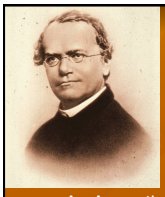
Mendel: Darwin's Savior or Opponent

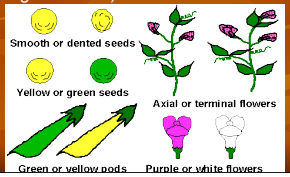


Gregor Mendel

- An Augustinian monk, Mendel studied physics and natural science in Vienna, but lived most of his adult life in the cloister at Altbrunn (now Brno in the Czech Republic)
- Starting in 1856 he conducted plant breeding experiments in the cloister's garden
  - Seeking the "law governing the formation and development of hybrids"

Mendel's Breeding Experiments

- An lucky choice of model organism. Chose to study peas because
  - They exhibit relatively easy to distinguish traints
  - They naturally self pollinated but are easy to cross-pollinate
- To characterize their behavior in crosses, Mendel introduced the vocabulary of *dominant* (traits that appeared in hybrid crosses) and *recessive* characters (one's that only appeared in subsequent generations)



Mendel's Procedure

- Began by cross-pollinating between pure breeding lines with alternative traits—yellow/green, smooth/dented
  - Found that all members of the F1 generation exhibited the dominant traits
- Allowed members of the F1 generation to self-pollinate, generating the F2 generation
  - And analyzed the numbers exhibiting the dominant and recessive traits

F2 Generation Created from Hybrids

Form of seed	Round / Wrinkled	5474	1850	2.96:1
Color of albumin	Yellow / Green	6022	2001	3.01:1
Color of seed coat	Violet flowers / White flowers	705	224	3.15:1
Form of pods	Inflated / Constricted	822	299	2.95:1
Color of unripe pods	Green / yellow	428	152	2.81:1
Position of flowers	Axial / terminal	651	207	3.14:1
Length of stem	Long / short	787	277	2.84:1

F2 Generation

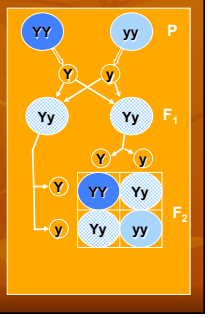
- Produced by self-pollination of members of the F1 generation
- When members of the F2 generation were allowed to self pollinate
  - Individuals with recessive traits bred pure
  - One out of three of those showing the dominant character produced only offspring with the dominant character
- **Theoretical problem for Mendel—what could *explain* these and other patterns Mendel found?**

Mendel's "Laws"

- Three laws commonly attributed to Mendel:
  - Law of segregation
    - Only one of a pair of alternative traits will be passed on through a gamete
  - Law of independent assortment
    - Different traits are inherited independently from each other
  - Law of dominance
    - One trait will "dominate" over the other in hybrids

Mendel's Hypothesis (in modern terms)

- Proposed that behind the characters lay *factors*
  - Pollen and egg cells each possessed the factor for either the dominant or recessive trait
- What evidence does Mendel have for these factors?
  - Only that they could account for the inheritance pattern he saw and others he predicted



Response to Mendel

- Presented results first at meeting of Brünn Natural History Society in 1865
- Paper was published in the Society's *Proceedings* in 1866
- No comments on the paper; few citations over next 35 years.
- Why neglect of Mendel?
  - Mendel in contact with Karl von Nägeli, but Nägeli's focus was different
  - Nägeli directed Mendel to work on Hawkweed, which unbeknownst to them, reproduced both sexually and asexually.
- Mendel did (could do) little to promote his results
  - Elected abbot of one of the richest cloisters in the Hapsburg Empire and spent much of the rest of his life in battle over taxation of the monastery—"Fight for the Right"

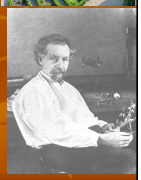
Rediscovery of Mendel in 1900

- **Carl Correns** (1864-1933) in Germany
  - Student of Nägeli, Mendel's main correspondent (who led Mendel to study hawkweed)

- **Hugo De Vries** (1848-1935) in Netherlands
  - Had been conducting experiments inspired by Darwin's account of pangenesis in the 1890s and from his observations reconstructed Mendel's laws

- **Erich Tschermak von Seysenegg** (1871-1962) in Austria
  - Grandfather had taught Mendel botany!

Mendelism as an Alternative to Natural Selection

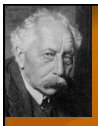


- De Vries' Mutation Theory
  - De Vries has observed evening primrose colonies outside Amsterdam in 1900
  - Offspring often differed dramatically from their parents
    - Termed these different offspring "mutations"
    - (Actually due to chromosome duplications)
  - Interpreted mutations as producing different species
    - Fast
    - No expectation of intermediate forms

An Uncelebrated Visit to San Diego

- In the month of June 1906, San Diego was visited by one of the greatest scientists of that time. His arrival was announced in the list of guests of the Coronado Hotel for 4 June 1906, where he was listed as Col. Hugo de Vries, Amsterdam. The "Col." cannot be a southern title, for Hugo de Vries never visited Kentucky, nor was he ever in military service. Except for this announcement, his visit went unnoticed. Nobody apparently greeted him at the railway station, nobody acted as his *Cicerone*. Alone, he wandered over San Diego's hills and the *mesa*, enjoying the plants which grew there and admiring the view.

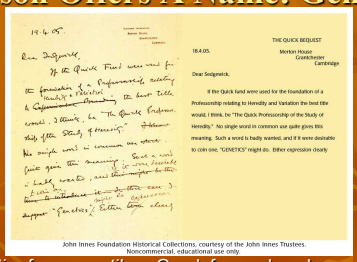
  HUGO DE VRIES VISITS SAN DIEGO
  By Peter W. van der Pas, *Journal of San Diego History, 1971*



The Arbiter

- William Bateson in England focused his evolutionary research on discontinuous variations
  - Bees with legs where there should be antennae
  - Humans with six fingers or extra ribs
- Was not one of the rediscovers of Mendel, but he got to settle the priority dispute by naming the view *Mendelism*
- Became champion of Mendelism (saltationism) in opposition to the biometricians (who emphasized gradualism)
  - Had Mendel's paper translated into English (1901-1902)

Bateson Offers A Name: Genetics



THE QUICK BEQUEST

18.4.05.

Merton House
Grantchester
Cambridge

Dear Sedgwick,

If the Quick fund were used for the foundation of a Professorship relating to Heredity and Variation the best title would, I think, be "The Quick Professorship of the Study of Heredity." No single word in common use quite gives this meaning. Such a word is badly wanted, and if it were desirable to coin one, "GENETICS" might do. Either expression clearly

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- *Genetics* from *genetikos*, Greek for produced
- Wilhelm Johansen in 1909 introduced the term *gene*
- Bateson also coined the terms *allelomorphs* (later shortened to *allele*), *zygote, heterozygote* and *homozygote.*

A Representational Tool: The Punnett Square

- The device for representing the genotypes that result from crosses in tables was developed by Reginald Punnett, a close collaborator of Bateson's at Cambridge
- A major contribution to making the theory intelligible

	R	**R**
R	RR	RR
r	Rr	Rr

	RY	**Ry**	**rY**	**ry**
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

Biometrician-Mendelian Conflict

Zoological Section, British Association, 1904

- William Bateson for Mendel
  - *Cinneraria* derived from hybridization in a wild population with many distinct (discontinuously-varying) varieties
- W.F.R. Weldon for Biometricians
  - *Cinneraria* originated through gradual selection from continuously-varying wild population (in Canary Islands)

Biometrician-Mendelian Conflict

- At stake:
  - For the Mendelians: Survival of the new field
  - For the Biometricians: continued control over "Evolution Committee" of the Royal Society (Composed of Galton, Pearson, Bateson and Weldon)

Contentions	Mendelians	Biometricians
Variation	Discontinuous	Continuous
Evolution	Rapid, step-wise	Slow, gradual
Selection	Small negative role: weeds out unfit	All-important moves mean of population in direction of selection

Linking Genes with Known Cell Structures

- For many biologists, genes (factors) were abstract, not physical, entities
- Chromosomes were identified in nucleus of dividing cells with the use of stains in the 1870s
  - Leading to studies of their role in development
- Link between Mendel's factors and chromosomes developed from work by Theodor Boveri and Walter Sutton
  - Boveri, working with sea urchins, showed that each chromosome contributed differentially to normal development
  - Sutton in 1902 proposed that chromosomes could provide the physical basis of Mendelian inheritance

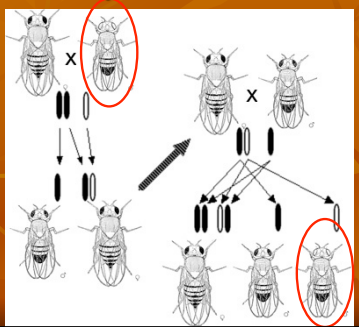
Cementing the Link: Thomas Hunt Morgan

- Morgan's initial focus was on development
  - Experimental studies of embryo formation, e.g., formation from separated blastomeres or in different salt concentrations
- Initially skeptical of both Darwinian natural selection and Mendelian inheritance
  - Bothered by the hypothetical and preformational character of Mendelian factors
  - Rejected chromosome theory: individual chromosomes did not carry hereditary information

Morgan's Conversion to Mendelism

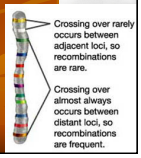
- Observed a white-eyed mutant in 1909
  - When crossed with normal red-eyed flies, all the offspring had red eyes
  - But the next cross yielded male flies with white eyes
  - Referred to such traits as *sex limited (sex-linked)*
  - Discovered other sex-linked traits (rudimentary wings and yellow body color) and determined that these were all inherited together
  - Concluded that the X-chromosome carried a number of discrete hereditary units
  - Developed the chromosomal theory of inheritance

Sex-Linked Inheritance of White Eyes--1911



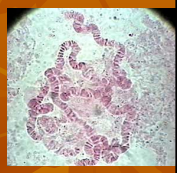
Thomas Hunt Morgan and the Fly Lab

- Discovered linkage groups: groups of genes that were inherited together
- Discovered crossover: paired chromosomes could exchange parts, leading to genes on different parts of one chromosome being separated in subsequent generations
- Established that the distance between genes determined probability of crossover
  - Genes further apart would be more likely to crossover
  - Rate of crossover became a tool for mapping location of genes on chromosomes
- Sturtevant developed the first genetic map in 1913
  - Discovered double crossovers



Mechanism of Mendelian Heredity

- Published with his graduate students Alfred Henry Sturtevant, Calvin Blackman Bridges, and Hermann Joseph Muller in 1915
- Bridges had established relations between crossover points and banding on the giant Drosophila chromosome allowing for the first physical mapping of genes to chromosomes



Mathematics meets Mendelism: Hardy-Weinberg Equilibrium

- Punnett felt unhappy with his attempt to explain why recessive phenotypes continued to exist, and asked his cricket partner and Cambridge mathematician Godfrey Hardy Hardy (1877-1947)
  - Question: what happens to a Mendelian mutation?
- Hardy's approach: Assumed a 2-allele case: **A** and **a**, with starting f = **AA** = 0.49, **Aa** = 0.42 and **aa** = 0.09 This gives an allele frequency of **A** = 0.7, **a** = 0.3
- He demonstrated that this ratio would remain constant from generation to generation provided:
  - Populations is large
  - Mating is random
  - No selection: All offspring combinations are equally successful
  - No migration in or out of the population
  - Mutation rate has reached equilibrium
- Independently derived by Wilhelm Weinberg (1867-1937), pediatrician in Stuttgart