Evolution and the Biological Sciences Since Darwin
Denis Alexander
Dorchester Lecture, 14 November 2009

DNA is the most amazing molecule in the world. Of course Darwin in the 19th century knew nothing about DNA, and in many ways the history of evolution since Darwin is like a long bridge bringing us all the way from his great theory of natural selection to our 21st century world of DNA and genetics.

DNA in the test-tube looks like a really boring little bit of squidgy white plastic. But it contains the language of life, the set of recipes that provides all living organisms with their basic structures and ways of living in the world.

DNA is found in every cell of our bodies, except our red blood cells. Each of the approximately 10^{13} cells in our bodies contains an astonishing six foot length of DNA packaged with proteins to form 23 pairs of chromosomes. That's really difficult to believe, because cells are very small: typically human cells are only about 10 microns in diameter, which means you can easily line up 100 cells across the top of a pin-head. In fact if all the tightly-packed DNA in all the 10^{13} cells in a single human being were stretched out fully, it could go round the equator 456,000 times! As millions of our cells divide every second, each individual cell produces thousands of miles of newly copied DNA every minute. We are all walking photocopying machines, but fortunately we don't have to think about it – DNA replication is on automatic.

Evolutionary theory has come a long way since Darwin and in its modern form involves two key steps which operate together to produce new forms of life. In step one, variation is introduced into the genomes of living organisms. The genome refers to the sum total of all the genetic information contained in the DNA of a single living thing. New variant DNA can be generated by more than a dozen different mechanisms, all of which are random in the sense that their occurrence is not connected to any particular requirement of the organism.

Step 2 is the one that Darwin discovered, ‘natural selection’, whereby the variant organisms produced by the variant genomes are tested out in the workshop of life. The variant organisms that are most successful in ‘being selected’ to pass on their genomes to subsequent generations will do so because they are best adapted for particular environments. The key measure is ‘reproductive success’: how many copies of these particular sets of variant genomes are passed on to the next and succeeding generations?

But in 1859 when Darwin published his great work *On the Origin of Species*, the mechanism of inheritance was completely unknown. So how did we get from there to here?

Darwin set out his own views on inheritance not in the *Origin of Species*, but in the second volume of his 1868 work, the *Variation of Plants and Animals under Domestication*. There Darwin presented his theory of Pangenesis. The idea was that multitudes of little physical units, ‘gemmules’ as he called them, were produced from each part of the body and ‘packaged’ in some way in the eggs and sperm, or pollen in the case of plants, from there to be passed on to the offspring. Darwin believed, like his forerunner Jean-Baptiste Lamarck (1744-1829), in the inheritance of acquired characteristics: the external environment could modify the inheritable gemmules. He also thought that inheritance resulted in a ‘blending’ of the characteristics of both parents, with the ‘gemmules’ playing a key role in the blending process. So Darwin himself was not actually a strict Darwinian – he believed in the inheritance of acquired characteristics.

But the problem for evolution, of course, is that if offspring inherit a blend of their parents’ traits, then even the most beneficial variation in any one individual eventually disappears through generations of breeding with normal types. Under any theory of blended inheritance, individual variations are “swamped” by the larger population.

So the other Big Idea that eventually became incorporated into our current theory of evolution came not from Darwin, but from a Moravian monk named Gregor Mendel (1822-1884). Ironically, at the very time that Darwin was puzzling over the question of inheritance and proposing his theory of Pangenesis, which was in fact wrong, Mendel had not only carried out the key experiments that would eventually lay the foundation of modern genetics, but also published his results in 1866. But Darwin knew nothing of his work.

Mendel was the only son of a peasant farmer. He failed his exam to obtain a teaching certificate, although by all accounts he turned out to be a great teacher. In 1843 he gained admission to the wealthy and scholarly St. Thomas Monastery of the Augustinian Order near the Moravian capital of Brunn where he remained for the rest of his life, eventually becoming its Abbott, and so Mendel had the great advantage that he had access to the garden of the monastery where he carried out his famous plant breeding experiments during the period 1856-1863, exactly the period of Darwin's publication of *On the Origin of Species*.

Mendel's experiments probably sound pretty boring to us know, because essentially they consisted of "growing, crossbreeding, observing, sorting and counting nearly thirty thousand pea plants of various carefully selected varieties" and tracking their pattern of inheritance. Yet his findings eventually changed our whole understanding of inheritance. Like much successful work in science, his experiments involved the right choice of materials to work with, a lot of patience, a sharp eye for detail, and smart mathematical skills. Mendel also had a great love of fine food and good cigars, both reportedly consumed in prodigious quantities, so no doubt that helped with the analysis.

And essentially what Mendel found was that the inheritance of characteristics was particulate. If he crossed pea-strains which were either tall or short, or that had either wrinkled or smooth seeds, then their offspring were either tall or short, not somewhere in between. Or they had seeds that were either wrinkled or smooth, not a blending of both. So Darwin’s blending theory of inheritance was wrong, but of course he never knew it because he never saw Mendel’s results.

Mendel also noticed that some characteristics of his peas were ‘dominant’ and some were ‘recessive’. When he crossed the tall pea plants with the short pea plants, then the ratio of tall to short plants in the next generation came to approximately 3:1: tall was a dominant trait, and short was a recessive trait. But if he crossed tall with tall then he got only tall, and likewise short with short yielded only short plants. Experiments with peas having multiple different characters suggested that each trait, e.g. height, color, texture, was inherited independently through subsequent generations.

These were key findings, we now know with the benefit of hindsight, but they were published in an obscure journal, buried away and largely forgotten for a period of 35 years.

Soon after Mendel’s publication, in 1869, the Swiss physician Friedrich Miescher discovered a weak acid in the nuclei of white blood cells, so he called it “nuclein”. He isolated his white blood cells from the pus on bandages collected from the local hospital in Tübingen where he was then working. Such is the dedication of scientists. It would be nearly a century until that substance, deoxyribonucleic acid (DNA), was identified as the molecule responsible for Mendel’s results. In the meanwhile, the mystery of inheritance continued to be a topic of curiosity for many.

Darwin died in 1882 and was buried in Westminster Abbey as a great British scientific hero with great pomp, the famous iconic scientist. But ironically for the next 50 years his theory of natural selection actually declined in popularity, and by 1900 some biologists were talking about the demise of Darwinism.

In 1903, the German botanist Eberhard Dennert proclaimed, “we are now standing by the death-bed of Darwinism, and making ready to send the friends of the patient a little money to insure a decent burial of the remains.” Evolution as an idea remained immensely widespread and popular, and was greatly strengthened by new fossil discoveries that I'm sure we'll be hearing more about from Simon Conway Morris later in the day - but how evolution actually happened was widely disputed. The significance of Mendel's key results remained unknown. Lamarckian evolution remained popular, the inheritance of acquired characteristics, because the sudden jumps that were observed in the fossil record seemed better explained in this way.

Even great enthusiasts for evolution, such as Thomas Henry Huxley, never really accepted slow, incremental, natural selection as the mechanism for evolution, much preferring the idea of big jumps or so-called saltations. Also Huxley was suspicious of the role of chance in generating variant phenotypes of organisms upon which natural selection then acted. For Huxley, chance sounded like an opening for God's special creation, whereas he wanted to see evolution as emerging out of natural scientific laws. So its ironic that in his day Huxley resisted the idea of chance, because he thought that it had theological overtones, whereas creationists today resist the idea of chance because they think that it has atheistic overtones. Often people interpret essentially the same data in quite different ways depending on their historical and cultural context.

The great Victorian idea of progress also seemed to fit better with Lamarckian ideas. Surely it is more rational, so the argument went, that the useful things that animals learnt during their lifetimes should be passed on to their offspring. Why waste what you've learnt – let it benefit a future generation. This perhaps illustrates the danger of imposing our own political or social ideologies upon the data of science – we should let the data speak for itself.

Another factor that encouraged the popularity of Lamarckian evolution was that the earth was actually getting younger during the latter decades of the 19th century. By the early decades of the 19th century everyone knew that the earth was really old, but there was still much discussion about exactly how old. Along comes William Thompson, the great physicist, later to become Lord Kelvin, who used his law of cooling to estimate (in 1862) that the world was only 20-40 million years old, far less than had previously been thought, and seemingly not long enough to allow natural selection to occur by acting on random variations in organisms. So Lamarckian evolution provided a convenient mechanism for speeding things up. Of course we now know that Lord Kelvin's estimates of the age of the earth were wrong, because he didn't know about the heat generated by the radiation in the earth's core, which changes the situation completely, and the earth's age is of course now estimated to be 4.6 billion years.

Meanwhile, increasingly powerful microscopes were being used by biologists to good effect. August Weismann (1834-1914) made the important observation, published in 1893, that there were two different types of cells in the body, the 'somatic cells' that made up the bulk of the body and did not pass on their information to succeeding generations, and the 'germ cells' (the egg and sperm cells) that did pass on information. Moreover, he noted that the two types of cell replicated in different ways. Somatic cells came from germ cells, but not vice-versa, rendering the inheritance of acquired characteristics impossible. As such, Weismann's finding contradicted the theory of Pangenesis. To make quite sure, he chopped the tails off fifteen hundred rats, repeatedly over 20 generations, and reported that no rat was ever born in consequence without a tail. It really did seem that the property of being a tailless rat was not inherited. So…Lamarck was wrong.

Finally at the turn of the 19th century Mendel's seminal work was rediscovered and extended by three fellow plant breeders: Hugo de Vries (1848-1935) Professor of Botany at the University of Amsterdam, son of a Mennonite deacon who later became Prime Minister of the Netherlands; Carl Correns (1864-1933) in Tübingen, orphaned at an early age, raised by an Aunt in Switzerland, who was encouraged to study botany by a correspondent of Mendel; and Erik von Tschermak (1871-1962) in Ghent, whose grandfather had taught Mendel during his time in Vienna. All three had been using different plant breeding systems to investigate inheritance, and each confirmed a 3:1 ratio between dominant and recessive traits in his own system.

With varying degrees of speed and enthusiasm, they recognized that their work had been foreshadowed in Mendel's work, and together they helped to launch Mendel to the central place that he still enjoys in the history of genetics.

All these results provided striking confirmation of the particulate theory of inheritance. In 1909 the Danish botanist Wilhelm L. Johannsen (1857-1927) introduced the term 'gene' to replace older terms like factor, trait, and character: the word was deliberately chosen to contrast with 'pangene', the older term associated with the now discredited ideas of Pangenesis.

Now you might have thought that once the Mendelian laws of inheritance had been rediscovered, then bingo they would be brought together with the idea of natural selection to quickly generate the kind of theory of evolution that we have today. But that didn't happen at all. During the early decades of the 20th century, Mendelism as it became called, the pattern of inheritance that Mendel had originally discovered, was actually seen as a <u>rival</u> to the theory of natural selection. How come?

Well the answer is that the particulate idea of inheritance readily lent itself to the idea that changes in evolution happened rather suddenly. The idea of 'saltations', sudden jumps, soon became identified with the idea of 'mutations', a term which at the beginning had a quite different meaning from the way we use the term today to refer to changes in physical genes contained within DNA. In the early 19th century the term referred much more to the apparently sudden appearance of different varieties of plants, so that speciation itself could be quite sudden.

For example, the botanist Hugo De Vries made extensive studies of the evening primrose, and observed that it seemed able to sprout new, differently colored varieties at random. The so-called 'mutation theory' of de Vries became the most popular theory of evolution in the early decades of the 20th century. And it seemed to many biologists to make Darwinian natural selection much less important, or even completely superfluous. If new varieties or mutations could come about suddenly, then why did you really need natural selection because the new variety or species had got there all in one jump? Other biologists, and de Vries himself was one of them, still retained a role for natural selection to allow the survival of the best mutational varieties that arose, but its role was deemed pretty minor. Instead it was just thought that species occasionally went through rapid bouts of mutation in which they sort of threw out a whole selection of new varieties, and this also then explained, so it was thought, the gaps in the fossil record.

Now what all this shows is that it's not a good idea to base general conclusions in biology on the study of just one or a few species. And by 1920 it became clear that actually the evening primrose that de Vries had been studying for so long was a complex hybrid, and so his apparently new forms of primrose were not new forms of mutation at all, but simply recombinations of existing characteristics.

Meanwhile genetic studies were being extended for the first time from plants to animals, and the key scientist who carried out this work was Thomas Hunt Morgan, the first American biologist to receive the Nobel Prize. Now ironically at the start Morgan used mutation theory to make a vitriolic attack upon Darwinian natural selection. In his book *Evolution and Adaptation* (1903) Morgan dismissed both the idea of natural selection and the idea that evolution could be driven by the ideas of adaptation. But it was Morgan's work that was soon to help lay the foundations of modern biology and our contemporary theory of evolution.

This happened because Morgan decided to shift from plants to fruit-flies, called Drosophila, as his organism for research. And geneticists have been using Drosophila ever since. "It's wonderful material", Morgan boasted in 1910, "they breed all the year round and give a new generation every 12 days". Within the first six years of his research, during which he had made his most profound discoveries, Morgan and his research team had watched more generations of fruit-flies go by than Mendel and de Vries could have seen in their peas or primroses in two centuries. His team worked in a small laboratory at Columbia University in New York, which soon became known as the "fly-room". Milk bottles filled with flies lined the desks and shelves. The stench of rotten bananas (used to feed the flies), and the ether used to anaesthetize them filled the air, together with swarms of flies that had escaped.

So what did Morgan discover? Well first that Mendel's laws of inheritance applied equally well to flies as they did to plants. After a year of breeding flies Morgan's team found their first fly mutation, a male white-eyed fly in a roomful of red-eyed flies. They then bred the male mutant with a normal, red-eyed female, and interbred their offspring. All the flies in the first generation were red-eyed, but in the next generation there was approximately one fly with the mutant white eyes compared to every three with red eyes. Morgan had demonstrated the famous 3:1 Mendelian ratio between a dominant and a recessive trait.

Soon Morgan's group discovered many more mutations, and by extensive breeding experiments during the years 1911-15 they showed that many fly traits or characteristics were linked together in their inheritance, and could be located on one of the four chromosomes that Drosophila were shown to possess by their scientific collaborator, the Belgian Franz Janssens. Out of this work came the key conclusion that genes were strung out on chromosomes, as Morgan put it: "like beads on a string". In 1915 Morgan co-authored with three other collaborators the famous book *The Mechanism of Mendelian Inheritance*, that completed a revolution in scientific thought by placing genes at the centre of biologists' ideas about heredity.

Now surely, you might have thought, Morgan would apply his brilliant new discoveries to evolutionary theory to show how genetic variation and natural selection could come together to generate a unified theory. But that didn't happen. Morgan was a reductionist laboratory-based experimentalist. He was very suspicious of theorizing and of speculating. And he continued to give a major role to mutations in making forward jumps in evolution, and a very minor role to natural selection. He was very focused on the flies kept in his milk-bottles in the lab, less interested in how different fly species actually behave out in the wild. He continued to minimize the role of adaptation in evolutionary change, since most of the mutations observed in the laboratory seemed to be negative in their effects anyway.

But without ever seeing a gene, by 1915 Morgan and his students had used their studies of mutant flies to establish the existence of genes, map their location on chromosomes, and elucidate the basic principles of classical genetics. That was an incredible achievement. But one person, one research team, cannot do everything.

The next key stage in the development of evolutionary ideas in biology came not from plant-breeders, nor from the fly-breeders, indeed not from the laboratory at all, but from population geneticists and mathematicians. The key question now was: how did evolution actually work in populations of living organisms out in the wild? There were three key figures associated with this shift in thinking, and these were the mystic British communist J.B.S. Haldane, the Anglican British eugenicist R.A Fisher, and the American Sewall Wright, the son of first cousins, who became a professor at the University of Chicago.

And for the first time they started analysing mathematically the consequences for populations of genetic variation. How do gene frequencies change in populations under evolutionary forces? And the four factors that they realised were important were genetic drift, gene flow, mutation, and natural selection. So unused were biologists at this time to mathematical treatments of their subject that Fisher’s first paper submitted to the journal of the London Royal Society was turned down because no-one could understand it!

Genetic drift means the change in the relative frequency in which a gene variant, known as an allele, occurs in a population due to random sampling and chance. The alleles in offspring are a random sample of those in the parents, and chance has a role in determining whether a given individual survives and reproduces. Imagine that you put twenty marbles in a jar to represent 20 organisms in a population. Half of them are red and half blue, and the colours correspond to two different gene alleles in the population. The offspring they reproduce for the next generation are represented in another jar. In each new generation the organisms reproduce at random. To represent this reproduction, randomly select any marble from the original jar and deposit a new marble with the same color as its "parent" in the second jar. Repeat the process until there are 20 new marbles in the second jar. The second jar will then contain a second generation of "offspring", 20 marbles of various colors. Unless the second jar contains exactly 10 red and 10 blue marbles, there will have been a purely random shift in the allele frequencies, and this will influence what happens in the next generations also.

Gene flow simply refers to the transfer of alleles of genes from one population to another in the same species. Lets imagine that two animal populations have been breeding quite separately on either side of the country. During this time they will accumulate quite different sets of allelic variants. They then migrate and mingle, and start inter-breeding again quite randomly. The transfer of variant alleles from one population to the other is then called gene flow.

Mutations now came to mean not the sudden emergence of new variations as previously, but more discrete changes in actual genes, resulting in different alleles even though chemically these changes weren’t yet understood because DNA hadn’t yet been discovered. And the role of natural selection once again began to be recognized as a powerful sieve, just as Darwin had always maintained, filtering out those sets of alleles that reduce the fitness of the organism.

And in time this combining of the ideas of genetic inheritance and variation, together with Darwinian natural selection, came to be known as the neo-Darwinian synthesis – the fusing together of the two key ideas in evolutionary theory that have stayed with us right up to the present day – so that one useful way of summarizing evolution is by this little mantra:

Genes mutate
Individuals are selected
Populations evolve

Sewall Wright in particular introduced the idea of adaptive landscapes – picturing Darwinian fitness as being like a well adapted set of genetic variants at the top of a mountain peak, whereas the valleys represent genomes that produced less fit organisms. Fitness here doesn't refer to what results when you go to the gym, but rather a short-hand way of expressing reproductive success. Organisms well fitted to their environment are those that generate plenty of progeny in succeeding generations.

Big ideas in science often benefit from scientists who are good at communicating the key results to a wider public, and the unusual J.B.S.Haldane played precisely such a role. Haldane has been described as "independent, nasty, brilliant, funny and totally one of a kind". He learned Mendelian genetics while still a boy by breeding guinea pigs and often served as one himself when he helped his father, who was professor of genetics at University College London. In one childhood episode, his father made him recite a long Shakespearean speech in the depths of a mine shaft to demonstrate the effects of rising gases. When the gasping boy finally fell to the floor, he found he could breathe the air there, a lesson that served him well later in the trenches of World War I.

Later Haldane himself quite often experimented using his own body, one time drinking a large quantity of hydrochloric acid to observe its effects on muscle action. I hasten to add that none of these experiments should be repeated by anyone here, but it's perhaps not surprising that the writer Aldous Huxley incorporated Haldane into at least one of his novels as the arch-typical eccentric scientist.

More relevant to our immediate topic is Haldane's ten highly mathematical papers published between 1924 and 1934, plus his influential book *The Causes of Evolution* (1932), in which he reestablished a central place for natural selection in the neo-Darwinian Synthesis. It's interesting that Haldane comments in his 1932 book that "Criticism of Darwinism has been so thoroughgoing that a few biologists and many laymen regard it as more or less exploded" (p. 32). This just shows how far the drift away from Darwinism had gone since 1882. But Haldane's aim was to resurrect Darwinism by showing that continuous, small-scale variation could also have a Mendelian basis and, especially, that tiny selection pressures, working in a cumulative manner on such minor variations, could effectively explain evolution.

Haldane was a theoretical biologist who never did much field-work, but he did use the famous results of the biologist Tutt on the peppered moth which had shown how increasing industrialization in Britain had led to a higher proportion of black moths that would be less visible to predators as they rested on sooty leaves. Haldane calculated that the observed increase of black moths from 1% in 1848 to 99% in 1898 required only a 50% higher survival rate of black moths over speckled ones. But if the increase was solely due to variation without selection, as the early Mendelians tended to argue, then this would require 1 in 5 moths to mutate from speckled to black an obvious impossibility.

Other influential biologists followed up in popularizing the new neo-Darwinian synthesis. Julian Huxley, brother of Aldous and grandson of Darwin's great defender, Thomas Henry Huxley, was the author of *Evolution: The Modern Synthesis* (1942), one of the most influential books on evolution in the 20th century. He carried out same famous studies on the Great Crested Grebe and on some other birds that mate for life, developing ideas that Darwin himself had originally discussed on the evolution of sexual selection. Like Haldane, Huxley was one of the biologists in the early 20th century to restore a prominent role to natural selection in the evolutionary narrative.

Other key figures who helped establish the neo-Darwinian synthesis include the Russian, later to become American, Theodosius Dobzhansky, a committed eastern Orthodox Christian who was a student of Morgan and was the one who first took genetics out to investigate natural populations of *Drosophila* in the field. The title of one of his popular papers - “Nothing in Biology Makes Sense Except in the Light of Evolution” published in 1973, has become almost a mantra in the field of evolutionary biology. It’s interesting to note how three of the great founders of the neo-Darwinian synthesis – Haldane, Fisher and Dobzhansky – represent such an interesting range in their own religious commitments. Haldane was the atheist albeit mystic-Marxist; Dobzhansky the Eastern Orthodox; Fisher a committed Anglican who sometimes preached in his College Chapel in Cambridge – a good example of how scientists of any faith or none can work together in the scientific enterprise to establish a common theory.

Ernst Mayr was another great influence on the development of evolutionary theory during the course of his long life. He died in 2005 aged 100, a year when he also published what turned out be his last scientific paper – an example to us all. Neither Darwin nor anyone else in his time knew the answer to the *species problem*: how multiple species could evolve from a single common ancestor. Ernst Mayr approached the problem with a new definition for the concept **species**. In his book *Systematics and the Origin of Species* (1942) he wrote that a species is not just a group of morphologically similar individuals, but a group that can breed only among themselves, excluding all others. When populations of organisms get isolated, the sub-populations will start to differ by genetic drift and natural selection over a period of time, and thereby evolve into new species. The most significant and rapid genetic reorganization occurs in extremely small populations that have been isolated (as on islands). Mayr called this allopatric speciation.

Whilst these great advances in evolutionary theory were being made in the 1920s, 30s and 40s, there was still a great mystery that remained: from a chemical perspective, what were genes made of? It had been realized since the work of Morgan that genes were located on chromosomes like beads strung out on a string. But where and how was the genetic information actually located? Many biologists thought that the genetic information was contained in the proteins. After all, proteins contain 20 different amino acids and each protein has a precise sequence of different amino acids, so that seemed to give plenty enough specificity for the transfer of genetic information. But there was just one problem. How could a single protein pass on its information? How could it divide?

The beginnings of the answer came in 1944 when DNA was identified as the genetic material. This key finding was carried out at the Rockefeller Institute in New York by Oswald Avery (1877-1955). Avery's research team found that the characteristics of one strain of bacteria could be transferred to another purely through DNA and not via proteins. Avery's results were initially greeted with disbelief, the world being in the turmoil of the Second World War. By the time the significance of Avery's results was fully appreciated, he was dead, and Nobel Prizes cannot be awarded posthumously. Yet Avery was entirely correct and his findings laid the groundwork for the new era of molecular biology.

The race was on to determine the structure of DNA. It was known that it contained specific sequences of the genetic alphabet known as nucleotide bases, there being only four types of nucleotide, four letters in the genetic alphabet. The question was: how were they assembled together? There were a number of different rival models. Linus Pauling preferred a triple-helix. But Jim Watson and Francis Crick based at the Cavendish Physics Laboratories in Cambridge had the huge advantage that they obtained the X-ray diffraction pattern results of DNA in advance of publication from a scientist working at Kings College London called Rosalind Franklin. Poor Franklin died at the age of only 38 from ovarian cancer, so was never able to really receive the recognition for her pioneering work at the time. But based on her results Watson and Crick set to work to build models that would satisfy the measurements that Franklin had obtained, until they finally published their famous DNA double-helical structure in Nature 1953. Their paper was barely a page long, but their double-helical model changed the face of biology. The last laconic sentence of their paper says it all: "It has not escaped our notice that [the structure] we are postulating immediately suggests a possible copying mechanism for the genetic material". Once you have a double-helix, then you have a mechanism for unzipping it and copying each strand to make two daughter molecules of DNA. Mendel's laws of inheritance finally found their chemical mechanism.

Soon the genetic code itself was broken in the 1960s, largely by the work of Sydney Brenner in Cambridge, the 64 triplet codons, consisting of three genetic letters, or nucleotide bases each, that encode the amino-acids that make up the sequence of proteins, each specific sequence giving each protein its particular properties. So now a gene became a specific sequence of nucleotides in DNA. Those sequences that encode proteins became known as 'Open Reading Frames'. Out of these advances came the so-called 'central dogma', information from DNA is transcribed into mRNA molecules and these are then translated into the amino acid sequence of the protein. Notice how the language of language has dominated this relatively new field of molecular biology, with its talk of transcription, translation, open reading frames, and so forth. It is now common to talk of the language of the gene.

So the gift that molecular biology gave to evolutionary biology was an actual set of molecular mechanisms that not only explain genetic inheritance, but also genetic variation. A huge array of mechanisms account for genetic variation: point mutations which affect a single genetic letter; deletions in which whole parts of a gene drop out; gene duplication in which more than one copy of the same gene is generated on the same chromosome and passed on to the next generations. And lots of other types of variation besides. So the same set of possibilities as before are still with us - genetic drift, gene flow, mutation, and natural selection – but now these same ideas are based on actual DNA-based information.

It was Richard Dawkins who popularised the idea of the *Selfish Gene* with his best-selling book published in 1976. But the idea is biologically rather misleading. The reality is that many genes cooperate together in the genome of each organism to produce the recipe that builds the organism. The genetic orchestra is made up of many different instruments, many different genes, that need to play well together in order to produce the music of life. And just as a musician can flourish in one orchestra and not in another, so the same gene can have different effects depending on the genetic company that it keeps.

Molecular biology has also stimulated the rise of evo-devo, which is not some new avant-garde artistic movement, but a reference to evolutionary development, the awareness that the regulation of development provides a key target for natural selection. For example, the hox genes are master genes that define which segment in the fruit-fly Drosophila does what, grow a leg, a wing or whatever it needs. The hox genes provide the cells in the different segments with a kind of GPS navigator so that they know where they are and what they are supposed to do – except this is a GPS system that uses chemical signals rather than radio waves. And in fact you find the hox genes involved in development in all vertebrates. Reach down and feel your own ribs – hopefully you can feel them – they are there in the right order because your master control hox genes made sure that they're there. Evo-devo investigates the roles of such genes in evolutionary history.

Stephen Jay Gould was an influential evolutionary biologist during the last few decades of the 20th century. Gould was fond of saying that if you could replay the history of life again, then it would end up looking quite different. Certainly we wouldn't be here. Gould liked to emphasise the stochastic, random aspects of evolutionary history. There is no doubt that there are some.

But more recent biological findings have suggested that if we take the evolutionary process as a whole, Gould was wrong. What is striking are those many discoveries that show that evolution is a highly constrained process. We can now see evolution as like a search engine for exploring design space. Most attempted solutions for filling design space are sterile – no flourishing living organisms result – those are the little red boxes in the diagram. But now and again evolution generates a genome that builds an organism that flourishes in a given ecological niche. Those are the green boxes, and they provide us with the evolutionary lineages that we in fact observe. And in generating the green boxes, living organisms come up with the same kind of adaptive solutions again and again in the phenomenon known as convergence. Evolution is a highly organized and constrained process, and to some extent predictable.

So as we look back at the history of evolutionary thought, summarized today in this highly compressed form, let us never think that this is somehow the end of the story, that somehow we've arrived. Not so. Scientific theories are like maps that render coherent lots of different bits of data. But maps are not static – they go through different editions as new data and insights come along. So it is with evolutionary theory. The map of evolution is being restructured and reshaped, and the new discoveries of these coming decades might just make it look very different indeed. And with that provocative thought I will close.