Heritable change in animals

If it chance that an egg cell unites with a pollen cell, we must then assume that when the fertilizing cells are developed, they reach a compromise for the life of the plant, but then, during gametogenesis, they go their separate ways, unchanged.

To describe this incredibly simple idea as influential would be akin to calling Michael Jordan a "pretty good shooting guard."

Sadly, this idea sat on the bench for the entire 1865-1900 season. More on why that happened — shortly.

Charles Darwin (1859)
The Origin of Species by Means of Natural Selection

1. Living organisms multiply; resources are limited.
2. Organisms vary. Some variation affects survival and reproduction.
3. Like begets like.
4. Populations of organisms will evolve: those organisms with characteristics most favourable for survival and reproduction will not only have more offspring, but will pass their characteristics onto those offspring.

→ the characteristics seen in the population will change

The problem with step 2

"What was missing from Darwin's theory was a source for the variations on which natural selection acted. ... Darwin addressed the problem of heredity. He believed that small units, which he called germules, were produced by the cells, and them migrated through the body, and some of them would be retained in the ... gonads." EA Carlson, Mendel's Legacy

"The most unfortunate of the assumptions underlying Darwin's mechanism of evolution was that of blending heredity; i.e., that parental differences are merged in the offspring of bisexual reproduction so that variation is constantly being diminished. The basis for this assumption was the so-called intermediacy of hybrids which Koelreuter regarded as a law for all "true" hybrids." R. Olby Origins of Mendelism

Sergei Chetverikov (1926)
On certain aspects of the evolutionary process from the standpoint of modern genetics

"mutational load"

1. Trap 239 Drosophila melanogaster near Moscow.
2. Self their offspring (brother sister).
3. 32 recessive loci (=186 in humans).

"... A species, like a sponge, soaks up heterozygous mutations, while remaining phenotypically homozygous."

Archibald Garrod (1902)
Higher frequency of children with alkaptonuria (urine turns dark on standing and alkalinization) from consanguineous marriages.

Why?
"There is no reason to suppose that mere consanguinity of parents can originate such a condition as alkaptonuria in their offspring, and we must rather seek an explanation in some peculiarity of the parents, which may remain latent for generations..."

Ah!

“It has recently been pointed out by Bateson that the law of heredity discovered by Mendel offers a reasonable account of such phenomena. …”


A useful term

If a trait follows in its inheritance Mendel’s first law, that phenomenon is described as “simple Mendelian inheritance” (SMI). Examples: cystic fibrosis; sickle cell anemia; hemophilia A.

An awful, awful term: “monogenic trait”

If a trait follows SMI – what does that say about its genetic architecture?
A highly pernicious school of lack of thought in biological instruction uses the term “monogenic trait.” It is most unfortunate.
In what sense is blood clotting a “monogenic” trait?

In no sense at all.

What is “simple” is the genetic difference between an unaffected individual and an individual who has hemophilia. It can be as small as a single base pair change. In other words, what the phenotype tracking allows us to do is look at the genetics of the difference.

If a particular phenotype follows SMI, then all that says is: The difference in genotype between an organism with that phenotype and without it is due to a genetic difference at a single position in the genome (= “a single locus”). Nothing can be learned from this analysis about the number of genes that are required for that phenotype to develop, or about the role this particular gene plays in having this phenotype develop.

PKU, for example, has to do with the breakdown of aromatic amino acids, and its lack causes mental retardation. What is the specific role of phenylalanine breakdown in cognition?

Motherhood – a monogenic trait?!

A Defect in Nurturing in Mice Lacking the Immediate Early Gene fosB
Brown et al.

Manhood – a monogenic trait

Note: SRY directly causes the conversion of a female embryo to a male one

XY  XX+Sry transgene


Prof. Cline – lecture 25
In other words

"Mendelian inheritance" of traits (note: OF TRAITS) is largely the exception, not the rule in Nature.

Mendel made two titanic contributions to science:

1. From an epistemological perspective, he created a fundamentally novel, enormously powerful experimental paradigm, one that replaces all previous heuristic, trial-and-error-based efforts in this field with a methodical, hypothesis-driven, rigorous quantitation-based approach, in which one sets up controlled crosses, determines the number of phenotypic classes that results from those crosses, analyses their incidence in each generation separately, and determines the ratios of organisms that fall into each class. This – to the letter – remains the core of the ENTIRE genetic research paradigm to this day. It is astonishingly powerful, as you shall see.

2. From an ontological perspective, he discovered two of the three most important principles of the behavior of genes (the equal segregation into gametes of two alleles of a gene during gametogenesis; and the independent behavior that two distinct genes exhibit in this process). The third – linkage – was discovered in 1906 by Bateson and Punnett, and we will discuss it at great length on Friday. All autosomal genes obey Mendel's first law, and all unlinked genes obey Mendel's second law.

"What are the genes? What is the nature of the elements of heredity that Mendel postulated as purely theoretical units? … Frankly, these are questions with which the working geneticist has not much concern himself… If the gene is a material unit, it is a piece of a chromosome; if it is a fictitious unit, it must be referred to a definite location in a chromosome. … Therefore, it makes no difference in the actual work in genetics which point of view is taken."

T.H. Morgan

*The Relation of Genetics to Physiology and Medicine*

Nobel Lecture, June 4, 1934

"The offspring of hybrids in which several differing traits are associated"

"In the experiments above described plants were used which differed only on one essential character. The next task consisted in ascertaining whether the law of development discovered in these applied to each pair of differentiating characters when several diverse characters are united in the hybrid by crossing." \( \rightarrow \) dihybrid cross

"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 color of the albumen; in the second in the form of the seed, in the color of the albumen, and in the color of the seed coat. Experiments with seed characters give the result in the simplest and most certain way.

In order to facilitate study of the data in these experiments, the different characters of the seed plant will be indicated by A, B, C, those of the pollen plant by a, b, c, and the hybrid forms of the characters by Aa, Bb, andCc."
Ta-daaa! The second law

“There is therefore no doubt that for all of the traits involved in the experiments this statement is valid: 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 traits are combined. It is demonstrated at the same time that the relation of each pair of different traits in hybrid union is independent of the other differences in the two parental plants.”

Narrow-sense heritability (prof. Brem, lecture 31)

Additive vs. dominance vs. interaction genetic variance.

Why Mendel’s second law makes the first one of those so important.
Gasp #2

“Even the validity of the law formulated for *Pisum* requires still to be confirmed, and a repetition of the more important experiments is therefore desirable … In the meantime we may assume that no basic difference could exist in important matters, since unity in the developmental plant of organic life is beyond question.”

Gasp #2 continued

“Indessen dürfte man vermuthen, dass in wichtigen Puncten eine prinzipielle Verschiedenheit nicht vorkommen könne, da die Einheit im Entwicklungsplane des organischen Lebens ausser Frage steht.”

This statement brings and “prescient” to new shades of meaning. Mendel – a peasant’s son who failed to graduate from college, working alone in a monastery – says here that he believes to have discovered a general law of life, because he thinks that the same core principles underlie the functioning of all living beings.

Gregor Mendel to Carl Nägeli, Dec. 31, 1866

“Highly esteemed Sir:
The acknowledged preeminence your Honor enjoys in the detection and classification of wild-growing plant hybrids makes it my agreeable duty to submit for your kind consideration the description of some experiments in artificial fertilization.”

Gregor Mendel to Carl Nägeli, Dec. 31, 1866

“I am not surprised to hear your honor speak of my experiments with mistrustful caution. … I knew that the results I obtained were not easily compatible with our contemporary scientific knowledge, and that under the circumstances publication of one such isolated experiment was doubly dangerous; dangerous for the experimenter and for the cause he represented. Thus I made every effort to verify, with other plants, the results obtained with *Pisum*.”

Apomixis

“In botany, apomixis is asexual reproduction, without fertilization and modified meiosis. The modified meiosis yields seeds that are genetically identical to the one of the parental plants.”

In zoology, the cognate phenomenon is known as parthenogenesis.