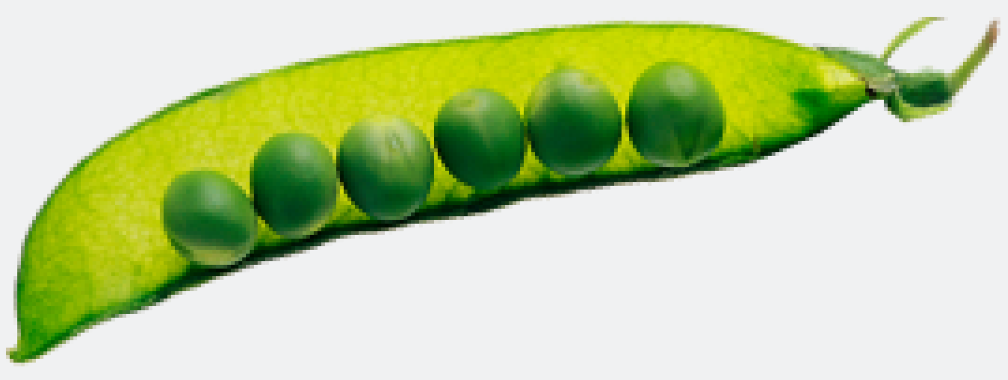
SCIENCE —

How Mendel started genetics by getting it mostly wrong

A good scientific law, like the speed limit imposed by light, may solve an ...

JOHN TIMMER - 4/26/2010, 9:17 AM



Pity Gregor Mendel. Far enough ahead of his peers that his work wasn't appreciated in his own lifetime. When the world was finally ready to deal with his results, the scientific community almost instantly went to work demonstrating that Mendel's Laws were wrong—or at least applied to such a narrow subset of inheritance that it was nearly impossible to generalize them. Yet, despite all these problems, most of the phenomena associated with inheritance, including the majority of exceptions to his eponymous Laws, continue to be termed Mendelian inheritance.

Why does the scientific world celebrate Mendel's achievement despite the fact that his work languished and then was quickly left in the dust? If we look at the history of his ideas (as we're about to do here), one key factor seems to be the fact that other researchers quickly linked his laws to the underlying biology. But perhaps more significantly,we'll see that, even if his laws were wrong, they provided some testable predictions that helped organize an otherwise mystifying field. It's OK to be wrong in science, as long as you're wrong in ways that lead to fruitful research.

Gregor Mendel

In a recent trip through the history of science, Chris Lee pointed out that Einstein used recently developed math to deal with problems that had been annoying scientists for decades, if not centuries. The law that resulted, in the sense that "nothing moves faster than light" can be considered a law, was little more than a happy side effect of tying together things like electromagnetism, the nature of light, and the structure of the universe.

Mendel's work was nothing like that. The people who thought about inheritance had found it pretty vexing, but not a lot of people thought about it, and the field was such a black box that there weren't even the equivalent of outstanding issues to neatly package together, as Einstein did. At the time that Mendel set to work, the only other scientific field that might immediately benefit from an understanding of inheritance—evolutionary biology—was still largely trapped in Darwin's brain, kept there by his general dislike of making waves.

Mendel's insights vs. Mendel's Laws

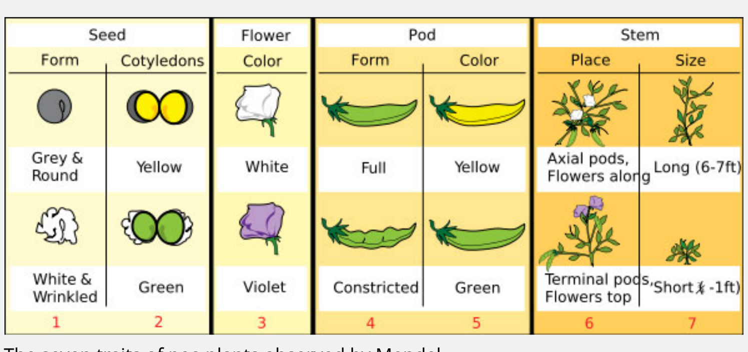
The claim that science is either physics or stamp collecting may be hyperbole, but, in a lot of ways, pre-Mendelian biology was a lot closer to stamp collecting than physics. The only thing that merited the status of theory—cell theory—was descriptive, not quantitative, and a lot of biology simply involved cataloging species. The Linnaean classification system provided this process with some structure, but the implication of this system—a branching tree of life—wasn't fully grasped or accepted, and no mechanism for producing one had withstood any scrutiny.

Mendel wasn't a stamp collector. He spent two years developing true-breeding plant lines, and learned how to control the fertilization of seeds in the process. He developed a precise scoring system for a variety of traits, and then set about breeding and analyzing tens of thousands of offspring.

By grouping the offspring together based on their appearances—their phenotypes—Mendel was able to begin to recognize patterns in the appearance of traits. In some types of crosses, two traits would appear in roughly equal numbers; in others, the ratio would be closer to 3:1. Eventually, he realized that these patterns could be created through the inheritance of pairs of genetic factors, which we now call genes.

The statistical power of these numbers (along, perhaps, with some observational bias) was absolutely necessary for recognizing some of the ratios that helped him formulate his ideas. With smaller numbers of offspring, random chance would probably have obscured the ratios that Mendel recognized. His achievement in recognizing them is all the more remarkable in that the statistical test we now use to identify results produced by chance wasn't developed by Fisher until over 50 years after Mendel did his work.

The other key insight was that units of inheritance are discrete and they remain discrete across generations. So, a tendency to yellow pea pods wouldn't be diluted or blend (as many biologists, including Darwin, suspected), even if it were to remain hidden for years in plants that produced green ones. Because of dominant traits, what we saw with our eyes when looking at a plant might only be a partial indication of the full genetic legacy they carried—looks not only could be deceiving, they often were.



The seven traits of pea plants observed by Mendel

Image source: Wikimedia Commons

Really, it's no surprise that Mendel's work wasn't widely recognized; biologists of the time probably didn't know what to make of it.

Mendel attempted to generalize his findings into laws, which governed inheritance of genes in organisms that have two copies of them. Germ cells obey the law of segregation, in that they only carry one of the two possible copies of the gene, and the genes follow the law of independent assortment, which suggested that individual genes would end up in those germ cells through an essentially random process.

Breaking the law

With his laws in hand, Mendel turned to other plants in an attempt to see just how general they were. One of them obeyed the law; the other cross turned into a technical nightmare of low fertility and phenotypes that didn't fall into a neat dominant/recessive pattern. So even Mendel realized that his ideas were not likely to be complete.

In a world where biologists weren't really experimentalists and most thought there had to be some sort of blended inheritance, not even the successful experiments went over well. Mendel ended up being promoted to abbot two years after his publication, effectively ending his scientific career.

In the intervening 35 years, anyone who attempted to take the same sort of experimental, big-numbers approach to inheritance would have been lucky to find a species and set of genes that obeyed Mendel's laws, for all the reasons we're about to go into. Even as experimental biology became more common, the conceptual leap that Mendel made remained a significant barrier; one of the three people once credited with rediscovering Mendel's ideas has since been removed from that list by science historians, who have become convinced that he didn't actually understand what he was doing.

Nevertheless, people eventually saw the sorts of patterns identified by Mendel, and quickly recognized he had beaten them there. But, with his laws being examined by the scientific community, it took less than a decade for researchers to start to identify some serious limitations to the patterns of inheritance seen by Mendel. Some of these will be familiar to anyone with a high school biology education: incomplete dominance, environmental influences, and so forth. But the basic insight Mendel had—that genes were more or less invariant across generations, even if the traits they promoted would sometimes be impossible to detect—could be used to explain all of these exceptions.

His experimental approach also turned out to be key in understanding a different phenomenon, which we now call linkage. Before the decade of rediscovery was gone, researchers had found that, in many cases, there were large deviations from Mendel's law of independent assortment. For some pairs of genes, the specific versions (called alleles) inherited from a parent tended to continue to be inherited together; once separated, they tended to remain separate.

Thomas Hunt Morgan, working with the fruit fly, used Mendel's approach of controlled matings and massive number of offspring to characterize linkage. He show that patterns of linkage were consistent and the frequency of reassortment was more or less additive, allowing the locations of genes to be mapped. Eventually, this enabled him to demonstrate that the linkage seen through genetic crosses had a direct relationship with the order of genes on a chromosome.

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