Fibrous proteins are especially abundant outside the cell, where they form the gel-like extracellular matrix that helps cells bind together to form a tissue. These proteins are secreted by the cells into surroundings, where they often assemble into sheet or long fibrils. Collagen is the most abundant of these fibrous proteins in animal tissues. The collagen molecule consists of three long polypeptide chains each containing the nonpolar amino acids glycine at every third position. This regular structure allows the chains to wind around one another to generate long triple helix.

Extracellular Proteins Are Often Stabilized by Covalent Cross-Linkages

To maintain their structures outside of the cell, proteins are often stabilized by covalent cross-linkages. These linkages can tie together two amino acids in the same protein, or connect different polypeptide chains into multisubunit protein. The most common cross-link in proteins are covalent sulfur-sulfur bonds. These disulfide bonds (also called S-S bonds) form are being exported from the cells.

How Proteins Work

Proteins are not inert lumps of material. Because of their different amino acid sequences, proteins come in an enormous variety of different shapes—each with unique surface topography of chemical groups.

All Proteins Bind to Other Molecules

The biological properties of a protein molecule depend on its physical interaction with other molecules.

| Antibodies | → | virus or bacteria |
| Hexokinase | → | Glucose |

All proteins stick, or bind, to other molecules. In some cases this binding is very tight; in others it is weak and short-lived. In all cases binding shows great specificity, in the sense that each protein molecule can bind to just a few molecules out of the many thousands of different molecules it encounters. Any substance that is bound by a protein is external to be a ligand for that protein. The ability of a protein to bind selectively and with high affinity to a ligand is due to the formation of a set of weak, non covalent bonds plus hydrophobic interaction.
The region of a protein that associates with a ligand, known as its binding site, usually consists of a cavity in the protein surface formed by a particular arrangement of amino acids. These amino acids belong to widely separated regions of the polypeptide chain that are brought together when the proteins fold.

Antibodies or immunoglobulins, are proteins produced by the immune system in response to foreign molecules. Each antibody binds to a particular target molecule extremely tightly, either activating the target directly or marking it for destruction. An antibody recognizes its target (called antigen) with a remarkable specificity. Antibodies are Y-shaped molecules with two identical binding sites that are each complementary to a small portion of the surface of the antigen molecules.
Enzymes Are Powerful and Highly Specific Catalysts

Enzymes bind to one or more ligands, called substrate, and convert them into chemically modified products, and doing this over and over again with amazing rapidity. They speed up reactions, often by a factor of a million or more, without themselves being changed. Enzymes can be grouped into functional classes that carry out similar chemical reactions. Each type of enzyme is highly specific, catalyzing only a single type of a reaction.

Lysozyme illustrates How an Enzyme Works

Lysozyme severs the polysaccharides chains that form the cell walls of bacteria. Because the bacterial cell wall is under the pressure due to the osmotic forces, cutting even a small number of polysaccharide chains causes the cell wall rupture and the bacterium to burst. The reaction is catalyzed by lysozyme as a hydrolysis: the enzyme adds a molecule of water to a single bond between two adjacent sugar groups in the polysaccharide chain, thereby causing the bond break.

Lysozyme severs the polysaccharides chains that form the cell walls of bacteria.
Tightly Bound Small Molecules Add Extra Functions to Proteins

Although the order of amino acids in proteins gives these molecules their shapes and versatility to perform different functions, sometimes the amino acids by themselves are not enough. Proteins often employ small nonprotein molecules to perform functions that would be difficult or impossible using amino acid alone. For example, signal receptor protein rhodopsin pigment made by the rod cells in the retina detects light by means of small molecules, retinal, embedded in protein. Retinal changes its shape when it absorbs a photon of light, and this change is amplified by the protein to trigger a cascade of enzymatic reactions that eventually leads an electrical signal being carried to the brain.

Another example of a protein that contains a non-protein is hemoglobin. A molecule of hemoglobin carries four heme groups, ringed shaped molecules each with single central iron atom. Heme gives hemoglobin its red color. By binding reversibly to oxygen gas through its iron atom, heme enables to pick up oxygen in the lungs and release it in the tissues.

How Proteins Are Controlled

Most proteins and enzymes do not work constantly, or at full speed in the cell. Instead their activity is regulated so that the cell can maintain itself in a state of equilibrium, generating only those molecules it requires to thrive under the current conditions.

Regulation of enzyme activity occurs at many levels.
1. The cell controls how many molecules of each enzyme it makes by regulating the expression of the gene that encodes that protein.
2. The cell controls enzymatic activities by confining sets of enzymes to particular subcellular compartments, enclosed by distinct membrane.
3. Enzyme’s activity changes in response to other specific molecules that it encounters.

The most common type of control occurs when a molecule other than substrate binds to an enzyme at special regulatory sites outside of active sites by altering the rate at which the enzyme converts it substrates to products.

Feedback inhibition regulates the flow through biosynthetic pathways

The end product Z inhibits the first enzyme that is unique to its synthesis and thereby controls its own concentration in the cell. This is an example of negative regulation.
Feedback inhibition at multiple sites tunes connected metabolic networks. In this example, which shows the biosynthetic pathways for four different amino acids in bacteria, the red arrows indicate positions at which products feed back to inhibit enzymes. Each amino acid controls the first enzyme specific to its own synthesis, thereby controlling its own levels and avoiding a wasteful buildup of intermediates. The products can also separately inhibit the initial set of reactions common to all the syntheses. In this case, three different enzymes catalyze the initial reaction, each inhibited by a different product.

Allosteric Enzymes Have Two Binding Sites That Influence One Another

There was one feature of feedback inhibition that was initially puzzling to those who discovered it: the regulatory molecule often has a shape that is totally different from the shape of the enzyme’s preferred substrate. This type of regulation was named as allosteric. These types of enzymes must have at least two different binding sites on their surface and recognize a substrate and a second site on their surface recognizes a regulatory molecule.

Example

An enzyme used in early studies of allosteric regulation was aspartate transcarbamoylase from E. coli. This large multisubunit enzyme catalyzes an important reaction that begins the synthesis of the pyrimidine ring of C, U, and T nucleotides. One of the final products of this pathway, cytosine triphosphate (CTP), binds to the enzyme to turn it off whenever CTP is plentiful. This diagram shows the conformational change that occurs when the enzyme is turned off by CTP binding.

Phosphorylation Can Control Protein Activity by Triggering a Conformational Change

Enzymes are not only regulated by the binding of small molecules. A second method commonly used by eukaryotic cells to regulate protein activity involves attaching a phosphate group covalently to one of its amino acids side chain. Phosphorylation of proteins cause change of conformation and eventually changes protein’s affinity towards substrates. Many proteins (approximately 10,000) are controlled by phosphorylation in eukaryotic cells. The reverse reaction—removal of the phosphate group, or dephosphorylation, is catalyzed by protein phosphatase.

Chapter 13

How Cells Obtain Energy

p427-452
Perhaps the most important fuel molecules are the sugars. Plants make their own sugars by photosynthesis, whereas animals obtain sugars by eating other organisms. If a fuel molecule such as glucose were oxidized to CO₂ and H₂O in a single step (as happens in nonliving systems), it would release an amount of energy many times larger than any carrier molecule could capture. Instead, living cells use enzymes to carry out the oxidation of sugars in a tightly controlled series of a reaction.

The Breakdown of Sugars and Fats

Animal cells make ATP in two ways. First, specific steps in a series of enzyme-catalyzed reactions are directly coupled to the energetically unfavorable reaction, ADP + Pi → ATP.

The second process takes place in mitochondria and uses the energy from activated carrier molecules to drive ATP production.

Food Molecules Are Broken Down in Three Stages

In stage 1, large food molecules are broken down into simpler forms either in intestine or within the cells by means of lysosomes. In both cases, digestive enzymes reduce large polymeric molecules in food into their monomers.

Proteins → amino acids
Polysaccharides → sugars
Fat → glycerol and fatty acids

Glycolysis is a Central ATP-Producing Pathway

Glycolysis produces ATP without the involvement of molecular oxygen. It occurs in the cytoplasm of many anaerobic microorganisms. During the glycolysis, a glucose molecule with six carbon atoms is cleaved into two molecules of pyruvate, each of which contains three carbon atoms. For each of glucose molecule, two molecules of ATP are consumed to drive the early steps, but four molecules of ATP are produced in later steps.
Step 1: Glucose is phosphorylated by ATP to form a sugar phosphate. The negative charge of the phosphate prevents passage of the sugar phosphate through the plasma membrane, trapping glucose inside the cell.

\[
\text{glucose} + \text{ATP} \rightarrow \text{glucose-6-phosphate} + \text{ADP} + \text{H}^+ \]

Step 2: The six-carbon sugar is dephosphorylated to produce the aldehyde form of glyceraldehyde-3-phosphate. Only glyceraldehyde-3-phosphate can proceed immediately through the glycolysis pathway.

\[
\text{fructose-1,6-bisphosphate} \rightarrow \text{fructose-6-phosphate} \rightarrow \text{glyceraldehyde-3-phosphate} \]

Step 3: The other product of step 4, dihydroxyacetone phosphate, is isomerized to form glyceraldehyde-3-phosphate.

\[
\text{dihydroxyacetone phosphate} \rightarrow \text{glyceraldehyde-3-phosphate} \]

Step 4: The two molecules of glyceraldehyde-3-phosphate are oxidized. The energy generation phase of glycolysis begins, as NADH and a new high-energy anhydride linkage to phosphofructokinase are formed (see Figure 6-8).
Step 7. The transfer to ADP of the high-energy phosphate group that was generated in step 6 forms ATP.

Step 8. The remaining phosphate ester linkage in 3-phosphoglycerate, which has a relatively low free energy of hydrolysis, is moved from carbon 3 to carbon 2 to form 2-phosphoglycerate.

Step 9. The removal of water from 2-phosphoglycerate creates a high-energy monophosphate linkage.

Step 10. The transfer of the high-energy phosphate group that was generated in step 9 forms ATP, completing glycolysis.
An outline of glycolysis

Each of the 10 steps shown is catalyzed by a different enzyme. Note that step 4 cleaves a six-carbon sugar into two three-carbon sugars, so that the number of molecules at every stage after this doubles. As indicated, step 6 begins the energy generation phase of glycolysis, which causes the net synthesis of ATP and NADH molecules.

Fermentations allow ATP to be produced in the absence of oxygen

For most animal and plant cells, glycolysis is only a prelude to the third and final stage of the breakdown of food molecules. In these cells, pyruvate formed at the end of glycolysis is rapidly transported into the mitochondria, completely oxidized to CO₂ and H₂O. But for many anaerobic organisms, which do not use molecular oxygen and cannot grow and divide in its absence, glycolysis is the principal source of the cell's ATP. The same is true in certain animal tissues, such as skeletal muscle, that can continue to function at low levels of molecular oxygen.