13

Multicellular Life: The Last Hurdle?

13.1 Multicellularity arrives

Most of us have read various accounts of the ways in which life, after some 2.5 billion years essentially restricted to a water environment, emerged on to land and eventually flourished there. Emotive terms such as 'conquest of the land' and 'invasion of the Earth' were suitable for the Empire-building nineteenth century when they were coined. I prefer descriptions such as 'greening of the Earth' or even 'colonization of the land'. The former is not merely descriptive but also reflects the order in which life, in a substantial way, first emerged on the land. Of the complex forms of life, plants came first. In reality things were difficult and success was by no means assured.

Thus far we have dealt with individual cells and some life forms are, as we have seen, single celled to this day. They gain nutrients from and excrete waste products directly to their environment through their cell membrane (and cell wall, if any). They move by means of tail-like flagella or the concerted beating of many cilia. We probably are more familiar, however, with multicellular organisms that live on land. Single-celled life forms such as bacteria, cyanobacteria, and protists have been highly successful for billions of years, so how did multicellular organisms evolve? What extra problems did they need to overcome to survive, not only in water where they evolved, but also on land?

Imagine the land slightly less than 1 billion years ago. The continents, vastly different in shape and position from what we see today, were apparently barren, rocky, scoured by intermittent streams but unable for lack of plants and organic soil to maintain much moisture, baking under a scorching sun, but often freezing at night. A number of microorganisms undoubtedly existed in these environments, including the atmosphere, with sufficient nutrients to support them, but overall 'land' was most likely almost bereft of life. Oxygen levels were building and an ozone layer was developing that was to protect any emerging organisms from the worst of ultraviolet radiation.

What changed all this? The oceans were populated by prokaryotic bacteria and by unicellular eukaryotic organisms, the protists that had already begun to diversify. These eukaryotes comprised both phototrophic and heterotrophic types, some of which had adopted a sexual mode of reproduction. Of the many tentative associations formed by the protists, undoubtedly most did not survive, but those which did laid the biological foundations for the truly multicellular organisms that were to come. What made eukaryote cells first associate is unknown. Some of the associations, fortuitously, must have possessed some survival advantages. These reproduced for long enough to undergo natural selection, which resulted in further survival, further improvements, further survival, and so on.

The close association of many cells is the most obvious characteristic of multicellularity. Association is considered as the first of several principles to have been involved in the evolution of multicellular organisms. Presumably, simple association led to improved reproductive success and thus it persisted. Merely by staying alive, by persisting, multicellular organisms, like all others, were inevitably subjected to natural selection pressures. More than simple association was needed. Some form of cooperation was required, which meant intercellular communication and transmission of information. However, the cell membrane presents a significant barrier to water and other polar molecules. Fortunately, cell membranes are more than just a lipid bilayer. They can accommodate proteins, for example. Some 50–70% by weight in modern animal cell membranes is protein. Non-polar sections of membrane proteins span the membrane, leaving polar heads and tails in the cytoplasm and extracellular fluid. Such transmembrane proteins can move laterally in the membrane. They are also capable of allosteric interactions with smaller molecules to alter their conformation and hence their uptake properties. Such regulatable property variations lend themselves to the formation of specific channels and receptors that allow cross-membrane and thus intercellular information exchange by molecular messengers.

Some experimental (in the evolutionary sense) multicellular types would have disappeared fairly quickly, while others must have begun to develop specialized tissues, that is they took advantage of simple association to develop cell differentiation, the second principle of multicellularity. Differentiation enhanced survival and so off the multicellular organisms went, ultimately to become flowers and fungi, dinosaurs and mushrooms, frogs and humans. From the early simple colonies emerged the means for cells to remain associated. The so-called slime-moulds are an instructive example. Their unicellular forms developed surface molecules that allowed them to adhere to others by a complementary, lock-and-key type of interaction. They probably developed the early equivalent of cell-surface receptors, which held them to the viscous slime they secreted. These association principles remain in force in modern organisms, for example in the cell-adhesion molecules and substrate-adhesion molecules of mammals. Unicellular organisms that were to become plants and fungi most likely developed their cellular association within a structure that became the cell wall of modern plants and fungi. Plant cell walls are complex structures and structurally very strong. The size of some modern trees attests to this. Fungal walls are somewhat less complex, but are well suited to their scavenging lifestyle. Cell walls are absent in animals, which for land-dwellers places a limit on the size they can achieve and even affects their body shape. These limitations are compensated for by greater mobility—animals can run, fly, swim, hunt, and hide to avoid predators.

Differentiation can only occur and tissues be maintained if the cells possess a well-developed capability for gene regulation. Superb control mechanisms are required. Genes need to be turned on and off, and their regulation by controlling the transcription of DNA into messenger RNA (and hence into protein) is important in several ways. Each somatic cell of an organism contains all the genes (the genome) of that organism, but only a small proportion of these genes is ever used in a given cell type. All cells have what are called 'housekeeping' genes, which code for structural proteins, enzymes for intermediary metabolism, etc, that is all the general functions needed to run the cell from moment to moment. These genes must be capable of being active when needed, and are under the control of a group of regulatory proteins. Special proteins called transcription factors bind to specific sites on DNA and either activate or deactivate their respective genes. Not surprisingly, the genes that make the transcription factors are called regulatory genes. A transcription factor that inhibits DNA transcription is called a repressor, and one that stimulates transcription is called an inducer. Depending on the activity levels of these essential transcription factors, the genes are either transcribed or not transcribed into messenger RNA, and thence to protein. A model for control of gene expression in *Escherichia coli* was first proposed by the French researchers Jacob and Monod (Maynard Smith and Szathmary 1999).

In the cells comprising any given tissue or organ, apart from the housekeeping genes, the genes that can be activated are those which define the type of tissue. For example, in muscle cells the genes coding for the special functional proteins of muscle are often activated, but the genes coding for the specialized functions of, say, the pancreas or liver, although present in the muscle cells, are deactivated early in development, when the embryonic cells undergo differentiation. Such deactivation of certain genes after cell differentiation is not always absolutely irreversible. An example well known to gardeners is that certain plants may be grown from a cutting or shoot. The end of the cutting in the ground will often grow roots and eventually an entirely new, complete plant will develop. This could occur only if there is a complete set of genes in the cells of the part of the stem placed in the ground and if these genes are capable of being reactivated to produce root cells.

Regulation of genes by transcriptional control is especially important during the development and maturation of an organism. There are many examples, but let's just consider briefly the onset of puberty in humans. Specific genes in the cells of organs concerned with puberty are activated, such as those that induce facial hair in boys and the development of breasts in girls. Steroid hormones that trigger a response in the appropriate cells are released into the bloodstream and on reaching the appropriate cells interact with specific cell-surface receptors. This triggers the activation of regulatory proteins, which bind to the complementary segments of DNA in the genes to be activated. Transcription can now take place in these genes and the processes leading to the development of hair or breasts commence. At the gene level much the same kind of control is involved in other stages of development.

The regulation of gene activity is actually much more complex than the above outline suggests, but I hope you have grasped the principles involved.

Thus differentiation leads to cell specialization, and to division of labour between the tissues and organs of a multicellular organism. We will deal with some more of the advantages and problems associated with cell specialization soon, but before leaving gene regulation an important question must be answered: What is the role of energy in gene regulation?

I said above that regulatory proteins bind to specific portions of the genomic DNA. The binding occurs because it is energetically favourable under the prevailing conditions. Complementarity of shape between the regulatory proteins and the DNA regions to which they bind is involved and this allows the short-range secondary bonding forces to act cooperatively, holding the two portions together. This is fine for binding, and 'unwanted' genes may thus stay inactivated quite long term. What about the reverse, the removal of, say, a repressor protein to allow the gene to become activated? Removal of a bound regulatory protein may be achieved if a third molecule, such as a hormone or a metabolite, binds to the regulatory protein and alters its shape. This is another example of the allosteric effect. If the altered shape does not have the same complementarity with DNA as before, secondary bonds cannot be maintained and the regulatory protein/DNA complex dissociates. There are some subtle variations on this theme, brought about by the four different types of regulatory protein so far known. I won't discuss these here. During the entire, incredibly complex, regulatory process, the laws of thermodynamics are satisfied—there's thermodynamics in everything!

To outline the story of the evolution from protists to humans could take anything from a large book to a small library. My approach has been to look at the major 'problems' that organisms faced along the way, particularly those involving energy. Put another way, what had to be 'invented' to 'take advantage' of the 'potential opportunities' that were 'offered' by multicellularity? As with all evolutionary developments, the existing life forms didn't actively seek to solve such problems or to make such inventions—hence my use of so many quotation marks.

As mutations occurred, the variety of resulting new life forms sampled the available niches. We don't know how many attempts were made. Depending on how a particular life form managed to cope with all the conditions confronted, it either survived or disappeared. Ultimately, the three main multicellular kingdoms emerged independently and survived: the plants, the fungi, and the animals.

13.2 The evolution of plants

The early history of plants is reflected in some of their modern counterparts, the algae and the seaweeds. Seaweeds and indeed all algae do not develop from any kind of embryo and are thus not classified as plants. Three main evolutionary lines of algae emerged and in each case endosymbiosis appears to have been involved. Depending on the type of cyanobacterium involved in the symbiotic relationship, the red, brown, and green algae emerged. All these algae are phototrophic, all contain green chlorophylls, and all produce molecular oxygen as a result of their photosynthetic activity. The different colours are caused by the presence of different pigments. The pigments typically have at least two functions: they act as secondary absorbers of light and/or as antioxidants to protect the algal tissues from the high reactivity of molecular oxygen and its products. Pigments look coloured in sunlight precisely because they absorb some wavelengths of white light (sunlight) preferentially. The colour we see is what is 'left over' from white light. The absorbed light energy, as we saw in Chapter 10, drives the endergonic photosynthetic processes via an electron transport chain. Within the three groups of algae, there is considerable diversity of size, shape, metabolism, and reproductive styles. Common to all algae is the cell wall, which contains the glucose polymer cellulose as its main component, plus a variety of other polysaccharides such as alginates or carrageenans, depending on the species. Structurally, algae are quite simple as they contain only a few specialized cell types such as those which anchor them to the bottom, floats filled with air, and simple sex cells. Their gradual adaptation to a life on land occurred some 450 million years ago.

As always, natural selection was at work. One advantage was the acquisition of a waxy cuticle, which prevented plant desiccation in their newly adopted environment. Because the cuticle prevented the free flow of gases and nutrients, another acquisition must have been the development of special surface cells containing pores to facilitate the uptake of carbon dioxide from the atmosphere, rather than from water, and to release oxygen to it. These pores eventually evolved into the stomata of present-day plants. Stomata are variable apertures that allow control of the exchange of carbon dioxide, water vapour, and oxygen between the plant and its environment.

For some unknown reason, green aquatic algae were the only protists to evolve into plants which became fully successful on dry land, so use of the term 'the greening of the Earth' is appropriate. The successful ones eventually evolved into three phyla, the mosses, the liverworts, and the hornworts, whose members are known collectively as the bryophytes. The need for water at the critical fertilization stage largely restricted the bryophytes to moist regions in temperate or tropical habitats. Their growth was also restricted, thus bryophytes are typically ground-hugging and small. This success story of the transition from an aquatic to a terrestrial way of life is hardly one of invasion or conquest in the accepted sense. Rather it is an example of the immense power of environmental factors in exerting a genetic load and influencing the direction of evolution. Humans have often deliberately increased the genetic load on organisms by selecting the characteristics they want and 'forcing' the chosen plants or animals to adapt. Examples include the selective breeding of dogs from their wolf ancestors to an extent that almost defies belief, the development of enormous sunflowers in Russia, and increased yields of cereal grains (without the application of genetic engineering).

The first terrestrial plants were restricted to coastal areas, where high humidity assisted the transition from water to land. The remaining vast terrestrial spaces were still barren of life, their surface layers largely dry and deserted. To spread further, the plants needed to develop root systems that could penetrate the ground to draw up precious moisture and nutrients. The aerial parts needed to grow larger and longer, to be more efficient in harnessing solar energy for conversion into larger and larger structures, as conditions permitted. A characteristic of land plants, the cuticle, would have prevented excessive evaporation from the early land plants and protected the tissues from damaging ultraviolet radiation.

The land plants were forced by their physical environment into developing two distinct zones. Above ground were the green, light-seeking leaves, which also functioned as gas exchangers with the atmosphere. Below ground were the colourless roots, lacking in chlorophyll. Joining these was a stem, which allowed the passage of water and nutrients from the roots upwards and of sugars formed by photosynthesis downwards. What was lacking in the bryophytes, but which was needed desperately for plants to have the best of both worlds, was an efficient transport system connecting all parts of the plants.

The vascular (vein) system, a fluid-conducting system that plants evolved, consists of the xylem tissues and phloem tissues. These were a vast improvement. The xylem is the tissue through which most of the water and minerals are circulated, whereas the phloem is the food-transporting system in vascular plants. The vascular systems of most land plants consist of these tissue types. Xylem tissues comprising the vascular system consist mainly of dead, heavily lignified cells and living phloem cells. The early vascular plants, such as the ferns and horsetails, lacked seeds and possessed spores only. The leafy ferns we see today are the dominant, adult, diploid sporophyte stage. Under the leaves, haploid spores are produced by meiosis, are discharged, and germinate into gametophytes. Omitting much of the detail, male and female gametophytes produce sperm and eggs, respectively, and when there is sufficient water present the sperm are released and swim into the female archegonium, where fertilization occurs, as in the bryophytes. The (now diploid) zygote then develops into the mature sporophyte stage.

Cell differentiation into xylem and phloem systems was one advance that allowed the vascular plants to solve the problem of efficient food and nutrient transport. Another, which helped start plants on their upward pathway towards the sun, was the ability to synthesize lignin. Lignin is a chemically complex, amorphous material that is deposited in the intracellular space as plant cells, particularly those of the stem, mature. It adds rigidity to the carbohydrate components of the cell wall, allowing some plants to grow to considerable heights. Land plants needed to cope with the Earth's gravitational field to support their stems and branches of increasing span. Large trees are heavily lignified, especially in the regions that support the large branches. On the other hand, the smaller, more flexible grasses contain less lignin. The presence of lignin makes the carbohydrate of plant cell walls inaccessible to the digestive enzymes of many grazing animals, which tend to prefer the grasses for a meal.

The ancient plants gradually evolved more highly differentiated, efficient systems suited to life on land.

About 400 million years ago, oxygen levels were about 10% of what they are today. Plants began to colonize the land on an increasing scale. Climatic changes assisted by making the atmosphere more humid, and once the plants took firm hold they also contributed to this by drawing up moisture from the soil and releasing it into the air through their stomata by the process of transpiration. Huge tropical swamps were formed, where large trees grew rapidly, and when these and other plants died, they decayed and were transformed to form vast deposits of carbonaceous material, which are mined today as coal. Some 50 million years later these swamps began to dry out as the continental masses then present drifted together to form a single massive land mass, Pangaea, a large portion of which was located over the South Pole, and as a result was covered in a thick layer of ice. Interior parts contained large deserts. The climate became colder, possibly because volcanic eruptions caused dust clouds, which blocked out much of the energy from the sun. More ice-sheets and glaciers formed. The large areas of snow and ice reflected more of the energy from the Sun back into space; more ice formed, the sea-level dropped, and the Earth entered its most severe Ice Age. These rapid changes in the energy balance of the Earth had a profound effect, especially on land species. As a result, the great Permian Extinction, which wiped out vast numbers of both land and marine species, took place.

We might be tempted to look on these events aghast as yet another example of disasters which seem periodically to affect life on our planet in a negative way. This would not be only wasted emotion, but in this case (and others) a decidedly misguided one. As with many events in the history of life on Earth, the Permian Extinction presented evolutionary opportunities for those organisms which were, fortuitously, at a stage to exploit it. One of the results was the emergence of true seeds and ultimately the flowering plants that give humans (again fortuitously) so much pleasure today. The flowering plants—Class Angiospermae—have steadily increased their influence on the living world since the early Cretaceous, some 130 million years ago. Since about 90 million years ago they have been dominant in the plant world. Today, some 90% of plant species are angiosperms. They range in size from the gigantic eucalypts of Australia to tiny duckweeds with 1 mm leaves. Angiosperm flowers range from pinhead size to those of the giant Indonesian *Rafflesia*, up to a metre across. The grains, fruits, and vegetables we eat are angiosperms, as are the plants that provide us with cotton and linen. Domestication of angiosperms (and animals) had enormous influence on the early history of humans, which was extended firstly by conventional plant breeding, through to today's genetically modified crops. Although angiosperms reproduce both sexually and asexually, it is aspects of the former method that have helped their evolution and fascinated humans. Flowers and fruits are two unique characteristics of angiosperms. With the aid of animals, in particular insects, flowers have helped plants to overcome one of the problems they encounter because of their immobility—their inability to reproduce efficiently with distant members of their own species. Rather than allowing the wind to carry pollen randomly, many angiosperms have developed complex relationships with insects. These range from the mutualistic interaction between bees and flowering plants, where both participants benefit, to the outright bizarre mating behaviour of male wasps of the species *Campsoscolia ciliata*, which attempt to copulate with the flowers of the Mediterranean orchid. The male wasp is apparently fooled into this act by a physical resemblance of the flower to the female wasp and also, more remarkably, by chemical compounds with a scent similar to that of a receptive female wasp. The wasp carries pollen to other orchid flowers and the species is efficiently fertilized. There is no apparent benefit to the wasp, in contrast to the efforts of bees, which gather nectar (and other materials to produce their propolis) as well as spreading pollen. Some plants and their attendant insects can truly be said to have coevolved, so much have their ways of life become enmeshed. Insects view the world at wavelengths different from ours. Studies have shown that bees perceive ultraviolet as a distinct colour, but don't perceive red. Bee-pollinated flowers are usually blue or yellow, with distinct markings that can be seen by ourselves if a photograph is taken by a camera sensitive to ultraviolet light. The most important plant pigments, which give flowers their colour, are flavonoids, complex organic compounds that block far-ultraviolet light and thus protect the plants, while selectively admitting blue-green and red light for photosynthetic purposes. An important class of flavonoids, the anthocyanins, are major determinants of flower colour. Their colour can range from red to blue depending on the pH. Some red, orange, and yellow flowers contain carotenoids, which also are found in leaves and stems. Various combinations of pigments give rise to the variety of colours we see in plants and their flowers. Reduced to the prosaic level of chemistry, all colours we perceive arise from the interaction between electromagnetic energy and the electrons in organic molecules. A rose by any other name.

13.3 The evolution of fungi

Difficult though it may be to believe, fungi are more closely related to animals than to plants, according to recent molecular evidence. Animals and fungi appear to have diverged from a common ancestor, possibly from a protist resembling a member of the colony-forming choanoflagellate family. Choanoflagellates are heterotrophic, aerobic protists with a single flagellum. The earliest fungi-like fossils are filaments from about 540 million years ago (Lower Cambrian).

Fungi are to be found almost everywhere on Earth. Their spores float in the air and settle on our faces, our food, and our fences. Well in excess of 70,000 fungal species have been named and it has been estimated that the total number of species exceeds 1.5 million, second only to the insects. Although they are principally land dwellers, about 500 known species are marine. I mention these numbers to emphasize the huge potential for fungi to influence their environment. Fungi obtain their food by secreting enzymes directly into their immediate environment, thereby digesting it externally rather than ingesting it as animals do. This way of feeding makes the fungi so distinctive that they have been assigned their own kingdom. They are characteristically multicellular, but a few, including yeasts, are unicellular. Although once believed to be primitive plants which lacked chlorophyll, the fungi in fact share little with the plant kingdom, except in general appearance and their lack of mobility. Fungi and plants both possess cell walls, but these are chemically different. Fungal cell walls consist mainly of the polysaccharide chitin, the same material found in the exoskeletons of insects, spiders, crabs, and shrimps. Chitin is more resistant to degradation by microbes than cellulose, the major component of plant cell walls.

Fungi are formed of slender filaments called hyphae. Typically, hyphae are divided into cells by septa, but these do not usually form a complete barrier between cells. Rather, the septa have large pores that let the cytoplasm stream through quite freely, allowing proteins synthesized anywhere in the hyphae to pass to the tip, which is the point of growth. As a result of this freedom of transport for essential molecules, the growth of hyphae may be very rapid during times when food and water are plentiful. It has been estimated that some individual (presumably large!) fungi can produce up to a kilometre of new hyphae within 24 hours. This astonishing growth rate reflects an equally impressive rate of metabolic energy flow and is only possible because of the structure and arrangement of the hyphae. Individual hyphae, which are barely visible to the naked eye, are arranged in a mass called a mycelium (from the Greek for fungus, *myketos*; the study of fungi is called mycology). The mycelium of a fungus may be many metres long. It penetrates into the surroundings, or substratum, and because of the filamentous form of the hyphae gives the fungus a relationship with its environment that is unique in muticellular organisms. The surface-area-to-volume ratio is very high, bringing fungi into intimate contact with their surroundings such that no somatic cells are more than a few microns from the environment, with only a thin cell wall and the plasma membrane separating them. The cell wall is nevertheless rigid, preventing microorganisms and particles from being engulfed directly. Instead, the fungi secrete a battery of enzymes into a substratum containing food and absorb the smaller molecules, which are released, mainly at or close to the growing tip of the hyphae. All fungi are heterotrophic, obtaining their food supply by growing on top of or inside their food source. Depending on the relationship with their food supply, fungi function as saphrophytes (which live on organic compounds from dead organisms), as parasites (living off other live organisms, usually harming them but giving nothing in return), or in mutual symbiotic association, where the association benefits both organisms. Ecologically, fungi are important as decomposers of the living and dead tissues of other organisms. In this role they release nutrients and other compounds to the environment, such as carbon dioxide to the atmosphere and nitrogen compounds to the soil. Fungi thus help to maintain the cycles that keep the limited amounts of these essential materials constantly in circulation in the biosphere. Keeping the balance of nature is a role not to be underestimated and the fungi are fully involved. They attack cellulose and lignin in wood and other plant material, but also impact negatively on many human activities. Fungi are great destroyers of human foods, as they grow on bread, fruit, meat, and vegetables. Amazingly, their digestive repertoire extends to cloth, paint, paper, rubber, leather, and even petroleum. Valuable crops are attacked by over 5000 species of fungi, causing billions of dollars in losses each year, while many trees and wild plants also succumb to pathogenic types. Over 150 species are involved in causing serious diseases in humans and domestic animals.

Other fungal types are commercially valuable. Yeasts, such as *Saccharomyces cerevisiae* (baker's yeast), produce alcohol and carbon dioxide, and are widely used in baking, brewing, and winemaking. A number of antibiotics, including penicillin, have been isolated from fungi, and in 1979 the 'wonder drug' cyclosporin became available. Continuing tissue rejection problems up to the late 1970s almost resulted in the cancellation of attempts develop organ transplants in humans. Cyclosporin was found to suppress immume responses causing rejection and allowed the programme to proceed. Truffles, morels, and some 20 types of mushrooms are enjoyed as food by people around the world. The ability of fungi to break down all kinds of substances has led to their use in toxic waste cleanup and also in non-toxic waste disposal.

What needed to be 'invented' by the ancestral protists that evolved into the fungi? Considering the relative simplicity of structure, and their way of obtaining food (and thereby energy), not a great deal. Development of a basic set of enzymes allowed fungi to take advantage of the many food sources that existed. The components of the basic set changed as new fungal species evolved along with new plant species and after animals became available as a food source on land. The development of a cell wall was essential for terrestrial organisms to maintain structures that were rigid enough to support them against gravity and to penetrate the substratum. The fungal cell wall does not need to be as structurally strong as in plants, as fungi don't need to grow large above-ground structures. Much of the fungus is in the form of mycelia, which are buried close to or well inside the food source. There is no need for a large light-collecting canopy, as in a tree or shrub, to maximize photosynthesis.

These then are the fungi, with a kingdom to themselves and deservedly so. As an integral part of the biosphere, their influence is often overlooked, but they are all around us, quietly helping to maintain the energy balance of the environment that we more spectacular organisms so readily take for granted.

13.4 The evolution of animals

The sources of cellular energy in multicellular organisms are essentially the same as those in unicellular life forms. The basic biochemistry of the cell is the same and ATP is still the major energy source. Mammals, as examples of complex multicellular organisms, have added layers of structural complexity compared with their unicellular cousins. Mammalian bodies are often described and studied in terms of the eight or so systems of which they are constructed. Their body complexity leads to extra requirements, such as the means to distribute and regulate energy supply in the mammal as a whole. To achieve this, the energy requirements of all cells, moment by moment, need to be monitored, collected, and collated, and the resulting information distributed appropriately. This distributed information is directed to various feedback mechanisms, which act to supply individual cells with their required amount of energy. The whole integrated ensemble of processes is working all the time to maintain the delicate balance of energy demand and supply essential for healthy cell life.

To reiterate: animals are heterotrophic; they depend for their energy on food derived from other living organisms. The search for food dominates the behaviour of animals in a much more visible way than it does that of green plants. The behaviour of animals is more obvious as they are relatively large, mobile, and readily catch our interest. Plants are autotrophic, and as such require water, nutrients, CO_2, and sunlight, all of which are readily accessible on much of the land and in the surface layers of oceans and other bodies of water. At about the same time as autotrophic protists began tentative steps along the multicellular pathway that was to lead to modern plants, early heterotrophic protists, the ancestors of the animals with which we are all familiar, also 'experimented' via mutation and natural selection, with the advantages and drawbacks of multicellularity. This exquisite sorting process, over time, generated an enormous variety of ways to improve the vital processes of feeding and reproduction. Success, at least that measured by the survival of enough organisms to provide today's astonishing diversity of animals, was achieved through the cooperative association of cells. As with plants, no doubt there were many trials and failures. First, cells formed into simple tissues; some individuals survived and succeeded. Ultimately, came the complex and specialized organs that we see today in the domesticated and wild animals around us. One of the differences between animal groups which strikes us immediately is that of body shape.

We could spend quite some time on the topic of animal body shapes, or, as evolutionary biologists would say, body plans. As an example, consider the dog. All dogs have the same body plan, but it is obvious that all dog breeds do not look (or behave) alike. All existing dogs (family Canidae) evolved from the wolf, and humans over thousands of years have had a major hand in the accelerated development, under domestication, of the major breeds. The story of the domestic dog is an example of evolution not by natural selection, but of selective pressure exerted by humans. Much the same can be said of the other animals domesticated by humans—pigs, cattle, sheep, goats, poultry, horses, pigeons, and all the rest, plus the domesticated plants. All have been subjected to selective breeding, sometimes with astonishing success.

Evolution has in general tended to favour conservation of animal body plans, rather than replacement of them. Many examples were noted by Darwin, and in the mammals these include the familiar comparison of the bones comprising the wing of a bat, the flipper of a whale, the forelimb of a mouse, and the human arm. These are examples of structural homology, or structures built from the same basic anatomical feature. The overall plan has been retained by the animals, despite considerable differences in their respective ways of life. Such similarities indicate a common ancestor and constitute one very powerful type of evidence for evolution, and for its ability to produce diversity within a basic plan—remember the principle of common descent.

The more closely two organisms are related, the more characteristics they share, both morphologically (i.e. in body shape and body plan) and genetically. The animal kingdom as a whole has a rather limited number of characteristic body plans, which developed broadly as follows. Early association of cells to form primitive animals and fungi could well have started with the aerobic protist family called the choanoflagellates. These organisms probably formed hollow, spherical structures initially, which, via mutations, gradually flattened into a pancake shape consisting of two layers of cells. The cells of the back or dorsal side were thinner than those of the bottom (ventral) layer. The ventral layer was thicker and used for movement and food gathering. Over time, the ventral layer developed a cavity, which evolved into a groove that served as a primitive digestive region. Eventually the groove sealed over, forming an early version of what is now, in animals ranging from worms to mammals, called the alimentary canal. These early animals had two distinct layers of cells: those on the 'outside' became the ectoderm, while those lining the alimentary canal became the endoderm. The process also formed a body cavity, or coelom, which had no contact with the outside world. In time the coelom became lined with a third layer of cells, the mesoderm. Thus arose the three-layered body plan of the triploblasts, which most of the animal world, including ourselves, subsequently adopted. The body became elongated in the direction of the alimentary canal and thus became bilaterally symmetrical, that is it possessed a right side and a left side, which were reflections of one another, as well as the dorsal and ventral aspects. The two ends of the alimentary canal eventually developed distinct functions and became the mouth and the anus, with food passing unidirectionally from the former to the latter, being digested and absorbed along the way. In order to control an increasingly complex body, the nervous system evolved in parallel, ultimately leading to a head and brain located in the anterior (front) region near the mouth, where they were best places to house other sensory systems such as those for sight, smell, hearing, taste, and touch. The sensory organs allowed the animal to keep in constant contact with many aspects of the surrounding environment, and allowed it to respond rapidly to stimuli received from that environment. Later still, a backbone evolved in some animals, along the path of the nervous system which ran the length of the body, and the vertebrates, ranging from fish to amphibians, reptiles, birds, and mammals, came into being. We have seen a number of times previously that 'successful' genetic mutation, as the main mechanism underlying evolution, usually results in relatively small changes in an organism at a time. An accumulation of small changes, over many successive generations, can result in large differences. Body plans that have proven successful need not change drastically to achieve quite different functions, as shown by our example of wings, arms, and flippers above, so the question arises: how are the basic animal body plans maintained, yet allowed to differ in detail, that is to generate the enormous number of animal shapes we see around us? For part of the answer, we must probe a little into the mysteries of animal development.

There is a period in the development process of an animal called a 'phylotypic stage'. Before the phylotypic stage the 'decision' as to which phylum the animal will belong to has not been made. Before the phylotypic stage, the threshold of commitment has not been crossed. Despite this lack of decision, there has been already programmed into the developing organism a number of blocks of undifferentiated cells, arranged relative to one another just as they will be arranged in the mature adult. The basic body plan is already in place, preserved because it has been advantageous, so in the evolutionary sense it does not 'need' to change much. As development proceeds, there comes a stage where these blocks of cells are allowed to differentiate more or less independently, leading eventually to an individual belonging the phylum to which its own parents belonged. The all-important decision at the phylotypic stage is, not surprisingly, determined by specific regulatory genes characteristic of the phylum.

For example, the animal Phylum Chordata includes the Subphylum Vertebrata, whose members possess a body plan characterized by having the familiar left/right (bilateral) symmetry, a head with a skull and brain, a tail, and a segmented vertebral column (the backbone). Depending on the class to which our example belongs, its phylotypic stage may become a jawless fish, a cartilaginous fish such as a shark, a bony fish such as a herring, a frog, a reptile, a bird, or a mammal; the basic body plan is the same. This plan and its inherent flexibility allow the development of fins, legs, wings or arms, to name a few easily observed variations on the theme. Although we may view elephants and toads as vastly different, their body plans are similar; they belong to the same phylum (Chordata) and subphylum (Vertebrata), and begin to differ in classification only at the class level (*Mammalia* and *Amphibia*, respectively).

Built into the genome of every multicellular species are the instructions to produce the body plan characteristic of that species. Body plans are the result of a combination of up to several hundred cell types, all of which are formed by division and differentiation from a single cell, a fertilized egg in the case of animals (or, in some plants, a spore). With great certainty, we can assert that pea plants will produce pea plants and ducks will produce ducks. This certainty reflects our experience, and underpinning it all is the regulation of gene expression, from the fertilized egg to the mature adult containing cells in their billions. If something should upset the regulatory mechanism, disaster for the individual is usually the result. For humans, malnutrition, disease (rubella), some drugs (smoking, heroin), or other chemicals can upset the exquisitely balanced sequence of events that culminate in birth. Those humans who are born 'normal' are fortunate, considering the plethora of hazards they face leading up to that event. Other species face similar problems.

New discoveries in developmental genetics that depend on the marvellous techniques of molecular biology are rapidly advancing our knowledge, taking us further and further into the evolutionary past to reveal some most surprising relationships. In the fruit fly *Drosophila*, the classic choice of classical geneticists, there was discovered a series of genes, called Hox genes, each of which is active in a different section of the embryo, from front to back. Each gene appears to act as a master switch that activates a series, or cascade, of other genes that are needed for the development of the respective regions of the embryo. The Hox genes have been sequenced comparatively recently. The surprise was the finding of a similar series of genes in the mouse and subsequently in other groups of animals. In summary, it is now believed that the common ancestor of all bilaterally symmetrical animals, such as flies, segmented worms, fish, and mammals, possessed a series of Hox genes which acted on different regions of the body and controlled the development of structures in those regions. Whereas flies have one set of Hox genes, the more complex vertebrates have four sets, each slightly different from the others. These genes have been conserved for about 500 million years and it has been suggested that their possession should be the defining characteristic of all animals. Natural selection seems to work on the principle 'if the system works, why change it, especially if there are hazards in doing so?' Perhaps some early 'attempts' by animals did sample other systems, but these didn't survive. The widespread occurrence of the Hox system was so unexpected because there is nothing in common between the animal structures it controls in different groups of animals. There is nothing in cats or in pigeons which corresponds to the six legs and two pairs of wings of the insect thorax. In retrospect, it was realized that the control mechanism, or signalling system, was being conserved. The Hox genes signalled 'build something here', while at the next level of control the structural genes responded, producing a fin, a wing, or a leg. Thus, the actual genes being controlled were the variables which, over time, evolved to produce the different detailed structures we see in animals today—fin, wing, or leg. The Hox signalling system itself was what evolution conserved at a fundamental level.

13.5 The organization of the mammalian body

Unless it is necessary, in the following discussion I won't distinguish between humans and other mammals, as many aspects of their physiology are common. The basic building blocks of the mammalian body are the familiar cells. In humans there are some 210 different cell types. Cells of the same type are grouped into tissues, the main tissues being: epithelial, connective, lymphoid, nervous, and muscular. Aggregations of various tissues form the familiar organs of the body. In turn, the organs and tissues are traditionally classified into a number of functional systems, of which there are eight.

1) The *musculo-skeletal system* comprises the bones of the skeleton, skeletal muscles, and a number of associated tissues, whose main functions are to provide a means of movement and support for the internal organs. The system is especially important in land animals, which also need to support themselves against gravity.
2) The *cardiovascular system* is necessary to transport oxygen and nutrients to all the cells in the body. This is usually done by blood, pumped by some kind of heart. Simpler, single-celled animals, which are in direct contact with their environment, do not need such a system.
3) The *respiratory system* (lungs and associated organs) extracts oxygen from the air and delivers it to the bloodstream, and removes carbon dioxide from the deoxygenated blood for expiration to the atmosphere. As such it is of primary importance in energy processing in mammals, all the cells of which are dependent on oxygen, but only a few of which are in contact with it. Once again, unicellular organisms don't require such a system.
4) The *digestive system (gastrointestinal tract, GIT)* is involved in extracting nutrients from the diet, that is it processes ingested food. The GIT is involved in the degradation and absorption of foodstuffs, and the removal of the depleted food residues. It is another specialized system not required by unicellular organisms.
5) The *urinary tract and the kidneys* are involved in the removal of the soluble, non-volatile waste products of metabolism. This system is also involved in the control of the composition and volume of the fluid surrounding the cells (extracellular fluid).
6) The *endocrine and nervous systems* act to coordinate and regulate the various bodily systems. Without this regulation, the body as a whole would not be able to function. The nerves use electrical signals for information transmission, whereas the endocrine system largely uses chemical messengers, such as hormones, which travel from their source via the bloodstream to the cells where their activity is needed. Each type of hormone usually has its own

receptor on the target cell surface, with which it interacts to elicit a response inside the cell.

7) The *reproductive system* produces the specialized sex cells, or gametes. In mammals these are the sperm (male) and the ova (female), which each contain half (the haploid number) the number of chromosomes normally found in the organism (the diploid number).
8) The *immune system* is the body's defence system against infection. It not only kills invading organisms and eliminates some foreign chemicals, but also destroys damaged or diseased cells that may be hazardous to healthy cells in the body.

All the organ systems listed above are unique to multicellular animals. As multicellularity developed from the simple association of similar cells, natural selection, as ever, conserved the 'good ideas' from the many that were undoubtedly generated, gradually honing each system as it arose to be increasingly efficient. Natural selection can only work on what has come before. There are therefore limits, both qualitative and quantitative, on what it can do in the short term.

Before mammals could evolve, other 'simpler' animals needed to emerge as intermediates on the journey to the complexity that was ultimately achieved by mammals. The interrelatedness and complexity of mammalian bodily systems require that they be suitably regulated and controlled. These are some of the defining characteristics of complex organisms, and of life itself. The two major regulatory systems in mammals are the endocrine system and the nervous system. One aspect of control in mammals that heavily involves the endocrine system is the maintenance of a stable environment in which each group of cells may work. The internal environment of a mammal consists of groups of cells in tissues and organs, surrounded by extracellular fluid. Both the cells and the surrounding fluid must be stabilized against rapid changes. The maintenance of a stable internal environment is called homeostasis. I don't mean to imply that the environment for all cells types is the same. Far from it. What is important is that the environment for any type of cell be maintained close to the optimum for that type of cell, under the conditions prevailing at the time. For example, for the heart muscle to continue beating strongly and regularly, the heart cells must continue to contract rhythmically. This depends on electrical signals, which depend on the relative concentration of sodium and potassium ions in the intracellular and extracellular fluids. An excess of potassium ions in the extracellular fluid may cause the cardiac muscle cells to contract irregularly instead of rhythmically, with potentially fatal results. Fine control of the extracellular potassium and sodium ion concentration is clearly essential.

Homeostasis is a property of unicellular organisms as well. Their internal environment must also be kept quite close to the optimal levels. The cytoskeleton, various organelles, and other components must have their essential gradients and concentrations carefully maintained for optimum activity. In general, monocellular organisms have little control over such variables as temperature or the chemical composition of their immediate environment. Multicellular organisms have the same problems, and the development of solutions to these problems has taken considerable evolutionary time.

One solution involved the adoption of an optimal extracellular environment in which the various cells could carry out their functions without having to continuously 'worry' about this aspect of their existence. Mammals also need to coordinate their various organs and tissues into an integrated whole. The eight mammalian organ systems listed above took some 500–600 million years to evolve. This seems a short time compared with the 3 billion years of life that preceded them and indicates that many of the necessary control mechanisms and principles had already been evolved by bacteria. Not a great deal needed to be 'invented' by natural selection, but what was invented made possible multicellular life as we see it today.

The evolutionary development of each organ system has been studied intensively across the whole range of animal groups. Although it is convenient for many purposes to recognize the individual functions of organs, the body functions as a whole. No organ or system is more important than any other in maintaining the overall health and wellbeing of an individual. If one part fails, it will affect the rest. For the brain, which must consume large amounts of energy continuously, glucose and oxygen depletion can be tolerated for only a short time before severe damage and death occur. This is one price we pay for our biological complexity, but at least we are capable of realizing, understanding, and coping with it. Medical experts often specialize in one of the systems, such as the nervous system or the GIT, or may concentrate on a very limited aspect, such as the heart or the kidneys. The complexity of the mammalian body precludes a single person being an expert in all its workings. There is still much to learn, even for the experts of today.

The study of biology is a never ending journey, whatever your view of life.

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