1 Introduction

In his theory of evolution, Charles Darwin gave a simple and logical explanation for the diversity and adaptability of species[372,1165]. Everything that used to be a mess of riddles and contradictions suddenly became comprehensible and coherent. The results of Darwin's theory were enormous and have had a dramatic effect on theoretical developments within the field of biology. The theory of evolution has subsequently been applied to an increasing number of disciplines.

Evolution occurs because there are differences in the hereditary characteristics of different individuals within a species, created through mutation and the transfer of genes, and because selection may or may not favour these different traits. The individuals who do best in a certain environment, i.e. produce the most offspring, are those who subsequently outcompete others in that species. The genetic traits of these successful and well-adapted individuals become increasingly common within the species while others gradually disappear. This process is called natural selection. Hence, evolution depends on elimination.

Natural selection benefits those that have more offspring than others. While carnivores become better hunters during evolution, their prey become better at fleeing. Bacteria attack animals that, in turn, develop defence mechanisms, which the bacteria then outsmart, and so forth. Plants develop toxins and other bioactive substances that are harmful to animals that feed off them. Evolution is an eternal, escalating struggle that continues to this day.

1.1 Why do we get sick?

Evolutionary theory has been applied sporadically within the field of medicine since the early twentieth century. The activation of the sympathetic nervous system during stressful periods has long been considered a part of the 'fight-or-flight response', and pain has been seen to encourage healing by forcing that part of the body to relax. Later, the appearance of microorganisms with resistance to antibiotics led to

Table 1.1 Mechanistic and evolutionary causes of diseases or symptoms.

	Mechanistic explanation	Evolutionary explanation
Breakdown of the immune system in AIDS	HIV binds to the CD4 molecule on the surface of helper T cells to invade and gradually destroy them	Attack: spread of HIV fostered at the expense of the host organism
Fever	Pyrogenes stimulate the synthesis of prostaglandin E2	Defence: increased body temperature appears to make cell division difficult in the microorganism
Myopia (nearsightedness)	Abnormal growth of the eye ball mediated by local growth factors	Lack of adaptability to new environment: we have left the life of hunting and gathering
Choking on pieces of meat	Inhalation during swallowing	Design error: airway and gastrointestinal systems are crossed

an understanding of how this resistance develops according to the laws of natural selection. The relative protection against malaria among heterozygous carriers of sickle cell anaemia has been thoroughly discussed. However, only recently has evolutionary thinking emerged as a wide-ranging discipline in medical science in the form of evolutionary medicine[1286,1716,1809].

Evolutionary medicine looks at health and illness from an evolutionary perspective and generally focuses on what is typical rather than what is the exception, more on evolutionary (ultimate) rather than mechanistic (proximate) explanations for disease (Table 1.1).

A proximate explanation for disease is therefore synonymous with pathogenesis, which provides a detailed, often physiological or biochemical, description of the origin of the disease. Evolutionary explanations for diseases or symptoms try to explain who or what benefits from the process and in what way. To the extent that something can be done in terms of environmental factors, this is of great interest.

Roughly speaking, evolutionary explanations for disease can be divided into four categories: attack, defence, lack of adaptation to unfavourable environments and design errors. Attack is thought to benefit the attacker, while defence benefits the person attacked. The methods can vary from the bite and scratch of an animal or the invasion of microorganisms to the pricks and poisons of plants. For hundreds of millions of years, in an escalating struggle for survival, both attack and defence have been strategies in the evolutionary history of the animals. This process is still going on, and no animal can be said with certainty to be the ‘winner’ in the game of survival of the fittest.

Humans with a tendency for anxiety may potentially create a more secure environment for their offspring than those who are clueless or foolhardy[1286]. It has been suggested that fever also has an evolutionary purpose by impeding the growth of bacteria[925].

However, diabetes can hardly be said to have a purpose, and therefore, it lands in the category of lack of adaptation. The fact that this lifestyle disease has affected an increasing percentage of the earth's population in the last few decades shows that genetics is not the only cause, since the timescale of genetic change is very much slower. In general, heredity has a great impact on individual resistance to a Western lifestyle but is rarely the sole explanation. These ideas are explained further in Section 4.6.

An even clearer example of a lack of adaptability to new eating habits is the loss of lactase activity during childhood, which leads to an inability to digest lactose in the adult. Such a loss is the rule in most ethnic groups, like in other animals. During human evolution, when cow's milk was not part of the diet, there was no advantage in maintaining lactase activity after childhood. On the contrary, natural selection benefited those groups that did not spend resources on an enzymatic activity that would not be used – in this case, that of lactase.

A design error can often be seen as the best design of the given alternatives, in contrast to the best theoretically imaginable design. The problem with choking on pieces of meat could have been avoided by separating the respiratory tract from the digestive apparatus. But we all descend from an ancestor with crossed systems[557] and now it is too late. Evolution cannot go backwards, and any species that might by chance develop the rudiments of a better system would, for other reasons, have been outcompeted.

Certain hereditary diseases can be seen as the result of design errors, but often one or more environmental factors are required for a disease to appear. Heredity therefore does not preclude environmental influence.

Past scientific discussion can sometimes give one the impression that the diseases of the Western world are caused by design flaws that can only be corrected with the help of pharmaceuticals or other medical procedures. I consider this book an argument for the case that this is a misunderstanding.

1.2 We are changing at pace with the continental drift

During the unbelievably slow process we call 'evolution', changes through natural selection have led to the appearance of our own species[1165]. These changes occur sometimes in great strides and sometimes more gradually in many small steps. Often there is no change in a certain trait across millions of years, when natural selection favours stability, say for the metabolism of glucose. Microevolution involves a slow process of adaptation within the species and the development of new species, which are relatively similar to the original. However, macroevolution involves the appearance of radically new strains and thereby new groups at a higher level than their relatives.

One way of clarifying how much time has passed from the first vertebrates to live on land until the appearance of humans is displayed in the 'evolutionary calendar' in Table 1.2. For the sake of simplicity, we will assume that the first vertebrate life forms to walk on land lived 365 million years ago, and then we can allow 1 day in the calendar to represent 1 million years in reality.

Table 1.2 The last 365 million years converted to a calendar year.

Time	Event
January 1	Amphibian ancestor
March 5	Reptile ancestor
June 10	Early mammal
July 20	'America' starts to separate from 'Europe' and 'Africa'
October 28	Primate ancestor
Christmas Eve	Bipedal ancestor (hominid)
New Years Eve	
19:30:00	*Homo sapiens* (modern humans)
21:30:00	Some of us leave Africa
22:45:00	Some go to New Guinea
23:00:00	Some of us go to Europe
23:40:00	And even to Scandinavia
23:45:00	Agriculture starts in Middle East
23:52:00	Agriculture starts in Scandinavia
23:53:00	The Ice Man dies in the Alps
23:59:00	The Black Death (the European pandemic of plague)
23:59:50	Cardiovascular disease

Note: 1 day = 1 million years, 1 hour = 41,700 years, 1 minute = 694 years.

The changes that occurred since one of our ancestors left the fish stage more than 400 million years ago primarily concerned size and form, temperature regulation and the methods for reproduction and obtaining food. We have stopped laying eggs, we have lost our tail and we no longer carry fur. We use tools to obtain food and obviously look different from our mammalian relatives.

But despite the enormous amount of time that has passed since our first amphibian ancestor crawled up onto land, there are still more similarities than differences between the current descendants in the chain of development. The cells of different mammals are essentially built up by the same protein-based information systems, regulated by the same DNA-based genetic language. Food is chewed and broken down in very similar ways by various types of animals. The few exceptions include the fact that mammals can move their lower jawbone sideways in relation to their upper jawbone, and that ruminants have bacteria in their digestive tract that can break down cellulose and 'disarm' some plant defences. Curiously, few changes in our ancestors' long history have occurred in terms of how our food is processed once it has been absorbed by the organism. Consequently, the metabolism between different mammals that are used in research is very similar to each other, despite the fact that their common ancestors may have lived 100 million years ago. It is thanks to this close similarity that we can perform experiments on animals to understand human biochemistry. We have obtained most of our knowledge of our own biochemistry from studies on rats and other types of animals.

For millions of years, species have been fine-tuning how they use the available food substances in the most beneficial manner possible. Notice the word 'available'; this process has not been able to change our bodies to handle food that did not appear during evolution, e.g. salted food or cheese sandwiches.

However, adapting to available food has not been problem-free. Most plants protect themselves from being eaten by mammals, insects and fungi by synthesising toxins and a host of antinutritional bioactive substances[721]. These include plant lectins, alkylresorcinols, protease inhibitors, tannins and polyphenols. Evolution has forced plant-eating animals (herbivores) to develop sophisticated defence systems, including variation of plants eaten in order to minimise the dose of each individual substance. Animal species that support themselves exclusively on one particular plant have been forced to develop defence mechanisms to minimise the damaging effects of its phytochemicals. One example is the ability of some herbivores to consume large quantities of cyanide-forming (cyanogenic) plants[596].

From this perspective, the term 'natural' somehow gets a new meaning. Naturally occurring substances in the plant kingdom are not necessarily as benign or as useful as we often imagine. Somewhat drastically, you could say that it is completely natural to die of mushroom poisoning, that this is part of the mushroom's natural strategy to make short work of its enemies. Today, it is natural to die of a myocardial infarction (heart attack), which is a natural consequence of the Western lifestyle. In the light of this, herbal medicines are given credit that is not truly justified. The fact that these medications have their origin in the plant world does not mean that they are safer than drugs that are manufactured synthetically.

Our primate ancestors have been consuming fruit, vegetables, nuts and insects for 50 million years or more. Meat was successively added, with a probable increase around 2 million years ago. Underground storage organs (roots, tubers, bulbs, corms) possibly become staple foods 1–2 million years ago (see Section 3.1)[1971]. The variability was large; single plant foods were rarely available in excess. Modern staple foods such as grains, milk, refined fats and sugar, and salt were not available, but are now providing the bulk of calories in most countries.

1.3 Are we adapted for milk and bread?

If milk and bread are capable of causing illnesses that would have reduced fitness in early agriculturalists, would not have Europeans been able to adapt to these items over the past 10 000 years? If that were the case, it would have been a result of the gradual elimination of people who suffered from early death or low fertility caused by such foods, and we, who are the descendants of the survivors, would accordingly be created differently. This is a multifaceted question[831]. First, it depends on which adaptations you look at. Genetic adaptation to a deadly threat in childhood, in certain cases, can apparently occur in less than 50 generations (which may correspond to less than 1200 years), starting at the time when 1% of the population carry the protective trait and ending at the time when the large majority, say more than 90%, are carriers. However, the necessary time from complete absence of the trait to its first appearance in an individual carrier may be very long, and is actually mathematically impossible to calculate. In addition, it may take several thousand generations for the prevalence to increase from 0 to 1%.

The timescale of genetic adaptation can be illustrated by the observed change in colour of the peppered moth (a winged insect) in the area of Manchester during the 1800s. In the 1700s, almost all of these moths were speckled grey and were therefore perfectly camouflaged against the lichen covering English birch trees. By chance, however, a small founder population of moths were black and therefore easier to be spotted by birds. This could have caused their elimination if an unexpected saviour had not appeared, namely industrialism. The soot from Manchester's smoke stacks blackened the area's birch trees so severely that suddenly it was the grey speckled individuals that were at the greatest risk of being eaten by the birds. Just 50 generations later – after 50 years in their case – the result was that almost all peppered moths in the area were black. This process of natural selection went unusually fast, but the danger was also very significant in the first day of life for those that had the wrong colour.

Now assume in our case that people in a downright barren Europe 10 000 years ago were forced to drink milk to survive the harsh winters after the hoofed mammals had been hunted down to near extinction by humans. Lactose intolerance, the hitherto normal condition for adult humans (and animals), would then be a serious threat to survival; i.e. the inability to thrive on milk would exert a strong negative selection pressure. Assuming also the presence of a large enough founder population, after a few hundred generations it is highly possible that most lactose intolerant families had been eliminated, which also seems to have been the case among the Scandinavian people[239].

Assume further that milk caused atherosclerosis (see Section 4.2), stroke and myocardial infarctions in most people in their 50s, apart from some individuals who were genetically resistant and did not develop these conditions before the age of 80. If such a resistance-promoting gene would be passed on to their children, how quickly can it spread in the population; i.e. how big of an advantage do these resistant relatives have despite drinking milk? Do they have more children? Barely, if a heart attack at age 50 years or later is the sole result. Do the children fare better? Perhaps, but the difference is marginal. When a mother is 50 years old, the children often deal quite well without her help. Other populations, by and large, can just as easily propagate their offspring, and the roughly 10 000 years since the dawn of agriculture is very unlikely enough time for the majority of Europe's population to belong to this resistant group. However, grandmothers could have had a certain amount of significance during evolution (which would explain the long time a woman can live after menopause). Adult children's independence of their elder parents became most apparent in civilised society, where competence and knowledge could be spread to a larger number of people than in hunter-gatherer societies.

However, a few thousand years may be enough if fertility is strongly and negatively affected. The relation between Western dietary habits and insulin resistance (a precursor to type 2 diabetes and hypothetically a partial cause of cardiovascular disease), as well as reduced fertility, is therefore an important issue that will be addressed in Section 4.6 on insulin resistance. In that section, the relatively low prevalence of type 2 diabetes in people of European descent, as compared to most other ethnic groups, will also be discussed.

While cow's milk is relatively easy to dismiss as optimal human food from the perspective of genetic adaptation, seeds (including beans) are slightly more complicated. Grass seeds from the Poaceae family, which includes wheat, rye, barley, oat, rice and maize, have not been staple foods before the advent of agriculture. In contrast, fatty seeds from various African plant species probably have been part of our ancestors' diets for millions of years. We know that seeds have high concentrations of phytochemicals[721]. Hence, if African fatty seeds were regularly consumed during human evolution there may have been some adaptation to these particular species, whereas grass seeds are just as recent as milk in the human diet. In addition, a narrow range of seeds are now consumed every day as staple foods, a very recent phenomenon in evolutionary terms.

The question of root vegetables is even more complex. As outlined in Section 3.1, humans may be highly adapted to a high intake of root vegetables. Such an adaptation would mainly pertain to the particular phytochemicals that are present in African roots, including those found in some species of *Dioscorea* or *Ipomoea*. However, the potato, which originates from South America, may contain bioactive substances that are too foreign for us to cope with. For example, the potato lectin (Solanum tuberosum agglutinin or Solanum tuberosum lectin) activates tyrosine kinase receptors not necessarily affected by lectins from more distantly related plant tubers[558]. Considering the amounts of potato consumed in Western countries, a higher degree of adaptation would have been preferable.