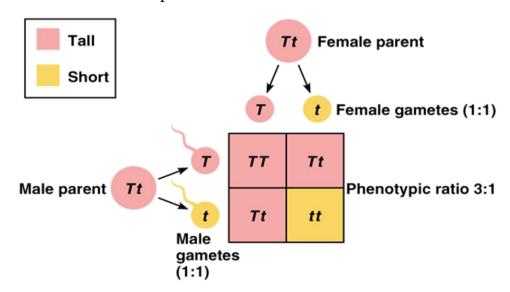
Dominant character is sign either by 2 capital letters (eg TT for tallness) or 1 capital and one small letter (eg Tt) and recessive character is signed by 2 small letters (eg tt for shortness).

For example:

Pea plants have 2 genes that control each trait located on the chromosomes.

Pea plants that have at least 1 allele for tallness (TT or Tt) are tall because the allele for tallness is dominant over the allele for shortness. The only way a plant can be

short is if both height alleles are for a short plant (tt). Dominant trait appears in the F_1 generation, while recessive trait disappears in the F_1 generation. The 2 alleles are located on different copies of a chromosome – one copy inherited from the female parent and one from the male parent.



Monohybrid Cross

The first crosses Mendel made were between inbred lines of peas that were true **breeding** for opposite types of a character, for example, tall x dwarf, yellow x green seed, round x wrinkled seed coat, etc (Table). These are called **monohybrid crosses** because the peas were inbred lines that differed for a single character (Fig.). In the progeny from the hybrid cross, called the **F1 generation**, he observed that all offspring were always just one of the two alternate types.

Example (1) tall x dwarf plants

Never were both types observed or were offspring of some intermediate type. Mendel then self-pollinated some F1 offspring to create an **F2 generation**, whose plants segregated for both characters found in the inbred parents (Fig.1). It was at this point that Mendel was at his scientific best. Not only did he observe the character types in the offspring, but he also counted them and calculated ratios of each type. In the F2 for all seven of the characters he was studying, he observed approximately three times as many plants of one character type as the other. Furthermore, the type observed in the F1 was the one in greater number in the F2.

Mendel interpreted the results of his monohybrid crossing experiments to develop his first three laws of inheritance. He surmised that there must be one factor for tall and one factor for dwarf, and that these factors are somehow paired (**Law 1**, Table 1). Later this became the basis of the concept of pairs of **homologous chromosomes** with the gene determining a particular character located at the same position (*i.e.* locus) in each homologue. A locus can have different forms of the gene, which are called **alleles**. For example, in Mendel's peas there was one allele coding for tall plants (*D*) and one allele coding for short plants (*d*) and these alleles segregated among the offspring. Plants that have the same allele at a locus on each of the homologous chromosomes are homozygous (*e.g. DD* and *dd*), whereas those with a different allele on each homologous chromosome are heterozygous (*e.g. Dd*).

Mendel further hypothesized that one unit factor (*i.e.* allele) is **dominant** to the other **recessive** factor (*i.e.* the dominant allele masks the effect of the recessive allele), based on the phenotypes he found in the F1 and F2 (**Law 1**, Table1). For example, the allele for tall (D) is dominant and the allele for dwarf (d) is recessive. This leads to the important distinction between genotype and phenotype. The three possible genotypes are DD, Dd, and dd, although with D being dominant to d, there are only two phenotypes. The DD and Dd genotypes are both tall phenotypes and the dd genotype is the dwarf phenotype.

A simple method to interpret the results of the monohybrid cross is through the **Punnett Square**, named after its inventor Reginald Punnett (Fig.1). It can be seen that when a heterozygous F1 is mated to itself (or crossed to an identical F1), three genotypes (*DD*, *Dd* and *dd*) are found in the 1:2:1 ratio (**genotypic ratio**), respectively. However, only two phenotypes are found, tall and dwarf, in the ratio of 3:1 (**phenotypic ratio**), respectively. Finally, Mendel proposed that the 3:1 ratio observed in the progeny of selfed F1 plants is expected if the *D* and *d* alleles are transmitted from each parent to the offspring at random (**Law 2**, Table). The frequencies of the offspring genotypes are the products of the frequencies of the

alleles transmitted from each parent. The frequency of the DD genotype is 1/4, the frequency of the heterozygous Dd class is 1/2, and the frequency of dd is 1/4. Because D is dominant to d and therefore, DD and Dd have the same phenotype, the expected proportion of tall offspring is 3/4 and the dwarf offspring is 1/4 (or a 3:1 ratio). Mendel confirmed the expectations of random segregation with another type of cross, called a **test cross**. Here he crossed a Dd plant with a dd plant and found that approximately half of the offspring were tall and half were dwarf.

Table 1. Mendel's laws of segregation and independent assortment.

Law 1. (law of segregation) states that every individual possesses a pair of alleles (assuming diploidy) for any particular **trait** and that each parent passes a randomly selected copy (allele) of only one of these to its offspring. The offspring then receives its own pair of alleles for that trait. Interactions between alleles at a single locus are termed dominance and these influence how the offspring expresses that trait (e.g. the color and height of a plant, or the color of an animal's fur).

≡Each genetic character is controlled by unit factors (alleles) that come in pairs in individual organisms. Paired unit factors for a given character are dominant and recessive to one another.

Law 2. (law of independent assortment=inheritance law) states that separate genes for <u>separate traits are passed independently of one another</u> from parents to offspring. That is, the biological selection of a particular gene in the gene pair for one trait to be passed to the offspring has nothing to do with the selection of the gene for any other trait.

≡the law states that alleles of different genes assort independently from one another during gamete formation.

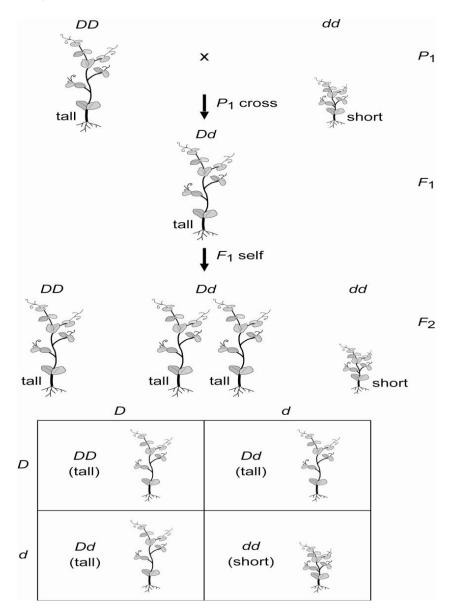


Fig.1 Mendel's monohybrid crosses with peas (tall x dwarf plant).

Example (2) yellow x green seed

Mendel grew seeds from a cross between green-seed and yellow-seed plants. All of the offspring in F1 generation had yellow seeds. Mendel allowed the plants in F1 generation to self pollinate. ³/₄ of the plants had yellow seeds and ¹/₄ had green forming ratio of 3:1 (3 yellow to 1 green).

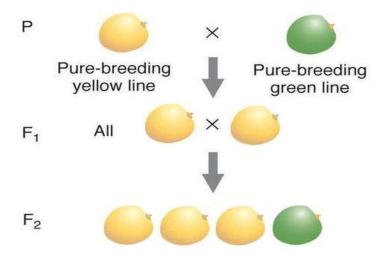


Fig. Mendel's monohybrid crosses with peas (yellow x green seeds).

Dihybrid Cross

A second type of experiment Mendel performed was the **dihybrid cross**, which was an extension of the monohybrid cross to two characters (Fig. 2). Mendel crossed a yellow and round seeded type to a green and wrinkled seeded type. The F1 offspring were all yellow and round and the alternate types of each character were found in 3:1 ratios in the F2, as observed in monohybrid crosses involving the same traits.

Mendel also counted the two-character phenotypes and these were in a 9:3:3:1 ratio in the F2. This is the expected ratio of two-character phenotypes given that both pairs of traits segregate randomly and completely independently of one another (**Law 4**, Table1). Under independent assortment, the expected frequency of any two-character phenotype is the product of the frequencies of each component character. Therefore, the frequency of yellow round offspring is 9/16 and the frequency of yellow wrinkled is 3/16. In this case, the genes controlling color and smoothness of seed coat reside on different chromosomes. The Punnett square shows the offspring resulting from selfing the F1. There are nine possible genotypes (genotypic ratio 1:2:2:4:1:2:1:2:1) but only four phenotypes (yellow and round, yellow and wrinkled, green and round, green and wrinkled) which segregate in a 9:3:3:1 ratio (phenotypic ratio).

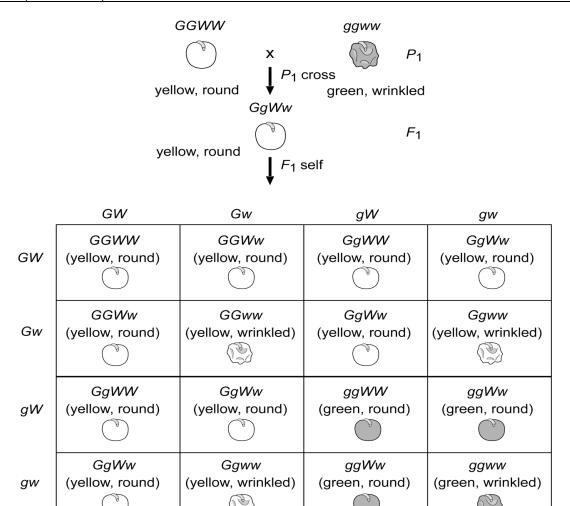


Fig. Mendel's dihybrid crosses with peas (yellow and round x green and wrinkled seeded type).

Lecture activity: Punnett square of the dihybrid cross (students solving and open discussion).

Trihybrid Cross

A trihybrid cross is between two individuals that are heterozygous for three different Traits: pea shape and pea color and then a new trait: pod shape. The same rules as before apply for shape and color (round is completely dominant to wrinkled, and green is completely dominant to yellow). Pea pod shape follows similar rules, with smooth pods being completely dominant to constricted pods. Therefore,

homozygous-dominant and heterozygous individuals will have smooth pods, while homozygous-recessive individuals will have constricted pea pods.

Lecture activity: Punnett square of the trihybrid cross (students solving and open discussion).

	ABC	ABc	AbC	aBC	Abc	aBc	abC	abc
ABC	AABBCC	AABBCc	AABbCC	AaBBCC	AABbCc	AaBBCc	AaBbCC	AaBbCc
ABc	AABBCc	AABBcc	AABbCc	AaBbcc	AABbcc	AaBBcc	AaBbCc	AaBbcc
AbC	AAbBCC	AAbBCc	AAbbCC	AabBCC	AAbbCc	AabBCc	AabbCC	Aabb Cc
aBC	aABBCC	AaBBCc	aABbCC	aaBBCC	aABbCc	aaBBCc	aaBbCC	aaBbCc
Abc	AAbBcC	A Ab Bcc	AAbbcC	AabBcC	AAbbcc	Aab Bcc	AabbcC	Aabbcc
aBc	aABBcC	aABBcc	aABbcC	aaBBcC	aABbcc	aaBBcc	aaBbcC	aaBbcc
abC	aAbBCC	aAbBCc	aAbbCC	aabBCC	aAbbCc	aabBCc	aabbCC	aabb Cc
abc	aAbBcC	aAbBcc	aAbbcC	aabBcC	aAbbcc	aab Bcc	aabbcC	aabbcc

Example of Trihybrid Punnett

Polygenic traits

Some traits are determined by the combined effect of more than one pair of genes. These are referred to as polygenic or continuous traits.

Forest geneticists and tree breeders have primarily concerned themselves with the genetic improvement of economic traits, such as stem volume and wood quality, which are under the control of many genes. Nevertheless, observant geneticists have identified a small number of morphological traits showing Mendelian inheritance in the progeny of controlled crosses in trees include cone color in *Pinus monticola* (Steinhoff, 1974), seedling foliage color in *Picea abies* (Langner, 1953), chlorophyll deficiencies and other morphological variants in *Pinus taeda* (Franklin, 1969), diameter growth in *Pinus patula* (Barnes *et al.*, 1987), blister rust resistance in *Pinus lambertiana* (Kinloch *et al.*, 1970), and the narrow-crown phenotype in *P. abies* (Lepisto, 1985).

An example of this is human stature. The combined size of all of the body parts from head to foot determines the height of an individual. There is an additive effect. The sizes of all of these body parts are, in turn, determined by numerous genes. Human skin, hair, and eye color are also polygenic traits because they are influenced by more than one allele at different loci (by about 12 genes). The result is the perception of continuous gradation in the expression of these traits.



Statistical Tests for Mendelian Inheritance:

Chi Square "Goodness of Fit Test"

- To determine if your data "good" or not.
- To find out if probability are due to chance alone

Data collection

As you know all too well by now, a valid test of your hypotheses, requires more than a mere visual inspection of the data. The investigator can make no claims about significance without first performing a statistical test on his/her data. When you have finished counting and tabulating your results, you will perform a simple, non-parametric test that will allow you to determine whether the observed results exhibit any significant deviation from the expected ratios.

Data analysis

<u>Remember:</u> a scientifically observed result is said to be statistically significant if there is less than or equal to a 5% ($P \le 0.05$) probability that the phenomenon is due simply to random chance. Conversely, this means that there is a 95% chance that the phenomenon is due to some factor other than chance.

To determine whether the variation in phenotype frequency you counted is significantly different from the frequencies expected from each of the parental genotypes, you will use the Chi square test.

The test

Before we count the offspring of each sample, we must ask whether the ratio of the phenotypes we actually count is likely to occur in a random sample produced by a monohybrid cross.

If our count is not significantly different from the expected, we have no reason to reject our null hypothesis. However, if our number is significantly different from the expected, we conclude that there is very little probability of obtaining such a ratio by random chance. Some other factor must be at work here--one we must try to explain in terms of other genetic events such as gene linkage, lethal genes, etc.(from lecture).

We will use a simple, non-parametric test called the Chi square (X^2) to determine whether our observed (counted) ratios of sample phenotypes are significantly different from the expected (from the known parental genotypes) ratios. The formula for this test is as follows:

the expected (from the known parental genotypes) rations follows:
$$X^{2} = \Sigma \frac{(\text{Observed frequencies} - \text{Expected frequencies})^{2}}{\text{Expected frequencies}}$$

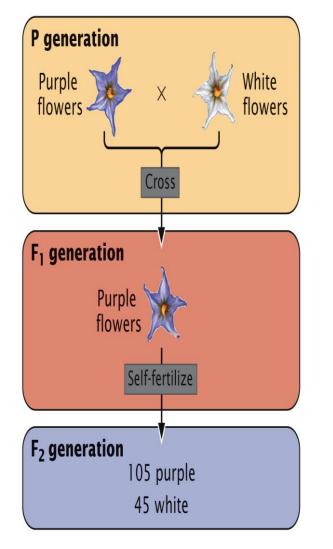
$$= \Sigma \frac{(\text{Fo - Fe})^{2}}{\text{Fe}}$$

in which

- Fo = the observed (counted) number of grains of a particular phenotype
- Fe = the expected number of grains of a particular phenotype.
- Σ represents the summation of X^2 values over every phenotypic category (1 through n)

Run the X^2 test on each samples to determine whether their phenotypic ratios deviate significantly from the expected. Test all three of your hypotheses, accept or reject each one, and explain your results.

Application on the test



Phenotype	Observed	Expected
Purple	105	$3/4 \times 150 = 112.5$
White	45	$1/4 \times 150 = 37.5$
Total	150	

$$\chi^{2} = \sum \frac{(O-E)^{2}}{E}$$

$$\chi^{2} = \frac{(105-112.5)^{2}}{112.5} + \frac{(45-37.5)^{2}}{37.5}$$

$$\chi^{2} = \frac{56.25}{112.5} + \frac{56.25}{37.5}$$

$$\chi^{2} = 0.5 + 1.5 = 2.0$$

Degrees of freedom = n-1Degrees of freedom = 2-1=1Probability (from Table 3.4) .1 < P < .5

Conclusion: No significant difference between observed and expected values.

Fig_03-14-1 Genetics, Second Edition © 2005 W.H. Freeman and Company

Fig_03-14-2 Genetics, Second Edition © 2005 W.H. Freeman and Company

* Please read and make sure you understand the following term before you go on:

The hypothesis is termed the **null hypothesis** which states that there is no substantial statistical deviation between observed and expected data.

For more reading: (in Botany Department Library)

- 1. Study guide and problems workbook: Principles of genetics, Peter Snustad, Simmons and Price (eds), 2nd edition, 2000.
- 2. Introduction to genetic analysis, Griffiths, Wessler, Lewontin and Carroll, 9th edition, 2008.