The Modern Synthesis

The genetic basis of natural selection,
the origin of life, and the evolution of human beings

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“Swamping”

Darwin and Galton had believed that the characteristics of the parents are blended in the offspring, and Galton had shown that those of the progeny will regress towards the mean of the population. This made it difficult to understand how advantageous traits could increase in the population.

In 1867, Fleeming Jenkin (1833–1885) pointed out that blending will render any advantageous variation ineffective because it will be “swamped” by intermixture with the rest of the population. This objection disturbed Darwin, and he was unable to see how to reconcile it with his theory.

This shows that both Darwin and Jenkin were still thinking of natural selection acting on *individuals*, with incrementally different characteristics. In order for the theory of evolution by natural selection to be established on a firm footing, it was necessary to change the perspective to one of selection acting on discrete factors in a *population*.

The biometricians and the ancestral law

Two of Galton's followers, Karl Pearson (1857–1936) and W.F.R. Weldon (1860–1906) founded the journal *Biometrika* in 1902 to publish and promote their work on continuous variation.

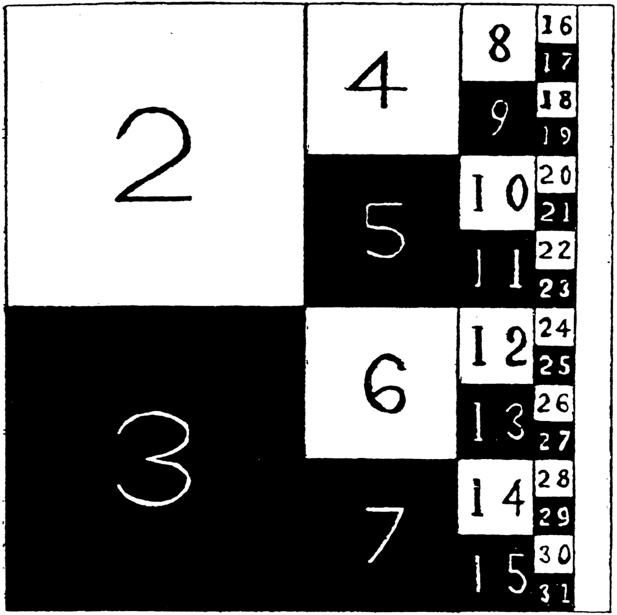
The biometricians used Galton's ancestral law of inheritance:

$$(0.5) + (0.5)^2 + (0.5)^3 + \cdots = 1.$$

By focusing on traits that tend to be blended, they argued that *the ancestral law of heredity* was more fundamental to inheritance than Mendel's law, which they thought operated only in special circumstances.

For example, in a classic dispute, William Bateson (1861–1926) showed that a biometrical analysis of albinism in mice in *Biometrika* was incorrect, and argued that the experimental results, in fact, supported Medelism.

Galton's *ancestral law of heredity*, from his "A diagram of heredity," 1898.



Yule's mathematical comparison

Udny Yule (1871–1951), who had been Pearson's best student, took a purely mathematical approach to modeling the difference between Galton and Mendel's laws. Yule was a gifted mathematician who had been working on applying statistical methods to social problems.

In two papers in 1902, he showed that both laws produce the 3:1 ratio. Then, in his treatment of recessive alleles, Yule dropped the assumption of complete dominance, assumed that the environment also affects the gametes, and showed that if variations in the contribution of the hereditary units…

Yule, *The Genetical Theory of Natural Selection* (1902)

"… take place by discrete steps only (which is unproven), discontinuous variation must merge insensibly into continuous variation simply owing to the compound nature with which one deals."

Muller in the USSR

Hermann Muller (1890–1967) – who had worked in T. Morgan's "fly room" – like many intellectuals in the west in the first half of the 20th century, was attracted to the economic and social ideals of communism and first visited the USSR for a few months in 1922 when Lenin was still alive, bringing with him a valuable collection of specially bred *Drosophila*. During this time, Muller communicated to his Russian colleagues his excitement about the prospects for Mendelism and his hope that it might be connected with Darwinism.

He must have formed a connection with the country because he returned to the USSR in 1933, fleeing Nazi Berlin, to work at the Institute for Genetics at Leningrad (now St. Petersburg), and then Moscow. He stayed for a number of years until the situation became untenable for geneticists, due to the rise of Trofim Lysenko and his persecution of geneticists.

Izrail I. Agol, H. Muller, K. Offerman and S.G. Levit at work in the Vavilov Institute, Leningrad (St. Petersburg), late 1930s. Muller left the country in 1937, with about 250 strains of *Drosophila*, after learning that Stalin was displeased with his book on eugenics, while Agol and Levit were shot due to their politics.

The Russian school of population genetics

In the interwar period, there was a group of active genetic researchers in who were also interested in more traditional natural history and field work, especially Sergei Chetverikov (1880–1959) at Koltsov Institute of Experimental Biology, Moscow, and his students D.D. Romashov (1906–??) and Nikolay Dubinin (1907–1998). They received Muller warmly and began a research program based on crossing the flies he brought with the wild populations in Russia.

Chetverikov used simple mathematical models to calculate the possibility that there were hidden recessive genes in the wild populations and used experimental crosses to test his models. He concluded that the smaller the population, the more chance that this *cryptic variability* would show up. Although this was later challenged, the approach brought quantitative methods to bear on considering the distribution of genes in a population.

The gene pool concept

Romashov and Dubinin continued this work by introducing more sophisticated methods from classical probability theory in an experimental system dubbed “the urn.” They placed different colored marbles, representing different alleles for one of two genes that will be inherited and found that the proportions of various genotypes will bear a relation to the frequency of each type of gene in the previous generation’s total gamete production. This model provided a mathematical description of equilibrium concepts, that allowed one to probe the effects of various initial conditions – positive or negative selection, non-random mating, etc. – on the gene frequencies in each subsequent generation.

With this work, they developed the explicit idea of the overall population as a sort of reservoir for genes – the so-called “gene pool” – in which all combinations of the available genes could be realized in various frequencies.

Ronald Fisher (1890–1962)

In the 1910s, R.S. Fisher – a Cambridge trained mathematician, most famous for having developed the mathematics of randomized control trials – took up the study of genetics from the perspective of mathematical modeling. He worked with idealized initial conditions, appealed to theoretical entities, and sought mathematical laws to encapsulate the phenomena of heredity and evolution. He constructed a *statistical genetics*, applying statistics to various combinations of alleles in a population.

He modeled the distributions of genes in a population, not just a mating pair, under the assumptions that such a population is reproductively isolated, and any male can mate with any female. The frequencies of alleles within the population can then be calculated and probabilities of survival at different life stages can be determined, so that evolutionary concepts such as "reproductive value" and "fitness" have computable or assigned values in the equations – and hence become *measurable* terms.

The Genetical Theory of Natural Selection (1930)

In *The Genetical Theory of Natural Selection* (1930), Fisher set out his mathematical models of population genetics and argued that "Mendelism validates Darwinism."

He stated the "fundamental theorem of natural selection" as *the rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time*. Comparing it with the second law of thermodynamics, he said…

Fisher, *The Genetical Theory of Natural Selection* (1930)

> "… 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 of a measurable quantity, in the one case the entropy of a physical system and in the other the fitness … of a biological population."

Two kinds of fitness

Fisher showed that the fitness – which he called the Malthusian parameter – measures the reproductive values of individuals at all ages of their life history, and hence would be different for each genotype. In this way, the Malthusian parameter is an index of the fitness of each genotype to survive *under specific environmental conditions*.

In fact, there are two measures of fitness that can be applied to populations. The first can be applied to two or more species of populations compared to each other and measured as an increase in the size of one population over the other. The second is applied to particular individuals, or specific genes, within a single population and measures the change in gene frequency over successive generations.

In general, Fisher's approach was highly abstract and mathematical, with little attempt to treat biological complexity.

J.B.S. Haldane (1892–1964)

Haldane – or JBS, as he was always known – was another British mathematician, classicist and biologist, who was an active communist when he was younger and spent his final years in India. He was interested in applying the mathematical approach pioneered by Fisher to various questions dealing with more practical situations in biological populations. For example, he was interested in the effects of immigration and emigration, and other situations that would arise in real world applications. He also sought to treat, mathematically, various factors that would influence the fitness of certain genes – such as complete versus incomplete dominance, random versus selective mating, self-fertilization versus cross-fertilization, and so on.

For both Fisher and Haldane, populations were abstractions that were described in terms of the *frequency of certain genotypes*.

Sewell Wright (1889–1988)

Wright was a Harvard trained geneticist who was a gifted, but mostly autodidact, mathematician, but was more interested in practical applications and tests of the mathematical theory than Fisher and Haldane. Wright began with the assumption of a population in equilibrium and investigated the factors that would upset that equilibrium. Write showed that mutation, selection and migration upset the genetic equilibrium and shifted gene frequencies.

One of his main claims is that gene frequencies may shift in a population *even without the pressures of selection* – a phenomena he called *genetic drift*. His models shows that this happens much more in small populations – particularly, in the *founder effect*, when a small group of organisms migrate to a new area, and in the *bottleneck effect*, when environmental changes kill off all but a small number of individuals in a population.

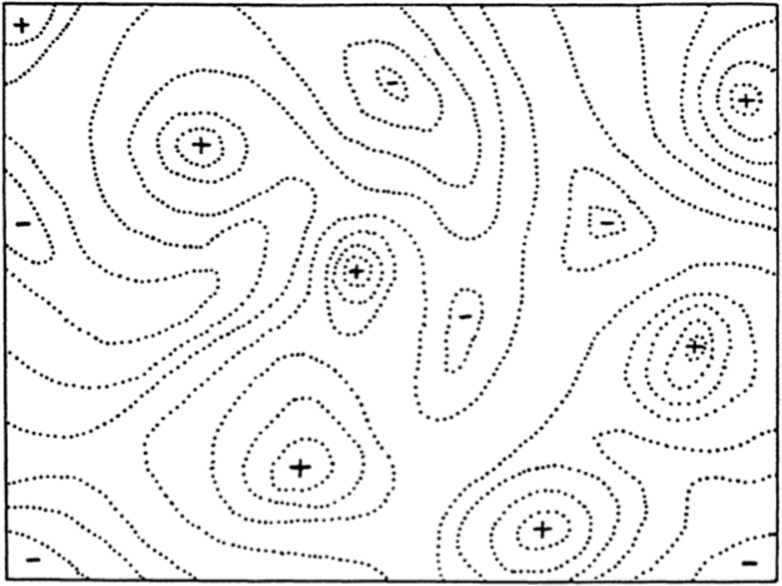
Genetic drift

Wright described the relationships among phenotypes in terms of *fitness surfaces* – a plot in which fitness, now a value, is the height, and the axes are allele frequencies and average phenotypes. A population occupies a hill in this landscape. Natural selection causes a population to climb a peak, while genetic drift may cause a population to move from peak to another passing through a saddle.

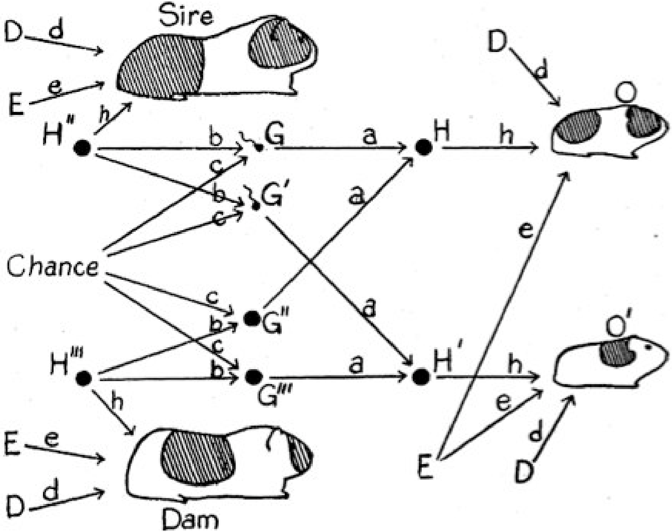
Wright also realized that the usual conception of dominance was inaccurate, stating…

Wright, "… theories of dominance," 1934

"… it is clear that dominance has to do with the physiology of the organism and has nothing to do with the mechanism of transmission, i.e. with heredity in the narrow sense."

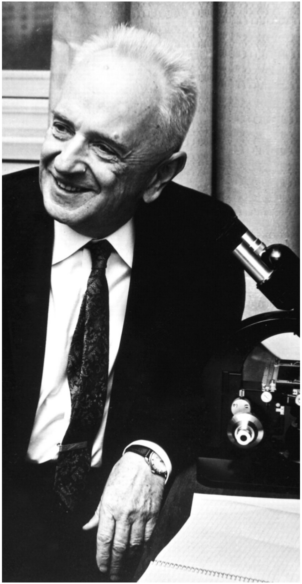


One of Wright's *fitness surfaces* – fitness is height, the axes are allele frequency and average phenotype.



Wright also developed the *path diagram* as a mathematical method for treating *causation*. This is his map for computing the causal effect of development, *D*, on guinea pig coat coloration.

Theodosius Dobzhansky (1900–1975)

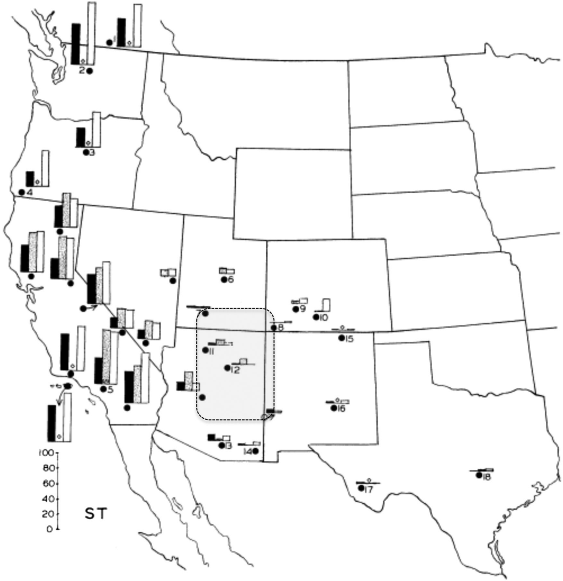


- Educated in Kiev, Russian Empire (now Ukraine), and then St. Petersburg (Petrograd), where he worked on entomology and genetics.
- He moved to the US in 1927 and worked with Morgan's group in Columbia, and then Caltech.
- He became a US citizen in 1937.
- He went back to Columbia in 1940 and then on to Rockefeller University, and finally University of California.
- He became a well-known public intellectual, arguing for the importance of the theory of natural selection, and contributing to the debate about the biological meaning of "race."

Drosophila pseudoobscura

Dobzhansky combined the techniques of classical genetics, naturalist field work, and the mathematics of population genetics to produce a new field of *evolutionary genetics*. Over the course of many years he collected wild samples of *Drosophila pseudoobscura* in the American west and studied their genetic make up. He was able to show that two "races" of *D. pseudoobscura* that are morphologically indistinguishable have different genetics and are actually separate species.

By placing the flies in population cages, he was able to show that the frequencies of certain genes would be changed by altering the temperature and light – thus bringing *micro-evolution* by selection into the lab. This showed that evolution by natural selection could be subjected to experimental testing and quantification, and that what was adaptive was not individual genes or phenotypic traits but the whole complex of genetic traits carried on the chromosome.



A “landscape genetics” study.

The bars represent three principal configurations of the chromosomes in *D. pseudoobscura* collected by Dobzhansky and his colleagues.

Genetics and the Origin of Species (1937)

Dobzhansky's 1937 book became one of the key works in the modern synthesis. He laid out his understanding of evolutionary genetics and the relationship between micro- and macro-evolution. He later laid out the case for treating micro-evolution through experiments, stating that…

Dobzhansky, "Adaptive changes induced by natural …," 1947

> "… the genesis of adaptation, which is possibly the central problem of biology, now lies within the reach of the experimental method."

In 1973, he wrote an essay titled "Nothing in Biology Makes Sense Except in the Light of Evolution." He argued against a creationist position and points out that the fact that evolution occurs explains the interrelatedness of the various facts of biology, and so unifies our understanding of biology.

The modern synthesis

In the 1940s, a large number of biologists began to become convinced of the importance of natural selection, and produced works that contributed to the modern synthesis. Of which we may mention a few examples:

Julian Huxley wrote *Evolution: The Modern Synthesis* (1942), giving the new approach its name and paying particular importance to the implications for human beings. Ernst Mayr's *Systematics and the Origin of Species* (1942) argued for natural selection from the perspective of a field naturalist, focusing on morphology and local speciation in birds. George Simpson's *Tempo and Mode in Evolution* (1944) applied the new methods to paleography and argued that the effects of micro-evolution compounded together to produce the macro-evolution found in the fossil record. G. Ledyard Stebbin's *Variation and Evolution in Plants* (1950) laid out the case for the combination of genetics and natural selection in the study of plants.

The principles of the modern synthesis

The main tenets of the theory by the 1940s were:

- Evolution is gradual. Small genetic changes and recombinations occur; the phenotypic results undergo natural selection.
- Selection is the main mechanism of change; slight advantages are important over many generations.
- Genetic drift occurs, but its importance to evolution is unclear.
- Discontinuities arise through reproductive isolation, and possibly through retention of juvenile features in the adult.
- Genetic diversity is a key factor in evolution.
- The fossil record can be explained by extrapolation from observed micro-evolution to non-observed macro-evolution.

The population concept of species

A major contribution of the modern synthesis was the development of a revised concept of species – known as the biological species concept – which states that species are…

Mayr *Systematics and the Origin of Species* (1942)

> “… groups of actually or potentially interbreeding natural populations, which are reproductively isolated from other such groups.”

This concept was further articulated to include all of the factors of concern to biologists – morphology, reproductive fertility, adaptations, and ecological situation.

That is, they argued that species really exist, but they exist as populations, or rather groups of populations.

Origin of Life (1938)

The Soviet biochemist Alexander Oparin (1894–1980) put forward the idea that *primordial spontaneous generation* should be thought of as a process of chemical development through which the building blocks of living organisms were gradually assembled – related to the Marxist philosophy of dialectical materialism. He argued that the earth's atmosphere originally contained no oxygen, which was produced in its free state as a result of the activity of living things. Chemical reactions in an atmosphere of hydrocarbons and ammonia produced a primordial soup of large, self-replicating molecules, in which the first formation of living organisms took place.

Oparin's ideas were taken seriously in the West despite the explicit link to Marxism. In the early post-war period, the American biochemist Stanley Miller (1930–2007) showed that amino acids could be produced by passing electricity through the kind of reduced atmosphere that Oparin postulated.

The origins of *Homo sapiens*

The modern synthesis shifted focus back on discussions of the evolutionary origins of humans. By the 1940s, it was clear from the fossil remains of the *Australopithecines* that the hominid family evolved in southern Africa. Mayr argued that fossil remains found in Java and China should be grouped together into the *Homo erectus* species, which had evolved from the *Australopithecines*. The *Homo neanderthalensis* were regarded as a variety of *Homo sapiens*, which had separated and then gone extinct relatively recently.

Scientist could then focus on questions about the sorts of adaptations that might have lead to the larger brains of *Homo sapiens*, as a result of natural selection. A number of different explanations were put forward, but they were no longer based on a concept of progress. For example, Sherwood Washburn (1911–2000) argued that the enlarged brain resulted from communal hunting as principle means of securing food.

Debates about race

The modern synthesis eliminated the tradition of *race science*. Although proponents of the modern synthesis disagreed about the extent to which differences between different “races” are biological or cultural, they agreed that human beings are a single species, and that we use the term “race” in popular speech differently from the way we use it in biology – in which there is no such thing as a “pure race” for a biological species. Indeed, many of them argued that the term “race” should not be used in science at all, because it had lost any sense of objectivity.

Whereas anthropologists were attempting to differentiate between different “races” by making measurements, biologists pointed out that this had little value because there was more genetic variation between the individuals of each population than there was among the group. They argued that it was, rather, only on the basis of genetic differences that it would be meaningful to talk about different “races.”

The Price Equation

In the 1960s and 70s, a number of scientists elaborated Fisher's mathematical approach to natural selection. In 1964, W.D. Hamilton (1936–2000) published a paper on the mathematics of *kin selection*. The American chemist and mathematician George Price (1922–1975) then applied concepts from game theory to provide a rigorous interpretation of Fisher's mathematics as well as a general equation that describes how a trait could increase or decrease in a subpopulation due to both a "selection" term and an "environmental" term. The equation can be thought of as a precise definition of the meanings of "survival" and "fitness." It allows one to interpret the "environmental" term as operating at various levels – encompassing ideas like genetic drift, group selection, and epigenetic environment.

After Price's death, Hamilton and others articulated his insights into a rigorous theory of the natural selection of altruism, and other traits, such as cruelty.

The neutral theory of molecular evolution

Motoo Kimura (木村資生, 1924–1994) studied biology and genetics in Japan before taking a PhD from Wisconsin from J.L. Lush and S. Wright. He produced highly sophisticated mathematical studies in population genetics that modeled the way gene frequencies might change from one generation to the next based changes to the genetic material at a molecular level.

In 1968, after the rise of molecular biology, he introduced his neutral theory of molecular evolution, which proposed that the majority of genetic change, which happens at a molecular level, is neutral with respect natural selection – making *genetic drift* the primary driver of evolutionary change.

Although his views were very popular in Japan, they were controversial among biologists – finding broad support among molecular biologists but opposed by most evolutionary biologists.

Lysenkoism

In the USSR, the progress of genetics and the acceptance of the modern synthesis was drastically reduced by the rise to prominence of the agronomist and biologist Trofim Lysenko (1898–1976). Lysenko was a Lamarckian who argued that genetics and natural selection were bourgeois Western theories that were incompatible with Marx's material dialectic – which, he claimed, was more compatible with Lamarckism.

After the famines of 1920 and 1927, the Soviet leaders were anxious to improve crop productivity and to prevent a reoccurrence of such famines. Emergency funds were spent to build an Institute of Applied Botany, and later the Institute of Applied Genetics, Moscow. During Stalin's rein, however, Lysenko came to control Soviet biological research and to effectively shut down his competitors and professional enemies.

Lysenko speaking at the Kremlin, 1936

The direct politicization of ideas

In the late 1920, Lysenko and his colleagues put into place a program to improve agriculture that rejected the slow methods of orthodox breeders and promised quick results by exposing organisms to the direct action of the environment. Although in many ways this was a successful agricultural program, it implemented theories that were based on considerable ignorance, little data, and pure speculation.

The most serious effects of Lysenkoism were on professional soviet science, since practitioners who disagreed with Lysenko were denied jobs, forced underground, sent to camps, and sometimes killed. Although Lysenkoism is usually associated with the Soviet Union, it was also developed in many other countries – particularly, in central and eastern Europe and China, sometimes with disastrous results. After Stalin's death in 1953, Lysenkoism gradually gave way to mainstream genetics and evolutionary theory.

Private institutes

The growth of the biological sciences in the first half of the 20th century was greatly spurred by two private American institutions, the The Rockefeller Institute and the Carnegie Institution – both founded by the eponymous tycoons.

The Rockefeller Institute for Medical Research was founded in 1901 to be America's answer to the Pasteur Institute or the Robert Koch Institute. The Rockefeller Foundation, which gave grants, was closely affiliated. For decades the Institute focused on basic research, applied research such as biomedical engineering, and clinical science. The Rockefeller Institute eventually became Rockefeller University while the Foundation supplied large and small grants in many different fields all over the world. In this way, the Foundation was able to help shape the direction of the life sciences, both internally, in terms of the types of theories and methods that were pursued, and externally in terms of the politics of the programs funded.

Overview

- We have looked at the way that population genetics addressed, and overcame, the problem of “swamping” in biometrical approaches to natural selection.
- We went over the way that population genetics was developed to treat natural selection as a process acting on gene frequencies in a population.
- We discussed the modern synthesis and the combination of the theory of evolution by natural selection and evolutionary genetics.
- We briefly treated the rise and fall of Lysenkoism.
- We touched on the influence of the The Rockefeller Foundation.