Genetics – the narrative so far

1. Mendel (1853-66):
   1. Heredity operates via particles of information (=genes).
   2. For any trait, two particles (=alleles of a gene) come together in an organism, but then separate into gametes, one per gamete.
   3. This process occurs independently for particles (genes) for different traits.

2. Häckel, Weissmann, Flemming, Boveri (1850-1900):
   1. The nucleus of the cell is the organelle that is responsible for heredity (Häckel, Boveri), and specific kinds of cells (the gametes) that are separate and distinct from the rest of the body, are responsible for generating progeny (Weissman).
   2. Inside the cell, lie the chromosomes (Flemming) that separate into daughter cells via mitosis.
   3. Proper development of an organism requires a specific set of a particular kind of chromosome (Boveri).

3. Sutton (and Cannon) – 1902:
   1. There is a striking concordance between the behavior of Mendel's particles and chromosomes during meiosis.

Genetics – the narrative to come

1. Morgan and Bridges – genes lie on chromosomes (1910-1915).
2. Bateson and Sturtevant (1906-15) – some genes appear to be physically linked; the nature of this linkage is the following: genes are arranged on a chromosome in a linear order, at particular distances from each other.
3. McClintock and Stern (1930) – genetic recombination occurs when homologous chromosomes can exchange parts.
4. Beadle and Tatum (1945) – some genes affect the development of traits by encoding biochemical functions (“one gene = one enzyme”).
5. Muller (1927) – the gene can be purposefully mutated.
6. Benzer – the gene itself can be split into smaller units.
7. Studying the molecular makeup of life via:
   1. The genetic screen – use of purposeful mutagenesis to identify genes required for the development of various traits.
   2. Mapping by linkage and association mapping – the study of “simple” and “complex” traits by analysis of pedigrees and populations.

What is being omitted for lack of time

1. The rediscovery of Mendel’s laws by Correns, Tschermak, and de Vries.
2. The finding – by Cuenot and by Castle – that Mendel’s laws also apply to mammals, such as mice and guinea pigs.

William Bateson

“... he privately subsidized his small book, Mendel's Principles of Heredity: A Defence and he sent copies to all of the leading students of heredity to make sure that Mendel would not suffer another 35 years of neglect.”
Carlson Mendel's Legacy

Modified Mendelian ratios → epistasis

“Repulsion and coupling” → linkage
results into Mendelian terms. Such an exercise would show that the change which must now appear over the conceptions of biology can only be compared with that which in the study of physical science followed the revelations of modern chemistry.

The outcome of such a revision of current conceptions it is impossible to foresee, but we propose in the present paper to consider some of the more important questions which are immediately raised.

To denote the new conceptions some new terms are needed. Several have already been suggested by Correns, but in practice we have not found his terminology altogether convenient, or that it meets the new requirements. Correns proposes the terms "heterozygous" and "homozygous" to express that an organism is dominant or not dominant in respect of a given character. There are unfortunately objections to the use of these terms, though in some respects they are very suitable. First, they are in use by Weismann and his followers in quite different senses, as Correns states. Secondly, it is not clear whether they are to be applied to the variety, the individual, or the character. Besides these objections, it is fairly clear that dominance is a phenomenon presenting various degrees of intensity, and while the single phenomenon of dominance is well expressed by that word itself, other conditions probably cannot of various phenomena which are not consistently defined by one word.

Correns' terms "heterozygous" and "homozygous" cannot as yet be used with precision to mean more than breeding "true" and not breeding "true," and, for reasons given later, the metaphor of splitting may be incorrect.

Thomas Hunt Morgan, the first native-born American to win the Nobel Prize, founder of modern genetics.

"As will be shown now, certain factors follow the distribution of the X chromosome and are therefore supposed to be contained in them."

Emphasis mine – fdu.

\[ \alpha \text{λληλος} = \text{"each other"} \]
"The supposition that particles of chromatin, indistinguishable from each other and indeed almost homogeneous under any known test, can by their material nature confer all the properties of life surpasses the range of even the most convinced materialism."


A problem and a solution

“The value and utility of any experiment…”

(Mendel)

“What was needed to open up genetics to new phenomena was an organism that bred rapidly, produced lots of progeny, and was inexpensive to maintain” (Carlson)

“Fruit flies can be raised on a mixture of corn meal, yeast, sugar, and agar. Flies complete their life cycle from fertilization to emergence of the adult fly in 10 days. A female can produce 3,000 progeny in her lifetime. A single male can sire well over 10,000 offspring.” (Hartwell)

Morgan and Drosophila (go Bears)

Morgan was not a geneticist by training (he was an embryologist), and he was not the first one to use Drosophila for purposes of genetic research (Castle was).

“One of the baffling problems of breeders in pre-Mendelian days had been the effects of inbreeding and crossbreeding. What these were was a much-debated question. We set out to give it an experimental test and found ready to hand a rapidly breeding little fly, Drosophila, being cultured in the laboratory by a graduate student as embryological material. This, he told us, would complete a generation within a fortnight. (Charles Woodworth, prof entomology at UC Berkeley). … We began culturing the fly on pulped Concord grapes, but this gave us poor results as many of the larvae would get drowned and then our population statistics were no good. As grapes became out of season, we tried other fruits, and finally hit the jackpot in bananas. …

The conclusion drawn [from our studies] was that inbreeding reduces very slightly the productiveness of Drosophila. … This was not a conclusion of world-shaking importance. The important outcome of this investigation was that it called to Morgan’s attention a new source of material for experimental study not subject to the limitations of slow-breeding laboratory mammals.”

WE Castle (prof genetics UC Berkeley) The Beginnings of Mendelism in America – in Genetics in the 20th Century, p. 73.
Tough early going

"... Morgan had been working on fruit flies for at least two years before he found his most significant mutation, a white-eyed fly. For this new approach, Morgan was his own first student. He bred the flies for two years without assistance. He pointed to the shelves with flies and [said] that he had wasted two years and had gotten nothing for his work."

Great opening passages in the history of the English language

"It is a truth universally acknowledged that a single man in possession of a good fortune must be in want of a wife."

"When Caroline Meeber boarded the afternoon train for Chicago, her total outfit consisted of a small trunk, a cheap imitation alligator-skin satchel, a small lunch in a paper box, and a yellow leather-snap purse, containing her ticket, a scrap of paper with her sister's address in Van Buren Street, and 4 dollars in money. It was in August, 1998. She was eighteen years of age, bright, timid, and full of the illusions of ignorance and youth."

Required reading for Morgan's Science paper

1. The paper itself.
2. The commentary to it, written by Robert Robbins, that precedes the paper itself in the ESP-generated PDF.
3. Morgan's own description in narrative form, pp. 15-20 of his 1915 book (also an ESP-provided PDF).

"May 1910 was when the revolution began. Morgan found a white-eyed male running around in one bottle."

"The Mechanism of Mendelian Heredity" (1915)

Thomas Hunt Morgan
Alfred Sturtevant
Hermann Muller
Calvin Bridges
Nothing special here. Just like seed color in peas.

Normal Mendelian ratio (3:1) – but where are the white-eyed females?!!

Nettie Stevens, discoverer of the sex chromosomes

Nettie Stevens was one of the first female scientists to make a name for herself in the biological sciences. She was born in Cavendish, Vermont. Her family settled in Westford, Vermont. Stevens' father was a carpenter and houseman. He did well enough to own quite a bit of Westford property, and could afford to send his children to school. Stevens was a brilliant student, consistently scoring the highest in her classes. In 1896, Stevens went to California to attend Leland Stanford University. She graduated with a master's in biology. Her thesis involved a lot of microscopic work and precise, careful detailing of new species of marine life. This training was a factor in her success with later investigations of chromosomal behavior.

After Stanford, Stevens went to Bryn Mawr College for more graduate work. Thomas Hunt Morgan was still teaching at Bryn Mawr, and was one of her professors. Stevens again did so well that she was awarded a fellowship to study abroad. She traveled to Europe and spent time in Theodor Boveri's lab at the University of Munich. Boveri, a German scientist, was very interested in the genetics of Drosophila. He showed a great deal of interest in the subject from her stay.

In 1903, Stevens got her Ph.D. from Bryn Mawr, and started looking for a research position. She was eventually given an assistantship by the Carnegie Institute. This research was done with Thomas Hunt Morgan, and her findings were published as a Carnegie Institute report in 1905.
The useful mealworm

"It is perfectly clear that an egg fertilized by a spermatozoon containing the smaller hererochromosome produces a male, while one fertilized by a spermatozoon containing the larger heterochromosome develops into a female."

→ XO is male and XX is female (until 1916)

Edmund Wilson – arguably, the first XY person on Earth

"In many species of insects there are two classes of spermatozoa, equal in number, which in the early stages of their development, differ visibly in respect to the nuclear constitution; while there is but one class of eggs. That is to say, if the two kinds of spermatozoa be designated as the X-class and the Y-class, respectively; the eggs are all of the X-class. The male may accordingly be designated as the heterogametic sex, the female as the homogametic."
**Verification of Hypothesis**

*First Verification.*—If the symbol for the white male is WX, and for the white female WWXX, the gametes will be WX: W (male) and WX: WX (female), respectively. Mated, these individuals should give

\[
\begin{align*}
\text{WX} & \quad \text{W (male)} \\
\text{WX} & \quad \text{WX (female)} \\
\text{WWXX} (50\%) & \quad \text{WWX} (50\%)
\end{align*}
\]

White female

White male

All of the offspring should be white, and male and female in equal numbers, this is in fact the case.

*Second Verification.*—As stated there should be two classes of female in the F₁ generation, namely, RRXX and RWXX. This can be tested by pairing individual females with white males. In the one instance (RRXX) all the offspring should be red.

\[
\begin{align*}
\text{RX} & \quad \text{RX (female)} \\
\text{WX} & \quad \text{W (male)} \\
\text{RWXX} & \quad \text{RWX}
\end{align*}
\]

and in the other instance (RWXX) there should be four classes of individuals in equal numbers, i.e.,

\[
\begin{align*}
\text{RX} & \quad \text{WX (female)} \\
\text{WX} & \quad \text{W (male)} \\
\text{RWXX} & \quad \text{WX} \\
\text{RWXX} & \quad \text{WX}
\end{align*}
\]

It now becomes evident why we found it necessary to assume a coupling of R and X in one of the spermatozoa of the red-eyed F₁ hybrid (RXO). The fact is that this R and X are combined, and have never existed apart.

It has been assumed that the white male parent was a male.

![Diagram](image-url)

![Image](image-url)