Unit 3: Evolution, Genetics, and Development

1. Mendel: Darwin's Savior or Opponent?

Reactions to Darwin

- For many biologists in the second half of the 19th century, Darwin had establish evolution: descent with modification
  - But they either rejected or ignored natural section
    - John Herschel referred to it as the "Law of Higgeldy-piggeldy"
- A small collective in England embraced natural selection and sought to understand its workings
  - One consequence of their work was the development of statistics
    - used to determine how traits changed in a population
  - Francis Galton, Darwin's cousin, was a leader in this movement

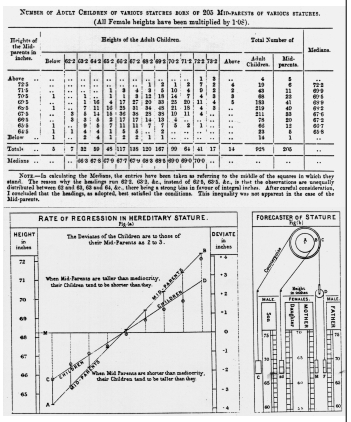
Regression to the Mean

- Galton first identified the phenomenon of regression to the mean in studies with peas:
  - Plants with larger peas give rise to plants with larger peas, but ones with very large peas do not give rise to ones with peas as large as their own
  - Likewise with plants with smaller peas
  - Reversion to the mean
  - Applied this framework to the study of the heritability of human traits —height, weight, visual acuity, "talent and character"
- Field came to be known as biometrics
  - The practitioners were biometricians

Diameter of Parent Peas	Mean Diameter of Offspring
21	17.26
20	17.07
19	16.37
18	16.40
17	16.13
16	16.17
15	15.98

Galton's studies of height

- Compared the mean height of parents in 205 families (calculated by multiplying the mother's height by 1.08 and averaging that and her husband's height) with the height of 928 adult children (multiplying daughters' heights by 1.08 again).
- Graphed the results comparing expected value (mid-parents) and actual (children)



NUMBER OF ADULT CHILDREN OF VARIOUS STATURES BORN OF 205 MID-PARENTS OF VARIOUS STATURES.
(All Female heights have been multiplied by 1·08).

Heights of the Mid-parents in inches.	Heights of the Adult Children.													Total Number of		Medians.
	Below	62·2	63·2	64·2	65·2	66·2	67·2	68·2	69·2	70·2	71·2	72·2	Above	Adult Children.	Mid-parents.	
Above	..	..	..	..	..	..	..	1	..	3	1	3	3	..	11	..
72·5	..	..	..	..	..	1	3	2	3	2	10	4	9	5	41	72·3
71·5	..	..	..	..	1	3	2	5	12	18	14	7	4	5	71	69·9
70·5	1	..	1	1	3	2	15	19	14	7	4	3	3	68	22	69·6
69·5	..	1	5	16	14	27	20	33	25	20	11	4	5	183	41	69·9
68·5	1	..	7	11	16	35	38	48	31	15	4	3	..	210	49	69·5
67·5	..	3	9	18	33	55	64	63	33	25	8	..	..	311	46	68·9
66·5	..	5	4	3	17	14	28	19	8	11	4	..	..	113	33	67·2
65·5	1	1	9	5	7	11	7	7	5	2	1	..	..	66	12	66·7
64·5	1	1	3	4	1	5	2	1	2	..	..	..	..	21	5	65·9
Below	..	1	..	2	4	1	2	1	1	..	..	..	..	14	1	..
Totals	..	5	7	32	99	45	117	135	135	107	59	24	17	14	928	205
Medians	..	..	..	68·3	67·8	67·9	67·7	67·9	67·9	68·3	68·5	69·0	69·0	70·5	..	..

NOTE.—In calculating the Medians, the entries have been taken as referring to the middle of the squares in which they stand. The reason why the headings run 62·2, 63·2, &c., instead of 62·5, 63·5, &c., is that the aberrations are unequally distributed between 62 and 63, 63 and 64, &c., there being a strong bias in favour of integral inches. After careful consideration, I concluded that the headings, as adopted, best satisfied the conditions. This inequality was not apparent in the case of the Mid-parents.

The Biometricians and Eugenics

- The success of breeders in shaping the traits of the organisms they breed suggested that the same could be done with humans
  - By controlling mating, one could produce populations with desired traits or lacking undesired traits
- Galton: "Eugenics is the study of agencies under social control that may improve or impair the racial qualities of future generations, whether physically or mentally."
- His chair at the University of London became the Chair of Eugenics
  - Succeeded by Karl Pearson (pioneer in the statistics of correlations)

SIR FRANCIS GALTON'S WILL.

BEQUEST TO LONDON UNIVERSITY.
THE STUDY OF EUGENICS.

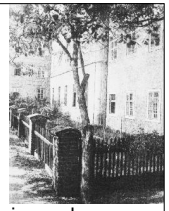
We understand that under the terms of the will of the late Sir Francis Galton, which has not yet been proved, the residuary estate is left to the University of London for the purpose of encouraging the study of national eugenics.

Sir Francis Galton may be described as the founder of the study of eugenics. His principal contributions to science consisted in his anthropological inquiries, especially into the laws of heredity, where the distinguishing feature of his work was the application of statistical methods. In 1869, in "Hereditary Genius," he endeavoured to prove that genius is mainly a matter of ancestry, and he followed that up with many other books and papers on various aspects of the subject. Some time ago, as Mr. Cracknanthorpe recalled in an interesting letter published in *The Times* of January 25, he ceased to engage in original research and devoted his energies to the spread of eugenics. In 1904 he endowed a Research Fellowship in the University of London for the promotion of the study of national eugenics, and in the following year he established for its prosecution a laboratory at University College.

A Crucial Gap in Darwin's Account

- In the *Origin* Darwin offered no account of heredity
- He later did propose an account of *pangenesis*:
  - Each cell of the body generated minute particles—gemmules—that migrated to the sexual organs and were passed to the offspring
  - In sexual reproduction, each offspring would get gemmules from both parents and develop new cells that reflected the average of those of its parents
- Fleeming Jenkin demonstrated that if true this were true, it would be a disaster for natural selection
  - The variability would be reduced with each generation and there would soon be no variants left to select among

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

Clicker Question

What was Mendel's objective in carrying out breeding experiments?

A. To repudiate Darwin's theory of natural selection
B. To defend Darwin's theory of natural selection
C. To identify the laws governing the formation of hybrids
D. To determine how to grow peas that produced more offspring

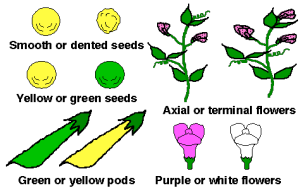
Clicker Question

Why did Mendel elect to work with peas?

A. He was interested in producing better varieties of peas
B. They exhibited useful characteristics such as well-differentiated traits and are able to pollinate themselves
C. Different varieties exhibited different colored seeds and leaves
D. They were relatively inexpensive so could be grown on a monks salary

Mendel's Breeding Experiments

- A lucky choice of a model organism. Chose to study peas because
  - They exhibit relatively easy to distinguish traits
  - They naturally self pollinated but are easy to cross-pollinate



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 one trait, which he called *dominant*
    - tall rather than short stem
- Allowed members of the F1 generation to self-pollinate, generating the F2 generation
  - Some plants exhibited the trait that had disappeared in the F1 generation—which he called *recessive*
  - Mendal analyzed the numbers exhibiting the dominant and recessive traits

F2 Generation Created from Hybrids

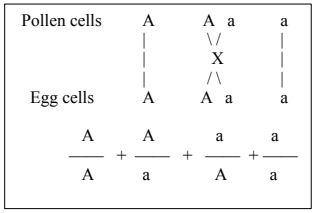
Form of seed	**Round / Wrinkled**	**5474**	**1850**	**2.96:1**
Color of albumin	**Yellow / Green**	**6022**	**2001**	**3.01:1**
Color of seed coat	**Violet flowers / White flowers**	**705**	**224**	**3.15:1**
Form of pods	**Inflated / Constricted**	**822**	**299**	**2.95:1**
Color of unripe pods	**Green / 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**

F3 Generation

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

Mendel's Hypothesis

- Having started with the observations of the inheritance of characters, Mendel shifts to advancing a hypothesis of what accounts for the distribution of characters he observed
- He now uses A and a to refer to types of pollen and egg cells and analyzes how they might be combined:



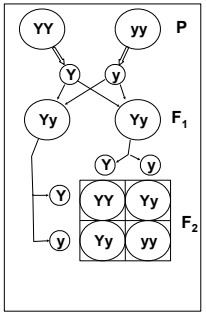
Discussion Question

When Mendel represents the results of his crosses and dominants with recessives, he writes the expression A + 2Aa + a rather than the now familiar AA + 2Aa + aa. What might account for this?

A. He thought it would be wasteful to write both letters when they duplicated each other
B. He was representing the characters that would be produced in offspring, not genes or factors
C. His mathematics was flawed—he didn't realize that two dominant factors and two recessive factors would be produced
D. He had a very different understanding of the genetics than we have today

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



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
- None of these is strictly true

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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; very few citations over next 35 years
- Mendel himself was led off onto an unproductive path by the leading researcher on heritability of traits, Karl von Nägeli
- Nägeli suggested that Mendel study inheritance in the Hawkweed, which unbeknownst to both of 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"

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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

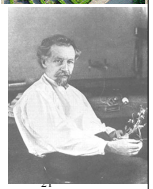
- Erich Tschermak von Seysenegg (1871-1962) in Austria
  - Grandfather had taught Mendel botany!

Clicker Question

When researchers rediscovered the work of Mendel at the beginning of the 20th century, why did they construe it as presenting an alternative to Darwinian natural selection?

A. Mendel never discussed evolution, so it was reasonable to assume that he did not believe in it
B. Mendel never discussed natural selection, so it was reasonable to assume that he did not believe in it
C. Change in Mendelian factors/characters seemed to produce evolutionary jumps, not gradual changes
D. These researchers rejected the eugenics program embraced by the Biometrians who defended Darwinian natural selection

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

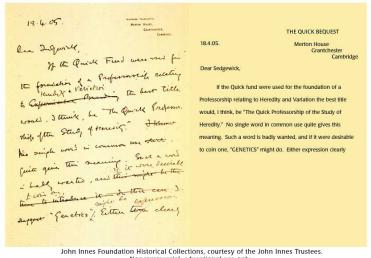
- In the month of June 1906, San Diego was visited by one of the greatest scientists of that time. His arrival was announced in the list of guests of the Coronado Hotel for 4 June 1906, where he was listed as Col. Hugo de Vries, Amsterdam. The "Col." cannot be a southern title, for Hugo de Vries never 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*

Arbitrating the Priority Dispute

- 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 the 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 Sedgewick,

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

- *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.*

Biometrician-Mendelian Conflict

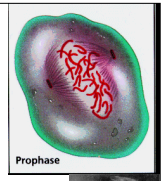
- Debate at the Zoological Section of the British Association's meeting in 1904
  - William Bateson for Mendel
    - Cinneraria derived from hybridization in a wild population with many distinct (discontinuously- varying) varieties
  - W.F.R. Weldon for Biometricians
    - Cinneraria originated through 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)

	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

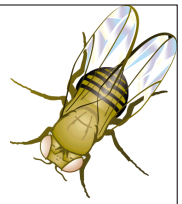


- For many biologists, genes (factors) were abstract, not physical, entities
- Chromosomes were identified in nucleus of dividing cells with the use of stains in the 1870s
  - Leading to studies of their role in development
- Link between Mendel's factors and chromosomes developed from work by Theodor 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

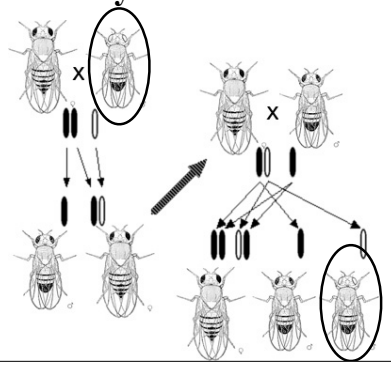
- Morgan's initial focus was on development
  - Experimental studies of embryo formation, e.g., formation from separated blastomeres or in different salt concentrations
- Initially skeptical of both Darwinian natural selection and Mendelian inheritance
  - Bothered by the hypothetical and preformational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

Morgan's Conversion to Mendelism



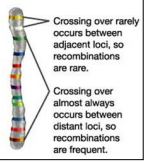
- Observed a white-eyed mutant in 1909
  - When crossed with normal red-eyed flies, all the offspring had red eyes
  - But the next cross yielded male flies with white eyes
  - Referred to such traits as sex limited (sex-linked)
  - Discovered other sex-linked traits (rudimentary wings and yellow body 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