Introduction to the Canto Edition

I was at first reluctant to agree to the re-issuing of this book. It was first published in 1958, and last brought up to date in 1975. A lot has happened since then. Two things have changed my mind. First, there is no other account of evolutionary biology available which is at the same time written for a non-professional readership, and which covers the whole field, from the origin of life to human evolution, and from molecular biology to animal behaviour. Second, I find on re-reading it that the picture it presents is close to the one I would paint if I were to start afresh, and write a wholly new book.

All the same, much has been discovered in the last twenty years. I now attempt to summarize some of these additions.

(i) Molecular Biology

Rapid advances in this field have transformed many branches of biology, and evolution theory is no exception. The account of molecular biology in Chapter 5 is still adequate, but there is more to say about the application of these facts.

(a) Molecular Weismannism. The central idea that underlies this book is that the origin of new heritable variation is not adaptive. Most new mutations are harmful. If evolution leads to adaptation, as obviously it does, it is because selection establishes the small fraction of mutations that are adaptive. The alternative, ‘Lamarckian’, view is that individual organisms adapt during their lifetimes, and pass those adaptations on to their offspring: the so-called ‘inheritance of acquired characters’. In
Chapter 4, I gave a brief explanation of how the Weismannist view had been given a molecular interpretation in the ‘central dogma’ of molecular biology: acquired characters are not inherited because information cannot pass from protein to DNA, but only from DNA to protein.

Since 1975, two groups of facts have emerged that might seem to challenge the central dogma. The first concerns ‘reverse transcription’. As explained in chapter 5, information passes first from DNA to an intermediate, messenger RNA, and then to protein. The first of these stages, from DNA to RNA, is called transcription. It depends on the pairing of complementary bases, just as does the replication of DNA (p. 71). It turns out that the transcription step is reversible: information sometimes passes from RNA to DNA. This process of ‘reverse transcription’ is of great practical importance – for example, it is essential for the replication of the virus that causes AIDS. But, despite claims to the contrary, it has no relevance to the central dogma. When I wrote (p. 80) that it is difficult to see how the flow of information could run backwards, the step I had in mind was that from RNA to protein. There is still no reason to think that this step can be reversed. Of course, even if the protein-to-RNA step could be reversed, the inheritance of an acquired character would also require that the change in phenotype be translated into a change in a protein, and in most cases it is hard to see how this could happen.

A second group of facts is much more controversial, and could lead to a bigger revision of our views of evolution. Cairns, and more recently Hall, have studied mutations in bacteria that are starved, and therefore not growing. For example, bacteria need the amino acid, tryptophane, in order to grow. Most can make it for themselves, but some ‘trp−’ bacteria have undergone a mutation in a gene coding for an enzyme that helps to make tryptophane: these can grow only if they are supplied with tryptophane. Cairns and Hall measured the rate of ‘back mutation’ of trp− bacteria to a state in which they can again grow in the absence of tryptophane. They found that the rate is higher in cells that are starved of tryptophane, and cannot grow, than it is in growing cells.

By itself, this finding is interesting, but does not challenge the
idea that mutation is non-adaptive. It would be explained if a cell which is in difficulties, and cannot grow, increases the mutation rate of all its genes. This would be a sensible thing to do: if in trouble, try anything. However, Cairns and Hall go further, and claim that the mutation rate increases only, or at least mainly, in those genes which, if they mutate, will help the cell to resume growth – in this case, the gene that synthesizes tryptophane. This claim is still highly controversial. If it does turn out to be true, how could it be explained? The difficulty if this: how does the cell ‘know’ which genes to mutate? Several mechanisms have been suggested. The one that seems most likely to me is as follows. Not all genes are transcribed (that is, copied into RNA) all the time. Suppose that genes that are being copied are more likely to mutate than those that are not. A cell that needs tryptophane to grow will be desperately trying to synthesize it: therefore, the relevant gene will be switched on, even if it is no good (the control mechanism involved is explained on p. 123). This could explain apparently adaptive changes in the mutation rate. I must emphasize that there is as yet no evidence that this is the correct explanation. But the idea is testable. I offer it to make the following general point. If we are faced with an apparent case of adaptive mutation, we now know enough molecular biology to seek a mechanism to explain it.

I have spent some time on this example because the ‘Weismann vs. Lamarck’ argument remains crucial for evolution theory. The snag with Lamarckian explanations is that there seems to be no way in which an organism could recognize the adaptive changes – and only the adaptive ones – it had undergone, and convert them into corresponding changes in DNA. It is too early to be sure of the significance of these recent bacterial experiments. It may be no more than that cells in difficulties increase the rate of mutation in a non-specific way. If, as seems possible, something more is happening, it will be fascinating to find out how it works. In any case, the process can only help a cell to meet an immediate molecular problem: it could not lead to morphological or behavioural adaptation.

(b) Sequence Data and the Mechanism of Evolution. One major technical advance has been in methods of determining the
sequence of nucleotides in DNA. This information has been useful to evolutionary biologists in two main ways: in determining relationships, and in analysing mechanisms of change. To shed light on evolutionary mechanisms, we need the sequence of the same gene from a number of closely related individuals – members of the same species, or of similar species. Such information is only just beginning to be available because, understandably, molecular biologists have preferred to sequence a gene as different as possible from anything that has been sequenced before.

The value of having a number of sequences, or other molecular information, from related individuals is that it can tell us about the nature of the variation upon which selection can act, the kind of changes that occur, and the extent to which genes are exchanged between populations. Some examples will make these points clearer. In Chapter 12, I discussed the idea that the evolution of social behaviour depends on genetic relatedness. Molecular methods have been used to measure relatedness in animal societies. In some cases, it has been shown that the degree of altruism displayed towards others varies in the predicted way with relatedness. In the comparable problem of parental care, one would expect the amount of paternal care to vary with confidence of paternity: no increase in fitness follows from caring for unrelated offspring. Molecular studies of birds that form monogamous pairs have shown that the frequency of ‘extra-pair copulations’ is surprisingly high. In some cases, males do reduce their care of the young if their mate has had opportunities to copulate with another male.

The evolution and maintenance of sex has received increasing attention. There are two contexts in which molecular information is crucial. One concerns the longevity of clones (that is, asexually reproducing lineages). It is accepted that the ancestors of animals, plants, and fungi were sexual, but in all three groups some lineages have wholly abandoned sex. For how long can a lineage survive without sex? As yet, we do not know whether any animal clones are really old – millions rather than thousands of years. The obvious candidates are the Bdelloid rotifers (small multi-cellular fresh-water ‘wheel animals’), a whole sub-order in which no one has ever seen a
male. Are they a genuinely ancient clone, many millions of years old, or have they invented some alternative to males as a means of exchanging genes? We should soon know.

A second question concerns the prokaryotes (bacteria and blue-green algae). These do not have the classical sexual processes of meiosis followed by gamete fusion, but, at least in the laboratory, there are ways in which single genes, or parts of genes, can be transferred from one cell to another. Have these parasexual processes been important in the evolution of bacteria? Sequence analysis has shown that gene transfer has been crucial in the evolution of drug resistance, and in antigenic changes that enable bacteria to escape the immune responses to their hosts. Infectious disease would be a good deal easier to cope with if our parasites did not have means of exchanging genes.

The availability of DNA sequences has had an important influence on the debate (pp. 102–6) about the ‘neutral mutation theory’: that is, the idea that most changes at the molecular level happen, not because they are selected, but because they are selectively neutral. If the theory is true, there are two predictions. First (p. 104), the rate of evolution of a particular gene, or region of DNA, should be constant. Second, the rate should be high for those DNA regions on which there are few selective constraints (that is, which can change with little effect on fitness), and low for highly constrained regions (that is, regions in which most changes would have deleterious consequences). If we compare the DNA sequences of the same gene in related individuals, we can distinguish two kinds of change, ‘synonymous’ and ‘substitutional’: a synonymous change is one which, because of the redundancy of the genetic code (p. 91), causes no change in the amino acid, and a substitutional change is one that does cause the substitution of one amino acid for another. We would expect there to be greater selective constraints on substitutional changes (although it has turned out that even synonymous changes can be selected for or against, because some codons are translated more slowly than others), and hence, if the neutral theory is correct, the rate of synonymous change in evolution should be higher. This is in fact the case. However, sequence analysis has provided evidence that, in at least some genes, most amino acid changes in
evolution are selective rather than neutral. Perhaps the strongest evidence is that, in the ADH gene of *Drosophila*, there are more amino acid differences between related species than would be predicted on the neutral theory, knowing that there is little variation within species.

Molecular data have been used extensively in determining population structure. For example, some 300 killer whales have been studied behaviourally for twenty years off Vancouver Island in British Columbia. They fall into two groups, one of which follows the seasonal salmon migrations, and the other of which feeds on marine mammals. The groups differ in DNA sequence to an extent as great as that which separates killer whales from the Pacific and Atlantic, suggesting that, although they inhabit the same region, they do not interbreed. Information of this kind is of obvious value in conservation. It is also relevant to the origin of new species among mammals: although the two killer whale populations should probably not be regarded as different species, the difference in behaviour could be a first step in the speciation processes.

(c) Molecular Data and Phylogeny. A curious omission from earlier editions of this book is the lack of any discussion of the theory of classification. I spent some time on the nature and origin of species, but said little about classification at higher levels, beyond saying that a hierarchical classification (species – genus – family – order – class – phylum) fitted the observed pattern of variation, as would be expected on evolutionary grounds. As to how classification should be carried out, I said only that species that resemble one another in many characteristics should be grouped together. I had not at that time digested the ideas of Willi Hennig, whose book on systematics, published in German in 1950 and translated into English in 1965, has become the orthodoxy among taxonomists. The application of his ideas owes a lot to molecular data, and to computers, but it will be clear from the date of publication that neither contributed to their origin. I will explain them with a morphological example. The fact that horses and zebras both have a single toe is regarded as evidence of close relationship, whereas the fact that humans and lizards both have five toes is not. Why should this
be so? The reason is that, for land vertebrates, to have five toes is the primitive condition, and to have a single toe is a derived character. Resemblance in a derived character is good evidence of relationship, but resemblance in a primitive character is not. The principle is a good one, but how does one decide which are primitive and which derived characters? Sometimes one can get an idea of the primitive state from the fossil record, or from development (p. 311), but the most widely applicable method is the use of an ‘outgroup’. For example, when classifying the Perissodactyls (horses, tapirs, rhinos, etc.), one would take as an outgroup some other mammal. The perceptive reader will notice that there is an element of circularity here: how does one choose a suitable outgroup until one knows the classification?

The relevance of molecular data is that they provide a vast number of additional characters that can be used in classification. Given computers, these data can be pressed into service. Do molecular data have any intrinsic advantage, other than sheer volume? Two features perhaps make them peculiarly useful. The first is the non-adaptive nature of many molecular changes. Adaptive characters may evolve independently in different lineages. Thus a single toe is an adaptation for running fast in open country: it evolved not only in horses but also in an extinct group of South American mammals, the Litopterns. A second feature of molecular changes, causally connected to their frequently non-adaptive nature, is their approximately constant rate. A molecular classification, therefore, may give, not only a reliable phylogeny, but also an approximate dating of the times of divergence of the various lineages.

What has emerged from molecular phylogenetic studies? In general, they have confirmed classifications made on morphological ground. Many details have changed, and doubtful points have been cleared up, but the basic picture remains unchanged. Perhaps the most important contribution has been to the relationships between major groups – phyla and kingdoms – which are so different that morphological information is unhelpful. The concordance between molecular and morphological phylogenies is to be expected if the theory of evolution is true, and inexplicable otherwise. An important novelty concerns the evolution of proteins themselves. It was already
familiar from morphological studies that new organs, with new functions, do not emerge from nothing, but by modification of already existing organs with different functions. Arms and legs are modified fins, wings are modified arms, feathers are modified scales, jaws are modified gill arches, and the swim bladders of fish are modified lungs (although, as it happens, Darwin thought it was the other way round). The same picture holds for proteins, as is shown by the similarity of sequence between proteins with quite different functions. For example, lysozyme, a bacteriocidal protein present in tears, has sequence similarity to an enzyme that helps to make lactose in the mammary glands. This could not have been predicted, but has been explained retrospectively by saying that the first protein breaks a chemical bond similar to that made by the second.

(d) \textit{Selfish and Ignorant DNA.} One surprise has been the discovery that a large proportion of the DNA in eukaryotes is never translated into protein. In humans, as little as ten per cent of the DNA is translated, and the proportion is still lower in newts, lungfish and lilies. Some of the untranslated DNA performs a useful function: it may regulate gene action, or be transcribed into RNA that plays a role in protein synthesis or in other ways. But the vast majority probably does nothing useful for the organism at all.

To understand why this is so, remember that the nucleus of a cell is packed with enzymes that replicate DNA, and others that cut it and splice it together again, the function of the latter being to repair damaged DNA, and to recombine chromosomes (p. 61). Hence a DNA molecule in the nucleus, particularly if it is inserted into a chromosome, will be replicated, even if it performs no useful function. It helps to think of the additional DNA as falling into two categories, ‘ignorant’ and ‘selfish’. The ignorant DNA does not have any special sequence that ensures its survival. Often it consists of short sequences of five to ten nucleotides, repeated over and over again. It is just there, and replicated because it is there. In contrast, selfish DNA has an evolved sequence that ensures its own increase. For example, in the chromosomes of wild \textit{Drosophila melanogaster}, there are some
fifty ‘P factors’. These are regions of DNA some 3000 nucleotides in length which are transcribed and translated into two proteins. One of these causes additional copies of the P factor to be inserted elsewhere in the chromosome set – a process called transposition – and the other controls the process. In most populations, P factors cause no particular harm, although it must cost the fly something to replicate all this useless DNA. But if strains of *Drosophila* with and without P factors are crossed, the control of transposition breaks down, causing death and infertility.

Such ‘transposable elements’ are universal. To give a second example, there are some 400,000 copies of the Alu element, 282 nucleotides long, distributed throughout the human genome, amounting to about five per cent of the DNA in the nucleus. The existence of transposable elements raises a problem for evolutionary biology. As the P factor example shows, an element that transposes too successfully can damage the organism. We are therefore faced with another example of selection operating on two levels. On pp. 193–200, I discussed the problem of group selection and the evolution of social behaviour: why do individuals cooperate in animal societies, despite selection for selfish behaviour? We are now faced with an analogous question: why do the genes in an organism cooperate to ensure the survival of the organism, despite selection for selfish replication? The question is easier to ask than to answer.

One last comment on molecular biology: the prospects discussed on the last page of the book come ever closer.

(ii) *Replicating molecules*

It is now possible to study evolution in a test tube, in the absence of any living organisms. A test tube is prepared containing the four nucleotides from which RNA is synthesized, a ‘primer’ molecule of RNA, and an enzyme, Qβ replicase, which copies RNA molecules. The enzyme repeatedly copies the primer, using the nucleotides provided. After some hours, when many copies exist, a drop of the solution is transferred to a second tube, also containing enzyme and nucleotides, but not, of course, a
primer, because RNA molecules ready to be copied are already present. The process can be repeated as often as one wishes. If replication was precise, this would merely produce many copies of the original primer. But replication is not perfect. Every time a new nucleotide is added, there is a chance of about 1/1000 that it will be ‘wrong’: that is, it will not be complementary to the nucleotide in the strand being copied. Other errors, or mutations, lead to changes in the length of the RNA molecule. Since some RNA sequences are replicated more rapidly than others, there is a process of evolution by natural selection. For a given set of physical and chemical conditions, the end point of this evolutionary change is repeatable – usually an RNA molecule some 200 nucleotides long. There is, apparently, some unique ‘best’ sequence, and natural selection can rather rapidly produce a population consisting of molecules with this optimal sequence, or one very like it, regardless of the sequence of the original primer.

Of course, these experiments are not an answer to the question of how life originated. Conditions in the test tube differ from those in the primitive ocean in one crucial respect: there could not have been any Qβ replicase molecules present in the primitive soup. Nevertheless, the experiments are interesting for two reasons. First, they demonstrate how, once replication has arisen, natural selection can generate structures which, without it, would be wildly improbable. Thus there are $4^{200}$, or $10^{120}$, different RNA molecules 200 nucleotides long, yet natural selection can repeatedly produce one specific sequence in a few days. The experiments are also important for a practical reason. Modifications of this procedure may make it possible to use natural selection to produce enzymes with specific desired activities.

(iii) *The Origin of Life*

In existing organisms, nucleic acids, DNA or RNA, act as carriers of genetic information, and proteins act as enzymes responsible for metabolism. This led to a ‘chicken and egg’ problem: did nucleic acids or proteins come first? How could