Genome 453 J. Felsenstein
Evolutionary Genetics Autumn, 2015

Outline of lectures 1-3

History of genetics in evolution

1. History has a persistent influence in biology. In a physics course, they do not teach it by first going over outdated ideas such as the caloric or the ether. But in biology the phenomena are so complex, and the understanding of them is at an early stage, that old ideas can persist and distort our current understanding more than they do in other fields. To get some sense of these influences we need to look back.

2. Monster movies are an amusing example of the survival of Victorian ideas about evolution (e.g. *The Lost World* by Arthur Conan Doyle, where explorers find dinosaurs on a plateau in the Amazon. The plateaus really are there but the dinosaurs aren't). This echos pre-evolutionary insistence that nothing can go extinct, but can always be found surviving somewhere, because surely a Creator would not allow his works to be lost. Generally a recent movie is a remake of a '50s version, which was based on a '20s silent film, which was based on a novel from at least 30 years before that (and whose author's exposure to biology was even earlier).

3. We'll start with systematics, the understanding of how natural diversity is arranged. Genetics comes into the story only later.

4. Aristotle. Categorized natural entities into "genus" and "species" (and did this not just for living things). This way of thinking, that real examples were imperfect reflections of ideal types, and that there were natural groups of entities, was a theme in the work of Aristotle's predecessors Socrates and Plato.

5. This was typological thinking – it assumed that the real organisms were imperfect examples of idealized "types". This was the dominant view through the Middle Ages, with people believing that Aristotle was correct by definition, and the medieval Church enforcing this view.

6. The Great Chain of Being. A linear order of entities from rocks up to worms and on up to us (and on to angels). Influential to this day when people think of "higher" and "lower" species. It is not necessarily an evolutionary view, as the linear order was originally thought of as static and divinely ordained. It goes back to the ancient Greeks.

7. (John Greene's book *The Death of Adam* is a very good account of this). From the 1500s on, developments in astronomy, anthropology, geology, and linguistics led to people being more ready to consider evolutionary ideas. Especially after the success of Isaac Newton's laws of motion in explaining orbits in astronomy, people became interested in simple laws

that could generate natural phenomena, rather than look for arbitrary divine patterns (such as having planets arranged on rotating celestial crystal spheres in a neat geometric arrangement).

8. As Europeans explored distant continents from the 1500s on, they began to report on the animals and plants that they found and send back specimens. This complicated the understanding of natural history. How to arrange all of these organisms?

9. Carl Linnæus (Karl von Linné) (usually called by his Latin name: Carolus Linnaeus). Swedish botanist of the mid-1700s. Made classifications of animals and plants using hierarchical classification with groups within groups (he also introduced the "type specimen" system, and codified binomial nomenclature). The system was presented as disclosing the true (static) order of nature as laid down at creation. In Linnæus's view he had just happened to be the one who discerned the true plan in the mind of God (Linnæus was not given to humility or modesty). However, he did ultimately begin to wonder whether each species was really created separately.

10. Linnæus's scheme was hierarchical, with groups within groups, and he gave names to levels (using Aristotle's terms "genus" and "species" as two of them). The binomial system of naming was used, calling each species by its genus and species name in Latin, instead of using the longer Latin phrases that had been common earlier, which were more elaborate descriptions like "big-grayish-brown-common-thrush-with-a-red-breast". Thus the American robin would be *Turdus migratorius*, with just those two words.

11. His system did so well that it became widely used, as it succeeded in summarizing biological diversity better than many other systems present at the time, which were based on arbitrary geometric or numerological schemes (everything coming in threes or being arranged in triangles, for example).

12. Classification being hierarchical fits well with organisms coming from a branching genealogy of lineages, so it suggests evolution as the cause.

13. If the groups we made in a classification system were entirely genealogical (so that each group consisted of a branch of the tree and all its descendants – a *monophyletic* group), then we would get a hierarchical classification system that was predicted by the phylogeny (evolutionary tree). Many textbook writers unthinkingly assume that this is exactly the kind of classification system we have had. The success of hierarchical classification then becomes a simple, neat story. But this isn't quite the kind of classification system we have had. The commonly used classification system in the recent past has been nearly but not quite genealogical.

14. The Linnean classification of organisms that has been in use most of the time since Linnæus has many groups that are not monophyletic. (A monophyletic group can also be defined as one that has its own common ancestor which is not the ancestor of anything else under discussion). Within the vertebrates, groups like Osteichthyes (bony fishes),

and Reptilia (reptiles) are not monophyletic (as we tetrapods are also descendants of the common ancestor of Osteichthyes but we're not in that group, and as the mammals and birds are also descendants of the common ancestor of reptiles but they do not get called reptiles). Since the 1960s there has been a trend away from this traditional classification, toward a purely monophyletic classification system, called "phylogenetic systematics". Most systematists would now not make a higher group called Reptiles, but would make one which has (for living species) the groups: amniotes (birds, mammals and reptiles) and divide it into turtles, mammals, crocodiles-plus-birds, and snakes-plus-lizards.

15. George-Louis Leclerc, Comte de Buffon (died 1788). Author of the first major account of natural history *Historie Naturelle*. Head of the Royal Botanical Garden in Paris. He described animal species as being graded into each other along a continuum, a version of the Great Chain of Being. But he also said that organisms changed and environment affected this. He primarily envisaged change by degeneration. (He also concluded that the earth was much older than 6,000 years). Did not give much of a mechanism for this evolutionary change.

16. Geologists in about 1800 began to understand that time was quite deep, that the Earth was much more than 6,000 years old. Starting in about 1700, they began to understand that fossils were remains of living organisms. By the mid-1800s they were to reject the idea that there had been a global flood which laid down all the geological layers and all of the fossils. The recent book *The Rocks Don't Lie: A Geologist Investigates Noah's Flood* by UW geologist David Montgomery is an excellent and readable account of this.

17. Jean Baptiste Pierre Antoine de Monet (Chevalier de Lamarck) (1744-1829). The first true evolutionary biologist. A man whose work is treated unfairly by biologists of our generation. After the French Revolution changed the Royal Botanical Garden into a public institution, he was offered a professorship of "worms" at the Natural History Museum in Paris. Before the Revolution he had been working on botany, with the encouragement of Buffon. He began work on "worms" reluctantly (he needed the money) but soon became fascinated. He was the great pioneer of invertebrate systematics, rearranging and clarifying it greatly. He invented the terms "invertebrate" and "biology".

18. In his *Philosophie Zoologique* (1809) he held that organisms had evolved, and that the mechanism was the effects of use and disuse, passed on by inheritance of acquired characters. Lamarck argued that in trying to cope with their surroundings, organisms had to use some organs more than others. These would grow larger, and (as everyone knew) those changes would be passed on to offspring, who would have slightly larger versions of those organs, and slightly smaller versions of the ones that were not used.

19. We now know that the mechanisms that increase the size of (for example) muscles when they are used are very specific and complicated adaptations, not general properties of all organs. These changes are also not passed on to offspring.

20. He did *not* popularize the inheritance of acquired characters, which was "common knowledge" at the time. "Lamarckian inheritance" was *not* invented by Lamarck or even particularly promoted by him, as it was widely believed in by everybody at that time – he just used it in his theory.

21. Lamarck started out using a linear Great Chain of Being, but felt forced by the data to start branching it into an evolutionary tree.

22. The discovery of dramatic fossils such as mammoths, mastodons, and large extinct reptiles such as dinosaurs in the early 1800s made it clear that there were major extinct species, some of which were quite different from any living organism.

23. There were controversies between Lamarckians and others in the early 1800s partly owing to political implications of Lamarckian views in medicine. Reformers in England, France, and elsewhere used Lamarck's views to argue for reform of medical education and other institutions ("you aren't teaching the new scientific anatomy"). Etienne Geoffroy Saint-Hilaire (1772-1844) was a major supporter of Lamarck (working at the same museum) who tried to use anatomy to connect vertebrates, invertebrates.

24. Georges Cuvier (1769-1832), Geoffroy's great opponent, was also at the Natural History Museum in Paris. The great founder of comparative anatomy. Also a central figure in purging French academia, in the period after the defeat of Napoleon, of supporters of republican rather than royalist views. Cuvier debunked Geoffroy's assertions of homology rather effectively (for example Geoffroy's supposed "homologies" between legs of crustaceans and fins of fish). Lamarck's work fell into disfavor among biologists. Adrian Desmond's book *The Politics of Evolution* goes over these controversies in detail, explains how Cuvier and others played a major role in defending the establishment, and suggests that Darwin delayed publishing his work because he didn't want to be associated with the disreputable Lamarckian position in these controversies.

25. Although Cuvier was the superior anatomist, recent findings in evolution of development ("evo-devo") have verified that some of Geoffroy Saint-Hilaire's wilder speculations are actually correct.

26. Views of the unity of nature became more popular in the early 1800s. The *Naturphilosophen* were a group of Romantic philosophers (centered in Germany) who asserted a unity of all life and that different life forms were explained by different amounts of development (but not evolution) along one common course. The Romantic movement also involved romantic poets such as Wordsworth, Shelley, Byron, and Keats, and romantic composers such as Beethoven, Paganini, and Schubert.

27. One major Romantic intellectual was both a poet and a scientist: Johann Wolfgang von Goethe (1749-1832), universally acknowledged ever since then as the greatest figure in German literature, just as Shakespeare is in English literature. He was allied with the Romantic philosophers, and was also the first person to make the connection

between flower part and leaves (by a developmental argument). He invented the term "morphology". He argued that flowers arose by the same developmental pathway that leads to leaves, that it gave flowers if continued further. By insisting on a unity of nature, and common processes, the Naturphilosophen had moved away from individual special creation of individual species towards a unified process.

28. In 1831, a Scottish landowner, Patrick Matthew proposed that living things had evolved, with natural selection explaining how they came to be well-adapted. This account was buried in an appendix to Matthew's book *On Naval Timber and Arboriculture* which was seen by almost no one.

29. In 1844 a publisher, Robert Chambers, wrote an anonymous book (with numerous errors in its biology) *Vestiges of the Natural History of Creation*. It describes life as having evolved, though it does not propose any mechanism to explain why adaptations arose. The book sold well. By this period many scientists were coming to the conclusion that life had evolved, which was then called "transmutation".

30. Charles Darwin (1809-1882). In his journey on the Royal Navy survey ship the *Beagle* around South America, and then home around the world, he saw geographic distributions of similar species, as well as fossils, that convinced him that they had evolved from common ancestors. After reading Thomas Malthus's book which argued that too many people were born for all to survive, he came up with natural selection, in about 1837, as the mechanism to explain the adaptations of organisms but he delayed publishing this.

31. Ever since then, natural selection, in which adaptation affects the probability that a genetic variation gets passed on to the next generation, has been the chief (almost the only) explanation for how organisms come to be adapted so well to their surroundings.

32. Alfred Russel Wallace (1823-1913) was the co-discoverer of natural selection (1858, also after reading Malthus). He sent a letter with a paper on this to Darwin, who he knew was interested in explaining species differences. This forced Darwin to publish (originally a small paper side-by-side with Wallace's). These events are described in an episode of the PBS program *Nova* entitled *Darwin's Darkest Hour*. Darwin's book was published in 1859 and was widely influential. Later Darwin tried to explain heredity as well, less successfully. His theory of heredity was called Pangenesis (the units were *gemmules*).

33. What were the chief differences between Lamarck's theory and Darwin's theory?

    (a) Natural selection is dependent on having genetic variations in the trait. Lamarck's theory does not need to have differences among individuals (as in principle all individuals could change their characters simultaneously by use and disuse).

    (b) Natural selection results from differential survival or reproduction of the different genetic variations. Lamarck's theory does not make use of differential survival or reproduction, relying instead on (what amounts to) directed mutation.

34. It turns out that the directed mutations that Lamarck was relying on don't actually occur for a simple reason – the path from the genes to the phenotype is so complex that a change in the phenotype does not have any way to go back and bring about a corresponding change in the genes in that direction. On the other hand, the genetic variation that Darwin and Wallace replied on is widespread, and so is differential survival and reproduction.

35. Fleeming Jenkin (1867) made an incisive criticism of Darwin. A pioneering electrical engineer and buddy of the famous physicist William Thompson (Lord Kelvin). Kelvin thought he had a fatal physical objection to Darwin's work based on the length of time the sun could remain hot if it were burning fuel such as coal. He calculated that it could not be very old. It turns out that nuclear fusion within the sun creates heat, and that invalidates his calculation.

36. Jenkin had a different objection than his friend Kelvin. It was based on blending inheritance. In blending inheritance, which was commonly assumed by everyone to be true, the offspring's hereditary substances ("blood", as in horse breeding today) was a mixture of the parent's, and hence intermediate between theirs. This averaging would reduce the variation in the population, as blending of phenotypes would eliminate half of the variance of the population every generation. That reduction of variation would cause progress to stall very quickly. Kelvin encouraged Jenkin to publish this. The criticism worried Darwin, who coped by increasing his emphasis on inheritance of acquired characters as a source of variability.

37. Gregor Mendel (1822-1884). Often called an "Austrian monk", he was actually a monk who was a science teacher at a Church secondary school in what is now Brno in the Czech Republic, but was then Brünn in the Austro-Hungarian empire. His school was the most prestigious in Moravia, a province where there was a lot of interest in plant hybridization. (The famous early twentieth-century composer Leos Janaček was a student of Mendel's and, as a young man, was the musician who played the organ at Mendel's funeral).

38. Under Mendelian inheritance (1864) there is no "blending" of different alleles. The variability does not disappear as it does with blending inheritance. A heterozygote Aa does not produce gametes with medium-sized A's in them, but instead half A and half a gametes. Mendel's work was cut short when his abbot, who had been supportive of his scientific work, died and, tragically, Mendel was chosen to be the new abbott. When he died he was a famous and beloved local figure but his scientific work languished almost unknown in minor journals.

39. In the 1890s there was increased interest in figuring out how inheritance worked. The chromosomes were known, and their segregation had been observed by cytologists such as August Weismann. There were even hints from work by the cytologist and developmentalist Theodor Boveri that improper segregation of chromosomes might cause developmental problems.

40. Mendel's laws were rediscovered by Karl Correns, Hugo de Vries, and Erich von Tschermak-Seysenegg in 1900. Maybe only Correns really discovered them independently, the others from finding Mendel's paper first (though that is not what they claimed).

41. In the meantime, although many biologists had accepted the reality of evolution (in the sense of "descent with modification" and common ancestry) after Darwin, the succeeding generation was often doubtful that natural selection was the explanation for adaptations. In that period, which has more recently been called (by historian Peter Bowler) "the eclipse of Darwinism" other mechanisms such as Lamarckism or orthogenesis were more often invoked.

42. The "Biometricians" (Francis Galton and Karl Pearson) from the 1880s through about 1920 put forward statistical formulas predicting the distribution of offspring phenotypes. They developed many regression and correlation methods which had a great effect on the development of statistics. They felt that they had put forward a scientific account of heredity, even though they had not identified structures within the cell that carried the hereditary influences. They argued that the Mendelians were concentrating on bizarre defects that had nothing to do with ordinary traits.

43. There was then controversy between the Biometricians and the Mendelians over evolution. Some Mendelians put forward mutation (discovered and named by De Vries) as the main mechanism of evolution as against natural selection. They ignored the fact that mutation without natural selection would not be able to explain the directionality of adaptation.

44. Population genetics theory was developed in the 1910s-1940s largely by three people: R. A. Fisher (1890-1962), Sewall Wright (1889-1988 (!)) and J. B. S. Haldane (1892-1964). Fisher also was the major figure in the development of modern mathematical statistics. Wright carried out years of work on the "physiological genetics" of guinea pig coat colors, and many of his graduate students became noted mammalian geneticists. Haldane made contributions to many fields, including the physiology of diving, and produced popular writings on science, but did most of his work in human genetics.

45. Fisher developed the theory of variance components and correlations among relatives in quantitative genetics (among many other things).

46. Wright developed inbreeding coefficients and the methods of calculating them. He and Fisher both developed the theory explaining what happens when genetic drift and other evolutionary forces interact in small populations.

47. Haldane published a series of papers in the 1920s setting forth the equations for gene frequency change in natural selection in many cases.

48. Between them they dominated the field well into the 1950s, when a new generation of theorists such as James Crow, Motoo Kimura, Richard Lewontin, Oscar Kempthorne, and C. Clark Cockerham emerged.

49. Fisher's, Wright's, and Haldane's work laid out the theoretical basis for this "Modern Synthesis", the combination of Mendelian genetics and evolutionary theory that began to emerge in the 1920s and was widely developed, applied and publicized in the 1940s in books by zoologists and botanists applying the theory to systematics and paleontology, notably Theodosius Dobzhansky, Ernst Mayr, George Gaylord Simpson, Julian Huxley, and G. Ledyard Stebbins (all but the last one published by Columbia University Press!).

50. A major effect of the Modern Synthesis was to vindicate natural selection as the mechanism explaining adaptation, and to undercut support of Lamarckism and orthogenesis.

51. This Modern Synthesis was the combination of genetics with evolution. It enabled quantitative arguments to be made about how fast natural selection would change phenotypes (if you knew their genetic basis), and how strong forces such as genetic drift, gene flow due to migration, and mutation would be. This will be the subject of the next block of lectures in this course.

Life	**A Timeline**	Life sciences
	1700	
	1735	Linnæus: editions of *Systema Naturae*
	–1759	
	1749	Buffon: *Histoire Naturelle, Générale et Particuliére*
	–1788	
US founded	1776	
French Revolution	1789	
	1790	Goethe: *Metamorphosis of Plants*
	1800	
steamships	1809	Lamarck: *Philosophie Zoologique*
Defeat of Napolean	1815	
railroads	1830	Debates between Cuvier and Saint-Hilaire
telegraph	1844	Chambers: *Vestiges of the Natural History of Creation*
	1859	Darwin: *Origin of Species*
U. S. Civil War starts	1861	
	1866	Mendel publishes his papers
	1889	Galton: *Natural Inheritance*
automobiles		
	1900	Rediscovery of Mendel
airplanes	1903	First papers on population genetics
World War I starts	1914	
electronics	1918	Fisher's quantitative genetics paper
	1921	Wright's papers on inbreeding theory
	1924	Haldane's first selection theory paper
Great Depression starts	1929	
	1930	Fisher: *Genetical Theory of Natural Selection*
	1931	Wright: paper: "Evolution in mendelian populations"
	1937	Dobzhansky: *Genetics and the Origin of Species*
World War II starts	1939	
large rockets, computers		
	1959	Darwin celebrations celebrate Modern Synthesis too
	1963	Protein sequences in different species compared
	1966	Lots of molecular polymorphisms found
	1979	DNA sequencing becomes possible
	1984	PCR reaction discovered
Internet widens	1988	Genbank DNA sequence database
the Web	1995	Comparative genomics becoming possible
	2000	
	2013	You take this class