5. PRINCIPLES OF BIOLOGY

...The natural world is full of excellent designs that we can learn from....There should be a lot more contact and interaction between good biologists and engineers.

- Andy McIntosh

Biology can be a very complex science, and its principles are not always easy to define. Defining life itself is not easy, either, and there has been no totally satisfactory definition of life. As more and more is known about subcellular structures that prey on living things (for example, prions and viruses) it is clear that the demarcation between living and nonliving things is not well defined.

Living things are complex, they use energy to grow and repair themselves, they respond to external stimuli, and they reproduce. However, inanimate things, like fire, possess similar, if not identical, qualities. Some computer programs seem to be almost living. Contrarily, some living things, like mules, cannot reproduce and others, like seeds, may lie dormant for many years before suitable environmental conditions are present for them to grow.

Living things are not passive players. All living things actively attempt to control their environments to better suit them. If that is impossible, they either become dormant until environmental conditions change or else they die. Sometimes (for example, the case of the seeds) it is difficult to distinguish between dormancy and death. So, perhaps it is easier to define life as anything that isn’t dead. Whatever that means (see Section 6.23).

Figure 5.0.1. The biological unit is at least partly defined by and helps to define the surrounding physical, chemical, and biological environment.
The study of biology is incomplete without considering the surrounding physical, chemical, and biological environment (Figure 5.0.1), for living things sense environmental attributes, react to them, and cause environmental changes. All this positions the being to compete and survive better.

From here we develop the principles of biology:

1. *The primary goal of life is survival and reproduction.* Of these two, reproduction is the ultimate goal because genetic material survives for another generation. Genetic survival extends to the interest an organism shows in the welfare of another organism depends upon the degree of relationship. In general, the more of a genetic code that two individuals share, the more sacrifice that one would make for the other. Sharing food, defense against predators, and nurturing care are some possible demonstrations of altruism. A parent that shares about 50% of its genes (assuming sexual reproduction) with its offspring will give a lot of nurturing care. Less genetic code in common with other individuals results in less willingness to share. The genes, apparently, look out for their own. See Section 5.4.

2. *Living things are constantly changing.* Unlike nonliving materials or entities, living things adapt, mature, reproduce, and otherwise react to environmental conditions surrounding them. Some of these changes are patterned and some are not, but living things are never the same from one time to the next. Changes in living things usually develop gradually.

3. *Long term changes to a species occur only if there is a reproductive advantage.* This is really a corollary of the first two principles, but it is important to realize when change does not occur. Without a reproductive advantage, there will be no natural selection of a particular genetic code. No matter if some genetic modification seems to confer some advantage, unless there is an actual reproductive advantage, there is no permanent genetic change that occurs. See Section 5.2.

4. *Life is redundant.* There are many redundant features incorporated into living things. This makes life very robust. Because of redundant structures and processes, living things will attempt to face environmental challenges with the most efficient means. When the most efficient means fail, alternatives are used. When redundant features are exhausted, catastrophic failure (death) ensues. See Section 5.2.
5. Coexistence of species requires that each adapts to a different ecological niche. Otherwise their competition would be detrimental to one or both, to the extent of disappearance. See Section 5.4.

6. Attributes passed from one generation to the next require an information legacy. Physical and behavioral attributes may be acquired in response to environmental pressures. However, these cannot automatically be transferred to progeny without some means to do so. Normally the information repository given credit for information transfer from one generation to the next is the genetic code of an organism. Changes in genetic code are passed, usually intact, to the next generation, whereas physical or behavioral changes acquired by an organism that do not involve genetic modification are not passed. Cultural information can also be used to modify physical and behavioral attributes of the next generation, including those individuals not directly in a bloodline. However, this type of information, while broadly more powerful than genes, is not as permanent. See Sections 5.3 and 5.4.

7. Each distinguishing biological trait is made valuable by its cost. Those traits that give survival or reproductive advantages to individuals or groups come at a price. For instance, male birds and mammals often have distinctive coloration, plumage, or other physical characteristics that convey messages of reproductive strength to females. But there are costs associated with these characteristics, either in resources required or vulnerability to threats, that make these characteristics too costly to fake. Their presences thus remain honest indicators of the messages they are intended to convey. See Section 5.4.

8. An individual is a product of both its genetic code and its environment. The genetic code is considered to be the basic blueprint of life. However, environment plays a very important role in the expression of genes and in the physical and behavioral attributes acquired by the organism over its life span. Different characteristics can be attributed in different percentages to either genes or environment, but, overall, the environment plays about an equal role with the genes in the development of an organism. See Section 5.3.

9. Life is conservative. By conservative we mean that living things use those structures and processes already present to achieve its purposes. Each new species does not start anew with no history and no models. Instead, structures and processes already present in ancestral species are modified when needed to new uses. This makes for structural connections among species, and explains why some life processes are
accomplished rather indirectly. Similarities among life forms can be used to predictive advantage. See Sections 5.1, 5.2, and 5.4.

10. Living things use simple building blocks with complex interactions. The biochemical bases for metabolic processes, biomaterials, growth, reproduction, and other essential processes are simple ones. There are only just so many combinations of things that are possible. Proteins, for instance, are composed of a small number of amino acids. Physical laws governing the combinations of amino acids are relatively simple. Nevertheless, there are large numbers of proteins and their functions are nearly innumerable because the number of combinations of these relatively simple building blocks is extremely high. And, many of these combinations occur simultaneously to add to the apparent complexity. See Section 5.6.

11. Extremes are not tolerated well by living things, nor do living things create extreme conditions. Life will exploit its environment to the maximum extent possible. There is almost no environment on Earth that will not support some form of life; even very hot, very isolated, or very cold environments contain life of some form. However, there are energetic penalties to pay for adaptation to extreme environments. Parasites or predators prey on most organisms, and many of these, in turn, are prey for other organisms. Rivals are controlled, not eliminated. This balance gives rise to an eternal struggle that is never resolved. See Sections 5.4 and 5.5.
5.1 Form and Function

Anatomy is to physiology as geography is to history; it describes the theater of events.

-Jean Fernel

There is an intimate relation between the form of something living and its function. Let us examine our own bodies to illustrate this. Our ears are meant to gather in sound, so their shapes are like funnels, beginning with the large part of the external ear, and continuing through the ear canal. The outer part of the ear is large in order to focus sound waves toward the smaller ear canal. Animals that depend more on hearing have larger outer ears than those that do not.

Our noses are intended to smell and to condition inspired air (make the inspired air match our body temperature and humidity). Heat is added to air by convection, and convection heat transfer is more effective for larger surface areas and for turbulent airflow. Humidity can be added to the air by the same process of convection. Again, larger surface area and turbulent flow is desired. Smelling a certain chemical in the air stream requires that the chemical come in contact with receptors on the surface of the epithelium lining the inside of the nasal passageway. Unless the air stream is turbulent, chemical molecules could pass through the nasal passage without ever coming in contact with the surface. Thus, to enhance the sense of smell, to add (or remove) heat, and to add (or remove) humidity, air turbulence is desired.

Turbulence is enhanced by a passage with non-uniform cross-section and by twists and turns and protrusions. Notice that the nasal cavity has a large surface area, it is of variable cross-section, and the path of the air makes a large turn before entering the throat. The large cross-sectional area means that the air velocity slows from its value at the nostrils, increasing the residence time of the air in the cavity and giving it time to be heated and humidified.

The location of the olfactory receptors are in the place (at the top of the cavity) where it is most likely that incoming chemical molecules will strike the surface. When chemical molecules do contact receptors, they must fit together before a nervous signal can be generated. This requires that the receptor must have a shape complementary to the shape of the chemical in order that the two join together. Each different class of chemicals generally has a different set of receptors sensitive to that chemical class. The form of the nasal passage and the form of the receptors are both determined by their functions.

Let’s go farther. The eyes are meant to gather light and to sense an image. Any transparent tissue could allow light to pass, but it takes a lens to focus the light to form an image. Thus, there is a lens in the eye along with transparent tissue. All human tissues require oxygen to live, but the normal way for oxygen to be transported to the cells is through the vasculature. An eye with many capillaries would not be sufficiently transparent to pass a lot of light. Thus, the cornea of the eye has no capillaries. The tissues get their
oxygen by diffusion from the air through the tears. Behind the eye is an array of very sensitive light receptors that are nerve cells most sensitive to electromagnetic radiation in the visual range. Thus, we can see that the form of the eye is determined by its function.

Among other things, the fingers must obtain touch information. Thus, the touch receptors are located close to the skin surface. These receptors are not sensitive to light, as are the receptors in the retina of the eye, but do have some sensitivity to temperature.

If we look at birds, we see that they are equipped with wings shaped to allow them to fly, and they have hollow bones to give strength without inordinate weight. The bones of vertebrates give strength from inside the organisms. The skeleton can also provide external protection, as for insects or arthropods. With an external skeleton, however, the size of the animal is limited by the size of the skeleton. In order to grow, a new skeleton must be formed. This is very energy inefficient for large animals. Thus, internal skeletons are seen for these.

Plants have skeletons, too, but plants are not usually mobile, so they have distributed skeletons. The cell walls of plants are made of rigid cellulose, thus giving plants the ability to withstand forces that would ordinarily drive animals to move to shelter.

Figure 5.1.1. The weight distribution of the hind leg of a horse is compared to the weight distribution of a bear. The horse’s weight is much higher on the leg, reducing its inertia (given here by the radius of gyration) and allowing faster acceleration and deceleration in running (from Hildebrand, 1987).
There are vestigial organs that retain forms related to previous functions. The human appendix is one of these. The appendix once served as an organ for digestion in ancestral organisms.

Horses are built for speed (Figure 5.1.1). Their legs are elongated relative to their body size, but not too far as to cause undue interference between forelegs and hind legs (as in giraffes). Muscle attachment points are closer to the joints than in other animals so that a small muscular contraction causes a faster movement of the end of the limbs (Hildebrand, 1987). Ligaments of the hind limb act as elastic bands to store energy upon impact and release it during movement of the leg. Leg bones are as light as possible and still have enough strength to sustain forces incurred during galloping and jumping. The weight of muscles is minimized because the structures of the joints lock the legs into movements in a plane; muscles and tendons are not needed to strengthen the joints in a transverse direction. Everything about the form of a horse’s leg is related to its function of generating running speed.

Form and function. They are enough related that function can often be inferred from the form of a part of a living being.

Applications and Predictions

1. The function of a biological structure can often be inferred from its shape.
2. Similar types of structures from different species will have similar shapes and properties if they perform the same function.
3. Similar structures with similar functions in different organisms could have evolved by different paths and still look and act similarly.
4. Ducks’ webbed feet mean that they are meant to swim.
5. Organisms adapted to similar environments will possess similar features.
6. Dogs have been bred to have forms determined by their uses.
7. Prehistoric environmental conditions can be inferred from fossil records.
5.2 Modularity and Incremental Change

Survival, whether as members of the human species or as professionals in a clinical, research, or commercial environment, depends on the ability to adapt.

- David Dewhurst

Biological systems are modular. There are a few fairly simple building blocks that are used for multiple purposes, and it is the adaptation of these building blocks for new purposes that makes biology unique.

When environmental conditions change, and a new biological organism is needed, existing organisms change to meet the need. An entirely new organism is not created. Thus, there is a similarity of forms between organisms, and, for the most part, the more closely related the organisms are, the more similarity there is. Thus, the bones and soft tissues are similar among mammals, with strikingly close similarity among the closest related mammals. There is a similarity between mammal hearts and reptile hearts; there is a similarity between fish muscle and amphibian muscle. There is a similarity, too, in enzymes produced and metabolic pathways. ATP is nearly universally used as an energy transfer compound. That means that use of ATP as an energy storage compound evolved very early in the history of life.

Challenged with antibiotics, microbes evolve to new forms capable of immunity. Challenged with insecticides, insect pests evolve to become immune. Adaptation of weeds under herbicide pressure also occurs. In each case, entirely new organisms were not created. Rather, there was an adaptation of existing parts, put together in new ways.

We have become so accustomed to this tendency that we have lost appreciation for the fact that unique functions can be achieved by existing forms assembled in new ways. Thus each cell in early fetal development can become nerve, bone, or liver; further modification fixes their functions.

It is obvious from their appearances that biological organisms share a close relationship. They share similar morphological features, each with some variation from the next. Indeed, the closer two species are related, the more similar they appear. Among humans, members of the same family often appear very much alike, and can be distinguished from unrelated individuals quite readily (see also Section 6.19.1). What is not so obvious is that even at the molecular level there is a great deal of commonality. All organisms use the same set of bases for their genetic codes. Plants and animals share at least 50% of the same genetic code; fruit flies and humans share 44% of the same genetic code; chickens and humans share 60% of the same genetic code; primates and humans share 99% of the same genetic code; and among humans there is only a 0.1% variation.

New genes, new organs, new species, and new family members do not appear spontaneously, but are derived from existing genes, organs, species, and family members. The differences are sometimes larger and sometimes smaller, but they are clearly related.
Because of this, it is often easy to guess at the function of an organ in a newly discovered species by knowing the function of a similar organ in familiar species. A stomach is a stomach is a stomach.

If a new form of life is necessary to adjust to a new environment, a new species is not formed from scratch, but the new species evolves from an existing species by incremental change. New functions are found for existing organs; improved function is derived from existing function. The old is not discarded, it is changed. (One might be tempted here to say that the old is improved upon, but improvement is relative; an improvement for one set of environmental pressures may be a worsening for a different set of environmental pressures.) The new does not erupt spontaneously; it is formed from the old.

We can therefore trace lineages by looking back over the incremental changes that are evident from one organism to a previous one. When we do that, it becomes clear that, whether we view a difference as either small or large, any differences we see are not revolutionary but evolutionary. The same gene that controls the process of cell division, and which, when defective, causes cancer in humans, is also responsible for allowing fruits, such as tomatoes, to achieve the unnaturally large sizes we expect from our orchards and gardens. This is an example of identical or similar biological structures having somewhat different outcomes in different species.

We have seen how biological form is related to biological function. That is, geometrical shapes are related to the functions of different parts of biological entities. Incrementality develops the form through many small changes over many generations (Figure 5.2.1), as long as each small change gives the possessor of the change some advantage to survive and reproduce. If the incremental change cannot be passed to succeeding generations, and give them survival and reproduction advantages, then the changes are not permanent and must begin anew for each generation.

Evolution from one form to another, more adapted, form is unlikely to occur if the intermediate form is less well adapted than the more primitive form from which it starts. Squid are less economical swimmers than salmon, but squid were unlikely to develop fishlike tails that would have made them better swimmers because there does not seem to be any conceivable evolutionary route from a squid to a fishlike animal that would not involve passing through a stage less fit than either (Alexander, 2003).

This is precisely why form and function are so closely related in biological organisms. Not all incremental changes are able to improve the functioning of the organism, but those that do are able to make better use of physical or chemical principles than previous forms. The fittest survive.

Behavior is also incremental. Biological organisms adapt much better to small changes than to large ones; small adjustments are more easily made than large ones. As an example, consider thermoregulatory adjustments in humans. Within a relatively small temperature range, called the thermoneutral zone, humans may regulate their body temperatures by cutaneous vasoconstriction or vasodilation (reducing or increasing blood flow to the
Figure 5.2.1. An example of incremental morphological change (National Geographic, 2001).
A warm skin surface loses more heat to the environment than a cooler skin surface (see Section 2.7). This adjustment is small, easily made, and usually not noticed. A large increase or decrease in temperature, however, results in much more noticeable and more difficult changes. Cold elicits shivering, going to the closet for more clothes, and turning up the thermostat. Hot elicits profuse sweating, removal of clothes, seeking cool spots, drinking extra fluids, and reduction of activity. If the onset of cold or hot is sudden, the person feels extremely uncomfortable. If the onset is slow, such as during the change of seasons, conditions that would feel very uncomfortable for a sudden change can be tolerated well when they occur slowly. This is called thermal acclimation, and involves hormonal and other physiological adjustments that occur relatively slowly. Conversely, thermal conditions that would feel comfortable for the unacclimatized may feel uncomfortable for the acclimatized. Biological engineers should be aware of these differences when designing environments for plants, animals, or microbes.

As a second example, consider the case of the common honeybee, *Apis mellifera* and its relation to a parasite mite, *Varroa destructor*. For years the mite coexisted with the Eastern honeybee, *Apis cerana*. It did not disturb the Eastern honeybee all that much, because the behavior of the honeybee kept mite populations relatively low; it was an insignificant pest. Sometime in the middle of the 20th century, *Apis mellifera* was introduced into Asia, and *Varroa* underwent a change that made it able to parasitize its new host. Since then, *Varroa* has become a major pest of *Apis mellifera*. The honeybee is slowly adapting to the new threat. There are small pockets of resistance to *Varroa*, and those bees that cannot tolerate *Varroa* are dying. The first defense by beekeepers was to depend on pesticides to control the mites, but the eventual solution will be resistance that develops in the honeybees themselves because of natural selection. As long as this sudden parasitic threat does not result in the catastrophic loss of all honeybees, slow adaptation will allow bees to be able to coexist with the mite. Incremental changes will occur to ensure the survival of this species of honeybee.

Nowhere is evolutionary adaptation more apparent than in the finches of the Galapagos Islands off the western coast of South America. These birds, known as Darwin’s finches after the famous biologist who described their similarities and differences, exhibit a wide range of adaptations to local environmental conditions on the islands where they live (Grant and Grant, 2002). Some have developed stronger beaks to crack strong seeds, some have become better adapted to dry conditions rather than rain forest, and some spend more time on the ground whereas others are found in trees. These adaptations have been so profound that interbreeding of the most distant of these birds does not happen; they have developed into entirely different species. By studying these birds, Darwin was able to describe what he stated was the way new species evolve from a common ancestor.

*Convergent evolution* is the term that describes the result of evolutionary pressures on organisms with different origins. For example, rotifers are small animals that live in soil and in water. Most rotifers have a
simple gut lined with cells running from the mouth to the anus. In a number of very small rotifer species, this gut is absent and replaced by a continuous cytoplasmic sac that forms food vacuoles at the mouth end and ejects wastes from the vacuoles at the anal end. This digestive system is exactly like that found in ciliate protozoa, organisms of the same size occupying a similar ecological niche. The small rotifer has apparently replaced its ancestral digestive system with the simpler digestive system of the protozoa because it was subject to the same environmental pressures as was the protozoa. This might indicate that the same genes present in protozoa are also present in rotifers, and are only expressed under the proper set of circumstances.

The degree of similarity between body shapes, biomechanical muscle forces and attachments, and swimming styles of sharks and tunas well illustrates convergent evolution brought about by nearly identical environmental factors (Shadwick, 2005). Although each of these organisms arose at different times from very different predecessors, both have developed constant and fast swimming styles with teardrop shaped bodies, to streamline water flow, specialized muscle biomechanics to isolate their swimming movement to the tail region, highly specialized gills to supply adequate oxygen amounts, and regions of nearly constant muscle temperature for dependable muscle contractions.

### The Evolution of Hemoglobin

Four billion years ago, when the earth was young and without life, it is believed that there was no oxygen in the air. The earth’s atmosphere contained mostly water vapor, nitrogen, methane, and ammonia (Hardison, 1999). When the first organisms developed about 3.8 billion years ago, these atmospheric constituents were used for food and energy. It seems plausible that these early metabolic reactions were facilitated (or catalyzed) by metals, such as iron and magnesium (Hardison, 1999).

Between 3.3 and 3.5 billion years ago, there appeared cyanobacteria that could convert energy from the sun into chemical energy through photosynthesis. Cyanobacteria removed electrons from hydrogen sulfide present in the atmosphere to produce elemental sulfur and ATP. Photosynthetic bacteria appeared sometime between one and two billion years ago that used water (H₂O) rather than hydrogen sulfide (H₂S) as the chemical substrate. As a result, the earth’s environment was remarkably transformed.

The oxygen so produced was released into the atmosphere and gradually came to be its most important constituent. With abundant oxygen, other life forms appeared that could use the highly reactive nature of oxygen to their metabolic advantage. It was not an easy trick: oxygen
Example 5.2.1 Cancer Cell Drug Resistance

Cancerous cells are resilient; they can develop effective defense mechanisms to avoid toxic or static effects of chemotherapeutic agents. Although therapeutic drugs may kill the vast majority of cancer cells, those that survive can form the nucleus for drug-resistant cancers. New cancer growth would be impervious to the chemotherapy that was previously effective. Predict the type of cancers that are most likely to be drug resistant.

Solution:

Gastrointestinal tract and kidney tumors are most likely to be drug resistant. These tissues have evolved to tolerate natural cytotoxins in foods.

One important defensive mechanism used by these and other drug-resistant cells is a natural drug pump dependent on a protein molecule called P-glycoprotein resident in the cell membrane. After the cytotoxic drug enters the cell by diffusion, this chemical draws it out again and lowers the intracellular concentration to sublethal concentrations. One solution to this
problem is to block the drug pump, either by a second drug or by inserting a gene into the cell that interferes with the drug pump mechanism.

Applications and Predictions

1. A majority of the genetic code of insects will match the genetic code of humans.
2. Vestigial organs will be seen at various stages in fetal development.
3. Related species will have similarity of structures.
4. Formation of new species will not be easy to detect because the differences will be small.
5. Microbes in a bioreactor will adapt to new conditions better if the new conditions are imposed slowly rather than suddenly.
6. Permanent changes in the characteristics of a population occur slowly, so they will only adapt to long-term average environmental conditions.
7. Adaptations to new environments will usually come from physical or behavioral traits already present to some extent in the population of organisms.
8. Any environmental change that kills the entire population will be too severe to be accommodated. The dinosaurs probably faced this challenge.
9. Human appendixes have no known remaining function, but unless there is a survival cost to retention of appendixes, humans will continue to have them.
5.3 Genetic Basis

*Evolution is blind; technology is mind.*

- Chris Calladine

It’s really the ultimate in biological control. That is the determination of structure and function of the next generation by the previous generation. This is the effect of genetic inheritability.

Genetic material has been called the blueprint of life. It is the material that stores accumulated information about the complexity determined from generations upon generations of adaptations and modifications to environmental pressures.

5.3.1 DNA as the Blueprint

*Instead of the book of life, DNA is more like the scrapbook of life. Sentences, paragraphs, or entire chapters are copied and haphazardly inserted into various parts of our genome. In some people, the same page repeats over and over, while other people don’t have that page at all.*

- Steve Olson

The basic storage code is found in very ancient biochemical molecules called *deoxyribonucleic acids* (DNA). These nucleic acids contain a phosphate group, a five-carbon sugar (deoxyribose), and a nitrogenous base. DNA strands are formed when the phosphate groups and sugars bond covalently to form a backbone, with the nitrogenous bases exposed like ornaments on a Christmas tree (Figure 5.3.1).

The bases are extremely important to DNA. They can either be in the form of a pyrimidine (a six-member ring of carbon and nitrogen), or a purine (a six-member carbon and nitrogen ring attached to a five-member carbon and nitrogen ring). Of the two, the purines are larger.

DNA contains four different bases: the pyrimidines cytosine (C) and thymine (T), and the purines adenine (A) and guanine (G). As it happens, DNA forms a double helix structure (Figure 5.3.2) composed of two complementary DNA strands. Hydrogen bonds between the two bases (called a *base pair*) of the complementary strands hold the two strands together. The only possible combinations of bases between the two strands are pairings of purines with pyrididines:

\[
\begin{align*}
A & \leftrightarrow T \\
G & \leftrightarrow C
\end{align*}
\]

Thus, if a sequence of bases on one strand is A A G T C, the sequence of bases on the complementary strand must be T T C A G.
5.3.2 RNA as the Fabricator

*In nature, technology has already been at work for millions of years.*

-Buckminster Fuller

The ultimate result of DNA is that proteins are formed regulating the behavior of the cell. DNA is not the means to do this directly, however. Proteins are formed from polypeptides (two or often more amino acids linked together), and these are formed from amino acids that bear a distant relationship to DNA. The organization of this process is found in simplified form in Figure 5.3.3.

Short sections of DNA act as templates for the formation (transcription) of messenger RNA (mRNA). RNA is *ribonucleic acid*, which differs from DNA in that the five carbon sugar is ribose instead of deoxyribose.

![Figure 5.3.1. The structure of DNA and RNA. Each unit has a phosphate group (yellow) and pentose sugar (green) to form the backbone. Pyrimidines or purines attach to the sugars to complete the strand. DNA and RNA include slightly different pyrimidines and sugars, but otherwise have the same structure (Campbell et al, 1999).](image-url)
deoxyribose. RNA forms a polymer structure similar to DNA, except that it is single-stranded and the pyrimidine base uracil (U) replaces thymine (T). When RNA is formed from a single DNA strand, base pairs can be:

\[ \begin{align*} 
A & \leftrightarrow U \\
G & \leftrightarrow C 
\end{align*} \]

Messenger RNA essentially carries information contained in one gene, which then results in one polypeptide.

Because there are 20 common amino acids and 4 nucleotide bases, 3 bases must be the minimum number to specify each amino acid. If each base coded for one amino acid, only 4 amino acids, each corresponding to one of the 4 bases,

Figure 5.3.2. The double helix. The DNA molecule is usually double-stranded, with the sugar-phosphate backbone of the polynucleotides (abbreviated here by blue ribbons) on the outside of the helix. In the interior are pairs of nitrogenous bases, holding the two strands together by hydrogen bonds (Campbell et al, 1999).

could be specified. If two bases were necessary for each amino acid, the number of base pair combinations is \( 4 \times 4 = 16 \), still less than the 20 amino acids to choose from. Three base pairs gives \( 4 \times 4 \times 4 = 64 \) possible
combinations, a number greater than the required 20. There are some combinations that redundantly specify the same amino acid, and some base pair combinations seem to encode for starting and stopping operations. The combination of the three base pairs required to specify one amino acid is called a codon. Whereas one gene is associated with one polypeptide made from several amino acids, many codons comprise one gene.

The polypeptide is actually formed outside the cell nucleus as a ribosome moves along the mRNA molecule. The ribosome is composed, in part, with ribosomal RNA (rRNA) that helps to align the amino acids with the mRNA codons. Transfer RNA (tRNA) molecules, formed of short strands of RNA, wander through the cytoplasm, linking with specific amino acids floating in the cytoplasm and transport them to the ribosome, where they are joined to form a polypeptide (Figure 5.3.4). All three types of RNA, and several other types also, are transcribed from different sections of DNA.

![Diagram of the production of proteins from DNA instruction set.](image)

As with most biological affairs, the strict association of one base pair with another is not always so. When the association between specific base pairs is relaxed somewhat, several forms of the same tRNA are possible as it folds on itself. This is called wobble.

The actions of mRNA and ribosome are similar to a tape playing instructions into a parts-assembly machine. The protein or polypeptide is assembled one amino acid at a time, and, once produced, can act as an enzyme, for example, to create the amino acids required for the next set of
proteins. In this way, the sequence of DNA bases is translated into the amino acid sequence of a protein. The feedback loop comprising protein formation, enzymes, amino acid synthesis, and ribosome action indicates that the process can be regulated so that the amount of an enzyme produced depends on the metabolic needs of the cells.

The genes determine the sequence of amino acids in a protein, but they do not, in and of themselves, determine how the protein is folded. Thus, the genes are only the foundation of cell activity, not the entire blueprint.

### 5.3.3 Gene Types

*Happy is he who gets to know the reasons for things.*

- Virgil

DNA material is found in chromosomes. Eukaryotic (higher level cells) chromosomes are each made of a single strand of DNA and several different kinds of proteins (Hale et al, 1995). These chromosomes exist in pairs (said to be *diploid*), except in some lower forms of algae or fungi that have single sets of chromosomes only (said to be *haploid*). Prokaryotes (bacteria) have but one chromosome arranged in a circular shape. Diploid cells thus have paired (*homologous*) chromosomes containing identical genetic loci. Both of these genetic locations (called *alleles*) may either have the same DNA base pair sequence or they may be different. If the same, then the cell is described as *homozygous*; if the alleles are different, then the term is *heterozygous*.

Heterozygous cells have two different genes encoding for the same trait, giving the possibility of a conflict between them. Many genes display either *dominance* or *recession*, the dominant gene determining the apparent trait and the recessive gene being hidden except in very nonobvious tests (as for example, by gene-mapping). If both genes are homozygous recessive, then the trait is determined by the recessive gene, and becomes apparent.

Crosses between homozygous dominant and homozygous recessive individuals (for one particular genetic trait) will give all heterozygous offspring that express the dominant trait (Figure 5.3.5). Crosses between two heterozygous individuals will, on average, yield one-quarter homozygous dominant offspring, one-quarter homozygous recessive offspring, and one-half heterozygous offspring (Figure 5.3.5). Three quarters of these offspring will, therefore, exhibit the dominant form of the trait, and only the homozygous recessive offspring will exhibit the recessive form. Gregor Mendel observed these results with his classic experiments on peas with white
Figure 5.3.4. Polypeptides are formed at the ribosome through a process called translation. Messenger RNA acts as a template, and transfer RNA acts as a scavenger, bringing the correct amino acids to the ribosome in the correct order determined by the mRNA (Campbell et al, 1999).

(recessive) and purple (dominant) flowers. It was his pioneering work that showed that genetic characteristics did not blend together, but instead retained their essential qualities (Hellman, 1998).

The genetic makeup of a cell is called the *genotype*, and is determined fully when every allele is known. The physical appearance and apparent physiological traits of a cell is called the *phenotype*. In the case of Mendel’s flowering peas, there were three separate genotypes resulting from a cross between two heterozygous individuals (purple-purple, purple-white, and white-white); there were, however, only two distinct phenotypes (purple or white).
5.3.4 Genetic Expression

The Austrian monk Gregor Mendel was also studying mice, which he bred with the goal of deciphering the inherited traits of coat color. However, to Mendel’s conservative bishop, the thought of a monk spending his time with copulating mice seemed inappropriate. He banned the mice, and Mendel set his sights on a less prurient subject for investigation, peas.

-Terri Peterson Smith

Mendelian experimental results were extremely simple, much simpler than many other real results. Although there are cases where traits are determined by two independent alleles, one dominant and one recessive, and Mendel happened to have observed these in his experiments, all is not that easy. There are cases of multiple alleles (human blood types are an example). There are cases of incomplete dominance and codominance when intermediate levels of biochemicals are either not sufficient to produce the full effect or when intermediate levels can produce the full effect. There is pleiotropy, where one gene can affect an organism in many ways, and there is epistasis, where one gene is affected by the presence of other genes. Some organismal traits are determined by multiple genes, a condition known as polygenic inheritance. And, finally, there is genetic linking between genes located on the same chromosome. It is possible that the effect of a gene can depend upon which parent contributed the gene. Thus, the Mendelian model is one of the simplest of possible genetic models, but it is the place to start.

Not all genes are expressed equally. Expression of genes means that RNA and proteins are formed from the DNA template (Figure 5.3.6). This can be seen by considering the many types of cells in the human body. Each cell contains the same genetic material, but some cells make certain hormones, other cells react to stimuli, and other cells yet have different structures. Although each cell has the same genotypical prototype, environmental factors change phenotypical properties. Similarly, environmental conditions outside the organism also affect gene expression (Table 5.3.1). Thus, knowledge of the genotype is no guarantee that the phenotype can be predicted.

Very few somatic cell genes are actively expressed. There appears to be something in the cell’s cytoplasm that directs genetic expression (Saltus, 2006). Some of this may have to do with methylation, wherein a methyl hydrocarbon group (CH₃) replaces a hydrogen atom on a genetic nucleotide base. A gene that is methylated lies dormant.

Fusing human embryonic stem cells with somatic cells can reawaken dormant genes. Sometimes this fusion leads to a double set of chromosomes, but sometimes the adult nuclei completely replaces stem cell nuclei (Saltus, 2006).
<table>
<thead>
<tr>
<th>Two Homozygous Dominant Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA x AA</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>AA AA AA AA AA 100% dominant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>One Homozygous Dominant and One Heterozygous Dominant Parent</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA x Aa</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>AA AA Aa Aa Aa 100% dominant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>One Homozygous Dominant and One Homozygous Recessive Parent</th>
</tr>
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<tbody>
<tr>
<td>AA x aa</td>
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<tr>
<td>↓</td>
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<tr>
<td>Aa Aa Aa Aa Aa 100% dominant</td>
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</tbody>
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<tr>
<th>Two Heterozygous DominantParents</th>
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<tr>
<td>Aa x Aa</td>
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<tr>
<td>↓</td>
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<tr>
<td>AA Aa Aa aa 75% dominant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>One Heterozygous Dominant and One Homozygous Recessive Parent</th>
</tr>
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<tbody>
<tr>
<td>Aa x aa</td>
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<tr>
<td>↓</td>
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<tr>
<td>Aa Aa aa aa aa 50% dominant</td>
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<table>
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<tr>
<th>Two Homozygous Recessive Parents</th>
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<tbody>
<tr>
<td>aa x aa</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>aa aa aa aa aa 0% dominant</td>
</tr>
</tbody>
</table>

Figure 5.3.5. Genetic outcomes from different crosses.
Figure 5.3.6. This hypothetical eukaryotic cell has 5 genes located in the nucleus. Only gene 1 and gene 5 are active in the control condition. Given a treatment consisting of a different set of environmental conditions (treated cell), genes 1 and 4 become active. RNA from these genes is formed in the nucleus; corresponding proteins are formed in the cytoplasm. This description leaves out several important intermediate details (Hamadeh and Afshari, 2000).

There is not a one-to-one mapping between DNA and mRNA sequences (Hamady et al, 2005). Through a process called splicing, certain portions of the RNA transcribed from DNA can be deleted or added. In alternative splicing, different pieces of transcribed mRNA are deleted under different circumstances. The result is several different mRNA forms from one DNA master sequence. In trans-splicing, mRNA molecules from different DNA sequences are spliced together. The result of this is mRNA from several DNA genes. In fruit flies, for instance, different mRNA forms are produced depending on the sex of the fly.

The phenotype (visible configuration) of the marsh plant *Sagittaria sagittifolia* depends on its environment. As shown in Figure 5.3.7, its leaf forms depend upon the degree to which it is submerged. Nowhere is there a better illustration of the interaction of environment with genetic expression than this.
Table 5.3.1 Genes or Environment? Estimates of Relative Contributions of Each to Personality Traits and Physical Conditions Based on Studies of Identical Twins

<table>
<thead>
<tr>
<th>Condition</th>
<th>Genetic Contribution</th>
<th>Environmental Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>60%</td>
<td>40%</td>
</tr>
<tr>
<td>Autism</td>
<td>90%</td>
<td>10%</td>
</tr>
<tr>
<td>Blood group</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>27%</td>
<td>73%</td>
</tr>
<tr>
<td>Children’s earache</td>
<td>71%</td>
<td>29%</td>
</tr>
<tr>
<td>Depression (women)</td>
<td>42%</td>
<td>58%</td>
</tr>
<tr>
<td>Depression (men)</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>Grip strength</td>
<td>65%</td>
<td>35%</td>
</tr>
<tr>
<td>Height</td>
<td>80-90%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Lean body mass</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>Musical pitch</td>
<td>76%</td>
<td>24%</td>
</tr>
<tr>
<td>Nightmares</td>
<td>36%</td>
<td>64%</td>
</tr>
<tr>
<td>Obesity</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>Type I (juvenile) diabetes</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>Voting in elections</td>
<td>60%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Although chimps and humans share about 99% of their genetic material, there are large differences between the two species. This is evidence that perhaps it takes more than a genetic blueprint to determine the characteristics of a species, and of an individual within a species.

Most genes have a switch, called a *promoter*, that controls the activity of the gene. Other regulatory elements, called *enhancers*, also are involved. Together, they determine how, when, and if a gene becomes active. Plant genes have been shown to be made ineffective by chemically attaching methyl groups to their surfaces (Brown, 2006). This is apparently the way plants regulate gene expression to control cell growth and development. In this way, fundamental genetic sequences are preserved but heritable changes in gene expression are made possible.

The transcription of mRNA from a gene requires the active presence of promoters, enhancers, and transcription factors produced from other genes. Thus, some genes regulate the activity of other genes, and the activities of both are dependent upon environmental influences. Apparently large differences in physical, intellectual, and emotional characteristics of animals can thus be determined not by changing the presence of certain genes, but by whether or not these genes are used, when they are used, and for how long.
Figure 5.3.7. The marsh plant *Sagittaria sagittifolia* as it appears: a) partially submerged, b) completely terrestrial, and c) completely submerged. This illustrates that genetic expression is highly dependent upon environmental factors (West-Eberhard, 2003).

Most chromosomes in the human cell nucleus are roughly 2 m long. Humans have 48 pairs of chromosomes tightly packed together; other species have other numbers of pairs of chromosomes (one copy coming from the female parent and one copy from the male parent). Along each chromosome are found sequences of DNA identified as genes, but there are many more long stretches of DNA for which the functions have not been determined. Some of these stretches transcribe into RNA that does not result in protein formation. Rather, these bits of RNA probably help regulate gene expression. Other parts of the non-gene DNA may have other functions, such as alignment of genes, coordination of replication, contributing to complex genes overlapping other genetic DNA, direct regulation of gene expression, and emergency genes that function only in extreme situations. Hox genes control the actions of other genes by turning them on or off. Thus, although the complement of genes for some species may be the same as for others, it is the action of the hox genes that enables some of them to be expressed and others to be quiescent, so that the various species turn out entirely different from each other. In this way, differences in a few genes can have profound effects on phenotypical behavior of an organism (Gilad et al, 2006).

Variable numbers of a gene can produce a greater or smaller amount of protein important to the body, but a duplicated section of DNA can also disrupt the function of an important gene. Structural differences in the genome (given as duplications, insertions, deletions, or inversions of genetic material) seem to be as important, or more important, to the causes of
genetically-linked diseases than are differences in the nucleotides A, T, G, and C (Olson, 2007).

Figure 5.3.8. Slightly different promoters lead to big differences in the expression of the same gene for size of the thorax.
The Hoxc8 gene determines the location of the thorax in a developing animal (Figure 5.3.8). If this gene is active for a long time during development, then the animal becomes almost all thorax, as is a snake. If the Hoxc8 gene is turned on for a short time, the animal has a short thorax, as with a chicken. An intermediate period of activity results in something like a rat. The snake has all of its vertebrae located in its thorax, the rat has 13 thoracic vertebrae, and the chicken has seven. The same gene is in all these three, but expressed differently.

There are approximately 15% of the U.S. population who are left-handed. It has been found that handedness is determined by a gene with two alleles, and the allele for right-handedness is dominant. Thus, anyone with at least one copy of this allele is right-handed. People who lack this allele, however, only have a 50-50 chance of becoming left-handed (Brodie, 2004). Coming from the father, the gene for left-handedness is active; coming from the mother, the gene has no effect. Incidentally, this same allele determines the direction that hair whorls at the back of the head; right-handed people have clockwise spirals. [It is interesting, from an engineering point of view, to note that a bolt that tightens as it is rotated clockwise is called a right-handed thread. Mathematical cross-products and vector notations also follow this convention. You see, after all, there is a sound biological basis for this convention.]

So, what are the external environmental influences on genetic activity? They are not all known, but they include the fetal environment, intellectual and emotional stimulation, and physicochemical environmental factors. All of these, it seems, can influence the activity of genes, and it is well known that there are critical periods during development for the genetic potential to be realized. Everything from ambient temperature to the presence of chemicals to learning to emotional trauma can influence the metabolism of an organism.

Muscle tissue is very plastic. Lack of exercise causes muscle to remodel itself into weak muscle, with a smaller amount of tissue, fewer mitochondria, and containing fewer capillaries. Exercise reverses this process to make the muscle stronger and more efficient. Muscular exercise is the trigger to activate genes in the muscle tissue to make this happen (Booth and Neufer, 2005).

Although it appears that only 10% of the human genome consists of genes that code directly for the formation of proteins, genetic material in the remaining 90% also appears to have useful function. There are short stretches of regulatory DNA that allow regulatory proteins, those involved in gene expression, to bind and influence gene activity in different ways. There are also stretches of DNA that encode RNA, and these can regulate gene expression through RNA interference. Many of these intermediate sites have DNA that is easily transposed, thus facilitating genetic diversity and species formation.
Polymerase Chain Reaction

Small samples of DNA are often not large enough to perform identification procedures, such as electrophoresis (see Section 2.11), or other manipulations that have been found useful in disease diagnosis or vaccine development. The Polymerase Chain Reaction (PCR) was perfected to overcome this limitation.
Polymerase Chain Reaction cont.

The DNA double helix is first heated so that it denatures and the double helix splits into two separate strands. Newer methods use enzymatic denaturation. Annealing (combining of nucleic acids) also occurs during this phase wherein a primer (a short segment of RNA) attaches to the DNA strands. Next a mixture of nucleic acids and thermophilic enzymes is added. As the mixture cools, complementary DNA (cDNA), using the original DNA strands as templates, completes the formation of new double-stranded helical DNA. This process duplicates the natural process of DNA replication. This process may be repeated as many times as necessary to multiply the original DNA to the quantity needed.

Refinements of PCR involve reducing the time it takes to produce sufficient DNA for required purposes, reducing error rates, and reducing the amount of sample needed at either the beginning or the end of the PCR process. The primers must be extremely specific to the template being amplified, and there is a limit to the maximum length of DNA that can be amplified. Any slight contamination with nonintended DNA can result in an incorrect product.

5.3.5 RNA Interference

Thomas Henry Huxley called Richard Owen a “lying Orthognathus Brachycephalic Bimanous Pithecus.” Owen charged that Huxley was “nothing but a thorough Archencephalic Primate.”

-Hal Hellman

RNA is now known to be much more than just an intermediary between DNA and protein. RNA can act as a catalyst (mRNA), a binding site for small molecules (tRNA), a regulator of gene expression (RNAi and siRNA), a structural component of ribosomes (rRNA), and perhaps much more.

As another example of the complexity of genetic operations, some RNA, along with some destructive enzymes, functions by interfering with the expression of some genes. Instead of acting simply as a means to convey genetic information to the ribosomes, some RNA actually keeps other genes from being effective. This process is called RNA interference, and often involves double-stranded RNA (iRNA or siRNA, standing for small interfering RNA). RNA interference can be an important tool in functional
genomics, the term used to describe matching functions with certain genes. RNA interference can be used as a tool to turn off specific genes, and then observations made to see what happens when they are no longer active.

siRNAs, many of which are commercially available, trigger the destruction of targeted mRNA species. MicroRNAs (miRNAs) bind to mRNA and block its translation into protein. miRNAs can also act to regulate transcription pathways and interfere with specific genetic expression. They are evolutionarily conserved and are critical in natural organism development, especially brain development, and in viral infection processes. RNA interference is a way to shut down defective genes and can be used therapeutically to treat genetic diseases.

Interfering iRNA fuses with mRNA to form a double-stranded molecule. This appears to the cell as a virus, and it is subsequently destroyed (Matushansky and Maki, 2005).

### 5.3.6 Genetic Variation

*The human genome is a misnomer. It’s been shown that big changes in DNA – insertions and duplications and deletions and inversions – are extremely common in the population.... These changes play a role in human disease- everything from HIV susceptibility to autism to mental retardation to epilepsy.*

-Evan Eichler

In the complete genetic sequences of nearly 100 of a wide range of organisms, it has been found that 30 to 40 percent of the genes are the same. About 98.5% of the genomes of humans and chimpanzees are identical (Tiffany-Castiglioni, 2003). There are about 20,000 to 30,000 human genes, which means that only 2% of the genome functions as genes. The rest has other functions poorly understood at present. It has been estimated that 99.9% of the human genome is identical for all humans; only 0.1% of base pairs are different. Considering those genes common only to all humans, 7% differ from individual to individual (Nesse and Williams, 1994). If there are about 3 billion base pairs in the human genome, then about 3 million of them may differ among individuals. About 8 percent of the human genome appears to be remnants of DNA from retroviruses (Ogle and Platt, 2004).

One advantage of genetic variation is that the capacity to meet the demands of environmental variations often lies within genetic variants. Through sexual reproduction, new genetic combinations are possible. There is an enormous amount of genetic variability maintained in natural populations. The amount of variability is greater than anyone would expect: average invertebrates are heterozygous at 14.6 percent of its gene loci, and vertebrates are heterozygous at 5.0 percent. The cost of maintaining this variability is high. If one or two of these genetic variants has some reproductive advantage, then the rest are at a disadvantage. It would be expected that the reproductively-disadvantaged genes should disappear eventually. However,
they are apparently maintained at a much higher level than can be explained by random mutation (Powell and Dobzhansky, 1976).

Perhaps some genetic variants are maintained at high levels because of the hybrid vigor exhibited by heterozygotes. Other variants may be useful in different habitats or at different seasons. Still others may have a selective advantage when they are rare but become disadvantageous when they become too frequent (Powell and Dobzhansky, 1976).

There is an estimate that much of the genetic material found in chromosomes does not function as genes; that there are about 20,000 to 30,000 genes in the human genome. Each gene can result in about 10 proteins in the human (there are only 3 proteins per gene in yeast), so the potential amount of variation is rather large even in the same species.

### 5.3.7 Replication

*A book of science is inexhaustible.*

-Samuel Johnson

Higher level plants and animals undergo two types of nuclear division as essential steps in genetic reproduction. In *mitosis*, chromosomes are duplicated through a complex process that depends upon the unambiguous linking of DNA base pairs (Starr, 2000). Copies of all pairs of chromosomes are passed on to daughter cells. In *meiosis*, chromosome pairs are separated and passed singly to reproductive cells. When two reproductive cells are joined in the process of *fertilization*, pairs of chromosomes are again formed.

### The Chicken or the Egg?

*Curiosity is, in great and generous minds, the first passion and the last.*

-Samuel Johnson

This is a philosophical question meant to imply mutual dependence and the difficulty separating steps in a cyclic situation. Asking this question usually ends the discussion, because the question is understood to mean that no resolution of the issue can be found.

Nevertheless, the question can be answered. An organism, such as a chicken, is composed of many cells, each with its own DNA. The DNA in most of these cells is identical to the DNA in all the other cells. The exceptions are the reproductive cells (gametes) that have only one-half the
5.3.8 Mutations

Let it also be borne in mind how infinitely complex and close-fitting are the mutual relations of all organic beings to each other and to their physical conditions of life; and consequently what infinitely varied diversities of structure might be of use to each being under changing conditions of life.... If such [variations] do occur, can we doubt (remembering that many more individuals are born than can possibly survive) that individuals having any advantage, however slight, over others, would have the best chance of surviving and of procreating their kind?... This preservation of favourable individual differences and variations, and the destruction of those which are injurious, I have called Natural Selection, or the Survival of the Fittest.

-Charles Darwin

During the process of chromosomal manipulation, mistakes sometimes happen. These are called mutations. Mutations (genetic changes) occur either spontaneously or they may be induced. Mutations are changes in genetic material that can occur either in non-reproducing (somatic) cells or in reproducing (germ cells or gametes) cells. Those mutations that occur in somatic cells are not passed to future generations, whereas those that occur in gametes are inherited. The spontaneous mutation rate in humans has been estimated at between $10^{-5}$ and $10^{-6}$ mutations per gamete. About 6% of us begin life with at least one brand-new mutation found in neither parent (Nesse and Williams, 1994). The spontaneous mutation rate differs considerably...
among different organisms, possibly reflecting efficiencies of different DNA repair systems at work (Hale et al, 1995). Structural mutations are classified as: 1) inversion, where a DNA segment is rearranged in reverse order, 2) duplication, where a DNA segment is repeated either next to the original segment or elsewhere along the chromosome, 3) translocation, the exchange of segments between nonhomologous chromosomes, and 4) deletion, the removal of a segment (Hale et al, 1995). No process as important as genetic duplication can be left without error-correction and repair mechanisms, however (see Section 6.18). There are enzymes that proof-read newly created DNA strands and fix mistakes (Campbell et al, 1999). That very few of these mutations are not self-corrected pays tribute to the robust system of error detection and correction in the living cell (Drake et al, 1983).

High-energy radiation, and some toxic chemicals are among the environmental mutagens that can change the genetic code, and these changes can be felt for many future generations (see Section 6.12). In addition, viruses and some bacteria are able to merge their genes with those of host cells and so become agents of genetic change.

Figure 5.3.9. Human antibodies must be immensely diverse to anticipate the unpredictable infections that beset us. The variable regions on the two arms of antibodies include three hypervariable segments (dark stripes) that bind directly to invaders. These segments mutate much more than other parts of antibodies’ variable regions (Caporale, 2003).
Most genetic mutations cause such drastic effects that they are lethal for the host cell. Others are not as drastic, but confer a comparative reproductive disadvantage that may cause this mutation to disappear within a few generations. Others, however, offer clear advantages, and, for these, it can be said that the environment can have profound effects on the BU that inhabit it.

There is evidence that genetic mutations are not random (Caporale, 2003). Some mutations occur orders of magnitude more often than others, and can even be predicted. Blood pathogens, for instance, can hide from their host’s immune system by changing their outside coats. These changes occur by changes in the genes that control coat protein formation. Natural selection has favored biochemical mechanisms that alter just these genes and no others. These genes are located in areas that are bracketed by conserved sequences of bases; these do not change, but the regions between them do.

Figure 5.3.10. One strand of repetitive DNA can slip during DNA copying or repair, leading to a mispairing that changes the length of the repeat. If the original strand loops out while being copied, a portion of the repeat is deleted. If the new strand loops out, the repeat becomes longer in the next generation (Caporale, 2003).
There are other examples, such as cone snails and scorpions, which use focused genetic variation to generate new components of their venoms. Human and animal antibody production is also subject to unequal distribution of mutations. Antibodies are composed of two regions: a constant region that links to other body proteins, and a variable region that binds to foreign bodies (see Section 6.20.3). The constant region almost never mutates; the variable region, and especially the part that binds to foreign antigens, mutates frequently (Figure 5.3.9). This gives the human or animal the ability to anticipate changes in pathogen surface coat configuration.

Figure 5.3.11. When a DNA segment forms a loop and pairs with itself, repair mechanisms can correct apparent mismatches. This leads to selective DNA mutations.
What mechanisms are there that foster selective mutation? These can be classified as:

1. repeats of sequences of bases, such as CCCCC… or AGTCAGTCAGTC…, increase or decrease in length as the two strands of the double helix slip and misalign during DNA copy or repair.
2. looping of one strand or other of the DNA during copy or repair means that some genetic material may be gained or lost (Figure 5.3.10).
3. looping of a portion of a DNA strand can cause pairing with itself (Figure 5.3.11). Various bases may then be exchanged by repair enzymes that recognize the arms of the loop as two separate strands.
4. the proteins involved in copying DNA can themselves mutate and change the probability of future mutations at specific sites.

There may be other mechanisms as well, but it is clear that these genetic changes can have profound effects on phenotypical genetic expression.

The conclusion from this is that there is at least a second order selection process going on. Not only is there natural selection from among mutations that occur that leads to a survival advantage, but there seems to be a selection for those individuals that can mutate their genes in regions that are likely to improve survival. Random mutations are still likely, but nonrandom mutations are more likely, because these give an organism an advantage to survive and reproduce.

Viruses contain RNA segments that encode for specific proteins encapsulated in a surrounding envelope of protein, lipid bilayer, and external proteins, that protrude from the viral surface (Figure 5.3.12). The surface proteins bind to surface receptors of the host cell (Figure 5.3.13), whereby the viral RNA strands move into the cell nucleus. Viral RNA strands encode messenger RNA that ultimately produce new virus particles. Other viral surface proteins enable the newly created viruses to separate from the host cell and invade other cells.

Because viruses contain RNA and not DNA, replication of viral genetic material is not subject to the same error-checking and repair mechanisms as is cellular DNA. Thus, mutations in viral RNA are relatively more common, and viruses, should they be able to survive the mutations, can evolve rather quickly to circumvent cellular or therapeutic drug antiviral countermeasures. Antiviral defenses oftentimes recognize viral surface proteins as foreign bodies, and deal with them accordingly. Cytokines such as interferon and tumor necrosis factor are used as the nonspecific first line of defense that does not require previous exposure to the virus. Immunoglobulin antibodies are produced specifically reacting to a certain viral surface configuration; antibody production depends on previous exposure. Some viral
RNA mutations result in different viral surface proteins, and these changes can be enough to make ineffective antibodies produced to defend against the previous form of the virus.

Figure 5.3.12. Diagram of a Type A influenza virus. These viruses are spherical with a diameter of about $10^7$ m. Surface proteins hemagglutinin (HA) and neuraminidase (NA) enable the virus to enter and leave host cells. Inside the viral coating are eight strands of RNA that code for 10 proteins, including HA and NA. The ion-channel protein M2 forms a conduit through which small molecules, such as water, can pass through the impermeable outer coating (Webster and Walker, 2003).
Figure 5.3.13. Viruses invade cells by first attaching to the cell membrane with viral fusion proteins. These proteins are configured as an alpha helix with a hinge. As the catalytic hinge closes, the two membranes are brought close together until they fuse. At that point, the virus contents enter the cell (Dutton, 2006).

### Ames Test for Mutagenicity

There are many toxic substances in the environment, some natural and some man-made. One issue of interest when a new material is identified is whether or not it is capable of changing the cellular genetic code. If so, then it is a likely cancer-causing substance. So, the search for *carcinogens* resolves into a search for *mutagens*.

The Ames test is extremely simple and fast. A strain of bacteria is cultured that is unable to grow on a minimal medium devoid of histidine. When mixed with the suspected mutagen, some of the bacteria may mutate into a bacterial strain capable of growth on the minimal growth medium. Presence of bacterial colonies growing on plates containing the minimal medium indicates that the substance is, indeed, capable of mutagenicity.

### 5.3.9 RNA Correcting DNA

*Why do some controversies resolve satisfactorily, while others seem to continue on and on? In the latter case, the science itself may be recalcitrant, just plain slow to develop. As a result, competing ideas go back and forth.*
More often, there is some subtle or not-so-subtle question of beliefs or values that underlies the whole debate.  

-Hal Hellman

One possible additional function of RNA is to correct abnormalities that appear in DNA. It has been found that certain plants with mutated genes could revert to the unmutated DNA forms possessed by the second previous generation. It has been speculated that the mechanism by which this happens is a cache of RNA that can be used to correct harmful DNA mutations (Pennisi, 2005). If true, this would: 1) extend the complexity of natural genetic processes, and 2) be somewhat similar to the way a retrovirus reproduces in a healthy target cell.

5.3.10 Mitochondrial and Chloroplast DNA

Microbiology has undergone an explosion of discovery...into realms that are as bizarre as anything appearing...in novels.

-Joan Slonczewski

Mitochondria in the cell carry their own DNA separate from that in the cell nucleus. Sperm of all animal species contain their mitochondria in their tails, which are separated from their heads at the moment of fertilization. Thus, the newly fertilized egg contains mitochondrial DNA from the female parent only. Tracing relatives through the female lineage is thus relatively simple. Mitochondrial DNA mutates at a relatively high rate, and thus differences in mitochondrial DNA can be used to study relationships among population groups. Knowing this, and the rate at which spontaneous genetic mutation occurs, can be used to estimate the age of different species.

DNA in the chloroplasts of plants is transmitted from one generation to the next through the egg (Juniper, 2007), similarly to the DNA of mitochondria. The DNA for both of these structures is circular, as it is in prokaryotes. Thus, for higher level plants that depend on photosynthesis to fix carbon from atmospheric carbon dioxide (and thus contain chloroplasts), there are three independent DNA stores in the cell: in the chloroplast, in the mitochondria, and in the nucleus.

DNA Inheritance

Female inheritability can be traced through mitochondrial DNA, because mitochondria come only from egg cells. Thus, lineage can be traced by comparing mitochondrial DNA from one generation to the next. The number of generations, and thus the time between two relatives, can be estimated by assuming a certain rate of DNA mutation and looking at DNA differences.
DNA Inheritance cont.

Male inheritability can be traced through the Y sex chromosome. Each male somatic cell contains two sex chromosomes, an X and a Y (Figure). Females have two X’s.

Images of X and Y sex chromosomes. The Y chromosome is much shorter than the X chromosome, and is carried only by males.

When pairs of chromosomes split to form germ cells by the process of meiosis, male germ cells (sperm) carry either an X chromosome or a Y chromosome. Female germ cells (eggs) carry only X chromosomes. Thus, the only way for a zygote (offspring) to inherit a Y chromosome is from the male parent.

Because of this, genes appearing on the Y chromosome can be compared similarly to comparisons of mitochondrial DNA, and reflect male-only lineage. Time between particular generations can be estimated by again assuming a normal rate of DNA mutation.

5.3.11 Plasmid DNA

Bacteria, far from being opportunistic loners, are highly social creatures that incessantly chatter among themselves, with the hosts they infect, and even with other species of bacteria....

-Paul Raeburn
Bacteria contain some extra-chromosomal genetic material in the form of a small, circular, self-replicating DNA molecule called a plasmid (Figure 5.3.14). Certain plasmids can be incorporated reversibly into the cell’s chromosome. The plasmid contains a small number of genes that supplement chromosomal genes; they are not required for the survival or reproduction of the bacterium under normal conditions. They do offer advantages to the bacterium in a stressful environment, however. The F (for fertility) plasmid facilitates genetic recombination involving other bacteria that may be required to survive in a changed environment that can no longer sustain existing bacterial strains (Campbell et al, 1999).

![Diagram of bacterial cell with chromosome and plasmid](image)

Figure 5.3.14. The plasmid is a packet of supplemental DNA material found outside the bacterial chromosome. Plasmids often contain DNA molecules that serve specific purposes supplemental to chromosomal DNA. Genes for specific antibiotic resistance are found in plasmids, and genes conferring virulence are also found there. Exchange of plasmid DNA among bacteria is relatively easy (Amábile-Cuevas, 2003).

**Example 5.3.1 Searching For the Causes of Autism**

Autism is a mental condition where people, mostly children, crave routine, have trouble communicating, and don’t understand intuitive social rules. Some autistics barely speak, while others have some very large vocabularies. Some are riotously overstimulated, while others are isolated and withdrawn.

It is thought that the causes for autistic behavior are a combination of genetic makeup and environmental factors. Although the right genes must be present, not all children with these genes develop autism. Speculate on possible environmental causes.
Solution:
There has been found a genetic variation present in 47% of the U.S. population that codes for a protein active in the brain, gastro-intestinal tract, and immune system. This gene is associated with autism. It is likely that there is a genetic predisposition to the condition that is triggered by unknown environmental events.

Because autism develops in the very young, only those happenings occurring in early development can be the trigger. After children are born, they may be placed in an incubator; they may be placed on a ventilator; they can be held much or little; they may be breast fed or not. Autistics seem to develop for all of these conditions.

More generally, drops of silver nitrate or other silver compounds are placed in the eyes of newborns to prevent infectious conjunctivitis (*ophthalmia neonatorium*). Vaccines are given shortly after birth. It has been speculated that vaccines could contribute to autism, although this is highly unlikely.

Before birth, immune system abnormalities of the mother may contribute to autism by interfering with the timing of fetal brain development. There is evidence of a link between autism and viral infection of the mother during pregnancy (see Section 6.22.8). Because autistic children exhibit extremely male brain characteristics, others are focusing on prenatal testosterone exposure.

Interestingly, high rates of autism seem to run in families of physicists and engineers. These are professions that require focus on details and not on language or social skills.

**Example 5.3.2 High-Energy Radiation**

High-energy radiation can damage DNA and cause mutations. How can this same radiation be used to advantage?

Solution:
High-energy radiation can be used intentionally to induce DNA damage in bacteria and viruses present in and on food. When high-energy photons strike the electrons of irradiated food, they send them flying in all directions. Some of these electrons strike the relatively huge double-stranded DNA of bacteria. Atoms become ionized and molecular bonds are disrupted. Breaking both DNA strands kills the organism; breaking one strand weakens the bacterium and renders it sterile. Targeting viruses is a little more difficult because they are smaller than bacteria and contain only short pieces of genetic material packed inside a protein coat. Thus, high-energy beams can be used to sterilize food to make it safer and store longer.
Example 5.3.3 Crossbreeding Tigers

The well-known illusionist team of Siegfried Fischbacher and Roy Horn had been performing together at the Mirage Casino in Las Vegas for over 34 years. In their act they worked with extremely rare white tigers, making them seem to disappear and appear at other times. This duo had become interested in propagating these tigers in order to increase their numbers. What strategy should they use in order to do this?

Solution:

If the white tigers were mated among themselves, they would soon become too inbred, and display all the weaknesses (and the strengths) of animals that are nearly homozygous. Although offspring of cross-matings between white tigers and yellow tigers will not display the desired white coloring (white being a recessive gene), these heterozygous tigers can subsequently be bred among themselves, with about one-quarter of the offspring expected to be white. The result is that the selected white tigers will be stronger because their genetic material will contain genes from a wider range of animals. Because many undesirable genetic traits are recessive, even one copy of a desired gene will avoid genetic weaknesses.

Cross-breeding is used often to add genetic strength to a breed, especially one that has limited numbers to start with. Cross-breeding is also used to develop new varieties of plants; the cross-breeding usually involves parents that display extremes of the trait of interest.

Example 5.3.4 Genetic Causes of Alcoholism

Marilyn Vos Savant authors a column for the weekly Parade magazine, in which she answers mostly intellectual questions from readers. The following appeared in the 12 October 2003 issue of Parade:

Why do you doubt the idea that certain people are genetically prone to alcoholism? – J. T., New York, N.Y.

One reason is that alcohol doesn’t exist in nature. Instead, alcohol is a creation of mankind: Our genes don’t know about it. Another reason is that about 80% of alcoholics are male. Yet no one suggests that problem genes are sex-linked, such as male-pattern baldness. So I am concerned that, in an effort to remove the stigma of alcoholism from individuals and to blame their genes instead, we are stigmatizing whole families and ethnic groups. In my opinion, that’s far worse.
Response:

Permanent changes in the genetic code of an organism, either the addition of new capability or the removal of an old liability, must come about as a result of a survival and reproductive advantage to the organism. The speed at which the change happens would be related to the degree of the reproductive advantage.

If humans had developed a genetic response to alcohol, there would have had to be some good reason why alcoholics were more procreative than nonalcoholics. It is hard to imagine this happening, so it is not likely that humans would ever develop a genetic proclivity towards alcoholism.

Alcohol and similar biochemicals have been present in nature for a lot longer than humankind. So, if there is a genetic component to alcoholism, it is likely that the genes were present in more primitive organisms. Because humans share approximately 30-40% of their DNA with all other organisms, it is likely that these vestigial genes could still reside in the human genome. If there were no strong reproductive disadvantages to the presence of these genes, they would probably be maintained.

Biologists have been searching for such a gene, and there is evidence of the gene in a worm *Caenorhabditis elegans* (Davies et al, 2003). Whether this gene is responsible for alcoholism, and whether it has been passed on to humans is still an open question. It could very well be that the gene influences the metabolism of a whole class of biochemicals, not just alcohol, and the intoxicating effects of alcohol are just an inadvertent side effect to the major function of the gene. Sickle cell anemia, for instance, is a genetic disease that confers a survival advantage to those who live in malaria-infested regions; the long-term effects of sickle cell are inadvertent.

Something like alcoholism can have complex causes, as we know. To attribute alcoholism to no genetic causes, would be too simplistic. If there are genes involved in alcoholism, they may influence such diverse attributes as metabolism, personality, and sensory perception, all of which are determined in part by genetic causes. Thus, there are probably many genetic components to alcoholism.

For these reasons, the answer that was given to the question was not complete, and wasn’t based on sound reasoning and knowledge about the workings of the genes.

**Example 5.3.5 Biochips for Disease Detection**

Disease detection is simple and fast with biochips that contain up to several hundred small wells (of the order of 10 µm in diameter) etched into a substrate carrier. In each well is a drop of gel containing a DNA segment, protein, peptide, or antibody that tailors each drop to recognize a specific biological agent or biochemical signature substance. These drops are placed in known locations on the biochip so that when a reaction takes place between
the test reagent and the detected sample, the sample can be identified by its location. A biochip scanner makes this process almost automatic.

Many biochips use dyes that fluoresce when illuminated. Different color dyes can be used to determine, not only whether a reaction has taken place, but specific details of sample reactants. Other biochips may work with small magnetic beads.

Detector substances in biochips can be tailored to identify diseases of human, veterinary, or horticultural importance, and samples can be processed in just a few minutes. Viral or bacterial genetic material can be detected with DNA fragments complementary to the candidates for detection; when the target DNA is present, it links with the DNA affixed to the biochip, and the resulting hybrid can be detected by fluorescence.

Other test wells may contain DNA strands (called aptamers) that stick only to specific proteins. These can then detect a single protein out of a mixture of many proteins.

Applications and Predictions

1. Complete knowledge of the genotype will never be able to be used to predict the phenotype.
2. Family resemblance will be determined by genes.
3. Not all traits possessed by an individual will be genetically determined. Thus, the process of selection for a particular trait must start with determination of its inheritability.
4. Certain behaviors will be linked to appearances.
5. A new breed of dog will be able to be established through genetic selection.
6. Most random mutations will be detrimental. Many will be deadly. A small few will be advantageous.
7. The accumulated successes of survival will be manifested in the genes.
8. Nothing will be as simple as you would like.
9. Knowledge about genetic mechanisms will be important for the development of new products and tests.
10. There will be vestigial genetic material present in the genome that has no present purpose.
11. Genetic approaches will cure many diseases and provide new vaccines.
12. Inbreeding will result in a higher than normal expression of recessive traits.
5.4 **Competition and Selection**

*Finding Toumai man, the oldest hominid, in Chad fits well with the theory of punctuated equilibrium developed by paleontologists Niles Eldridge and Stephan Jay Gould* [the theory explains why new species, rather than evolving gradually over millions of years, seem to suddenly appear in the fossil record, punctuating long periods of species stability, or equilibrium]. *People derided the theory, calling it evolution by jerks. Gould’s famous retort was that the alternative theory is evolution by creeps.*

- David J. Melvin

There is perhaps no process more important for anyone working with living systems to be familiar with than the process of competition and selection. All biological units (BU) are in competition with each other and with different types of BU. An environment without BU is unnatural, and will soon contain BU as the opportunity arises. It is difficult to sterilize packages containing food, medical instruments, or even enclosures for humans with weakened immune systems, but it is very easy for these environments to be colonized by BU at just the slightest opportunity.

The vast amount of variation of BU and the adaptability of BU ensures that there will be a BU to thrive in all but the most harsh environments. Even there, BU may take forms such as spores, seeds, or hibernating BU to survive the worst conditions imaginable until these conditions ameliorate and growth can again take place. There is hardly a place that does not contain BU in some form (see also Sections 3.4, 6.5, 6.15, and 6.21).

BU will grow and reproduce to the extent allowed by the environment. As long as sufficient resources are available, the only limit to growth will be time. With sufficient time, all available resources will be used by BU. These resources include chemical substrates, light, heat, or space. Negative resources useful to some BU are lack of toxins, lack of heat (or cooling), and lack of light.

With unchecked growth, it should be apparent that BU will expand limitlessly. Other BU will also tend to do the same thing. There are many cases where growth of one type of BU can enhance the growth of another type (for instance, growth of nitrogen-fixing bacteria can enhance growth of legumes, or growth of humans enhances the growth of human immunosuppressive viruses (HIV)). There are also many cases where growth of one type of BU limits the resources available to another type. Competition between these two types is the natural result.

Competition is a natural part of biology. When two or more BU could use the same resources, but each BU limits the opportunities for growth and reproduction of the others, then the competition becomes severe. The result is that some BU may thrive, some may barely survive, and some may die. As Gillespie (2005) has put it, “Ecologists who have examined communities over time have shown that [introduction of new species] may be stochastic, but deterministic processes can dictate the community’s set of species at
equilibrium. However, communities are complex, dynamic systems, so many factors decide whether stochastic forces dominate deterministic ones or vice versa…. Early on, species just pile in, with nothing to stop any one species from arriving and existing in a community. Over time, the early colonists ‘settle down’ during which competition may bump out certain species. After this competitive jostling, the remaining species are not a random bunch of those that arrived, but rather a set that is more tightly co-adapted – they’ve figured out how to live together. So any species can get into a community to start with, but only those that form cohesive co-adapted sets remain.”

Each BU is a carrier for its genetic material, and can be considered to be the vehicle at present to deliver genetic material to the future. Thus, progress in biology travels in one direction only, from the past to the future. Genetic material survives only by being transported from the past into the future. If genetic material is lost or changed in some way in its journey from the past into the future, it cannot be recovered in its original form, and so is lost forever. In this way, time can be considered to be an effort variable.

### Cheating Genes

Certain genes are able to out-compete their homologues in an interesting way (Ganetsky, 2000). When certain chromosome pairs split during meiosis, genes of one type and its corresponding gene on the other chromosome find themselves in different gametes. The gene for red-eyed fruit flies (dominant gene) in certain males can eliminate the gene for white-eyed fruit flies (recessive) by killing sperm with the recessive gene. Thus, a cross between a heterozygous male and a female homozygous for the recessive gene should yield 50% offspring recessive homozygous (white eyes) and 50% offspring heterozygous (red eyes).

Not all crosses end this way. Some of the red-eye genes can destroy white-eye sperm and the results are 100% heterozygous offspring (red eyes).

Thus, when a BU dies as a result of competition, not only does that BU fail to survive, but all potential future generations also fail to survive. This has enormous consequences. It means that:

- those BU that are best adapted to their environment will stand the best chance of populating that environment.
- future generations will be well adapted to that environment because those less well adapted will be crowded out.
• competition among all future BU will become even stronger.
• genetic material contained by BU that do not survive will be forever lost.

Because the future is so vast, and the number of generations represented by the future is so numerous, it does not take much of a competitive advantage to have a huge ultimate effect on a population. A competitive advantage of 0.0001% can become 100% in 693,148 generations. So, when we talk about natural selection, we usually do it in terms of reproductive advantage and genetic survival rather than the immediate effects on one generation only.

**Darwin’s Legacy**

Charles Darwin has been recognized as the person most responsible for the recognition of biological evolution and continual creation of new forms of life. Before Darwin, biological scientists had sought purpose and meaning in the relationship among organisms. Darwin asserted that the order was the purpose; that relationships themselves were derived from history (Gould, 1986). Form and function of organisms and their parts resulted from adaptations of things that were already there, modified under the influence of environmental pressures. That’s why Darwin’s ideas were so novel; he removed the order and purpose from the creation of an individual, and placed it on the environment to which the individual responded.

![Selection pressures lead to evolution of biological forms better adapted to their environments.]({})

Perhaps now we can understand why intermediate forms of BU (the so-called “missing links”) are not easy to find. If we suspect that two types of BU are related through natural selection, then the intermediate BU between these two forms would probably have been lost completely due to their
competitive disadvantages. They would no longer exist, and their genetic material would survive only in changed form.

Changes in environment change selective pressures and change reproductive potentials. These environmental changes can be physical, chemical, cultural, legal, or may take other forms. We can easily see the effects of physical selection pressures on the animals that populate tropical contrasted to arctic regions (see Section 2.7). Tropical animals tend to be lanky with long limbs to help lose heat. Arctic animals are stocky with short limbs; their low surface area to volume ratios conserve heat. Chemical pressures have led to bacteria populating ocean vents that use sulfur compounds as sources of energy; other bacteria would find these extreme environmental conditions too harsh for survival. Cultural reproductive

### Selfish Genes

According to Dawkins (1976), genes are impersonal replicators, dedicated to multiplying as widely as possible. This idea considers the organism as the means to pass genes from one generation to the next. Aggression and selfishness are natural attributes of genes locked in a competition to dominate. Altruism, love, and generosity would only be expected to be shown toward those other individuals who share the same genes, and the closer the relationship, the more care and attention would be lavished on the relative. Parents and their offspring share 50% of their unique genetic material; grandparents and grandchildren share 25%; siblings share, on average 50%. This is an interesting idea, and seems to have some merit in the animal kingdom.

Humankind, however, does not always act this way. There is care and concern for even total strangers. There is even care and concern for other species, especially those kept as pets. This is a cultural attribute.

Perhaps the paradigm for selfish genes are genes called transposons, or “jumping genes”. The transposon encodes a protein that cuts the transposon DNA free of its place in the chromosome and then reinserts it in another unrelated place in the genome. DNA repair mechanisms of the cell then mend the hole at the original transposon position by recreating the transposon nucleic acid sequence. After this, the cell has two copies of the transposon rather than one. This is an example of competition even among different genes within the same cell (Gould et al, 2006). Transposons make up about 50% of the human genome (Burt and Trivers, 2006), and make up a large part of the so-called “junk DNA” that appears to have no purpose except to replicate itself.

The conflict among genetic elements is sharpened by the existence of gamete killer genes in certain fungi. The gamete killers are a series of tightly-linked genes (genes that nearly always are replicated together, just
advantage can be seen among groups of humans less likely to use birth control methods than other groups. As long as higher birth rates are not accompanied by lower survival rates, groups not using birth control methods will continue to increase disproportionately to other groups. Legal changes can also affect selection pressures.

Most of our food that we eat today, the food that we call “natural”, is really evolved food (Palumbi, 2001). Seedless oranges, pink grapefruit, Idaho potatoes, sweet corn and popcorn, Angus beef, and huge Thanksgiving turkeys are all among these. Our different breeds of dogs and cats are also products of not-so-natural selection that illustrates how reproduction can be used to alter characteristics of living organisms.

Not all characteristics are subject to successful selection pressure. There must be natural variation, differences in reproduction, and inheritability of the trait in order for selection to produce results. Natural selection requires not only that there be genetic variation, but also that the genes be expressed (Mulcahy and Mulcahy, 1987). Without the latter, the genetic code present in a BU is simply irrelevant. Those traits that are not genetically determined cannot be selected for. Predation can select for different traits than would otherwise be chosen. An example of this is the color of male guppy fish: females breed preferentially with the most colorful ones, but predators can most easily locate and eat the most colorful ones. Thus, male guppies in upland streams where there are few predators are more colorful than guppies downstream where predators abound (Palumbi, 2001).

*Underdominance* is the term used to describe a counterintuitive competitive situation where the more fit group of interbreeding strains does not result in the fitter group surviving (Figure 5.4.1). This can happen when these conditions prevail (Gould et al, 2006):

1. there are two (or more) distinct genetic groups, one of which has higher numbers of surviving progeny
2. the two groups cross-breed
3. the progeny of the cross-breeding are less able to survive than either of the two pure-bred (homozygous) groups.
Figure 5.4.1. Underdominance describes a condition when a mating between two strains (A and B) results in offspring (AB) less fit than either parent. This mechanism has been proposed as a means to eliminate malaria-carrying mosquitoes from the environment (Gould et al, 2006).

The result is that the total population begins with dominance by the more fit genetic group: their numbers are greater than the group with less fit genes. It is more likely that the less fit individuals mate with more fit individuals than with individuals similar to themselves. The progeny of this mating have a small likelihood of survival. Some of the better fit individuals will mate with the less fit individuals. These progeny will also not survive in great numbers. Eventually, the proportions of the two sub-populations equalize. At this point, interbreeding is very likely, and few progeny survive. The total breeding population may then collapse.

Biodiversity is an essential element of a natural selection process in the face of continuous competition. Biodiversity is valuable for two reasons:

1. It leads to a greater abundance of the species in question, because different populations can exploit different habitats and resources in unique ways.
2. It fosters enhanced long-term stability by spreading the risk and providing redundancy in the face of unpredictable catastrophes.
Responses to environmental pressures are often gradual and incremental, resulting from slight changes in genetic expression from one generation to the next. There have appeared in the fossil record, however, periods of time when changes seemed to have occurred suddenly, more widespread, and of much greater magnitude than at other times. This effect still happens in the present, when microbes well adapted to one species suddenly jump to another species, and then evolve quickly to adapt to their new host. This seems to have been the case for the influenza virus that chronically infects birds, but has the ability to move to swine, and from there to humans. It is also the case for the human immunosuppressive virus (HIV) that was apparently a mild infectious agent of monkeys (simian immunosuppressive virus, or SIV).

Technology progresses in a similar fashion. There is discovered a completely new technology (for example, solid-state transistors) that have potential advantages over older technologies (for example, vacuum tubes), and people begin exploiting the new technologies. Over the years, with more and more experimentation and experience, the new technologies are incrementally advanced until they reach the point where the returns on further efforts are not worth additional resources (called the point of diminishing returns). At that point, completely new technologies are required for improvements. Thus, there is a parallel between advances made in human technology and the biological world: slow increments punctuated by sudden and large changes that seem to come from out of nowhere.

Those who deal with living systems need to understand that these systems are not static. They will change in response to the things done to them. Just because BU are of a certain form and function now, does not guarantee that they will be the same after changes are imposed. Whether we are considering new laws to protect the environment, the implantation of an artificial heart in a human, or cooling a bioreactor, the BU involved will change. If the change we make is permanent, and affects the reproductive potential of the BU involved, then the BU can change very dramatically. We must keep this in mind as we extend technological control over our domain.

**Memes**

There is the idea that humans, and, perhaps, some animals, too, have found an alternative to genetic determination of physical and behavioral qualities. This alternative takes the form of cultural information passed from one generation to the next. Simple packets of cultural information are called memes, analogously to the simple packets of physical information called genes.

Culture has been likened to the genome, and individual ideas (memes) to genes. Memes are now in a competition to survive, and evolution of ideas (and knowledge) can be much faster than genetic
Memes cont.

evolution. This may lead to a new paradigm for survivability and improvement of performance. It is unclear how these new evolutionary rules may affect future life, but Palumbi (2001) suggests that they may interact, with ideas, and the knowledge that comes from the accumulation of ideas, forming the basis for future evolution of humans and other species with which we come into contact. Perhaps this can be said to have happened already through the products of plant breeding, agricultural selection, and domesticated animal improvement. Humans have had inadvertent evolutionary effects on the disease-causing microbes that they had hoped to subdue and on plants and animals whose territories they have invaded. Add to this mix the new knowledge of biotechnology and the ability to directly select those genes that will not only survive but also come to dominate the planet. Ideas may have their own evolutionary course to follow, but they certainly have been a powerful force for natural selection in more physical ways.

The examples of individual adaptability directly dependent upon cultural information are many. Humans, for instance, learned how to domesticate animals and plants for their own purposes, and thus begat agriculture. Those who had the best agricultural knowledge were the ones who had the best chance of surviving and reproducing. This knowledge, when passed from one generation to the next, clearly gave reproductive advantage to that human line. Thus, information became a determinant of survival alternative to genetic makeup. Some animals do the same by teaching their youngsters about tools, plants safe to eat, avoidance of predators, and migratory patterns (see box on Mother Bear Man, Section 6.22.7).

For instance, adult meerkats (small members of the mongoose family) teach their pups how to catch and eat dangerous prey. Adults bring dead scorpions, lizards, and spiders to very young offspring. As the pups get older, they are given prey disabled by, for example, biting off the stinger of a scorpion. The pups are eventually taught how to handle normal live prey (Thornton and McAuliffe, 2006).

Sheep and goats do not innately know the difference between poisonous and nonpoisonous plants. They learn about this through the social interactions of the herd. Young goats learn about edible forages by imitating older goats, and eating what they eat when they eat it (NIAA, 2007).

This book is an example of how information can modify behavior and thus lead to better survivability through successful applications of knowledge. Understanding of biology results in control of living things, and the control is meant to benefit (in some way) human beings.
Example 5.4.1. Natural Selection from Genetic Variation.

Color of the moth *Biston betularia* was profoundly influenced by the rise of industry in Britain. Moth collections spanning more than fifty years record the rise in frequency of darker colored moths as the deposition of soot on surfaces visited by the moths made them darker. Darker colored moths were thus better protected against bird predation. Although darker genotypes had existed at a low prevalence in Briton before the Industrial Revolution, the darker genotype came to dominate genes for lighter colors after the Industrial Revolution (Koehn and Hilbish, 1987).

Applications and Predictions

1. Organismal changes will occur most rapidly where competition is most severe, environmental selection pressures are the greatest, and generation time is the shortest.
2. An organism that can adapt easily to environmental conditions will not evolve. Likewise, an organism that cannot survive in an environment will not evolve.
3. Evolution will not apply to an individual organism, but to a progenitor and progeny.
4. A mother will be more likely to care naturally for her own children than to care for her step-children.

Memes cont.

Although it is easy to see how knowledge can affect behavior, knowledge passed from one generation to the next can also change physical characteristics of the recipients of that knowledge. Examples of this are male circumcision among Jews, foot-binding of Chinese girls, neck-elongation among some African women, plastic surgery, and human selection of cultivars of fruits, vegetables, grains, and flowers.

Among species for which cultural information can be taught and learned, the notion that memes have become powerful forces for survivability rivaling, or even overshadowing, genes is not very far-fetched. It seems likely that the future of the human race will depend on its ability to discover new information and to transfer that information to others. This is the ultimate response to new environmental challenges.
5. Competition will be present for all biological systems.
6. Social groups with cultural information passed from one generation to the next will have a competitive advantage over social groups without that cultural information. Knowledge about the preservation and storage of food is one such piece of cultural information. Proper sanitation and medical care information is another example. Still another is information about the use of tools in hunting, domestic activities, and fighting.
7. Spatial or temporal isolation is necessary for the formation of a new species.
8. Symbiosis will improve competitive advantage for the species involved, cooperation among organs in a body will improve the survival of all.
9. Humans have changed selection pressures for many other species; all species modify selection pressures for other species.
5.5 Biological Hierarchies

EPIDERMIS, n. The thin integument which lies immediately outside the skin and immediately inside the dirt.

- Ambrose Bierce

Those who deal with biological systems might offer that, beginning with the simplest biological unit (BU) and classifying to the most complex BU, a biological hierarchy could be constructed as:

1. cell
2. tissue
3. organ
4. system
5. organism
6. population or colony
7. biome
8. ecosystem

We will see in this Section that the cell is distinguished as the basic BU. Any group of cells of similar structure that performs a specific function is called a tissue. Examples of these are muscle tissues in animals and phloem tissues in plants. A multicellular structural or functional unit to perform a specific role of an animal or plant, which may be composed of different tissues, is known as an organ. Examples are the liver, a leaf, or an eye. A system is a functional unit made up of correlated and semi-independent parts. Examples of these are vascular or digestive systems. An organism is any living thing, be it animal, plant, microorganism, or other (depending on the classification scheme, which will be avoided in this text). A population is a group of similar individual organisms inhabiting a particular locality or region. A biome is a major regional community of organisms defined by the habitat and determined by the interaction of the substrate, climate, fauna, and flora. An ecosystem is a collection that includes all the biotic organisms and abiotic components of the total environment.

From the above definitions one can see that there is a certain increase in complexity from the cell to the ecosystem. However, this increase in complexity is largely definitional. Each of these levels can be considered to be a biological unit (BU), and, as such, has similar responses to its external and internal environments. For instance, consider competition and cooperation. Two cells can compete, and this is basic to nearly all of life and to the natural selection process. If these cells cooperate in a certain way, they can form a tissue. Likewise two biological systems can cooperate for mutual support of an organism, or they can compete as when the digestive system and the muscles compete for blood flow in an exercising animal.

If we consider each of these as BU’s, then the responses of these BU’s can be studied in general and applied in the context in which they arise. Thus,
Biological Responses in Context (BRIC) form the basic building blocks for the study of predictive biology. Part III is devoted to developing the BRIC concept.

Ecology or bionomics is the study of plants and animals in relation to their total environment. The techniques and methods are more powerful than this, however, because they can be related to all BU. Studying the BRIC of a tissue BU is the same as studying the BRIC of a population BU. Thus, the approach here will be largely the same as the application of ecology to all BU, no matter what the level.

There are thus certain hierarchies in biology, and these hierarchies are often hardly more than conceptual in nature. There are overlaps, such as when a cell can be an organism or a part of a tissue, and there are different ways to classify the same biological units. However, many of the same principles apply no matter what the classification scheme, and no matter what level in the particular scheme is being considered.

5.5.1 The Cell

...an embryo is the result of the union of a live human egg and a live human sperm. If either is dead, no viable embryo is produced. Therefore, life does not begin at conception, at the transition between embryo and fetus, or at birth. It continues. -John Majka

The cell is the basic biological unit in a way similar to the atom as the basic unit of physics and chemistry. Particles smaller than the atom exist, but chemistry as we know it doesn’t exist below the atomic level, and the laws of physics are completely changed at that scale. At levels lower than the cell, we do not have biology, but rather have chemistry. This is an example of an emergent property where the properties and actions of the whole entity are greater than the sum of its parts.

Because the cell exhibits all the properties and actions that we would call living, the cell is considered to be the basic biological entity. All combinations of cells will also be considered to be living (Figure 5.5.1).

Figure 5.5.1. One combination of cells considered to be a living unit.
There are two basic types of living cells. Prokaryotes are the most primitive of organisms, and this includes all bacteria (Figure 5.5.2). They have no true cell nucleus, nor do they have internal organelles (specialized regions separated by membranes to perform certain functions such as food storage or energy production). They have a single chromosome made up of nucleic acid only, and they reproduce by binary fission (see Section 6.17). They are small, where diffusion does not severely hamper cell function. Many of these functions are performed within or along the cell membrane.

Figure 5.5.2. Comparative diagram of different particle sizes showing where typical bacteria fit into the size scheme.

Eukaryotes are distinguished by the fact that they have a membrane-bound nucleus with several chromosomes made of nucleic acids complexed with protein (see Section 5.3). They have an internal structure including organelles such as golgi apparatus, endoplasmic reticulum, lysosomes, and mitochondria (Table 5.5.1). Their relatively large sizes might incur materials transport limited by diffusion. Thus, they have specialized transport proteins and vesicles to move materials and store them at sites throughout the cell. Cell division is by mitosis (asexual) and meiosis (sexual). All plants, fungi, and animals contain eukaryotic cells.

Outside the cell is a membrane. The structure of the cell membrane (Figure 5.5.3) is believed to be a bimolecular lipid layer covered on both sides by protein coats (Schneck, 1990). The lipids cause the membrane to exclude water and polar molecules. The membrane behaves as if it contains pores slightly larger than a urea molecule (5-10 \(\text{Å}\)), so small molecules can pass freely from one side to the other. The outer surface of the cell is replete with linkage sites for external biomolecules (see Section 4.4.1) and is very active in transport of chemicals (see Section 6.19.3) and in detection of foreign bodies. The cell membrane is populated with proteins that perform several functions. Some proteins act as attachment sites for other molecules, and these can be very specific. When a mating molecule attaches to these receptors, some
Figure 5.5.3. Schematic representation of the bi-lipid configuration of the cell membrane.

Action is usually triggered in the cell, from the formation of an action potential in a neuron in response to a neurotransmitter to the formation of reactive proteins. Other proteins included in the cell membrane are shaped in such a way that they form channels (or tunnels) through which small ions or molecules may pass. Depending on the shape of the channel, its size, and the surface charges inside, the channel may be a good gate-keeper for specific molecular species.

Within the cell there is a gel-like substance composed of water, proteins, sugars, lipids, ions, and complex organic compounds. Various organelles, many enclosed within their own membranes, perform functions such as storage, metabolism, regulation, and so on. Together these substances and structures perform the complex functions we characterize as a living cell. The inside of a cell is packed full of ions, molecules, and inclusions (see Figure 3.7.7).

The cellular cytoskeleton gives the cell some structure and rigidity. Actin filaments that, among other things, form parts of the cellular cytoskeleton, prefer to polymerize at one end and depolymerize at the other. Hence, one end grows and the other shortens. Actin filaments thus stream from one end location to the opposite end, forming a one-way transport system for molecules linked to the filaments (Brodie, 2004).
<table>
<thead>
<tr>
<th>Cell Component</th>
<th>Function</th>
<th>PROKARYOTIC</th>
<th>EUKARYOTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Archaeobacteria, Eubacteria</td>
<td>Protists</td>
</tr>
<tr>
<td>Cell wall</td>
<td>Protection, structural support</td>
<td>yes*</td>
<td>yes*</td>
</tr>
<tr>
<td>Plasma membrane</td>
<td>Control of substances moving into and out of cell</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Nucleus</td>
<td>Physical separation and organization of DNA</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>DNA</td>
<td>Encoding of hereditary information</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>RNA</td>
<td>Transcription, translation of DNA messages into polypeptide chains of specific proteins</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Nucleolus</td>
<td>Assembly of subunits of ribosomes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Ribosome</td>
<td>Protein synthesis</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Endoplasmic reticulum (ER)</td>
<td>Initial modification of many of the newly forming polypeptide chains of proteins; lipid synthesis</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Golgi body</td>
<td>Final modification of proteins, lipids; sorting and packaging them for use inside cell or for export</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Lysosome</td>
<td>Intracellular digestion</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Mitochondron</td>
<td>ATP formation</td>
<td>**</td>
<td>yes</td>
</tr>
<tr>
<td>Photosynthetic pigment</td>
<td>Light-energy conversion</td>
<td>yes*</td>
<td>yes*</td>
</tr>
<tr>
<td>Chloroplast</td>
<td>Photosynthesis; some starch storage</td>
<td>no</td>
<td>yes*</td>
</tr>
<tr>
<td>Central vacuole</td>
<td>Increasing cell surface area; storage</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Bacterial flagellum</td>
<td>Locomotion through fluid surroundings</td>
<td>yes*</td>
<td>no</td>
</tr>
<tr>
<td>Flagellum or cillum with 9+2 microtubular array</td>
<td>Locomotion through or motion within fluid surroundings</td>
<td>no</td>
<td>yes*</td>
</tr>
<tr>
<td>Cytoskeleton</td>
<td>Cell shape; internal organization; basis of cell movement and, in many cells, locomotion</td>
<td>no</td>
<td>yes*</td>
</tr>
</tbody>
</table>

* Known to be present in cells of at least some groups.
** Oxygen-requiring (aerobic) pathways of ATP formation do occur in many groups, but mitochondria are not involved.
Epi-, Meso-, Endo-, and All Those Kinds of Cells

Epithelial cells comprise closely-packed monolayers that separate different tissue compartments. One side of the epithelium faces the outside of the body, or the side occupied by the external environment. The other side faces the inside of the body, or the side containing the blood and extracellular fluids. The skin is made of epithelial cells, as are the lumens of the gastrointestinal tract, the kidneys, the lungs, and the urinary bladder (Putnam, 1995). Simple epithelium is one cell thick, and compound epithelium is several cells thick. The cells usually cover connective tissue, and are held together by a cementing substance to form a sheet (Hale et al, 1995). Their shapes give rise to descriptive names of columnar, cubical, and squamous (flat).

Epithelia sometimes have a secretory function (in the liver), but otherwise function as a barrier between the external environment and the internal environment. They also selectively transport substances between compartments. To enhance this task, the outward-facing membrane, called the apical membrane, is often covered by microvilli (small, finger-like protrusions that increase surface area for absorption). The inward-facing membrane, called the basolateral membrane, has a different lipid and protein composition from the apical membrane. Because of these specialized structures, and the tight junctions between cells, the only substances that normally enter the body from the outside are those transported through the cells.

Endothelial cells are a single layer of flattened epithelial cells lining a tube such as the heart, blood vessels, and lymph vessels of vertebrates. Mesothelium cells are similar to epithelial cells, but they line the inside of the body cavity. The endoderm is a single layer of tissue found outside the vascular layer in many angiosperm plants.

Ectoderm (or ectoblast) is the germ cell layer lying outside of the developing embryo that eventually gives rise to epidermis, nervous tissues, and nephridia (a primitive tubular excretory organ present in many invertebrates such as the earthworm). Endoderm is the embryological germ layer in animals that develops into the gut and its associated organs. Mesoderm is the layer of embryonic cells lying between ectoderm and endoderm in all higher animals that forms the muscles, blood system, connective tissues, kidney, the skin dermis, and the axial skeleton. The limbs of some animals, such as newts, can be regrown if cut off. The tissue from which the limb arises comes from the mesoderm at the middle layer of the embryo (Tickle, 1981). The ectoderm, endoderm, and mesoderm are all embryonic cells that develop into epithelium, endothelium, and mesothelium, respectively.
Cell types resulting from undifferentiated fetal cells.
Although the cell is the basic unit of living organisms, cells are not always completely autonomous and separate units. Fusion of cells appears to be commonplace (Ogle and Platt, 2004). Skeletal and cardiac muscles, and some liver tissue, is composed of giant cells with multiple nuclei that appear to be fused from multiple precursor cells. These are termed syncytia.

Cell fusion within the same organism, and even between cells from different species, is possible. If the nuclei fuse and contain DNA from both precursor cells, the resulting hybrid is called a synkaryon. If the nuclei remain separate within the cell, the hybrid is called a heterokaryon. In both cases, DNA from both precursor cells exerts an influence over proteins and other complex molecules fabricated by the cell.

Fused hybrids possibly have a major role in the differentiation of fetal cells during early development. Fusion also might allow a mature cell whose location and function are well established, to induce an immature cell, a stem cell for instance, to assume the function of the mature cell. This may well be the mechanism that regulates the ability of stem cells to differentiate into tissues that need augmentation. Fused hybrids may also have a survival advantage by introducing superior DNA from one species into another.

Embryonic stem cells are useful if they retain the ability to transmute into many other types of cells. This pluripotency becomes compromised the longer a cell line is maintained in culture. Therefore, frequently freezing vials of stem cells as the line is expanded helps to maintain cells from validated batches, and is crucial to success with a stem cell line.

### Epi-, Meso-, Endo-, and All Those Kinds of Cells cont.

The epidermis is a designation of location rather than type of cells. The epidermal layer of vertebrates, which is the outer layer of skin, is usually made up of stratified epithelium with an outer layer of dead cells and an inner layer of growing and dividing cells. The invertebrate epidermis is normally one cell thick and often forms a protective cuticle (Hale et al, 1995). The epidermis of plants is a one-cell thick tissue that surrounds young roots, stems, and leaves. The epidermal cells (not epithelium) of stems and leaves secrete a cuticle (a protective layer of protein or lipids).
5.5.2 What is Life?

*If you call a tail a leg, how many legs has a dog? Five? No; calling a tail a leg doesn’t make it a leg.*

-Abraham Lincoln

Defining the basic living unit as the cell begs the question about what life really is. The separation between living and nonliving is not sharp. Viruses are little more than RNA enclosed in a protein coat. Yet, they reproduce in the right environment of a host cell. Prions are bits of protein that become active within cells, and also reproduce. Neither of these carries on all the functions that we would call “life”, but they do exhibit some living properties.

So what are these properties? They are numerous, and depend on who is doing the listing. Some examples are as follows:

1. Life is (Starr, 2000):
   - an outcome of ancient events by which nonliving matter – atoms and molecules – became assembled into the first living cells as a way of capturing and using energy and raw materials
   - a way of capturing and using energy and raw materials
   - a way of sensing and responding to changes in the environment
   - a capacity to reproduce, grow, develop and change over generations.

2. Life is (Hazen, 1999):
   - highly complex chemical systems
   - composed of cells
   - able to obtain and use energy
   - able to reproduce using the same genetic mechanism
   - able to grow and develop
   - able to respond to changes in the external environment while maintaining a relatively constant internal environment.

3. Life is a condition characterized by (Campbell et al, 1999):
   - order and complex organization
   - reproduction
   - growth and development
   - utilization of energy for its own purposes
   - responses to environmental stimuli
   - maintenance of relatively steady internal environment
   - evolutionary adaptation.

4. Life is (Webster’s New World Dictionary, in Anbar, 2001):
• that property or quality of plants and animals that distinguishes them from inorganic matter or dead organisms; specifically, the cellular biochemical activity or processes of an organism, characterized by the ingestion of nutrients, the storage and use of energy, the excretion of wastes, growth, reproduction, etc.

5. Life is (NASA, in Anbar, 2001):
   • a self-sustained chemical system capable of undergoing Darwinian evolution.

6. Life is (Anbar, 2001):
   • a process that spontaneously organizes matter to higher levels of complexity and then maintains that complexity in potentially destructive environments.... We may search for living systems or for tangible products of life, but not for life itself.

Rasmussen et al (2004) have given sufficient properties of life as localized molecular assemblages that regenerate, replicate, and build new functionality through evolution. Three essential functions to life are:

1. a genetic system for transmission of hereditary information
2. a metabolic system for extracting energy and materials from the environment
3. a containment system to maintain separation from the surroundings.

They did not, however, consider sensing and reactive functions that often characterize living things.

Stec (2004), however, brought a chemical perspective to the issue of the definition of life. Stec maintains that living things must contain chemicals (usually proteins) with alternate forms at the same or nearly the same energy levels to allow the living system to adapt. If one form of the protein clearly predominates (that is, its energy level is much lower than those of alternate forms), then the system is not adaptable, and appears to be more physical than biological. It takes a protein system with many possible forms at nearly equal energy levels to exhibit the adaptability characteristic of living matter.

Each of these descriptions begs the question of “what is life?” enough so that none can be called a definition, although the one by Anbar (#6) probably comes close. Rather, most of these are descriptions of a combination of attributes. Taken together, they describe a living cell and combinations of cells, but they do not describe sub-cellular components. Hence, the cell is considered to be the basic unit of life.

5.5.3 Synthetic Biology
Evolution prefers short-term survival at the expense of long-term function. -J. Douglas Bremner

There are many reasons for trying to define what constitutes life. One of these is the attempt to create forms that have many of the same characteristics of life, including reproduction, information storage, complex behavior, and others. These artificial life forms have never existed before, and may be like no other living thing.

Some are attempting to create life from the bottom up. They are locating the molecular machinery for their protocell on the outside, where a membrane is not needed. A clump of hydrophobic fatty acid molecules glues the protocell together as a structure called a micelle (Stroh, 2005).

Genetic material for the protocell will be supplied by peptide nucleic acid, or PNA, which has the same double-helix structure and the same four chemical bases as DNA, but has a peptide backbone. A light-sensitive molecule will be able to provide the energy to convert precursor molecules into new fatty acids and PNA molecules.

Newly created fatty acids will be incorporated into existing micelles, making them larger and larger. At some point they become unstable and split into two, as a simple form of binary fission.

A top-down approach to artificial life is also being attempted. One team starts with a simple 517 gene organism called Mycoplasma genitalium, and pares away as many genes as possible while still maintaining a semblance of life. As many as 215 genes may be unnecessary. A substitute genome is to be constructed from scratch and will require 300,000 chemical bases. If successful, the artificial life form could be loaded with genes to perform useful functions.

Synthetic biologists change the behavior of a cell by designing and rewiring the complex genetic foundation inside. They utilize existing biological (mostly genetic) parts, fitting them together to transform cells into micromachines capable of performing whatever is their designed function. This may range from building cells that move especially fast, to cells that produce desirable compounds, to cells that turn color in the presence of ultraviolet light. This is true genetic engineering, where a set of standard genetic parts are created and characterized, and which can then be combined with other standard genetic parts to implement intended purposes.

5.5.4 Ecology on Micro- and Macro-Scales

With man gone, will there be hope for gorilla? With gorilla gone, will there be hope for man? -Daniel Quinn

When a biological engineer looks at BU responses to various environmental stimuli (or BRICs, as we have called them), it is best to think
about the myriad of interactions as an ecological system. This applies no matter at which hierarchical level the BU happens to reside.

Ecology as popularly defined is the study of communities of organisms and how they all fit together (May and Seger, 1986). Yet this can be considered to be macroecology, or ecology on a large scale. In essence, all BU are subject to environmental influences, and every cell affects the flora and fauna around it. This is microecology, or ecology on a scale that can resolve to the smallest possible level, even if there is no identifiable biological component present. Without microecology, biochemicals could not be produced through biotechnology, biological homeostasis could not be maintained within a transplanted liver, and your radio would not be able to deliver music to your ear.

A colony or other type of social structure acts in a coordinated way because information flows both horizontally (at the same level) and vertically (between levels). The same is true within a cell, within a tissue, or within an organism. The social structure thus acts as an entity unto itself with independent and identifiable organization, actions, and input-output relations. Taken another step farther, the definition of BU extends to symbiotic relationships, parasite-host pairs, and predators with prey. Indeed, each of these has predictive physical and behavioral responses to environmental stimuli (Grene, 1987). These will be considered further in Part III of this text.

### Human Ecology System

Each of us is composed of roughly 100 trillion cells, but only 10 trillion of these are human. The other 90 trillion are bacteria, parasites, fungi, and other small creatures (Buckman, 2003).

Humans provide a complete and varied ecosystem, and like other ecosystems, theirs is balanced in the sense that various species cooperate and compete, with no species dominating. Included in the bacteria of note are the common *Staphalococcus aureus*, the microbes that can cause deadly Staph infections. *S. aureus* is present in great numbers on the skin, but they are kept in check by other bacteria and viruses that compete and limit their populations. *Escherichia coli* is a common intestinal bacterial parasite that is normally harmless unless the ecosystem of the gastrointestinal tract becomes upset in some way. It is this balance that is the key to human health. The indiscriminate use of antibiotics and disinfectants can upset this balance and give competitive advantage to dangerous microbes. Their use can also keep the human immune system unchallenged and thus much more vulnerable to infection than if full immunities were allowed to develop. Related to this is accumulating evidence that allergies are more likely to develop in children who are kept too clean and their environments too sterile. It is the balance of nature that we have accommodated. To believe that we can conquer or control all other species is very egotistical. We have allies in our struggle to survive, and it is not a good idea to ignore or harm them.

### Human Ecology System cont.

unchallenged and thus much more vulnerable to infection than if full immunities were allowed to develop. Related to this is accumulating evidence that allergies are more likely to develop in children who are kept too clean and their environments too sterile. It is the balance of nature that we have accommodated. To believe that we can conquer or control all other species is very egotistical. We have allies in our struggle to survive, and it is not a good idea to ignore or harm them.
5.5.5 Food Pyramid

*Time flies like an arrow. Fruit flies like a banana.*

-Groucho Marx

Energy is captured from primary sources for use by BU by primary producers. These may be plants that convert solar energy into energy-rich

![Classification scheme for organisms by energy and carbon sources](image)

Figure 5.5.4. Classification scheme for organisms by energy and carbon sources (Tortora et al, 2001).

carbon compounds such as glucose, cyanobacteria that do the same, or thermophilic microbes that use sulfur compounds from deep ocean vents as
their primary energy sources. These BU are called autotrophs because they are not dependent on other sources of organic substrates to manufacture their own organic requirements; they use inorganic sources. Heterotrophs obtain their basic organic materials from the environment; they may dine directly on autotrophs or obtain organic wastes attributable to other biological sources.

![The food pyramid, also called trophic levels. Energy is transferred from the bottom to the top with an efficiency between levels of about 10% (Fried and Hademenos, 1999).](image)

There are four general classifications of organisms made by combining energy and carbon sources (Figure 5.5.5):

1. **photoautotrophs.** These use light as the energy source and carbon dioxide as the source of carbon.
2. **photoheterotrophs.** Light is the source of energy, and carbon comes from organic compounds such as alcohols, fatty acids, other organic acids, or carbohydrates.
3. **chemoautotrophs.** These use electrons from reduced inorganic compounds as their energy source, and carbon dioxide as their
source of carbon. Inorganic compounds can include hydrogen sulfide \( \text{H}_2\text{S} \), elemental sulfur \( \text{S} \), ammonia \( \text{NH}_3 \), nitrite ions \( \text{NO}_2^- \), hydrogen \( \text{H} \), and ferrous ions \( \text{Fe}^{2+} \).

4. **chemoheterotrophs.** Both energy and carbon come from the same organic compound, such as glucose. These organisms are medically important, but some can be beneficial for bioremediation.

Once the primary producers fabricate organic compounds from inorganic sources, they can become sources of food for other heterotrophs. The ideal order of feeding is called the food pyramid (or food chain, or trophic levels), and is classically described as herbivores grazing on plants, carnivores eating the **herbivores**, and higher-level **carnivores** eating the lower-level carnivores. This is not the way it always happens, but gives the idea.

Energy levels are degraded at every step of a process (Section 2.4). That is, there is always some inefficiency in converting energy from one form to another, and some energy is unrecoverable (see Section 2.4.3). Because of this, there is lost energy (about 90%) at each step on the food chain. Consequently, whether we consider numbers of BU, total biomass, or energy equivalence, the bottom of the food chain always is larger than the top. That is, there are more autotrophs than grazers, more grazers than lower-level carnivores, and more lower-level carnivores than higher-level carnivores.

Diagrammatically, these statements describe a pyramid shape (Figure 5.5.5). Trophic levels in the sea were originally defined as discrete steps describing the food chain (Pauly et al, 2000). For instance, tiny zooplankton (second level) feed on phytoplankton (first level). See Figure 5.5.6. Many marine creatures don’t feed exclusively on the level just below. Instead, like anchovies (level two), they may feed on organisms from several lower levels. Depending on the relative amounts of their diets, these creatures can be assigned a fractional trophic level number. Anchovies have thus been assigned to level 2.2. Humans who fish for anchovies would then be assigned to level 3.2, one above anchovies.

The difficulty comes when a lower trophic level is fished nearly to extinction. Then the entire ecosystem above this trophic level collapses.

Incidentally, humans are not always at the top of the food chain. Ask any shark.
Figure 5.5.6. Trophic levels were initially defined to include only discrete steps (left). Organic detritus and microscopic plants (phytoplankton) occupy the first trophic level. Tiny zooplankton, which feed on phytoplankton, reside at the second level. Creatures that eat zooplankton sit at the third level, and so forth. But many marine creatures feed from multiple trophic levels and so could not be fit into this classic scheme. Thus the modern approach allows the assignment of trophic level to span a continuum rather than forcing it to take on integral values. Marine biologists would, for example, assign the anchovy, which supplements its main diet of phytoplankton with some zooplankton, to a trophic level of about 2.2; people fishing for anchovies (and eating a diet of only these small fish) would then be assigned a trophic level of 3.2 (right) (Pauly et al, 2000).
Applications and Predictions

1. Colonies of ants and human livers will have similar responses to environmental challenges.
2. Cells are necessary for more complex life forms.
3. Life requires sources of energy and nutrients to develop, grow, and reproduce.
4. All life is connected.
5. Certain nutrients and biochemicals will become more concentrated in BU at higher trophic levels.
6. Some living things are difficult to distinguish from nonliving things.
7. Nutrients and energy are recycled.
8. Trophic levels of societies will be higher than the trophic levels of individuals within the societies.
9. Higher trophic level organisms depend for their survival on lower trophic level organisms.
5.6 Is Biology Complex or Simple?

There are known knowns; there are things we know we know. We also know there are known unknowns; that is to say, we know there are some things we do not know. But there are also unknown unknowns – the ones we don’t know we don’t know. -Donald Rumsfeld

There is an aura surrounding biology that attributes great complexity (Trefel and Hazan, 1998) that even tends to the metaphysicality of a special life force. The huge numbers of biochemicals within the cells, the way in which they interact in strangely efficient ways, the apparent self-organization, and the emergent properties of higher biological levels reinforce the notion that we are dealing with entities that somehow suspend the limits of physics and chemistry. Complexity, some say, is the key to understanding biology (Capra, 1996) and this very notion makes it nearly impossible to completely understand biological foundations.

Yet, each biological property that is studied turns out to be surprisingly simple. Whether it is the attachment of the gecko’s feet to vertical surfaces or the height to which water rises in the xylem tubes of the giant Sequoia, that which was once not understood and so thought to be very complex turns out to be based on very simple principles. And because the principles are simple, the effects are robust.

Could it be that biology is not so complex, but instead is an accumulation of a vast number of very simple outcomes based upon simple modes of action? It is indeed possible, because, at least in many instances thus far, mechanisms of biological action that have been discovered and consequently understood have not required that any new principles or modes of action be postulated. The study of biology has not revolutionized the fields of physics and chemistry. Rather, it has reaffirmed them.

Engineering predictions about biological phenomena are usually based upon (mostly empirical) mathematical equations. The usefulness of these equations depends upon the accuracy of their predictions. Sometimes, however, biological behavior is too complex to be described in simple mathematical form.

The biological beings that are the subjects of these equations, however, are not able to understand mathematics, and, indeed, have been operating successfully for many generations. Thus, there must be a simpler basis for biological activity than the submission to equations that require a high degree of generalized intelligence and many years to understand.

Wolfram (2002) asserts that biological complexity can be derived from relatively simple rules of behavior. In his computational experiments with cellular automata, he has been able to generate complex geometric patterns that he insists are examples of complex natural phenomena (Figure 5.6.1). As one might expect, such assertions are controversial.

Wolfram’s ideas may not be entirely correct, but there can be, at least, a simple basis to biological behavior. Depending on the rules governing
interactions between biological units and their neighbors, Wolfram has found complexity, nested patterns related to fractals, optimization, and random responses. Whether or not it becomes useful to identify these simple rules, the robustness of biological activity must depend almost solely on simple processes. The simplest, we know, is the gene.

There is a problem with the burgeoning and overwhelming aggregation of information being learned about genetic structure, placement, and function. Such a vast information aggregate cannot be easily classified and presented. Manipulation of genetic knowledge is one domain of bioinformatics, but the ideal pictorial representation of genetic structure and function has not yet been demonstrated. Is there a genetic analog to the periodic table of chemical elements? One can look at the table and immediately infer generalizations about chemical properties. Will there be possible such a representation for genetic elements? The search continues.

Figure 5.6.1. This fractal-like form was spontaneously produced on a computer with some relatively simple manipulations (Wolfram, 2002).

In many natural environments, from biological cells to clusters of galaxies, complex geometric forms can appear spontaneously and propagate into other forms under very simple conditions (Madore and Freedman, 1987). The Belousou-Zhabotinskii chemical reaction, for instance, develops into waves of chemical activity propagating through a receptive liquid medium. These can be seen in a series of photographs (Figure 5.6.2). Other structures can be formed spontaneously in biological gels under relatively simple conditions. The conditions under which these structures are formed are just beginning to be discovered, but the implication is that subcellular biological structure may be thermodynamically preordained.

In a very lucid book on the interior conditions of cells, Pollack (2001) takes issue with many of the assumptions of cellular structure and organization. Integrity of the cellular membrane is not required for proper functioning of the cell, and the number of active transport mechanisms thought to be required to maintain chemical equilibrium inside the cell is much too high to be realistic. Instead, Pollack asserts, there is a basic
Figure 5.6.2. The Belousov-Zhabotinskii reaction produces complex geometric forms without human intervention (Madore and Freedman, 1987).

intracellular gel maintained by the interactions of polar water molecules and surface charges on the actin filaments of the cytoskeleton (Figure 3.7.7). He has explained many cellular actions based upon this structure. Again, the basic functional mechanisms are extremely simple and do not require levels of complexity previously thought necessary to explain cellular activity.
If there is complexity in biological systems, it is most apparent in the relationships among simple elements. In Figure 5.6.3 is shown a diagram of the interactions among contributors to a model of the limits of human work performance while wearing a respirator mask (Johnson and Dooly, 1995). This diagram has been described as looking like a “plate of spaghetti” with its interconnecting lines between elements of the model. Each element is fathomable and modelable, and therefore relatively simple, but the overall appearance seems to be complex.

Biological materials, also, show this same feature. There are a very limited number of macromolecules available to produce all the materials present in biological systems (Section 3.6.4). However, the appearance of an

![Figure 5.6.3. Schematic overview of a model to predict human performance. The appearance is that of a complex pattern involving simple elements (Johnson and Dooly, 1995).](image_url)

infinite variety of biomaterials is due more to the interconnections of this small number of building blocks rather than to a large number of precursors.

Reductionists (those who study the most fundamental scientific states) often believe that all properties of more complex states can be explained by their fundamental laws. All science could then be classified as either: 1) related to the discovery of fundamental laws, or 2) explaining natural
phenomena in terms of known fundamental laws (Anderson, 1972). Biological scientists, however, talk about emergent properties, or characteristics of a higher-level biological organization that cannot be deduced simply by adding the characteristics of its component parts. In other words, it may be that there is no unique set of fundamental laws that can be used to explain all phenomena at all hierarchical levels. At each new level, there are new laws, concepts, and generalizations that are necessary to apply to that level. Thus, they say that biology is not just applied chemistry.

The view taken in this text sidesteps the reductionist and emergent properties views. As engineers or technologists who are concerned more with the application and use of biology than with its explanation, it is sufficient to become familiar with generalizations that apply across all hierarchical levels, those principles that apply at certain levels only, and exceptions to both that modify the biological behavior expected when challenged with a certain set of environmental conditions.

Thus, the view here is that basic biological activity is based upon very simple and robust physical and chemical principles. The complexity of biology comes in the multitude of different activities that work together to achieve the common goals of survival and replication.

Summary of scientific principles related to the understanding of biological systems:

1. There are places with higher potential and places with lower potential. Things move from higher to lower potential.
2. The maintenance of order requires energy.
3. What goes in but doesn’t come out is stored inside.
4. Different forms of energy can be used to perform mechanical work.
5. The transfer of something from one place to another depends directly on the surface area and is inversely proportional to the distance between the two places.
6. Mechanical strength depends on geometrical configuration, the amount of material present, and properties of the material.
7. Unbalanced mechanical forces cause acceleration.
8. Heat is the ultimate nonspecific form of energy.
9. Hydrostatic pressures are equal in all directions.
10. Flowing fluids require energy to overcome resistance.
11. There is a periodicity of properties of elements, and these properties are related to numbers of electrons and their energy states in elemental atoms.
12. Elements can combine to form compounds with different properties.
14. Chemical reactions occur spontaneously when they yield energy to the environment.
15. Reaction rates depend upon reactant concentrations, temperatures, and pressures.
16. Intermediate reactions are most important to living things.
17. There is an element of randomness in biology.
18. Appropriate responses require control systems, and each of these needs sensors, actuators, processing, and information pathways.
19. Optimization conserves resources.
20. Information implies order.
21. The primary goal of life is survival and reproduction.
22. Living things are constantly changing.
23. Long term changes to a species occur only if there is a reproductive advantage.
24. Life is redundant.
25. Coexistence of species requires that each adapts to a different ecological niche.
26. Attributes passed from one generation to the next require an information legacy.
27. Each distinguishing biological trait is made valuable by its cost.
28. An individual is a product of both its genetic code and its environment.
29. Life is conservative.
30. Living things use simple building blocks with complex interactions.
31. Extremes are not tolerated well by living things, nor do living things create extreme conditions.
QUESTIONS
Chapter 5

5.0.1 Formulate additional principles of biology and justify them.

5.1.1 Choose a biological example, and show how form is related to function.

5.1.2 How does the relation between form and function affect a biological engineering design?

5.1.3 What characteristics of a plant are most important for designs involving it?

5.1.4 Give examples where the forms and functions of these biological units influence engineering designs involving them:
   - slithering animal
   - plant
   - animal that communicates verbally
   - bacteria
   - virus
   - intestinal wall cell
   - muscle cell
   - flying insect
   - finfish

5.1.5 Add to the list of Applications and Predictions.

5.2.1 Describe how you would infer relationships among organisms from their forms.

5.2.2 Describe the conceptual design of a new biological function by combining elements from different biological forms.

5.2.3 What happens to intermediate biological forms once better adapted forms have been developed?

5.2.4 Why is it important to know about normal living conditions when providing for a new habitat for living things?

5.2.5 Contrast the expected optimal environments for hepatic cells compared to dermal cells.

5.2.6 Development of resistance to a new pathogen, parasite, or biochemical challenge requires what?
5.2.7 What is convergent evolution and explain why it might occur.

5.2.8 Add to the list of Applications and Predictions.

5.3.1 Why is it that the sequences of bases on both DNA strands can be determined if the base sequence on one strand is known?

5.3.2 What are the relationships among DNA, a gene, a codon, amino acids, RNA, and proteins? Why is a codon considered to have a minimum length of three bases?

5.3.3 Compare the process of development of a computer operating system (like DOS or Windows) with the operation of protein formation.

5.3.4 Explain why the dominant-recessive genetic model is much simpler than most genetic trait determinations.

5.3.5 Speculate on the difficulty in identifying the relationship between a gene and its effect.

5.3.6 Why is it surprising that genetic variability is maintained in an organism? What is the advantage to maintaining genes that result in individuals less suited to their environments than others?

5.3.7 Of what importance is PCR? Think of some unique uses for PCR.

5.3.8 Discuss the chicken or egg question.

5.3.9 If sufficient knowledge about the genetic makeup of an individual is known, what factors would be important to determine if individualized medicines would or would not be made?

5.3.10 What is the role of mutation in genetic progress? What factors determine whether mutations occur and survive? How can these be used in biological engineering designs?

5.3.11 Why can it not be said that genetic mutations occur randomly?

5.3.12 Discuss the simple elegance of the Ames test.

5.3.13 Why is it important to know about extra-nuclear genetic material?

5.3.14 List specific factors influencing gene expression.

5.3.15 Of what use is the fact that chloroplast and mitochondrial DNA is transmitted separately from nuclear DNA?
5.3.16 Describe the function and use of biochips.

5.3.17 Add to the list of Applications and Predictions.

5.4.1 Why is competition necessary for biological selection?

5.4.2 Name an Earthly environment where no life would be expected to exist.

5.4.3 The fact that some sort of microbe will grow almost everywhere means what to a biological engineer?

5.4.4 If less competitive species are constantly being lost, does that necessarily mean that competition for a species becomes greater in the future? Why?

5.4.5 Discuss the theory that the closer the relationship, the more interest one individual shows in another. How does this relate to biological engineering designs?

5.4.6 Is there a sudden advance in technology that can be anticipated in biology? What is it?

5.4.7 How can the idea of memes be used to advantage by biological engineers?

5.4.8 Will evolution always result in a new species? Why?

5.4.9 Give examples of evolution that does not result in genetic changes. How can these be used by biological engineers?

5.4.10 Describe the competition among individual genes or groups of genes.

5.4.11 How are the reproductive strategies of transposon genes and gamete killer genes similar and how are they different?

5.4.12 Add to the list of Applications and Predictions.

5.5.1 List similarities and differences among different hierarchical levels in biology.

5.5.2 List ways in which eukaryotes differ from prokaryotes. Why are these differences important?
5.5.3 Which definition of life do you prefer? Why do you think it best, and what could be improved?

5.5.4 How would you define life?

5.5.5 Why is it important for a biological engineer to be able to distinguish between living and nonliving forms?

5.5.6 If all of life is considered to be a component of an ecological system, what implications does this have for the ultimate outcomes of engineering uses of biology?

5.5.7 Describe ways in which the ecological balance of nature can be used as a potent tool for biological engineering design. How can a balance be incorporated and nurtured?

5.5.8 Where would you place humans on the trophic level scale if all human food is considered? Why?

5.5.9 How does synthetic biology differ from conventional biology?

5.5.10 How would you go about counting the many microscopic organisms living on and in the human body?

5.5.11 Add to the list of Applications and Predictions.

5.6.1 Give an example where a biological characteristic can be attributed to a multitude of simple building blocks.

5.6.2 Is biology simple or complex? Why?

5.6.3 Is the summary of scientific principles sufficient? Is there need for others? Are some not necessary?