1) **(2 pts)** Define catabolism and anabolism. One sentence each should be fine.

Catabolism - group of metabolic pathways that break down molecules to gain energy and precursors for biosynthesis  
Anabolism - group of metabolic pathways that build macromolecules such as RNA, DNA, lipids, proteins and various cell and organ structures

2) **(3 pts)** Two peptides are listed below using the one letter code for each amino acid.

   a) RKDE  
   b) LYWF

   i) Which peptide is more hydrophobic __b__ : L, Y, W and F are all have hydrophobic R groups

   ii) Which peptide has more charged groups __a__ R, K positive R groups; D, E neg. R groups

   iii) Write each peptide, using the usual first three letter for each amino acid. Example: APL would be AlaProLeu

      a) ArgLysAspGlu  
      b) LeuTyrTrpPhe

3) **(3 pts)** Entropy reduction, acid-base catalysis, metal ion catalysis, and covalent intermediate formation are four ways that enzymes catalyze reactions.

   a) Which is one the chymotrypsin mechanism does NOT use: **Metal Ion Catalysis** (no metal ions in mechanism)

   b) Which most directly involves the catalytic triad serine: **Cov. intermediate formation** (attached to Ser OH group)

   c) Which most directly involves the catalytic triad histidine: **acid-base catalysis** (His R group accepts and donates H+ during reaction cycle)

4) **(2 pts)**

   a) For a given reaction converting S to P. Draw a sketch of the energy diagram to depict the ΔG and the ΔG‡

5) **(2 pts)** For a simple, Michaelis-Menton type enzyme, write the term for fraction f of maximum rate as a function of substrate concentration. Hint: the term only goes between 0 and 1

   \[ f = \frac{S}{(S+K_m)} \]
6) (2 pts) As you know, $k_{cat} = V_{max} / E_T$ What property of an enzyme does $k_{cat}$ describe, in English?

$k_{cat}$ describes the number of reactions catalyzed per second per enzyme molecule at maximum velocity

7) (3 pts) You have a beaker with S and P in equilibrium. You add an enzyme E that increases the S to P rate by $10^7$. Describe what happens to the P to S rate, and the ratio $[P]/[S]$. One sentence:

The P to S rate will increase by $10^7$ (just like the S to P rate) and the ratio will stay the same.

8) (4 pts) The following branched pathway has a reaction catalyzed by Rase, that "decides" how much S becomes P1 or P2.

\[ \begin{align*}
A & \rightarrow B \rightarrow S \\
C & \rightarrow D \rightarrow P_1 \\
E & \rightarrow F \rightarrow P_2 \\
\end{align*} \]

a) Describe a plausible scheme in which P1 and P2 are allosteric regulators of Rase that would tend to keep the production of each product in balance. (One sentence):

Let P1 be an allosteric inhibitor of Rase, and P2 be an allosteric activator of Rase, that way, high P1 will promote the synthesis of P2, and high P2 will promote the synthesis of P1.

b) Draw a graph showing the Rase reaction rate as a function of S with no added regulator, added P1 or added P2, according to your scheme.

No regulator is in \textbf{BLACK}, plus \textbf{P1 is in RED}, and \textbf{plus P2 is in GREEN}.

9) (4 pts) The picture below is the "business end" of the NAD cofactor.

a) Is this the oxidized form or the reduced form? \underline{oxidized from} \underline{red}.

b) Draw the other form \underline{next to} the one depicted. \textit{Anything like this is fine; key points: no charge, no aromatic, two Hs}.

c) Name one enzyme that uses this cofactor in its catalytic cycle:
10) (1 pt) An enzyme allows ATP to drive a chemical reaction. The reaction without ATP has a \( \Delta G^o \) of 10 kJ/mole, and the ATP \( \Delta G^o \) is -36 kJ/mole. What is the \( \Delta G^o \) of the enzymatically catalyzed reaction?

\[
10 + (-36) = -26 \text{ kJ/mole}
\]

11 (4 pts) The following skeletal picture of glucose has the carbons each labeled with a number.

a) Which carbon(s) is oxidized by NAD+ in glycolysis? \( 3, 4 \)

b) Which carbons receive phosphate from ATP in glycolysis? \( 1, 6 \)

c) Which pairs of carbons end up being indistinguishable as glycolysis proceeds? a) 1 and 5; b) 3 and 4; c) 1 and 6; B and C; d) none

Correct letters: b (3 and 4), c (1 and 6)

12) (2 pts) Draw the structure of glyceraldehyde 3 phosphate. any number of variations accepted…

13) (2 pts) The product of the glyceraldehyde 3 phosphate dehydrogenase enzyme is 1,3 bisphosphoglycerate. Where do each of these phosphates come from during glycolysis? The 1-P is on the carboxyl (One sentence)

The 1 phosphate comes from free phosphate ion that enters the G3PDH reaction, and the 3 P comes from ATP added during the preparatory phase.

14) (3 pts) In class we discussed the two hexokinase isozymes: hexokinase and liver-specific glucokinase.

a) Sketch an enzyme rate curve as a function of glucose concentration for each isozyme, to the right. No need for concentrations.

b) Why are the liver-specific isozyme's kinetic properties useful? One sentence

The liver-specific glucokinase has a saturation curve that allows it to act over the broad range of glucose concentrations encountered by the liver without saturation.
15) (5 pts) Word problem!! You have developed a drug, Tristatin, that is a potent inhibitor of the triose phosphate isomerase (TPI). You add Tristatin to cells in culture, using enough to completely inhibit TPI. Let's think about the effect of this drug.

   a) Write the reaction catalyzed by TPI. Use the provided structure to complete the reaction. If you need cofactors or other stuff, add them. Write the names of reactants and products.

   TPI converts DHAP into G3P, allowing use of all six glucose carbons in later glycolysis steps

   ![DHAP and G3P structures]

   We will now explore the effects of complete inhibition of TPI by Tristatin on glycolysis.

   b) How many ATP will be produced per glucose molecule in drug treated cells? ___2 total___

   c) How many ATP will be consumed per glucose molecule in drug treated cells? ___2 total___

   d) How many NADH will be produced per glucose molecule in treated cells? ___1 total___

   e) Which glucose carbon(s) will be in the carboxyl group in pyruvate produced in Tristatin-treated cells, using the numbers 1-6 above ___only carbon 4___

16) (4 pts) What are the two main products produced by the pentose phosphate pathway. Write them below and briefly describe their function:

   a) ___NADPH___: major anabolic reducing agent in cell

   b) ___Ribose-5 phosphate___: used in backbone of DNA, RNA (and for synthesis of a variety of sugars)

17) (1 pt) The pentose phosphate pathway and glycolysis share a common substrate molecule. What is it?

   ___Glucose-6-P_____
18) (6 pts) Look! It is our BMFF (best molecular friend forever) pyruvate (chi-co-coo). Answer the following questions about pyruvate.

(2 pts) In organisms or cells that are only using glycolysis for energy production, it is critical to restore NAD+. Why is this so?

NAD+ is required for glycolysis to proceed; the G-3-P dehydrogenase reaction can not occur without NAD+, and without this step, glycolysis can not occur.

What are two ways involving pyruvate that allows cells using only glycolysis to restore NAD+

a) Convert pyruvate to lactate with lactate dehydrogenase, which transfers electrons from NADH to lactate, producing NAD+

b) Oxidative decarboxylation of pyruvate by production of ethanol and NAD+

Write the balanced reaction (no need for structures) for the enzymatically catalyzed reaction in which ethanol is generated from pyruvate. Include all reactants and products. No need for cofactors such as TPP.

\[
CH_3-CO-CO_2^- + NADH + 2H^+ \rightarrow CO_2 + EtOH + NAD^+
\]

19) (2 pts) Speaking of cofactors, the cofactor TPP, first introduced during our discussion of fermentation, has the indicated "business end". Describe how this "business end" functions chemically (One sentence; you can label the picture too if it helps)

The H on the circled C has a very low pKa, being easily released to create a carbanion that can attack carbonyls

20) (3 pts) TPP is also involved in the pyruvate dehydrogenase complex PDH, a fancy enzyme. Using just word representations, such as CoA-SH (as opposed to structures) write the balanced reaction of the PDH complex.

\[
CH_3-CO-CO_2^- + NAD + CoA-SH \rightarrow CH_3-CO-CoA (or AcCoA) + NADH + CO_2
\]
21) (3 pts) The "business end" of the lipoic acid cofactor is depicted.
a) Next to it, draw the lipoic acid business end carrying the group it carries in the PDH reaction.

b) Besides the chemical group it carries, what else is the lipoic acid business end carrying when it does its job?

The lipoic acid cofactor carries electrons when it is in the reduced HS-------SH, open ring sulphhydril form.

22) (2 pts) The lipoic acid is restored to its original form (drawn above) after it reacts with CoA in the PDH reaction. Describe how the resulting "spent" lipoic acid is restored by the sequential action of two cofactors (one sentence):

The lipoic acid is restored to its closed ring, oxidized form by oxidation with FAD, and then oxidation of the resulting FADH2 by NAD+ to produce NADH

23) (4 pts) Citric acid is produced in the first reaction of the Krebs Cycle. The structure is shown to the right. Notice there are two acetate groups. The top one is added in the first reaction.
a) Where did it come from?:

The acetate on the top was added from AcCoA in the reaction with OAA that formed the citrate

b) Isocitrate is produced in the next reaction, draw the structure of isocitrate, to the right paying attention to the identity of the two acetyl groups in the substrate.

c) What is the name of the enzyme that produces isocitrate: aconitase

24) (2 pts) The glyoxalate cycle, a variant of the Krebs cycle that uses some of the Krebs steps and two other reactions that are unique. Why can't the Krebs cycle reaction depicted below also be a glyoxalate cycle reaction? You don't need to have memorized the glyoxalate cycle to know the answer. One sentence

Isocitrate + NAD+ $\rightarrow$ NADH + CO$_2$ + αKG

Any reaction that produces CO2 is not part of the glyoxalate cycle, which functions to get acetate carbons into anabolism by avoided the oxidative decarboxylations that are part of the Krebs cycle.
25) (2 pts) One of the Krebs enzymes functions in exactly the same manner as the PDH, but uses a Krebs cycle molecule as a substrate instead of pyruvate.
   a) What is the name of that enzyme? 
   \[ \text{alpha ketoglutarate dehydrogenase} \]
   b) What is the Krebs cycle molecule that is produced in this reaction? Name only is fine:
   \[ \text{succinyl-CoA} \]

26) (2 pts) 500 molecules of AcCoA are run through the Krebs cycle. How many molecules of CO₂ are produced by this occurrence?
   \[ 1000 \text{ molecules of CO}_2 \]

27 (6 pts) Succinate dehydrogenase and isocitrate dehydrogenase are two enzymes of the Krebs Cycle. For each, write whether the statement applies to the first (S), the second (I), both (B) or neither (N) reactions:
   a) Generates CO₂ in reaction __I___
   b) Produces NADH in reaction __I___
   c) Uses FAD in reaction __S___
   d) Consumes water in reaction __N___
   e) Uses lipoic acid cofactor __N____
   f) Has dicarboxylic acid product __B____
   g) The enzyme hastens only the forward reaction __N___

28) (2 pts) You are studying cultured cells. When you add citrate to the culture medium, the rate of glycolysis slows, and fructose-6-phosphate levels increase. If you remove the citrate, glycolysis speeds back up, and the fructose-6P levels drop. What is going on? Use specific enzyme or enzymes in your explanation. One sentence
   \[ \text{Citrate allosterically inhibits phosphofructokinase-1 (PFK1) which slows glycolysis and causes a buildup of the substrate of PFK1, fructose-6-phosphate.} \]
29) (4 pts) The reaction catalyzed by succinyl-CoA synthetase produces GTP (Δ).
   a) Write the reaction (words like Suc-CoA, no structures), including all substrates and products.
      Succinyl-CoA + GDP + P → Succinate + CoASH (or CoA) + GTP

   b) How come this reaction has a negative ΔG, when GTP is a "high energy" compound like ATP?
      The ΔG for hydrolysis of Succ-CoA is sufficiently negative to overcome the positive ΔG of the
      GTP production reaction, giving a net negative ΔG

30) (1 pts) What is the primary function of anapleurotic reactions? One sentence.
      The provide Krebs cycle molecules to replenish or “fill” the cycle when its intermediates are
      lost or used by other pathways.

31) (5 pts) Describe where in the cell the following pathways occur:
      Glycolysis: cytosol
      Pentose phosphate pathway: cytosol
      Pyruvate dehydrogenase reaction: in the matrix of the mitochondrion
      Krebs Cycle: in the matrix of the mitochondrion
      Electron transport chain: along the inner membrane of the mitochondrion
True and false questions

For each phrase below, decide if the question is true or false

32) ___ T _______ Enzyme-catalyzed reactions in the cell can have a positive $\Delta G$

33) ___ F _______ Mammalian cells have a glyoxylate cycle

34) ___ F _______ The Krebs cycle is an oxygen dependent set of reactions

35) ___ F _______ The mitochondrion does not have ribosomes

36) ___ F _______ The mitochondrion synthesizes ATP on its outer surface

37) ___ T _______ Allosteric enzymes usually have quaternary structure

38) ___ F _______ Enolase is one of the regulated enzymes of glycolysis

39) ___ T _______ ATP is a negative allosteric regulator of PFK-1

40) ___ T!!! _______ Randy promised never to go away and abandon his merry band of Metabolites again.

Presto Metabolino pictured with one of his masterpieces