Page 19:

Add to Section 1.4.4:

Example 1.4.4 Animal Models for Drug Testing

Animal models are often used to test predictions of effects of drugs intended for human use. However, animals meant for this purpose have many disadvantages (Dove, 2010):

1. there are ethical and moralistic concerns about animal use and care.
2. animals often give poor predictions of human responses.
3. animals are expensive and inconvenient.
4. animal populations used for drug testing usually have uniform genotypic and phenotypic characteristics, and so do not display idiosyncratic reactions.

For these reasons, alternatives have been sought. Human cell cultures hold promise; they can be fast and inexpensive, but cultured human cells rarely act the same as identical cells in the body. Mathematical models of drug reactions are another possibility, but, until model results are validated by animal experiments, there is little confidence in model predictions. Indeed, validation of mathematical models could actually increase animal usage rather than decrease it.

Page 23:

Example 1.6.4 Unintended Consequence of Roundup-Ready Crops

Glyphosate (commercially sold with the name "Roundup") is a very popular herbicide because it kills both grasses and broadleaf weeds at any stage in their development. It works as a chelating agent that ties up minerals like iron, manganese, zinc, calcium, nickel, and copper. Some of these are essential for critical enzyme formation. Glyphosate kills plants by blocking the essential shikimic acid enzyme pathway required for plant respiration. It also interferes with enzymes necessary for disease resistance (Lehnert, 2010).

A plant gene conferring resistance to glyphosate had been inserted into popular genetically-engineered crops in the mid-1990s. This allowed these crops, called "Roundup Ready", to be grown with minimal herbicide use. One spray of glyphosate replaced four or five sprays of other, more environmentally-damaging herbicides. Glyphosate-resistant cotton and soybean crops became dominant due to their economic and management advantages. More than 143 million acres were planted to Roundup Ready crops worldwide, and 92 percent of the U.S. soybean crop was planted to glyphosate-resistant varieties in 2010 (Lancaster Farming, 2010).

Such reproductive pressure has rapidly led to the emergence of glyphosate-resistant weeds. There were no resistant weed species in 1995; there were 19 resistant species in

2010 (Lancaster Farming, 2010). Resistant weeds were a problem on 2.4 million acres of crops in 2007, 5.4 million acres in 2009, and 11.4 million acres in 2010.

The biological realm depends on redundancy for effectiveness. Scientists who developed Roundup Ready crops inserted just one gene into their plant genomes. The probability that effectiveness of one gene can be overcome is small, but finite. If there were two or three genes to overcome, the probability of developing resistance would be nearly zero. Biotechnologists, engineers, and scientists who wish to avoid the unintended consequence of making their creations widely ineffective need to depend on more than one mechanism to safeguard their works.

Page 58:

In Section 2.8.1, in the paragraph beginning "Within the cell, vesicles …", Replace the last sentence of the paragraph with:

In the opposite process of *endocytosis*, the cell can incorporate material by surrounding it and forming a vesicle to either store or transport it to the interior of the cell. Endocytosis is important for lymphocytes to ingest invading microbes, and for other cells to transport materials too big to pass through membrane pores from the environment into the cell. Endocytosis is more likely to be developed in adherent cells than in suspended cells.

Page 61:

Add to Section 2.8, this Example 2.8.5:

Example 2.8.5 Water Bears Need No Circulatory or Respiratory Systems

Water bears (also called *Tardigrades*) are extremely small aquatic animals found almost everywhere on Earth (Miller, 2011). Terrestrial water bears live in damp places in moss, lichens, leaf litter, and soil. They have amazing survival strategies, including *cryptobiosis*, or the ability to cease all metabolic activity in the absence of water. They are so small (Figure 2.8.5) that they contain only a little over 1000 cells, with enough access for water, oxygen, and nutrients that they lack circulatory or respiratory systems.

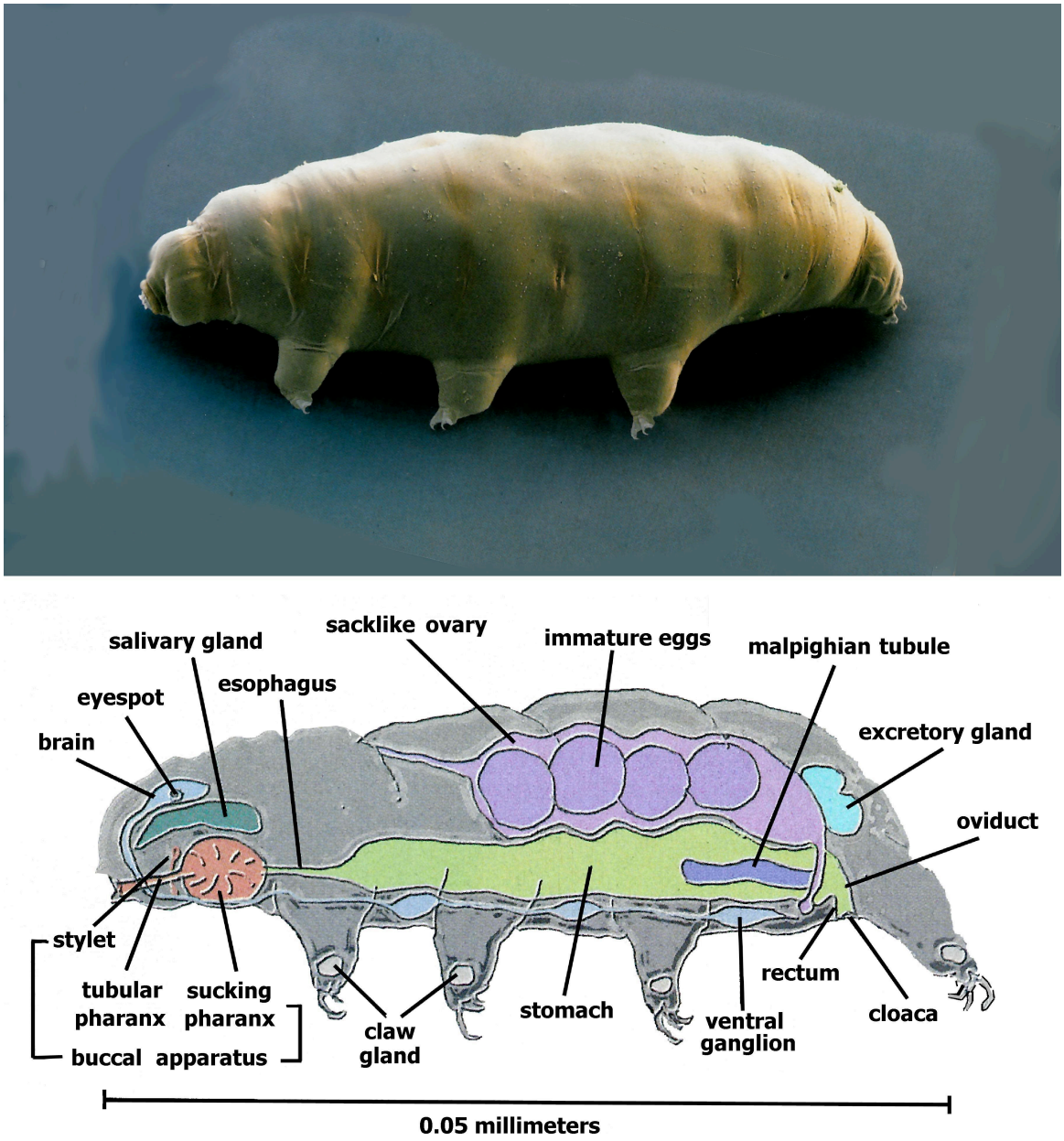


Figure 2.8.5 Water bears are microscopic animals with extreme survivability. They are small enough that they need no respiratory or circulatory systems.

Page 69:

Add to Section 2.9.5, after the last paragraph:

Counteracting high internal pressures requires strong surrounding structures. Bacteria, fungi, plants, and some archea have tough, sometimes flexible outer cell walls that offer structural support, protection, and limited filtering. The cell wall prevents the cell from bursting when too much water enters the cell in a hypotonic (low solute

concentration) environment. Different bacteria have generally two different kinds of cell walls that either stain or not with a standard blue dye. These are called gram-positive or gram-negative.

Page 78:

Add to Section 2.11.2, just before the paragraph that begins “Neural signals and muscular …”:

DNA electrical conductivity can be used as the basis for biosensors giving information about the state of the organism they are associated with. DNA has an electrical conductivity equivalent to that of other conductive polymers, but the actual conductivity value depends on DNA configuration and composition, which is why DNA configuration can be detected electrically.

Page 81:

Add these sentences in Example 2.11.1, just after the sentence in the second paragraph beginning “Another means is electroporation, …”:

Once the pulse stops, the pores close.

Add after the sentence beginning “Large molecules such as DNA …”:

When the pores close, they are locked inside the cell.

Add as the last sentence, after the sentence beginning “Electroporation can also be used …”:

This approach is highly efficient, but can sometimes be deadly to the cell.

Page 81:

Add these examples at the end of Section 2.11:

Example 2.11.2 Use of Electroporation to Increase DNA Vaccine Effectiveness.

Vaccines typically use an inactivated pathogen injected into a host to elicit an immune response. When subsequent exposure to a live pathogen happens, the immune system is primed to respond and fight the infection (see Section 6.20.3). New approaches to vaccine development use snippets of DNA called plasmids (see Section 5.3.11) instead of the entire pathogen. These plasmids enter the cells of the host, produce proteins identified as belonging to the pathogen, and elicit an immune response without any danger that could come from the entire pathogen. The host’s own cells do the work of eliciting the immune response (Morrow and Weiner, 2010).

It is the protein produced from the plasmid that provokes the immune system, not the DNA plasmid itself. Thus, a critical step in the process is moving plasmids into enough of the host's cells so that the cells can begin producing the protein in large enough quantities.

DNA material does not easily translocate across the cell membrane. For this, a vector is needed. Vectors can include adenoviruses (common cold viruses) for humans or agrobacteria for plants. However, adenoviruses by themselves provoke an immune response that may not allow the plasmids to be incorporated into host cells.

Electroporation momentarily opens pores in the cell membranes to allow injected plasmids to translocate into host cells. This is thus a preferred method to move DNA past the cell membrane barrier.

DNA vaccines have been developed to treat or protect against human immunodeficiency viruses (for humans), West Nile virus (horses), infectious hematopoietic virus (salmon), melanoma (humans and dogs), fetal loss (pigs), hepatitis C (humans), human papillomavirus (humans), and liver cancer (humans).

Example 2.11.3 Deep Brain Stimulation

Deep brain stimulation via an electrode array implanted at some location in the brain is a standard treatment to calm the tremors of Parkinson's disease. It can also be used as an intervention for depression, obsessive-compulsive disorder, or other psychological disorders. Magnetic coils placed against the scalp and induce electrical currents in the brain in response to magnetic pulses. These can either increase or decrease brain activity. This technique has been used successfully to block migraine headaches when they first appear.

Page 89:

Add to Section 3.1, just before the paragraph beginning "The periodic table of elements …":

Before English physicist Henry Moseley, the periodic table of elements was ordered according to atomic mass. Moseley, using the frequencies of X-rays reflected from material samples, was able to detect the nuclear charges of different elements. From these, he ordered the periodic table based on atomic number (Scerri, 2014).

Page 90:

Add to Section 3.1, after the sentence beginning "They do not take part …", this phrase and this sentence:

(although xenon has been found to form bonds with halogens, oxygen, carbon, and gold, under certain conditions). Looking at the periodic table, flammability decreases from left to right, and toxicity increases from top to bottom.

Page 91:

Add to Section 3.1, after the sentence beginning "Arsenic (33) is dangerous …":

Although toxic to almost all life, arsenic can apparently substitute for phosphorous without ill effect in a bacterium called GFAJ-1 (Wolfe-Simon et al, 2010). The arsenic was incorporated in the nucleic acids (as the DNA backbone), proteins, and cell membranes of healthy bacteria.

Page 91:

Add this box:

ARSENIC AND OLD LACE

In the Joseph Kesselring 1939 play "Arsenic and Old Lace", two misguided spinster sisters decide to help lonely old men relieve their loneliness by inviting them to their house for dinner and poisoning them with home-made elderberry wine laced with arsenic, strychnine, and just a pinch of cyanide.

Arsenic is acutely poisonous. It has been known as the "poison of kings" because it is nearly odorless and tasteless and could be discretely slipped into food or drink to assassinate persons of wealth or power. It was not able to be detected as a poison until sensitive tests were developed in the 19th century. The Borgias of 15th and 16th century Italy used arsenic-tainted wines to rid themselves of influential popes and cardinals in order to further their own ambitions.

Arsenic competes with phosphorus to interfere with cell metabolism. Acute arsenic exposure causes necrotic cell death. Long-term arsenic exposure can lead to cancer. Arsenic poisoning is now considered to be an environmental toxin of particular harm to fetuses and very young children, in whom it can cause neuropathological conditions and death to develop (Yosim et al, 2015).

Page 93:

Add to the end of Section 3.1, this example:

Example 3.1.1 Phosphates in Detergents Cause Algal Bloom

Phosphorous as phosphate (phosphorous with the addition of four oxygen atoms) is an important constituent of many detergents. Cleaning agents remove dirt from dishes or

clothes, and phosphorous binds to the dirt and keeps it suspended in water. The problem that results, however, is that phosphorous added to waste water acts as a fertilizer that stimulates algal growth. When the algae die, they decompose and absorb oxygen from the water, suffocating other forms of aquatic life.

Page 114:

Replace in the last sentence of the second paragraph of Section 3.6.3, the references with:

(Everts, 2013; MacDermott and Tranter, 1990).

Page 115:

Add this sentence to Section 3.6.3, third paragraph, after the sentence that begins "The amino functional group…":

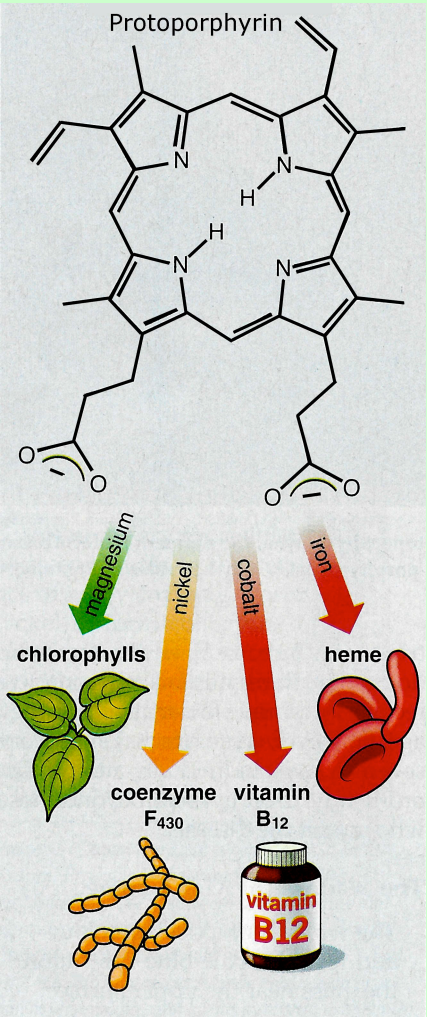
Protein contains approximately one part by weight of nitrogen for each 6.25 parts of protein (Lane, 2010).

Page 115:

Add this box at the end of Section 3.6.2:

THE IMPORTANT PORPHYRIN RING
(Reprinted From Dayan and Dayan, 2011)

The porphyin pathway is ubiquitous in the biochemical realm, serving throughout the plant and animal kingdom as the assembly line for the most abundant pigments in nature. The ring-shaped porphyrin molecules bind an array of metal ions, with each combination associated with different biological functions. Chlorophylls bind magnesium to play a pivotal role in photosynthesis. Heme binds iron to coordinate molecular oxygen and carbon-dioxide transport chains necessary for cellular respiration and contributes to the catalytic activites of many enzymes. Porphyrins bind nickel to form ccoenzyme F_{430}, which plays critically important roles in bacteria that metabolize methane. Vitamin B_{12} is formed from the binding of cobalt to a derivative of porphyrin; lack of the vitamin can result in pernicious anemia and impair the function of the brain and nervous system. Taken together, these porphyrin-derived pigments can be called the "colors of life", in the sense that these rings are necessary to sustain key activities in nearly all organisms (Figure)

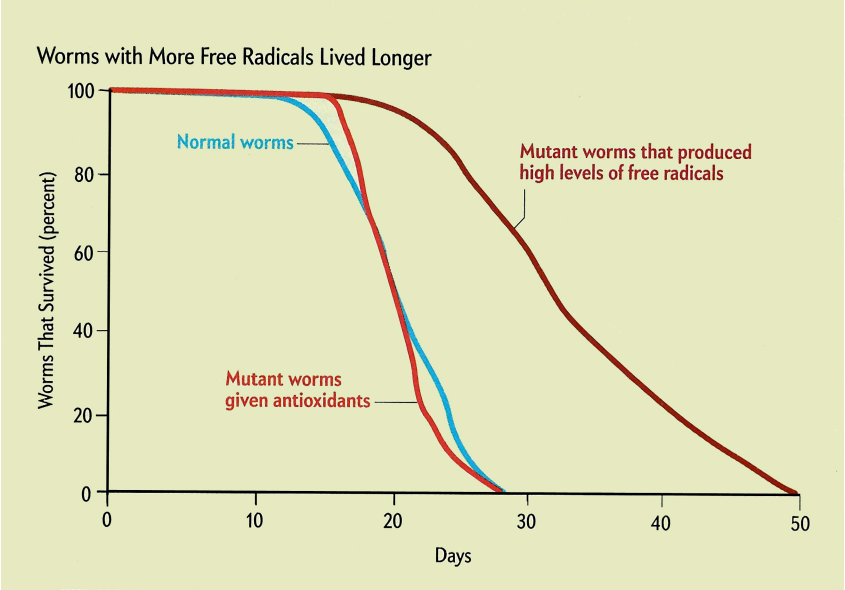


The porphyrin ring-shaped molecule can accept different metals to produce pigments essential to metabolism in various organisms. Heme and vitamin B_{12} are vital to animals, chlorophyll to plants, and coenzyme F_{430} to methane-processing bacteria.

Page 119:

Add to Section 3.6.7, in the box entitled “Antioxidants”, just after the paragraph beginning “Antioxidants derived from foods …”

But the story of free radicals and antioxidants may be much more complicated than commonly believed. Some level of free radicals in certain locations may be necessary to stimulate cellular repair and defensive mechanisms. Free radicals at higher levels and at other places in the body may lead to cellular damage. Just as with other substances, the concentration of antioxidants may be important, with a *hormetic* effect (beneficial at low concentrations but toxic at higher concentrations). Antioxidants in foods seem to be healthy; antioxidants as vitamin supplements are not always so (Yang and Hekimi, 2010; Moyer, 2013).



Round worms genetically modified to produce high levels of certain free radicals lived 32% longer than unmodified worms. Feeding Vitamin C to the worms shortened their life spans (Moyer, 2013).

Page 120:

Add Example 3.6.2 to the end of Section 3.6:

Example 3.6.2 C:N Ratio for Composting.

Composting is used to turn discarded or infected organic waste into a pathogen-free soil amendment. Composting is used to remediate pathogenic threats from animal carcasses as well as from infected plant matter. Composting uses mezophillic (medium warm temperature loving) and thermophillic (hot temperature loving) bacteria to metabolize organic matter, producing heat in the process. If the temperature rises high enough, pathogenic bacteria are killed and weed seeds are inactivated. The end product is a nitrogen and micronutrient rich fibrous material.

Nitrogen is required for the composting bacteria to form microbial tissue. Nitrogen and other essential nutrients are supplied by the organic matter to be composted. Carbon, however, must be added to supply energy for aerobic metabolism. Carbon may come from any number of sources: sawdust, straw, chopped newsprint, or other cellulosic material. Oxygen must also be available to achieve aerobic digestion. Anaerobic digestion, due to insufficient oxygen, results in an odorous product without killing pathogens.

The ideal ratio of carbon to nitrogen is in the range of 20 or 30 to 1. Table 3.6.3 gives a list of carbon to nitrogen ratios of common compost materials. It is apparent from this table that the required C:N ratio must be achieved with a mix of carbon-rich and nitrogen-rich sources.

Table 3.6.3. Common Compost Materials (Payne and Pugh, 2010).

Compost Material	C:N
Sawdust	442:1
Straw-wheat	127:1
Rice hulls	121:1
Straw-general	80:1
Corn stalks	60-73:1
Finished compost	30-50:1
Hay-general	15-32:1
Horse manure-general	30:1
Cattle manure	19:1
Grass clippings	17:1
Sheep manure	16:1
Turkey litter	16:1
Broiler litter	14:1
Swine manure	14:1
Cottonseed meal	1-7:1
Soybean meal	4-6:1
Animal carcass	5:1

Page 126:

Add to Section 3.7.2, to the figure caption of Figure 3.7.8, after the sentence beginning "This cross section through the cytoplasm …":

Macromolecules typically occupy 20 to 40 percent of cytoplasm volume (Clabby, 2011).

Page 130:

Add to Section 3.8, at the end of the paragraph beginning “This problem is the result …”:

As might be expected, protein folding and other natural processes proceed more slowly in the crowded environment within the cell than they do in a test tube (Ebbinghaus et al., 2010).

Page 132:

Add to Section 3.8, as the last sentence of the paragraph beginning “Proteins are originally synthesized ….”:

Chaperone molecules work by encasing an unfolded protein in an isolation compartment. Safely inside, the proteins fold correctly by themselves. Without the isolation, the proteins clump together and kill the cell (Goforth, 2012).

All cells, from yeasts to humans, and at least some bacterial cells, attach complex sugars to their proteins in a process called *glycosylation*. These sugars help the proteins fold and function properly.

Page 133:

Add to Section 3.8, as the last sentence of the paragraph beginning “Mutant proteins, …”:

Cellular mechanisms for destroying misfolded proteins weaken with age, allowing proteins to accumulate and cause diseases.

Page 133:

Delete the top paragraph on page 131 of Section 3.8, beginning “If the protein fails to fold properly …” and delete the last paragraph on page 133, beginning “There are many diseases …” . Insert these paragraphs at the end of Section 3.8:

If the protein fails to fold properly, its shape is incorrect and it cannot perform its intended function. Aberrations in protein folding appear to contribute to human and animal diseases. Among these are Alzheimer’s disease, prion diseases, emphysema and cirrhosis, amyelotrophic lateral sclerosis (Lou Gehrig’s disease), cystic fibrosis, some tumors, osteogenesis imperfecta (King et al., 2002), and transmissible spongiform encephalopathy (TSE). Unclustered prion molecules are harmless and found in all mammals. When bunched together, however, these same prions become infectious (Wilham et al, 2010).

Prions are instrumental in stabilizing neural synapses involved with long-term memory formation. When an electrical impulse is passed from one neuron to another in the brain, a chemical change in an associated prion allows the synaptic connection to be retained even after the initial stimulus has been removed. Thus, the memory of the stimulus remains (White-Grindley et al., 2014)

Prions are misfolded proteins. When a protein converts to a prion, it polymerizes from coiled alpha helices that dominate normal protein structure into an aggregate of tightly packed beta sheets (Saltus, 2010A). The prion that is implicated in the cause of bovine TSE (mad cow disease), for instance, appears as a pleated sheet rather than a smooth helix. Prions have the unusual property that they can replicate without DNA or RNA (Saltus, 2010A). This gives the possibility that prions can act as an evolutionary route parallel to the genetic code for the organism. Whereas some prions have been identified as causing debilitating diseases, others in yeast, have been shown to change the pattern of gene expression in cells, at times enabling the cell to cope with radically different environmental pressures. The ability to self-replicate may also be important in the retention of memories through prion alteration of frequently-used neural synapses.

Treating these diseases at the protein level may be easier and more ethical than using gene therapy. The strategy would be to restore missing or nonfunctional proteins with pharmacological chaperone molecules inserted into the cells.

Page 133:

Add to Section 3.8, this box:

CARRIER PROTEINS

Within the crowded cell interior, there are molecules, usually proteins, that are critical to cell functioning and must be located in the correct place, be it the cell nucleus, the outer cytoplasm, or the cell membrane. These necessary molecules are transported along actin microtubules inside the cell by other carrier proteins. It is the function of these carriers to pick up the necessary cargo molecules and facilitate their transport within the cell. One carrier protein, *kinesin*, similar in structure to myosin, carries molecules into the interior of the cell; another, *dynein*, carries molecules in the other direction from the interior to the outer cytoplasm. Still other molecules freeload on the actin as it streams within the cell. In these ways, necessary proteins are delivered to the places where they are needed, and in a timely fashion. If these transport processes are disrupted, cells cease functioning correctly and physical disorders result (Williams, 2013B).

Page 138:

Add to Section 3.9, this box:

UNFOLDED, UNSTRUCTURED, AND MEANT TO BE THAT WAY

Most cellular proteins have a particular structure that they assume in order to serve their specific purpose. Enzymatic proteins are this way, and are ineffective if misfolded. Elaborate mechanisms inside cells detect misfolded proteins and either destroy or repair them.

However, about 35% of human proteins have long unstructured regions with no particular shape (Dunker and Kriwacki, 2011). Nearly all eukaryotic cells, but few, if any prokaryotes, depend upon these unstructured proteins for signaling and regulation functions. Enzymes must still form highly-regulated structures in order to be effective, but unstructured proteins are functionally flexible because they can wrap around many different types of molecules. When they wrap around enzymes, for instance, the enzymes are rendered ineffective. Hence, their functions are regulated by proteins that can assume any necessary shape. The ability to fold or unfold as the need arises presents many different possibilities.

Long, thin proteins can thread through small openings in the cell and carry other molecules with them. They can thus help regulate the availability of necessary chemicals, or help signal the cell of the chemical nature of the surrounding environment.

Not all proteins must have rigid structures to be effective; some work best if they can assume a multitude of shapes.

Page 163:

Add to Section 4.2, this box:

PETO'S PARADOX

If every living cell in an organism theoretically has an equal probability of developing cancer, then large animals with more cells should have higher cancer rates compared to smaller animals with fewer cells. However, it has been found that all mammals, regardless of size, have similar rates of cancer. This effect is called *Peto's Paradox* (Sneed, 2014).

Page 163:

Add to Section 4.2.1, as the first sentence, and before the sentence that begins "Mathematicians …":

The more variation in the results of an experiment, the harder it is to conclude that there are any meaningful differences between treatments and untreated control.

Page 181:

Add to Section 4.2.4, this example:

Example 4.2.5 Flu Vaccine Effectiveness

Quite a few studies in the literature have demonstrated that seniors who were vaccinated against influenza had nearly one-half the death rate of seniors who were not vaccinated. The implication of this is that influenza vaccination is highly effective in preventing influenza-related deaths. But is vaccination really so effective?

Upon further investigation, it can be seen that these studies looked at seniors either vaccinated or not, and how many died during flu season. Because it is difficult to know which senior died of flu, they looked at deaths from any cause. Included in the death rate had to be causes such as stroke, car accidents, heart attacks, and every other cause. The flu vaccine should have had no effect on most of these (Saulnier, 2009).

In order to see this big of a difference between seniors vaccinated and not, there had to be other differences between these two groups besides the fact that one received vaccination and the other did not. Those who chose to be vaccinated were generally healthier. They were mobile, they took care of themselves, they were younger, and they were less likely to suffer from chronic diseases. Frail and less functional seniors were less likely to seek vaccination.

So, the classical double-blind studies (those in which neither investigators nor the subjects know who is receiving which treatments) were not able to distinguish adequately between groups because the groups were not matched for all factors except the one of interest, in this case, vaccination or no vaccination.

Correct interpretation of test results cannot always be made without looking carefully at the methods used to obtain those results. In this case, flu vaccination was made to look to be much more effective than it really was because confounding factors also contributed to final results.

Page 193:

Add to Section 4.4.1, this sentence after the first sentence of the paragraph beginning "Surfaces of cell membranes …":

Each receptor is configured with a pocket into which a specific external molecule can fit.

Page 193:

Add to Section 4.4.1, this sentence at the end of the paragraph beginning “Surfaces of cells …”:

Modern drug therapies are now targeting these receptors or the chemicals (often hormones) that bind to them in order to produce desired results (Amábile-Cuevas, 2010).

Page 204:

Add to Section 4.4.3, to the box on Action Potentials, a phrase to make the last sentence on the page:

When the depolarization of the action potential reaches the synapse, a neurotransmitter is released by exocytosis into the small gap between the neurons.

Page 213:

Add to Section 4.6, this box at the end:

BODILY MICROBES AS AN INFORMATION LEGACY

The mix of microbes on organismal body surfaces is different for each individual plant or animal. These microbes have personalized effects, ranging from disease cause or prevention, odor production, digestion of nonfood compounds, essential biochemical production, and proper development of the immune system. Some types of microbes are essential to all members of an organismal species. Examples are endophytes in certain grasses, nitrogen-fixing bacteria in legumes, cellulose-digesting microbes in termites and cud-chewing animals, and probiotics in humans and animals. These microbes (called the *microbiome*) are so important that behavioral mechanisms have evolved to assure the passage of specific microbes from one generation to the next. In certain animals, essential microbes are passed through fecal exposure; in mammals, probiotics are introduced through mammary gland secretions.

The effects of these transfers are so profound that offspring may not survive without them. Somatic microbes thus are often as important as the genome and cultural information (memes) as a means to pass information from one generation to the next. Realizing this, the biological engineer should be sure not to impede this process.

Page 216:

Add to Section 4.7, at the end of the Section:

Table 4.7.1. Number of Neurons in the Brains of Selected Species.

Species	Number of Neurons
Roundworm	302
Fruit Fly	100,000
Mouse	75 million
Cat	1 billion
Chimpanzee	6.7 billion
Human	86 billion

Page 225:

Add this example to the end of Section 5.1, before the Applications and Predictions:

Example 5.1.1 Species that Mimic Each Other

Mimicry, the situation where an unrelated species develops an appearance similar to another species, is sometimes an important strategy in biology. There are survival benefits to the mimicking species if the species being mimicked has some kind of defense against predators. This type of mimicry confers a selective advantage as long as the mimicking species remains scarcer than its model. Even defenseless species may mimic each other if it reduces the chance that any individual may be lost to predators (Vogel, 2010).

Page 226:

Add to Section 5.2, at the end of the sentence that begins “If the incremental change … “:

(Gould , 1986).

Page 228:

Add to Section 5.2, this box after the sentence that begins “By studying these birds, …”:

PARSIMONY PRINCIPLE

The *Parsimony Principle in Biology* posits that natural selection operates as simply as possible over time. Therefore, one can judge the traits of an ancestor by looking at traits of present day individual groups. Traits shared by several related groups are even more likely to have been the same or similar to traits possessed by common ancestors (Boehm, 2012). This principle is thus recognition of the modularity of biological physical and behavioral characteristics.

Page 232:

Add this paragraph to the end of Section 5.3.1. Figure 5.3.3 must be added, and numbering for present Figure 5.3.3 through Figure 5.3.14 must be changed.

DNA is a very stiff molecule, with its double-helix structure and surface charges that repel other DNA surface charges (Babbit, 2011). Because of this, DNA does not curl up unaided into a tight ball inside the cell. Instead, DNA is wrapped spool-like around histone protein cores, called *nucleosomes*, that keep the DNA strands from straightening out into their full 2 m length (in human cells) and disrupting chromosome structure inside the five micron cell nucleus (Figure 5.3.3). Nucleosome positions with respect to one another help to determine gene expression within the cell, and these positions appear to have evolved over time by natural selection pressures exerted by the environment.

Methyl groups and other molecules can bind to the helix itself or to its histone protein core and cause the whole assembly to flex. As that happens, some genes are exposed and others are obscured. The exposed genes are the ones that can be actively expressed.

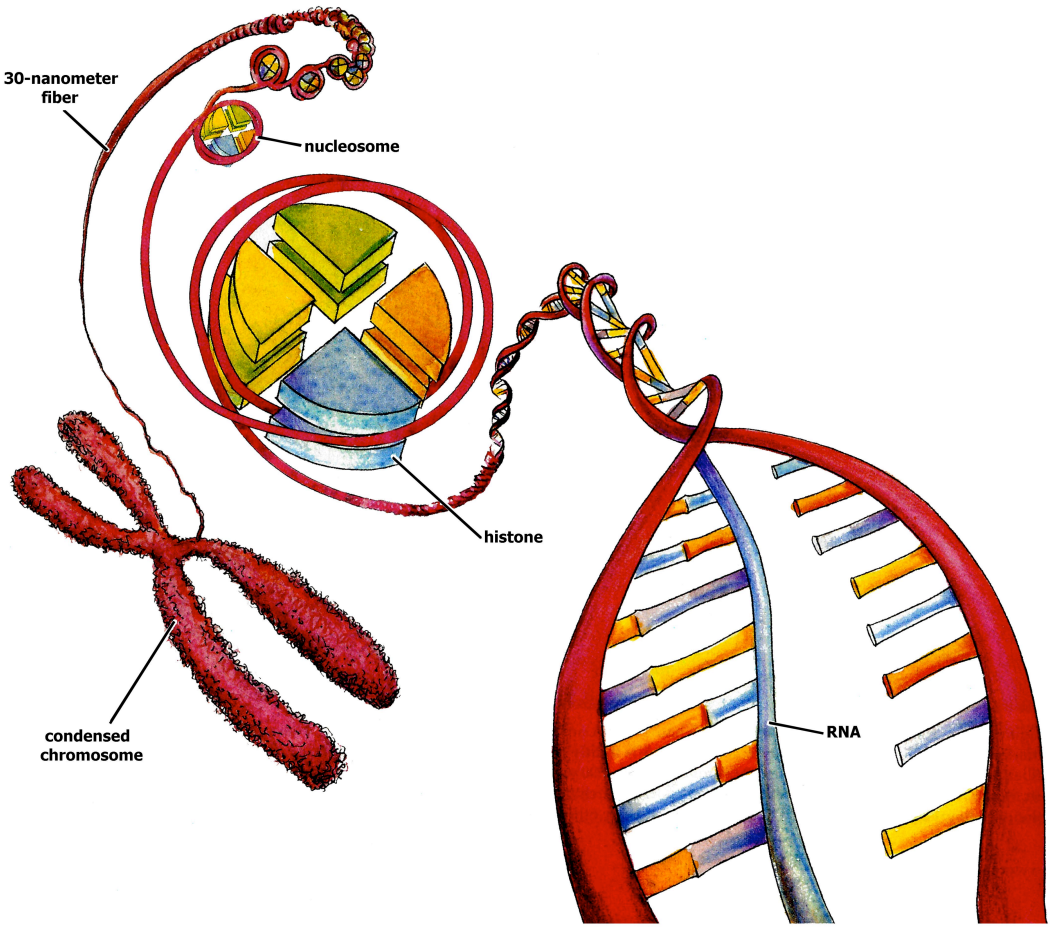


Figure 5.3.3 DNA is such a stiff molecule that it would not coil up enough by itself to fit inside the cell nucleus. Instead, it is wrapped around histone proteins to form nucleosomes that are serially located along the chromosome fibers 30 nanometers in diameter. The positions of different genetic materials (genes) in the nucleosomes probably influences genetic expression. Here, a single-stranded RNA molecule is also seen to be transcripted from one side of the DNA double helix (Babbit, 2011).

Page 233:

Add to the end of Section 5.3.2, these last paragraphs and Table:

Only about 1.5-2% of the human genome contains sequences that code for proteins. This genetically expressed part of the genome is called the *exome*. There are some transcribed strings of RNA that do not produce proteins; these are called noncoding RNA, or ncRNA (or, lincRNA for linear ncRNA). These appear to function by regulating gene expression. One type of ncRNA is called a *riboswitch* that helps to turn genes on and off. Riboswitches attach to the genes they regulate and can be sensitive to the levels of compounds targeted by those genes. The genes can then be made to produce more or less of substances regulating the target compound amounts. Long non-coding RNA (lncRNA) is a type of ncRNA that regulates gene activity in the nucleus. As with many

regulatory systems in biology, there are mechanisms to turn on a system and mechanisms to turn off the same system and the final system action is given by the difference between these two tendencies; lncRNA, for instance, can upregulate genes (enable them to be expressed), whereas RNAi downregulates genes. Some ncRNAs are important for the expression of Hox genes in human epithelial cells (Gupta et al., 2010; Williams, 2011). In summary, the ncRNAs control the genes and the genes control the production of the target compound in a multi-level regulation process.

The *transcriptome* is the translation of genetic information into cellular responses, and includes all RNA molecules mRNA, rRNA, tRNA, and ncRNA produced in a cell. This transcriptome is different between *in vitro* (cell culture) and *in vivo* (in natural context). Different mRNAs are expressed in each, so drugs tested in cell cultures can have different effects in isolated cells compared to cells in their natural environment. Even cells living next to one another, although appearing to be identical, can have different transcriptomes (Stein, 2014).

Table 5.3.1. Correspondence Between Amino Acids and DNA Codons From Which They Come.

Three Letter Code	Amino Acid	Possible DNA Codons
Ala	Alanine	GCA, GCC, GCG, GCT
Asx	Asparagine or Aspartic acid	AAC, AAT, GAC, GAT
Cys	Cysteine	TGC, TGT
Asp	Aspartic acid	GAC, GAT
Glu	Glutamic acid	GAA, GAG
Phe	Phenylalanine	TTC, TTT
Gly	Glycine	GGA, GGC, GGG, GGT
His	Histidine	CAC, CAT
Ile	Isoleucine	ATA, ATC, ATT
Lys	Lysine	AAA, AAG
Leu	Leucine	CTA, CTC, CTG, CTT, TTA, TTG
Met	Methionine	ATG
Asn	Asparagine	AAC, AAT
Pro	Proline	CCA, CCC, CCG, CCT
Gln	Glutamine	CAA, CAG
Arg	Arginine	AGA, AGG, CGA, CGC, CGG, CGT
Ser	Serine	AGC, AGT, TCA, TCC, TCG, TCT
Thr	Threonine	ACA, ACC, ACG, ACT
Val	Valine	GTA, GTC, GTG, GTT

Trp	Tryptophan	TGG
Tyr	Tyrosine	TAC, TAT
Glx	Glutamine or Glutamic acid	CAA, CAG, GAA, GAG
*	stop codon	TAA, TAG, TGA

* The three codons (TAA, TAG, and TGA) are termination codons (also called stop codons or nonsense codons) that do not code for amino acids, but signal the end of the mRNA message (with U substituted for T) and provide the "stop" signal for protein synthesis.

Page 236:

Add to Section 5.3.4, in the paragraph that begins “Mendelian experimental results …”, just before the sentence that begins “Some organismal traits …”:

Antagonistic pleiotropy is the term applied to a gene that has a strong positive, normally reproductive, effect on the young, but an adverse impact on the old individual.

Page 237:

Replace entries in Table 5.3.1, Section 5.3.4 with:

Table 5.3.2. Genes or Environment? Estimates of Relative Contributions of Each to Personality Traits and Physical Conditions Based on Studies of Identical Twins.

	Genetic Contribution (%)	Environmental Contribution (%)
Apple fruit size	25	75
Brain Structures		
Corpus callosum (connects brain hemispheres)	95	5
Parietal lobe white matter (logic and visual-spatial skills)	85	15
Temporal lobes (learning and memory)	45	55
Human Diseases		
Age-related macular degeneration	50	50
Asthma	60	40
Breast cancer	27	73
Children’s earache	71	29
Crohn’s disease	23	77
Depression (men)	29	71

Depression (women)	42	58
Schizophrenia	50	50
Type 1 (juvenile) diabetes	70	30
Type 2 diabetes	10	90
Human Personality		
Having confidence	51	49
Impulsiveness	49	51
Optimism	50	50
Procrastination	46	54
Resilience	50	50
Human Attributes		
Autism	70-90	10-30
Blood group	100	0
Blood pressure	55	45
Body composition	80	20
Body weight	75	25
Grip strength	65	35
Hair texture (straight or curly)	90	10
Height	80-90	10-20
Lean body mass	70	30
Musical pitch	76	24
Nightmares	36	74
Obesity	70	30
Voting choices in elections	60	40
Livestock Animals (sheep):		
Birth weight	30	70
Mature body weight	40	60
Multiple births	15	85
Rate of weight gain	30	70

Page 238:

Add the following paragraph to Section 5.3.4, immediately prior to the paragraph beginning "The Hoxc8 gene …":

Human cancer cells are overwhelmingly *aneuploid*, that is, some cells have an extra chromosome and some have fewer than normal (Scudellari, 2014). The extra aneuploidy chromosome seems to allow quicker responses to environmental stresses, and also to promote genetic mutations that help the cell to survive. Different parts of cell proteins originate in different chromosomes, so aneuploidy cells have such large amounts of some protein subunits that they overwhelm protein quality control mechanisms within the cell. Aneuploidy also alters the balance of tumor suppressor genes and tumor

promoter genes; cancer genomes select for extra chromosomes containing tumor promoter oncogenes and against chromosomes containing extra tumor suppressor genes.

The Hox genes are a set of genes present in nearly all animals from insects to humans, including worms, frogs, chickens, and mice. These genes regulate the animal's basic body configuration, organizing the arrangement from head to tail (Figure 5.3.8). The order of the Hox genes along the chromosome corresponds to the order of body segment development, starting from the head and ending at the tail (Willmore, 2010).

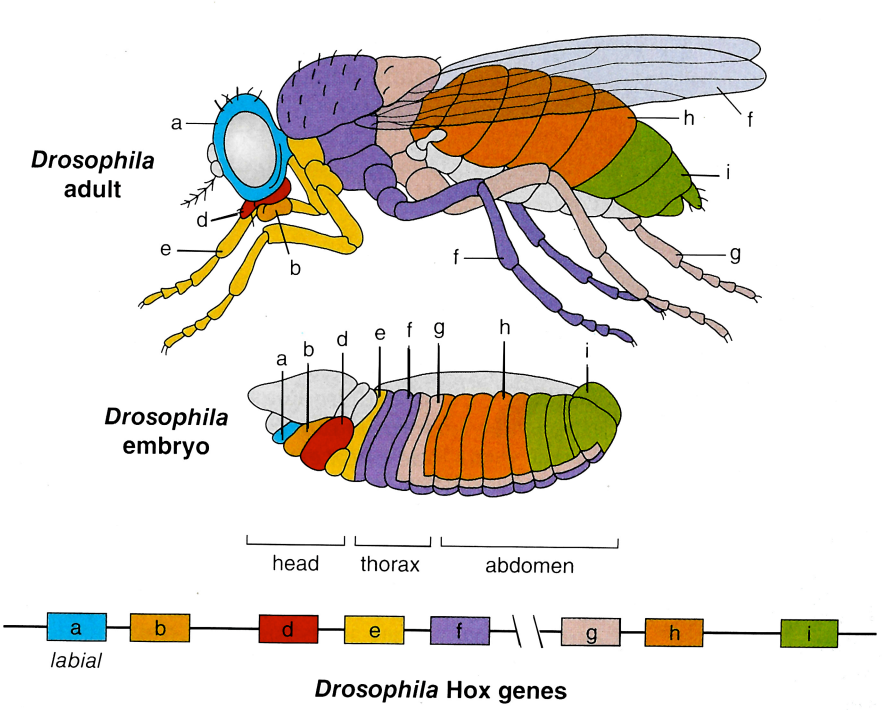


Figure 5.3.8. Hox genes in the fruit fly and the portions of the body that they help form. The first gene, known as *labial*, is necessary for the genes to be expressed. The order of the genes on the chromosome corresponds to the order of body part development (Willmore, 2010).

Also, change the numbers of subsequent figures 5.3.8 through 5.3.14 to be 5.3.9 through 5.3.15. Change figure references in the text.

Page 240:

Add just after the sentence that ends: "…(Booth and Neufer, 2005).":

These genes have wide-ranging effects on health, metabolism, and skeletal muscle strength.

Page 241:

Add to the box entitled “Polymerase Chain Reaction”, just before the sentence that begins “The primers must be extremely specific …”:

PCR is normally used to identify only the type of genetic material present in the sample; qPCR can be used to measure, in addition, the amounts of genetic material present in the sample. dPCR stands for digital PCR, which amplifies DNA at the single molecule level. The sample to be amplified is diluted so that only one molecule is present in each detector cell.

Page 241:

Add these paragraphs to the end of Section 5.3.4:

Epigenetic markers include methylation, phosphorylation, or acetylation at one or more genetic sites. Methyl groups and other molecules can bind to the helix itself or to its histone protein core and cause the whole assembly to flex. As that happens, some genes are exposed and others are obscured. The exposed genes are the ones that can be actively expressed. When a methyl group is added to a gene, it keeps other regulatory molecules from binding to that gene.

The chemical switches and markers in the *epigenome* that affect how genes are expressed are important to direct each body cell into the type of cell it needs to become. These switches assure that the proper set of genes is expressed and that other, interfering genes present in precursor cells are not. The epigenome is vulnerable to disruption by environmental toxins, pollutants, and poor nutrition, thus leading to organic diseases such as various types of cancer.

Reversible epigenetic changes have been shown to be associated with behavior in honeybees. Young honeybees function as nurses to unemerged brood larva and nurse bees later become foragers. With methylation of a majority of genes these foragers have been made to revert to nurse behavior (Herb et al, 2012).

It has also been found that methylation of the nucleic acid cytosine (the “C” in DNA base units) occurs chronologically in the human genome. Thus, epigenetic changes occur that are correlated with age of the individual (Bocklandt et al, 2011).

Page 241:

Add to Section 5.3.5, in the paragraph that begins “siRNAs, many of which …”, toward the end, just before the sentence that begins “RNA interference …”:

There are two tags on miRNA molecules, the first being a methyl group which allows the miRNA to be retained and the second a uridine group that signals destruction of the miRNA. In this way, miRNA may sometimes be turned on and sometimes have no effect. Each microRNA molecule can regulate up to hundreds of target protein-encoding genes, and each target gene can be regulated by multiple microRNAs (Stein, 2012).

Page 242:

Add to Section5.3.4, as the last paragraph:

Another genetic regulation mechanism is the presence of *antisense molecules*, complementary *oligonucleotides* (nucleic acid molecules with few (up to 200) bases formed by cleavage of longer nucleic acid segments) that bind to target RNAs or DNAs to inhibit normal functions. An antisense strand contains nucleotides complementary to the target mRNA, thus forming double-stranded RNA (dsRNA) that are ineffective in the translation process to form proteins. dsRNA are rapidly degraded in the cell.

Single-stranded noncoding RNA (ssncRNA), 19-23 nucleotides long, can regulate gene expression by decreasing levels of target messenger RNA (mRNA). Short hairpin RNA (shRNA) consists of a sense strand, short loop sequence, and antisense strand that interferes with gene expression in the cell in a similar fashion to the action of short interfering RNA (siRNA) (Moriarty, 2012).

Genomics (associated with the genes), proteomics (associated with proteins), or metabolomics (associated with metabolic processes) together are referred to as the field of study of *omics*.

Page 242:

Add to Section 5.3.5, as the last paragraph before the box entitled "Genetic Diversity Repositories":

Bacteria subject to virus (bacteriophage) infections can acquire new DNA sequences identical to sequences in the infecting phages. They then become immune to further infection by the same phages through a mechanism similar to the iRNA mechanism in eukaryotic cells (Baker, 2011; Haurwitz et al, 2010).

Page 245:

Insert in Section 5.3.8, in the second paragraph, third sentence, immediately following the words "There are enzymes …":

Insert these words: "(Figure 5.3.9)"

Insert a new Figure 5.3.9, and renumber Figures 5.3.9 through 5.3.14.

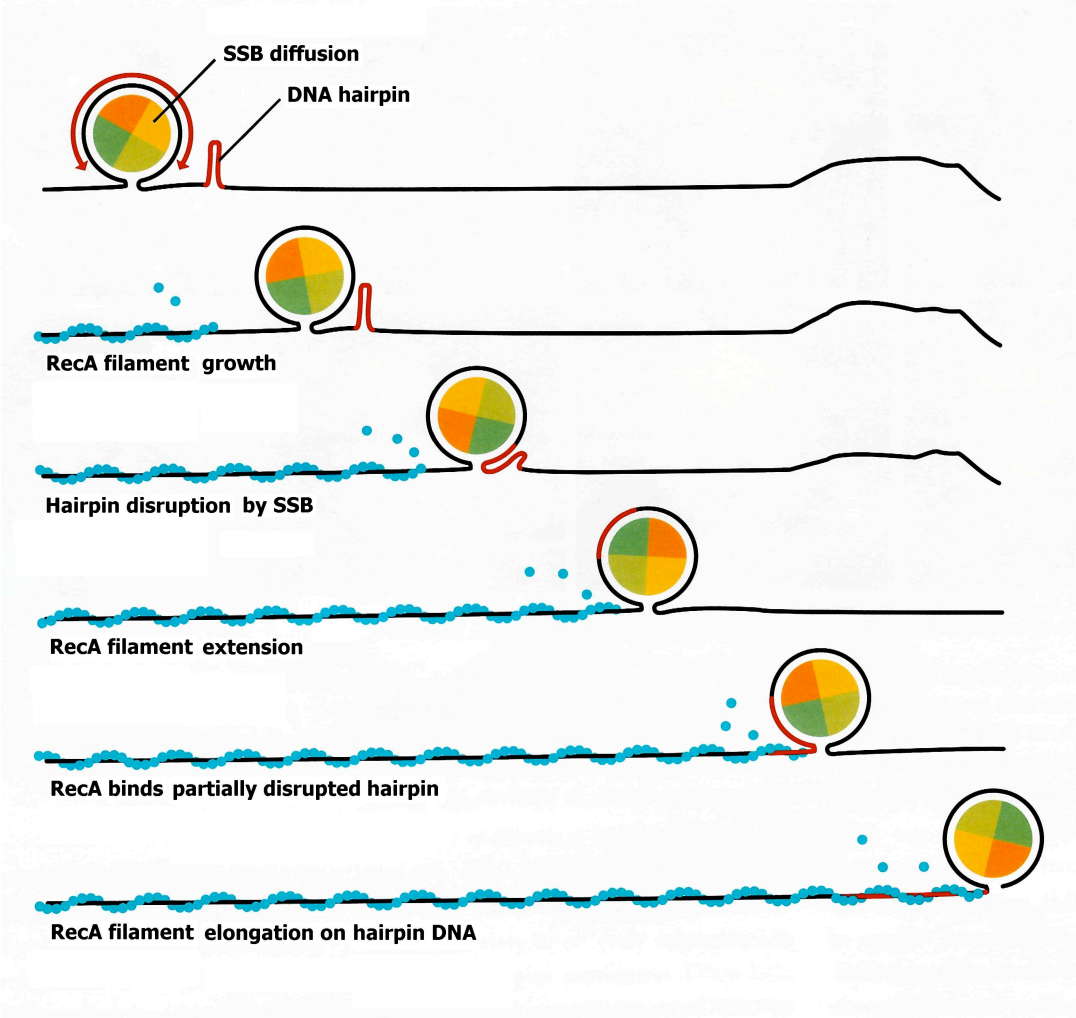


Figure 5.3.9. Part of the repair and maintenance operation for single-stranded DNA involves two proteins: single-stranded binding protein (SSB), and Rec A. Double helix DNA unwinds and separates into two single strands during replication. Immediately after separating, each single strand wraps itself around SSB proteins. SSB shuttles back and forth along the strand, fixing small defects known as hairpins. Rec A builds behind SSB and binds to the DNA strand. This action keeps SSB moving along the strand in the right direction and makes the SSB leave the DNA strand at the right time (Schnabel, 2010).

Page 245:

Add to Section 5.3.8, just before the paragraph that begins "There is evidence that …":

The successful persistence of genetic mutations with favorable effects depends at least in part on where and when the mutations occur (Hawks, 2014). Some mutations arise in places where there is no survival or reproductive advantage to having them, even though they would have huge advantages elsewhere. Other very advantageous mutations happen only after other mutations with advantages only partially as large as the later mutations, but the better mutation doesn't survive because the lesser mutation has largely

assumed most of the reproductive advantage that would have happened with the better mutation.

The ways in which genes affect the organism is highly nuanced and more complex than once thought. Mutations in noncoding genes were once thought to have no effect on the organism because they do not directly result in protein formation. These so-called "silent mutations", however, have effects that can be felt in health and disease (Chamary and Hurst, 2009).

Page 247:

Add to Section 5.3.8, Figure 5.3.12 caption, just before the sentence that begins "Inside the viral coating …":

Different forms of HA and NA give the influenza virus its unique designated identification (e.g., H1N3, or H7N5).

Page 248:

Replace in Section 5.3.9, the sentence that begins "If true …":

RNA involved in genetic modification during cell replication is known as *reverse transcription* (Gage and Muotri, 2012), and is somewhat similar to the way a retrovirus reproduces in a healthy target cell.

Page 249:

Section 5.3.10, first paragraph, replace the last two sentences with:

Mitochondrial DNA (mtDNA) suffers a higher rate of mutation compared to nuclear DNA due to factors such as proximity to highly reactive free radicals, lack of histone protection, and poor fidelity of mtDNA replication and repair. Because of this, differences in mtDNA can be used to study relationships among population groups. Knowing the rate at which spontaneous genetic mutation occurs can be used to estimate the ages of different species.

Page 250:

Insert in Section 5.3.11, third sentence, between "… number of genes …" and "… that supplement …":

(designated as *pDNA* for plasmid DNA)

Page 250:

Add to Example 5.3.1, just before the sentence that begins "Because autistic children …":

There is also evidence that the human SHANK3 gene causes autism-like changes in behavior.

Page 256:

Add to the box “Selfish Genes” in Section 5.4 after the paragraph that begins “Perhaps the paradigm …”:

Transposable segments of DNA are present in all organisms, and were found in maize (corn) many years ago. Transposable elements comprise about 85% of maize DNA and affect the color of corn kernels (Figure). The maize genome with ten chromosomes and 2.5 billion base pairs is almost as big as the human genome (ASABE, 2010). Because of their activities, transposons have been called “genetic parasites”. They do serve a useful purpose sometimes. In the fungal disease called powdery mildew, transposons disguise the pathogen by changing the genomic structure determining target molecules that identify it to the host plant (Spanu et al, 2010). Transposons appear to be important in animal, including human, brains and brain activity (Gage and Muotri, 2012). It has been speculated that the genetic variation that results from transposon insertion makes at least some brains better able to confront environmental challenges and improve species survival.

Figure caption: Transposons are responsible for the different colors of kernels in these corn ears.

Page 256:

Add to Section 5.4, this box:

HAMILTON'S RULE

William D. Hamilton was a theoretical evolutionary biologist who, among other contributions, expounded on altruistic actions performed by individuals for others (Hamilton, 1964 A&B). Each of these actions is considered to have a cost in resources that could be used to support reproductive success. On the other hand, each action by a benefactor could enhance the resources available to the recipient to boost the recipient's chance of reproductive success. So, each action has a cost to some genes, and a benefit to other genes. Hamilton's Rule states that the altruistic action will be performed if the cost to the benefactor (C) is less than the fitness benefit to the recipient (B) times the probable degree of genetic relatedness (R) between the two:

$$B \bullet R > C$$

The probable degree of genetic relatedness is a number, less than or equal to 1.0, that expresses the probability that two individuals share the exact same genes. The closer the relationship between two individuals, the larger the degree of relatedness.

Table of Probable Degree of Genetic Relatedness

Relationship	R
Parent-offspring	½ (0.5)
Grandparent-grandchild	¼ (0.25)
Great grandparent-great grandchild	1/8 (0.125)
Identical twins	1.0
Full siblings	½ (0.5)
Half siblings – one parent the same out of two	¼ (0.25)
First cousins	1/8 (0.125)
Second cousins	1/32 (0.03125)
Full hymenopteran sisters – ants, termites, bees, wasps, etc.	¾ (0.75)
Full siblings, sex linked genes	¼ (0.25)

Hamilton's Rule has been identified as leading to the field of *sociobiology*, that posits a genetic basis for all actions among individuals (Dawkins, 1989). According to sociobiology, all genes are in competition with one another to reproduce to the maximum extent possible.

Page 266:

Insert, in Section 5.5.2, just after the second sentence:

This definition is more than just an academic exercise if we are to search for life outside the Earth, called *exobiology*. In the next chapter of this book there will be descriptions of organisms living in some extreme environments of the Earth. Even these organisms could be classified as alien or highly unusual. Life outside the Earth might be expected to be even more unusual. Will they be classified as living or not?

The separation between ….

Page 268:

Add to Section 5.5.3, after the paragraph beginning "Newly created fatty acids …":

Artificial nucleic acid base pairs have been produced that have been found to be accepted as part of cellular DNA (Malyshev et al, 2014; Thayer and Ellefson, 2014). Further work along these lines could result in a completely new synthetic biology.

Page 268:

Add to Section 5.5.3, after the paragraph beginning "A top-down approach …":

Enough is now known about genetic expression that synthetic genes can be fabricated to produce a protein in a specific organism like *E. coli.* Algorithms have been developed to design synthetic genes to express target proteins optimally (May, 2010). These proteins can be used in pharmaceutical research.

Page 268:

Add at the end of Section 5.5.3:

Mathematical simulation modeling of single cell activities, including metabolic energy and nutrient flows, has largely been accomplished for the small organism *Mycoplasma genitalium*, and could lead to computer models of more complex cells (Covert, 2014). These models could be useful for everything from predicting the outcomes of biological experiments to designing new organisms with desirable properties.

Page 269:

Insert in the box entitled "Human Ecology System", in Section 5.5.4, in the first line after "100 trillion", and before "cells":

(10^{14})

Insert in the first line after "10 trillion (", and before "10%)":

10^{13}, or

Insert, after the second sentence:

On every square centimeter of human skin there are 10^7 microbes.

Page 273:

Replace, in Section 5.6, in the paragraph beginning "There is a problem …", the sentence that begins "Such a vast information aggregate …", with:

Such a vast information aggregate cannot be easily classified and presented, although the multidisciplinary approach called *systems biology* attempts to understand how individual cellular components are organized, function, and, especially, interact within live cells.

Page 278:

Add to the end of Section 5.6, this box:

NAMING OF GENES

Discovering and describing a new gene confers with it the privilege of naming that gene.
Some genes carry prosaic names related to their location in the genome, such as *SDCCAG8* in humans (related to a kidney failure disease). Others, however, are named creatively and imaginatively by investigators (Kresge, 2013). Thus, we have, in fruit flies, *couch potato* and *benchwarmer* (related to laziness), *tweek* (quivering), *Piwi* (small testes), *ken* and *barbie* (external genetalia), *kojak* (baldness), *cheapdate* (sensitive to alcohol), *VanGogh* (hair patterns), *fruitless* (sex differences in the fruit fly's brain that make females get drunk faster than males), and *18wheeler* (stripes on larvae). There are others, such as *superman* (flowers with extra stamens), *tiggywinklehedgehog* (neural patterning in Zebra fish), *werewolf* (plants with hairy roots), and *tigger* (human transposon).

Page 278:

Add to the end of Section 5.6:

Example 5.6.1 How Wolves Saved Yellowstone (Ward, 2010).

Wolves historically inhabited Yellowstone Park in the western US, but were exterminated in the early 1900's to protect livestock herds bordering the area. This set off an ecological chain of events that ended up drying streams, creeks, marshes, and springs.

Without wolves, native elk overpopulated Yellowstone. They chewed and overgrazed willow and aspen seedlings while they were still small. Without replacements, the population of these trees declined dramatically. Beavers, which normally ate these trees and used them for building dams and lodges, fell into decline. Without the beavers to build dams and ponds, wetlands disappeared, and so did the natural habitats for insects, amphibians, fish, birds, and plants. Water runoff that was no longer slowed and distributed by ponds, rushed down streams and was soon lost to the uplands.

Yellowstone's overgrazed river banks eroded and silted spawning beds for fish. Amphibians lost precious shade, and nearly disappeared. Birds that once thrived in the lushness of Yellowstone soon flew on by. The area dried up, and turned arid. Springs that had been recharged by pond water seeping into the ground no longer flowed, and drought became common.

Wolves were reintroduced into Yellowstone in 1995-1996, and immediately began to have a beneficial ecological effect. They killed fat elk, thinning the herd and improving the genetic quality of the survivors. Without so many elk, the trees regrew. With the trees came beavers and water to recharge springs and create habitats. Wolves had regulated the Yellowstone ecosystem from the top down, and restored ecological balance.

Page 283:

Insert, in the first page of Chapter 6, just after the list at the bottom of the page, this paragraph:

There are extremophiles (genus *Shewanella*) found in very harsh environments that grow electrically-conductive proteins from their outer membranes to exchange electrons directly with metal surfaces (Powell, 2015). There are others that use manganese instead of iron in essential enzymes (to most other organisms, iron is required). There are extremophiles in regions of high salt concentrations (Dead Sea bacteria and other osmophiles), extreme water pressures (Blobfish and Devil Worms) and some able o survive in space without air or water (Tardigrades).

Page 284:

Add to Section 6.0, this paragraph before the paragraph beginning "Generally, the same responses …"

There is a surprising similarity across all levels of biology. In many ways, an environmental wetland can act the same as the human kidney. Conditions for soil bacteria are very similar to conditions for bacteria in the human gut.

Page 292:

Add this paragraph to Section 6.3, just after the second paragraph:

Having a stable food supply is important at all biological levels. Humans, of course, had stabilized their food supply when they changed from hunting and gathering to agriculture. But versions of farming, or investing in a crop, are practiced by simpler organisms as well. There are fungus-growing ants that cultivate fungi inside their nests; they harvest leaves, feed the leaves to the fungi, and eat the fungi. There are damselfish that care for algal plots, removing unwanted algal types to benefit the types that they prefer to eat. There are solitary amoebas that engulf and keep intact bacteria inside themselves, searching for and feeding nutrients to the bacteria to help them survive and grow. At some point, the bacteria are released to reproduce and become a food supply for the amoebas (Burke, 2014).

Page 292:

Section 6.3.1. Replace the Table in the parentheses at the end of the first sentence to be "(Table 6.3.1 and Table 6.3.2)".

Page 294:

Add this Table before the box "How Evolution Shaped Nutrient Needs":

Table 6.3.2. Nutrients Necessary for Plant Growth Media.

Chemical Symbol	Element Name	Functions
B	Boron	Essential in cell division, Flower formation
Ca	Calcium	component of rigid cell walls, slows aging
Cu	Copper	Required to form pollen, lignins in woody plants
Fe	Iron	Releases energy stored in starches
K	Potassium	Drives photosynthesis, prevents wilting
Mg	Magnesium	Component of chlorophyll molecules
Mn	Manganese	Releases oxygen from water during photosynthesis
Mo	Molybdenum	Aids in the absorption of nitrogen
N	Nitrogen	Part of proteins, enzymes, DNA, RNA, and more

P	Phosphorus	Helps store end transport energy
S	Sulfur	Used in amino acids that form proteins
Zn	Zinc	Needed to build chlorophyll for photosynthesis

Page 295:

Add at the end of Section 6.3.2, this new paragraph:

Vitamin D can be produced in the skin when exposed to the ultraviolet rays of the sun. It was once thought that the only effect of a vitamin D deficiency was a childhood disease called rickets, where the bones grew weak and malformed. Lately, however, vitamin D has been found to be very important in the adult years (Park, 2010). It has been found that vitamin D dramatically reduces the risk of cancers by suppressing cell growth and blood vessel formation. Vitamin D controls the release of stress hormones that lead to high blood pressure and inflammation. Because of this, it can reduce incidence of heart disease. The vitamin has also been found to protect against autoimmune diseases, such as multiple sclerosis, lupus, and rheumatoid arthritis. It may also help to reduce depression by promoting the release of the mood enhancing hormone serotonin. Perhaps related, vitamin D helps to alleviate back pain.

Page 296:

Add to the box entitled “Codependence of Food and Genes”, as the first sentence in the box:

Diet, and the ability to adapt to eating a variety of foods, may have been a factor in the rapid evolution of our own *Homo* species as climates changed dramatically and shifted available plants and animals in prehistoric times (deMenocal, 2014).

Page 296:

Insert a new Section 6.3.3:

6.3.3 Microbes Assist Digestion

Simplicity is the ultimate sophistication.

- Leonardo DaVinci

Microbes (bacteria, protozoa, algae, and fungi) are extremely important to the nutrition of animals, insects, and plants. Microbes in the soil decompose complex organic matter into simpler forms that can be readily absorbed by plant roots. This is especially true for nitrogen and phosphorus compounds. Some microbes, called *mycorrhizal fungi*, are

necessary to pine species and other conifers to form root structures that allow these species to absorb water and nutrients from the soil. Some soil microbes degrade harmful pesticide chemicals residing in the soil that might otherwise accumulate and kill or depress growth of plants growing in those soils.

Microbes living in the mammalian gut, called *microflora* and collectively called the *microbiome*, are important to supply certain nutrients that cannot be synthesized by the animal or human. They either extract these nutrients from undigested foods or aid in the digestion of otherwise indigestible compounds. Dietary fiber, lactose, and sugar alcohols are examples of non-starch polysaccharides that escape digestion in the upper part of the intestine. Microflora ferment these foods into short-chain fatty acids that are readily absorbed in the colon.

There are between 300 and 1000 different microfloral species in the human gut that collectively add over 1 kg to body mass. These microbes are first introduced to babies through breast milk and more can be added through ingestion of fermented milk (yogurt), and uncooked fruits and vegetables. One of the most beneficial microbe types belongs to the genus *Lactobacillus*, found in yogurt.

Taking antibiotics kills beneficial as well as disease organisms, and it is important to reestablish thriving microfloral colonies after discontinuing the drug. Other ingested substances that kill gut microbes are alcoholic beverages, chlorinated water, and food preservatives.

Herbivores with rumens are particularly dependent on microbes to digest cellulosic materials into sugars, fatty acids, and vitamins. Termites also rely on the same types of microbes for their nutritional requirements. Without these microbes, the animals or insects would die of starvation.

Bacteria and yeasts in honey bee saliva ferment the tough outer shell of pollen grains and partially digest them for bee food. Without these microbes, pollen would be indigestible; with them, pollen becomes the major protein source for honey bees.

Page 296:

Rename the present Section 6.3.3 to:

6.3.4 Synthetic Growth Media

Change the Table of Contents accordingly.

Page 296:

Add a box at the end of new Section 6.3.3:

THE REALLY BIG DINOSAURS HAD REALLY BIG APPETITES

Dinosaurs lived on Earth between 65 and 230 million years ago (Lane, 2010). The sauropods were the largest class of these, and were much larger than any animal of our time. The most massive of these was the *Argentinosaurus,* longer than 100 feet and weighing 100 tons. The largest African elephant weighs only a tenth as much.

Argentosauruses were herbivores that ate leaves, ferns, and shrubs. They likely maintained in their digestive systems populations of fiber-fermenting microbes to help digest this plant material, similar to herbivorous animals of today. If they ate only 1-1.5% of their body weights in a day, then they consumed 2000-3000 pounds of dry matter each day. Plant material was probably about 75% water, so these dinosaurs needed to consume more than 8000 pounds of leaves per day. They had to keep moving just to find enough forage to eat.

Fiber fermentation does not happen efficiently at low temperatures. In order for the fiber-digesting microbes to survive and perform as needed, they must be kept at 60˚ F or above. Thus, the dinosaur probably had some body temperature regulation mechanism uncharacteristic of cold-blooded animals of today.

Page 297:

Add to Section 6.3.3, Example 6.3.1, just before the sentence that begins “Fat in foods …”:

In addition to the four other types of taste sensation, bitter, sweet, sour, and savory (or umami), it is likely that there are taste receptors for detecting fat.

Page 305:

Insert these additional sections in Section 6.5, after section 6.5.4. Insert the examples after Example 6.5.1:

6.5.5 Too Hot

No amount of experimentation can ever prove me right; a single experiment can prove me wrong.

- Albert Einstein

Excessive temperatures can pose a threat to life. At high temperatures, critical enzymes become denatured and metabolism goes awry. Neural circuits misfire, causing seizures and loss of thermoregulation. Intercellular clefts open and allow microbes access to

physical body interiors. Cognition, dexterity, and coordination suffer. Human decision-making becomes impaired; plants just bake.

Responses of living organisms to excessive temperatures include:

1) moving to cooler locations, if possible.
2) enhancing water evaporation.
3) increasing heat loss surface area.
4) making use of convective or conductive heat loss.
5) increasing surface temperature to increase heat loss.
6) shedding or adding surface insulation, depending on radiation exposure.
7) reducing metabolic heat production.

So, important physical parameters in the heat relate to air temperature, air humidity levels, and radiant energy. Each of these directly affects heat gain or loss.

There is a metabolic advantage to high body temperatures. Higher temperatures allow for faster chemical reactions, quicker responses, and higher signals-to-noise in sensors. Movement becomes sustainable. Honeybees, for instance, must tense their flight muscles on cold mornings to raise their temperatures and allow them to contract fast enough to sustain flight. If they did not perform this pre-flight ritual, they would fall from the air and die.

The disadvantage of high body temperature is the proximity to the lethal temperature limit. Thus, it is imperative that living organisms be able to confine body temperature increases to the safe range.

The issue of human activity in the heat is so critical that indices have been developed to estimate the ability for people to continue work during hot exposure (Moran and Pandolf, 19990. Some of these are calculated from physical measurements only (temperatures, humidity, wind speed, and radiation), and some use physiological data also (heart rate and rectal temperatures). When these heat stress indices reach threshold values, the exact value depending on the index used, employers are legally obligated to ameliorate the stress, either by stopping or modifying work schedules or by providing cooling strategies.

6.5.6 Too Cold

Simplicity is the ultimate sophistication.

-Leonardo DaVinci

Cold temperatures can pose a threat if they are very low and convective heat loss is very high. Under these conditions, flesh can freeze. If this is a continuing problem, then the organism has likely developed strategies to lessen the threat. Deciduous plants, for instance, lose their leaves and greatly decrease their water dependences. Some arctic poikilotherms circulate glycoproteins throughout their bodies to act as natural antifreeze. Other homeotherms develop thick insulating furs or feather coats. For humans able to move freely and dress warmly, cold temperatures are mostly of interest from a comfort standpoint.

Weather bureaus in various countries have empirically developed correlations of physical weather factors with comfort, and often report these as wind-chill temperatures. The wind-chill temperature is influenced largely by convective heat loss caused by air

moving across bare skin. The wind-chill temperature is supposed to be the temperature equivalent to that with the sensation of bare skin under minimal wind speed (usually taken to be 1.8 m/sec) conditions.

Example 6.5.2 Heat Stress in Cattle

Cattle, too, are susceptible to heat stress (Figure 6.5.2). This stress can be accompanied by diminished appetite, reduced growth rate, compromised disease resistance, or death (McGinnis, 2010). People who raise cattle want none of these.

Cattle, like humans, use sweating to remove heat. Some animals are more able to control body temperature in this way, and some are not. In order to identify individual animals that may require targeted management of their thermal environment, agricultural engineers developed index values that evaluate animals susceptible to heat stress (Brown-Brandl, 2008).

The index they came up with relates to respiration rate of cattle in the heat (above 80˚F):

Breathing rate index = 2.83×air temperature (˚F) + 0.58×relative humidity (fractional)
+ 0.76×wind speed (mi/hr) + 0.039×solar radiation (Watts/m^2)
- 196.4

If no solar radiation data are available, use 1000 W/m^2.

A score < 90	cattle are fine
90 – 110	cattle are on alert
110 – 130	cattle in danger
> 130	emergency

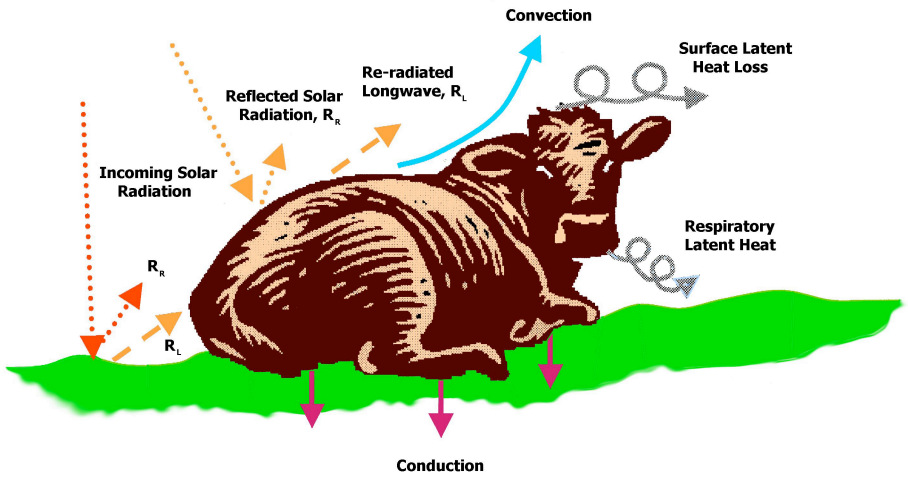


Figure 6.5.2. Heat transfer modes for a bovine outside without shade (Brown-Brandl, 2008).

Example 6.5.3 Wind Chill Temperature

The U.S. National Weather Service provides wind-chill equivalent temperatures as charts of equivalent temperature with ambient temperature and wind speed. Values in these charts are based on the formula:

$$T_{\text{wind chill}} = 35.74 - 0.6215\, T_{\text{ambient}} - 35.75\, \text{wind speed}^{0.16} + 0.4275\, (T_{\text{ambient}})(\text{wind speed})^{0.16}$$

Temperatures are in ˚F and wind speeds are in mi/hr. This equation is limited to temperatures at or below 50 ˚F and wind speeds above 3.0 mi/hr.

Be sure to add these sections to the Table of Contents.

Page 309:

Add to Section 6.6.3, after the paragraph beginning "Brightly colored insects …":

Mimicry is common in biology, especially in insects, when one species adopts the color, habits, or structure of another, less vulnerable, species usually to enhance chances of survival (Nelson, 2014). When one species (the model) is either distasteful or toxic to predators, and another nontoxic species (the mimic) assumes the appearance of the model, it is called *Batesian mimicry*. When both model and mimic appear similar and are both distasteful, it is called *Mullerian mimicry*. Predators learn to avoid eating both species based on appearance.

Page 310:

Add to Section 6.6.5, to the box entitled "Fetal Influences Last a Lifetime", at the end of the first paragraph:

Maternal nutrition modulates DNA methylation and shapes the phenotype of the offspring, thus leading to the era of *environmental epigenomics* (Jirtle and Skinner, 2007).

Page 310:

Add to Section 6.6.5, to the box entitled "Fetal Influences Last a Lifetime", after the fifth paragraph:

Prenatal stress of female sheep (ewes) was found to affect adversely the brains of lambs (Coulon et al, 2013). Researchers observed structural changes in brain neurons associated with emotion, behavior, and awareness. Similar results have been found in experiments with mice and rats (SRC, 2013). Prenatal stress in humans can result in childhood development of depression, post-traumatic stress disorder, and schizophrenia.

Page 313:

Add to Section 6.6, Example 6.6.4, second paragraph, after the last sentence:

The relation between cleanliness and immunities is called the *hygiene hypothesis*.

Page 313:

Add to Section 6.6, this example:

Example 6.6.5 Genetic Expression of Fruit Fly Larvae Hairs

The tiny hairs that exist on the surface of newly-hatched fruit fly larvae are called *trichomes.* The pattern of trichomes is governed by a gene called *shavenbaby*, which is influenced by at least six other enhancer DNA sections, some of which are far removed from the shavenbaby gene. Mutations in these enhancers can produce different trichome patterns in different species (McGregor et al, 2010; Michalowski, 2010).

These different patterns do not show up when fruit flies are reared in the laboratory with comfortable temperatures. The only time larvae have been found to have different trichome patterns is when the flies are raised in more natural temperature conditions of hot days and cold nights. Environmental conditions can have a direct bearing on genetic expression.

Page 318:

Add to Section 6.9, just before the paragraph that begins "Those, such as biological engineers …":

Cell actin cytoskeletons do more than just stabilize the integrity of the cell; they are also instrumental in cell locomotion, extending by branching into cell protrusions and dissolving in the parts of the cell following behind (Lamar, 2012). The cell probes possible pathways for movement by growing and branching the actin cytoskeleton. At the same time, actin filaments at the tail end disappear. The cell can respond to surfaces over which it travels, needing some traction to move, but not so much stickiness that it cannot escape. The cell can also respond to chemical signals from other cells; this is the means by which *keratocytes* (highly mobile cells found in the basal layer of epidermis) move to injured skin areas to repair them.

Page 320:

Add to Section 6.9:

Example 6.9.2 Slithering Snakes.

Snakes and some lizards move with body undulations that depend on friction between their bodies and surfaces underneath. As the snake wiggles, it produces reaction forces both normal and axial to its body segments (Figure 6.9.1). The sum of the forward normal forces must exceed the backward axial forces in order to propel the snake forward.

On their undersides, snakes have overlapping scales that snag on the ground more in the backwards direction than in the forward direction (*frictional anisotropy*). Measurements made of friction coefficients of a milk snake on a cloth surface were 0.10 in the forward direction, 0.14 in the backward direction, and 0.20 in the sideways direction (Goldman and Hu, 2010). This helps snakes turn body undulations into forward motion.

To reduce friction even further, snakes raise parts of their bodies off the ground when moving. This dynamic load balancing can increase speed by 35% and efficiency by 50%. Snakes slithering on land use a similar amount of energy as a legged organism of the same weight.

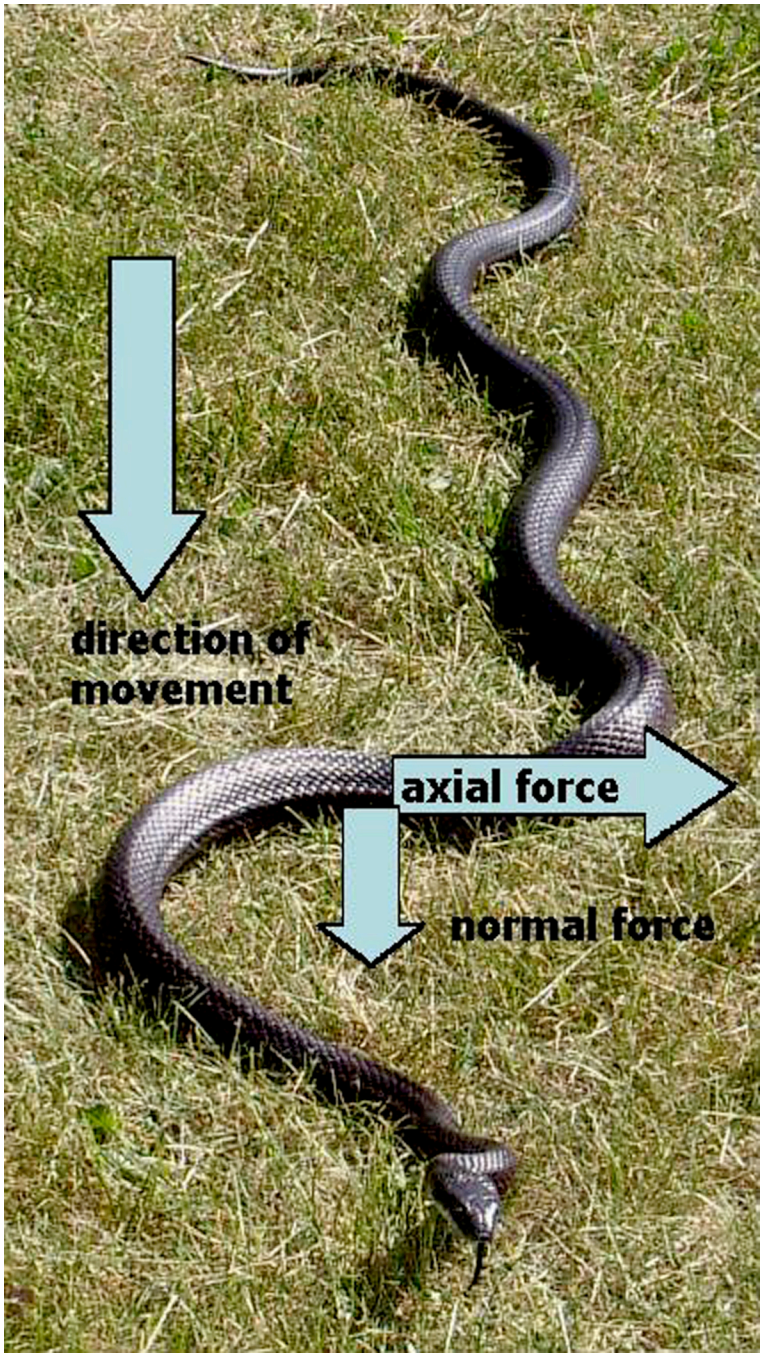


Figure 6.9.1. As the snake slithers, its forward reaction forces normal to its body propels it forward; axial reaction forces hold it back.

Page 321:

Add to Section 6.10, insert after the paragraph beginning: “Genes will survive best …”:

Before the discovery of epigenetics, it was easy to distinguish between adaptation and evolution. Adaptation affected only the present generation, and did not involve

genetic changes. Epigenetic changes make this incorrect on both accounts; epigenetics changes the expression of genes, and may last for several generations. Thus, the essential difference between adaptation and evolution is that adaptation reduces growth and reproduction, whereas evolution enhances both of these.

Page 321:

Add to Section 6.10, at the end of the paragraph that begins “Various environmental conditions …”:

It was shown previously that adaptations require extra energy and resources that could otherwise be used for growth and reproduction, thus reducing growth and reproduction. Adaptation, as a term used in this book, is meant to mean a nonpermanent, non-genetic, change in a BU. Before the discovery of epigenetic gene silencing, it was easy to distinguish between adaptation and evolution. The latter involved a change in the genetic code whereas the former did not. However, epigenetic changes can persist for many generations without a fundamental genetic change. Therefore, the feature most distinguishing between adaptation and evolution must then be that adaptation reduces growth and reproduction, whereas evolution leads to BU more successful at growth and reproduction.

Page 321:

Add to Section 6.10, this box:

SPECIES FORMATION

At some point, when portions of a population are isolated from one another, their genetic codes begin to diverge due to mutations and natural selection, allowing them to survive and reproduce better in their individual environmental conditions. There are two theories about the emergence of a new species. The first is that two species diverge from a common ancestor; the second is that a new species emerges as gradual changes take place in a previous species, making the evolved species significantly different from its previous form. In both cases, the new species would not be able to reproduce with other species.

Barriers that isolate a population and lead to a new species formation (Shermer, 2010) are:

1. geographic (such as a mountain range, desert, ocean, or river),
2. morphological (changes in coloration, body type, or reproductive organs), or
3. behavioral (a change in breeding season, mating calls, or courtship actions).

Page 323:

Replace in Section 6.10, in the box entitled “Directed Evolution”, at the end of the first sentence of the second paragraph, the references:

(Brown, 2012; Keats, 2006).

Page 324:

Add to Section 6.10:

Example 6.10.2 Microbes Respond to External Pressures

An alternative to recombinant DNA methods with microorganisms (see Section 8.2) is growth under selective environmental pressure. Microbes have very short generation times and high populations in small spaces. If it is desired to produce a microbe with particular characteristics, that microbe may result from growth in an environment that selects for those particular capabilities. This is especially true if the genes giving those capabilities are already present, but some enhancement is needed. This technique has been used to produce algae capable of increased production of biofuels and to produce microbes to remediate certain environmental pollutants.

Page 330:

Add to Section 6.11.6, just before the paragraph beginning “Agriculture is tending …”:

Crowding also exposes animals and plants to parasites. Cliff swallows in large breeding colonies suffer from high infestations of swallow bugs that feed on the blood of adults and brood alike (Brown, 2010). The infestation is worse for large bird colonies. Similarly, plants that occupy spaces with high population densities are more likely to attract animals that prefer to graze on them than plants of the same species sparsely located.

Page 331:

Modify the first statement of Section 6.21.1 to read:

"The following always holds for substances foreign to the organism:"

Add to Section 6.21.1, just before the paragraph that begins "Many nonpolar molecules …":

Despite the statement above, there is an effective exception to the rule that smaller molecules are more toxic than larger molecules. In the case of enzymes, molecule activity depends on the configuration of the entire molecule. One part of the enzyme molecule may conform to one type of substrate and another part of the enzyme molecule fits with another reactant. Bringing those two substances together on the surface of the enzyme allows them to combine much more readily than they would otherwise. Splitting the enzyme molecule destroys its ability to catalyze its intended reaction. Therefore, breaking an enzyme molecule into smaller pieces makes each piece just as ineffective as denaturation.

Enzymes are not usually classified as toxins. However, antibiotics, many of which act directly or indirectly enzymatically, are toxic to bacterial cells. Cleaving antibiotic molecules removes their toxic effects. Beta-lactamases in certain antibiotic-resistant bacteria, for example, cleave penicillin molecules and render them ineffective as antibiotics.

Page 332:

Replace the quote at the beginning of Section 6.12.2 with:

All things are poison, and nothing is without poison; only the dose permits something not to be poisonous.

Paracelsus (500 years ago)

Page 335:

Replace the references in Section 6.12.5 at the end of the first sentence with:

(Adams, 2007; Karn and Matthews, 2007)

Page 335:

Replace the sentence in Section 6.12.5 "other nanoparticles are used in electronics, medicine, and coatings." With:

Nanoparticles can be used to deliver medicines, for sun blockers, to strengthen materials, as antimicrobials, as environmental cleansers, and coloring agents. However, they also may cause physical harm to those who contact them (Wu, 2010). Nanoparticles have very high ratios of surface area to volume. This can affect their chemical reactivity, electrical conductivity, melting point, and color. Their chemical and physical properties are size-dependent, and so can be manipulated for particular purposes. Even shapes of nanoparticles can affect their interactions with living cells.

Page 336:

Add to Section 6.12.6, after the last paragraph:

Fungi and bacteria produce natural antibiotics to protect themselves from infectious agents. These can be the sources of many of the antibiotic drugs that we humans use to fight disease. These same fungi and bacteria also produce compounds that make them immune to their own antibiotics.

Page 338:

Add to the end of the sentence that begins "4. Changes in enzymatic pathways …":

(Figure 6.12.5).

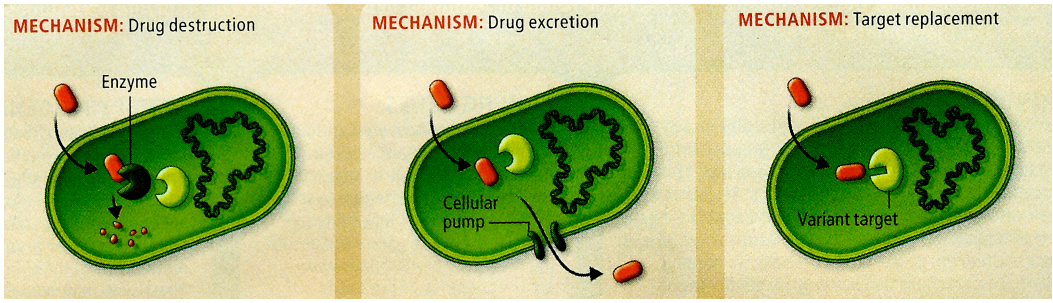


Figure 6.12.5. The three common forms of antibiotic resistance development are: 1) deployment of an enzyme that destroys or disables the antibiotic drug, 2) pumping the drug back through the cell wall before it can be effective, and 3) replacement of the target protein with a variant that is not affected by the drug.

Change the figure number of the current Figure 6.12.5 to Figure 6.12.6.

Page 338:

THE FIRST BIOLOGICAL THERAPY

The first biologically-based drug therapy was very expensive when first used around 1940. When used clinically, the drug was transported in armored trucks with police escort. The drug was even recovered from the urine of patients to whom it had been administered because that procedure was less expensive than manufacturing it anew. The name of that drug is penicillin, which is now cheaper than the glass vials in which it is sold (Amábile-Cuevas, 2010).

Add as a box to Section 6.12.7 just before the box entitled "Mysterious Foal Deaths in Kentucky".

Page 342:

Add this example at the end of Section 6.12:

Example 6.12.4 Chemical Fungicides to Control Fungal Infections in Corn

Sometimes chemical toxicity is sought, especially when it is selectivity toxic to pathogenic organisms that damage crops. Chemical fungicides are used separately or together in combination to control to maize fungal pathogen *Bipolaris maydis* (southern corn leaf blight). Wang et al (2015) have determined the fungicide effectiveness response curves of several common fungicides. The results for one of these, polyoxin, appears in Figure 6.12.6, and displays the typical dose-response curve expected of a chemical compound.

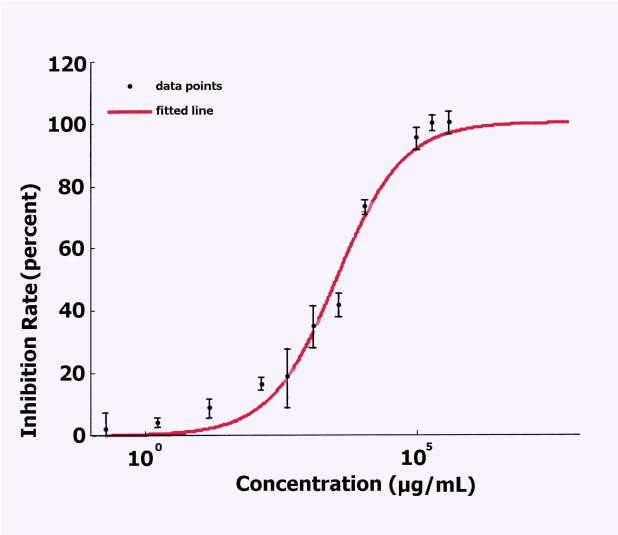


Figure 6.12.6. Dose-response curve for the fungicide polyoxin applied to the maize pathogen *Bipolaris maydis*.

Page 345:

Add to the paragraph beginning “Shear stress also causes …”, after the first sentence:

This temporary disruption of the cell membrane allows many types of external materials, including nucleic acids, to enter the cell (Bradley, 2014).

Page 345:

Add to Section 6.13.3, as the last paragraph:

Mechanobiology is the area of study that relates cell behavior to its physical surroundings. Different physical forces exterior to a stem cell, for instance, can cause the cell to morph into various cell types (Piccolo, 2014), or cause differentiation of somatic cells subject to different forces.

Page 346:

Add to Section 6.13.4 after first paragraph:

Page 346:

Add to Section 6.13.4, after the paragraph beginning “Also, the ability …”:

Somatic and stem cells grown outside the body prefer three-dimensional matrix and basement membrane growing environments to two-dimensional flat plates or Petri dishes (Saltus, 2010B). Cells nurtured in 3-D environments experience more normal physiological, biochemical, metabolic, and physical conditions, and, in turn, function more like the types of cells they began as. The microenvironment of the cell plays a large role in directing its growth and shaping its behavior.

Page 346:

Insert a new box at the end of Section 6.13.4 and before Example 6.13.1:

BIOPRINTING

ing technology similar to that in a common inkjet printer, bioprinting uses materials
produce three dimensional scaffolds for tissues and to insert cells of the correct types
thin these scaffolds to form organs, parts of organs, or patches to repair organs. These
printed parts can be made from tissue building materials and have the advantages
t:

1) they can be custom-made for a particular patient,
2) they can avoid immune system rejection,
3) they can supplement or replace limited organ bank stores, and
4) they can form standardized tissues for drug and other types of testing.
5) they can form three-dimensional matrices for natural cell or tissue growth.

sting drug toxicity and efficacy on animals is expensive, possibly unethical, and does
t always duplicate effects seen in humans. These difficulties can be avoided when
printing is used to provide living tissue for *in vitro* testing and drug screening.

Page 346:

Insert a new section at the end of Section 6.13.4 and before Example 6.13.1:

6.13.5 Whole Plant Responses

If anything, living systems consistently violate all of the criteria for reducibility. The number of elements that compose any living system – an ecosystem, an organism, an organ, or a cell – is enormous. In living systems, the specific identities of these parts matter. Unlike chemistry, for instance, in which an electron in a lithium atom is identical to an electron in a gold atom, all proteins in a cell are not equivalent or interchangeable. Each protein is the result of its own evolutionary trajectory. We understand and exploit their similarities, but their differences matter just as much. Perhaps most importantly, the relations between the components of living systems are complex, context-dependent, and weak.

- Robert L. Dorit

Physical stresses impose limits or otherwise affect cellular responses, as was presented in the previous sections. When cells join to form multicellular organisms, the possible range of physical effects increases greatly. Not only can individual cells respond to mechanical stresses, but the integrity of the whole organism can be compromised when intercellular connections become stressed beyond limits.

Plants, for instance, can be challenged by high winds, hail, or herbivore grazing. Plants that are habitually eaten sometimes develop tougher tissues that are less palatable

than rapidly-growing stems and leaves. This is in addition to the chemical responses discussed elsewhere in this text.

When mechanical stresses exceed strength limits, limbs may break or the plant may snap off at ground level. These stresses may take the form of bending, tension, compression, shear, or torsion. Mature wood has maximum stress levels in the range of 5000-1000 pounds per square inch (psi). Green (immature) wood may tolerate a greater degree of bending than can mature wood, but is more likely to tear off (weaker in tension and bending). Plants constantly challenged by mechanical stresses that do not exceed physical limits often develop extra tissue to help cope with chronic mechanical stress. Although this extra tissue does not significantly alter the ultimate strength stress that can be tolerated, it does add bulk that when multiplied by stress results in larger forces that can be resisted:

$$\text{Stress} \times \text{area} = \text{force} \qquad (6.13.1)$$

This is analogous to the myocardial hypertrophy that develops in a human heart resisting high blood pressure.

Wood is a composite material made from linear polymer cellulose fibers embedded in a *hemicellulose* matrix. *Lignin* acts as a glue to hold the fibers together. The *grain* of the wood is the direction parallel to the cellulose fibers. Wood is stronger in this direction than in any other.

Some trees grow more slowly than others, and these produce wood that is denser than faster-growing species. More dense wood translates into stronger wood. Dried wood is also stronger than green wood. The values in Table 6.13.1 are for dried wood. These values should be degraded by at least 50% for wood still part of a tree.

Table 6.13.1. Strengths of Some Wood Species

Wood Species	Specific Gravity	Compressive Strength (psi)	Bending Strength (psi)
Ash	0.60	7,410	15,000
Aspen	0.38	4,250	8,400
Basswood	0.37	4,730	8,700
Beech	0.64	7,300	14,900
Birch, Yellow	0.62	8,170	16,600
Butternut	0.38	5,110	8,100
Cedar, Aromatic Red	0.47	6,020	8,800
Cedar, Western Red	0.32	4,560	7,500
Cherry	0.50	7,110	12,300
Chestnut	0.43	5,320	8,600
Cypress	0.46	6,360	10,600
Elm	0.50	5,520	11,800
Fir, Douglas	0.49	7,230	12,400
Hemlock	0.45	7,200	11,300
Hickory	0.72	9,210	20,200
Lauan	0.40	7,360	12,700

Mahogany, African	0.42	6,460	10,700
Maple, Hard	0.63	7,830	15,800
Maple, Soft	0.54	6,540	13,400
Oak, Red	0.63	6,760	14,300
Oak, White	0.68	7,440	15,200
Pine, White	0.35	4,800	8,600
Pine, Yellow	0.59	8,470	14,500
Poplar	0.42	5,540	10,100
Redwood	0.35	5,220	7,900
Sassafras	0.46	4,760	9,000
Spruce, Sitka	0.40	5,610	10,200
Sycamore	0.49	5,380	10,000
Teak	0.55	8,410	14,600
Walnut	0.55	7,580	14,600

6.13.6 Bodies in Motion

There are no things man was not meant to know.
Michael Kurland

As long as human beings are using only their own bodily capabilities to move or perform work, then they most likely easily remain within tolerable limits of strength, comfort, and tissue failure. However, when they use modern tools, devices, or modern transportation modes, humans can experience discomfort, injury, or even death when physical limits are exceeded.

Dealing with a sentient being goes beyond the mechanical limits of physical failure discussed in the previous section on plants. There are also issues of comfort, psychological damage, and chronic health effects to consider.

Rapid accelerations and decelerations of the human body can cause many problems. The maximum deceleration ever recorded for a human was 46 times the acceleration due to gravity (9.8 m^2/sec), also called 46 g's (Ward, 2011). At this rate of deceleration, the human body was distorted, with some organs shifting position. The eyes, for instance, displace from their eye sockets. Some representative accelerations for different events appear in Table 6.13.2.

Table 6.13.2 Acceleration and the Human Body

Acceleration (g's)	Event
2.9	Sneezing
3	Space Shuttle flight
3.5	Coughing

3.6	Crowd jostle
3-4	Roller coaster, maximum
4.1	Slap on back
4-6	Induces blackout in fighter planes
6	maximum gravitational force exerted during suborbital launch
8	Fighter pilot, brief maximum
8.1	Hopping off a step
10.1	Plopping down in a chair
30-35	Car crash, wearing a seat belt
60	Chest acceleration limit during car crash at 48 km/h with airbag
70 – 100	Crash that killed Diana, Princess of Wales, 1997
150 – 200	Head acceleration limit during bicycle crash with helmet

Rapid accelerations cause large forces, and these can be enough to cause breakage. Without tissue cushioning and elastic energy storage in the muscles and tendons, a jump of less than ½ meter would be enough to break a femur (Johnson, 2007). Over time, such forces would result in extra strength added to the bone.

The maximum tolerable acceleration depends both on the direction of the force and the type of restraint used. A seat belt or shoulder harness helps to protect against horizontal accelerations, for instance (front-to-back inertial force, called *Gx,* is the most tolerable, but can peel skin back; sideways inertial force, called *Gy*, is rare, but can move or dislodge organs). Forward thrust horizontal accelerations are tolerated better than reverse-thrust acceleration. Both the brain and the eyes may be damaged with horizontal forces. Accelerations of 70-100 g's during car crashes can tear the pulmonary artery from the heart.

Vertically-upward acceleration, called *Gz*, drives the blood down to the feet. This deprives the eyes and the brain of needed oxygenation. Induced tunnel vision, loss of consciousness, or even death can result. The remedy for fighter pilots, who commonly experience up to 4-6 g's vertically, is a "g-suit" that applies external pressure to the legs to push blood back up again. Vertically-downward acceleration does just the opposite, forcing blood to the eyes and the retina, causing a "red-out" of vision.

It is important to maintain comfort for humans. Commercial standards in the U.S. limit acceleration to 1.5 g and deceleration to 1 g (Ward, 2011). These are applied to various modes of transportation. Commercial airplanes can accelerate passengers by no more than 1.6 g's, and banking angles on turns can be no more than 30˚. Horizontal

WOODPECKERS DO NOT SUFFER CONCUSSIONS

One interesting example of accommodation to mechanical shock is the odpecker. This bird pounds into wood to find insects hidden underneath the surface. though their heads decelerate at 1200 times the acceleration due to gravity, their ock-absorbing structures consisting of elastic beaks, musculotendinous attachments the tongue and throat muscles (called *hyoids*), skulls with a minimum of rebrospinal fluid, and partially spongy skulls that attenuate rapid accelerations protect ir brains from injury (Yoon and Park, 2011). Brain injury is caused by a combination acceleration and duration resulting in internal shear and excessive tensile forces lexander, 2015). Studying the woodpecker can potentially benefit humans who suffer ncussions, most notably from violent sports participation.

movement can be very uncomfortable also. These motions are tolerated better in the prone position than in the seated position.

This natural frequency of the human viscera is about 6-8 cycles per second. Vibration in that range can be extremely uncomfortable and must be avoided. Rocking back and forth, as riding on an animal, is more tolerable at higher frequencies (a horse) than at lower frequencies (a camel). This rocking can produce a condition called *motion sickness*.

Chain saw vibrations of 30 g's or more have been recorded on the hands and arms (Cundiff and Suggs, 1976), and these exceed international standards for tolerable vibration (Bingham et al., 1992). Other hand-held devices can also vibrate beyond tolerance. One common consequence of excessive hand vibration is constriction of the peripheral arteries shutting off the blood supply to the hands and fingers. This occupational condition, called *Raynaud's Syndrome*, can become permanent and result in loss of feeling, dexterity, and, in extreme cases, entire hand function.

Add this box at the end:

Add this example at the end of Section 6.13.1, after Example 6.13.1:

Example 6.13.2 Wind Load on a Small Poplar Tree.

Assume a small poplar tree as diagrammed in Figure 6.13.4. The wind blows against the tree at 30 miles per hour. Will the tree trunk break?

Solution: Determining the answer to this problem requires knowledge of statics and strength of materials. Wind load (F) in pounds can be calculated from:

$$F = A \times P \times C_d$$

Where A is the area presented to the wind in ft^2
P is the wind pressure in lb/ft^2
C_d is the drag coefficient, unitless

$$P = 0.00256\ v^2$$

Where v = wind speed in mi/hr

$$P = 00256\ (30)^2 = 2.304\ lb/ft^2$$

Assuming the tree top is spherical in shape, and relatively non-porous (opaque) to the wind,

$$A = \pi\ d^2/4 = 7.069\ ft^2$$

For a brisk wind, $C_d \approx 0.4$ for a spherical shape (Johnson, 1991). So,

$$F = 7.069\ ft^2 \times 2.304\ lb/ft^2 \times 0.4 = 6.51\ lb$$

The wind force can be considered to act at the center of the tree top. Thus, the moment (M) it causes at ground level is:

$$M = F \times L = 6.51\ lb \times (4\ ft + 1.5\ ft) = 35.8\ ft{\bullet}lb$$

From strengths of materials, the maximum bending stress on the trunk at ground level is:

$$\sigma_{max} = M \times c / I$$

Where σ_{max} is the maximum bending stress in lb/ft^2
M is the moment produced by a force acting over a distance in ft•lb
c is the maximum distance from the axis of rotation in ft
I is the moment of inertia of the circular cross-section in ft^4

For the circular cross-section of the trunk (Eshbach and Souders, 1975),

$$I = \pi\ d^4/64 = \pi \times (3\ in/\ [12\ in/ft])^4 / 64 = 1.917 \times 10^{-4}\ ft^4$$

Thus,

$$\sigma_{max} = 35.8\ ft{\bullet}lb \times (1.5\ in/[12\ in/ft]) / 1.917 \times 10^{-4}\ ft^4 = 23{,}360\ lb/ft^2$$

From Table 6.13.1, The maximum bending stress for poplar wood is 10,100 lb/in^2, or 1,454,400 lb/ft^2. This is over 60 times higher than the wind-induced maximum bending stress. Hence, even the green wood of the tree trunk should be able to withstand the 30 mi/hr wind without breaking.

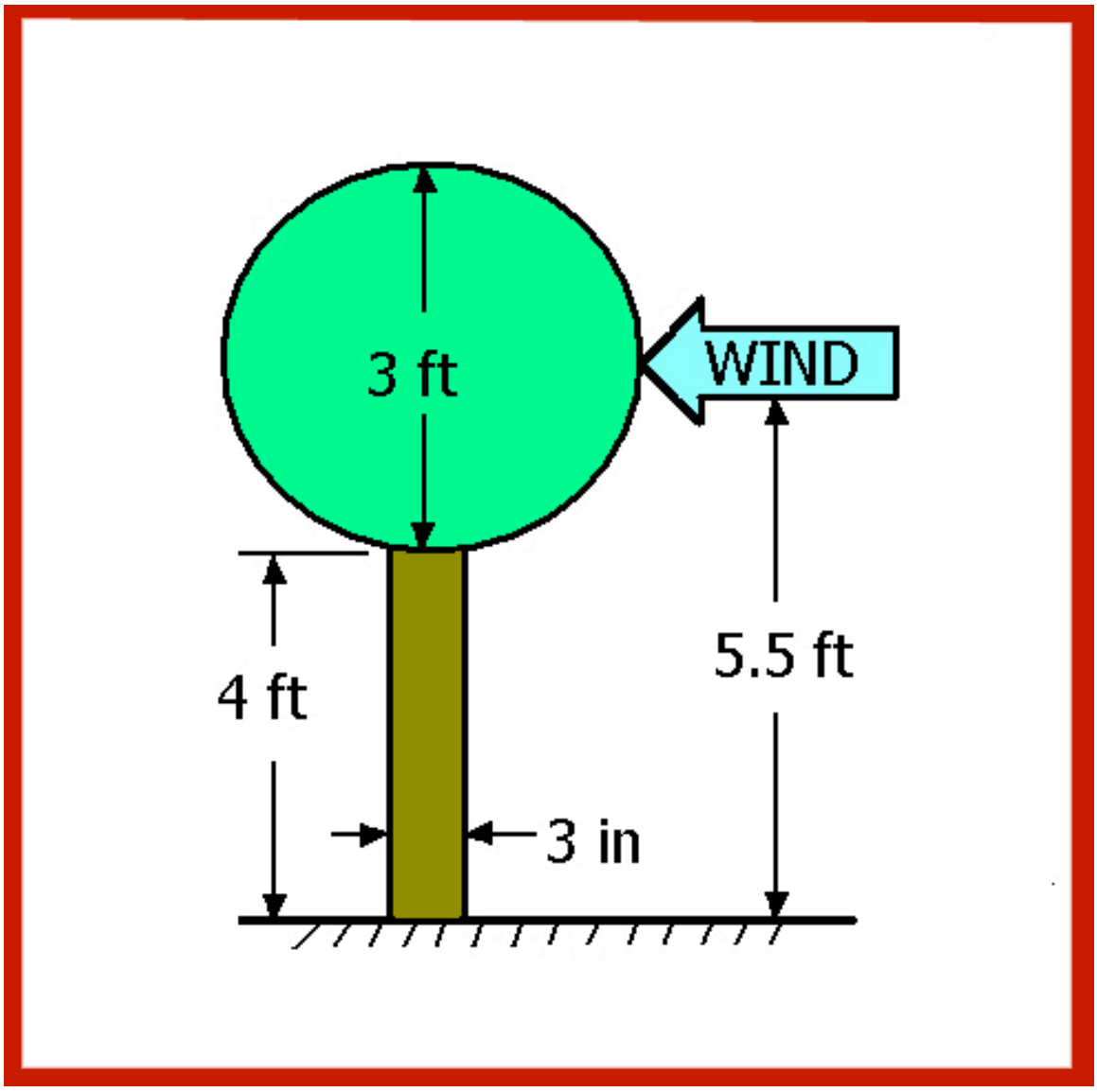


Figure 6.13.4 Simplified diagram of the poplar tree in Example 6.3.2.

Example 6.13.3 Entertainment Engineering for Fun and Excitement

Entertainment of visitors to highly technical shows and theme parks combines engineering with thrill solicitation. Shows such as the Cirque du Soleil bring extreme human gymnastic and artistic expression together with mechanical technology. The result is awe-inspiring.

Theme parks combine technology with interesting settings to elicit excitement from ride participants. These must convey a sense of danger without being dangerous.

There is a good deal of biomechanical engineering in entertainment engineering. Capabilities of humans to be accelerated, thrown about, and psychologically-challenged must be known and limits strictly observed. Yet, within these limits, a great deal of

latitude results in unique experiences for participants. Entertainment engineering academic programs have been established to instruct students in the specialized knowledge applicable to the entertainment industry (Creighton, 2005).

Example 6.13.4 Enhancing Safety and Performance with Sports Engineering

Combining mechanical engineering, materials science, and applied physiology, sports engineering applies modern technology to sports equipment and sports measurements. Women tennis players, for instance, are four times more likely to injure their ankles than men (Grose, 2004). Realizing this, sports engineers can design better shoes for women tennis players; such shoes would differ from men's.

Sports engineers can also tackle designs of tennis racquets, golf clubs, rowing oars, and baseball bats. Of special importance is protective gear to minimize injury while skiing, playing baseball, football, or hockey, or even riding a bicycle. Sports engineers need to know the limits to human strengths and endurance. Along with knowledge of materials and mechanical design, they can make sports participation safer and more rewarding.

Example 6.13.5. Drug Delivery Using Cell-Penetrating Peptides.

Delivering large molecules for medicinal purposes into cells is impeded by the bilayer cell membrane that repels hydrophilic compounds. For this reason, cell membrane penetration techniques have been developed that include viral vectors and membrane disruption. These methods, however, can have significant toxic and immunogenetic side effects.

Cell penetrating peptides (CPPs) can be used to evade the membrane barrier. These peptides are either: 1) positively-charged amino acids, 2) hydrophobicity, or 3) amphipathicity (both hydrophilic and lipophilic). When they contact and attach to the membrane, they are ingested through endocytosis, forming peptide-inclusive vesicles and being transported into the interior of the cell (Figure 6.13.5). Once there, they are released and free to conjugate with other biochemicals inside the cell (Thundimadathil, 2013).

Therapeutically-significant biomolecules can be attached to these CPPs and be ingested into the cell at the same time.

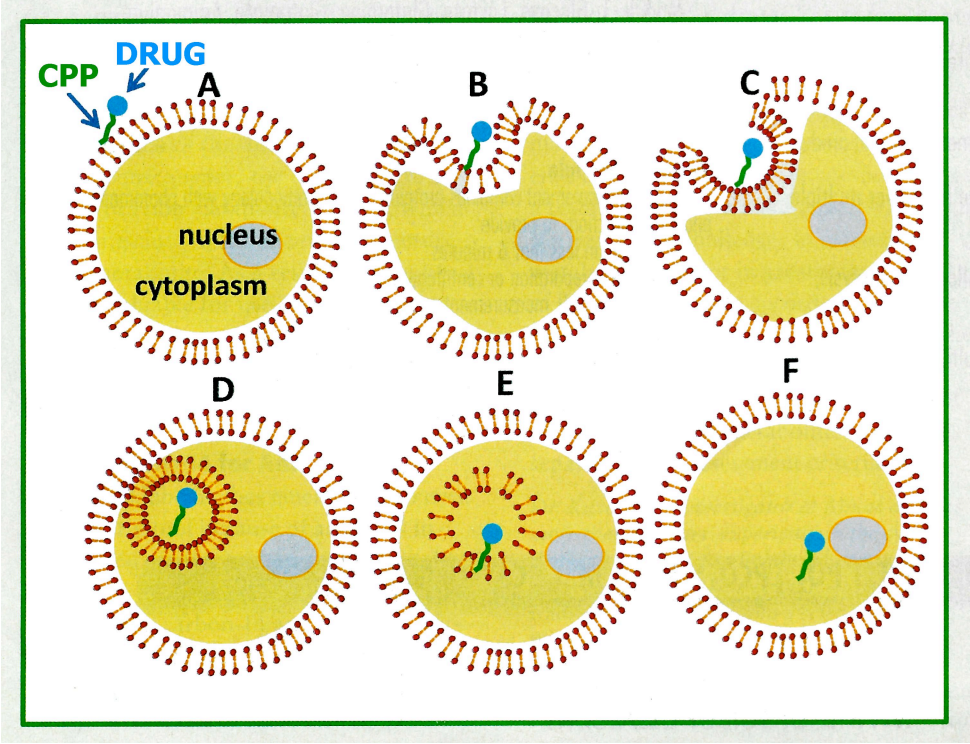


Figure 6.13.5. Steps in cell penetration of a cell-penetrating peptide (CPP) through endocytosis: A) membrane interaction, B) endocytosis, C) vesicle formation, D) endosome in cell, E) endosomal release of the CPP, F) CPP conjugates with other biomolecules inside the cell (Thundimadathil, 2013)..

Add these two sections to the Table of Contents.

Page 351:

Insert a new Section 6.14.4, and renumber current Sections 6.14.4 and 6.14.5. Also renumber Figures 6.14.5, 6.14.6, and 6.14.7 and change their references in current Section 6.14.5. Add the new Section 6.14.4 and renumbered Sections 6.14.5 and 6.14.6 to the Table of Contents.

6.14.4 Genetic Variability

Biology has traditionally had more success when driven by good data rather than by theory.

- Robert H. Carlson

It was mentioned in Section 5.3.6 that there is genetic variation within a species that cannot be easily explained. The principle of survival of the fittest (natural selection) should result in the elimination of all but the most survival successful genes. This means that genes not optimum for survival in a competitive environment should not persist, no matter how small their disadvantage. However, a few of them remain, and they give the

species the possibility that, should the environment change, there would be genes already present that could be better able to allow the species to adapt correctly.

If this is considered to be an optimization problem, then the unexplained genetic variation could be a consequence of the broad optima that characterize biological systems. Optima can be broad or narrow (Figure 6.14.5). Narrow optima are very selective, and don't tolerate much variation before the cost of locating at a nonoptimum point becomes too high to be sustained. Broad optima can still have the same optimum, but the costs of deviation from the exact optimum point do not rise significantly quickly. Biological systems seem to have broad optima.

Therefore, genetic variation could be explained by the fact that carrying nonoptimum genes does not turn out to be too expensive for the species as long as the result of those genes being present does not differ too much from the results of the fittest genes. As with all other biological optima, this means of genetic optimization turns out to be energetically less expensive (and maybe more likely for species survival) than an optimum that confers too much advantage to the best genes.

The broad genetic optimum can be a consequence of several properties characteristic of living things. The first is the ability of a living system to sense its environment and to communicate in various ways. The second is the ability to respond to the immediate environment that results in a mathematically chaotic system. That is, the end result is dependent on the pathway it takes to get there. The third property is the appearance of alternate forms that differ very little in energy levels. As a result of these properties, it is easy for biological systems to have varying forms with very little additional energy costs, but which have been determined by the history of the organism. In the case of the genome, each individual's genes are determined by history of the individual and its predecessors, but there persists genetic variability within a population because of somewhat different histories. The genes, once in place, cannot be routinely changed (despite some possibility of random mutations or of epigenetic expression modifications). In the case of optima for breathing rate, heart rate, and stride length, responses can vary with time.

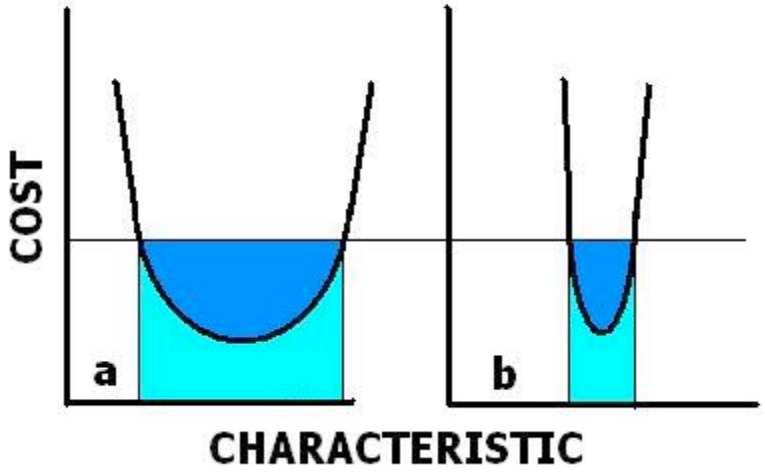


Figure 6.14.5. Illustration of broad (a) optimum and narrow (b) optimum. For the same level of cost, the broad optimum allows a greater range of the optimized characteristic. Biological systems seem to prefer broad optima.

Page 360:

Change the name of Section 6.15.4 to:

6.15.4 Plant Responses

Add to Section 6.15.4, these sentences at the beginning of the section::

Vegetative plants produce a natural stress hormone, abscissic acid (ABA) to help them survive drought by curtailing growth. Plants exposed to environmental stress, such as drought, can adjust their responses so that they respond better to the next episode of drought. Plants that have not been prestressed wilted faster than those that had survived a previous period of dryness. This adaptation has a limited memory time, however. After a certain period of adequate moisture, the drought tolerance can be lost (Ding et al, 2012).

Page 361:

Add to Section 6.15, this Example:

Example 6.15.2 White Nose Syndrome in Bats

Since 2006, millions of bats in the eastern U.S. have died from a fungal disease called White Nose Syndrome. The disease attacks bats while they hibernate in caves in the winter. The disease irritates the bats and wakes them from their deep sleep. This increases their metabolism to nearly summertime levels. In winter, there is no food available, and the bats die of starvation. The disease is so pervasive that all the bats in the affected area

die out. They have long generation times and low reproductive rates, so the threat is very serious. Bats are important ecologically because of the prodigious numbers of insects that they eat. One hundred fifty bats can eat millions of potentially-damaging insects in a year.

Page 362:

Add to Section 6.16, just after the paragraph that begins "Although one might be tempted …":

Cooperation, it appears, evolved in life amid a highly competitive environment. Despite the direct disadvantages that helping others confers on an individual, there are several ways that cooperative tendencies could survive and grow through evolution in a population (Nowak, 2012):

1. Direct reciprocity. Doing something positive for another and the other does something positive for the first.
2. Special selection. Clusters of cooperating individuals exist amid highly competitive environments, as in neighbors helping other neighbors.
3. Genetically related. Helping kin promotes survival of related genes.
4. Indirect reciprocity. Cooperating with another individual of higher stature reflects back on the one of lower stature and confers rewards.
5. Greater good. Cooperating with other individuals of a group helps the whole group to survive and prosper.

Page 368:

Insert in Section 6.16.4, after the first paragraph:

Various social insects, microbes, birds, and mammals have developed distinctive structures in which to live cooperatively. In addition to the example given above, bird nests differ according to species, ant hills are characteristic of the species, bee hives vary depending on the race, and termites of different kinds have much different habitat structures. It appears that the architecture for each of these is genetically-determined and subject to the same evolutionary pressures as all other features of living organisms (Dunn, 2014).

Page 370:

Add to Section 6.16.4, after the paragraph beginning "Hepatocyte cells in the liver …":

The ecology of bacteria in the human gut has been called the *human microbiome* (Williams, 2010). These 10^{11} microbes in residence are different for each person. They stimulate immune responses, help detoxify food compounds, enhance new blood vessel growth, allow proper tissue development, produce vitamins, and transform undigestible compounds into useful forms. It's the balance of microbial populations that keeps

individuals healthy or sick. Disrupting normal bacterial populations can lead to asthma, allergies, obesity, and weakened immune systems.

Page 370:

Add to Section 6.16.4, after the paragraph beginning "Cooperation can aid individuals …"

A dramatic example of common benefit over individual benefit involves the programmed cell death (*apoptosis*) of single-cell organisms (Durand et al, 2011; Youngsteadt, 2011). Should an individual single-cell organism be stressed to the point that it cannot survive, it commits suicide, actively expending energy to shrink, disassemble its own DNA, and release beneficial chemicals into the surrounding environment. These substances stimulate surrounding cells, probably having the same DNA or DNA similar to the suicidal cells, to grow robustly, even more effectively than would fresh nutrient broth or leftovers from unprogrammed cell death (*necrosis*). Necrotic substances contain toxics that can sometimes poison their neighbors. Therefore, it appears that some cells that would have trouble surviving turn their demise into a benefit for related neighboring cells.

Page 370:

Add to Section 6.16.4, just before the paragraph that begins "One concept of evolution …":

Social cooperation among groups of humans and among other animals has had profound effects on survival and reproduction over time (Stix, 2014), but, in addition, the expectations for behavioral responses of individuals within these groups can have large implications for successful biological engineering designs, influencing, for example, complexity of operation, meaningful symbology, placement of modules, and number of operations required. Consider, for example, piloting an airplane with its heads-up displays rich in symbols for different gauges and operations, and that requires a copilot to perform tasks supplemental to those of the pilot. Such a highly sophisticated and cooperative operation would be impossible without the design assumptions of intelligence, experience, and willing cooperation expected of adult human beings.

Page 370:

Add to Section 6.16.4, in the paragraph beginning "One concept of evolution …", just before the sentence beginning "Adaptation at any level …":

The higher levels provide the environment for the levels below.

Page 371:

Insert, in Section 6.16.4, at the end of the sentence that ends with "… others at that level.":

(Buston and Wong, 2014).

Page 374:

Add this example to the end of Section 6.16.

Example 6.16.4 Probiotic Treatment for Diabetes

Intestinal epithelial cells secrete insulin when stimulated by either of two proteins, GLP-1 or PDX-1 (Duan et al, 2008). The first of these causes secretion of insulin in response to blood glucose levels, and, with the second, insulin is secreted irrespective of blood glucose concentration. A common probiotic strain of *E. coli* was engineered to secrete either of these two proteins. It was found that ingestion of these bacteria could be a promising treatment for Type 1 (insulin-dependent) diabetes. A pancreas is not necessary for insulin secretion.

Page 375:

Add to Section 6.17.1, the end of the first paragraph:

Plant eaters outnumber meat eaters in nearly all ecosystems.

Page 376:

Add to Section 6.17.2, box entitled "Spiders and the Web of Life", at the end:

Biological cycles are sometimes incredibly complex. Such is the case with other parasites that assume behavioral control over the actions of their hosts so that those hosts may become agents for the reproduction of the parasites: a male sheep crab is changed by a parasitic barnacle into a female so that the barnacle may hatch in the crab; a house cricket can be made to commit suicide in a body of water by a parasitic worm that emerges as the cricket drowns; a female wasp can sting a ladybug and leave behind a single egg that then hatches, eats the ladybug from the inside out, forms a cocoon, and is protected from enemies by the ladybug; a flatworm burrows into a bullfrog tadpole and causes the tadpole to develop deformed limbs, making it easy prey for birds, and, and, finally, the flatworm reproduces inside the bird; Amazonian ants are penetrated by a fungus that enters its brain causes the ant to climb a nearby tree and fasten itself to a leaf where the fungal stalks burst forth and rain spores on other ants below (Maure et al, 2011; Zimmer, 2014).

Page 377:

Add to Section 6.17.3, after the paragraph beginning "Whereas the predator-prey competition …"

Mycoplasmas (not to be confused with mycobacteria, a normal sized bacterium) are exceptional parasites descended from bacteria that had lost their cell walls and shed much of their genomes and metabolic capacities. They became highly dependent upon host environments and biomolecules (including cholesterol for their cell membranes), and, in the process, became the smallest (less than 1 μm in diameter) and simplest free-living organisms. They have extremely small genomes ranging from 450-1,000 million *Daltons* in size (a Dalton is a number equal to the molecular weight of the molecule), which makes them an obvious choice to be the starting point for synthetic biology (Morowitz, 2011).

Page 378:

Add to Section 6.17.4, just before the paragraph that begins "Coevolution is at work …":

Fungi and bacteria that produce natural antibiotics (the sources of many of the antibiotic drugs we use) also produce compounds that make them immune to these same antibiotics.

Page 378:

Add to Section 6.17.4, after the paragraph beginning: "Other means of expulsion …":

Diseases caused by bacteria are often more threatening when caused by gram-negative, rather than gram-positive, bacteria. The cell walls of gram-negative bacteria are often toxic, and their cell membranes are highly protective and antibiotic-resistant.

Many pathogens have evolved to be specific to one or several specific host(s). It has long been considered that pathogenic viruses are exclusively found in their preferred host. Plant viruses have never before been found to spread from plants to animals. However, the tobacco ringspot virus (TRSV) has been seen to infect honey bees, a representative of the animal kingdom (Li et al, 2014) in the first known shift of a plant virus to an animal.

Page 379:

Add to Section 6.17, these examples:

Example 6.17.5 Cat Parasite Has Unusual Neural Effects

Toxoplasma gondii is a parasitic microbe of cats with unusual characteristics (Shepherd, 2020). Cats come in contact with the microbe when they eat an infected mouse or bird. They don't usually get sick, but the parasite reproduces in the cat's gut, forming eggs (or *oocysts*) that develop and are shed in the cat's feces.

When another warm-blooded animal, such as a mouse, ingests the oocysts through contact with the cat's feces, the oocysts enter its gut. There they release cells that

migrate mostly to the muscles and brain, forming cysts to protect themselves from the mouse's immune system.

But *T. gondii* must get back to into a cat to reproduce again. In order to do that, it needs the mouse to be eaten by the cat. So, it changes mouse behavior to induce it to take risks, including an attraction to the smell of cat urine. This makes mice vulnerable to attack by cats.

T. gondii has two unusual genes that contain instructions for an enzyme that makes the neurotransmitter dopamine. This is likely the mechanism that *T. gondii* uses to change normal mouse avoidance behavior. It may also explain a statistical link between *T. gondii* infection of humans and human schizophrenia. Some anti-schizophrenic drugs are dopamine antagonists.

Example 6.17.6. Pathogens in Produce.

There is always a risk of eating produce contaminated with pathogenic microbes. This risk is made larger by the produce preparation and distribution system that serves a large portion of the consuming public and so that any defect in the safety of the produce is spread to a large number of consumers. There is also the greater chance that a larger number of food handlers come in contact with the food before it is sent out.

Even before then, however, the proliferation of antimicrobial and antibiotic chemicals used on the produce as it grows may be partly to blame for produce contamination (Figure 6.17.2). These chemicals have the greatest effect on the weakest microbes, and eliminate them from competing with stronger and more pathogenic microbes. Without this check on their growth, pathogenic bacteria can grow quickly to toxic levels (Fonseca and Ravishakar, 2007).

Figure 6.17.2. Leaf lettuce growing in the field, where it could be exposed to pathogenic bacteria.

Page 381:

Insert, in Section 6.18.2, at the end of the sentence that begins “Transduction occurs when viruses …”:

(*transfection* is placing nucleic acids into cells without using viruses).

Page 382:

Add in Section 6.18.3, at the end of the paragraph that begins “The human body is made of …”:

There are many tumor suppressive and tumor-supportive (oncogenes) in the genome, and it is the cumulative effect of these two types that determines if cell growth is limited or not. The immune system continuously eliminates tiny tumors in a process called *immune editing*, until some tumor cells develop the ability to turn off the immune system.

Page 384:

Add to the end of the first full paragraph of the page, Section 6.18.4, after the sentence that begins “Human telomeres consist of …” and before the sentence beginning “Telomeres in other species …”:

The length of human telomeres is about 15,000 base pairs at conception, 10,000 base pairs at birth, and the rate of loss is about 50 base pairs a year after birth. At about 5000 base pairs, human cells have largely lost the ability to divide (Hooper, 2011).

Change the next sentence to read:

Telomere sequences in other species vary from one to another, but usually consist of repetitions of 6-10 base sequences.

Page 384:

Add to the second full paragraph on the page in Section 6.18.4, just before the sentence that begins “Prokaryotes avoid this problem … “:

Laboratory cultured cells, not immortal stem cells or cancer cells, can divide about 50-70 times before they die; this number of divisions is known as the *Hayflick Limit* (Hooper, 2011).

Page 384:

Add to Section 6.18.4, just before the paragraph that begins “There is an enzyme …”:

Shortened telomeres have been associated with age-related health like heart disease, obesity, diabetes, cancer, and mental decline. Chronic mental depression is

HeLa CELLS

The HeLa cells are a line of immortal cervical cancer cells biopsied from Henrietta Lacks at Johns Hopkins University in 1951. They are amazingly resilient and robust. As such, they have been shared among many researchers world wide and used for research on cancer, Acquired ImmunoDeficiency Syndrome (AIDS), radiation, toxic substances, and gene mapping. This cell line is so hardy, prolific, and overpowering that it is a contaminant in perhaps 10-20% of all research cell lines.

Page 384:

Add to the end of Section 6.18.4, this box:

HeLa cells differ from normal human somatic cells because of the presence of powerful telomerase that prohibits the shortening of the telomeres during cell division. These cells also have 82 chromosomes, unlike the normal human number of 46. The additional chromosomes apparently came from Human Papilloma Viruses (HPV) that fused with the original cancer cells. Although some variation in the HeLa cell genome has been reported when cultured under different environmental conditions, the HeLa genome has been remarkably stable over the course of hundreds of cell divisions.

The Hayflick Limit is the number of times that normal human somatic cells can divide before their telomeres are completely consumed. This number is a value somewhere between 40 and 60. When the Hayflick limit is reached, senescence sets in, eventually leading to cell death (apoptosis). The HeLa cell line has shown no evidence of a Hayflick Limit.

associated with shortened telomeres, with the most severely depressed having the shortest telomeres (Verhoeven et al. 2013).

Page 387:

Add at the end of Section 6.18.5, after the paragraph beginning “Then follows a set …”:

Low light levels in deep ocean depths of 500 m or more can challenge animals that live there to find food and also to find mates. Bioluminescense is one way to signal the presence of an individual looking to reproduce (McClain, 2010). Also of importance in the quest to find a mate is the sense of smell. Small male anglerfish seek out females by smell. When a male contacts a much larger female, enzymes fuse his mouth to her

WHY ARE HUMAN BABIES BORN AT NINE MONTHS?

Human babies are born after a gestation period of nine months despite the fact that their brains and cognitive development would require gestation times of 18-21 months to be comparable to the relative level of development of chimpanzee births. Why this 9 month gestation period is relatively so short is not completely known. One theory is that human mothers are limited at 9 months to a metabolic rate that can no longer supply the needs of both the fetus and the mother. Thus, the babies are born and derive most of their metabolic needs outside the body of the mother (Wong, 2012; Dunsworth et al, 2012).

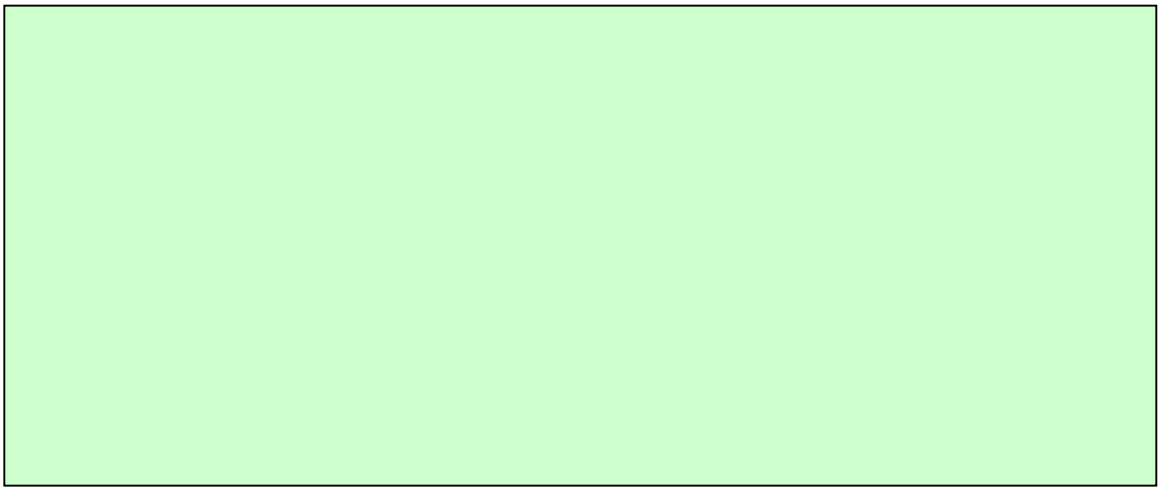
Page 389:

Add to Section 6.18.6, just after the last sentence, inside the square brackets:

As evidence of this observation of physical similarities, a study of married couples in the U.S. show that paired couples share a higher share of genetic material than would randomized pairings (Domingue et al., 2014).]

Page 389:

Add to the end of Section 6.18.6, this box:



Page 391:

Add to Section 6.18.9, after the paragraph beginning: “Some flowers contain …”

Pollen grains are formed on male flower parts called *stamens*. The male gametes in pollen are encapsulated in several tough outer polymer layers to protect against drying and physical damage. There is a very small opening in the pollen grain, called a *micropore*, through which the gametes can leave when they land on the female flower structure, called a *pistil,* the top part of which is called a *stigma* (Figure 6.18.6). They then grow into the pistil to fertilize the ovule.

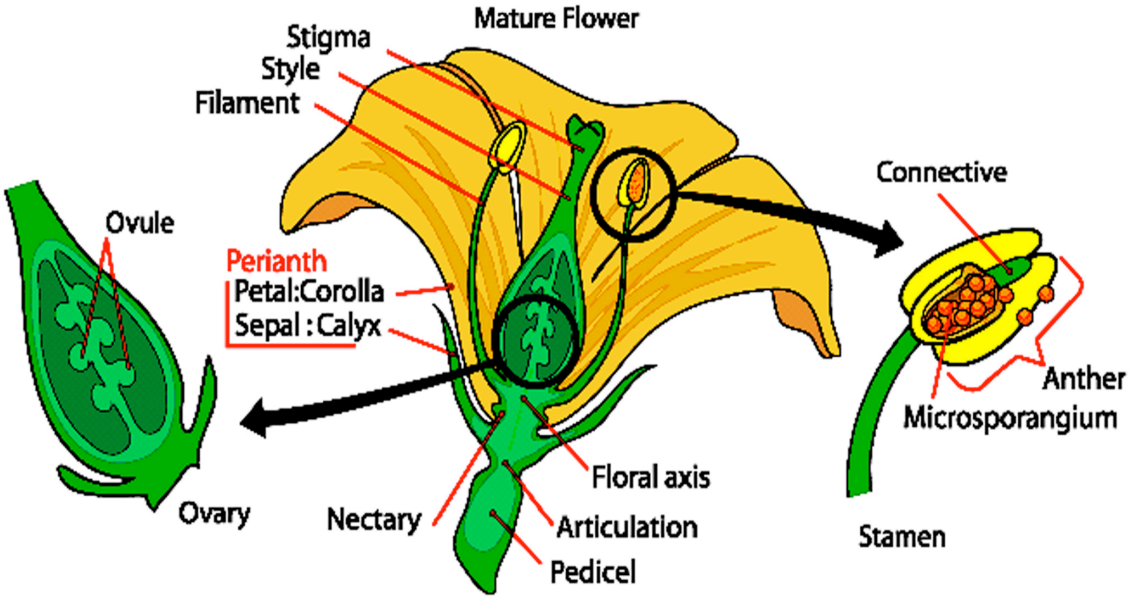


Figure 6.18.6. The reproductive parts of an angiosperm flower (source: Wikipedia, Marianna Ruiz, 2011).

Page 391:

Add to Section 6.18.9, after the paragraph beginning "The other strategy …":

Plants sometimes also have difficulty with fertilization by cross-pollination. There may be no other plants around to provide pollen, as at the edge of the geographical range of the species, or neighboring plants may still be many years away from sexual maturity. There are genes in some plants that control fertilization by interfering with self-pollination. The absence of one of these genes can allow the plant to become self-fertile under some environmental circumstances (Fessenden, 2010).

Some insects, especially bees, collect pollen as a protein source for raising their young. After they bring it back to their nests or hives, the pollen is partially digested to make the protein nutritionally available. Perhaps as a reproductive strategy, plants that depend upon insects for pollination have more protein in their pollen than plants that depend upon the wind for pollination.

Page 396:

Add to the end of Section 6.19.1:

Polychlorinated biphenyls (PCBs) are synthetic chemical pollutants that have been used to remove heat from electrical components and have also been widely dumped into the environment. PCBs have been demonstrated to have detrimental toxic and developmental effects on humans and wildlife. A study of two bird species, black-capped chickadees and song sparrows, has shown higher total blood PCB concentrations in

regions of the Hudson River valley where environmental PCB contamination has historically been higher. High blood PCB concentrations were shown to affect bird songs adversely, thus interfering with avian intraspecies communications necessary for satisfactory reproduction (DeLeon et al, 2013).

Vervet monkeys (small monkeys common throughout Africa) communicate among themselves about various predators. They have different alarm calls for leopards, eagles, and pythons, their chief predators. When the alarm call is made for leopards nearby, the monkeys run to the nearest trees and climb to the smaller branches where they are safe. The eagle alarm causes vervets to scan the sky and dive into the underbrush to avoid being seen from the air. The python, or snake, call causes monkeys to stop and alertly determine where the snake is located. Once located, the vervets pounce on the snake and drive it off. Lions, hyenas, and cheetahs as a group also have an alarm call (Shumaker, 2010).

Vervets fighting other vervets and getting the worst of the fight sometimes give the leopard call as a ruse to save themselves from further beatings. Once the call is given, all vervets stop fighting and display their defensive behavior.

Page 397:

Add to Section 6.19.2 as the first sentence of the paragraph beginning "Odors are important …"

The human nose, it has been estimated, can distinguish among 1.7 trillion different odors (Bushdid et al, 2014).

Page 401:

Add to Section 6.19.2, after the paragraph beginning "Quorum sensing also coordinates …":

Populations of bacteria can appear to be much more antibiotic resistant than expected. That is because some bacteria in the population will have resistance and some will not. Those resistant bacteria challenged with antibiotics emit a compound called *indole* that signals to surrounding non-resistant bacteria to expel antibiotic and to change chemical pathways to neutralize toxins produced inside the cell by the antibiotic (Williams, 2010; Lee et al, 2010).

Page 402:

Add to Section 6.19.3, after the paragraph beginning "Touch is extremely important …":

Touch is one of the first sensations to be developed after birth, and seems to be important in classification of one's own physiological states and interpersonal relationships later in life. Skin-to-skin tactile sensation has been found to be beneficial for physiologic and

neurologic maturation of newborn premature infants (Feldman et al, 2014). This intervention, called *Kangaroo Care*, features maternal to newborn contact for at least one hour per day, and results in improved physiological and cognitive function lasting at least ten years in the life of the child.

Human touch, especially as sensed through the hands, associates with relevant mental concepts. For instance, physically touching a warm object promotes interpersonal warmth (Williams and Bargh, 2008). Having heavy objects in one's hands associates with importance and seriousness in other people and other matters (Ackerman et al, 2010). Handling rough objects forms an impression associated with difficulty and harshness (Ackerman et al, 2010). Hard objects made others appear more strict, more stable, less emotional, and less flexible (Ackerman et al, 2010). Thus, we have the expressions that associate touch with personal attributes, such as:

1. warm-hearted
2. weighty thoughts
3. rough day
4. coarse language
5. hard-hearted
6. rock-solid
7. cold personality
8. keep in touch
9. smooth operator

Physical pain also has a psychological analog in depression or rejection (as exemplified by "I'm crushed" or "I'm hurt by that remark"). Acetaminophen (Tylenol) has been found both to relieve physical pain and, at the same time, social or moral conflicts that tend to cause depression (Stix, 2010).

These observations have biological engineering implications. The type of packaging may critically determine the attitude of customers toward the product inside. The design of human-occupied spaces may depend upon the use of the space and the impressions that are to be fostered. Manipulations of the human environment can be made easier if the correct tactile choices are made.

It is likely, too, that these results extend to the animal kingdom, too. Classical studies by Harlow(1958) on maternal-infant bonding in macaque monkeys demonstrated that infants preferred to stay close to a cloth surrogate mother warmed with a 100 W light bulb rather than a bare wire surrogate mother with a baby milk bottle as a source of food. Harlow's conclusion was that contact comfort was very important to the monkey infants compared to meeting nourishment needs. Monkeys raised with the warm cloth mother developed relatively normal social skills, in contrast to infants with only wire mothers.

The cell membrane has many receptors, each with a specific function. Many of these provide the means for substances to be transferred into or out of the cell; the cell membrane is otherwise nearly impervious to transmembrane movement of larger ions or compounds. These receptors can also act as portals through which viruses access the cell

interior. The Transferrin Receptor 1, for instance, which usually brings the element iron into the cell, can also act as access for the deadly Machupo virus to enter the cell (Vastag, 2010).

Add to Applications and Predictions:

1. Conversations are friendlier with a warm beverage rather than cold.

Page 405:

Add to box "Seeing Inside Us", Section 6.19.4, at the end of the paragraph beginning "MRI detects individual …":

In order to detect rapid changes in blood oxygenation, images from fMRI must be faster than regular anatomical MRI; fMRI images consequently have lower resolution.

Page 405:

Insert in Section6.19.4, to the box entitled "Seeing Inside Us", in the paragraph beginning "Optical coherence tomography …", after the words "tissue interfacial boundaries"

(echo location). Rate of flow can be measured using phase shift information.

Page 405:

Insert in Section6.19.4, to the box entitled "Seeing Inside Us", just before the sentence beginning "NIRS is particularly useful …":

NIRS uses pulses of infrared light to excite different tissues. Chemical bonds in molecules that make up the tissue differentially absorb certain wavelengths. By measuring the absorption fractions of different infrared wavelengths as they pass through tissues, the types of tissues present can be identified. This method can be used widely in animal and plant tissues, foods, and inanimate objects.

At the end of that same paragraph, add:

There is at present a minimum compound concentration that can be reliably detected with NIR.

Page 405:

Add to the box, "Seeing Inside Us". Section 6.19.4, after the paragraph beginning "*Electron tomography …"*:

Fluorescence resonance energy transfer (FRET) can be used to determine the locations of individual molecules. When two light-absorbing molecules lie close to one another, they can pass absorbed energy between them. The efficiency of this energy

transfer depends precisely on the distance between donor and acceptor molecules. Measuring luminosities of each molecule can determine the distance between them. FRET has been used to track molecular movements along a DNA strand (Schnabel, 2010).

In *Laser Ablation Imaging* (LAI), short-duration high-power laser pulses are used to vaporize thin sections of a sample as images are taken of each level. These images are then combined to produce a full three-dimensional view of the anatomy of the sample (Clabby, 2014). LAI is very quick, easy, and accurate. LAI destroys the samples it analyses, so it cannot be used with live specimens. This technique, nevertheless, could be found valuable for determining the anatomical structure of plants, insects, and other items to be screened.

Optogenetics is a technique wherein a gene is inserted inside neurons that then produce a light-sensitive protein (called an *opsin*). The opsin is sensitive to a particular color of light introduced through a fiber optic thread. The result is that the neuron can either be excited or depressed by shining a light on it. Optogenetics is used to study neural circuits in the brain (Palmer, 2014).

Combinations of these imaging modalities are proving useful. PET-CT and PET-MR can locate tissues, such as cancer with high metabolic rates. Photoaccoustic tomography uses light pulses to heat target tissues or cells, and the heat reflects back to the transducer with less scattering than with light.

Some small transparent creatures can be observed through a microscope to elucidate life processes in living organisms. But, light images are distorted when passing through intervening biological tissues. Astronomers have faced a similar problem in the way the atmosphere distorts light emanating from distant heavenly bodies. Wang et al (2014) have used a similar technique to clarify and sharpen images from nerve cells deep in the brains of zebrafish

Page 405:

Add to Section 6.19.5, before the first paragraph:

Nonverbal communication with animals is also a possibility. Mice, like humans, express pain through facial expressions (Dove, 2010). Knowing this, laboratory scientists can assure that animals under their care do not suffer unnecessarily. The same characteristic can also lead to improved pain-relief drugs for humans.

Pet owners usually agree that their animals can tell from non-verbal cues when there will be a change in normal routines; they can tell when their owners will go on vacation, take them to see the veterinarian, or give them baths. Communications with animals can happen at several levels, and there is opportunity for biological engineers to extend communication devices for human hearing or seeing impaired to connect to animals as well.

Page 405:

Add to Section 6.19.5, the box entitled “Perception of Stimuli”, after the sentence that begins “Any particular input stimulus …”

For instance, the human eye can distinguish 2.3 million colors despite only three types of retinal color sensors (called *cone cells*).

Page 409:

Add to Section 6.19, this example:

Example 6.19.4 Pheromones for Your Cat

Sara was the name of a cat owned by Andrea Sachs (Sachs, 2010). Sara had come nine years ago from an animal shelter. She was a gentle cat, but skittish, afraid of new situations and strange people, a proverbial scaredy-cat.

Sammy was an aggressive and competitive cat which Andrea brought home two months ago from the shelter. Once Sammy moved in, he and Sara fought over and over until she would run to the nearest safe hideout. This continual fighting disrupted the peace and quiet of the household.

Desperate to get some sleep, Andrea consulted her veterinarian, who gave her pheromone collars and electric plug-in pheromone diffusers. The diffusers emitted a chemical that mimics a pheromone that cats leave behind when they rub their cheeks on furniture or people; the collar had a pheromone that mother cats emit while nursing. Both calm agitated cats.

Pheromones are known to have behavioral effects on many kinds of animals, from alarm alerts to soothing siblings. Besides cats, pheromone products are also available for dogs and humans.

Page 410:

Add to Section 6.20.1, at the end of the paragraph beginning "Taste and smell are both …":

Sensing magnetic fields is called *magnetoception*, and involves the presence of small bits of the mineral magnetite located in subcellular organelles called a *magnetosomes*.

Page 416:

Add to the box on immune system, Section 6.20.3, after the sentence beginning "There are probably more than a million …":

Insects are among the number of animals that do not produce antibodies as part of their immune responses. Instead, they depend on RNA interference mechanisms to defend against foreign invaders.

Page 418:

There is also within a cell a mechanism to screen all RNA molecules to detect foreign particles or cells that have evaded immune system protections (Ashe et al, 2012; Shirayama et al, 2012; Williams, 2013). This mechanism particularly protects against viral infections that incorporate viral RNA within the genetic duplicating mechanisms of the host cell. This system uses a type of RNA, called *Piwi-interacting RNA* (piRNA) to check if the foreign RNA has been seen before. If it has not, then it is recognized as "non-self" and epigenetically silenced (RNAe, or RNA-induced epigenetic silencing).

Add to the box on the immune system, Section 6.20.3, just before the paragraph beginning "Microbes attempting to enter…":

Page 419:

Add to the box, Section 6.20, to the last sentence on the page:

(see hygiene hypothesis).

Page 420:

Add to Section 6.20.3, to the box on the immune system, before the paragraph beginning "If bacteria such as *Listeria* …", this paragraph:

Newborn ruminant mammals have very low protease activity in their digestive tract, which means that ingested proteins, including antibodies, are not degraded. Specialized receptors on small intestinal epithelial cells bind to antibodies and incorporate them into the body by endocytosis. This allows antibodies appearing in mother's first milk, called *colostrum*, to be passed to their offspring. Six to 12 hours after birth, the newborns lose the ability to absorb antibodies directly from the mother (Stewart, 2011).

Page 421:

Add this box at the end of Section 6.20.3:

PLANT IMMUNE RESPONSES TO DISEASE THREATS

There are also parasitic viruses (called *virophage*) that infect other viruses. The uses they infect belong to a recently-discovered class of giant viruses as large as ne prokaryotic cells (Van Etten, 2011).

lants, too, have multiple responses to combat diseases caused by microbes. These nclude:

1. Stomata close when certain proteins near the stomata detect signature molecules in bacterial membranes or flagella.
2. Infected cells die (e.g., apple scab immunity works in this fashion).
3. Nutrients necessary to bacterial growth are removed from open spaces inside the stomata.
4. Biochemicals are produced inside the leaf that disable pathogenic compounds.
5. Plant cell death compounds are activated by high humidity when infection is most likely to happen.

lants, too, have microbiomes, collections of microbes living in, on, and around the lants. These microbes apparently assist with plant metabolism, nutrient uptake, lisease resistance, and reproduction (Gould, 2012; Wagner et al, 2014).

Page 427:

Add to the end of the box entitled “Phages to the Rescue” in Section 6.20.7:

Page 430:

Add the following examples at the end of Section 6.20:

Example 6.20.5 Paleobiologists Using Immunities

There is epidemiological as well as forensic interest in identifying ancient parasites, bacteria, and viruses. Learning about these can shed light on the causes of famed pandemics, reasons that historical figures suffered or died, and the coevolution of microbes and hosts. The detection, identification, and characterization of ancient microbes in the environment or human remains have largely been based on analysis of tiny recovered samples of ancient DNA (aDNA). However, potential contamination by modern DNA and altered aDNA can make these methods unreliable. An alternative is to use nonnucleotidic biomolecules, including mycolic acids and proteins remaining from ancient microbes or other tissues. Assaying techniques include immunohistochemistry,

immunochromatography, enzyme-linked immunosorbent assays (ELISA), and mass spectrometry.

Example 6.20.6 Oncolytic Virotherapy

An Italian woman in 1904 who was diagnosed with cervical cancer suffered a bite from a rabid dog. She was given the live virus rabies vaccine for the bite, and subsequently, her large tumor disappeared. She lived cancer-free for eight more years.

The idea that viruses could be useful cancer therapy grew out of this case. Viruses can either be selected or engineered to selectively attack and kill cancer cells while leaving normal healthy cells unaffected. These viruses can do this because there are a number of characteristics of cancer cells that are different from normal cells, among them numerous receptors on cancer cell surfaces, and the large amount of viral-supporting raw materials inside the rapidly-growing cancer cells.

The viruses attack cancer cells with multiple mechanisms, and so do not depend on a single means of killing cancer. When the viruses have matured within the cancer cell, they burst forth, killing the cell and releasing compounds that are then recognized by the body's immune system as foreign. The immune system T cells contribute to the extermination of the cancer. Thus, oncolytic virotherapy engages the redundancy so successfully used by living things to fight off infections (Mahoney et al, 2014).

Example 6.20.7. Antibiotic Effects Are More Profound When Given Early in Life.

The hygiene hypothesis was supported by research results that showed that two common antibiotics given to neonatal mice significantly affected their internal microbiota diversity and made them more susceptible to severe allergic asthma. The same antibiotics administered to adult mice had almost no effect on either the microbiota or asthma susceptibility (Russell et al, 2012).

Page 432:

Add to Section 6.21.2, a new third paragraph:

Seeds dormant in the soil can sense when a forest fire has burned all the underbrush that would normally successfully compete with the seedlings for light and nutrients. The seeds contain a protein that changes shape in the presence of a chemical compound of smoke and ash. When this component, called *karrikin*, is sensed, the seeds begin to germinate, thus restoring the forest environment (Gammon, 2013; Zheng et al, 2013).

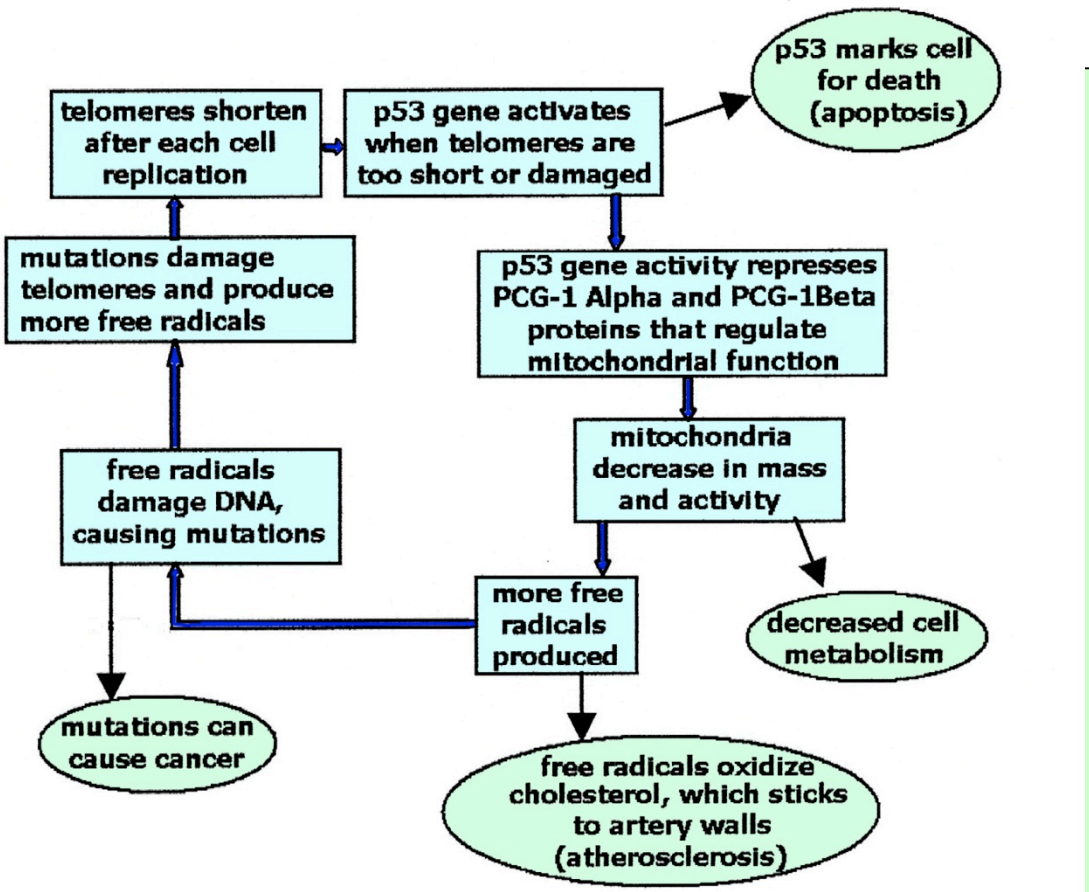
Page 432:

Add to Section 6.21.2, just before the paragraph beginning "The concept of ecological steady-state …":

COMPREHENSIVE THEORY OF AGING

A theory of aging has been proposed by DePinho and colleagues (Sahin et al, 2011) hat incorporates many possible mechanisms having an effect on aging and symptoms f aging. This theory is diagrammed in the figure, and incorporates telomere length, he p53 guardian of the genome gene, two master protein regulators of metabolism, nitochondrial number and function, free radical production and effects, therosclerosis, and DNA mutation. Although this is still only a theory of aging, it loes illustrate the interactions that can occur among the various components ssociated with aging effects.

The human microbiome has been found to undergo ecological succession just like with other ecosystems. The distribution of microbes is originally seeded at birth and changes over time with diet, exposure to other bacteria, maturity of the human, medicine use, overall health, and general environment. Eventually, up to 30,000 different microbial strains reside in and on different areas of the body (Dorit, 2014).



Comprehensive theory of aging as proposed by Sahin et al (2011).

SLEEP AND HEALTH

ep is an important part of health, and not just human health, because other animals, luding insects, sleep as well. Plants, too, have resting cycles synchronized to a cadian rhythm. In humans, sleep has profound effects on digestive processing, cancer, art disease, neurodegenerative diseases, memory formation, and general body repair.

A good night's sleep may do much more than refresh the psyche. *Melatonin* is a rmone that acts as an antioxidant that combats the free radicals (see Section 3.6.6) that n cause genetic damage. *Cortisol* is another hormone that helps regulate the immune stem. The disruption of normal sleep cycles results in less melatonin production and ver cortisol activity. Perhaps that may be one reason that female shift workers have gher rates of breast cancer than women who sleep normal hours. Regular sleep may help battle cancer.

Page 439:

Add to Section 6.21.7, just before the paragraph that begins "Approximately 24 h circadian rhythms …":

Obesity, diabetes, cardiovascular disease, liver disease, cancer, and depression may all be related to malfunctions of the body's diurnal rhythm through genetic mechanisms related to protein formation. Immune responses appear to be stronger at certain times of the day and night than at others (Silver et al, 2012). Circadian rhythm controls protein levels by:

1) altering when genes are transcribed from DNA into RNA, and
2) influencing when RNA is used to make proteins (Hardin et al, 2013).

Certain genes have DNA-binding sites that allow control by circadian proteins. Genes called *clock*, *period*, and *timeless* help regulate circadian rhythms; *sleepless* and *redeye* control sleep cycles.

Page 440:

Add to Section 6.21.7, as the last sentence of the paragraph beginning "Plants, too, have a so-called …":

Even metabolic and immune responses in plants are regulated to some extent by circadian rhythm (Wang et al, 2011; Teng et al, 2013).

Page 442:

Substitute in Section 6.21.7 for the box entitled "Sleep and Cancer", this box:

THE CONSEQUENCES OF FEAR

Fear is a very powerful emotion useful for survival. Fear alerts humans and animals to potential dangers, and readies them for combat or escape (the so-called *fight or flight reaction*). Fright speeds the heart and constricts some blood vessels to shunt blood to the arms and legs. Some prey animals freeze when frightened, so predators won't see them move. Fear maximizes sensory input by widening the eyes, dilating the pupils, and flaring the nostrils (Lilienfeld, 2010). People recognize facial expressions of fear quicker than those of other emotions, perhaps because fear almost always associates with some kind of danger. Fears distort reality for sufferers. Some of this is due to physiological effects and some is due to psychological changes. People with fear and phobias tend to overestimate real threats (Lilienfeld, 2010).

Women react to fear differently than do men. Whereas men prepare for fight or flight in a fearful situation, women tend to cling to those around them and bond to other females in a collective defensive posture (*tend and bond reaction*).

Some fears appear to be innate, but others are learned. Monkeys with no prior fear of snakes have learned that fear from other monkeys who have experienced the consequences of snake predation (Shumaker, 2010). This is an example of memes in action.

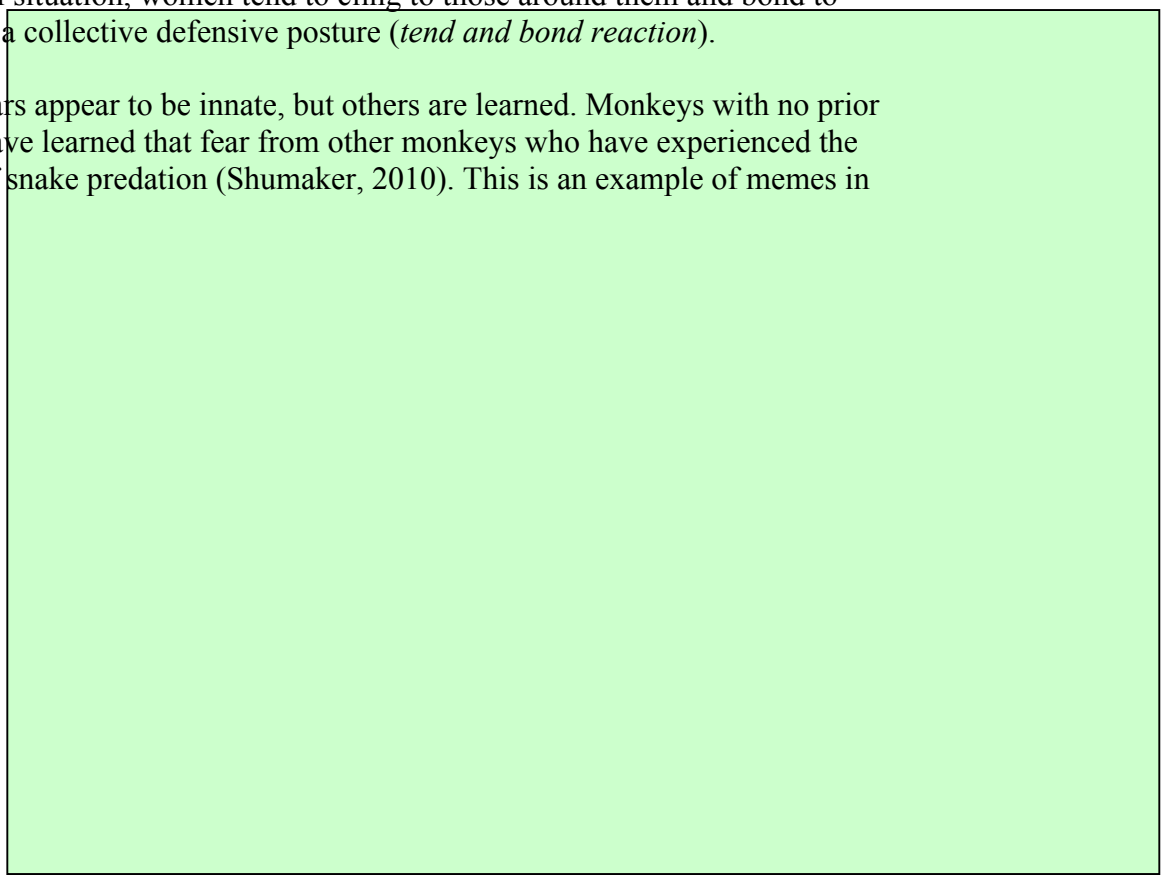
Page 450:

Insert in Section 6.22.1, in the paragraph that begins "Körner and Matsumoto (2002) …", just before the sentence that begins "The important self-image …":

Consciousness is derived from feelings and emotions (Pontin, 2014).

Page 451:

Add to the end of Section 6.22.1, this box:



Page 453:

Add to Section 6.22.3, just before the paragraph that begins "Blood glucose levels …":

How the brain recognizes sensory inputs, builds memories, and recalls past experiences is a topic of much study. The brain apparently has different codes for different types of information (Koch and Marcus, 2014). Some information is represented by neural firing rate, while other information resides in specific neurons or neuronal groups that fire. There are differences among different types of information such as new sensations, recognition of familiar entities, or general concepts. Different parts of the

brain code information differently. Memories are related to certain synaptic connections. These are all areas of ongoing work and interest.

Page 454:

Section 6.22.4, replace the term "*Emotional Intelligence*" with "The *Empathy Quotient*", an add at the end of the list of four factors:

The Empathy Quotient (EQ), or *Emotional Intelligence*, varies across the population as the familiar bell-shaped curve (Figure 6.22.5), or normal distribution. Females in the general population have slightly higher EQ scores than do males; humanities students score slightly higher than do science students. It appears that empathy arises from the amygdala and at least 10 interconnected regions of the brain (Baron-Cohen, 2011).

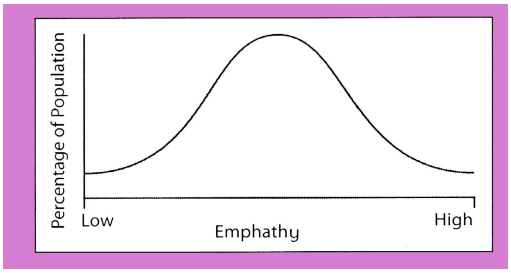


Figure 6.22.5. Empathy in the general population is expected to be distributed as a Normal Distribution.

Change all subsequent figure numbers and places in the text that refer to them.

Page 453:

Add to Section 6.22.4, paragraph 3, after the first sentence:

They have different vocal calls for things such as discovery of food, sighting predators, types of predators, empathy for others, care of offspring, and social relations with others of the same or opposite sex or status. Examples of these kinds of animals are mammals such as wolves, dolphins, sheep, and prairie dogs, and birds such as crows, chickens, ducks, and parrots.

Page 455:

Add this paragraph at the beginning of Section 6.22.5:

Learning about the environment and how to respond best to environmental challenges take time. Those animals that learn more and learn better take more time to mature and require longer parental care than do those animals with hard-wired (innate) responses.

ANIMAL INGENUITY

Maya is the name given by researchers to a matron of an isolated chimpanzee community in Africa. She has been observed to engage in the most sophisticated form of serial tool use by any nonhuman animal (Estes, 2010):

"Maya arrives at the termite mound, a rock-hard, bulbous structure three times her height, carrying in her mouth several plant stems that she will use to fish out its high-calorie occupants. First she rams a thick twig into a termite hole and widens it by jiggling the stick vigorously. Then she grabs a thin, flexible stem that she plucked off a nearby *Sarcophrynium* plant. Chimps in other parts of Africa are known to fish for termites with implements like this, but Maya goes one step further and modifies the tool. She drags the last six inches of the stem through her teeth to create a wet, frayed end, like a paint brush, and pulls it through her closed fist to straighten out the bristles. With the dexterity of a professional lock picker, she then threads the brush-tipped stem into the same hole, pulls it out, and nibbles off a couple bugs that cling to the wand's frayed edges.

"What's so remarkable about that fishing probe is that it represents a refinement. It's not just that some clever chimp figured out that it could break off a plant stem and use it to fish for termites – an impressive enough discovery in its own right – it's that some other chimp figures out a way to do it even better."

Another incident illustrating animal intelligence involves coyotes and sheep dogs. Shepherds located in regions with many sheep predators often keep sheep guard dogs with their flocks for protection. The dogs are trained to stay with the flock and ward off interlopers. Janet McNally (2010) is one of these shepherds, and described one of the incidents this way:

"I watched and listened as a coyote, just a stone's throw from a young … livestock guard dog, yapped at the dog, enticing her to chase. The [dog] would dash at the coyote, then retreat back toward the sheep. The coyote would come back and yap again, trying to lure the dog out into the woods. The coyote persisted for over three hours, but the dog] was only 8 months old. Typical of her breed, she stayed close to the flock and would not be enticed out toward the freeway. The week before, this coyote succeeded in drawing three older, bolder livestock guard dogs out onto the highway where they were promptly struck and killed by cars in three separate incidents over the course of two days. These were older dogs that were familiar with navigating traffic. Is a coyote smart enough to know the cars would kill the dogs?"

Humans, in particular, seem to be geared to learn; their brains take twenty years or more to mature because immature brains are flexible and can form new neural connections easily. Children explore creatively and easily; adults plan and act effectively. Each of these requires a different brain function and structure (Gopnik, 2010).

Page 456:

Add this box to the middle of section 6.2.5:

Page 466:

Insert in Section 6.22.8, in the paragraph that begins “Cardiovascular disease in animals …”, before the sentence that begins “These results demonstrate …”:

Just the presence of human observers has been shown to change wild animal behavior, allowing them to be less vigilant for the presence of natural predators (Nowak et al, 2014).

Page 471:

Add to Section 6.22:

Example 6.22.6 Dominance is Reinforced by Body Position

There is a psychological, physiological, and behavioral positive feedback system working in the minds and bodies of human beings that reinforces correlations among these three variables such that they cannot be easily separated. Just the act of smiling has been found to influence disposition toward a more positive outlook; nodding the head “yes” inclines a person to be more open to suggestion.

It has been found that the simple act of posing in a powerful position (exhibiting dominance or expanding occupied space) results in higher levels of the aggression hormone testosterone, lower levels of the stress hormone cortisol, and greater assumption of risk than posing in less powerful positions (closed, receptive, and subordinate). As shown in Figure 6.22.15, these two types of positions by themselves had profound physiological and physical consequences (Dana et al, 2010).

It had been known that higher levels of testosterone correlate with human dominance, and that lower levels of cortisol are related to lower stress levels. This research showed that these hormonal adjustments can be induced solely by the act of demonstrating power.

The relationship between social dominance and poses extends to other animals: peacocks spread their tail feathers and strut to attract mates; cats advance sideways to give the appearance of size to ward off intruders; chimpanzees inflate and thrust their chests forward to intimidate others. It is likely that these poses were enhanced by testosterone, and it is likely that testosterone was enhanced by the assumption of these poses.

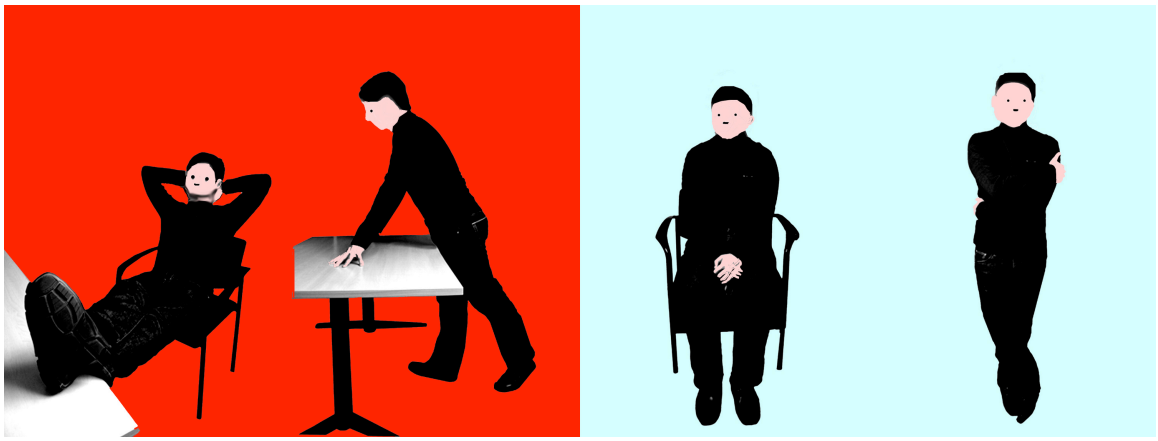


Figure 6.22.15. On the left are two poses found to demonstrate power and enhance testosterone and reduce cortisol. On the right are two poses that demonstrate conciliation, withdrawal, or subservience. Testosterone for the right hand poses was lower and cortisol higher (Redrawn from Carney et al, 2010).

Example 6.22.7 Sensory Overload in the Driver's Seat

Modern automobiles are designed and built for comfort by insulating the driver from noise, road bumps, and ambient conditions. The driver is isolated from the surrounding environment so well that a myriad of warning systems have had to be installed to indicate when there is trouble. There are dashboard lights for doors ajar, gas filler access flaps open, parking brake engaged, low fuel, engine trouble, air-bag malfunction, anti-lock brake condition, and many others.

When engineers decided to improve safety by warning drivers of nearby vehicles traveling in the blind spot for the driver, that place just to the left and slightly behind the driver (at least for autos driven on the right hand side of the road), they faced a decision about the best means to warn the driver (Corley, 2010). The visual sense was already overloaded while driving.

Engineers, instead, installed vibrators in the driver's seat. Surrounding vehicles activated vibrators in seat locations corresponding to positions of nearby cars; vehicles to the left activated left vibrators and vehicles to the right activated right-side vibrators. The closer the approaching vehicle, the more intense was the vibration. Engineers hope that using tactile feedback for drivers will help them take more appropriate actions in a timely manner.

Example 6.22.8. Healing Gardens

Gardens on hospital grounds have been shown to facilitate patient healing and recovery (Franklin, 2012). These areas should allow young children to have places for moderate activity, have interesting, contemplative areas for middle-aged adults, and have stimulatory locations for older adults. Research has led to the following checklist for hospital gardens:

1. **Keep It Green.** Lush, layered landscapes with shade trees, flowers, and shrubs at various heights should take up roughly 70% of the space; concrete walkways and plazas about 30%.
2. **Keep It Real.** Abstract sculptures do not soothe people who are sick or worried.
3. **Keep It Interesting.** Mature trees that draw birds and chairs that can be moved to facilitate private conversation foster greater interaction.
4. **Engage Multiple Senses.** Gardens that can be seen, touched, smelled, and listened to soothe best. But avoid strongly fragrant flowers or other odors for patients undergoing chemotherapy.
5. **Mind the Walkways.** Wide, meandering paths that are tinted to reduce glare allow patients with low eyesight, wheelchairs, or walkers to get close to nature. Paving seams must be narrower than one eighth of an inch to prevent trips by patients trailing wheeled IV poles.
6. **Water with Care.** Fountains that sound like dripping faucets, buzzing helicopters, or urinals do not relax anyone, and neither does the strong smell of algae.
7. **Make Entry Easy.** Gardens should not be far away or behind doors that are too heavy for frail or elderly people to open.

Example 6.22.9. Helping Autistics Achieve a Quality Life

Autism of many different degrees of severity affects one in 68 children in the U.S., with four times the incidence in boys compared to girls. Autism appears to be related to new mutations in DNA that affect neurological development and function (Hall, 2015). Autism disorders cover a spectrum of atypical behaviors ranging from somewhat affected to severe intellectual disability.

For those with mild cases, strengths of autistic thinking include:

1. Bottom-up thinking that renders unrelated details unimportant.
2. Associative thinking that places together all similarities.
3. Creative thinking that puts details together differently from others.

Therefore, autism can be considered, not a disease, but rather a neurological difference.

Biological engineers can help provide facilities to accommodate the special needs of autistic people (Robison, 2015):

1. Help them organize their lives, manage their schedules, and deal with sensory overload by supplying quiet spaces and calming lighting.
2. Provide engineering solutions to autistic deficiencies, such as formulating verbal communications for those who cannot speak, and designing machines that can read expressions of those around them for those who cannot interpret body language.

Page 477:

Add to the end of Section 6.23.2:

Example 6.23.2 The Use of Animals for Food

Temple Grandin has made several observations related to animal use and animal welfare (Klein, 2010):

1. the natural cycle of birth and death means that for one living thing to survive, another living thing must die.
2. animals in the wild usually die a violent death from starvation, predators, or exposure.
3. wild animals seldom die from natural causes or old age.
4. killing animals for food at a slaughter house can be much gentler and more humane than death in nature.
5. prey animals hide their pain to keep predators from singling them out; however, they don't hide fear.
6. livestock have been bred to supply food for humans. They exist in their present forms because of human breeding. They deserve a decent life and a quick, painless death.

Page 477:

Add to Section 6.23.3, after the first sentence, this reference:

(Fries and Crapo, 1981).

Page 478:

Add to the paragraph beginning "There is a possibility that …", after the word "resveratrol", this reference:

(Yuan and Marmorstein, 2013)

Page 496:

Add to Section 74, at the end of the first paragraph, immediately following the sentence ending with the word "mountains":

Other fractally-organized (scale independent) biological features are chromosome organization (Babbit, 2011) and correlation lengths among birds flying in flocks (swarm intelligence; Hayes, 2011).

Page 529:

Insert in Section 7.4.13, paragraph 3, after the sentence that reads "They have higher photosynthetic efficiency than do C3 plants.":

C4 crops use far less water and nitrogen than do C3 crops, and they typically have 50% higher yields.

Page 531:

Add to Section 7.4:

Example 7.4.4 Cats Lapping Water

When cats lap water, they do not cup their tongues, as dogs do. They use their tongues to slap the water, rather than scooping the water into their mouths. When a cat lifts its tongue, a column of water adheres to the tongue, and is drawn into its mouth by inertia (Reis et al, 2010).

Lapping frequency was found to be dependent upon cat body mass:

$$f = 4.6\ m^{-0.181}$$

where f is lapping frequency, in laps/sec
m is body mass, in kg.

Larger cats lap water slower than smaller cats. This makes sense, because larger cats have larger tongues that require more power to move as fast as smaller tongues.

Page 531:

Add to the end of Section 7.4:

Example 7.4.5 King Kong's Structural Constraints.

King Kong was a fictional movie character who appeared as a gorilla much larger than normal. All of his proportions were the same as a normal gorilla.

In real life, structural proportions of bone limit animal sizes and proportions. If King Kong were five times as tall as a normal gorilla, then his mass would scale as his volume, or $5^3 = 125$ times the mass of a normal gorilla. However, the strengths of his bones (limited by critical stresses) would depend on their cross-sectional areas, or $5^2 = 25$ times as strong as normal bones. Thus the forces on his leg bones would be $125/25 = 5$ times larger than normal; his bones would be crushed. Apes can be smaller or larger, but structural considerations impose constraints (Willmore, 2010).

Page 531:

Add to the end of Section 7.4, this example:

Example 7.4.6 Animals Shaking Off Water

Dogs aren't the only animals that shake when wet. Other animals also use this means to dry their bodies. The smaller the animal, the faster it shakes. Shaking frequency data in

Table 7.4.6 appeared in *National Geographic* magazine (Bloch, 2011). Investigate to see if an allometric relationship can be developed between shaking frequency and body mass.

Solution: Nominal body mass data were obtained from Table a.1 in the appendix, and are given in Table 7.4.6. Because it is reasonable to suspect a power-law relationship between shaking frequency and body mass, data for each of these variables were converted into logarithms and the values plotted (Figure 7.4.23). The apparent straight line relationship is consistent with a power-law equation.

Using the least-squares technique explained in Section 4.2.3, the best-fit equation was found to be:

$$\log f = 1.07 \log m - 0.21 \qquad (7.4.74a)$$

Converting this into a power-law equation requires taking the antilog of 1.07 to yield:

$$f = 11.8\, m^{-0.21} \qquad (7.4.74b)$$

This equation predicts a shaking frequency of 4.1 cycles per second for the tiger and a frequency of 4.8 cps for a 70 kg human.

Table 7.4.6 Shaking Frequencies of Animals

Animal	Body Mass (kg)	Log (mass)	Shaking Frequency (cps)	Log (frequency)
Mouse	0.023	-1.64	29	1.46
Rat	0.25	-0.602	18	1.26
Guinea Pig	0.345	-0.462	14	1.15
Cat	3.3	0.519	9	0.954
Poodle	12	1.08	6	0.778
Lab Retriever	14	1.15	5	0.699
Sumatran Tiger	160	2.20	4	0.602
Brown Bear	550	2.74	4	0.602

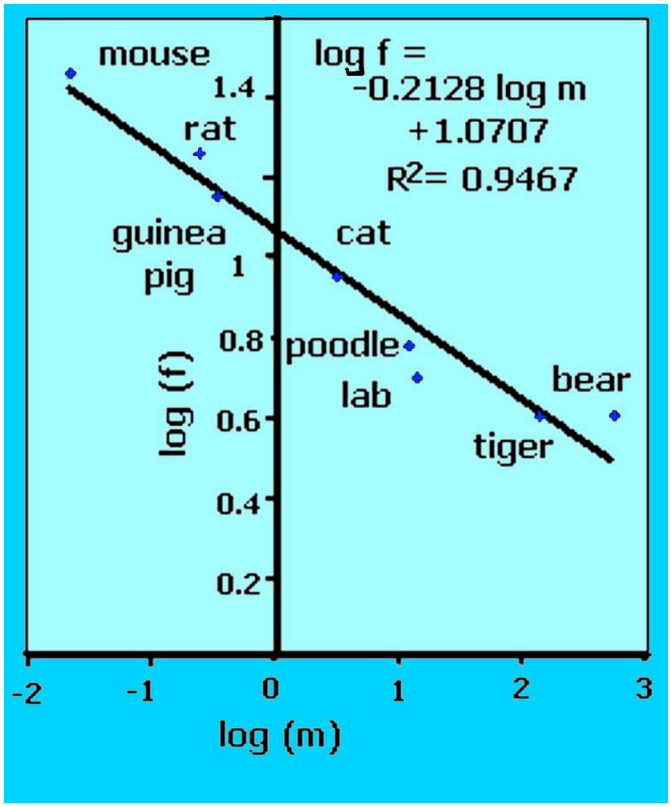


Figure 7.4.23 Graph of the logarithmic relationship between shaking frequency (cps) and body mass (kg) for several animals.

Page 535:

Add to Section 7.6.3, as the last sentence of the first paragraph:

The shape of the curve relating species type to relative abundance in an ecosystem is lognormal (Dorit, 2014).

Page 539:

Add this example to the end of Section 7.6:

Example 7.6.2 Poaching of Rhinos

Powdered rhinoceros horn is prized in some parts of the world for its supposed ability to cure fever, arthritis, high blood pressure, and cancer. This demand has led to the unauthorized and illegal killing of rhinos in Africa and Asia. The horns are sawed off the carcass and smuggled to horn dealers.

The numbers of rhinos has plummeted due to this poaching. African black rhinos numbered about 100,000 in the early 1960s, but the population had waned to just 2400 in the early 1990s (Beech and Perry, 2011). At the beginning of the twentieth century, there were only about 50 African white rhinos alive. Now, thanks to conservation efforts, the

number is about 20,000. The Sumatran and Javan rhinos, however, are on the verge of extinction.

Saving the African black rhino requires protection for a long enough time for the population to build up to sustainable levels. The mass of a black rhino is about 1200 kg (Clauss et al, 2005). The maximum population doubling time calculated from equations 7.6.8 a-d is 7.2 years. The actual number of black rhinos had doubled to about 4800 by 2011, giving a population doubling time of about 20 years. The difference can probably be attributed to the lasting effect of illegal killing.

Page 554:

Add at the end of the paragraph beginning "Biomimetics has been the inspiration …":

Besides encapsulating repair materials in microcapsules, vascular capillaries can be incorporated in the material to deliver healing agents to the required location. Other techniques used are integrating the healing agents directly in the object and using microcapsuled bacteria to fabricate repair materials on the spot (Grose, 2014).

Page 560:

Insert this paragraph in Section 8.2.3 immediately before the paragraph that begins: "Gene therapy is another technique …"

Genetically-edited organisms (GEOs) can be made with a system called *CRISPER* (clustered regularly interspaced short palindromic repeats) that is not only efficient but also applicable to virtually any living species. The *gene editing* using CRISPER allows the desired insertion of genes from different strains of the same species that convey beneficial characteristics to the target organism rather than the insertion of genes from other species, as in genetically-modified organisms. This method can be used for adding, disrupting, changing the sequence of specific genes, or gene regulation in many species at all hierarchical levels. The CRISPER system uses certain genetic patterns to identify the specific site on the chromosome where the desired gene is to be inserted. Using this marker sequence, a *restriction enzyme* is used to cleave the double-stranded DNA at the sequence-specific designated site, and the gene of interest is inserted where it is supposed to go. *Guide RNA* (gRNA) and a special protein (Cas9) are used to direct the restriction enzyme to a specific target site to cleave the DNA molecule. gRNA consists of a string of nucleotides that are complementary to the target cleavage sequence. Cellular mechanisms are enacted to repair the breaks including the newly-inserted gene. Antibiotic selection is not necessary with this gene editing technique (Knox, 2014).

Page 560:

Add to Section 8.2.3, after the paragraph beginning "Gene therapy is often conducted *ex vivo* …":

There are generally four choices to deliver nucleic acid (DNA or RNA) into a target cell:

1. transfection reagents and endocytosis
2. electroporation
3. viruses
4. biolistics (shooting DNA- or RNA-coated pellets into the cell)

Of these, the first three are usually used with animal cells and the fourth can be use for agricultural work. *Lentiviruses* are sometimes used to transfect genetic material into non-dividing cells.

Page 562:

Add to the paragraph beginning "There are many economic advantages …", just after the sentence that ends "(Marvier, 2007)":

Genetically- modified switchgrass can grow polyhydroxybutyrate (PHB) that can be used to fashion plastic bags, thermal foam, food packaging, and other objects (Cooper, 2008). PHB grown in this way is easy to harvest and does not require further chemical alteration. The switchgrass byproduct can be used as a biofuel.

Page 562:

Add at the end of Section 8.2.3:

Because mitochondria are passed from one generation to the next only through the maternal line, and it sometimes happens that there are genetic disorders of the mitochondria, these disorders are transmitted to subsequent generations no matter how healthy are paternal mitochondria. One solution is to use in vitro fertilization (IVF) with three gamete cells. The nucleus of the intended maternal cell with mitochondrial disease can be inserted to replace the nucleus of a second maternal cell with healthy mitochondria and then the resulting hybrid cell can be fertilized with the male gamete. The result is an offspring with intended nuclear genetics and healthy mitochondria that are passed down to subsequent generations.

Page 566:

Add to Section 8.2.4, after the second paragraph:

There is a growing involvement of robotics in medicine and engineers have a large role to play in their development. Robots can be used as components of prosthetic devices, as adjuncts to surgery or diagnosis, as means to collect data from otherwise inaccessible environmental locations, or as means to complete unsafe or highly repetitive

tasks. *Behaviomedics* is the practice of training robots to spot changes in patients caused by medical conditions like pain or depression.

Page 573:

Add to Section 8.2.5, after the paragraph that begins "Works of civil construction …":

Freshwater ecosystems, which provide vital goods and services such as clean water, biodiversity, flood protection, and recreation, are as endangered as any other type of ecosystem on the planet, given all the damming, dumping, draining, and diverting to which they have been subjected.

Page 577:

Add at the end of Section 8.2, this example:

Example 8.2.6 Bioleaching of Metal Ores

Bacteria are increasingly being used to extract metals from low-grade ores or from ores difficult to mine. Strains of the bacterium *Thiobacillus ferrooxidans* thrive on mineral-rich rock. Many of these rocks contain heavy metal sulfides, and form acidic solutions when rainwater leaches through them. *T. ferrooxidans* facilitates this leaching when it uses the compounds for its metabolism. This process is called *bioleaching.*

Low-grade ores that contain concentrations of metals uneconomical to extract through conventional smelting can be ground and piled on a water-impermeable surface, and treated with *T. ferrooxidans.* The metals are recovered economically from the solutions of acidic water runoff coming from the pile (Rawlings and Silver, 1995).

More than 25% of the world's copper is extracted using bioleaching. Bioleaching also shows promise for recovering gold, cobalt, and uranium. Because *T. ferrooxidans* survives in the harsh environments of acidic rock, this bacterium has been nominated as a means to extract valuable minerals from the surfaces of other planets (Olsson-Francis and Cockell, 2010).

Page 577:

Add to the end of Section 8.2, this example:

Example 8.2.7 Cyborg Beetles

Tiny robots that could fly inside caves, tunnels, and barricaded rooms could provide needed reconnaissance for the military, law enforcement personnel, or emergency first responders. Fully synthetic micromechanical robotic fliers require too much energy to be powered by present battery technology. Beetles have very efficient flying mechanisms,

but they need to be able to carry miniature cameras and to be controlled to fly where they are needed. Beetles large enough to carry miniature radios, batteries, and controllers have been used for this purpose (Maharbiz and Sato, 2010). Several very thin wires implanted in the insect's brain and flight muscles permit humans to control beetles to start or stop flying, and to turn left or right in flight (Figure 8.2.22).

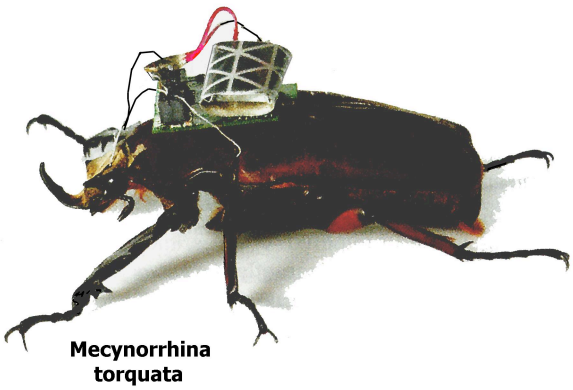


Figure 8.2.22 This beetle carries a miniature radio, controller, and battery and can be controlled in flight (Maharbiz and Sato, 2020)

Page 579:

Add to Section 8.3, in the box entitled "Bionanotechnology", just after the sentence beginning "The LDL could then be used …":

Venoms from bees, snakes, scorpions, or others can become effective anticancer agents when encased in nanoparticles that target cancer cells.

Page 580:

Add to Section 8.4, before the quote by Bessie Anderson Stanley:

I have not failed – I have just found 10,000 ways that won't work.
-Thomas Edison

Science is more than a body of knowledge, it's a way of thinking.
-Carl Sagan

The job of the artist is to fight against entropy. Entropy in its simplest form refers to the tendency of everything to collapse. If you smash a vase and throw the pieces in the air, they won't re-land in the shape of a perfect vase. But the job of the artist is to smash the vase and then fashion something coherent out of those shards.
-William Kentridge

Page 580:

Add to Section 8.4, after the quotes:

No consideration of biology for engineers, where the objective is to manipulate and use what is known about living things to produce useful new products and processes, can be complete without some consideration about whether the manipulation should be done. Certainly, with the tools that are now known and about to be known, a good number of capabilities can lead to unacceptable results, not unacceptable from a biological viewpoint, because biology is effectively neutral regarding new applications, but they can be unacceptable from a *bioethics* point of view. As Randy Oliver has said:

> *"Nature does not favor specific traits nor reward success. Nature only penalizes failure. Those left after penalization are called survivors, or 'more fit'."*

What makes these new applications acceptable or not is up to the general societal consensus of acceptability. It is up to the biological engineer to limit her or his activities to the confines of ethical acceptability.

There are so many applications possible these days that test the bounds of acceptability (King et al, 2015):

1. new assisted reproductive technologies (Fisher, 2015).
2. human brain manipulation.
3. prosthetic devices with independent control
4. what to do about degrees of sentience in other non-human species
5. environmental control of ecosystems
6. introduction of new life forms
7. possibility of human immortality
8. legal ramifications of free will
9. introduction of human emotions into machines
10. conflict between food production and environment

and many others. The burden is then on the shoulders of those who understand the implications of the technology to help identify those areas of questionable ethical concern and help to guide the conversation towards rational decisions of acceptability. That means you.