Section 1: Multiple Choice. 15 questions, 2 points each. Fill in the blank with the appropriate letter.

1. Which of the following statements is NOT true? In order for the Michaelis-Menton treatment of enzyme kinetics to be true,
   A) The concentration of substrate must be much less than $K_M$.
   B) The concentration of enzyme must be much less than substrate.
   C) The rate of the reaction must be measured as an initial rate.
   D) The reaction must be zero order with respect to enzyme.
   E) The enzyme–substrate complex must be at steady-state concentration.

2. Most enzymes have a pH optimum which can be represented as a _______ curve.
   A) rectangular hyperbolic
   B) bell-shaped
   C) linear
   D) sigmoidal
   E) Inversely proportional

3. During the early stages of an enzyme purification protocol, when cells have been lysed but cytosolic components have not been separated, the reaction velocity versus substrate concentration is sigmoidal. As you continue to purify the enzyme, the curve shifts to the right. Explain your results.
   A) This is an enzyme that displays Michaelis–Menten kinetics, and you purify away an allosteric inhibitor.
   B) This is an enzyme that displays Michaelis–Menten kinetics, but you must use a Lineweaver–Burk plot to determine $K_M$ and $V_{max}$ correctly.
   C) This is an allosteric enzyme, but you must use a Lineweaver–Burk plot to determine $K_M$ and $V_{max}$ correctly.
   D) This is an allosteric enzyme, and during purification you purify away an allosteric activator.

4. The antibiotic penicillin is an example of a _______ inhibitor.
   A) competitive
   B) noncompetitive
   C) transition state analog
   D) mechanism based
   E) affinity label
5. **C** In this catalytic strategy, a cofactor serves as an electrophile to stabilize a negative charge on a reaction intermediate.
   A) covalent catalysis
   B) allostERIC catalysis
   C) metal ion catalysis
   D) catalysis by approximation and orientation
   E) irreversible catalysis

6. **A** Evidence for this catalytic strategy was suggested for chymotrypsin by burst kinetics.
   A) covalent catalysis
   B) general acid–base catalysis
   C) metal ion catalysis
   D) catalysis by approximation and orientation
   E) irreversible catalysis

7. **C** Which statement concerning the structure of myoglobin and hemoglobin is FALSE?
   A) Myoglobin is a single subunit, but hemoglobin is a multisubunit protein.
   B) Both bind oxygen through a heme-bound iron atom.
   C) Both myoglobin and hemoglobin bind 2,3-BPG tightly.
   D) Both myoglobin and hemoglobin have α-helices as their dominant secondary structure.
   E) Both myoglobin and hemoglobin coordinate an iron atom through a histidine residue.

8. **D** Which of the following lipids would not be involved in a lipid bilayer structure?
   A) phospholipid
   B) cholesterol
   C) glycolipid
   D) triacylglyceride
   E) All of the above are involved in lipid bilayers.

9. **C** Which of the following statements concerning glycoproteins is FALSE?
   A) Some glycoproteins are more carbohydrate than protein by weight.
   B) Glycoproteins are either N-linked or O-linked.
   C) Glycoproteins are integral or peripheral membrane proteins with oligosaccharides facing the cytosolic side of the membrane.
   D) Glycoproteins are often involved in recognition and protection of the cell.
   E) Blood-types A, B, and O differ based on the oligosaccharide antigen on glycoproteins in red blood cells.
Questions 10-11 refer to the chart below.

The graph below shows several oxygen binding curves. Assume that curve 3 corresponds to hemoglobin with physiological concentrations of CO₂ and 2,3-BPG at pH 7.

10. C If the concentration of 2,3-BPG were to increase, the binding curve would
   A) Shift from curve 3 to curve 1.
   B) Shift from curve 3 to curve 2.
   C) Shift from curve 3 to curve 4.
   D) Remain at curve 3.

11. A If hemoglobin lost its quaternary structure, the binding curve would
   A) Shift from curve 3 to curve 1.
   B) Shift from curve 3 to curve 2.
   C) Shift from curve 3 to curve 4.
   D) Remain at curve 3.

12. D The signal transduction pathway for β-adrenergic receptor follows the following pattern
    A) Ligand → receptor tyrosine kinase → G-protein → protein kinase A → cAMP → effects
    B) Ligand → receptor → transducer → G-protein → second messenger → effects
    C) Hormone → G-protein → receptor → cAMP → protein kinase A → effects
    D) Hormone → 7-TM helix → G-protein → second messenger → protein kinase A → effects

13. A Which of the following is a digestive enzyme for polysaccharides that operates in the intestine.
    A) amylase
    B) pepsinogen
    C) maltase
    D) lipase
    D) nuclease
14. **E** The catalytic parameter that measures the efficiency of an enzyme is
   A) $K_M$
   B) $k_{cat}$
   C) $V_{max}$
   D) $k_{on}$
   E) $k_{cat}/K_M$

15. **D** Which of the following statements concerning gastric proton pump is TRUE?
   A) The proton pump in the stomach pumps protons and potassium out of the cell and into the stomach through an antiport mechanism.
   B) The proton pump, also known as $K^+/H^+$ ATPase, is a passive transporter.
   C) Protons are pumped out of the stomach lining cells, leaving a high concentration of hydroxide in the cells.
   D) Medicines such as omeprazole (Prilosec) lower stomach acid levels by irreversibly inhibiting the gastric proton pump.

Section 2: Fill in the blank. 15 questions 2 points each

16. According to the Bohr effect, a proton stabilizes the __________ (relaxed/tense) form of hemoglobin, and therefore the oxygen binding affinity of hemoglobin __________ (increases/decreases) at low pH.

17. An example of a hexoketose is __________.

18. A Michaelis-Menten graph is plotted with __________ as a function of __________.

19. In plants, glucose molecules can be linked through $\beta(1 \rightarrow 4)$ glycosidic bonds into __________, which serves structural roles.

20. $\omega$-3 fatty acids must be part of the human diet because they are __________ fatty acids.
21. **Ras** is a G-protein involved in pathways that involve cell growth and division.

22. Triacylglycerides and other lipids are packaged into **chylomicrons** in intestinal cells so that they can be transported in water-soluble form through the lymph.

23. ABC transporters are part of a superfamily of transporters that have two transmembrane domains and two domains that bind **ATP**, which is necessary for active transport.

24. **α-D-glucose** is an anomer of β-D-glucose.

25. **β-D-mannose (or galactose)** is an epimer of β-D-glucose.

26. A gene that has been mutated, leading to cancer, is known as an **oncogene**.

27. Proteolytic enzymes do not digest tissues because they are made in **zymogen** form prior to activation.

28. Subunits of hemoglobin behave **cooperatively**; the binding of the first oxygen molecule to hemoglobin increases hemoglobin's affinity for more oxygen molecules.

29. When the product of a reaction at the end of a metabolic pathway inhibits an enzyme near the beginning of the pathway, this is called **feedback** inhibition.

30. Receptor tyrosine kinases are activated through the process of **autophosphorylation** when two subunits are brought close together upon ligand binding.
Section 3. Problems. 5 questions 10 points each.


Draw the alpha-anomer of a disaccharide in which mannose is linked to galactose through $\beta(1\rightarrow6)$ linkage. (The mannose is on the reducing end of the disaccharide.)
Problem 7.24

32. Enzyme catalysis of the cleavage of peptide bonds in small peptides by a proteolytic enzyme is described in the following table. (The arrows indicate the peptide bond that is cleaved in each case.)

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Substrate</th>
<th>$K_m$ (mM)</th>
<th>$k_{cat}$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>EMTA↓G</td>
<td>4.0</td>
<td>24</td>
</tr>
<tr>
<td>B</td>
<td>EMTA↓A</td>
<td>1.5</td>
<td>30</td>
</tr>
<tr>
<td>C</td>
<td>EMTA↓F</td>
<td>0.5</td>
<td>18</td>
</tr>
</tbody>
</table>

A. If a mixture of these peptides were presented to the enzyme with the concentration of each substrate being the same, which peptide would be digested most effectively? Explain.

- Use enzyme efficiency, $\frac{k_{cat}}{K_m}$

- Exp C has highest $\frac{k_{cat}}{K_m}$, so EMTAF is best substrate

B. If the peptide EMTA↓F is digested, $K_m = 9$ mM and $k_{cat} = 18$ s$^{-1}$. What do these data suggest about the specificity of the enzyme?

- $\frac{k_{cat}}{K_m} = \frac{18 \text{ s}^{-1}}{9 \text{ mM}} = 2$, so not a good substrate.

- This suggests a large hydrophobic like isoleucine should not be in the first position

C. Fill in the table below with appropriate values for $K_m$ and $k_{cat}$ if Experiment A were re-run under these altered conditions. (For instance, “lower than ___” is an acceptable response.)

<table>
<thead>
<tr>
<th>Conditions</th>
<th>$K_m$ (mM)</th>
<th>$k_{cat}$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.0</td>
<td>24</td>
</tr>
<tr>
<td>[E] doubled</td>
<td>4.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Competitive inhibitor added</td>
<td>higher 4.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Noncompetitive inhibitor added</td>
<td>4.0</td>
<td>lower than 2.4</td>
</tr>
</tbody>
</table>
33. The catalytic triad of chymotrypsin is shown below:

![Catalytic Triad Diagram]

A. What type of reaction does chymotrypsin catalyze?

② peptide hydrolysis

B. What is the role of each member of the catalytic triad in catalyzing this reaction?

① A. Asp Increase basicity of His through H-bond

② B. His General base to activate ser Nu:

③ C. Ser Nucleophile (Covalent catalysis)

C. What is the purpose of the oxyanion hole in chymotrypsin?

② stabilize the alkoxide anion of the tetrahedral intermediate

D. Predict the effect of mutating aspartate in the active site of chymotrypsin to asparagine.

③ Asn is neutral, so it would not stabilize the protonated His as well. Therefore serine would not be as active of a Nu:, decreasing enzyme activity
34. Reversible inhibition

A. All reversible inhibitors bind to an enzyme, but how does an uncompetitive inhibitor act differently than a noncompetitive inhibitor in its binding?

An uncompetitive inhibitor binds only to ES complex, but noncompetitive binds to Free enzyme or ES complex

B. The following graph was determined for an enzyme with no inhibitor, represented by curve 1. The enzyme was then treated with a competitive inhibitor, an uncompetitive inhibitor, and a noncompetitive inhibitor. Which type of inhibitor produced curves 2-4?

<table>
<thead>
<tr>
<th>Curve</th>
<th>Type of Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>competitive</td>
</tr>
<tr>
<td>3</td>
<td>non competitive</td>
</tr>
<tr>
<td>4</td>
<td>uncompetitive</td>
</tr>
</tbody>
</table>

C. Draw a Lineweaver-Burk plot of the enzymatic rate data of an enzyme with no inhibitor present. Label the axes of the graph, and label the curve as “no inhibitor.” Then, on the same graph, draw a curve for the enzymatic rate data with a competitive inhibitor present.
35. Consider the following Figures in answering the questions below.

A. A scheme of the sodium-glucose linked transporter is shown above. If this symporter were inhibited, what effect, if any, would such inhibition have on the sodium-potassium pump?

+4 It would eventually inhibit the pump. If Na⁺ were not coming back into the cell, its gradient would build up so much that the energy of ATP could not increase the gradient more.

B. If ouabain, a specific inhibitor of the sodium-potassium pump, were added to this system, what would happen to the curve relating the rate of glucose transport to concentration of glucose? Draw this graph below.

+3 Glucose transport would be inhibited. (Secondary transport.)

Any graph suggesting lower rate

C. What does the curve for indole transport suggest about its mechanism of crossing the membrane?

+3 It is not under saturation kinetics, so it does not use a channel. It must diffuse across the membrane.