Week 12: 11/10 - 11/14

Topic(s): Nucleic Acid Structure & Reactions, DNA Topology and Chromatin

Nucleic Acid Structure & Reactions

1. Which of the following contributes most to DNA stability?
    a. Hydrogen bonding
    b. Base Stacking
    c. DNA coiling
    d. DNA backbone

2. Base Pairing Specificity
    a. Draw the base that pairs with guanine and label hydrogen bonds

    b. Which base pair (A-T or G-C) is more stable and why?

3. What are tautomers?

    a. Try to draw an imino C:amino A base pair. Is this possible? If so, how many hydrogen bonds form?

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4. Polarity:
    a. Label the 5' and 3' ends of both strands of DNA

    b. Why must new nucleotides be added only to the 3' end?

DNA Topology and Chromatin

1. You have a plasmid template that is 3,400 bp. What is the linking number (Lk), Twist (Tw), and Writhe (Wr) of this plasmid when it is in the relaxed state?

2. Topology influences the physical properties of DNA with important implications for gene expression and genome replication.

    a. Given a strand of DNA with 252 base pairs, what is its Lk_0?

    b. What does Lk_0 tell us about DNA?

    c. If ethidium bromide is added to the DNA, does Lk_0 change? Why or why not? If it changes, what is the new Lk_0?

3. You introduce 5 turns of negative supercoiling — what happens to Tw and Wr if Lk is constant?

Week 11: 11/3 - 11/7

Topic(s): Fatty Acid Metabolism and Amino Acid Metabolism

Fatty Acid Metabolism

1. Consider the catabolism of a saturated fatty acid, stearic acid ($C_{18}H_{36}O_2$), which has an 18-carbon chain. This fatty acid undergoes beta-oxidation in the mitochondria.
    a. Calculate the total number of beta-oxidation cycles required to completely break down stearic acid.

    b. Based on the number of beta-oxidation cycles calculated above, determine how many molecules of NADH and $FADH_2$ are generated in total.

    c. Calculate the total number of acetyl-CoA molecules produced from the complete breakdown of stearic acid.

    d. Assuming each NADH produces 2.5 ATP and each $FADH_2$ produces 1.5 ATP in the electron transport chain, calculate the total ATP generated from the NADH and $FADH_2$ produced in beta-oxidation.

2. Describe the role of acetyl-CoA carboxylase in fatty acid metabolism and how it is regulated.

3. Explain how elevated cytosolic malonyl-CoA levels can inhibit fatty acid oxidation and promote fatty acid synthesis, and describe one physiological situation where this occurs.

Amino Acid Metabolism

4. Evaluate the consequences of overexpressing chorismate mutase in transgenic plants.

5. A field population of weeds shows resistance to glyphosate, but DNA sequencing reveals no mutation in the EPSPS active site. What are two other possible molecular explanations for their resistance?

6. If a mutation caused overactive anthranilate synthase (Trp pathway), how might this affect levels of Tyr and Phe?

Week 10: 10/27 - 10/31

Topic(s): Citric Acid Cycle & Oxidative Phosphorylation

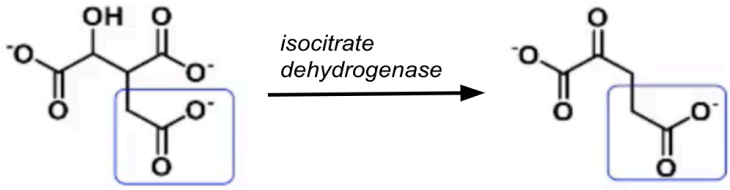
Citric Acid Cycle

1. The conversion of Pyruvate to Acetyl-CoA is an important step that prepares us for TCA.
    a. What are the five cofactors involved in this reaction?

    b. What are the roles of the cofactors? Expand on each of the cofactors.

    c. Explain the role of each enzyme: E1, E2, and E3. What is the name of these complexes combined?

2. Consider the following step of the citric acid (TCA) cycle:



isocitrate *α-ketoglutarate*

a. What cofactors are needed to catalyze this reaction?

b. Isocitrate dehydrogenase is the enzyme that catalyzes this reaction. If isocitrate dehydrogenase were subject to feedback regulation, what products might be inhibitory?

c. What are the important end products of the citric acid cycle and where do they go?

3. During intense exercise, oxygen supply to muscle temporarily drops. Researchers find that the mitochondrial [NADH]/[NAD^+] ratio increases sharply, while [α-ketoglutarate] and [succinate] accumulate. Meanwhile, [oxaloacetate] levels remain very low.

a. Why does limited oxygen availability cause NADH to accumulate in the mitochondrial matrix?

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b. How does this high NADH level affect the activity of isocitrate dehydrogenase and α-ketoglutarate dehydrogenase, and what happens to flux through the TCA cycle?

c. Explain why succinate levels might rise even though the overall cycle slows down

Oxidative Phosphorylation

1. How much H+ is pumped per NADH? What about FADH2? What accounts for the difference, and how does this relate to the "spin" of ATP synthase with regards to ATP production?

2. Photophosphorylation is a key process for plants to produce energy.

    a. What molecule acts as the source of electrons?

    b. What molecule is the ultimate electron acceptor?

c. Draw the path of electrons starting from P680 through PS I to PS II and ultimately to NADPH.

d. What is the net product of C02 assimilation?

Week 9: 10/20 - 10/24

Topic(s): Regulation of Glycolysis and Gluconeogenesis

Regulation of Glycolysis

1. Immediately after a meal, insulin signaling increases, activating phosphoprotein phosphatase in hepatocytes.
    a. Describe the change in phosphorylation state of the bifunctional enzyme PFK-2/FBPase-2.

    b. How does this alter fructose-2,6-bisphosphate (F2,6BP) levels?

    c. Predict the resulting direction of metabolic flux between glycolysis and gluconeogenesis.

d. Which glycolytic enzymes' expression will increase transcriptionally due to insulin? (Hint: Lecture 5 Table 15-5 → HK II/IV, PFK-1, PK L).

Regulation of Gluconeogenesis

1. A person is 12 hours into an overnight fast. Glucagon levels rise and PKA is active in the liver.
    a. Describe the phosphorylation state of the bifunctional enzyme PFK-2/FBPase-2 and the resulting F2,6BP concentration.

b. How do these changes influence PFK-1 and FBPase-1 activities?

c. Name one additional glycolytic enzyme that is directly inactivated by phosphorylation and explain the physiological reason for this.

d. Overall: which pathway dominates—glycolysis or gluconeogenesis—and why?

Week 8: 10/13 - 10/17

Topic(s): Glycolysis, Gluconeogenesis, and Regulation

Glycolysis

1. What is the **first committed step** of glycolysis, and why is this enzyme considered a major regulatory point?

2. Why does glycolysis continue under anaerobic conditions, even though no additional ATP is generated beyond substrate-level phosphorylation?

Gluconeogenesis

1. What is the role of **biotin** in pyruvate carboxylase, and what molecule activates this enzyme?

2. List the three **irreversible steps of glycolysis** and the **corresponding bypass reactions** in gluconeogenesis.

Enzyme Regulation

1. Why are **PFK-1** and **FBPase-1** considered reciprocal control points rather than reversible enzymes?

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2. Compare the total ATP yield from glycolysis with the total ATP **cost** of gluconeogenesis. Why is this difference important for regulation?

3. A mutation causes **fructose-1,6-bisphosphatase (FBPase-1)** to lose sensitivity to **AMP inhibition**. What is the most likely physiological consequence?
    a. Excessive glycolysis and hypoglycemia
    b. Accumulation of pyruvate and lactate
    c. Uncontrolled gluconeogenesis and hyperglycemia
    d. Increased ATP synthesis through substrate-level phosphorylation

Week 7: 10/6 - 10/10

Topic(s): Bioenergetics, Redox Reactions

Bioenergetics

This problem set is designed to provide supplemental practice problems related to course concepts. While we do not post the solutions, we would be happy to discuss the problems with you in drop-in services.

1. What information can:
    a. $\Delta G^{\circ\prime}$ tell us?

    b. ΔG tell us?

2. What is the difference between a reaction being favorable and a reaction being fast?

    A. What are the favorable steps in glycolysis? Unfavorable? How can you tell?

3. Given:
   $\Delta G^{\circ\prime}$ for glucose + Pi → glucose-6-phosphate + H2O = +13.8 kJ/mol.
   $\Delta G^{\circ\prime}$ for ATP + H2O → ADP + Pi = −30.5 kJ/mol.

a. Write the overall coupled reaction catalyzed by hexokinase.

b. Compute the overall $\Delta G^{\circ\prime}$.

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c. With [glucose] = 0.20 mM, [glucose-6-P] = 1.0 mM, [ATP] = 2.5 mM, [ADP] = 0.20 mM, compute the actual ΔG and state if the step is favorable.

Redox

1. A redox reaction has a E'o of 0.77 V. Given that 2 electrons are transferred in this reaction, find the ΔG° of this cell.

2. In the complete oxidation of the three-carbon molecule Lactate ($CH_3CH(OH)COO^-$) to Carbon Dioxide (CO_2), how many electrons are formally lost from the entire molecule?

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Week 6: 9/29 - 10/3

Topic(s): Nucleic Acids, Lipids

Nucleic Acids

1. Identify and draw the nucleic acid base that is only found in RNA and **not DNA**. Number the heterocyclic atoms accordingly.

2. Draw the structure of the thymine nucleotide.

    a. Number the carbons in the sugar and the nitrogenous base.

    b. What are the hydrogen bond donors and acceptors?

c. Add the nucleotide that thymine bonds to in your drawing. Be sure to indicate where the hydrogen bonds are formed.

d. Add a guanine nucleotide to the 3' end of the thymine nucleotide, and add its appropriate base pair to the opposite strand.

e. Did you draw DNA or RNA? How would you change your drawing if you wanted to switch between DNA and RNA?

3. What base is found in RNA, but not DNA? Draw the structure below.

4. Rank the following complexes in terms of stability in heat: DNA:DNA, DNA:RNA, RNA:RNA

5. What is the key structural difference in the sugar between RNA and DNA nucleosides?

a. What explains these differences in stability?

b. Many techniques can be used to analyze nucleic acids in the lab. When is melting temperature relevant in using these techniques?

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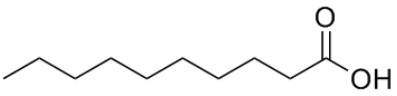
Lipids

1. How does the presence of one or more double bonds in a fatty acid chain affect its physical properties, such as melting point and shape? Give an example.

2. When phospholipase C acts on a membrane glycerophospholipid, what are the two main products formed?
    a. Diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP_3)
    b. Phosphatidic acid and ceramide
    c. Sphingosine and cholesterol
    d. Phosphatidylcholine and fatty acids

3. How do each of these lipids contribute to the fluidity of a cell membrane?

I.



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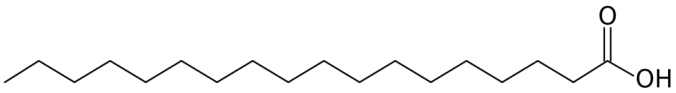

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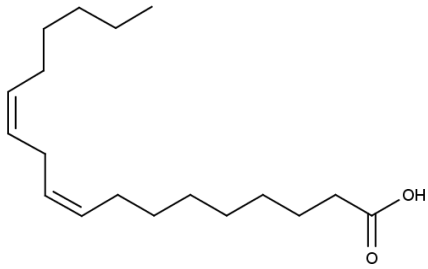

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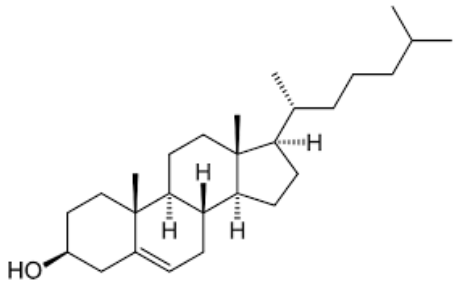
IV. 

Week 5: 9/22 - 9/26

Topic(s): Enzyme Mechanisms (Chymotrypsin), Binding, Regulation, Carbohydrates

1. **α-Chymotrypsin Catalytic Mechanism**
    a. Describe the role of the catalytic triad (Ser195, His57, Asp102) in the mechanism of α-Chymotrypsin. How do these residues cooperate to facilitate peptide bond hydrolysis?

    b. **Multiple Choice:** Why does α-Chymotrypsin specifically cleave peptide bonds following large hydrophobic amino acids like phenylalanine, tryptophan, and tyrosine?
        i. Because the active site has charged residues that bind hydrophilic groups
        ii. Because the enzyme's specificity pocket is hydrophobic and accommodates bulky aromatic side chains
        iii. Due to covalent bonding formed only with small amino acids
        iv. Because the enzyme has flexibility to cleave any peptide bond regardless of residue

2. α-Chymotrypsin Enzyme Regulation

a. **True or False:** The S1 pocket in α-Chymotrypsin is responsible for determining substrate specificity based on the shape and chemical properties of the side chain of the amino acid preceding the peptide bond.

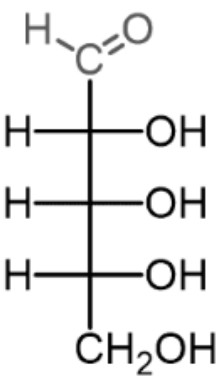
b. How might cooperative binding or allosteric regulation affect the activity of serine proteases related to α-Chymotrypsin?

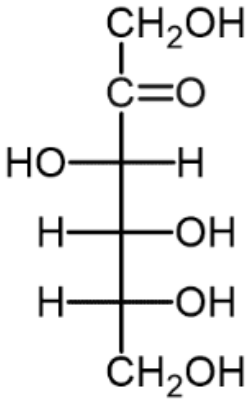
3. Answer the following questions about carbohydrates:

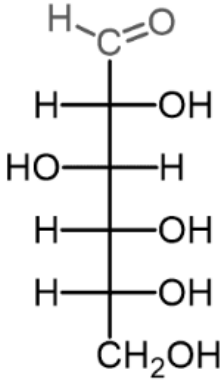
a. Examine each sugar in the diagram. For each, indicate whether the structure is a pentose or hexose and if it contains an aldehyde or ketone functional group. Mark the functional group directly on the diagram.

b. Identify all chiral centers within each sugar. For one sugar, number the carbons and list which carbons are chiral. Explain how to determine the absolute configuration (R/S) at one selected carbon using the Cahn-Ingold-Prelog rules.

c. If each sugar were converted to its cyclic (Haworth) form, predict whether the resulting ring would be a furanose or pyranose. Provide reasoning based on the position of the reactive groups in the Fischer projection.





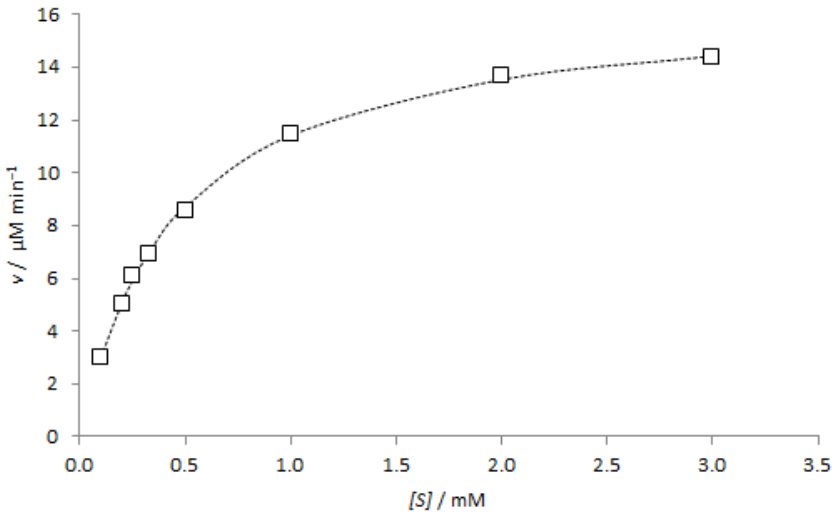


4. The graph below shows the activity of a particular enzyme.

   a. Approximate V_{max}. What is the substrate concentration at V_{max}?

   b. What is K_m? How would you use the graph below to find the K_m of this enzyme?

   c. Use the Michaelis-Menten equation to find the V_0 of this enzyme at [S] = 2 mM.



   d. Describe two limitations of Michaelis-Menten in which the model no longer holds up.

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Week 4: 9/15 - 9/20

Topic(s): Amino Acids, Henderson-Hasselbach, Protein stability and folding, Michaelis-Menten Equation and Enzyme Kinetics, ΔG° (Free energy calculations)

1. Suppose that you are studying a polypeptide chain consisting of the following Amino Acid sequence: G - T - D - K - S - Q - N - R. Find the net charge of the polypeptide chain at the following pH's (if pKa is within 1.0 of the given pH, assume it is half protonated, half deprotonated):4

    a. pH = 2

    b. pH = 8

    c. pH = 11

2. **True or False:**
    a. T/F At physiological pH, arginine will have at least one ionizable group that is uncharged.

    b. T/F Beta turns are necessary for antiparallel chains to interact through H-bonds

    c. T/F Hydrophobic interactions explain why the olive oil in an open bottle does not readily evaporate.

3. **Bioenergetics**
    a. At equilibrium, what is your ΔG and K'eq?

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4. **Michaelis-Menten and Enzyme Kinetics:** Two enzymes, E1 and E2, both act on the same substrate in a metabolic pathway.
    i. E1 has a very **low Km** (high affinity) but also a relatively **low Vmax**.
    ii. E2 has a **high Km** (low affinity) but a **high Vmax**.

    b. In a cellular environment where substrate concentration is usually low, which enzyme would be more effective? What about if the substrate concentration suddenly spikes very high? Explain in terms of Michaelis–Menten kinetics.

5. **Henderson-Hasselbach:** You are studying a peptide containing a **histidine** side chain (pKa ≈ 6.0). The peptide is placed in a buffer at **pH 7.4**.
    a. Use the **Henderson–Hasselbalch equation** to calculate the ratio of deprotonated to protonated histidine side chains.

    b. How would the charge state of histidine influence the peptide's ability to bind to a negatively charged phosphate group at this pH?

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