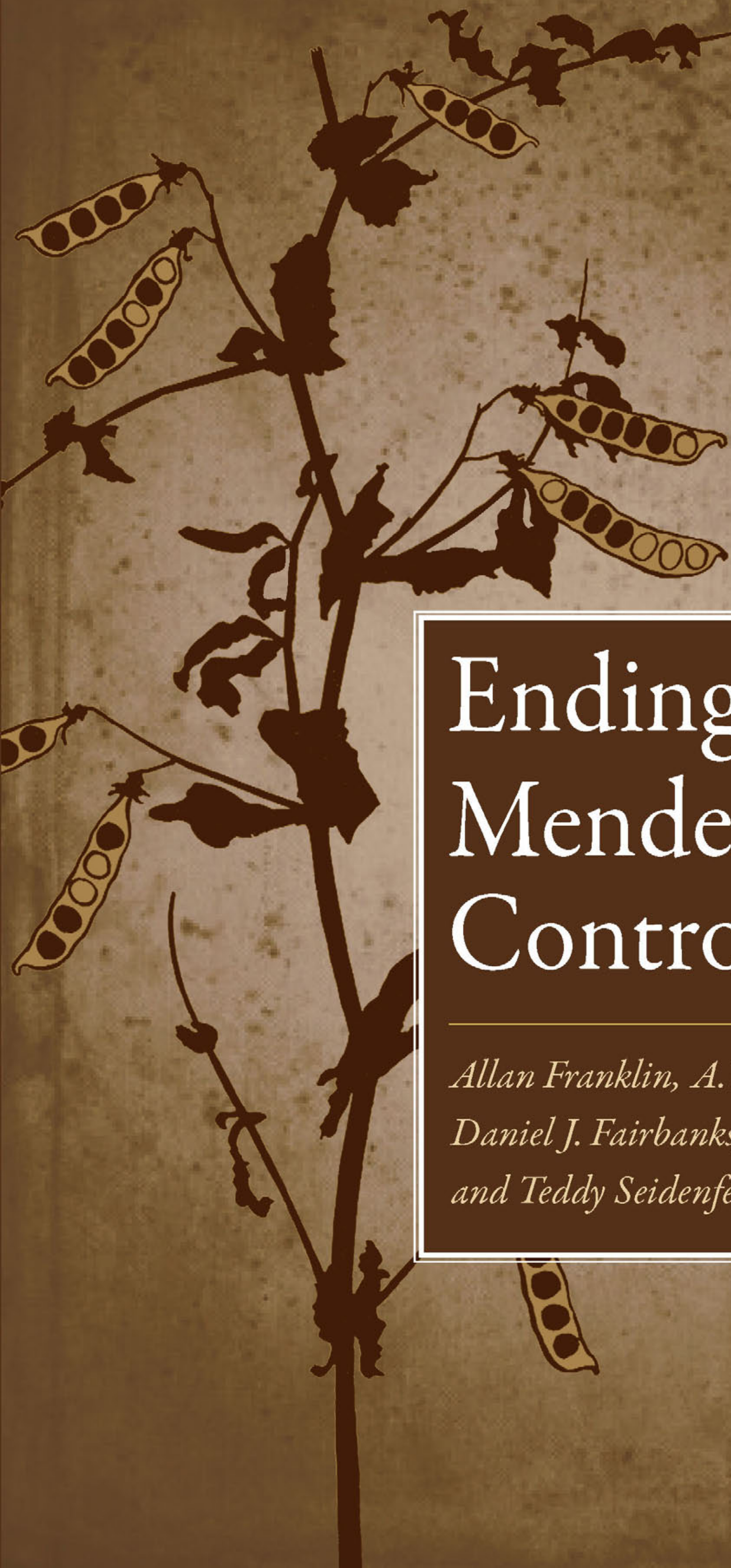


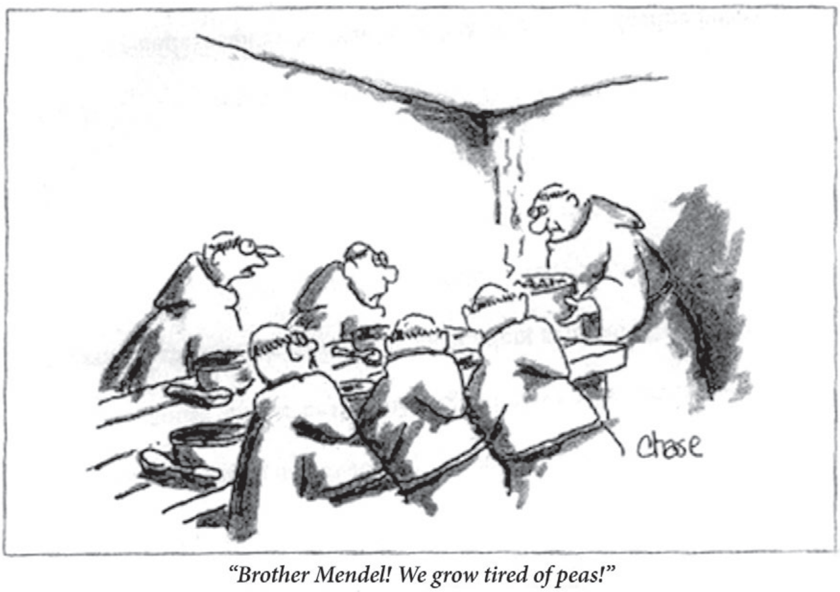
Ending the Mendel-Fisher Controversy

Allan Franklin, A. W. F. Edwards, Daniel J. Fairbanks, Daniel L. Hartl, and Teddy Seidenfeld

Ending the Mendel-Fisher Controversy

In 1859 I obtained a very fertile descendant with large, tasty seeds from a first generation hybrid. Since in the following year, its progeny retained the desirable characteristics and were uniform, the variety was cultivated in our vegetable garden, and many plants were raised every year up to 1865.

—Gregor Mendel to Carl Nägeli, April 1867, in *The Origin of Genetics: A Mendel Source Book,* ed. C. Stern, C. and E. R. Sherwood, 61–62. San Francisco: W. H. Freeman and Co., 1966.



"Brother Mendel! We grow tired of peas!"

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The History of Science has suffered greatly from the use by teachers of second-hand material, and the consequent obliteration of the circumstances and the intellectual atmosphere in which the great discoveries of the past were made. A first-hand study is always instructive, and often . . . full of surprises.

—R. A. Fisher, 1955. In *Experiments in Plant Hybridisation by Gregor Mendel, with Commentary and Assessment by Sir Ronald A. Fisher,* ed. J. H. Bennett, 6. Edinburgh: Oliver and Boyd, 1965.

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PREFACE

Gregor Mendel is justly admired as the founder of modern genetics. His experiments on pea plants, reported in 1865, established the principles of segregation and independent assortment, which form the basis of that field of study. Yet Mendel's reputation remains under a cloud. This is due to a 1936 paper by R. A. Fisher, the distinguished British statistician and geneticist, in which he reanalyzed Mendel's data and concluded that they fit his hypotheses too well. They were too good to be true. Fisher concluded that "the data of most, if not all, of the experiments have been falsified so as to agree closely with Mendel's expectations." (To be fair, Fisher attributed the falsification not to Mendel, but to an unnamed assistant.) It was this paper that created the cloud over Mendel's reputation and that, after some time, initiated the Mendel-Fisher controversy.

It is well known that Mendel's work was neglected until its rediscovery in 1900. Similarly, Fisher's paper was overlooked for some 28 years, until just about the centenary of Mendel's work. Since then the Mendel-Fisher controversy has simmered quietly, and sometimes not so quietly, for more than 40 years. It is still ongoing with both attacks on, and defenses of, both Mendel and Fisher.

It is our contention that this controversy should end. The purpose of this book is to present the reader with good reasons for that conclusion. The book includes an overview of the controversy, the original papers of Mendel and Fisher, and four of the most important papers on the controversy (in the judgment of Allan Franklin, who suggested which papers should be included). The book also includes brief updates, by the authors, of the latter four papers. This is not to say that all questions have been answered, but rather that we believe that the most important ones that can be answered have been answered. Barring a miraculous rediscovery of Mendel's notebooks, which are said to have been burned, and which would certainly answer the question of fraud, there seems to be little more of value to be said.

More specifically, we conclude that: (1) Mendel was not guilty of fraud; (2) Fisher's conclusion, based on χ^2 analysis, that Mendel's data fit his expectations extraordinarily well is correct, but may be explained without invoking fraud; (3) Fisher's criticism of Mendel, that in the experiments on the second generation of plants bred from hybrids the ratio of heterozygous to homozygous offspring should not be 2 : 1 but rather 1.7 : 1, is incorrect; and, finally, that (4) Fisher had great admiration for Mendel and his work and that he would have been quite unhappy with those who used his work to diminish Mendel's achievements.

It should be emphasized that this is a collaborative work. Since its initial suggestion, we have each benefited from discussions and visits with one another, which have been of great value to all of us. This has not only improved the book, but has also led to a new paper on the controversy by Daniel Hartl and Daniel Fairbanks (2007). Our collaboration has been both enjoyable and rewarding.

The previously published papers that appear in this volume have been reproduced using their original spellings, styles, and reference systems. Stylistic consistency has been imposed only across the new material (the introduction, postscripts, and appendix).

One change has been made to the original articles: this book is intended to be self-contained, so that all page references to papers that are included in this volume refer to those versions contained in this book (even when alternate translations are cited), and these page numbers are noted in italics for ease of use.

Ending the Mendel-Fisher Controversy

CHAPTER 1

■ The Mendel-Fisher Controversy

An Overview

ALLAN FRANKLIN

Gregor Mendel (1822–1884) is regarded as the founder of modern genetics. His experiments on pea plants reported in 1865 established the principles of segregation and of independent assortment. The former states that variation for contrasting traits is associated with a pair of factors that segregate to individual reproductive cells. The latter states that two or more of these factor-pairs assort independently to individual reproductive cells. It is well known that Mendel's work was neglected until its "rediscovery" in 1900 by Hugo de Vries, Carl Erich Correns, and Erich von Tschermak. It is less well known, however, that in 1936, the great British statistician and biologist R. A. Fisher analyzed Mendel's data and found that the fit to Mendel's theoretical expectations was too good (Fisher 1936). Using χ^2 analysis, Fisher found that the probability of obtaining a fit as good as Mendel's was only 7 in 100,000. Fisher also argued that because Mendel used only a limited sample of 10 plants in his experiment to determine the ratio of heterozygous plants (*Aa*) to homozygous plants (*AA*) in the F_2 generation produced by the self-pollination of hybrids, there was a 5.63% chance of misidentifying heterozygous plants as being homozygous. Thus, the ratio should be approximately 1.7 to 1, rather than Mendel's expectation of 2 to 1, although Mendel's data agreed more closely with the 2 to 1 ratio. Fisher concluded: "This possibility is supported by independent evidence that the data of most, if not all, of the experiments have been falsified so as to agree closely with Mendel's expectations" (*134*).[1] Fisher did not believe that Mendel was responsible for the falsification, but attributed it to an unknown assistant.

Fisher's work was overlooked. The first published comments on it appeared in 1964, about the time of the centenary of Mendel's paper, and since then at least 50 papers, letters, and discussions have been published on the controversy as to whether Fisher adequately showed that Mendel's data were falsified. These publications include explanations of Mendel's results and both criticisms and defenses of Fisher.

This chapter will provide an overview of that controversy, including summaries of both Mendel's and Fisher's papers, along with a discussion of most of the papers on the debate. It is not, however, a substitute for reading the original works. Therefore, this book contains the work of both Mendel and Fisher as well as four of the most significant discussions of the controversy, and updates by those four authors. I believe that taken together, these voices argue for an end to the controversy.

Mendel's Experimental Results

Mendel began his experiments on garden peas (*Pisum sativum* L.) in 1856 and continued them until 1863, a period of approximately eight years. His stated purpose was to investigate whether there was a general law for the formation and development of hybrids, something he noted had not yet been formulated:

> Those who survey the work done in this department will arrive at the conviction that among all the numerous experiments made, not one has been carried out to such an extent and in such a way as to make it possible to determine the number of different forms under which the offspring of hybrids appear, or to arrange these forms with certainty according to their separate generations, or definitely to ascertain their statistical relations.
>
> It requires indeed some courage to undertake a labour of such far-reaching extent; this appears however, to be the only right way by which we can finally reach the solution of a question the importance of which cannot be overestimated in connection with the history of the evolution of organic forms. (*79*)[2]

Mendel proposed to remedy the situation and did so. As Fisher remarked, "Mendel's paper is, as has been frequently noted, a model in respect of the order and lucidity with which the successive relevant facts are presented" (Fisher 1936, *121*). I will follow Mendel's plan in describing his experiments and will allow Mendel to speak for himself as much as possible.

In order to carry out such experiments successfully, Mendel required: "The experimental plants must necessarily—1. Possess constant differentiating characters. 2. The hybrids of such plants must, during the flowering period, be protected from the influence of all foreign pollen, or be easily capable of such protection. The hybrids and their offspring should suffer no marked disturbance in their fertility in the successive generations" (79). He further noted: "In order to discover the relations in which the hybrid forms stand towards each other and also towards their progenitors it appears to be necessary that all members of the series developed in each successive generation should be, *without exception*, subjected to observation" (79–80).

[F_2] The First Generation [Bred] from the Hybrids

Mendel began with 34 varieties of peas, from which he selected 22 varieties for further experiments. He had confirmed, in two years of experimentation, that these varieties bred true. He reported experiments on seven characters that had two easily distinguishable characteristics. I have listed these below, with the dominant form first:[3]

1. Seed shape: round or wrinkled
2. Cotyledon color: yellow or green
3. Seed-coat color: colored (gray, gray-brown, or leather-brown) or white. Colored seed coats were always associated with violet flower color and reddish markings at the leaf axils. White seed coats were associated with white flowers.
4. Pod shape: inflated or constricted
5. Pod color: green or yellow
6. Flower position: axial (along the stem) or terminal (at the end of the stem)
7. Stem length: long (six to seven feet) or short (three-quarters of a foot to one and a half feet)

The first two are seed characters because they are observed in seed cotyledons, which consist of embryonic tissue. Each seed is thus a genetically different individual and such characters may differ among the seeds produced on a heterozygous plant. Both yellow and green seeds may be observed on a single heterozygous plant. One may, in fact, observe these characters for the next generation, without the necessity of planting the seeds. The latter five are plant characters. As William Bateson remarked, "It will be observed that the [last] five are *plant-characters*. In order to see the result of crossing, the seeds must be sown and allowed to grow into plants. The [first] two characters belong to the *seeds* themselves. The seeds of course are members of a generation later than that of the plant which bears them" (Bateson 1909, 12). Because of this, Mendel would have had a reasonable expectation of what the results of his plant character experiments would be from his observations of the seed characters, before the plants of the next generation were grown.

Mendel's first experiment was to breed a generation of hybrids from his true breeding plants for each of the seven characters. His results for this generation (F_1) clearly showed dominance. He remarked: "In the case of each of the seven crosses the hybrid-character resembles that of one of the parental forms so closely that the other either escapes observation completely or cannot be detected with certainty" (*84*).

He then allowed these monohybrids to self-fertilize. He found a 3 : 1 ratio for plants that showed the dominant character to those that possessed the recessive character in this generation (F_2).[4] He found that this ratio held for all the characters observed in the experiments and that "*Transitional forms were not observed in any experiment*" (*85*). His results are shown in table 1.1. He concluded, "If now the results of the whole of the experiments be brought together, there is found, as between the number of forms with the dominant character and recessive characters, an average ratio of 2.98 to 1, or 3 to 1" (*87*).

Mendel also noted that the distribution of characters varied in both individual plants and in individual pods. He illustrated this with data from the first ten plants in the seed character experiments (see table 1.2). The variation in both the ratios of the characters and in the number of seeds per plant is considerable. Mendel also presented the extreme variations.

TABLE 1.1 **Mendel's results for the F_2 generation of monohybrid experiments** (from data in Mendel 1865, *85–87*)

	Expected ratio 3 : 1				
Trait	*Dominant*	*Number*	*Recessive*	*Number*	*Ratio*
1. Seed shape	Round	5474	Angular	1850	2.96
2. Cotyledon color	Yellow	6022	Green	2001	3.01
3. Seed coat color	Colored	705	White	224	3.15
4. Pod shape	Inflated	882	Constricted	299	2.95
5. Pod color	Green	428	Yellow	152	2.82
6. Flower position	Axial	651	Terminal	207	3.14
7. Stem length	Long	787	Short	277	2.89
Total	Dominant	14,949	Recessive	5010	2.98

TABLE 1.2 Mendel's results for the first 10 plants in the experiments on seed shape and seed color (from data in Mendel 1865, *86*)

	Experiment 1: Shape of seeds		*Experiment 2: Coloration of albumen*	
Plant	*Round*	*Wrinkled*	*Yellow*	*Green*
1	45	12	25	11
2	27	8	32	7
3	24	7	14	5
4	19	10	70	27
5	32	11	24	13
6	26	6	20	6
7	88	24	32	13
8	22	10	44	9
9	28	6	50	14
10	25	7	44	18
Ratio	3.33 : 1		3.08 : 1	

Note: The fact that the number of seeds in each plant differs for each numbered plant shows clearly that the plants for Experiments 1 and 2 are different plants. Thus, plant 1 in Experiment 1 has 57 seeds, whereas plant 1 in Experiment 2 has 36 seeds.

"As extremes in the distribution of the two seed characters in one plant, there were observed in Expt. 1 an instance of 43 round and only 2 angular, and another of 14 round and 15 angular seeds. In Expt. 2 there was a case of 32 yellow and only 1 green seed, but also one of 20 yellow and 19 green" (*86*). Mendel was clearly willing to present data that deviated considerably from his expectations.[5]

Mendel also noted: "In well-developed pods which contained on the average six to nine seeds, it often happened that all the seeds were round (Expt. 1) or all yellow (Expt. 2); on the other hand, there were never observed more than 5 wrinkled or five green ones in one pod" (*86*).[6]

[F3] The Second Generation [Bred] from the Hybrids

At the end of the section describing the first-generation experiments, Mendel remarked that the dominant character could have a "*double signification.*" It could be either a pure parental (dominant) character or a hybrid character. "In which of the two significations it appears in each separate case can only be determined by the following generation. As a parental character it must pass over unchanged to the whole of the offspring; as a hybrid-character, on the other hand, it must maintain the same behaviour as in the first generation" (*87*).[7] He further noted that those plants that show the recessive character in the first generation (F_2) do not vary in the second generation (F_3).[8] They breed true. That was not the case for those plants showing the dominant character: "Of these *two*-thirds yield offspring which display the dominant and the recessive characters in the proportion of 3 to 1, and thereby show exactly the same ratio as the hybrid forms, while only *one*-third remains with the dominant character constant"(*88*). In other words, of those F_2 generation plants showing the dominant character, two-thirds were heterozygous (*Aa*), or hybrid, and one third homozygous (*AA*). For the seed characters Mendel reported the following results: (1) from 565 plants raised from round seeds, 372 produced both round and wrinkled seeds in the proportion of 3 to 1 whereas 193 yielded only round seeds, a ratio of 1.93 to 1; (2) for plants raised from yellow seeds, 353 yielded both yellow and green seeds in the proportion 3 to 1, whereas 166 yielded only yellow seeds, a ratio of 2.13 to 1.

The experiments on plant characters required more effort: "For each separate trial in the following experiments [on plant characters] 100 plants were selected which displayed the dominant character in the first generation [F_2], and in order to ascertain the significance of this, ten [F_3] seeds of each were cultivated" (*88*).[9] A plant was classified as homozygous if all of the 10 offspring had the dominant character and classified as heterozygous otherwise.[10] Mendel's results for the plant characteristics are shown in table 1.3. Mendel noted that the first two experiments on seed characters were of special importance because of the large number of plants that could be compared. Those experiments yielded a total of 725 hybrid plants and 359 dominant plants that "gave together almost exactly the average ratio of 2 to 1" (*89*). Experiment 6 also yielded almost the exact ratio expected, whereas for the other experiments, as Mendel noted, "the ratio varies more or less, as was only to be expected in view of the smaller number of 100 trial plants" (*89*). Mendel was, however concerned about Experiment 5 (the color of unripe pods), in which the result was 60 to 40. He regarded these numbers as deviating too much from the expected 2 to 1 ratio.[11] Mendel repeated the experiment and obtained a ratio of 65 to 35, and was satisfied: "*The average ratio of 2 to 1 appears, therefore, as fixed with certainty*" (*89*). It is clear that Mendel did not attempt to hide any of his results, especially those that deviated from his expectations, because he presented the results for both the original Experiment 5 as well as its repetition. The sum totals for the six plant characteristic experiments, in-

TABLE 1.3 Mendel's results for the heterozygous-homozygous experiment (the 2 to 1 experiment) (from data in Mendel 1865, *88*)

Experiment	*Dominant*	*Hybrid*
3. Seed coat color (grey-brown or white)	36	64
4. Pod shape (smooth or constricted)	29	71
5. Pod color (green or yellow)	40	60
6. Flower location (axillary or terminal)	33	67
7. Stem length (long or short)	28	72
8. Repetition of Experiment 5	35	65
Total	201	399
	Ratio (hybrid to dominant) 1.99	

cluding the repetition of Experiment 5, were 399 (hybrid) to 201 (dominant), or 1.99 to 1.

Mendel's conclusion was quite clear:

> The ratio of 3 to 1, in accordance with which the distribution of the dominant and recessive characters results in the first generation, resolves itself into a ratio of 2:1:1 if the dominant character be differentiated according to its significance as a hybrid-character or as a parental one. Since the members of the first generation [F_2] spring directly from the seed of the hybrids [F_1], *it is now clear that the 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.* (*89*)

The Subsequent Generations Bred from the Hybrids

Mendel suspected that the results he had obtained from the first and second generations produced from monohybrids were probably valid for all of the subsequent progeny. He continued the experiments on the two seed characters, shape and color, for six generations; the experiments on seed-coat color and stem length for five generations; and the remaining three experiments on pod shape, color of pods, and position of flowers for four generations, "and no departure from the rule has been perceptible. The offspring of the hybrids separated in each generation in the ratio of 2:1:1 into hybrids and constant forms [pure dominant and pure recessive]" (*89*). He did not, however, present his data for the experiments on the subsequent generations.[12] He went on to state, "If *A* be taken as denoting one of the two constant characters, for instance the dominant, *a*, the recessive, and *Aa* the hybrid form in which both are conjoined, the expression $A + 2Aa + a$ shows the terms in the series for the progeny of the hybrids of two differentiating characters" (*89*).[13]

The Offspring of Hybrids in which Several Differentiating Characters Are Associated

Mendel's next task, as he put it, was to investigate whether the laws he had found for monohybrid plants also "applied to each pair of differentiating characters when several diverse characters are united in the hybrid by crossing" (*90*).

He went on to describe the experiments. "Two experiments were made with a considerable number of plants. In the first experiment the parental plants differed in the form of the seed and in the colour of the albumen; in the second in the form of the seed, in the colour of the albumen, and in the colour of the seed-coats. Experiments with seed characters give the result in the simplest and most certain way" (*91*). He was no doubt referring to the greater number of seeds than plants, which provides data with greater statistical significance, and also to the fact that the shape of the seeds and the color of albumen (cotyledons) could be seen in the second generation, without the need to plant a third generation. Daniel Fairbanks and Bryce Rytting (2001) later remarked with reference to seed-coat color, which, as noted above, was correlated with the presence or absence of axillary pigmentation, could be scored in seedlings, and was also used as the third factor in the trifactorial experiment: "Because this trait can be scored in seedlings, it is an excellent choice for the third trait in the trihybrid experiment because it creates at most a three-week delay between data collection for the first two traits and the third. Garden space is not as critical because many seedlings can be grown in the space occupied by a single mature plant" (*276*).

In these experiments Mendel distinguished between the differing characters in the seed plant and the pollen plant. *A*, *B*, and *C* represented the dominant characters of the seed plant and *a, b,* and *c* the recessive characters of the pollen plant, with hybrids represented as *Aa*, *Bb*, and *Cc*.[14]

First Experiment (Bifactorial)

Mendel's first experiment used two seed characters in which the seed plant (*AB*) was *A* (round shape) and *B* (yellow cotyledon), and the pollen plant (*ab*) was *a* (wrinkled shape) and *b* (green albumen). The fertilized

TABLE 1.4 Mendel's results for the bifactorial experiment (from Mendel 1865, *91–92*)

	A (round)	*Aa (hybrid)*	*a (angular)*
B	*AB* (round, yellow): 38	*AaB* (round yellow and angular yellow): 60	*aB* (angular, yellow): 28
Bb	*ABb* (round yellow and green): 65	*AaBb* (round yellow and green and angular yellow and green): 138	*aBb* (angular yellow and green: green): 68
b	*Ab* (round green): 35	*Aab* (round and angular green): 67	*ab* (angular green): 30

seeds were all round and yellow, as expected. He then raised plants from these seeds and obtained 15 plants with 556 seeds distributed as follows:

315 round and yellow
101 wrinkled and yellow
108 round and green
32 wrinkled and green[15]

All of these seeds were planted in the following year and Mendel's results are shown in table 1.4.

Mendel separately recorded the results for each set of the 556 seeds (i.e., round and yellow, round and green, wrinkled and yellow, wrinkled and green).[16] He noted that there were nine different forms (we would say genotypes) and classified them this way:

> The whole of the forms may be classed into three essentially different groups. The first includes those with the signs *AB, Ab, aB, ab*: they possess only constant characters and do not vary again in the next generation. Each of these forms is represented on the average thirty-three times. The second group includes the signs *ABb*, *aBb*, *AaB*, *Aab*: these are constant in one character and hybrid in another, and vary in the next generation only as regards the hybrid-character. Each of these appears on an average sixty-five times. The form *AaBb* occurs 138 times: it is hybrid in both characters, and behaves exactly as do the hybrids from which it is derived.
>
> If the numbers in which the forms belonging to these classes appear to be compared, the ratios of 1, 2, 4 are unmistakably evident. The numbers 32, 65, 138 present very fair approximations to the ratio numbers of 33, 66, 132. (*92*)

Mendel had a very good feel for his data and an ability to see the underlying patterns in his results despite statistical fluctuations. Mendel concluded that these results "indisputably" showed that the results could be explained by the combination of $A + 2Aa + a$ and $B + 2Bb + b$ (i.e., $AB + 2AaB + aB + 2ABb + 4AaBb + 2aBb + Ab + 2Aab + ab$).

Second Experiment (Trifactorial)

In this experiment, Mendel investigated whether the results he had obtained in both the monohybrid and bifactorial experiments held for an experiment in which three different characters were examined, the trifactorial experiment. He remarked, "Among all the experiments it demanded the most time and trouble" (*93*). The characters investigated for the seed plant (*ABC*) were: *A* (round shape), *B* (yellow albumen), and *C* (gray-brown seed coat); and for pollen plant (*abc*): *a* (wrinkled seed), *b* (green albumen), and *c* (white seed coat). The first two were seed characters and could be observed immediately, whereas seed-coat color, a plant character, required plants from the next generation.[17] Mendel obtained 687 seeds from 24 hybrid plants, from which he successfully grew 639 plants and "as further investigations showed,"[18] he obtained the results depicted in table 1.5. He summarized his data as follows:

The whole expression contains 27 terms. Of these 8 are constant in all characters, and each appears on the average 10 times; 12 are constant in two characters, and hybrid in the third; each appears on the average 19 times; 6 are constant in one character and hybrid in the other two; each appears on the average 43 times. One form appears 78 times and is hybrid in all of the characters. The ratios 10, 19, 43, 78 agree so closely with the ratios 10, 20, 40, 80, or 1, 2, 4, 8, that this last undoubtedly represents the true value. (*94*)[19]

TABLE 1.5 **Mendel's results for the trifactorial experiment** (Mendel 1865, *93*)

8 plants		*ABC*	22 plants		*ABCc*	45 plants		*ABbCc*
14	"	*ABc*	17	"	*AbCc*	36	"	*aBbCc*
9	"	*AbC*	25	"	*aBCc*	38	"	*AaBCc*
11	"	*Abc*	20	"	*abCc*	40	"	*AabCc*
8	"	*aBC*	15	"	*ABbC*	49	"	*AaBbC*
10	"	*aBc*	18	"	*ABbc*	48	"	*AaBbc*
10	"	*abC*	19	"	*aBbC*			
7	"	*abc*	24	"	*aBbc*			
			14	"	*AaBC*	78	"	*AaBbCc*
			18	"	*AaBc*			
			20	"	*AabC*			
			16	"	*Aabc*			

Mendel went on to say that this series resulted from combining $A + 2Aa + a$, $B + 2Bb + b$, and $C + 2Cc + c$. He had a strong feeling about the expected results and was willing to accept conclusions despite limited statistics. As Fisher remarked, "He evidently felt no anxiety lest his counts should be regarded as insufficient to prove his theory" (*121*).

Mendel remarked that he had conducted several other experiments in which the remaining characters were combined in twos and threes and that these gave approximately equal results, but he presented none of his data for these experiments. He concluded:

> There is therefore no doubt that for the whole of the characters involved in the experiments the principle applies that *the offspring of 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.* It is demonstrated at the same time that *the relation of each pair of different characters in hybrid union is independent of the other differences in the two original parental stocks.* (*94*)

In Mendel's opinion, his results justified belief that the same behavior applied to characters that could not be so easily distinguished. He noted, however, the difficulty of such experiments: "An experiment with peduncles of different lengths gave on the whole a fairly satisfactory result, although the differentiation and serial arrangement of the forms could not be effected with that certainty which is indispensable for correct experiment" (*95*).

The Reproductive Cells of Hybrids

In his bifactorial and trifactorial experiments, Mendel used seed plants with the dominant characters and pollen plants with the recessive characters. The question remained whether his results would remain the same if those parental types were reversed. He stated that in hybrid plants, it was reasonable to assume that there were as many kinds of egg and pollen cells as there were possibilities for constant combination forms. He further noted that this assumption, combined with the idea that the different kinds of egg and pollen cells are produced on average in equal numbers, would explain all of his previous results.

Mendel proposed to investigate these issues explicitly in a series of experiments. He chose true breeding plants as follows: seed plant (*AB*); where *A* and *B* were round shape and yellow albumen, respectively; pollen plant *ab*, where *a* and *b* were wrinkled shape and green albumen, respectively. These were artificially fertilized and the hybrid *AaBb* obtained. Both the artificially fertilized seeds, together with several seeds from the two parental plants, were sown. He then performed the following fertilizations:

1. The hybrids with the pollen from *AB*
2. The hybrids with the pollen from *ab*
3. *AB* with pollen of the hybrid
4. *ab* with pollen of the hybrid

For each of these experiments, all of the flowers on three plants were fertilized. Mendel stated that if his assumptions were correct, then the hybrids would contain egg and pollen cells of the form *AB*, *Ab*, *aB*, and *ab*. When combined with the egg and pollen cells from the parental plants *AB* and *ab,* the following patterns emerge.

1. *AB*, *ABb*, *AaB*, *AaBb*
2. *AaBb*, *Aab*, *aBb*, *ab*
3. *AB*, *ABb*, *AaB*, *AaBb*
4. *AaBb*, *Aab*, *aBb*, *ab*

These genotypes should occur with equal frequency in each experiment. Experiments 1 and 3, as well as experiments 2 and 4, would demonstrate that the results are independent of which parent is used for pollen and which is used for seed. Mendel also noted that there would be statistical fluctuations in his data.

> If, furthermore, the several forms of the egg and pollen cells of the hybrids were produced on an average in equal numbers, then in each experiment the said four combinations should stand in the same ratio to each other. A perfect agreement in the numerical relations was, however, not to be expected, since in each fertilisation, even in normal cases, some egg cells remain undeveloped or subsequently die, and many even of the well-formed seeds fail to germinate when sown. The above assumption is also limited in so far that, while it demands the formation of an equal number of the various sorts of egg and pollen cells, it does not require that this should apply to each separate hybrid with mathematical exactness. (*97*)

Mendel predicted that in Experiments 1 and 3 all of the seeds produced would be round and yellow, the result of dominance. For Experiments 2 and 4, his expectations were that round yellow seeds, round green seeds, wrinkled yellow seeds, and wrinkled green seeds would be produced in equal proportions. He reported: "The crop fulfilled these expectations perfectly" (*98*). Experiments 1 and 3 produced 98 and 94 exclusively round and yellow seeds, respectively. Experiment 2 produced 31 round yellow seeds, 26 round green seeds, 27 wrinkled yellow seeds, and 26 wrinkled green seeds. Experiment 4 produced 24 round yellow seeds, 25 round green seeds, 22 wrinkled yellow seeds, and 27 wrinkled green seeds. Mendel noted: "There could scarcely be now any doubt of the success of the experiment; the next generation must afford the final proof" (98).

Mendel sowed all of the seeds obtained in the first experiment, and 90 plants from 98 seeds bore fruit. In the third experiment, 87 plants from 94 seeds bore fruit.[20] Mendel reported on his other results:

> In the second and fourth experiments the round and yellow seeds yielded plants with round and wrinkled yellow and green seeds, *AaBb*.
>
> From the round green seeds plants resulted with round and wrinkled green seeds, *Aab*.
>
> The wrinkled yellow seeds gave plants with wrinkled yellow and green seeds, *aBb*.
>
> From the wrinkled green seeds plants were raised which yielded again only wrinkled green seeds, *ab*. (98)

Mendel's results are also shown in tables 1.6 and 1.7. He concluded, "In all the experiments, therefore, there appeared all the forms which the proposed theory demands, and they came in nearly equal numbers" (99).

TABLE 1.6 **Mendel's results from the gametic experiments 1 and 3** (Mendel 1865, *98*)

1st Exp.	*3rd Exp.*		
20	25	round yellow seeds	*AB*
23	19	round yellow and green seeds	*ABb*
25	22	round and wrinkled yellow seeds	*AaB*
22	21	round and wrinkled yellow and green seeds	*AaBb*

TABLE 1.7 **Mendel's results from the gametic experiments 2 and 4** (Mendel 1865, *99*)

2nd Exp.	*4th Exp.*			
31	24	plants of the form		*AaBb*
26	25	"	"	*AaB*
27	22	"	"	*aBb*
26	27	"	"	*ab*

TABLE 1.8 Mendel's results for the flower color-stem length experiments (Mendel 1865, *100*)

Class	*Color of flower*	*Stem*	
1 [*AaBb*]	violet-red	long	47 times
2 [*aBb*]	white	long	40 "
3 [*Aab*]	violet-red	short	38 "
4 [*Ab*]	white	short	41 "

TABLE 1.9 Mendel's subsequent results for the flower color-stem length experiments (from Mendel 1865, *100*)

Trait	*Number*
violet-red flower color (*Aa*)	85 plants
white flower color (*a*)	81 plants
long stem (*Bb*)	87 plants
short stem (*b*)	79 plants

Mendel conducted a second set of experiments to test his assumptions. For these trials, he made selections so that each character should occur in half the plants if his assumptions were correct. In these experiments, *A* conferred violet-red flowers, *a* conferred white flowers, *B* long stems, and *b* short stems. He fertilized *Ab* (violet-red flowers, short stem) with *ab* (white flowers, short stem) producing hybrid *Aab*. In addition, *aB* (white flowers, long stem) was also fertilized with *ab*, yielding hybrid *aBb*. In the second year, the hybrid *Aab* was used as the seed plant and hybrid *aBb* as pollen plant. This should produce the combinations *AaBb*, *aBb*, *Aab*, and *ab*. In the third year, half the plants would have *Aa* (violet-red flowers), half *a* (white flowers), half *Bb* (long stems), and half *b* (short stems). The results are shown in tables 1.8 and 1.9. Mendel modestly concluded, "The theory adduced is therefore satisfactorily confirmed in this experiment also" (*100*). Mendel also performed other experiments, with fewer plants, on pod shape, pod color, and flower position, and "results obtained in perfect agreement" (*100*). No numerical data were presented.

As a result of this research, Mendel deduced, "Experimentally, therefore, the theory is confirmed that *the pea hybrids form egg and pollen cells which, in their constitution, represent in equal numbers all constant forms which result from the combination of characters united in fertilisation*" (*100*). He also stated, "It was furthermore shown by the whole of the experiments that it is perfectly immaterial whether the dominant character belong to the seed-bearer or to the pollen-parent; the form of the hybrid remains identical in both cases" (*84*).[21]

In discussing his results, Mendel demonstrated that he understood, at least qualitatively, the statistical nature of his data. He stated:

> This represents the average results of the self-fertilisation of the hybrids when two differentiating characters are united in them. In individual flowers and in individual plants, however, the ratios in which the forms of the series are produced

may suffer not inconsiderable fluctuations. Apart from the fact that the numbers in which both sorts of egg cells occur in the seed vessels can only be regarded as equal on the average, it remains purely a matter of chance which of the two sorts of pollen may fertilise each separate egg cell. For this reason the separate values must necessarily be subject to fluctuations, and there are even extreme cases possible, as were described earlier in connection with the experiments on the form of the seed and the colour of the albumen. The true ratios of the numbers can only be ascertained by an average deduced from the sum of as many single values as possible; the greater the number the more are merely chance effects eliminated. (*102*)

All of Mendel's numerical data from his pea experiments have now been presented, and these are the data on which Fisher based his analysis.

Mendel's Experiments on Other Species

Mendel also reported several experiments on *Phaseolus* (beans). The experiments on *Phaseolus vulgaris* and *Phaseolus nanus* "gave results in perfect agreement" (*103*). Those with *Phaseolus nanus,* L., as the seed plant, and *Phaseolus multiflorus*, W., as the pollen plant, did not. The former had white flowers and small white seeds, whereas the latter had purple-red flowers and seeds with black flecks or splashes on a peach-blood-red background. Mendel reported that the hybrids more closely resembled the pollen plant. He obtained only a few plants but, within limited statistics, he found that for recessive plant characters such as axis length and the form of the pod were the ratio of recessive to dominant was 1:3.

Mendel summarized his work as follows.

Despite the many disturbing factors with which the observations had to contend, it is nevertheless seen by this experiment that the development of the hybrids, with regard to those characters which concern the form of the plants, follows the same laws as in *Pisum*. With regard to the colour characters, it certainly appears difficult to perceive a substantial agreement. Apart from the fact that from the union of a white and a purple-red colouring a whole series of colours results [in F_2], from purple to pale violet and white, the circumstance is a striking one that among thirty-one flowering plants only one received the recessive character of the white colour, while in *Pisum* this occurs on the average in every fourth plant. (*105*)

Thus, Mendel not only reported blending inheritance, but also results that disagreed with his previous experiments.

Mendel also conducted experiments on *Hieracium* (hawkweed) (Mendel 1870). Again, the results did not always agree with those he had obtained previously. He remarked on the difficulty of the experiments and that he had obtained very few hybrids.

If finally we compare the described results, still very uncertain, with those obtained by crosses made between forms of *Pisum*, which I had the honor of communicating in the year 1865, we find a very real distinction. In *Pisum* the hybrids, obtained from the immediate crossing of two forms, all have the same type, but their posterity, on the contrary, are variable and follow a definite law in their variations. In *Hieracium* according to the present experiment the exactly opposite phenomenon seems to be exhibited. (qtd. in Stern and Sherwood 1966, 55)[22]

Summary

There are several points worth noting about Mendel's paper that will be important in the discussion of the Mendel-Fisher controversy. The first is that, as he remarks on several occasions, Mendel did not publish all of his data. The published data, however, also include results that differ considerably from Mendel's expectations. Mendel also knew what results he expected, either from theory or from his early observations. It also seems clear that Mendel had a good understanding of the principles of segregation and of independent assortment that form the basis of modern genetics.

Fisher's Analysis of Mendel's Data

Fisher's Early Thoughts

Although it was not until 1936 that R. A. Fisher published the paper on Mendel that would engender the longstanding controversy, that paper was not his first comment on Mendel's results. In a 1911 talk given to the Cambridge University Eugenics Society, Fisher commented, "It is interesting that Mendel's original results all fall within the limits of probable error;[23] if his experiments were repeated the odds against getting such good results is about 16 to one. It may just have been luck; or it may be that the worthy German abbot, in his ignorance of probable error, unconsciously placed doubtful plants on the side which favoured his hypothesis" (qtd. in Norton and Pearson 1976, 160). Fisher later changed his mind and attributed these results to the work of an assistant.

Fisher, in all probability, based these early comments on the analysis of Mendel's results provided by W. F. R. Weldon (1902). Weldon thought Mendel's work quite interesting and, in a letter to Karl Pearson, wrote, "About pleasanter things I have heard of and read a paper by one, Mendel, on the results of crossing peas, which I think you would like to read" (qtd. in Froggatt and Nevin 1971, 13). In his comments on Mendel, Weldon discussed Mendel's results on the 3 : 1 ratio in the first generation bred from hybrids. He presented Mendel's data along with the deviation of obser-

TABLE 1.10 Individuals with dominant characters in the second hybrid generation (Weldon 1902, 233)

Characters crossed	*Individuals of second hybrid generation*	*Number of dominant individuals*	*Dominant individuals on Mendel's theory*	*Probable error of theory*	*Deviation of observation from theory*
1. (Shape of seeds)	7324	5474	5493	±24.995	−19
2. (Color of cotyledons)	8023	6022	6017.25	±26.160	+4.75
3. (Color of seed coats)	929	705	696.75	±8.902	+8.25
4. (Shape of pod)	1181	882	885.75	±10.037	−3.75
5. Color of pod)	580	428	435	±7.034	−7
6. (Distribution of flowers)	858	651	643.5	±8.555	+7.5
7. (Height of plant)	1064	787	798	±9.527	−11

vation from theory along with a calculation of the probable error (table 1.10). He remarked:

Here are seven determinations of a frequency which is said to obey the law of Chance. Only one determination has a deviation from the hypothetical frequency greater than the probable error of the determination, and one has a deviation sensibly equal to the probable error; so that a discrepancy between the hypothesis and the observations which is greater to or equal to the probable error occurs twice out of seven times, and deviations much greater than the probable error do not occur at all. These results then accord so remarkably with Mendel's summary that if they were repeated a second time, under similar conditions and on a similar scale, the chance that the agreement between observation and hypothesis would be worse than that actually obtained is about 16 to 1. (Weldon 1902, 233)

Weldon also commented on Mendel's experiments on the 2 : 1 ratio and noted, "Mendel's statement is admirably in accord with his experiment" (Weldon 1902, 234). He then went on to discuss the results of the trifactorial experiment and commented, "Applying the method of Pearson (No. 25)[24] [χ^2 analysis] the chance that a system will exhibit deviations as great or greater than these from the result indicated by Mendel's hypothesis is about 0.95, or if the experiment were repeated a hundred times, we should expect to get a worse result about 95 times, or odds against a result as good as this or better are 20 to 1" (235). This was one of the early uses, perhaps even the first use, of the χ^2 test.

Weldon did not comment further in his paper on the goodness of fit of Mendel's data to his expectations, nor did he give even the slightest hint that he believed that Mendel's results were fraudulent in any way.[25] In a letter to Karl Pearson of November 1901, however, Weldon wrote: "Remembering his shaven crown [an allusion to Mendel's status as a monk] I cannot help wondering if they [Mendel's results] were not too good" (qtd. in Magnello 2004, 23). This line was crossed out and followed by the statement, "I do not see that the results are so good as to be suspicious." This was, in all probability, the first suggestion that Mendel's data were "too good." When Weldon wrote again to Pearson on 28 November 1901, he stated that he was certain that Mendel "cooked his figures, but that he was *substantially* right" (qtd. in Magnello 2004, 23).

In his 1902 paper, Weldon did comment further on both the value of Mendel's work and on some difficulties with Mendel's conclusions:

> Mendel's experiments are based upon work extending over eight years. The remarkable results obtained are well worth even the great amount of labour they must have cost, and the question at once arises, how far the laws deduced from them are of general application. It is almost a matter of common knowledge that they do not hold for all characters, even in Peas, and Mendel does not suggest that they do. At the same time I see no escape from the conclusion that they do not hold universally for the characters of Peas which Mendel so carefully describes. In trying to summarise the evidence on which my opinion rests, I have no wish to belittle the importance of Mendel's achievement. I wish simply to call attention to a series of facts which seem to suggest fruitful lines of inquiry. (Weldon 1902, 235)

The rest of Weldon's paper is devoted to a discussion of some of the evidence for his reservations about Mendel's work.[26]

Fisher's Seminal Paper

In 1936, R. A. Fisher published a paper entitled "Has Mendel's Work Been Rediscovered?" (*117*). This is the paper that engendered, albeit after a considerable delay, the so-called Mendel-Fisher controversy. Fisher did not question whether people knew of Mendel's work, but rather whether they really understood what Mendel had written. He noted that the story of Mendel's work and its rediscovery had become traditional in the teaching of biology: "A careful scrutiny can but strengthen the truth in such a tradition, and may serve to free it from such accretions as prejudice or hasty judgment may have woven into the story" (*117*). Fisher proposed to provide such a careful scrutiny and remarked, "When the History of Science is taken seriously the number of enquiries which such a story suggests is somewhat formidable. We want to know first: What did Mendel discover? How did he discover it? And what did he think he discovered? Next, what was the relevance of his discoveries to the science of his time, and what was its reaction to them?" (*118*).

Fisher was concerned that misconceptions about Mendel's work had been propagated by Bateson, particularly claims that Darwinism was responsible for the neglect of Mendel's work and that Mendel was hostile to Darwinism. Fisher presented persuasive arguments against both these views. He was also concerned about Bateson's assertion that Mendel's description of his experiments should not be taken literally. Bateson, in commenting on the monohybrid experiments, stated: "This statement of Mendel's in the light of present knowledge is open to some misconception. Though his work makes evident that such varieties may exist, 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 (*wesentliches Merkmal*). The point is probably of little theoretical or *practical consequence, but a rather heavy stress is thrown on 'wesentlich'*" (Bateson 1909, 332).[27] Fisher proposed two possible solutions to this problem. Mendel might have arbitrarily chosen one factor for which the particular cross was designated as an experiment and ignored other factors; or he might have scored each plant in all factors and assembled the data for that factor from all of the crosses in which it had been involved and reported the result as a single experiment on a single factor. Fisher noted that the first solution seemed incredibly wasteful of data, but added, "This objection is not so strong as it might seem, since it can be shown that Mendel left uncounted, or at least unpublished, far more material than appears in his paper" (*121*). Fisher believed that the second option was what most modern geneticists would do, but thought it unlikely that Mendel had done so: "[T]he style throughout suggests that he [Mendel] expects to be taken literally; if his facts have suffered much manipulation the style of his report must be judged disingenuous. Consequently, unless real contradictions are encountered in reconstructing his experiments from his paper, regarded as a literal account, this view must be preferred to all alternatives, even though it implies that Mendel had a good understanding of the factorial system, and the frequency ratios which constitute his laws of inheritance, before he carried out the experiments reported in his first and chief paper" (*122*).

Fisher's Reconstruction of Mendel's Data

As far as the subsequent controversy is concerned, the most important section of Fisher's paper is the one entitled "An Attempted Reconstruction." Fisher constructed a chronology of the eight years of Mendel's experiments, including which experiments were done and how many plants were grown in a given year, what Mendel's results were, and in what order those results were obtained.

Fisher inferred that the experiments on seed characters (yellow or green and round or wrinkled) were completed in 1859 and that "Mendel does not test the significance of the deviation, but states the ratios as 2.96 : 1 and 3.01 : 1, without giving any probable error" (*123*). He went on to remark, "The discovery, or demonstration, whichever it may have been, of the 3 : 1 ratio was evidently the critical point in Mendel's researches" (*124*). Fisher believed that Mendel's satisfaction with these approximate ratios was intelligible if "he had convinced himself as to their explanation, and framed the entire Mendelian theory of genetic factors and gametic segregation" (*124*). He further noted:

> In 1930,[28] as a result of a study of the development of Darwin's ideas, I pointed out that the modern genetical system, apart from such special features as dominance and linkages, could have been inferred by any abstract thinker in the middle of the nineteenth century if he were led to postulate that inheritance was particulate, that the germinal material was structural, and that the contributions of the two parents were equivalent. I had at that time no suspicion that Mendel had arrived at his discovery in this way. From an examination of Mendel's work it now appears not improbable that he did so and that his ready assumption of the equivalence of the gametes was a potent factor in leading him to his theory. *In this way his experimental programme becomes intelligible as a carefully planned demonstration of his conclusions.* (*125*, emphasis added)

In other words, Fisher believed that Mendel was, in fact, a Mendelian.[29]

Fisher went on to discuss Mendel's experiments of 1860 in which the 3 : 1 ratio was shown to be 1 : 2 : 1, where 1 is the homozygous dominants or recessives and 2 is the heterozygous hybrid. On several occasions, Fisher commented on the comparison of the observed deviations from the expected results to the standard deviation expected. Thus, in discussing the experiments on plants raised from yellow seeds (which yielded 166 plants with only yellow seeds and 353 plants with both yellow and green seeds) and that on plants grown from round seeds (which yielded 193 plants with only round seeds and 372 plants with both round and wrinkled seeds), Fisher stated: "The ratios in both cases show deviations from the expected 2 : 1 ratio less than their standard errors" (*126*). For the 1861 experiments on plants bred from colored flowers and from tall plants (see table 1.3), Fisher commented, "In neither case does the ratio depart significantly from the 2 : 1 ratio expected, although in the second case the deviation does exceed the standard deviation of random sampling" (*126*). For the experiment on yellow pods (which yielded a 60 : 40 ratio), Fisher remarked on "a relatively large, but not a significant, deviation" (*127*). He further noted, "It is remarkable as the only case in the record in which Mendel was moved to verify a ratio by repeating the trial" (*127*).

TABLE 1.11 Classification of plants grown in the trifactorial experiment (Fisher 1936, table II)

	CC				*Cc*				*cc*				*Total*			
	AA	*Aa*	*aa*	Total	*AA*	*Aa*	*aa*	Total	*AA*	*Aa*	*aa*	Total	*AA*	*Aa*	*aa*	Total
BB	8	14	8	30	22	38	25	85	14	18	10	42	44	70	43	157
Bb	15	49	19	83	45	78	36	159	18	48	24	90	78	175	79	332
bb	9	20	10	39	17	40	20	77	11	16	7	34	37	76	37	150
Total	32	83	37	152	84	156	81	321	43	82	41	166	159	321	159	639

Fisher, obviously concerned, went on to critically examine the experiments in which such deviations occurred. It was at this point that he first announced the problem of the 2:1 ratio:

In connection with these tests of homozygosity by examining ten offspring formed by self-fertilization, it is disconcerting to find that the proportion of plants misclassified by this test is not inappreciable. If each offspring has an independent probability, .75, of displaying the dominant character, the probability that all ten will do so is $(.75)^{10}$ or .0563. Consequently, between 5 and 6 per cent of the heterozygous parents will be classified as homozygotes, and the expected ratio of segregating to non-segregating families is not 2:1 but 1.8874:1.1126 or approximately 377.5:222.5 out of 600. Now among the 600 plants tested by Mendel 201 were classified as homozygous and 399 as heterozygous [see table 1.3]. Although these numbers agree extremely closely with his expectations of 200:400, yet, when allowance is made for the limited size of the test progenies, the deviation is one to be taken seriously. It seems extremely improbable that Mendel made any such allowance, or that the numbers he recorded are "corrected" values, rounded off to the nearest integer, obtained by dividing the numbers observed to segregate by .9437. We might suppose that sampling errors in this case caused a deviation in the right direction, and of almost exactly the right magnitude, to compensate for the error in theory. A deviation as fortunate as Mendel's is to be expected once in twenty-nine trials. Unfortunately the same thing occurs again with the trifactorial data [table 1.11] (*127*).

Fisher's further examination of those trifactorial data yielded detailed comments that are also worth examining.

In the case of the 600 plants tested for homozygosity in the first group of experiments Mendel states his practice to have been to sow ten seeds from each self-fertilized [F_2] plant. In the case of the 473 plants with coloured flowers from the trifactorial cross he does not restate his procedure. It was presumably the same as before. As before, however, it leads to the difficulty that between 5 and 6 per cent of heterozygous plants so tested would give only coloured progeny, so that the expected ratio of those showing segregation to those not showing it is really

TABLE 1.12 Comparison of numbers reported with uncorrected and corrected expectations (Fisher 1936, table III)

	Number of plants tested	Number of non-segregating progenies observed	Number expected		Deviation	
			Without correction	Corrected	Without correction	Corrected
1st group of experiments	600	201	200.0	222.5	+1.0	−21.5
Trifactorial experiment	473	152	157.7	175.4	−5.7	−23.4
Total	1073	353	357.7	397.9	−4.7	−44.9

lower than 2:1, while Mendel's reported observations agree with the uncorrected theory.

The comparisons are shown in Table III [table 1.12]. A total deviation of the magnitude observed, and in the right direction, is only to be expected once in 444 trials; there is therefore here a serious discrepancy. (*130*)

The reliability of Mendel's results had been called into question.

Fisher then offered several possible solutions to the 2:1 ratio problem. He pointed out that if Mendel had backcrossed the 473 trifactorial plants, the probability of misclassification of heterozygotes would be reduced by a factor of 50. (This would have involved a considerable amount of labor.) If, for example, the plants were backcrossed with a recessive plant, then the probability of observing the recessive character in a single plant would be 0.5 for a heterozygote. For 10 plants, the probability of misclassification is then (0.5),^{10} or 0.00098.

A second possibility was that Mendel had used a larger number of progeny in his test, say 15 instead of 10. The probability of misclassification, in this case, is reduced to 0.013, which gives a ratio of 1.974:1.026 = 1.924, much closer to 2. Fisher noted, however, that this would have required a larger number of plants grown in a single year than Mendel had, in fact, ever planted. In addition, it would not apply to the earlier experiments, in which Mendel had explicitly stated that he used 10 progeny.

The third possibility was that the selection of plants for testing favored the heterozygotes. Fisher remarked that in some crosses, it was possible that the heterozygote plants were larger and that "the larger plants might have been unconsciously preferred" (*131*). Fisher presented three arguments against this possible solution: (1) in the trifactorial experiment all plants were counted; (2) it was improbable that the compensating selection would work equally well for all five plant characters; and (3) the total compensation for all plants was unlikely to have given the exact number needed.