

Controversies about Mendel's work

Although Mendel is now recognized as the founder of genetics, significant controversy ensued about his work throughout the 20th century.

Fairbanks and Rytting (2001) reviewed five of the most contentious issues:

- Are Mendel's data too good to be true?
- Is Mendel's description of his experiments fictitious?
- Did Mendel articulate the laws of inheritance attributed to him?
- Did Mendel detect but not mention linkage?
- Did Mendel support or oppose Darwin?

Are Mendel's data too good to be true?

- 1902, Weldon (χ^2 test): **Mendel's observed ratios were astonishingly close to his expectations.**
- 1936, Fisher: **Mendel's results were consistently so close to expected ratios that the validity of those results must be questioned.**
- He concluded that **Mendel should have misclassified some heterozygotes as homozygotes** in obtaining 2: 1 genotypic ratio.
- Mendel chose 100 F_2 plants with the dominant phenotype for each of the five plant traits and grew only ten F_3 descendants from each of these plants.
 - If all ten F_3 descendants had the dominant phenotype: F_2 plant as constant (homozygous).
 - F_3 descendants had both dominant and recessive phenotypes, the F_2 plant as hybrid (heterozygous).
 - If each offspring has an independent probability, 0.75, of displaying the dominant character, the probability that all ten will do so is 0.75^{10} , or 0.0563.
 - Consequently, between 5 and 6 percent of the heterozygous parents were misclassified as homozygotes.
 - The expected ratio of segregating to nonsegregating families should not be 2 : 1, but 1.8874 : 1.1126, or approximately 377.5 : 222.5 out of 600.
 - A χ^2 test of Mendel's observed values of 399 and 201 and Fisher's expected values of 377.5 and 222.5 yields a χ^2 value of 3.3020 with one degree of freedom, **which is not statistically significant because its probability is 0.0692 (> 0.05).**
 - Piegorsch (1983) calculated the summed χ^2 value to be 7.6582 with a corresponding probability of 0.2642 with six degrees of freedom. When this probability is halved to 0.1321, the differences between Mendel's observed ratio and Fisher's expected ration becomes nonsignificant.
- 1986, Edwards: **Only two of Mendel's 22 experiments yield χ^2 values with probabilities <0.5 and six yield χ^2 values with probabilities >0.90, -- bias toward expectation in Mendel's data.**
 - Random distribution: $P = 0.05$ to 0.95 , nonsignificant and hypothesis is accepted.

The proximity of Mendel's F_3 progeny data to an incorrect expectation is not as questionable as it might seem when viewed in a botanical context.

- ***Mendel probably sowed more than ten seeds in a space to be occupied by ten plants, then thinned the seedlings to ten to ensure that there were ten F_3 progeny from each F_2 plant.*** Indeed, Mendel's description of his method, reported cultivating rather than sowing **10 seeds**.
- Had Mendel sown more than ten seeds from each F_2 plant, then he could have scored two of the plant traits in seedlings before thinning.
 - **Differences in stem length, as Mendel noted in his paper, can be easily scored in seedlings a few days after germination.**
 - **Variation for flower and seed-coat color was perfectly correlated with variation for axillary pigmentation in his experiments.** Mendel could score F_3 plants for the **presence or absence of axillary pigmentation** as early as two to three weeks after germination.
- Wright (1966) and Beadle (1967) proposed that Mendel might have ***unconsciously misclassified*** individuals with questionable phenotypes to favor his expectations.
 - **Mendel was careful about misclassification of phenotypes and had mentioned that "with a little practice in sorting, however, mistakes are easy to avoid".**
 - **Mendel identified not only the phenotypes, but also the genotypes of individual seeds through examination of their self-fertilized progeny.**
- Mendel might have stopped counting individuals when the numbers were close to the ratios he expected [Olby (1985) and Beadle (1967)].
 - The average **number of seeds per plant is close to 30** (16 590 seeds divided by 550 plants = 30.16 seeds per plant from the monohybrid, dihybrid, and trihybrid experiments for seed shape and cotyledon color).
 - Is 30 seeds per plant too low for 19th century pea cultivation?
 - Dr. J. Rasmussen, a pea geneticist wrote to Fisher: "**About 30 good seeds per plant is, under Mendel's conditions.**"
 - Fairbanks and Rytting (2001) found that average number ***of seeds per plant was 47.18*** among 24 garden-pea varieties grown at the New York Agricultural Experiment Station in Geneva, during 1888 (Curtis, 1889).
 - ***Of the 24 varieties tested, four produced averages of less than 30 seeds per plant.***
- In Mendel's second letter to Nägeli, he referred to his paper as "***the unchanged reprint of the draft of the lecture mentioned; thus the brevity of the exposition, as is essential for a public lecture***".
- Fairbanks and Rytting (2001) concluded that, "***although the bias in Mendel's experiments is evident, there are reasonable statistical and botanical explanations for the bias, and insufficient evidence to indicate that Mendel or anyone else falsified the data.***"

Is Mendel's description of his experiments fictitious?

- Bateson (1913): “*It is very unlikely that Mendel could have had seven pairs of varieties such that the members of each pair differed from each other in only one considerable character.*”
- According to Fairbanks and Rytting there is little foundation for claims that ***Mendel's experiments were fictitious*** when viewed from a botanical perspective.
 - Much of the confusion on this issue arises from the fact that *Pisum sativum* is a domesticated species and among the many cultivated varieties there are several different phenotypes.

Three general categories of pea varieties:

- ***Garden varieties (also called shelling varieties), field varieties, and sugar varieties.***
- **Garden varieties** display
 - white seed coats, white flowers and no axillary pigmentation, inflated pods, green pods, and axillary flowers; they vary for:
 - ***seed shape, cotyledon color, and stem length***
- **Field varieties** display
 - ***dominant phenotypes for all seven traits.***
- **Sugar varieties** display
 - dominant phenotypes for all traits except ***pod shape.***
- **Pod Shape:**

Mendel's monohybrid experiment for ***pod shape*** may have included a field variety and a sugar variety as parents.
- **Seed-coat color:**

There are several possibilities for Mendel's monohybrid experiment for ***seed-coat color***. He could have hybridized ***a field variety with a garden variety*** that differed only for seed-coat color.
- **Flower position:**

The most readily available terminal-flowered variety in the 19th century was called the ***Mummy Pea*** and it is probably the variety that Mendel used.
- **Pod color:**
 - Garden and sugar varieties, called ***gold varieties, have yellow pods.***
 - Mendel could have matched any one of the gold varieties with another garden or sugar variety in a monohybrid experiment for ***yellow pod.***

A mathematical minimum of eight varieties is required for seven monohybrid experiments.

Fairbanks and Rytting (2001) ***concluded that Mendel could have easily designed and conducted seven monohybrid experiments with 22 varieties at his disposal.***

Evidence, however, is insufficient to advocate for either way.

Did Mendel articulate the laws of inheritance attributed to him?

The two laws of inheritance most often attributed to Mendel are *segregation* and *independent assortment*.

1. The law of segregation, stated in modern terms, is that *during meiosis two alleles of a single locus, one inherited from each parent, pair with each other, and then segregate from one another into the germ cells so that each germ cell carries only one allele of that locus*. Segregation in heterozygous individuals produces in equal proportions two different types of gametes, each with one of the two alleles.
2. The law of independent assortment, stated in modern terms, is that *the segregation of alleles of a single locus has no influence on the segregation of alleles at another locus*. The result is completely random and uniform combinations of alleles of different loci in the self-fertilized progeny of dihybrid (or multihybrid) individuals.

The law of segregation:

Genetic terms, such as *allele*, *locus*, and *chromosome*, had not been coined in Mendel's day, nor was the cellular process of meiosis understood.

Mendel referred to segregation of hereditary elements several times in his paper. He concluded:

- *“the differing elements succeed in escaping from the enforced association only at the stage at which the reproductive cells develop. In the formation of these cells, all elements present participate in completely free and uniform fashion, and only those that differ separate from each other. In this manner the production of as many kinds of germinal and pollen cells would be possible as there are combinations of potentially formative elements.”*

This paragraph, however, is a remarkably lucid summary of the law of segregation.

- Mendel's reference to "potentially formative elements" implies the existence of **invisible particulate determinants of inherited traits**. We might well view the term "element," as the equivalent of the modern term "allele."
- Mendel's reference to the "enforced association" of differing elements indicates that he perceived the **differing elements as being paired in hybrids** (heterozygotes).
- His statement that differing elements "**separate from each other**" shows a clear understanding of segregation that is similar to the modern view.
- He also correctly recognized that segregation takes place "**only at the stage at which the reproductive cells develop**" (i.e., during meiosis).

This paragraph, however, reveals one aspect of Mendel's perception that differs from the modern concept of segregation.

- *Mendel perceived segregation as an anomaly restricted to hybrids (heterozygotes).*
- He called the differing elements "antagonistic elements" whose association in the hybrid is a "compromise," and wrote that "only those elements that differ separate from one another."

Mendel represented heterozygotes with a two-letter designation (*Aa*), as modern geneticists usually represent them, he consistently represented homozygotes with a single letter (*A* or *a*), rather than the two letters (*AA* or *aa*) used today.

- For example, Mendel represented the genotypic ratio of the F_2 generation of a monohybrid experiment as $A + 2Aa + a$, instead of $AA + 2Aa + aa$.

Mendel may have concluded that like elements (alleles) do not pair with one another and do not segregate in plants that are not hybrids (i.e., are not heterozygotes), and that therefore a single letter was an accurate way to represent such plants.

"Mendel's view of segregation occurring only in the heterozygotes (i.e., with different alleles) could easily be defended as being completely consistent even with the modern use of the term." – [Fairbanks and Rytting (2001)].

The law of independent assortment:

The following statement immediately after Mendel's presentation of his di- and trihybrid experiments is the often-quoted statement of independent assortment:

"The progeny of hybrids in which several essentially different traits are united represent the terms of a combination series in which the series for each pair of differing traits are combined. This also shows at the same time that the behavior of each pair of differing traits in a hybrid association is independent of all other differences in the two parental plants."

"He articulated the laws of inheritance attributed to him insofar as was possible given the information he had." – [Fairbanks and Rytting (2001)].

Did Mendel detect but not mention linkage?

- Mendel concluded "the behavior of each pair of differing traits in a hybrid association is independent of all other differences in the two parental plants".
- Dunn (1965), under the assumption that Mendel studied one gene on each of the seven chromosomes, calculated the probability of doing so as $6/7 \times 5/7 \times 4/7 \times 3/7 \times 2/7 \times 1/7 = 0.0061$ (<1%), again calling Mendel's experimental results into question.

Mendel studied: <http://www.jic.bbsrc.ac.uk/germplas/pisum/zgs4f.htm>

- two genes on chromosome 1 (a and i),
- no genes on chromosomes 2 and 3, either two genes (fa and le) or three genes (fa , le , and v) on chromosome 4,
- one gene (gp) on chromosome 5,
- possibly one gene (p) on chromosome 6,
- and one gene (r) on chromosome 7.
- The gene in doubt is the one that governs pod shape. Recessive alleles of the v gene on chromosome 4 and the p gene on chromosome 6 both confer constricted (unparchmented) pods when homozygous, and it is not known which of the two Mendel studied.

Genes on the same chromosome are said to be linked only if they are so close to one another that the frequency of crossovers between them is significantly less than the frequency of recombination for independent assortment.

In most testcross experiments (the most reliable type of linkage experiment), linkage often cannot be distinguished from independent assortment for genes located more than ~ 60 cM.

- The two genes that Mendel studied on chromosome 1, i , which governs seed color, and a , which governs flower color, are 204 cM apart, so distant that they assort independently.

- The same is true for two of the genes that Mendel studied on chromosome 4; *fa*, which governs flower position, and *le*, which governs stem length, are 121 cM apart.
- Mendel would not have detected linkage if he studied the *p* gene, which governs pod shape, on chromosome 6. He could have observed one case of linkage if he studied the *v* gene, which also governs pod shape. The *v* gene is located 12 cM from the *le* gene on chromosome 4.
- If Mendel did study the *v* gene and would had the opportunity to observe linkage.
- Lamprecht (1968) reported that observed recombination between *le* and *v* may vary from 2.6 to 38.5% and that, according to Lamprecht (1941), the mutation rate for *v* may be as high as 40%. Had either or both of these values been on the higher side in Mendel's experiments, he would not have detected linkage for the *v* and *le* genes.
- Mendel conducted his experiments with F₂ progeny, which are not as reliable for detection of linkage as are testcross progeny.
- Mendel did not report data for his experiment with stem length and pod shape, we are fortunate that he described such an experiment in his second letter to Nägeli.
- The experiment was a tetrahybrid experiment in which one parental variety had **green cotyledons, white seed coats, short stem, and inflated pods** (if *v*, then in repulsion phase linkage with *le* for stem length [short stem]), and the other had yellow cotyledons, colored seed coats, constricted pods, and long stems.
- Mendel obtained a true-breeding F₃ plant in 1859, the fourth year of his experiments, that had yellow cotyledons, white seed coats, **inflated pods, and long stems**.
- Thus, the dominant alleles for **pod shape and stem length, if they were linked, were in repulsion conformation in the F₁ generation** and were recombined into coupling conformation in the true-breeding descendent that Mendel described.

Segregation of F₂s for two linked loci mapped 12 cM map apart:

Linkage	<i>L-V-</i>	<i>llV-</i>	<i>L-vv</i>	<i>llvv</i>
Repulsion	8	4	4	0
Coupling	11	1	1	3
Independent Assortment	9	3	3	1

Linkage for loci that are 12 cM apart in repulsion conformation may escape detection in an F₂ population.

- If, as Mendel stated, he examined a small number of individuals in this experiment and he observed at least one recombinant type, he probably did not detect linkage, if indeed the genes he studied were linked.

Di Trocchio (1991) raised another question: *Why Mendel did not consider more than seven characters?*

Mendel studied the literatures before initiating his studies. Before him:

- Knight (1799, 1823) studied **seed coat color** and described the phenomenon of dominance.

- Goss (1824) studied **cotyledon color** and described dominance, as well as segregation, although in purely qualitative terms.
- Seton (1824) studied **stem length and cotyledon color**.
- Gärtner (1849) reviewed Knight's work with seed coat color, and described his own work in *Pisum* with **stem length, flower color, cotyledon color, and seed shape**.

Mendel studied Gärtner's (1849) book on plant hybridization in detail before and during his experiments, as he indicated in his first letter to Nägeli and as evidenced by his 17 references in his paper.

Thus, he was familiar with both Knight's and Gärtner's pea hybridization experiments.

- The type of analysis that Mendel conducted relies on traits that display discontinuous variation, as does detection of linkage. The traits that Mendel chose to study are among only a few that varied in a discontinuous fashion among commercially available 19th century varieties.
- Mendel's varieties certainly differed in more than the seven traits on which he reported data.
 - For example, he also reported in his paper that he conducted experiments on the timing of flowering, peduncle length, and brownish-red pod color but he did not report the data for these experiments.
 - However, most of the other traits display continuous variation and are governed by multiple genes and environmental influences and cannot be easily analyzed in a simple Mendelian fashion.

Mendel's choice of traits apparently was based:

- first on those studied by his predecessors and,
- second on those that had distinct discontinuous phenotypic differences that permitted conclusive analysis.

Fairbanks and Rytting (2001) concluded “*because of the locations of the genes that governed such traits and the design of his experiments, it is unlikely that he could have detected linkage. There is no botanical or historical evidence to support the claim that Mendel observed and then disregarded linkage.*”

Did Mendel support or oppose Darwin?

Mendel was clearly interested in evolution and he considered his experiments as relevant to an understanding of evolution.

At the time Mendel wrote his paper, the *Origin* was well known and evolution through natural selection was a popular topic for discussion in scientific societies.

- According to Orel (1971, 1996), Mendel probably first heard of Darwin in September 1861 during a lecture. He might have read the *Origin* during the latter part of 1862 or early 1863 when the Brünn Natural History Society acquired a copy of the German translation of the first English edition (Darwin, 1859). The 1863 publication date of Mendel's personal copy of the *Origin* coincides with the last year of his experiments with peas.

- Therefore, the *Origin* had no effect on the design or conduct of those experiments, although it may have influenced Mendel's interpretation of those experiments on hybridization.
- ***Darwin's explanation of the uniformity of hybrids in the F_1 generation and the variability of their F_2 offspring differs substantially from Mendel's in that Darwin places the cause on altered reproductive systems rather than constant inherited traits.***
- Mendel never mentioned Darwin in his paper although he mildly contradicted some of the points that Darwin made in the *Origin* and supported a few others.
- **Mendel's apparent reserved rather than intense interest in the *Origin* may be due to his well-known concern for detail.**
- Although the passages Mendel marked in the *Origin* briefly address phenomena that he observed experimentally, the book had little in the way of detailed results and explanations that would have been useful to him. Mendel may not have contacted Darwin because, under the circumstances, there was little to gain in doing so.

Fairbanks and Rytting (2001) concluded that there was not enough evidence to believe that ***Mendel either strongly supported or opposed Darwin when he wrote his paper.***

CONCLUSION

[Fairbanks and Rytting (2001)]

- Although Mendel's paper is considered a classic in the history of biology, it generated much controversy throughout the century that elapsed since the rediscovery of Mendelian laws in 1900. Scholars disagree about Mendel's integrity in his presentation, his articulation of the fundamental laws of inheritance, his experimental design, his motives for conducting his experiments, and his conclusions.
- There is no credible evidence to indicate that Mendel was inaccurate or dishonest in his description of his experiments or his presentation of data. The main questions about his results can be resolved by an appeal to botanical principles and historical evidence.
- Mendel did not fabricate his data, his description of his experiments is literal.
- He articulated the laws of inheritance attributed to him insofar as was possible given the information he had.
- He did not detect linkage.
- He neither strongly supported nor opposed Darwin.