A Brief History of Modern Biology

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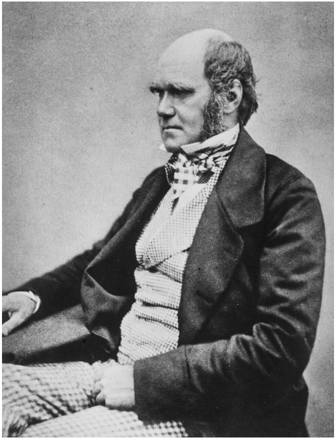
Ideas of biological evolution in the 19th century

- In the 19th century, there were many conflicting ideas about evolution and the meaning of the existence of *variations* among organisms.
- In the 1810s, Jean-Baptiste Lamarck outlined a comprehensive theory of evolution in which animals in the course of their lives, *individually*, become more complex and better adapted and then pass these changes onto their offspring. This kind of theory is known as Lamarkism.
- In 1844, the *Vestiges of the Natural History of Creation* (Robert Chambers) presented a cosmic natural history in which all forms were in transformation and everything develops from previous forms.

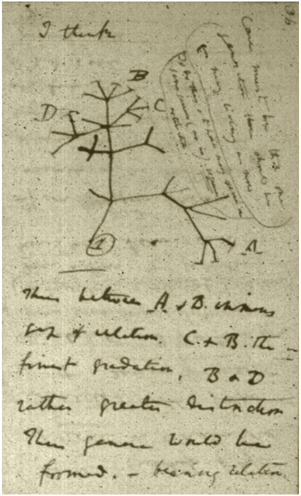
Charles Darwin (1809–1882)

- Darwin was born to a wealthy family of Unitarians and freethinkers, but was baptized as an Anglican.
- He graduated from Cambridge University, ordinary degree.
- Voyage of the Beagle, 1831–1836.
- Became familiar with the work of Charles Lyell on geology and formulated his own theory of evolution.
- Spent many years studying the variation of species and arguing that species change through natural selection.



Darwin at age 45

Darwin's theory of evolution by natural selection



On the Origin of Species, 1859. (6 eds.), argued that just as individual variations can be selected for by animal breeders, so there are natural mechanisms which effectively select locally advantageous traits.

Two key concepts of natural selection: (1) variations are random, and that (2) these variations are then selected by the environment.

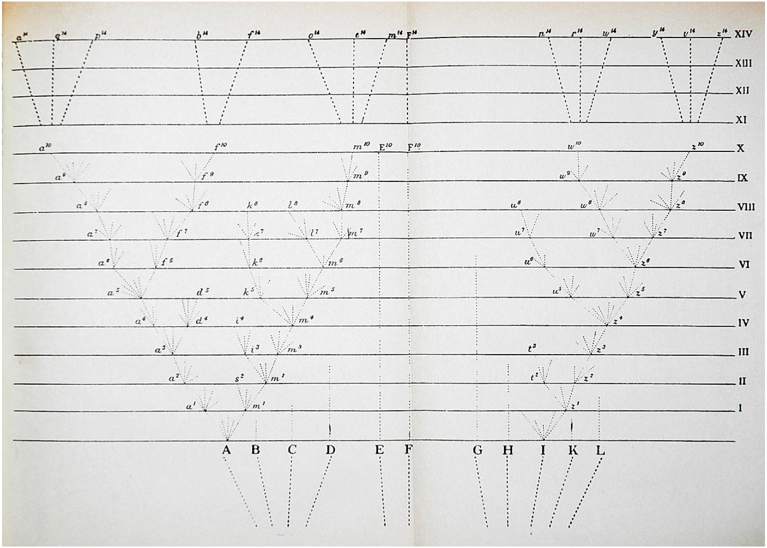
Under these two conditions, over long periods of time new species are produced while others die out.

Natural Selection of Survival of the Fittest

On the Origin of Species, 6th edition, 1872:

> *Can it, then, be thought improbable, seeing that variations useful to man have undoubtedly occurred, that other variations useful in some way to each being in the great and complex battle of life, should occur in the course of many successive generations? If such do occur, can we doubt (remembering that many more individuals are born than can possibly survive) that individuals having any advantage, however slight, over others, would have the best chance of surviving and of procreating their kind? On the other hand, we may feel sure that any variation in the least degree injurious would be rigidly destroyed. This preservation of favorable individual differences and variations, and the destruction of those which are injurious, I have called Natural Selection, or the Survival of the Fittest.*

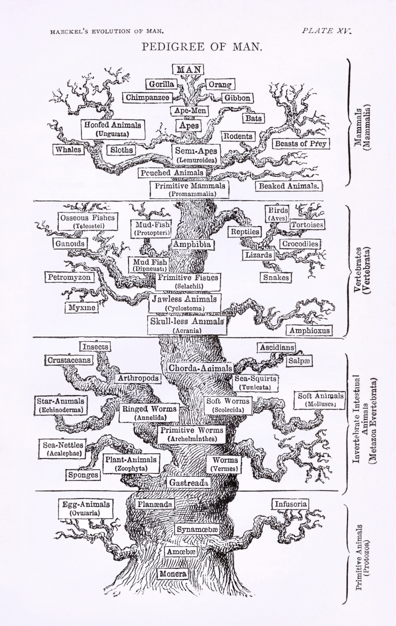
Darwin’s concept of divergence



The reception

- *On the Origin of Species* was very popular, but this was mostly because it was so controversial. Most of the early press was negative.
  - There was a lot of social, religious and scientific resistance to Darwin's ideas.
  - Contrary to most popular accounts of this history, there was no sharp divide between religious and scientific camps.
- Including the book itself, there was a growing body of evidence in support for evolution, and by the end of the century, most biologists accepted the fact of evolution.
- Nevertheless, there was very little support for the theory of natural selection. The early evolutionists had a preference for ideas of *evolutionary progress*, like Lamarkism.

- Ernst Haeckel's "tree of life," *The Evolution of Man*, 1879.
- This is a sort of linear, teleological version of evolution.
- In this view, every lower animal is seen as a stage in the process by which life matures towards the human form, as the final product. (Living fossils.)
- It violates the most important implication of Darwin's branching model, in which forms are rarely preserved unchanged.



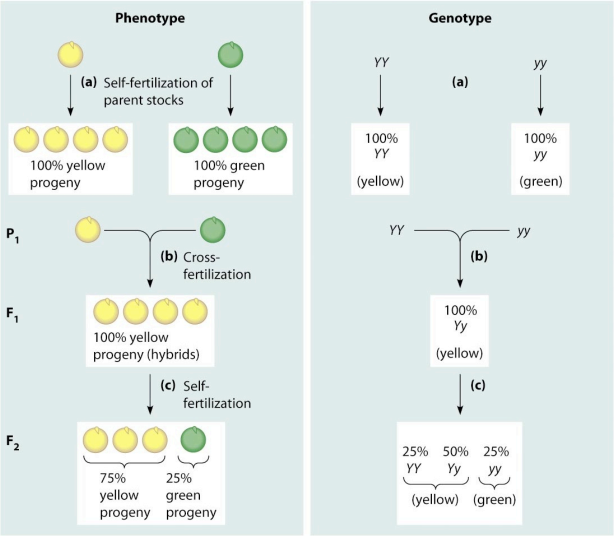
Gregor Johann Mendel (1822–1884)

- Mendel was an ethnic German, born in the Austrian Empire (now, Czech Republic), to a farming family.
- He was a friar, but attended university at both Olomauc and Vienna.
- He carried out his experiments in plant breeding at St. Thomas' Abbey.
- He was a physics teacher and head of the Abbey.
- We will look at some results from *Experiments on Plant Hybridization*, 1865.

Mendel's laws of heredity

- He was interested in how hybridization might be related to the emergence of new species.
- He did breeding experiments on pea plants.
- He chose a number of contrasting pairs of traits, such as *stem height*, *seed shape*, and *seed color*; and bred plants having opposite traits over a number of generations.
- He found that in the first generation (F1) one of the traits would dominate, which he called dominant, but in the next generation (F2), the other trait would reappear, which he called recessive.
- He distinguished between what we call genotype (factor), and what we call phenotype (the plant).
- The paper made a novel argument for the idea that heredity is *hardwired*, and that some traits are transmitted unchanged from one generation to the next.

Schematic of Mendel's law of heredity



The reception

- Mendel's paper was distributed to 134 libraries and scientific institutions. 40 reprints of the paper were made and Mendel sent some of these to a number of prominent biologists.
- Nevertheless, the paper was neglected by geneticists for almost 30 years, to be "rediscovered" when three biologists — Carl Correns (1864–1933), Hugo de Vries (1848–1935) and Erich Tschermak (1871–1962) — independently rediscovered his laws.
- There are a number of reasons why his contemporaries were not interested in his work.
  - Mendel was writing about hybridization, not genetics. He was interested in the production of species through hybridization, a degenerating research program at the time.
  - His contemporaries were interested in the origin of species, but Mendel gave no account of how new species would be produced by crossing hybrids in this way.
  - Mendel did not belong to a social network of biologists.

Drosophila melanogaster, the common fruit fly

- The fruit fly has had a long career in science; they are ubiquitous and breed easily and quickly.
- The fruit fly first came into genetic labs in 1901 as a control for other experiments.
- Gradually, however, researchers noticed that they show a large number of easily observable mutations which display Menelian traits.
- The fruit fly was made most famous by the Fly Lab at Columbia and remains an essential tool for genetic research.

The Fly Room at Columbia University

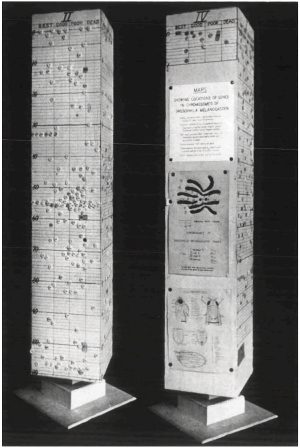
- The "Fly Room" was the nickname of Thomas Morgan's (1866–1945) laboratory, where he and his students (esp. Sturtevant, Muller and Bridges) studied the genetics of fruit flies.
- Morgan began studying the flies in order to prove the mutation theory of de Vries, a Dutch botanist; but he soon discovered that the flies had a lot to teach us about Mendelian traits.
- He discovered a white-eyed recessive mutant, which was nearly always related to male offspring.
- This lead to a research program of trying to determine the degree of the relationship between various traits through *linkage analysis*.
- In this way, the Fly Room became the center of research on the nature and structure of chromosomes.

Thomas Morgan in the Fly Room

Calvin Bridges in the Fly Room

Cromosome theory

- The idea that chromosomes might be the carriers of genetic material had been around for years, but it was Morgan's work that proved this point.
- Although initially there was no direct, observational evidence that chromosomes were linear arrays of Mendelian *genes*, the researchers in the Fly Room modeled the positions of the genes on the chromosomes using *linkage analysis*.
- Here we see an idealized model of the chromosomes made by Bridges. →



Bridges' "Totem pole"

The modern evolutionary synthesis

- In the 1930s-40s, there was a revival of the theory of evolution through the mechanism of natural selection.
- It was now argued that the new science of genetics made it clear that mutations in genes could be completely random and that these could then be adaptively selected for by environmental pressures.
- The modern synthesis brought together many different branches of the biological sciences — field studies, paleontology, embryology, genetics, population genetics, etc. — and interpreted their findings through the adaptive mechanism.
- As a result, there was a renewed interest in the evolution of the human race and in thinking about the implications of evolution through natural selection as a basis for understanding our social and moral place in the world.

Erwin Schrödinger's *What is Life?*

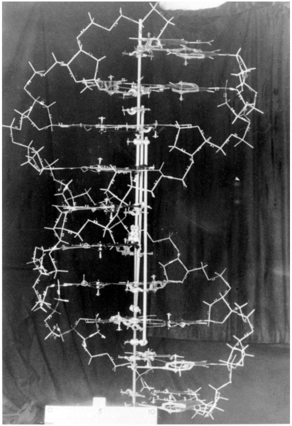
- In 1944, E. Schrödinger, the quantum physicist, turned his attention to the basic questions of life.
- He argued that the carrier of the gene itself had to be a molecule.
  - "How can we ... reconcile the fact that the gene structure seems to involve only a comparatively small number of atoms ... and that nevertheless displays the most regular and lawful activity — with a durability or permanence that borders on the miraculous? ... These material structures can only be molecules."
- He argued that the code of the genetic *information* could be carried by a small number of total atoms.
  - "What we wish to illustrate is simply that with the molecular picture of the gene it is no longer inconceivable that the miniature code should precisely correspond with a highly complicated and specified plan of development and should somehow contain the means to put it into operation."

Molecular biology

- Based on these kinds of ideas, physicists and chemists began to become interested in biology and began a process of *"colonization" of the biological sciences* with physical and chemical methods and ways of thinking.
- Using techniques such as x-ray crystallography, physicists and chemists began to study the internal structure of biological molecules.
- Biochemists, such as Erwin Chargaff (1905–2002), began to use chemical techniques to analyze biological molecules into their components.
- Linus Pauling (1901–1994), who had worked extensively on the nature of the chemical bond using quantum theory, showed that a polypeptide chain of proteins is a single helix, the alpha-helix.

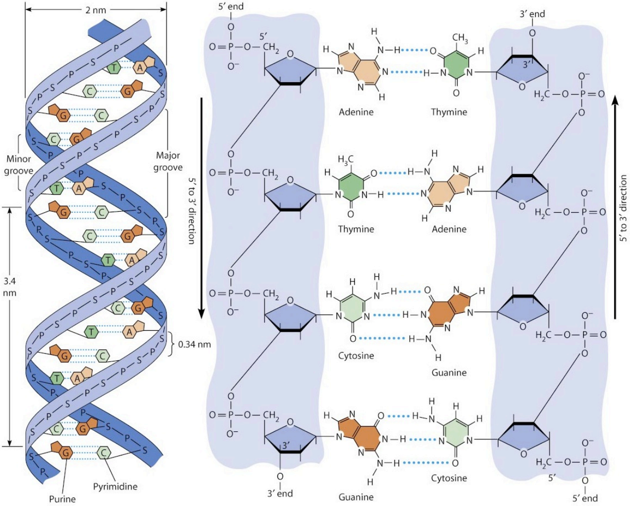
The structure of deoxyribonucleic acid (DNA)

- Over a period of a couple of years, James Watson (1928–) and Francis Crick (1916–2004), combined these different types of approach to work out the structure of DNA.
- Chargaff showned that the percentage of adenine and thymine were the same, as was the percentage cytosine and guanine. ($A/T \approx 1$, $G/C \approx 1$.)
- Rosalind Franklin had taken very good x-ray photographs, which they were able to see.
- They used Pauling's model building techniques.
- The model was announced in 1953.



Watson & Crick's model

DNA schematic



(a) Double helix

(b) Antiparallel orientation of strands

Reductionism and its discontents

- In the 1950s, Crick's reductionist model became known as the Central Dogma: DNA determines messenger-RNA which in turn determines proteins.
- In the 1960s, this view required modification. It became clear that a broader, holistic or systems approach was necessary.
- For one thing, it became clear that not all DNA was strictly genetic. There was also so-called "redundant" or "junk" DNA — now called introns.
- DNA was not simply transcribed into mRNA, but also acted as, or was acted on by, various regulators. Also, in some cases RNA could write to DNA (ex., in retroviruses).
- That is, the DNA would transcribe mRNA differently in different cells, or different parts of the organism, so that the focus had to shift back to these structures as well.

The Human Genome Project

- The study of DNA and mRNA lead to a new type of genetic analysis on a detailed level.
- The Human Genome Project was a "big science" project in the life sciences.
- It was a coordinated international effort to sequence the full list of chemical base pairs (A–T, C–G) of the human genome (20,000–25,000 genes).
- The official project lasted 13 years and cost around $3 billion to sequence a composite of 269 peoples' DNA.
- A private company headed by Craig Venter, Celera Genomics, also sequenced a composite genome of just 6 people, using their own techniques at a fraction of the time and cost.
- Now we can map individual genomes for less than $1,000, and the costs will probably continue to come down.

Biology and Information

Starting from the discovery of the molecular structure of DNA, biologists began to think more seriously about how the genetic material might contain, and transmit, *information*. The Russian-American physicist Grerorge Gamow (1904–1968) wrote a letter encouraging biologists to look for the *genetic code*, and outlining in principle how this might function.

Following this, detailed experimental work established that sets of three base pairs of nucleotides in the RNA encoded for just 20 amino acids, with some *redundancy*, and omissions.

The further problem of how series of the 20 amino acids would fold together to produce the solid structures of protein molecules was much more difficult and took decades to work out, and is still being worked on now. Recently this problem has been essentially solved by AI (Google's AlphaFold).

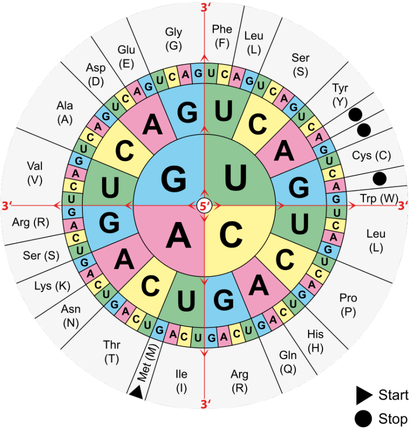
The Genetic Code

A schematic for understanding the way RNA codes for amino acids.

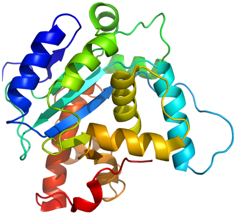
Here we see the three-pair sets of the four the nucleotide bases in the middle (A,G,C,U), and the resulting amino acids in the outside ring. (Compared with DNA, in RNA thymine (T) is replaced with uridine (U).

The 3′ and 5′ terms have to do with the directionality of the RNA strand.

This just gives a simplified code for what sequence of acids are produced. It tells us nothing about how the final protein will be structured.



Protein folding



The problem of determining the physical structure of proteins, given the sequence of amino acids, is massively harder than than of working out the genetic code.

For decades researchers from all over the world worked on the problem, and made some headway in individual cases, but did not come up with a general method of solution.

This began to change in 2018. Using a specially developed AI, AlphaFold, Googles' Deepmind dominated a contest for testing such solutions called Critical Assessment of Protein Structure Prediction, or CASP. AlphaFold2 can predict the solution with almost 90% accuracy.

Final remarks

- The two most dominant themes of 20th century biology are evolutionary theory, and genetic analysis.
  - Other major themes, which we have not discussed today, have been the application of systems thinking to biology and the rise of ecological thought.
- With the rise of the DNA-based notion of heredity and genetic transmission, we see a strong role for the function of information in biology.
- Hence, in various areas — like the life sciences, the physical sciences and the information sciences — we begin to see an increased emphasis on the role of information and control and communication systems.
- This gives new meaning to the concept of information society.