The Evolutionary Synthesis

"Nothing in biology makes sense except in the light of evolution."
Dobzhansky, 1973, *American Biology Teacher*

The Seeming Impotence of Natural Selection

- Selection can only eliminate variants—it cannot produce anything.
- Variants must arise from somewhere else—mutation, etc.
- The source of variation is the true cause of evolution
- "We are now standing at the deathbed of Darwinism, making ready to send the friends of the patient a little money to insure a decent burial. . ." (E. Dennert, *At the Deathbed of Darwinism,* 1904)

Mathematics meets Mendelism: Hardy-Weinberg Equilibrium

- Punnett felt unhappy with his attempt to explain why recessive phenotypes still exist, and asked his cricket partner and Cambridge mathematician Godfrey Harold 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:
  - Population 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

Pearson and Fisher

How (not?) to treat an up and coming star:

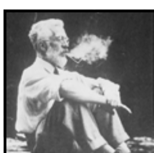
"…Fisher…received an offer from Professor Pearson at the Galton Laboratory. Fisher's interests had always been in the very subjects that were of interest at the Galton Laboratory, and for five years he had been in communication with Pearson, yet during those years he had been rather consistently snubbed. Now Pearson made him an offer on terms which would constrain him to teach and to publish only what Pearson approved. It seems that the lover had at last been admitted to his lady's court—on condition that he first submit to castration. Fisher rejected the security and prestige of a post at the Galton Laboratory and took up the temporary job as sole statistician in a small agricultural research station [viz., Rothamsted Experimental Station] in the country." (Box, 1978, p. 61)

Ronald Aylmer Fisher and *Population* Genetics

- Strategy of merging Mendelism and Darwinism through statistical analysis

- 1918: 1st paper, on "The Correlation between Relatives on the Supposition of Mendelian Inheritance."
  - Argued that discrete Mendelian gene was the focus of selection
  - That from many independent Mendelian factors one could account for the continuous variation the Biometricians observed
  - Opposed Darwin's and Pearson's view of blending inheritance, and Galton's "Laws"

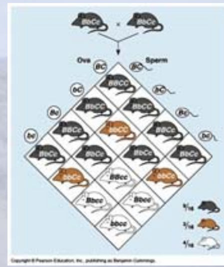
- Major contributions to the development of statistics, including the analysis of variance (ANOVA)



Genetical Theory of Natural Selection (1930)

- First half of book involved developing Fisher's concepts of genetics at the population level:
  - Idea of a "gene pool"
  - Fitness of alleles
  - Role of selection
- Fundamental theorem of natural selection: *The rate of increase of fitness of any organism is equal to its additive genetic variance in fitness at that time.*
  - Importance of *additive variance*
  - Downplayed but did not deny "genetic residue" – linkage, epistasis (interaction between genes at different loci)
- Second half applied these principles to human breeding as an argument for *eugenic control* of reproduction (eliminating the "unfit" and promoting the more fit by providing an allowance for children proportional to income)

The Problem of Epistasis

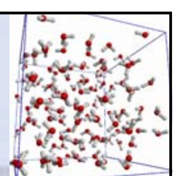


- Interaction between genes at two loci
  - The c-locus determines whether there is color in hair
    - cc individuals are albino
  - The b-locus determines color
    - B (dominate)—brown
    - b (recessive)—tan
- Effects at b and c locus are not individually additive

Fisher’s project of population genetics

- Evolution occurs in large, virtually unlimited populations
- Variation and environmental change are random
- Selection produces a gradual shift in gene *frequency*
- Evolution leads inevitably to better *adaptation*
- Populations are simply collections of independent alleles combining and recombining every generation
- Aimed to make population genetics do for evolution what kinetic theory of gases did for physics

Fisher and Thermodynamics

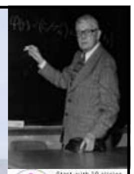


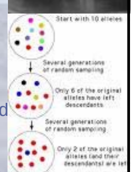
- Attracted as a student to the model of statistical mechanics as an explanation of phenomenological thermodynamics
- “The investigation of natural selection may be compared to the analytic treatment of the Theory of Gases, in which it is possible to make the most varied assumptions as to the accidental circumstances, and even the essential nature of the individual molecules, and yet to develop the natural laws as to the behaviour of gases, leaving but a few fundamental constants to be determined by the experiment.” (Fisher 1922).
- The organism disappears: selection as a coefficient operating on genes

Fisher’s Theorem

“It will be noticed that the fundamental theorem .... bears some remarkable resemblances to the second law of thermodynamics. Both are properties of populations, or aggregates, true irrespective of the nature of the units which compose them; both are statistical laws; each requires the constant increase in a measurable quantity, in the one case the entropy of the physical system and in the other the fitness .... of a biological population .... Professor Eddington has recently remarked that ‘The law that entropy always increases - the second law of thermodynamics - holds, I think, the supreme position among the laws of nature’. It is not a little instructive that so similar a law should hold the supreme position among the biological sciences.” (Fisher 1930 *The Genetical Theory of Natural Selection*).

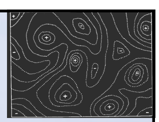
Sewall Wright’s Alternative

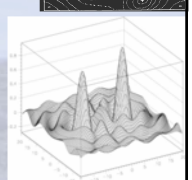




- Early experience with animal breeding and development of a manual for cattle breeding for the U.S. Department of Agriculture
- Developed mathematical framework while at the University of Chicago
- Concluded that small, inbreeding groups were the key to evolution—**Shifting balance theory**
  - Gene frequencies could more easily become fixed (100%), frequently by chance (genetic drift)
  - Inbreeding would promote homozygosity and hence expose genes more effectively to selection
  - Each population would become adapted to a micro-niche, or would become extinct
  - Genes often interact in production of traits, and fortuitous combinations more likely in small groups
  - Some migration & interbreeding between groups

Adaptive landscapes





- Peaks represent maximal adaptation
- Valleys represent low adaptation
- Sub-populations (demes) adapt to a particular peaks
- If not at a peak, move to one or go extinct
- Only small populations could move through valleys to new peaks—hence small populations were the key to evolution
- Competition both between organisms and between groups
- Adaptive landscapes constantly changing due to:
  - External conditions
  - Activity of the organisms themselves

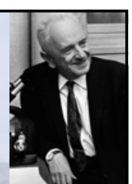
Fisher-Wright Dispute

- Are natural populations sufficiently small, or divided into nearly isolated inbreeding groups, for genetic drift to be a factor (Wright)
- Or do they consist of large enough numbers of organisms sporting sufficient independent genes for selection to find and promote variants (Fisher)
  - Selection the most important factor and resulted in very precise adaptation (since the large number of variable alleles allowed for highly targeted selection)
- Conflict between alternative modeling assumptions
- Need more than theory—evaluation of natural populations

Field Studies of Evolution

- Russian tradition initiated by Chetverikov and continued by Dubinin studying large wild populations of *Drosophila melanogaster* collected in the Caucuses
  - Found large percentage (16%) of recessive lethals on 2nd chromosome
  - Natural populations are loaded with hidden genetic variability
  - Since much of it is lethal, referred to as *genetic load*
- Dobzhansky brought this tradition to the U.S.

From Theory to Field: Theodosius Dobzhansky



- Unlike his more mathematically inspired predecessors, Dobzhansky's focus was the field (also true of Ernst Mayr and G. Ledyard Stebbins and of paleontologist G. G. Simpson)
- From the field he derived a very strong impression of both diversity and the adaptiveness of diverse forms to local circumstances
- Recognized the importance of variability:
  - ". . . the accumulation of germinal changes in the population of genotypes is . . . a necessity if the species is to preserve its evolutionary plasticity. . . . The environment is in a constant state of flux, and its changes...make the genotypes of the past generations no longer fit. . . . Hence the necessity for the species to possess at all times a store of concealed, potential, variability."

From Drift to Selection

- In 1937 (*Genetics and the Origin of Species)* Dobzhansky viewed much of the variability as non-adaptive and thus likely due to drift
  - Defined evolution as "a change in the frequency of an allele within a gene pool."
  - Emphasized isolating mechanisms for differentiating populations
- By 1951, he downplayed drift and emphasized selection
  - But a broadened conception of the power of selection not just in winnowing but in promoting particular traits
  - Result: balance selection—heterozygote superiority
- Increased emphasis on selection referred to as the "hardening" of the synthesis

Dobzhansky's Isolating Mechanisms

1. Premating or prezygotic mechanisms.
(a) Ecological or habitat Isolation.
The populations concerned occur in different habitats in the same general region.
(b) Seasonal or temporal Isolation.
Mating or flowering times occur at different seasons.
(c) Sexual or ethological Isolation.
No attraction between the sexes of different species:
(d) Mechanical Isolation.
Physical non-correspondance of the genitalia of the flower parts prevents copulation or the transter of pollen.
(e) Isolation by different pollinators.
In flowering plants, related species maybe specialized to attract different insects as pollinators.
(f) Gametic Isolation.
Female and male gametes are not attracted to each other. In organisms with internal fertization, the gametes of one species may be invialble in other species sexual ducts.
2. Postmating or zygotic isolating mechanisms
(g) Hybrid Inviablity.
Hybrid zygotes have reduced viability.
(h) Hybrid sterility.
The F_1 hybrids of one sex or both sexes fail to produce functional gametes.
(i) Hybrid break down.
The F_2 or backcross hybrids have reduced viability.

The Synthetic Theory of Evolution

- International Conference on Genetics, Paleontology, and Evolution, Princeton, 2-4 January, 1947

The "Hardening" of the Synthesis

- Apparently neutral traits, such as patterning in *Cepaea*, shown to result from selection by predators (Cain & Sheppard, 1950)
- Selection came to be viewed as playing the primary role in directing evolution.
- Mutation and drift downplayed
  - But the dead do not always stay dead!