Introduction

Today, when the word “genetics” is mentioned the mind is at once occupied with terms like cloning, PCR, the genome project, and genomics. Just a few decades ago, however, the word genetics conjured up a very different set of terms including crossing, segregation, Punnett square, and binomial expansion. It is not that these terms have disappeared or have been replaced since, it is, rather, that genetics moved full force into the molecular era in the late 1970s and, in the beginning of the twenty-first century, has passed on to the post-genome era. So much has genetics expanded and diversified that it is no longer adequate to study just genetics. To properly identify an area of study today requires the use of modifiers such as molecular genetics, quantitative genetics, behavioral genetics, plant genetics, human genetics, medical genetics, anthropological genetics, biochemical genetics, functional genomics, pharmacogenomics, and so on. In the minds of some who can still remember when you could take a genetics course and have the whole field covered in a single book that a person of average strength could actually carry to class, the unmodified term “genetics” refers to “Mendelian Genetics,” the transmission of whole traits from one generation to the next.

While such a reduction may appear to be a quibble, it does reflect the historical truth that, prior to the elucidation of the genetic code in 1966, the development of DNA sequencing in the late 1970s and the discovery of the polymerase chain reaction in the early 1980s, all of genetics was in some way Mendelian Genetics concerned with the transmission of whole traits in families, pure lines, or breeding stocks. Here, a brief history of genetics up to the dawn of the molecular era is presented with a focus on Mendel and the laws of transmission genetics he discovered.
Heredity Before Mendel

The basic concept of heredity is at least as old as civilization itself. It was no coincidence that animals and plants produced offspring very similar to the parents and that reproduction was usually restricted to members of the same general group. In the ancient world it was clear that there was a process in which both parents made some form of contribution for it was observed that exact copies were never made, there was always some slight variation to be seen. Indeed, as long ago as the time of the Babylonians, farmers were aware that desirable traits could be manipulated by carefully selecting which specific parent animals or plants were allowed to reproduce. Records left by the ancient Egyptians clearly indicate that they practiced cross-pollination of plants as a means of improving crops. And yet, while the practical benefits of hereditary manipulation were recognized by the ancients, there are no records prior to those of the Greeks that suggest their thoughts concerning the mechanism of heredity.

Pythagoras wrote some 2,500 years ago that semen was the product of fluids collected from the entire body and that there was a complete being preformed in the semen that was transferred intact to the female. This preformation theory was accepted, with various modifications, for more than two thousand years. Only occasionally did the notion that the female was simply the receptacle and had no role in determining traits appear to bother anyone. One such objection was raised by Empedocles about a century after Pythagoras when he proposed that there was, in fact, a blending of male and female that created an embryo and that the result was a combination of traits. This, and other objections, were shelved until well into The Reformation because of the pronouncement of Aristotle who held that while the female did make a contribution it was in the form of undifferentiated matter upon which the male imprinted life and form. Aristotle believed that semen was purified blood that carried the essence of the offspring to the less pure matter contributed by the female. Writing this in his great treatise On the Generation of the Animals in the 4th century BC, Aristotle had simply applied his view that all matter was formless until acted upon by an essence to the realm of biology. With the imprimatur of Aristotle firmly affixed, this was how things stood until the 17th century as there were no means available with which a skeptic could truly determine how heredity worked.

In the late 17th and early 18th centuries the English physician William Harvey (1578-1657) and the Dutch biologist Anton van Leeuwenhoek (1632-1723) independently discovered with the aid of new technology that female animals produced eggs, that embryos were formed by the union of egg and sperm, and that the embryo underwent a subsequent development that was similar regardless of the animal being investigated. This, of course, meant that Empedocles’ notion was closer to the truth but there were detractors. Another Dutch scientist, Jan Swammerdam (1637-1680), proposed that what van Leeuwenhoek was actually seeing in his microscope when he looked at sperm was in fact a tiny, pre-formed being, a homunculus, that entered the egg and used it for its source of nourishment as it grew. About a century later a Swiss scientist called Charles
Bonnet (1720-1793) reversed the role completely by suggesting that it was the eggs that held the homunculus and that each succeeding generation was similarly housed within in the manner of an endless succession of Russian matryoshka dolls (Figure 1).

Figure 1. A classic set of Russian nesting “matryoshka” dolls in which each doll is housed, fully formed, within the next larger doll in series. This is the view of heredity suggested by Bonnet in the 17th century. One objection never addressed was what happened when the last doll (homunculus) was reached.

Alternative theories were advanced by the French scientist Pierre Louis Moreau de Maupertuis (1698-1759) and the German anatomist Kaspar Friedrich Wolff (1733-1794). Both dismissed the notion that there were preformed homunculi carried by either sperm or egg and proposed instead that the actual reproductive material consisted of particles contributed by each parent and carried by both sperm and egg into union as the embryo. Both envisioned these particles as jointly determining not only form but sex as well. Maupertuis even held that some particles from one parent could exert a stronger influence than those from the other. However, both of these theories were advanced in the absence of actual experimental evidence.

Had they known of the work of a German botanist named Joseph Gottlieb Koelreuter (1733-1806), both Maupertuis and Wolff would have had the experimental evidence they needed. Koelreuter originally studied medicine at Tübingen but became interested in natural history at the Academy of Sciences in St. Petersburg. There, he studied the structure of flowers and the mechanisms of pollination. In 1763 he was appointed Professor of Natural History at Karlsruhe and also Director of the Gardens. He began to carry out experiments in cross pollination in the tobacco plant that he carefully recorded and later published. The most important discovery made by Koelreuter was sexual differentiation in plants that led to his demonstrations that traits in offspring were equally determined by the parents.

Unfortunately, apart from a very few attempts to reproduce his results, Koelreuter’s work was largely ignored except by those who dismissed it as completely wrong. He had found that the characters exhibited by the first generation of a cross (called the F1 generation) would lie intermediate between those of the parents in many cases but that the next generation (called the F2) would display a range of types including those of the original parents. Koelreuter was dismayed by this because he viewed the F1 blending as evidence of natural harmony and perfection and the F2 results as a breakdown of this
harmony. The explanation of these disturbing breakdowns was soon to be discovered by an obscure Silesian (Austrian) monk named Johann Gregor Mendel (1822-1884).

Mendel and the Laws of Heredity

Gregor Mendel was born in the Silesian village of Heizendorf (now called Hynčice) one of five children. Originally named Johann, he was renamed Gregor in 1843. Mendel demonstrated his intellectual abilities at an early age and was sent at age eleven to the Piarist High School in Leipnik and then to the Gymnasium at Troppau (now called Opava). He completed his education there in 1840 and moved on to the University in Olmütz (Olomouc). After a brief illness he was advised to enter the priesthood in the monastery in Brno (Figure 2). Here, he entered a world in which, unlike the conventional view of a monastery, he was immersed in a well respected seat of scientific learning. Many of the members of the Augustinian order at Brno held professorships in the local university or left to assume similar positions at other universities. Thus he was able to continue on an academic track. In 1851 he was sent to the University in Vienna where he was influenced by a number of great minds who were leaders in their fields. The most influential of these to Mendel was Franz Unger (1800-1870), Professor of Plant Physiology. However, in addition to his studies with Unger in which he learned of the work of influential biologists such as Carl Naegeli (1817-1891) and Matthias Schleiden (1804-1881), Mendel learned the value of precise observation and the importance of statistical evaluation from the physicists in Vienna, notably Christian Doppler (1803-1853) and Andreas von Ettinghuasen (1796-1878).

During his years in Vienna Mendel, by virtue of his relationship with Unger, was well aware of a raging controversy in which Unger figured prominently. One of the dominant views in biology at the time was the fixity of species. That is, species were set and constant and, therefore, could not change and certainly could not evolve. Unger was a vocal proponent of the view that variants would arise in natural populations and that slight variants gave rise to varieties and sub-species while large variants would result in new species. So controversial was this view at the time that Unger was almost dismissed from the faculty in Vienna in 1856. One of the motivations ascribed to Mendel for beginning his plant hybridization experiments in the first place was to resolve this issue [1].

Figure 2. On the left is a portrait of Gregor Mendel from 1880 and on the right is a photograph of the gardens at the Brno monastery taken in the 1920s.
Regardless of his motivation, Mendel had set himself a monumental task. He was determined to catalog all of the different forms that hybrids could take and to carry out a statistical analysis of these forms. The experimental system he chose was the common garden pea, *Pisum sativum* (Figure 3). He began his crosses in earnest in the summer of 1856 and over the course of the next fifteen years he identified several traits in his plants that appeared to breed “true” and used them in his crosses. In all, he made tens of thousands of observations of which only a few are well known. However, it is these few well known traits that led to the formulation of what are now called Mendel’s Laws of Heredity.


In his paper, Mendel laid out his experimental procedures and noted that the traits he had selected to use, among others, related to the difference in the form of the ripe seeds, to the difference in the color of the seed albumin, and to the difference in the form of the ripe pods (Mendel, 1866 translation in Peters, 1959). Mendel noted the number of plants used for each cross and the forms of the hybrids. He then noted the circumstances and results of the next generation (the F2) of crosses. For example, Mendel noted for albumen color 258 plants yielded 8,023 seeds, 6,022 yellow, 2,001 green; their ratio, therefore, is as 3.01 to 1. He noted the results of various combinations of traits such as round and wrinkled seeds with yellow and green albumin.

Among his observations was that, in the single trait crosses, one of the two forms of the trait would appear in the F1 generation intact and, therefore, “those characters which are transmitted entire, or almost unchanged in the hybridization, and therefore in themselves constitute the characters of the hybrid, are termed the dominant, and those which become latent in the process recessive.” Among his traits round seeds were dominant over wrinkled, yellow albumen was dominant over green, and smooth pods were dominant over rough. This led him to formulate his First Law, “... hybrids form seeds having one or the other of the two differentiating characters, and of these one-half develop again the hybrid form, while the other half yield plants which remain constant and receive the dominant or the recessive characters [respectively] in equal numbers.” This is now called segregation. Take the character of albumin color, yellow is dominant over green. If Y is the symbol for yellow and y is the symbol for green, then, starting with pure lines in the parental generation;

\[
P1: \quad YY \times yy \\
F1: \quad Yy \\
F2: \quad YY \ Yy \ Yy \ yy
\]
The F1 will all be yellow and the F2 will display the 3 to 1 ratio of yellow to green. The outward, physical appearance is called the **phenotype** (literally, the form that is shown). The "particles" that create the phenotype are now known to be genes and, therefore, each phenotype has an underlying **genotype**. (Note: the terms gene and genotype did not exist in Mendel's day, these terms were coined later by the Danish geneticist Wilhelm Johannsen, 1857-1927). Segregation refers to the separating of the particles in the F1 cross. A convenient means of keeping track of the segregating particles no matter how many there are was developed by and named for the English geneticist Reginald Crundell Punnett (1875-1967). Called the **Punnett Square**, the two forms of the gene (called **alleles**) are segregated by parent to permit an easy tabulation of the resulting offspring’s genotypes:

<table>
<thead>
<tr>
<th>Male Parent</th>
<th>Y</th>
<th>y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>YY</td>
<td>YY</td>
</tr>
<tr>
<td>y</td>
<td>Yy</td>
<td>Yy</td>
</tr>
</tbody>
</table>

Parents: all yellow Yy

Offspring: 1 yellow YY, 2 yellow Yy, 1 green yy

Mendel went on to consider various traits in combination. He observed that, “the hybrids in which several essentially different characters are combined exhibit the terms of a series of combinations, in which the developmental series for each pair of differentiating characters are united.” Further, “the relation of each pair of different characters in hybrid union is independent of the other differences in the two original parent stocks.” This is Mendel’s Second Law of Heredity called **Independent Assortment**. Taking yellow and green albumen together with round and wrinkled seeds, if the pure lines are yellow (YY) and round (RR) and green (yy) and wrinkled (rr):

P1:         YYRR x yyrr  
F1:          YyRr  
F2:       YYRR yYRR YyRR yyRR  
            YYRr  yYRr  YyrR yyrr

Again, using the Punnett Square and assorting the two traits independently,

<table>
<thead>
<tr>
<th>Male Parent</th>
<th>YR</th>
<th>yR</th>
<th>Yr</th>
<th>yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>YR</td>
<td>YYRr</td>
<td>YyRR</td>
<td>YYRr</td>
<td>YyRr</td>
</tr>
<tr>
<td>yR</td>
<td>YyRR</td>
<td>yyRR</td>
<td>YyRr</td>
<td>yyRr</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Female Parent</th>
<th>YR</th>
<th>yR</th>
<th>Yr</th>
<th>yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>YR</td>
<td>YYRr</td>
<td>YyRr</td>
<td>YYrr</td>
<td>Yyrr</td>
</tr>
<tr>
<td>yR</td>
<td>YyRr</td>
<td>yyRr</td>
<td>Yyrr</td>
<td>yyrr</td>
</tr>
</tbody>
</table>
Parents: all yellow, round

Offspring: 9 yellow, round; 3 yellow, wrinkled; 3 green, round; 1 yellow, wrinkled

Many examples of using of the Punnett Square to work out various crosses and combinations of traits are presented in the Supplemental Material at the end of this tutorial.

The “Rediscovery” of Mendel

Despite the fact that copies of the issue of the Proceedings in which Mendel’s work appeared were sent to numerous institutions such as the Royal Society and the Linnean Society as part of a regular mailing list, apart from a few letters exchanged with contemporary scientists, notably Carl Naegeli, the paper and its results went completely unnoticed until 1900. During the latter part of the 18th century, scientists were grappling not only with concepts of heredity but also with incorporating them into Darwin’s model of evolution. Notable among these scientists were the Dutch botanists Hugo de Vries (1848-1935) and Carl Correns (1864-1933), Austrian botanist Erich von Tschermak (1871-1962), and English biologist William Bateson (1861-1926). Correns, de Vries, and von Tschermak were all independently working along the same lines as Mendel and were reaching the same general conclusions at the close of the 18th century. Then, in 1900, each became aware of Mendel’s paper and de Vries sent a copy of a report on his own work to Bateson that contained a mention of Mendel. Bateson searched out the original publication of Mendel’s paper and an English translation appeared in 1901. An excellent account of the facts surrounding the rediscovery of Mendel is provided by Olby (1966).

Most historians of science set the year 1900 as the birth of genetics because that is the year that Mendel’s paper was “rediscovered.” Much of what we regard as standard terminology and concepts were developed in the first few years after the translation of Mendel’s paper appeared. Bateson himself coined the term genetics, Johannsen defined and refined the terms gene, genotype, and phenotype, and the essential blending of Mendelian inheritance and Darwinian evolution was well under way. One of the lesser-known stories about the rediscovery of Mendel’s work was that some, including Bateson, believed that Mendel had enunciated three laws of heredity. In addition to segregation and independent assortment, many regarded the phenomenon of dominance as a hereditary law at the beginning. It was viewed as an inherent property of traits and that it was immutable. Evolutionary geneticists grappled with the idea that dominance was just another trait subject to Darwinian selection until, in 1928, Sir Ronald Fisher (1890-1962) published his view that dominance could be modified by modest levels of selection. Fisher reiterated and expanded upon this in his monumental
1930 treatise *The Genetical Theory of Natural Selection*. Instead of settling the debate over the nature of dominance, Fisher’s work sparked a debate about the nature and role of selection with the great American population geneticist Sewell Wright (1889-1988) that had dominance as the center piece and lasted well into the 1980s with many of Fisher’s students and colleagues carrying on after his death [2]. The story of the evolution of dominance is a fascinating tale in its own right as it involved nearly all of the giants of twentieth century genetics, years of arduous field and laboratory breeding work, and some of the most elegant mathematics theoretical population genetics has to offer [3, 4, 5, 6, 7, 8].

**The Misuse of Mendel**

The rediscovery of Mendel’s laws of segregation and independent assortment set genetics on a sound theoretical footing in the early 20th century. Among those that used that footing to build up a solid edifice of genetic science many have already been mentioned such as Johanson, Correns, and Punnett. Another group that deserves special mention all worked in the same laboratory at Columbia University in New York. Under the guidance of the great American geneticist Thomas Hunt Morgan (1866-1945), a group of students that included Herman Joseph Muller (1890-1967), Calvin B. Bridges (1889-1938), and Alfred H. Sturtevant (1891-1970), studied the transmission of phenotypes cataloged by them in the fruit fly *Drosophila melanogaster*. From this work emerged most of the founding principles of modern genetics including chromosomal linkage and mutation [9].

So powerful were the discoveries of the early years of the 20th century and so compelling were the models built to explain them, that some carried genetic principles to an unfortunate and, ultimately, tragic extreme. A number of scientists and non-scientists alike saw the elegant simplicity of Mendel as the answer to everything. Ignoring the complications and the exceptions that were piling up as experiments in Mendelian genetics became more sophisticated and the traits being studied more complex, some seized upon very simple models as all that were needed to explain even the most convoluted biological characteristics. Nowhere was this more evident than in the rapidly expanding discipline of human genetics.

Attracted by the allure of simplicity, some of the attempts to explain complex human traits with basic Mendelian principles are humorous when viewed from a 21st century perspective. Many of the texts of the period contained family histories that purported to demonstrate simple Mendelian inheritance of artistic ability or musical ability. One extensive pedigree displayed evidence for the inheritance of ship building skill over several generation of a Norwegian family. Another prominently showed that three generations of band directors followed a basic Mendelian pattern. It is often common even today for people to casually note that doctors or lawyers “run in certain families” and, while no one today would seriously believe that medicine or law or music or even ship building is determined by a single Mendelian gene, such comments were taken very
seriously in the early 20th century. In fact, such belief was strong enough for a field of scientific inquiry to arise that sought to enhance traits deemed to be beneficial and to eliminate traits held to be deleterious. This science was called eugenics.

Eugenics comes from the Greek roots for “good” and “origin” or “generation.” The term was first used to refer to good breeding through selective heredity around 1883. By the 1920s the eugenics movement in the United States and Europe was gaining wide acceptance and was being championed by the respected American geneticist Charles Davenport (1866-1944). Eugenics was being portrayed as a sound mathematical science based upon Mendel’s law that could produce superior offspring via selective mating. Eugenicists held that desirable traits should be encouraged and numerous societies like the Race Betterment Foundation were established. Contests were held and prizes were awarded to “good families” at fairs and other events (Figure 4).

The other side of the eugenics movement was much darker. The goal of promoting the inheritance of “good” traits was being mirrored by the goal of preventing the inheritance of “bad” traits. Complex human traits like alcoholism, feeblemindedness, criminality, and even poverty were attributed to a simple model of Mendelian transmission. Prevention in the United States took the form of designating certain countries and groups as being prone to these traits and banning immigration. In addition, there was a massive program of involuntary sterilization of those already here. As late as 1942 the ethics of “euthanizing” children with disabilities was seriously debated in the pages of a major medical journal. In all, thousands of American citizens and immigrants were sterilized by court order.

Figure 4. This family was awarded a prize in a eugenics contest at a 1923 Kansas fair. Thousands of similar examples of “good breeding” were recognized during the heyday of the eugenics movement. Source: PBS Science Odyssey.

In Europe the eugenics movement gained equal acceptance but its power was nowhere exceeded than in Germany when it became an official policy of the Nazi Party. There, its precepts were taken to the ultimate extreme when the Nazi Party came to power in the 1930s. Soon, the list of traits to be eliminated grew quite long and “undesirables” were being rounded up and sent to camps. Selective human breeding programs, called the “liebensborn,” were established and “stocked” with young women who, by the criteria...
established under the Nazis, displayed the desired traits. Eventually the Nazis took this movement to the “final solution” of the question of the unfit and the concentration camps became death camps (Figure 5).

Figure 5. A photo taken at the liberation of one of the many Nazi death camps discovered as WWII came to an end. In all, the Nazis exterminated more than seven million people of whom six million were Jews.

Mendel in the Modern World

The laws of heredity established by Mendel form the backbone of modern genetics. Nowhere is this more evident than in the ongoing search for genes that cause diseases in humans, animals and plants. The sophisticated, contemporary methods for mapping and, ultimately, identifying individual genes that either increase risk for developing diseases or actually cause them is firmly rooted in Mendelian genetics. Genetic linkage analysis is based upon the co-transmission of genetic material that is physically linked together on the same region of a chromosome. The mathematics of linkage analysis works because of segregation and independent assortment. A genetic marker that displays independent assortment in families relative to a trait of interest such as cystic fibrosis, Huntington’s Disease, Breast Cancer, or Alzheimer’s Disease cannot be physically linked to that trait whereas a marker that segregates along with the trait is likely to be near the gene that causes the illness. Through this method literally hundreds of human, animal and plant genes have been mapped, cloned, and studied. Indeed, while the various genome sequencing projects, including the Human Genome Project, have made this search far easier than it was just a few years ago, the initial genetic maps that were used as the guides for ordering the sequences were made using mathematical and laboratory techniques, like linkage, that are grounded in the application of Mendel’s Laws.

References and Resources


Supplemental Material

Exercises in Mendelian Genetics
A range of hands-on exercises that can be used to present various aspects of basic Mendelian genetics are presented here. Most of these are straight-forward pencil and paper problems. In addition, some on-line resources of materials are listed.

I. Basic Mendelian Segregation
a. Complete Dominance

Phenotype: flower color

Alleles: R (red), r (white); R is dominant

Genotypes: RR, Rr = red; rr = white RR and rr are the homozygotes and Rr is the heterozygote.

Parental Pure Line Cross (P1): RR x rr

F1 generation: all Rr heterozygotes

F1 cross: Rr x Rr
In his paper Mendel reported that he observed 705 red flowers and 244 white flowers on a total of 929 F2 plants. His observed phenotypic ratio was 3.15 to 1.

Consider the problem of backcrossing. Given the following F2 backcrosses and the resulting F3 phenotype ratios, what are the genotypes of the F2 parents?

<table>
<thead>
<tr>
<th>F2:</th>
<th>Red x Red</th>
<th>Red x White</th>
<th>Red x Red</th>
</tr>
</thead>
<tbody>
<tr>
<td>F3</td>
<td>712 Red</td>
<td>505 Red; 490 White</td>
<td>740 Red; 260 White</td>
</tr>
</tbody>
</table>

b. Partial or Incomplete Dominance
Sometimes you can see a difference between the phenotype of the F1 hybrids and the two parental pure lines. This occurs when dominance is incomplete. The phenotype of the heterozygote F1 may lie in between that of the parental lines.

Phenotype: flower color

Alleles: R (red), r (white); R is dominant

Genotypes: RR, Rr = red; rr = white  RR and rr are the homozygotes and Rr is the heterozygote.

Parental Pure Line Cross (P1): RR $\times$ rr

F1 generation: all Rr heterozygotes

F1 cross: Rr $\times$ Rr
It is possible to know exactly what the F2 genotypes are now. Of course this is very easy when the F1 is a clear intermediate phenotype. Many times the heterozygote will not be so obvious. Take the case:

**Parental Pure Line Cross (P1):** RR \( \times \) rr

**F1 generation:** all Rr heterozygotes

Here, the F1 actually has a completely different color from the parental lines. The actual relationships that are possible with dominance, even in simple crosses, range from various degrees of partial dominance, through complete dominance, and on to what is called **overdominance** such as shown here where the F1 heterozygote is a deeper red than even the homozygous parent. Clearly, this is an oversimplification but the range of potential dominance effects is shown graphically below.

It is important to note here that an observation that looks like a departure from simple dominance may not be simple at all. In the case of the F1 in which the flower color is a deeper red than the pure line parent red, overdominance is only one possible explanation. Other possibilities include a mutation creating a new allele (which will be presented next) and **epistasis**, the phenomenon that occurs when the genotype of one trait interacts to change the phenotype of another (which will be presented later).
c. Multiple Alleles

Now, consider the case in which the gene that encodes a trait has not two but three alleles. Again using a flower color example, pure lines of red and white flowers are crossed and a third color appears on one plant. Now there are \( \text{red} \), \( \text{white} \) and \( \text{third color} \) and you want to know where the new color comes from. Set up the following crosses:

\[
\begin{array}{ccc}
\text{Cross #1} & \text{Cross #2} & \text{Cross #3} \\
\text{All} & 3 & 1 & \text{All} \\
3 & 1 & \text{All} & 3 \\
3 & 1 & \text{All} & 3 \\
\end{array}
\]

Now there are four phenotypes but the genetics can now be worked out. Numbering the alleles, call the pure red 1,1 and the pure white 3,3. The new phenotype can be called 2,- for the time being since the dominance relationships are not known.

In Cross #1 all of the flowers are red so 1 must be dominant. New mutants are always heterozygous, so the genotypes of Cross #1 must be 1,1 x 2,3 and the F1 must be an equal mixture of 1,2 and 1,3. Cross #2 is fairly simple to work out. In the F1 of Cross #1 the genotypes are a mixture of 1,2 and 1,3. This means that there are three possible F1 crosses in Cross #2: (1,2 x 1,2); (1,2 x 1,3); and (1,3 x 1,3). The results of these crosses are:

\[
\begin{align*}
1,2 \times 1,2 & \quad 1,2 \times 1,3 & \quad 1,3 \times 1,3 \\
1,1; 1,2; 2,2 & \quad 1,1; 1,3; 2,3 & \quad 1,1; 1,3; 3,3
\end{align*}
\]

Thus, Cross #3 must be 2,2 \( \times \) 3,3 since there are no white flowers the genotypes can only be 2,3. Therefore,

1 is dominant over 2 and 3 and 2 is co-dominant with 3.
If this seems complicated, it is. However, this is what Karl Landsteiner (1868-1943) had to work out when he discovered the human ABO blood groups in 1900. He observed that mixing human blood samples together gave a pattern of reactions that could only be explained if there were three alleles. He called them A, B, and O and found that tracing the reaction patterns did conform to Mendel’s laws if;

1. A and B were both dominant over O
2. A and B were co-dominant with each other

Landsteiner could not set up crosses so he did the next best thing. He traced the blood group reaction patterns in families. This method is known as pedigree analysis. Consider the following basic family pedigree:

By convention, squares denote males and circles denote females. This is a simple nuclear family with two parents and four children. Taking this basic pedigree and the two conclusions of Landsteiner regarding the ABO blood groups, fill in the genotypes based on the following phenotype patterns;

Note that the genotypes of a number of the children can not be determined precisely. When this occurs, additional information needs to be obtained by extending the pedigrees vertically and horizontally. An example of such an extended pedigree for the
ABO blood groups is shown below. It is easy to fill in each genotype uniquely by working through the pedigree using Landsteiner’s observations.

Observing traits such as simple genetic diseases in extended pedigrees was the way in which the inheritance of many traits was discovered. The patterns formed in extended pedigrees are often all that is needed to determine whether a trait is dominant, recessive, or sex-linked. Examples of these patterns are shown below:

**Dominant Inheritance Pattern**
The differences among the three pedigrees are related to the density of the affected individuals (the black symbols) and the sex distribution. A dominant trait will exhibit a higher density than a recessive trait since the dominant allele only requires one copy, that is, heterozygotes will be affected, while a recessive trait must be homozygous for the trait to be expressed in the phenotype. In the sex-linked, or X-linked, pattern, expression is limited to males only.

What pattern of inheritance is represented in the following four pedigrees?
II. Independent Assortment
Mendel’s careful recording of single trait crosses clearly established the ubiquitous nature of allelic segregation. Fortunately, he did not stop there. Considering two traits at a time is called dihybrid crossing. As an example, take Mendel’s observation of the two traits of yellow and green albumin and round and wrinkled seed. Noting that yellow (Y) is dominant over green (y) and that round (R) is dominant over wrinkled (r), pure lines for both traits simultaneously will have the genotypes YYRR and yyrr. If these lines are then crossed as the P1 generation, the F1 will all be yellow and round, or YyRr. In subsequent F2 dihybrids Mendel observed phenotypic ratios approximating the following distribution:

- 9 yellow, round
- 3 yellow, wrinkled
- 3 green, round
- 1 green, wrinkled

Mendel reasoned that this pattern could only be produced if the two traits were acting independently. We can see this easily using a Punnett Square for the F1 cross.

F1 gametes: 

\[
\begin{array}{c}
Y \\
Y \\
y \\
y \\
R \\
R \\
r \\
r \\
\end{array}
\]

F2 Genotypes:

\[
\begin{array}{c|c|c|c|c}
 & YR & Yr & yR & yr \\
YR & YYRR & YyRR & YyRr & YyRr \\
Yr & YYRr & YYrr & YyRr & Yyrr \\
yR & YyRR & YyRr & yyRR & yyRr \\
yr & YyRr & Yyrr & yyRr & yyrr \\
\end{array}
\]

Keeping the dominance relationships in mind, the 9:3:3:1 dihybrid phenotype ratio can be found in the 16 squares:

- 9 yellow and round: YYRR, 2 YYRr, 2 YyRR, 4 YyRr
- 3 yellow and wrinkled: YYrr, 2 yYrr
3 green and round: yyRR, 2 yyRr

1 green and wrinkled: yyrr

Of course, this can be extended to a trihybrid cross. Add blue (B) and white (b) flowers to the cross shown above:

Parental pure lines: YYRRBB and yyrrbb

F1 trihybrids; YyRrBb

If all three traits assort independently there will be eight possible gametes:

YRB, YRb, YrB, yRb, yRB, yRb, yrB, yrb

And the Punnett Square will have 64 cells:

<table>
<thead>
<tr>
<th></th>
<th>YRB</th>
<th>YRb</th>
<th>YrB</th>
<th>Yrb</th>
<th>yRB</th>
<th>yRb</th>
<th>yrB</th>
<th>yrb</th>
</tr>
</thead>
<tbody>
<tr>
<td>YRB</td>
<td>YYRRBB</td>
<td>YyRRBB</td>
<td>YYRrBB</td>
<td>YYRrBb</td>
<td>YyRRBB</td>
<td>YyRrBB</td>
<td>YyRrBb</td>
<td>YyRrBb</td>
</tr>
<tr>
<td>YRb</td>
<td>YYRRBb</td>
<td>YyRRbb</td>
<td>YYRrBb</td>
<td>YYRrbb</td>
<td>YyRRBb</td>
<td>YyRRbb</td>
<td>YyRrBb</td>
<td>YyRRbb</td>
</tr>
<tr>
<td>YrB</td>
<td>YYrRBB</td>
<td>YYrRbB</td>
<td>YYrrBB</td>
<td>YyRrBB</td>
<td>YyRRBB</td>
<td>YyRrBb</td>
<td>YyrrBB</td>
<td>YyrrBb</td>
</tr>
<tr>
<td>Yrb</td>
<td>YyRRBb</td>
<td>YyRRbb</td>
<td>YyRrBb</td>
<td>YyRrbb</td>
<td>YyRRBb</td>
<td>YyRRbb</td>
<td>YyRrBb</td>
<td>YyRRbb</td>
</tr>
<tr>
<td>yRB</td>
<td>YyRRBB</td>
<td>YyRRBb</td>
<td>YyRRBb</td>
<td>YyRRBB</td>
<td>YyRRBB</td>
<td>YyRRBb</td>
<td>YyRRBb</td>
<td>YyRRBb</td>
</tr>
<tr>
<td>yRb</td>
<td>YyRRBb</td>
<td>YyRRbb</td>
<td>YyRrBb</td>
<td>YyRrbb</td>
<td>yyRRBb</td>
<td>yyRRBb</td>
<td>yyRRBb</td>
<td>yyRRBb</td>
</tr>
<tr>
<td>yrB</td>
<td>YyRrBB</td>
<td>YyRrBb</td>
<td>YyrrBB</td>
<td>YyrrBb</td>
<td>YyRrBb</td>
<td>YyrrBb</td>
<td>YyrrBb</td>
<td>YyrrBb</td>
</tr>
<tr>
<td>yrb</td>
<td>YyRrBb</td>
<td>YyRrbb</td>
<td>YyrrBb</td>
<td>Yyrrbb</td>
<td>yyRrBb</td>
<td>yyrrBb</td>
<td>yyrrBb</td>
<td>yyrrBb</td>
</tr>
</tbody>
</table>

The phenotype ratio is:

Yellow, round, blue: 27
Yellow, round, white: 9
Yellow, wrinkled, blue: 9
Yellow, wrinkled, white: 3
Green, round, blue: 9
Green, round, white: 3
Green, wrinkled, blue: 3
Green, wrinkled, white: 1

Note that, because each of the three traits is assorting independently, each individual phenotype ratio is 3 : 1; i.e., 48 yellow to 16 green; 48 round to 16 wrinkled; 48 blue to 16 white!

There is an additional mathematical treatment that can be demonstrated with each of the crosses that have been worked out. Segregation of alleles means that there are known probabilities associated with gamete formation. For any monohybrid cross, for example, the probability that a AA parent will donate an A allele to an offspring is 1.00 and the probability that a AA parent will donate an a allele is 0.00. If the parent is Aa these probabilities are both 0.50. Thus, if one parent is AA and the other parent is aa, the chances that their offspring will be either AA or aa is 0.00 and the probability that their offspring will be Aa is 1.00.

Extending this to a dihybrid cross, if the parental genotypes are AABb and AaBb, the probability of each possible off spring genotype can be easily calculated by multiplying the individual probabilities of the independent genotypes:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Probability</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AABB</td>
<td>0.125</td>
<td>(0.5 x 0.25)</td>
</tr>
<tr>
<td>AABb</td>
<td>0.250</td>
<td>(0.5 x 0.5)</td>
</tr>
<tr>
<td>AAbb</td>
<td>0.125</td>
<td>(0.5 x 0.25)</td>
</tr>
<tr>
<td>AaBB</td>
<td>0.125</td>
<td>(0.5 x 0.25)</td>
</tr>
<tr>
<td>AaBb</td>
<td>0.250</td>
<td>(0.5 x 0.5)</td>
</tr>
<tr>
<td>Aabb</td>
<td>0.125</td>
<td>(0.5 x 0.25)</td>
</tr>
<tr>
<td>aaBB</td>
<td>0.000</td>
<td>(0.0 x 0.25)</td>
</tr>
<tr>
<td>aaBb</td>
<td>0.000</td>
<td>(0.0 x 0.5)</td>
</tr>
<tr>
<td>aabb</td>
<td>0.000</td>
<td>(0.0 x 0.25)</td>
</tr>
</tbody>
</table>

The total probability will always add up to 1.000. This exercise can be extended to include any number of traits so long as they assort independently. For example, given the parental genotypes AABbcccDd and AabbCcdd in a tetrahybrid cross, what is the probability that an offspring will be AAbbCcDd? (0.0625 from 0.5 x 0.5 x 0.5 x 0.5) What is the probability that another offspring will be AabbccDD? (0.000 from 0.5 x 0.5 x 0.5 x 0.0)

III. Epistasis
The final issue to be raised here is that of epistasis. This phenomenon is defined as the influence of one genotype on another. For example, in the trihybrid cross shown above, the phenotype ratios will be distorted if the genotype for flower color influences that for seed shape such that a homozygous white (bb) makes all seeds round regardless of their
genotype. In such a case, any occurrence of bb and rr will result in round seeds and the phenotype ratios will become:

- Yellow, round, blue: 27
- Yellow, round, white: 12
- Yellow, wrinkled, blue: 9
- Yellow, wrinkled, white: 0
- Green, round, blue: 9
- Green, round, white: 4
- Green, wrinkled, blue: 3
- Green, wrinkled, white: 0

What would the ratios be homozygous white made yellow albumin green but only if the albumin genotype was heterozygous Yy?

- Yellow, round, blue: 27
- Yellow, round, white: 3
- Yellow, wrinkled, blue: 9
- Yellow, wrinkled, white: 1
- Green, round, blue: 9
- Green, round, white: 9
- Green, wrinkled, blue: 3
- Green, wrinkled, white: 3

These are effects that distort the phenotype ratios overall but note that the phenotype ratios for the unaffected traits remain at expectation; i.e., the ratio of yellow to green albumin in the first example is still 48 : 16 and the ratio of round to wrinkled seeds is still 48 : 16 in the second example.

**Resources**

There are many sources for additional questions and problems available on the web. A few of these are listed below.

http://people.whitman.edu/~hutchidw/Mendelanswers.html

http://web.mit.edu/esgbio/www/mg/problems.html

http://www.biology.arizona.edu/mendelian_genetics/mendelian_genetics.html

In addition, a nice coin toss exercise for Mendelian genetics can be found at,

http://www.wsu.edu/~omoto/papers/cointoss.html
MENDEL’S LAWS OF INHERITANCE AND EXCEPTIONS TO THE LAWS

History

The assertion that life can instantaneously arise from non living matter is called spontaneous generation. Here are the critical experiments that busted the myth. Although today we understand that living things arise from other living things, the idea of spontaneous generation was entrenched in the minds of man throughout most of history. Spontaneous generation is the belief that, on a daily basis, living things arise from non living material. This debunked belief is not the same as abiogenesis, the study of how life on earth could have arisen from inanimate matter billions of years ago.

Aristotle and Spontaneous Generation (383-322)

Aristotle was one of the first to record his conclusions on the possible routes to life. He saw beings as arising in one of three ways, from sexual reproduction, asexual reproduction or nonliving matter. According to Aristotle, it was readily observable that aphids arise from the dew on plants, fleas from putrid matter, and mice from dirty hay; and this belief remained unchallenged for more than two thousand years.

Francesco Redi's Experiments (late 1600s)

Redi was an Italian physician and one of the first to formally challenge the doctrine of spontaneous generation. Redi’s question was simple, “Where do maggots come from?” According to spontaneous generation, one would conclude that maggots came from rotting food. Redi hypothesized that maggots came from flies and designed an experiment, elegant in its simplicity, to challenge spontaneous generation.

Redi put meat into three separate jars:

Jar #1 he left open. He observed flies laying eggs on the meat and the eventual development of maggots.

Jar #2 he covered with netting. Flies laid their eggs on the netting and maggots soon appeared.

Jar #3 he sealed. Flies were not attracted to this jar and no maggots developed on the meat. This seems to be a clear demonstration of life giving rise to life. Yet it took another two hundred years for people to accept spontaneous generation as a fallacy.

Anthony van Leeuwenhoek’s “Animalcules” (1600-1700s)

Leeuwenhoek was a Dutch cloth merchant, and due to his trade, he frequently used lenses to examine cloth. Rather than employing lenses made by others, he ground his own, and the expertise that he gained through lens crafting combined with a curious mind eventually led
to an interest in microscopy. During his life, Leeuwenhoek assembled more than 250 microscopes, some of which magnified objects 270 times. Through magnification, he discovered presence of “micro” organisms - organisms so tiny that they were invisible to the naked eye. He called these tiny living things “animalcules,” and was the first to describe many microbes and microscopic structures, including bacteria, protozoans and human cells.

**John Needham & Lazzaro Spallanzani (1700s)**

The debate over spontaneous generation was reignited with Leeuwenhoek’s discovery of animalcules and the observation that these tiny organisms would appear in collected rainwater within a matter of days. John Needham and Lazzaro Spallanzani both set out to examine Leeuwenhoek’s animalcules.

**Needham’s Experiment**

John Needham was a proponent of spontaneous generation, and his beliefs were confirmed when, after boiling beef broth to kill all microbes, within the span of a few days, cloudiness of the broth indicated the respawning of microscopic life.

**Spallanzani’s Experiment**

Lazzaro Spallanzani noted a flaw in Needham’s experiment. The containers holding Needham’s beef broths had not been sealed upon boiling. So Spallanzani modified Needham’s experiment, boiling infusions, but immediately upon boiling he melted the necks of his glass containers so that they were not open to the atmosphere. The microbes were killed and did not reappear unless he broke the seal and again exposed the infusion to air.

**Louis Pasteur (1800s)**

Pasteur, a French scientist who made great contributions to our understanding of microbiology and for whom the process of “pasteurization” is named, repeated experiments similar to those of Spallanzani’s and brought to light strong evidence that microbes arise from other microbes, not spontaneously.

**Pasteur’s Swan-Necked Flasks**

Pasteur created unique glass flasks with unusual long, thin necks that pointed downward. These “swan-necked” flasks allowed air into the container but did not allow particles from the air to drift down into the body of the flask.

**The End of Spontaneous Generation**

After boiling his nutrient broths, Pasteur found that these swan-necked containers would remain free of microbes until he either broke the necks of the flasks, allowing particles from the air to drift in, or until he tilted the flask so that the liquid came in contact with dust that had accumulated at the opening of the flask. It was these carefully controlled experiments of Pasteur
that finally put to rest the debate over spontaneous generation.

**Preformation theory (Swammerdam and Bonnet, 1720-1793)**

Preformation theory proposes that the only male and female is responsible for heredity. The male gamete consists of a miniature figure of man’s body called as homunculus which is responsible for heredity. Epigenesis (C.f.wolf (1733-1794) and K.E. Von Baer (1792-1876) said that the different organs and tissues of adult plant and animals developed from the uniform embryonic tissue and not from mere growth expansion of the miniature homunculi present in eggs / sperms. Von Baer proposed that they developed through a sequential modification of the embryonic tissue. This concept is universally accepted.

Swammerdam (1637-1680), for example, thought that a tiny preformed frog occurred in the animal hemisphere of the frog egg and that became simply larger by feeding on the food stored in the vegetal hemisphere of the egg. Another biologist, Hartsoeker (1695) published a figure showing a miniature man known as mankin or homunculus in the head of the human spermatazoa. Such preformation theories had been supported by Leeuwenhoek (1632-1723), Malpighi (1673), Reaumur, Bonnet (1720-1793), Spallanzani (1729-1799) and other workers of 17th and early 18th centuries. With the development of improved microscopy and other cytological techniques in 17th and 18th centuries, it became clear to biologists that neither the egg nor the sperm contained a preformed individual but that each was a relatively uniform, homogeneous mass of protoplasm.

**Particulate Theory**

A French biologist Maupertius in 1698-1759 discards the preformation theory and forwarded the concept of biparental through many tiny particles. According to him both the parents produce the semen, which composed of many tiny particles. The semen of both the parents unite and the embryo formed each organ of the embryo was supposed to be formed by two particles. Each of which came from each parent. In the year 1732-1806 J.C. Koelreuter was the first person to get fertile hybrids by artificial crossing two species of tobacco and concluded that the gametes were the physical basis of heredity.

**Pangenesis**

Charles Darwin proposed this theory. According to pangenesis that each organ of an individual produces very small almost invisible identical copies of itself called gemmules or pangenes. These gemmules from various parts collected into the blood stream of animals. The blood transports the gemmules into the reproductive organ, which produce gametes. Male and female gametes unite to form zygotes. When these gives rise to a new organism, the gemmules of different parts of the body give rise to the same kind of organs, tissues and cells, which
produced them in the parents.

**Lamarckism**

A French biologist Lamark (1774-1829) considered the inheritance of acquired characters to be the most important, if not the sole, mechanism of evolutionary changes. According to urgent need, use and disuse of organs, the modification thus acquired will be transmitted to their offspring.

**Germplasm theory August Weismanís (1834-1914)**

Germplasm theory explains that body of individual consists of two distinct types of tissues, (1) somatoplasm (2) germplasm. Somatoplasm consists of all body tissues, which do not contribute to the sexual reproduction. The germplasm on the other hand produces gametes that are the basis of heredity. It is only applied to animals and plants in which distinction between soma and germ can be made. Weismannís famous experiment of cutting off the tail of mice for 22 generations and observing that the progeny still had tail of normal length, proved that the somatoplasm is not responsible for transmission of characters.

**Cell Theory(1838)**

Schleiden and Schwann proposed cell theory 1838. They concluded that all plant and animal tissues were made of cells. It was also postulated that cell is the functional unit of living organism. In 1846 Negeli said that all cells originated from preexisting cells. Virchow 1853 elaborated this and referred it as cell linkage theory.

**Mendelian concept of hereditary**

The laws of inheritance were derived by Gregor Mendel, a 19th century monk conducting hybridization experiments in garden peas (*Pisum sativum*). Between 1856 and 1863, he cultivated and tested some 29,000 pea plants. From these experiments he deduced two generalizations which later became known as Mendel's Laws of Heredity or Mendelian inheritance. He described these laws in a two part paper, "Experiments on Plant Hybridization" that he read to the Natural History Society of Bruno on February 8 and March 8, 1865, and which was published in 1866.

Mendel's findings allowed other scientists to predict the expression of traits on the basis of mathematical probabilities. A large contribution to Mendel's success can be traced to his decision to start his crosses only with plants he demonstrated were true-breeding. He also measured only absolute (binary) characteristics, such as color, shape, and position of the offspring, rather than quantitative characteristics. He expressed his results numerically and subjected them to statistical analysis. His method of data analysis and his large sample size gave credibility to his data. He also had the foresight to follow several successive generations
(f2, f3) of his pea plants and record their variations. Finally, he performed "test crosses" (backcrossing descendants of the initial hybridization to the initial true-breeding lines) to reveal the presence and proportion of recessive characters. Without his careful attention to procedure and detail, Mendel's work could not have had the impact it made on the world of genetics.

**Mendel's Laws**

Mendel discovered that by crossing white flower and purple flower plants, the result was not a hybrid offspring. Rather than being a mix of the two, the offspring was purple flowered. He then conceived the idea of heredity units, which he called "factors", one which is a recessive characteristic and the other dominant. Mendel said that factors, later called genes, normally occur in pairs in ordinary body cells, yet segregate during the formation of sex cells. Each member of the pair becomes part of the separate sex cell. The dominant gene, such as the purple flower in Mendel's plants, will hide the recessive gene, the white flower. After Mendel self-fertilized the F1 generation and obtained the 3:1 ratio, he correctly theorized that genes can be paired in three different ways for each trait; AA, aa, and Aa. The capital A represents the dominant factor and lowercase a represents the recessive.
Mendel stated that each individual has two factors for each trait, one from each parent. The two factors may or may not contain the same information. If the two factors are identical, the individual is called **homozygous** for the trait. If the two factors have different information, the individual is called **heterozygous**. The alternative forms of a factor are called **alleles**. The genotype of an individual is made up of the many alleles it possesses. An individual's physical appearance, or phenotype, is determined by its alleles as well as by its environment. An individual possesses two alleles for each trait; one allele is given by the female parent and the other by the male parent. They are passed on when an individual matures and produces gametes: egg and sperm. When gametes form, the paired alleles separate randomly so that each gamete receives a copy of one of the two alleles. The presence of an allele doesn't promise that the trait will be expressed in the individual that possesses it. In heterozygous individuals the only allele that is expressed is the dominant. The recessive allele is present but its expression is hidden. Mendel summarized his findings in two laws; the **Law of Segregation** and the **Law of Independent Assortment**.

**Law of Segregation (The "First Law")**

The Law of Segregation states that when any individual produces gametes, the copies of a gene separate, so that each gamete receives only one copy. A gamete will receive one allele or the other. The direct proof of this was later found when the process of meiosis came to be known. In meiosis the paternal and maternal chromosomes get separated and the alleles with the characters are segregated into two different gametes.

**Law of Independent Assortment (The "Second Law")**

The Law of Independent Assortment, also known as **"Inheritance Law"**, states that alleles of different genes assort independently of one another during gamete formation. While Mendel's experiments with mixing one trait always resulted in a 3:1 ratio between dominant and recessive phenotypes, his experiments with mixing two traits (dihybrid cross) showed 9:3:3:1 ratios. But the 9:3:3:1 table shows that each of the two genes are independently inherited with a 3:1 ratio. Mendel concluded that different traits are inherited independently of each other, so that there is no relation, for example, between a cat's color and tail length. This is actually only true for genes that are not linked to each other.

Independent assortment occurs during meiosis I in eukaryotic organisms, specifically metaphase I of **meiosis**, to produce a gamete with a mixture of the organism's maternal and paternal chromosomes. Along with chromosomal crossover, this process aids in increasing genetic diversity by producing novel genetic combinations.
In independent assortment the chromosomes that end up in a newly-formed gamete are randomly sorted from all possible combinations of maternal and paternal chromosomes. Because gametes end up with a random mix instead of a pre-defined "set" from either parent, gametes are therefore considered assorted independently. As such, the gamete can end up with any combination of paternal or maternal chromosomes. Any of the possible combinations of gametes formed from maternal and paternal chromosomes will occur with equal frequency. For human gametes, with 23 pairs of chromosomes, the number of possibilities is $2^{23}$ or 8,388,608 possible combinations. The gametes will normally end up with 23 chromosomes, but the origin of any particular one will be randomly selected from paternal or maternal chromosomes. This contributes to the genetic variability of progeny.

**Rediscovery of Mendel's work**

Mendel's conclusions were largely ignored. Although they were not completely unknown to biologists of the time, they were not seen as generally applicable, even by Mendel himself, who thought they only applied to certain categories of species or traits. A major block to understanding their significance was the importance attached by 19th century biologists to the apparent blending of inherited traits in the overall appearance of the progeny, now known to be due to multigene interactions, in contrast to the organ-specific binary characters studied by Mendel. In 1900, however, his work was "re-discovered" by three European scientists, Hugo de Vries, Carl Correns, and Erich von Tschermak. The exact nature of the "re-discovery" has been somewhat debated: De Vries published first on the subject, mentioning Mendel in a footnote, while Correns pointed out Mendel's priority after having read De Vries's paper and realizing that he himself did not have priority. De Vries may not have acknowledged truthfully how much of his knowledge of the laws came from his own work, or came only after reading Mendel's paper. Later scholars have accused Von Tschermak of not truly understanding the results at all. Regardless, the "re-discovery" made Mendelism an important but controversial theory. Its most vigorous promoter in Europe was William Bateson, who coined the term "genetics", "gene", and "allele" to describe many of its tenets.

The model of heredity was highly contested by other biologists because it implied that heredity was discontinuous, in opposition to the apparently continuous variation observable for many traits. Many biologists also dismissed the theory because they were not sure it would apply to all species, and there seemed to be very few true Mendelian characters in nature. However, later work by biologists and statisticians such as R.A. Fisher showed that if multiple Mendelian factors were involved in the expression of an individual trait, they could produce the diverse results observed. Thomas Hunt Morgan and his assistants later integrated the
theoretical model of Mendel with the chromosome theory of inheritance, in which the chromosomes of cells were thought to hold the actual hereditary material, and create what is now known as classical genetics, which was extremely successful and cemented Mendel's place in history.

**Mendel's Laws of Inheritance**

Mendel postulated three laws, which are now called after his name as Mendel’s laws of heredity. These are:

1. Law of dominance and recessive
2. Law of segregation
3. Law of independent assortment

**1. Law of Dominance**

**Definition:** When two homozygous individuals with one or more sets of contrasting characters are crossed, the characters that appear in the $F_1$ hybrids are dominant characters and those do not appear in $F_1$ are recessive characters.

**Explanation:** The dominance and recessive of genes can be explained on the basis of enzymatic functions of genes. The dominant genes - are capable of synthesizing active polypeptides or proteins that form functional enzymes, whereas the recessive genes (mutant
genes) code for incomplete or non-functional polypeptides. Therefore, the dominant genes produce a specific phenotype while the recessive genes fail to do so. In the heterozygous condition also the dominant gene is able to express itself, so that the heterozygous and homozygous individuals have similar phenotype.

**Critical appreciation of Law of Dominance**

Scientists conducted cross-breeding experiments to find out the applicability of law of dominance. The experiments were conducted by Correns on peas and maize, Tschermak on peas, by De Vries on maize etc., by Bateson and his collaborators on a variety of organisms, by Davenport on poultry, by Furst on rabbits, by Toyama on silk moth and by many others. These scientists observed that a large number of characters in various organisms are related as dominant and recessive.

**Importance of law of dominance**

The phenomenon of dominance is of practical importance as the harmful recessive characters are masked by the normal dominant characters in the hybrids. In Human beings a form of idiocy, diabetes, haemophilia etc. are recessive characters. A person hybrid for all these characteristics appears perfectly normal. Thus harmful recessive genes can exist for several generations without expressing themselves.

Exceptions to Law of Dominance is the Incomplete Dominance. After Mendel several cases were recorded by scientists, where F1 hybrids exhibited a blending of characters of two parents. These hybrids were found to be midway between the two parents. This is known as incomplete dominance or blending inheritance. It means that two genes of the allelomorphic pair are not related as dominant and recessive, but each of them expresses itself partially. As for example, in four-o'clock plant, *Mirabilis jalapa*, when plants with red flowers (RR) are crossed with plants having white flowers (rr), the hybrid F1 plants (Rr) bear pink flowers. When these F1 plants with pink flowers are self-pollinated they develop red (RR), pink (Rr) and white (rr) flowered plants in the ratio of 1 : 2 : 1 (F2 generation).

**2. Law of Segregation (Purity of Gametes)**

**Explanation** - The law of segregation states that when a pair of contrasting factors or genes or allelomorphs are brought together in a heterozygote (hybrid) the two members of the allelic pair remain together without being contaminated and when gametes are formed from the hybrid, the two separate out from each other and only one enters each gamete.

Example - Pure tall plants are homozygous and, therefore/possess genes (factors) TT; similarly dwarf possess genes tt. The tallness and dwarfness are two independent but contrasting factors or
Determiners. Pure tall plants produce gametes all of which possess gene T and dwarf plants t type of gametes.

During cross fertilization gametes with T and t unite to produce hybrids of F₁ generation. These hybrids possess genotype Tt. It means F₁ plants, though tall phenotypically, possess one gene for tallness and one gene for dwarfness. Apparently, the tall and dwarf characters appear to have become contaminated developing only tall character. But at the time of gamete formation, the genes T (for tallness) and t (for dwarfness) separate and are passed on to separate gametes. As a result, two types of gametes are produced from the heterozygote in equal numerosity. 50% of the gametes possess gene T and other 50% possess gene t. Therefore, these gametes are either pure for tallness or for dwarfness. (This is why the law of segregation is also described as Law of purity of gametes).

\[
\begin{array}{c}
\text{F₁ Plants} \\
Tt \\
X \\
Tt
\end{array}
\]

Gametes unite at random and when gametes are numerous all possible combinations can occur, with the result that tall and dwarf appear in the ratio of 3 :1. The results are often represented by Punnett square as follows:

**Critical appreciation of law of segregation**

It has been confirmed by cytological studies that dominance or no dominance, the law of segregation holds good to all cases. Its far reaching applicability has made it rare biological generalization.

\[
\begin{array}{c}
\text{RR} \\
\text{have only gene for round} \\
\text{Rr, rR} \\
\text{have gene for round and wrinkle} \\
\text{Rr} \\
\text{have only wrinkeld gene}
\end{array}
\]

\[
\begin{array}{c}
\text{RR} \\
\text{Rr}
\end{array}
\]

\[
\begin{array}{c}
\text{R} \\
\text{r}
\end{array}
\]

\[
\text{Rr}
\]

\[
\text{Rr}
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\[
\text{Rr}
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\[
\text{Rr}
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\[
\text{Rr}
\]
3. Law of Independent Assortment

**Definition:** The inheritance of more than one pair of characters (two pairs or more) is studied simultaneously, the factors or genes for each pair of characters assort out independently of the other pairs. Mendel formulated this law from the results of a dihybrid cross.

**Explanation:** The cross was made between plants having yellow and round cotyledons and plants having green and wrinkled cotyledons.

The F₁ hybrids all had yellow and round seeds. When these F₁ plants were self fertilized they produced four types of plants in the following proportion:

(i) Yellow and round

9
(ii) Yellow and wrinkled 3
(iii) Green and round 3
(iv) Green and wrinkled 1

The above results indicate that yellow and green seeds appear in the ratio of $9 + 3 : 3 + 1 = 3 : 1$. Similarly, the round and wrinkled seeds appear in the ratio of $9 + 3 : 3 +1 = 12:4$ or $3 : 1$. This indicates that each of the two pairs of alternative characters viz. yellow-green cotyledon colour is inherited independent of the round-wrinkled character of the cotyledons. It means at the time of gamete formation the factor for yellow colour enters the gametes independent of R or r, i.e, gene Y can be passed on to the gametes either with gene R or r.

**Cytological explanation of the results:** In the above experiment yellow and round characters are dominant over green and wrinkled characters which can be represented as follows:

(i) gene for yellow colour of cotyledons Y
(ii) gene for green colour of cotyledons y
(iii) gene for round character of cotyledons R
(iv) gene for wrinkled character of cotyledons r

Therefore, plants with yellow and round cotyledons will have their genotype YYRR and those with green and wrinkled cotyledons will have a genotype yyrr. These plants will produce gametes with gene YR and yr respectively. When these plants are cross pollinated, the union of these gametes will produce F₁ hybrids with YyRr genes. When these produce gametes all the four genes have full freedom to assort independently and, therefore, there are possibilities of four combinations in both male and female gametes.

(i)RY  (ii)Ry  (iii)rY  (iv)ry

This shows an excellent example of independent assortment. These gametes can unite at random producing in all 16 different combinations of genes, but presenting four phenotypes in the ratio of 9:3:3: 1.

**Dihybrid ratio:** RR yy - Round, yellow seeded ; Rr yy - Wrinkled and greed seeded
Critical appreciation of law of Independent Assortment-

The law of independent assortment fails to have a universal applicability. Cytological studies have revealed that only those allelomorphs assort independently during meiosis, which are located in different homologous pairs of chromosomes. But, if the allelomorphs for different characters are present in the same homologous pair of chromosomes, these are passed on to the same gamete. Law of independent assortment does not apply to such cases.

BIOLOGICAL SIGNIFICANCE OF MENDEL’S LAWS

Mendel’s work remained buried for about three decades, but after its rediscovery, the laws are being used for the various branches of breeding. These are used for improving the varieties of fowls and their eggs; in obtaining rust-resistant and disease-resistant varieties of grains. Various new breeds of horses and
dogs are obtained by cross breeding experiments. The science of Eugenics is the outcome of Mendelism, which deals with the betterment of human race.

**Mendelian deviation**

Mendelian deviations or exceptions or anomalies includes

1) Incomplete dominance

2) Codominance

3) Lethal genes etc.

**1. Incomplete dominance**

Mendel always observed complete dominance of one allele over the other for all the seven characters, which he studied, in garden pea. Later on cases of incomplete dominance were reported. For example, in four éöí clock plant (Mirabilis jalapa) there are two types of flower viz., red and white. A cross between red and white flowered plants produced plants with intermediate flower colour i.e. pink colour in F1 and a modified ratio of 1 red: 2 pink: 1 White in F2.

**Parents**

<table>
<thead>
<tr>
<th>Red flower (RR) x White flower (rr)</th>
</tr>
</thead>
</table>

**F1**

Red (Rr) x White (rr) 

**F2**

1 Red (Rr) : 2 Pink (RR) : 1 White (rr)

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Incomplete dominance in flowers of *Mirabilis jalapa*
2. Codominance

In case of codominance both alleles express their phenotypes in heterozygote greater than an intermediate one. The example is AB blood group in human. The people who have blood type AB are heterozygous exhibiting phenotypes for both the IA and IB alleles. In other words, heterozygotes for codominant alleles are phenotypically similar to both parental types. The main difference between codominance and incomplete dominance lies in the way in which genes act. In case of codominance both alleles are active while in case of incomplete dominance both alleles blend to make an intermediate one.

3. Lethal genes

Gene, which causes the death of its carrier when in homozygous condition is called lethal gene. Mendel’s findings were based on equal survival of all genotypes. In normal segregation ratio of 3:1 is modified into 2:1 ratio. Lethal genes have been reported in both animals as well as plants. In mice allele for yellow coat colour is dominant over grey. When a cross is made between yellow and grey a ratio of 1:1 for yellow and gray mice was observed. This indicated that yellow mice are always heterozygous. Because yellow homozygotes are never born because of homozygous lethality. Such genes were not observed by Mendel. He always got 3:1 ratio in F2 for single gene characters.

Lethal genes can be recessive, as in the aforementioned mouse experiments. Lethal genes can also be dominant, conditional, semilethal, or synthetic, depending on the gene or genes involved.
MONOHYBRID CROSS

A cross is made between two true-breeding parents differing for a single trait, producing an F1 generation. These plants are intercrossed to produce an F2 generation.
**Dihybrid Crosses**

The following legends were described for peas by Mendel:

- **T** - Tall
- **tt** - dwarf
- **G** - green (pod)
- **gg** - yellow

Pure breeding parents can be crossed to produce a dihybrid meaning that 2 genes affecting different traits are heterozygous (segregating) in all the f1 progeny.

Examples:
- TT, GG X tt, gg ➔ Tt, Gg
- TT, gg X tt, GG ➔ Tt, Gg

When the F1 is self fertilized (plants) or crossed with another Tt, Gg individual, the progeny will show the expected 3 dominant : 1 recessive phenotypic ratio for each trait. If the two traits are independent, the two 3 : 1 ratios will interact to give a ratio based on 16ths.

<table>
<thead>
<tr>
<th>#</th>
<th>Genotypes</th>
<th>Phenotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>T_, G_</td>
<td>Tall, Green</td>
</tr>
<tr>
<td>3</td>
<td>T_, gg</td>
<td>Tall, yellow</td>
</tr>
<tr>
<td>3</td>
<td>tt, G_</td>
<td>Dwarf, Green</td>
</tr>
<tr>
<td>1</td>
<td>tt, gg</td>
<td>Dwarf, Yellow</td>
</tr>
</tbody>
</table>
Backcrossing is a crossing of a hybrid with one of its parents or an individual genetically similar to its parent, in order to achieve offspring with a genetic identity which is closer to that of the parent.

The Testcross

Because some alleles are dominant over others, the phenotype of an organism does not always reflect its genotype. A recessive phenotype (yellow) is only expressed with the organism is homozygous recessive (gg). A pea plant with green pods may be either homozygous dominant (GG) or heterozygous (Gg). To determine whether an organism with a dominant
phenotype (e.g. green pod color) is homozygous dominant or heterozygous, you use a testcross.

The breeding of an organism of unknown genotype with a homozygous recessive. If all the progeny of the testcross have green pods, then the green pod parent was probably homozygous dominant since a GG x gg cross produces Gg progeny. If the progeny of the testcross contains both green and yellow phenotypes, then the green pod parent was heterozygous since a Gg x gg cross produces Gg and gg progeny in a 1:1 ratio. The testcross was devised by Mendel and is still an important tool in genetic studies.