The biological revolution: from Darwin and Mendel to the discovery of the DNA

Christian Wüthrich

http://www.wuthrich.net/

Introduction to the history and philosophy of science
Faculté des sciences, Université de Genève

Plan

1. The emergence of evolutionary theory
   - Precursors: Hutton, Lamarck, Cuvier, Saint Hilaire, Lyell
   - Darwin
2. In search of a theory of heredity
   - Mendel's theory of heredity
   - From the modern synthesis to the discovery of DNA

From mineralogy to geology

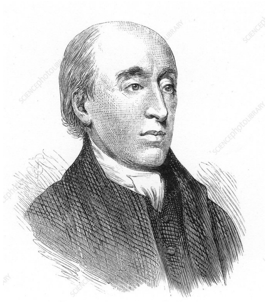
Characterisation (Mineralogy, ca. 1650-1800)

Often conducted by mining engineers, mineralogy in the 18th century was concerned with the classification of specimens of materials taken from the earth's crust (rocks, salts, minerals, etc) based on physical properties such as solubility, ignitability, etc. Its base assumption was that all minerals were originally fluids, which underwent solidification by cooling or drying. Its practice was based on the collection of specimen, observation, and some laboratory experiments.

Characterisation (Geology)

Geology, as we understand it today, arose from mineralogy roughly in the period 1800-1830 (culminating in Lyell's Principles). Its aim is to formulate 'theories of earth', i.e., to explain the emergence of earth as we find it today.

James Hutton (1726-1797)



- important enabler of modern geology, was a gradualist defending the idea that changes on earth's crust were gradual transformations.
- Hutton was a stead-state theorist, i.e., saw earth as having emerged from balanced changes between erosion and elevation.
- Importantly, he stressed the importance of natural laws underwriting the relevant causal proceedings.
- precursor of what later became known as uniformitarianism (see Lyell), according to which geology explains present-day feature of earth's crust as the result of continuing natural processes of long (geologic!) time scales.

Hutton (1788). The Theory of the Earth, 304:

> *The result, therefore, of our present enquiry is, that [in geology] we find no vestige of a beginning,—no prospect of an end.*

Jean-Baptiste Lamarck (1744-1829)

- French botanist, zoologist, naturalist
- proposed that biological evolution proceeded in accordance with natural laws
- *Système des animaux sans vertèbres* (1801): classification of invertebrates
- Lamarckism: theory of inheritance of acquired characteristics, based on idea of use and disuse (*Philosophie zoologique* 1809)

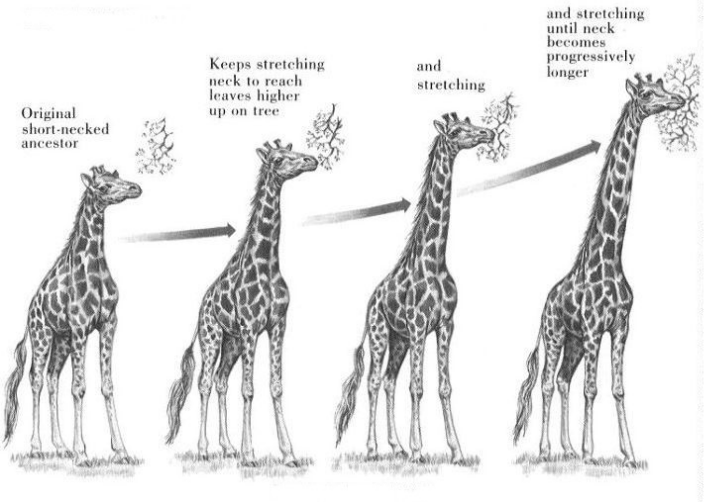
Thesis (Lamarck's theory of biological evolution)

Two factors drive evolution:

1. *complexifying force driving animal body plans towards higher levels creating a hierarchy of phyla*
2. *adaptive force causing animals with a given body plan to adapt to environment (use and disuse, inheritance of acquired characteristics), creating a diversity of species and genera*

Lamarck's evolutionary theory: use and disuse

Example: increase in length of giraffe's cervical vertebrae through use



- Problem: use of heart over decades should lead to hypertrophy...

Geoffroy Saint Hilaire (1772-1844)

- French naturalist, defender of Lamarck's theory, and believer in the possibility of the transmutation of species in time—transformism
- established the principle of unity of composition, the idea that there is an underlying unity of organismal design
- collected lots of specimens and evidence for his ideas in comparative anatomy, paleontology, and embryology
- pre-runner of idea of 'evo-devo'

Georges Cuvier (1769-1832)

- French zoologist, naturalist
- founder of (vertebrate) paleontology (= study of fossils) and comparative anatomy, comparing living animals with fossils, and expanding Linnean taxonomy by grouping classes into phyla and including extinct species
- established extinction as fact
- Against Lamarck and Saint Hilaire, he denied there was evidence for evolution (mummified cats and ibises from Egypt same as living animals)—fixism;
- instead, he thought there was evidence for cyclical creations and catastrophic extinctions of species e.g. through deluges—catastrophism.
- provided part of the foundation of scientific racism

Charles Lyell (1797-1875)

- Scottish geologist
- demonstrated the power of known natural causes acting over long periods of time ('deep time') in explaining earth's history
- *Principles of Geology* (1830-1833): earth was shaped by the same natural processes still in operation today, such as volcanoes, earthquakes, deluges

⇒ gradualistic view of uniformitarianism, as opposed to Cuvier's catastrophism

Charles Darwin, *On the Origin of Species* (1859, 282):

> *He who can read Sir Charles Lyell's grand work on the Principles of Geology, which the future historian will recognise as having produced a revolution in natural science, yet does not admit how incomprehensibly vast have been the past periods of time, may at once close this volume.*

Lyell and geology

Charles Lyell, *Principles of Geology* (1830-33, 1):

> *Geology is the science which investigates the successive changes that have taken place in the organic and inorganic kingdoms of nature. It inquires into the causes of these changes. And it describes the influence which they have exerted in modifying the surface and external structure of our planet.*

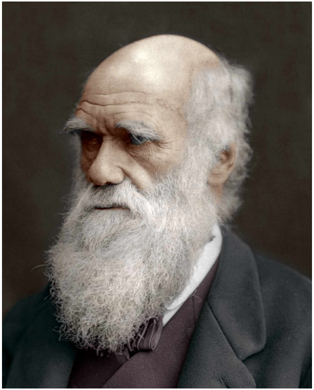
- "organic and inorganic kingdoms of nature": history of life is part of geology, which uses fossils as evidence of introduction and extinction of species
- "the causes of these changes": not mere empirical investigation, included theoretical task of giving explanations
- Volume II focuses on vicissitudes to which species are subject, and deals with biogeography, i.e., the influence of the inanimate on the animate world.

⇒ The origin of species is part of geology, rather than zoology.

Lyell's guiding 'philosophy'

- actualism: explanations of past phenomena ought to only rely on (kinds of, and degrees of) causes now operating ("the present is the key to the past")
- gradualism: forces of change operate 'at current intensities'
- commitment to (causal) empiricism: restriction to existing causes, which must be empirically accessible, but access can be indirect (rather than 'vera causa', i.e., the true cause of a natural phenomenon which must be shown by direct evidence to exist)
- steady-state earth: history is cyclical, rather than directed (not an 'arrow'), e.g. cycles of erosion and deposition, of subsistence and uplift, of the extinction and introduction of species, etc. (problem: there seems to be some evidence that some processes are directed)
- uniformitarianism

Charles Darwin (1809-1882)



- English geologist, biologist, naturalist
- reads divinity at Christ College, Cambridge (1828-1831)
- embarks on *Beagle* (December 1831-October 1836), to South America, the Galapagos Islands, and Australia, reads Lyell's *Principles* on trip
- makes observations on the formation of mountain ranges in South America, and on the islands and atolls
- collects plant and animal specimens, as well as fossils
- observes indigenous populations

Incipient ideas on the *Beagle*

- Already during his journey on the *Beagle*, Darwin realizes that the idea of a separate creation of different species is false.
- Instead, the only explanation of the similarities between fossils in a region and extant organisms, or of the presence on islands of species which are similar, but distinct from those found on the nearby continent, is to admit a progressive transformation of species.
- Darwin applies an idea by Thomas Malthus (*An Essay on the Principle of Population*, 1798) to the realms of animals and plants: the growth of a population leads to a competition for food and resources in which only the best adapted varieties survive.
- Upon his return to England, Darwin develops these ideas by collecting information both through a network of corresponding botanists and zoologists (by analogizing the process of evolutionary selection to selection used by breeders of pigeons) and by his own studies (of different species of barnacles, of pollination of orchids, of grain and egg transport, etc).

On the Origin of Species (1859)

by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life

Thesis (Evolution through natural selection)

The diversity of life arose by common descent through a branching pattern of evolution by means of natural selection operating on a large variation in a population of animals or plants competing for resources in constantly shifting environmental conditions.

- The *Origin* was written for a non-specialist audience and included a carefully crafted argument for the thesis above, summarising evidence from almost three decades of scientific work by Darwin.
- Darwin has no clear demarcation between variation within a species—varieties—sub-species—species.
- support by unification achieved by the Master Argument:

On the Origin of Species

Argument (Master argument)

- *Descent of modifications is by means of selection.*
- *Regional (comparing e.g. birds on Galapagos Islands and mainland) or temporal (comparing fossils and extant species) similarities are due to descent from common ancestry.*
- *Differences are due to specific environment favouring particular variations over others.*

The logic of Darwin's theory of natural selection

Ernst Mayr (1982). *The Growth of Biological Thought*. Cambridge, MA: Harvard University Press.

Mayr (1982, 479f):

Darwin's theory consisted of three inferences based on five facts derived in part from population ecology and in part from phenomena of inheritance.

Fact 1: All species have such great potential fertility that their population size would increase exponentially (Malthus called it geometrically) if all individuals that are born would again reproduce successfully.

Fact 2: Except for minor annual fluctuations and occasional major fluctuations, populations normally display stability.

Fact 3: Natural resources are limited. In a stable environment they remain relatively constant.

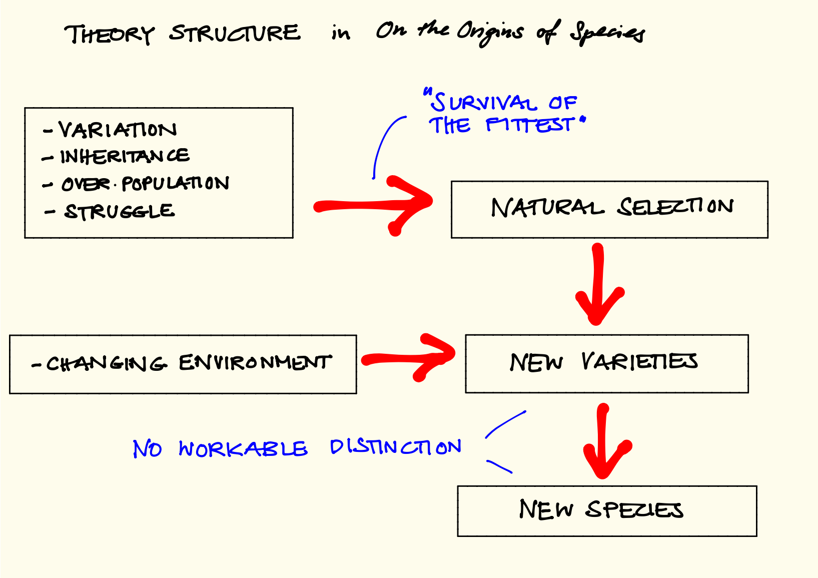
Inference 1: Since more individuals are produced than can be supported by the available resources but population size remains stable, it means that there must be a fierce struggle for existence among the individuals of a population, resulting in the survival of only a part, often a very small part, of the progeny of each generation.

The logic of Darwin's theory of natural selection

Mayr (1982, 479f), continued:

> *These facts derived from population ecology lead to important conclusions when combined with certain genetic facts.*
>
> *Fact 4: No two individuals are exactly the same; rather, every population displays enormous variability.*
>
> *Fact 5: Much of this variation is heritable.*
>
> *Inference 2: Survival in the struggle for existence is not random but depends in part on the hereditary constitution of the surviving individuals. This unequal survival constitutes a process of natural selection.*
>
> *Inference 3: Over the generations this process of natural selection will lead to a continuing gradual change of populations, that is, to evolution and to the production of new species.*

On the Origin of Species: theory structure



Discussion and implications

- Darwin endorses Lyell's gradualism and his actualism.
- A central assumption of Darwin's is that only variations with a small amplitude at the level of the organism are tolerable by living systems.
- Darwin's theory has biogeographic consequences. Consider
  - why there are (compared to the mainland) different though similar bats on islands, but no terrestrial mammals, and
  - why they are not the same (in locally different environments).
- Creation cannot explain these facts, evolution by natural selection of favourable traits is the most natural explanation.
- Darwin offers a convergent network of arguments in favour of evolution drawing from all parts of biology, from biogeography to paleontology and to embryology.
- Darwin's theory has implications for classification: Linné's system must be replaced by classifications based on evolutionary genealogy.

In search of a theory of heredity

Main lacuna of the theory of evolution:

The main puzzle piece which is lacking in Darwin's theory is a convincing theory of heredity: how is it that similarities (and, occasionally, dissimilarities) are inherited from one generation of organisms to the next?

- In the 1860s, several important developments in this respect take place:
  - Darwin offers a (false) theory of heredity.
  - Mendel undertakes systematic studies concerning the inheritance of traits in peas and formulates his laws of heredity.
  - Cytologists make important observations of cell division and fecundation, providing evidence for chromosomes.

Darwin's theory of pangenesis

Charles Darwin (1868). *The Variation of Animals and Plants under Domestication*. London: John Murray.

- Darwin realises that a theory of heredity is indispensable to his theory of evolution.
- His theory of pangenesis, a developmental theory of heredity, is hardly different from those of Buffon and indeed Hippocrates: minute particles called 'gemmules' are shed from all cells in an organism, circulate throughout the body to congregate in the gonads, the hormone-producing glads of sexually reproducing organisms.
- These gemmules participate in the construction of the organism of the offspring.
- Although this theory is a complete failure—it contradicts cytological evidence (e.g. produced by his cousin, Francis Galton) and is incompatible with other theories in biology—it opens a route to improved theories, e.g. by August Weismann and Hugo De Vries, which in turn lead to modern genetics.

Do smartphones give our thumbs superpowers?

Web links for the original study and the press release by U Fribourg:

https://pubmed.ncbi.nlm.nih.gov/25542777/
https://www.unifr.ch/scimed/en/info/news/13642/

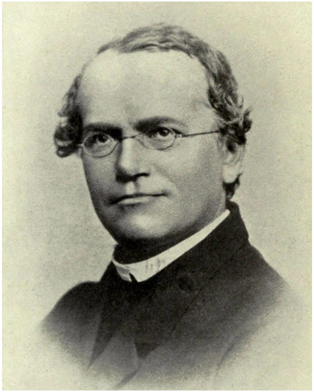
- According to a recent study (of researchers at U Fribourg and U Zürich and ETH Zürich), the frequent use of touchscreen reshapes sensory processing in our brains and the sensitivity in our thumbs. And may make our thumbs stronger and more agile...

Question:

Are such acquired characteristics or physical changes transmitted to progeny?

- Lamarckianism: yes.
- Darwin's theory of pangenesis: yes
- Alfred Russel Wallace (1823-1913): decidedly no ⇒ 'neo-Darwinism'
- Today: not so clear anymore

Gregor Mendel (1822-1884)

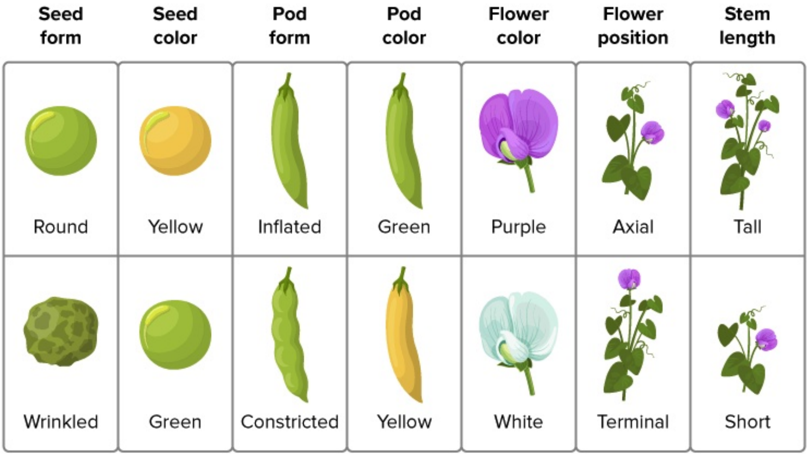


- Austrian-Czech biologist, meteorologist, mathematician, and Augustinian friar (and later abbot)
- trained in natural science (particularly physics) and mathematics at U Vienna, uses statistics, combinatorial mathematics in breeding experiments of pea plants, conducted between 1856 and 1863
- chooses to work with seven discrete characteristics of pea plants (rather than continuously varying ones): plant height, pod shape and colour, seed shape and colour, and flower position and colour

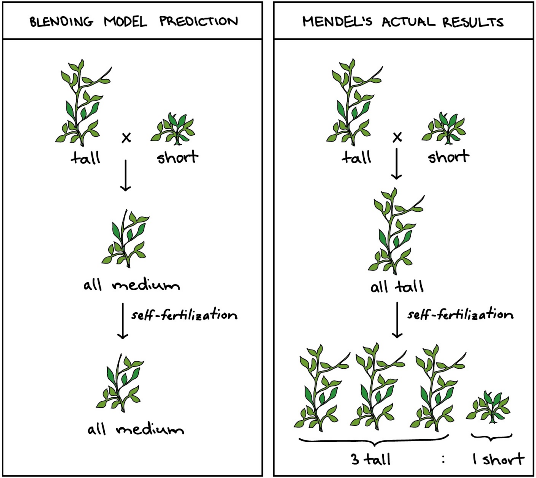
Gregor Mendel (1866). Versuche über Pflanzen-Hybride. *Verhandlungen des Naturforschenden Vereines in Brünn* 4, 3-47.

Mendel's pea plant experiment

Each of the seven characteristics take one of two determinate expressions ('phenotypes'):



- Mendel avoided the self-pollination of the pea plants and cross-bred them first, to create 'hybrids', and studied the prevalence of the two phenotypes in each subsequent generation.

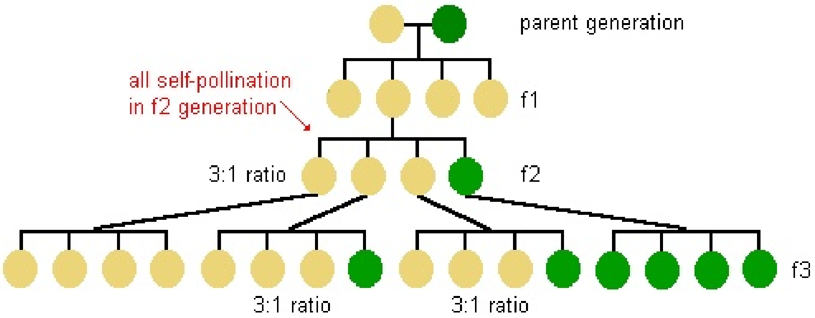


- The results actually looked more like this:

F_1 Crosses for Seven Charecters In Pea Plants

Character	Dominant Trait × Recessive Trait		F_2 Generation Dominant: Recessive	Ratio
Flower Color	Purple	White	705:224	3.15:1
Seed Color and Seed Shape	Green	Yellow	6,022:2,001	3.01:1
	Round	Wrinkled	5,474:1,850	2.96:1
Pod Color and Pod Shape	Green	Yellow	428:152	2.82:1
	Inflated	Constricted	882:299	2.95:1
Flower Position and Stem length	Axial	Terminal	651:207	3.14:1
	Tall	Dwarf	787:277	2.84:1

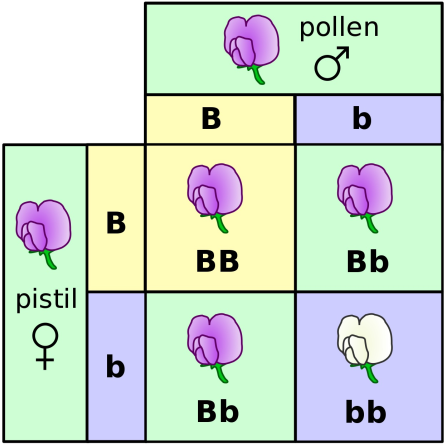
P-, F1-, F2-, and F3-generation



Explaining the results

- Mendel first recognized that for each pair of expressions of the same trait, one was dominant, the other recessive (his new terms).
- He inferred that there must be invisible 'factors' (now called 'genes'), which predictably acted to produce the phenotypes.
- The distinction between phenotypes (observable traits) and genotypes (an organism's hereditary information) was introduced by Wilhelm Johannsen in 1911.
- Using these concepts not yet available to Mendel, we see that the genotypes of the plants in the P-generation are 'homozygous' (i.e., both alleles are the same), using uppercase letters for the dominant trait and lowercase for the recessive one: AA and aa.
- (An allele is one of two or more possible versions of genetic information at a given genomic location. An organism inherits two alleles, one from each parent.)
- In F1, all plants are 'heterozygous' (the two alleles are different), i.e., all are Aa.
- In F2, combinatorics gives four possibilities:

Explaining the ratio of phenotypes in F2 using a ‘Punnett square’



Exercise:

How will the phenotypes and genotypes of plants in F3 look like, if we let them self-pollinate?

Mendel's laws of heredity (or 'rules', or 'principles')
(in contemporary terms)

Source: **Wikipedia**, https://en.wikipedia.org/wiki/Mendelian_inheritance

Law (Dominance and uniformity)

Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.

Law (Segregation)

During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.

Law (Independent assortment)

Genes of different traits can segregate independently during the formation of gametes.

Discussion

- Initially overlooked, Mendel's work was rediscovered in 1900 and spurred the development of modern genetics.
- Today we know that inheritance is often much messier than in the clean cases Mendel discovered, e.g. because many phenotypical traits are not controlled by single genes ('non-Mendelian inheritance').
- Two innovations of Mendel's are particularly important:
  1. He shows the possibility of establishing laws of heredity without knowing the embryological mechanisms responsible for character formation.
  2. By carving up the organism into discrete characteristics, he theorized on a level of organisation distinct from other levels important in biology at the time, such as tissues and cells.

The modern synthesis

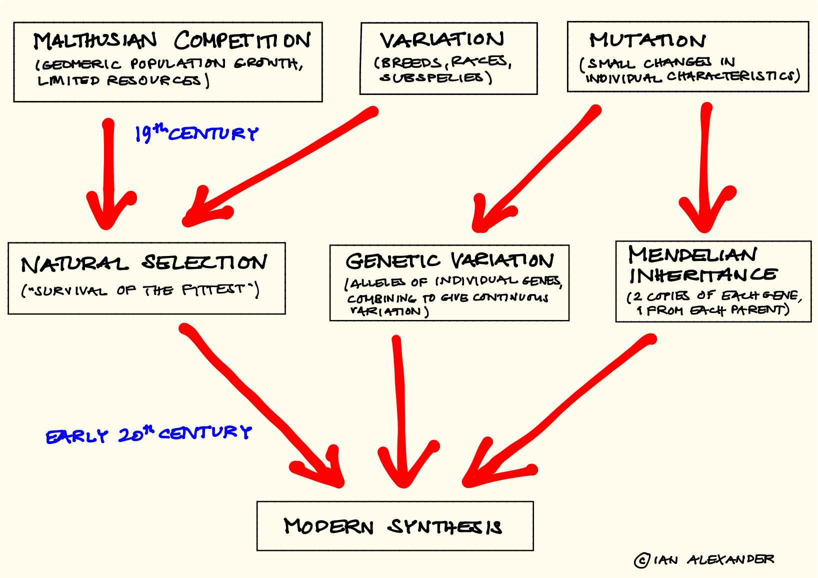
Characterisation (Modern synthese)

Coined by Julian Huxley in a 1942 popular science book on evolution, the 'modern synthesis' encompasses the main points of Darwin's theory of evolution, Mendel's ideas on heredity, as well as ideas from population genetics into a joint framework in first few decades of the 20th century.

The modern synthesis embraces the following components as central to biological theory:

1. Mutation: undirected source of random variation, producing new genotypes
2. Recombination: undirected, random variation in recombination or fertilisation
3. Natural selection: the only direction-giving factor, enabling adaptations to environment, guiding evolutionary changes in the gene pool
4. Reproductive isolation: limits the direction in which selection guides population, making divergence irreversible in sexual organisms

The modern synthesis: overview



The modern synthesis: contributing developments

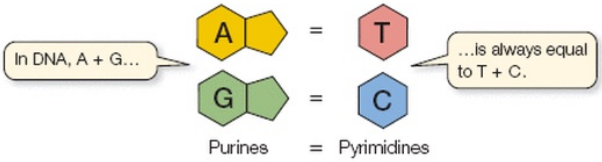
- 1905: William Bateson coins the term 'genetics'
- 1908: G H Hardy and Wilhelm Weinberg propose Hardy-Weinberg equilibrium model (describes frequencies of alleles in gene pool of population)
- 1909: Wilhelm Johannsen coins term 'gene'
- 1910: Thomas Hunt Morgan demonstrates that genes reside on chromosomes (based on work on *Drosophila melanogaster*)
- 1912: Morgan shows that mutations increase genetic variation in population, rather than creating new species
- 1900-1918: mutationists like de Vries and Bateson (evolution is driven by mutation) vigorously debates the biometricians around Karl Pearson and Walter Weldon (variation is continuous, not discrete like mutationism suggests)
- by 1918: Bateson, de Vries, Morgan, Punnett formed a synthesis of Mendelianism and mutationism

The modern synthesis: contributing developments

- 1918: Ronald Fisher clearly states modern synthesis by combining ideas of evolution, genetics, and—importantly—population genetics
- 1920s: JBS Haldane analyzes concrete examples of natural selection—famously the evolution of industrial melanism in peppered moths in England
- 1930: Gavin de Beer contributes developmental considerations from embryology
- 1932: Sewall Wright introduces the concept of 'adaptive landscape', where in general mutations, cross-breeding, genetic drift move population away from adaptive peaks, but may occasionally open the path to higher optima
- 1937: Theodosius Dobzhansky's work in evolutionary genetics bridges gap between population geneticists and field naturalists
- 1942: Julian Huxley promotes his synthetic point of view, bringing together ideas from genetics, developmental biology, ecology, systematics, palaentology, cytology, and the mathematical analysis of biology, and particularly of evolution

The molecularisation of biology

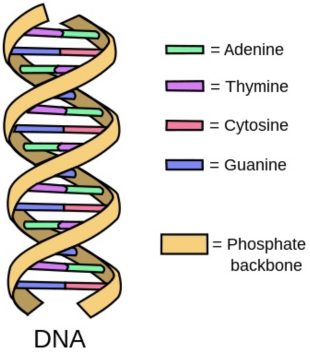
- In the 1940s, it becomes clear that it will be molecular genetics, which identifies the genetic material: the Avery-MacLeod-McCarthy experiment isolates deoxyribonucleic acid (DNA) as the carrier of genetic information; in 1952, the Hershey-Chase experiment proves the genetic information in phages to be DNA.
- Also in the 1940s, Barbara McClintock discovers mobile genetic elements (such as 'transposons').
- In 1950, Erwin Chargaff finds that in DNA, (1) the amount of guanine (G) and of cytosine (C) are the same, (2) The amount of adenine (A) and thymine (T) are also the same, and (3) the ratio of pyrimidines (G, A) to purines (C, T) is 1:1, i.e., $A + G = T + C$ ('Chargaff's rules')



The double-helix structure of the DNA

- In 1952, Rosalind Franklin's student Raymond Gosling takes the first X-ray diffraction image of DNA.
- In 1953, James Watson, Francis Crick, and Rosalind Franklin show that the DNA has the structure of a double helix.

The double-helix structure of the DNA



The structure of DNA

Nucleotides in a single strand of DNA are covalently attached to each other in a linear fashion. The backbone of the helix is composed of a sugar phosphate, the inside of the helix consists of the nucleotide bases which hold to the two strands together by hydrogen bonding (C-to-G and A-to-T pairing). This structure immediately suggests how the gene duplicates itself (at least partly). None of this delivers a mechanism of gene expression.

The central dogma

Francis H Crick (1958). On protein synthesis. In F. K. Sanders (ed.), *Symposia of the Society for Experimental Biology*. Cambridge University Press, 138-163.

The central dogma of molecular biology

The Central Dogma [...] states that once 'information' has passed into protein it cannot get out again. In more detail, the transfer of information from nucleic acid to nucleic acid, or from nucleic acid to protein may be possible, but transfer from protein to protein, or from protein to nucleic acid is impossible. Information here means the precise determination of sequence, either of bases in the nucleic acid or of amino acid residues in the protein. (Crick 1958, 153; emphases in original)