Student Solutions Manual, Study Guide, and Problems Book for Garrett & Grisham's

Biochemistry

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5th Edition

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Biochemistry

FIFTH EDITION

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Preface

In one scene in the movie Stripes (Columbia Picture Corporation 1981), privates John Winger and Russell Zissky (played by Bill Murray and Harold Ramis) attempt to persuade their platoon to an all night training session to prepare for the next day's final parade. The troops are skeptical of the plan; however, Zissky wins them over by his testimony of the importance of cramming. He proudly reports that he had, in fact, once learned two semesters of geology in a single three-hour all nighter.

It would seem unlikely that this approach would work well with biochemistry (or even geology). Rather a steady diet of reading, problem solving, and reviewing might be a better plan of attack. This study guide was written to accompany "*Biochemistry"* by Garrett and Grisham. It includes chapter outlines, guides to key points covered in the chapters, in-depth solutions to the problems presented in the textbook, additional problems, and detailed summaries of each chapter. In addition, there is a glossary of biochemical terms and key text figures.

Several years ago I spent part of a sabbatical in Italy and in preparation took a year- long course in elementary Italian. I had not been on the student-end of an academic interaction for several years and taking a language course was an excellent opportunity to be reminded of the difficulties of learning something for the first time. Memorization is part and parcel to the study of any language and so I found myself committing to memory nouns, verbs, adverbs, adjectives, and complex, irregular verb conjugations. The study of biochemistry has parallels to language studies in that memorization is necessary. What makes the study of biochemistry somewhat easier, however, are the common themes, the interconnections between various facets of biochemistry, and the biological and chemical principles at work. The authors have done a marvelous job in presenting these aspects of biochemistry and I have attempted to highlight them here. Biochemistry is a demanding discipline but one well worth the effort for any student of the sciences. *Buona fortuna.*

Acknowledgments

It is often stated that teaching a subject is the best way to learn it. In teaching my one-semester biochemistry course at Vassar College, because there is never enough time to cover all the topics, I used to worry about forgetting certain aspects of biochemistry. Thanks to Charles Grisham and Reginald Garrett, this fear is no longer with me. I thank both authors for the marvelous text and the opportunity to relearn all of biochemistry. I also thank my co-author Steven Theg. To my wife Kristen I give special thanks for putting up with me during this project.

David K. Jemiolo
Poughkeepsie, NY August 2011

Every time I work on this project I am grateful for the chance to learn and relearn aspects of biochemistry from Reginald Garrett and Charles Grisham through their scholarly and readable text. My co-author Dave Jemiolo displays the same vast knowledge of biochemistry, and I am grateful for the opportunity to work with him on this book. I am especially thankful for Jill, Chris, Alex and Sam for providing the context in which all this makes sense.

Steven M. Theg Davis, CA August 2011

Why study biochemistry?

This excerpt from *Poetry and Science* by the Scottish poet Hugh MacDiarmid (1892-1978), which first appeared in *Lucky Poet* (1943), might help with an answer.

Poetry and Science

Wherefore I seek a poetry of facts. Even as The
profound kinship of all living substance Is made clear
by the chemical route.
Without some chemistry one is bound to remain
Forever a dumbfounded savage
In the face of vital reactions. The
beautiful relations Shown only by
biochemistry
Replace a stupefied sense of wonder With
something more wonderful Because natural
and understandable. Nature is more
wonderful
When it is at least partly understood. Such an
understanding dawns
On the lay reader when he becomes
Acquainted with the biochemistry of the glands
In their relation to diseases such as goitre
And their effects on growth, sex, and reproduction. He will
begin to comprehend a little
The subtlety and beauty of the action
Of enzymes, viruses, and bacteriophages, These
substances which are on the borderland Between the
living and the non-living.
He will understand why the biochemist
Can speculate on the possibility
Of the synthesis of life without feeling
That thereby he is shallow or blasphemous. He will
understand that, on the contrary, He finds all the
more
Because he seeks for the endless
---'Even our deepest emotions
May be conditioned by traces
Of a derivative of phenanthrene!'

Science is the Differential
Calculus of the mind,
Art is the Integral Calculus;
they may be Beautiful apart, but are great
only when combined.

Sir Ronald Ross

In this poem, MacDiarmid argues strongly for the importance of studying biochemistry to understand and appreciate Nature itself. The poem was published in 1943, well before the molecular revolution in biochemistry, well before the first protein structure was solved or the first gene cloned yet MacDiarmid seems to have appreciated the importance of enzyme kinetics and enzyme catalysis and to anticipate the value of recombinant DNA technology: "The subtlety and beauty of the action of enzymes, viruses, and bacteriophages…." He even suggests that a fundamental understanding of life itself might be possible through biochemistry.

It is interesting to see how biochemists are portrayed in movies and films in this electronic age. In the 1996 film *The Rock* staring Sean Connery and Nicholas Cage, Cage plays a biochemist enlisted by the FBI to deal with a threat involving VX gas warheads. (VX is a potent acetylcholinesterase inhibitor.) Cage's character, Stanley Goodspeed, delivers this memorable line, which informs the audience of his expertise: " Look, I'm just a biochemist. Most of the time, I work in a little glass jar and lead a very uneventful life. I drive a Volvo, a beige one. But what I'm dealing with here is one of the most deadly substances the earth has ever known, so what say you cut me some friggin' slack!" Perhaps Stanley is overstating the danger inherent in his work but he is surely understating the importance of his occupation.

Chapter 1

The Facts of Life: Chemistry Is the Logic of Biological Phenomena

Chapter Outline

- Properties of living systems
  - Highly organized - Cells > organelles > macromolecular complexes > macromolecules (proteins, nucleic acids, polysaccharides)
  - Structure/function correlation: Biological structures serve functional purposes
  - Energy transduction: ATP and NADPH –energized molecules
  - Steady state maintained by energy flow: Steady state not equilibrium
  - Self-replication with high, yet not perfect, fidelity
- Biomolecules
  - Elements: Hydrogen, oxygen, carbon, nitrogen (lightest elements of the periodic table capable of forming a variety of strong covalent bonds)
    - Carbon -4 bonds, nitrogen -3 bonds, oxygen –2 bonds, hydrogen -1 bond
  - Compounds: Carbon-based compounds –versatile
  - Phosphorus- and sulfur-containing compounds play important roles
- Biomolecular hierarchy
  - Simple compounds: H_2O, CO_2, NH_4^+, NO_3^-, N_2
  - Metabolites: Used to synthesize building block molecules
  - Building blocks: Amino acids, nucleotides, monosaccharides, fatty acids, glycerol
  - Macromolecules: Proteins, nucleic acids, polysaccharides, lipids
  - Supramolecular complexes: Ribosomes, chromosomes, cytoskeleton
- Membranes: Lipid bilayers with membrane proteins
  - Define boundaries of cells and organelles
  - Hydrophobic interactions maintain structures
- Organelles: Mitochondria, chloroplasts, nuclei, endoplasmic reticulum Golgi, etc.
- Cells: Fundamental units of life
  - Living state: Growth, metabolism, stimulus response and replication
- Properties of biomolecules
  - Directionality or structural polarity
    - Proteins: N-terminus and C-terminus
    - Nucleic acids: 5'- and 3'- ends
    - Polysaccharides: Reducing and nonreducing ends
  - Information content: Sequence of monomer building blocks and 3-dimensional architecture
- 3-Dimensional architecture and intermolecular interactions (via complementary surfaces) of macromolecules are based on weak forces
  - Van der Waals interactions (London dispersion forces)
    - Induced electric interactions that occur when atoms are close together
    - Significant when many contacts form complementary surfaces
  - Hydrogen bonding
    - Donor and acceptor pair: Direction dependence

- Donor is hydrogen covalently bonded to electronegative O or N
- Acceptor is lone pair on O or N

- Ionic interactions
  - Stronger than H bonds
  - Not directional
  - Strength influenced by solvent properties
- Hydrophobic interactions: Occur when nonpolar groups added to water
  - Water molecules hydrogen bond
  - Nonpolar groups interfere with water H-bonding and to minimize this nonpolar groups aggregate

- Structural complementarity
  - Biomolecular recognition depends on structural complementarity
  - Weak chemical forces responsible for biomolecular recognition
  - Life restricted to narrow range of conditions (temperature, pH, salt concentration, etc.) because of dependence on weak forces. Denaturation: Loss of structural order in a macromolecule
- Enzymes: Biological catalysts capable of being regulated
- Cell types
  - Prokaryotes: Bacteria and archaea: Plasma membrane but no internal membrane-defined compartments
    - Archaea include thermoacidophiles, halophiles and methanogens
  - Eukaryotes: Internal membrane-defined compartments: Nuclei, endoplasmic recticulum, Golgi, mitochondria, chloroplasts, vacuoles, peroxisomes
  - Viruses and bacteriophages: Incomplete genetic systems

Chapter Objectives

Understand the basic chemistry of H, O, N and C.

H forms a single covalent bond. When bound to an electronegative element, like O or N, the electron pair forming the covalent bond is not equally shared, giving rise to a partial positive charge on the hydrogen (this is the basis of H bonds which will be covered in the next chapter). In extreme cases the H can be lost as a free proton.

O forms two covalent bonds and has two lone pairs of electrons. It is an electronegative element and when bound to hydrogen it will cause H to be partially positively charged. O is highly reactive due to its high electronegativity.

N forms up to three covalent bonds and has a single lone pair of electrons. It is an electronegative element and will create a partial positive charge on a hydrogen bonded to it.

C forms four covalent bonds. With four single bonds, tetrahedral geometry is predominant. With one double bond, carbon shows trigonal planar geometry, with an additional pair of electrons participating in a pi bond.

Macromolecules and subunits

Proteins are formed from amino acids composed of C, H, O, N, and in some instances S.
Nucleic acids are formed from nucleotides that are composed of phosphate, sugar and nitrogenous base components. (Nucleosides lack phosphate).
Polysaccharides are made of carbohydrates or sugar molecules.
Lipids are a class of mostly nonpolar, mostly hydrocarbon molecules.

Macromolecular structures

Macromolecular structures are composed of complexes of macromolecules (i.e., proteins, nucleic acids, polysaccharides and lipids). The ribosome, made up of protein and ribonucleic acid, is a prime example.

Organelles

Organelles are subcellular compartments defined by lipid bilayer membranes.

Cell types

There are two fundamental cell types: eukaryotic, having organelles and a defined nuclear region, and prokaryotic, lacking organelles and a membrane-enclosed region of genetic material. The archaea and bacteria comprise the prokaryotes.

are told nothing about modifications in the question and so we should select "nothing (in reduced form)", which is the default anyway. We can leave nearly everything else on the default setting except the "Display the peptides with a mass bigger than" option. Use the pull down menu to select "0" (i.e., zero). Activate the program by clicking on the "Perform" button.

The number of amino acid residues, average molecular mass and monoisotopic mass are all given on the line preceding the list of tryptic fragments. Human insulin receptor substrate-1 has 1242 amino acid residues, has a theoretical isoelectric point (pI) of 8.83 (so it is a basic protein) and an average mass of 131,591. The sequence of the tryptic peptide with mass 1741.9629 is LNSEAAAVVLQLMNIR.

ExPASy is a very useful database devoted to proteins. To get an idea of the kinds of information stored there activate the link to P35568 (located three lines above the table listing the tryptic fragments).

Preparing for the MCAT® Exam

15. Proteases such as trypsin and chymotrypsin cleave proteins at different sites, but both use the same reaction mechanism. Based on your knowledge of organic chemistry, suggest a "universal" protease reaction mechanism for hydrolysis of the peptide bond.

Answer: Peptide bonds are generally quite resistant to hydrolysis. Catalysis, however, might require attack on the carbonyl carbon by a negatively-charged group. For water to be the attacking group, it must be activated to a hydroxide. This would require an environment on the protein in which a water molecule binds and subsequently loses a proton to become activated. For catalysis to be initiated by an amino acid side chain on the protein likely candidates would include serine, threonine and tyrosine. These, however, would have to be activated because they have very high pKa's in solution and do not readily deprotonate. Aspartic acid, glutamic acid and cysteine can be more readily deprotonated but their charge density is low.

16. Table 5.4 presents some of the many known mutations in the genes encoding the α- and β-globin subunits of hemoglobin.

a. Some of these mutations affect subunit interactions between the subunits. In an examination of the tertiary structure of globin chains, where would you expect to find amino acid changes in mutant globins that affect formation of the hemoglobin $\alpha_2\beta_2$ quaternary structure?

b. Other mutations, such as the S form of the β-globin chain, increase the tendency of hemoglobin tetramers to polymerize into very large structures. Where might you expect the amino acid substitutions to be in these mutants?

Answer: Subunit interactions leading to a stable quaternary structure occur between groups on interacting surfaces of the subunits. Often these groups are hydrophobic. So, amino acid mutations on the surfaces of the subunits leading to removal of hydrophobic amino acids might be good candidates for quaternary structure mutants.

Hemoglobin S is a mutation from glutamic acid to valine, which represents a change from a negatively-charged amino acid to a hydrophobic amino acid. The presence of glutamic acid on the surface of hemoglobin is expected to block polymerization due to charge repulsion. In hemoglobin S, however, the valine allows for hydrophobic inaction leading to polymerization.

Questions for Self Study

1. Fill in the blanks. Proteins are linear chains of ___ ___ held together by covalent ___ ____ bonds. Although these bonds are typically drawn as C-N single bonds, they in fact have partial double-bond characteristics because of delocalization of ___ ___. The result of this delocalization is to constrain four atoms in a single plane termed the ___ plane. The four atoms are ___, ___, ___, and ___. Thus, linear chains of amino acids can be considered as a string of ___ carbons joined together by amide or peptide planes.

15. Calculate the frequency of occurrence of an RNAi target sequence
The RNAs acting in RNAi are about 21 nucleotides long. To judge whether it is possible to uniquely target a particular gene with a RNA of this size, consider the following calculation: What is the expected frequency of occurrence of a specific 21-nt sequence?

Answer: The probability of finding a specific 21-nucleotide sequence is simply $(1/4)^{21}$ or 2.27×10^{-12} assuming that we are working with nucleic acid with roughly equal amounts of A, G, C and T. The frequency of occurrence of this sequence is $1/2.27\times10^{-12}$ or one in 4.40×10^{12} nucleotides. The general formula used is $(1/4)^n$ where n is the number of bases and (1/4) is the probability or frequency of a particular base.

16. Calculate the length of a nucleotide sequence whose expected frequency is once per haploid human genome
The haploid human genome consists of 3×10^9 base pairs. Using the logic in problem 15, one can calculate the minimum length of a unique DNA sequence expected to occur by chance just once in the human genome. That is, what is the length of a double-stranded DNA whose expected frequency of occurrence is once in the haploid human genome?

Answer: To answer this we need to solve the following equation for n:

$$\left(\frac{1}{4}\right)^n = \frac{1}{3\times10^9}$$

This is done by taking the log. Thus,

$$n\times\left(-\log 4\right) = -\log\left(3\times10^9\right) \text{ or}$$

$$n = \frac{\log\left(3\times10^9\right)}{\log 4} = 15.7 \approx 16$$

17. Design a sequencing strategy for nucleic acids
Snake venom phosphodiesterase is an a-specific exonuclease (Figure 10.28) that acts equally well on single-stranded RNA or DNA. Design a protocol based on snake venom phosphodiesterase that would allow you to determine the base sequence of an oligonucleotide. Hint: Adapt the strategy for protein sequencing by Edman degradation, as described on pages 10-11 and 114-115.

Answer: One approach might be to simply partially digest the oligonucleotide for varying lengths of time and then analyze the products by mass spectrometry, specifically MALDI-TOF (Matrix assisted laser desorption ionization –time of flight). Complete digestion will only produce individual nucleotides but partial digestion will produce a collection of nucleotides with ragged ends and whose molecular weights differ by loss of a particular nucleotide.

In Edman degradation controlled cleavage of an immobilized peptide releases one amino acid at a time and something similar could be tried with a nucleic acid and an exonuclease, but it could be tricky.

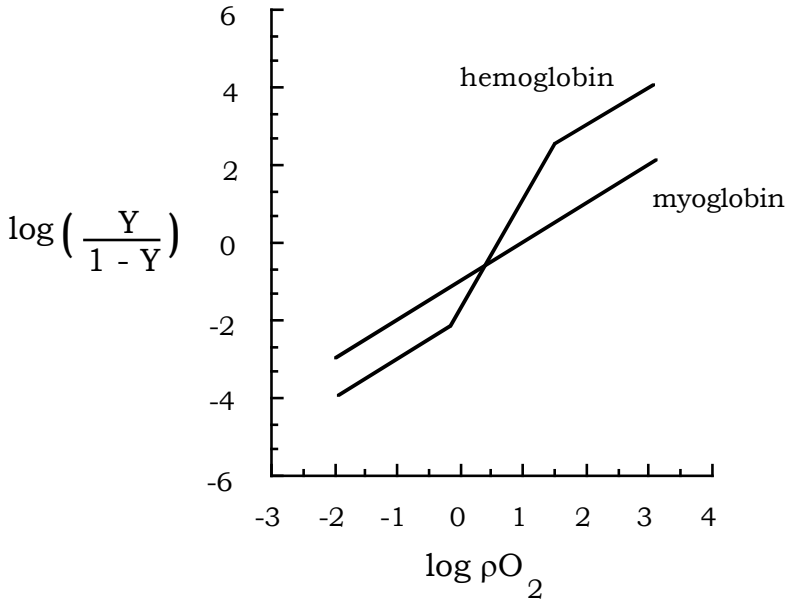
18. Calculate the mass of DNA in a human cell
From the answer to problem 4 and the molecular weights of dAMP (331 D), dCMP (307 D), dGMP (347 D), and dTMP (322 D), calculate the mass (in daltons) of the DNA in a typical human cell.

Answer: In problem 4 we calculated the moles of A, T, C and G in a typical diploid human cell and found the following: A = T = 3.14×10^9 and G = C = 2.68×10^9. The molecular weights given above need to be corrected for loss of water upon phosphodiester bond formation since what gets incorporated into a DNA is a nucleoside monophosphate residue. So, one needs to correct the molecular weights given above by subtracting 18 from each.

Mass of DNA =(331-18)×mole of A + (322-18)×mole of T +(347-18)×mole of G +(307-18)×mole of C
Mass of DNA = 3.59×10^{12} D

Preparing for the MCAT® Exam

19. The bases of nucleotides and polynucleotides are "information symbols." Their central role in providing information content to DNA and RNA is clear. What advantages might bases as "information symbols" bring to the roles of nucleotides in metabolism?



Abbreviated Answers

1. Variations in [product], [S], and [cofactors] have immediate consequences for enzyme activity. The same is true for allosteric regulation. Further, these controls last as long as the signals are present. Genetic controls, such as induction and repression leading to an increase or decrease in enzyme synthesis, are fast, although not immediate, and can be long lasting. Clearly, degradation is long-lasting. However, a delicate balance between synthesis and degradation can lead to a very responsive system of control. Covalent modification may lead to rapid and long lasting changes in enzyme activity. Balancing the activity of modifying enzymes against enzymes that can reverse these modifications creates a sensitive system of enzyme control. Finally, zymogens and isozymes are examples of enzyme control mechanisms that can be extremely long lasting.

2. This histidine, known as the distal histidine because it is on the opposite side of the oxygen-binding site where the so-called proximal histidine is located (see following question), is one of the iron coordinates in both myoglobin and hemoglobin. In hemoglobin, movement of the distal histidine in a single subunit of Hb can influence the accessibility of the oxygen-binding site in the other subunits.

3. The proximal histidine is located close enough to the heme iron so as to prevent carbon monoxide from binding to hemoglobin with optimum geometry.

4. By forming a protein:heme complex, the apparent solubility of heme is greatly increased. Thus, higher concentrations can be maintained without the problem of limited solubility, especially in the presence of oxygen. Because the heme is partially buried in a hydrophobic pocket, it is protected from oxidation. Oxidation produces met-Hb which does not transport oxygen.

5. Oxygen is supplied to the fetal blood system via the placenta where gas exchange occurs between fetal and maternal circulatory systems. Thus, the fetus must successfully compete with adult, maternal hemoglobin for oxygen. This is possible because fetal hemoglobin has a higher affinity for oxygen than adult hemoglobin. The β-chains of adult-Hb are replaced by γ-chains in fetal-HB. A critical function of β-chains is formation of the 2,3-BPG binding-site at the β/β interface of the (αβ) dimer junction. The binding site is composed of eight positive charges, four from each β chain of which three are from side chains and the fourth is from the N-terminus. In fetal-HB, the 2,3-BPG binding-site is considerably weaker due to an amino acid substitution, Ser-143 for His-143, at the 2,3-BPG binding site. As a consequence fetal-HB binds 2,3-BPG less avidly and therefore has a high oxygen affinity.

6. In arterial blood, hemoglobin is oxygenated whereas in venous blood, deoxy-hemoglobin predominates. The change in color upon change in oxygenation state is due to an alteration in the iron coordination. In

$$\frac{3\ H^+}{e^-} \times \frac{e^-}{2\ \text{quanta}} = \frac{3\ H^+}{2\ \text{quanta}}$$

But, ATP is produced by

$$\frac{3\ \text{ATP}}{14\ H^+} \times \frac{3\ H^+}{2\ \text{quanta}} = \frac{9\ \text{ATP}}{28\ \text{quanta}} = \frac{0.32\ \text{ATP}}{\text{quanta}}$$

Quanta (number of photons) per ATP is the inverse of this

$$\frac{3.11\ \text{quanta}}{\text{ATP}}$$

In cyclic photosynthetic electron transport, photosystems I is excited by absorption of light quanta. Thus, one quantum is needed to excite one electron, which translocates 2 protons.

$$\frac{2\ H^+}{e^-} \times \frac{e^-}{1\ \text{quanta}} = \frac{2\ H^+}{\text{quanta}}$$

But, ATP is produced by

$$\frac{3\ \text{ATP}}{14\ H^+} \times \frac{2\ H^+}{\text{quanta}} = \frac{6\ \text{ATP}}{14\ \text{quanta}} = \frac{0.43\ \text{ATP}}{\text{quanta}}$$

Quanta (number of photons) per ATP is the inverse of this

$$\frac{2.33\ \text{quanta}}{\text{ATP}}$$

6. Delta pH and delta psi in the chloroplast proton-motive force
(Integrates with Chapters 20.) In mitochondria, the membrane potential ($\Delta\psi$) contributes relatively more to $\Delta\rho$ (proton-motive force) than does the pH gradient (ΔpH). The reverse is true in chloroplasts. Why do you suppose that the proton-motive force in chloroplasts can depend more on ΔpH than mitochondria can? Why is ($\Delta\psi$) less in chloroplasts than in mitochondria?

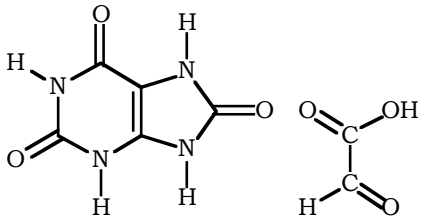
Answer: Both processes involve translocation of protons in response to electron transport. Since protons are charged species, net movement should produce both a proton gradient and a charge separation, leading to an electrical potential. In chloroplasts, however, movement of protons into the thylakoid lumen is countered by movement of Mg^{2+} out of the lumen. The chloroplast is, in effect, leaky to charge and so the electrical potential does not build up to the extent it does in mitochondria. The electrochemical potential across the thylakoid membrane is dominated by the proton gradient. In mitochondria, both a proton gradient and a membrane potential occur.

The pH change that occurs in mitochondria happens in the matrix of the mitochondria and in the cytoplasm of the cell (because the outer mitochondrial membrane is permeable to small molecules). In chloroplasts, however, the change in pH is restricted to the stroma and the lumen of the thylakoids. Mitochondrial pH changes may be restricted in magnitude because of pH-induced activity changes that might accompany large pH changes. The cytoplasm of plant cells does not experience the pH change due to chloroplast activity and so a bigger pH change may be tolerated.

7. The role of Try161 in PSII
Predict the consequences of a Y161F mutation in the amino acid sequence of the D1 and the D2 subunits of PSII.

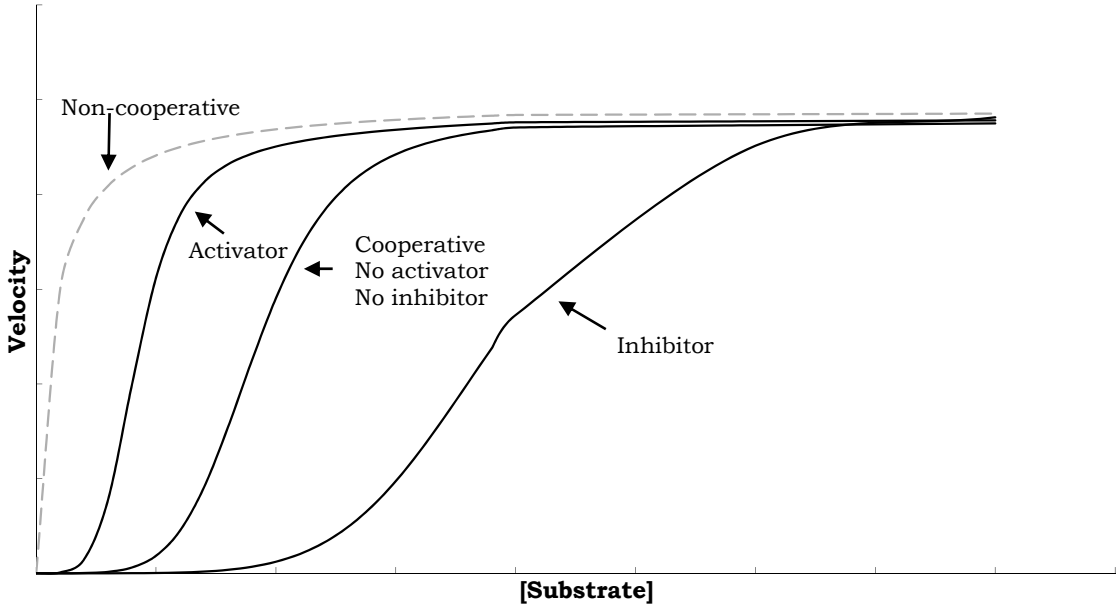
Answer: The notation Y161F indicates a mutation changing the amino acid located at position 161 from tyrosine (Y) to phenylalanine (F). (The codons for tyrosine are UAU an UAC and those for phenylalanine are UUU and UUC. So, a simple one-base transversion of A to T would cause this change.) In photosynthesis, movement of electrons from H_2O to P680 involves manganese and tyrosine 161, which becomes a free radical in its oxidized form. Tyrosine's hydroxyl group participates in the mechanism of electron transfer to a nearby manganese ion. Replacing tyrosine with phenylalanine would clearly prevent this interaction from occurring. This would prevent P680, once activated by light to $P680^*$ and then to $P680^+$ by electron transfer, from returning back to the ground state.

Net: Uric acid + 5 H_2O + ½ O_2 → 3 CO_2 + 4 NH_3 + Glyoxylic acid
By counting elements on both sides of the reaction, you will see that the equation is balanced. The structures of uric acid and glyoxylic acid are shown below.



12. The allosteric kinetics of aspartate transcarbamoylase
E. coli aspartate transcarbamoylase (ATCase) displays classic allosteric behavior. This $\alpha_6\beta_6$ enzyme is activated by ATP and feedback-inhibited by CTP. In analogy with the behavior of glycogen phosphorylase shown in Figure 15.15, illustrate the allosteric v versus [aspartate] curves for ATCase (a) in the absence of effectors, (b) in the presence of CTP, and (c) in the presence of ATP.

Answer: The plot shown below indicates activity of the cooperative enzyme in the absence of allosteric inhibitor and activator and then in the presence of either activator or inhibitor. The dashed line represents a non-cooperative protein. It is clear that activator shifts the cooperative curve to lower substrate concentrations. Inhibitor has the opposite effect. It shifts the cooperative curve to lower substrate concentrations.



13. The functional organization of a heteromeric allosteric enzyme
(Integrates with Chapter 15.) Unlike its allosteric counterpart glycogen phosphorylase (an α_2 enzyme), E. coli ATCase has a heteromeric ($\alpha_6\beta_6$) organization. The α-subunits bind aspartate and are considered catalytic subunits, whereas the β-subunits bind CTP or ATP and are considered regulatory subunits. How would you describe the subunit organization of ATCase from a functional point of view?

Answer: Since each catalytic subunit should be associated with a regulatory subunit we could consider ATCase as a hexomer of $\alpha\beta$ heterodimers or $(\alpha\beta)_6$. When we discussed hemoglobin its structure suggests it is a dimer of heterodimers or $(\alpha\beta)_2$.

when activated go on to phosphorylate other downstream targets, greatly amplifying the original signal. The specificity of these kinases for their immediate targets is enhanced by protein interaction domains located in separate regions of the enzyme. Because catalytic and interaction domains can often fold independently, the activity of one is often independent of the activity of the other. The modular nature of these signaling proteins thus allows for use of common and recognizable protein interaction and catalytic domains to be expressed in different contexts and provide for the high specificity required of signal transduction pathways.

Questions for Self Study

1. Name three classes of chemical species that act as hormones.

2. List the three receptor superfamilies that mediate transmembrane signal processing and give a brief description how signal processing occurs.

3. What two enzymatic activities are responsible for regulating cAMP levels?

4. cAMP is an example of a second messenger. Name five other second messengers.

5. A large family of second messengers can be derived from phospholipase C activity on phosphatidylinositol and its derivatives. Explain.

6. Protein kinase C is sensitive to what two intercellular signals?

7. Membrane-bound guanylyl cyclases and soluble guanylyl cyclases are stimulated by very different signals. What are they?

8. Match a term with its definition.

a. Node of Ranvier	1. Connects to sensory receptor.
b. Synapse	2. Carries nerve impulses away from cell body.
c. Schwann cell	3. Moves nerve impulses to the cell body.
d. Interneuron	4. Insulating layer around axons.
e. Sensory neuron	5. Gap between an axon and a dentrite.
f. Dendrite	6. Moves signals from one neuron to another.
g. Axon	7. Gap between Schwann cells along an axon's length.

9. Answer True of False.
a. Typically, action potentials are induced by a hyperpolerization of the membrane voltage.___
b. Resting potential of an axon is determined by the concentration gradients of all impermeable ions.____
c. During an action potential, the membrane voltage changes from approximately -60 mV to +40 mV because of changes in sodium permeability. ___
d. Potassium permeability changes alone are responsible for returning the action potential back to resting values. ___
e. Action potentials attenuate with distance. ___

10. Fill in the blanks. In cholinergic synpases, small vesicles termed ____ are localized on the inside of the synaptic knob and contain large amounts of the neurotransmitter ____. When an action potential arrives at the synaptic knob, voltage-gated ____ channels open. This is followed by fusion of vesicles with the plasma membrane and release of neurotransmitter into the synaptic cleft. Neurotransmitter induces action potentials in postsynaptic cells by binding to receptors. There are two kinds of receptors ____ and ____ distinguished by there responses to a toxic alkaloid in toadstools or to nicotine. Neurotransmitter action is usually short lived because it is rapidly hydrolyzed by the enzyme ___.

11. Match

a. Endorphin	1. Binds to nicotinic receptors and blocks their opening.
b. Catecholamine	2. Insecticide that blocks muscarinic receptor.
c. Glycine	3. Excitatory amino acid transmitter.
d. Glutamate	4. Epinephrine.
e. Malathion	5. Peptide neurotransmitter.
f. d-tubocurarine	6. Inhibitory amino acid transmitter.