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7.016 Problem Set 1- 2018

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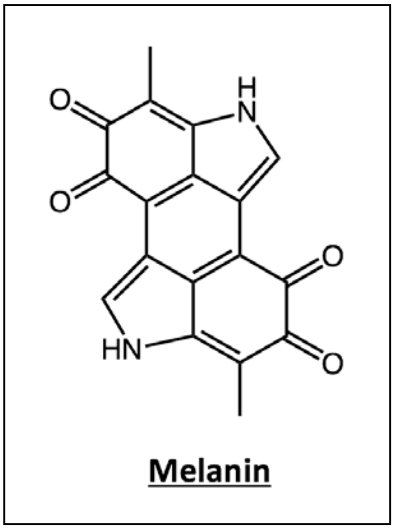
Question 1

The following is the "line-angle" drawing of melanin, a pigment that determines hair color. **Note:** *The carbon (C) and the hydrogen (H) atoms are not shown but implied.*



Melanin

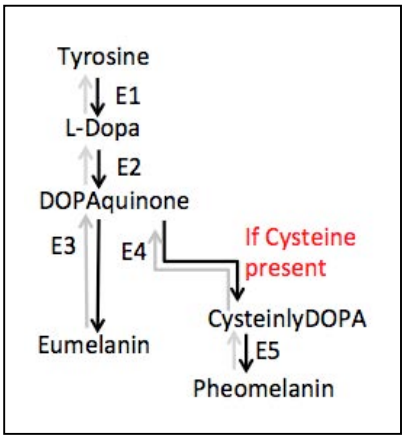
a) Clearly label **ALL** C and H atoms on the line angle drawing and write the **molecular formula** of melanin in the space below.

b) On the line angle drawing, **box one** nonpolar functional group and **circle all** electronegative elements.

c) Do you think melanin would dissolve in water? **Why or why not?**

Question 2

There are two types of melanin pigment in hair follicles: **pheomelanin** (which promotes red or blond hair color) and **eumelanin** (which promotes black or brown hair color). The following is the simplified outline of eumelanin and pheomelanin synthesis.



a) The E1-E5 catalyzed reactions proceed spontaneously in the forward direction (shown by an →) and NOT in the reverse direction (shown by ←) within a cell. **Explain** why this is so.

b) You identify three individuals: **Individual A** lacks a functional E2, **Individual B** has a hyperactive form of E3 enzyme and **Individual C** has a functional E5 but lacks a functional E4.

i. Which metabolite(s) would build up in the melanin synthesizing cells of **Individual A**?

ii. Which metabolite(s) would build up in the melanin synthesizing cells of **Individual B**?

iii. What would be the hair color of **Individual C**? **Explain** your choice assuming that cysteine is present.

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Question 2 continued

c) Which class of macromolecules is cysteine a monomer of: **carbohydrates/ lipids/ nucleic acids/ proteins**? Briefly **explain** why cysteine is different from other monomers that make the class of macromolecules that you chose.

Question 3

a) Complete the statements below by choosing from the following: **the same/ higher/ lower.** The reaction catalyzed by a hypoactive form of E3 (1000- fold less active than the normal form of E3) has …

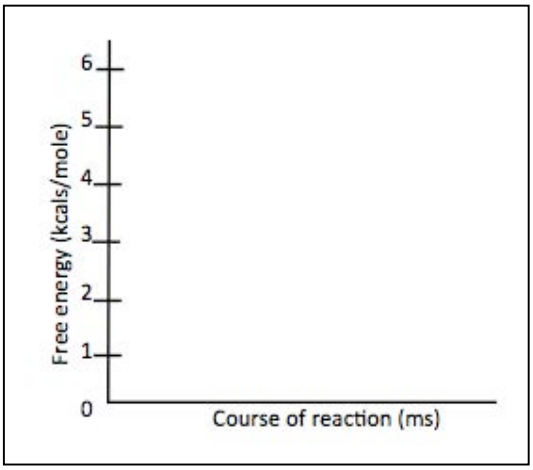
i. _____ **free energy** change as the reaction catalyzed by normal E3.

ii. _____ **reaction rate** compared to the reaction catalyzed by normal E3.

iii. _____ **reaction equilibrium** compared to the reaction catalyzed by normal E3

iv. _____ **activation energy** compared to the reaction catalyzed by normal E3

b) For the E3 catalyzed step, the free energy change (**ΔG) = -1.8 kcals/mole**.



i. The E3 catalyzed reaction is an example of an **exergonic/ endergonic** reaction.

ii. On the left, draw the energy profile of the reaction catalyzed by E3. Label the reactants (R), products (P), ΔG and activation energy (E_{AC}) of the reaction.

c) E3 is optimally active at pH 7.4 and 37^{O}C. If the same E3-catalyzed reaction were conducted *in vitro* (in a test tube) at pH 7.4 and 50^{O}C, would you expect to see **more/ less/ the same level** of melanin synthesis? **Explain why. Note:** *Provide an explanation with respect to the three dimensional (3D-) conformation of E3 enzyme. Your explanations may vary.*

d) You identify two inhibitors of E3: **Drug A** and **Drug B**. Further analysis shows that Drug A alters the 3D-conformation of E3 and prevents it from binding its substrate. Drug A does not bind to the active site of E3. Drug B on the other hand binds to the active site of E3 and prevents the binding of the substrate to E3. Which of the above drugs is an **allosteric inhibitor: Drug A or Drug B**? **Why?**

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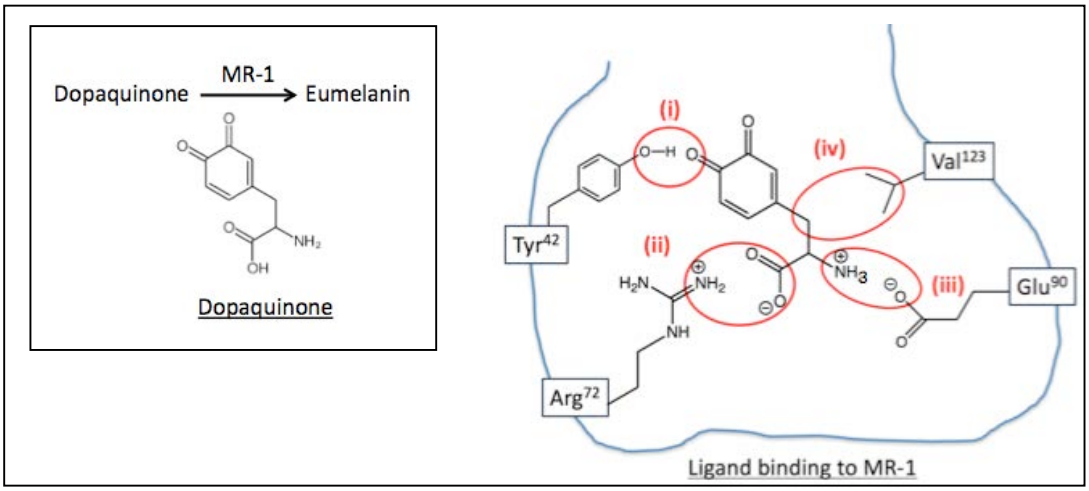
Question 4

E3 (or the Melanocortin receptor (MR-1)) catalyzes the conversion of dopaquinone to eumelanin as shown below. ***Note:*** *Each circled interaction is critical for dopaquinone-MR-1 binding.*

a) For each position (i)–(iv), name the **non-covalent interactions** between MR-1 receptor and dopaquinone by choosing from **ionic/ hydrogen/ hydrophobic interactions.**



(i): _____ **(ii):** _____

(iii): _____ **(iv):** _____

b) You identify four individuals (1-4), each having an amino acid substitution in the MR-1 protein at the positions outlined below.

Individuals	Amino acid substitutions
1	Tyr^{42} → Ile^{42} at position (i)
2	Arg^{72} -> Asp^{72} at position (ii)
3	Glu^{90} -> Asp^{90} at position (iii)
4	Val^{123}→ Ala^{123} at position (iv)

Explain, in terms of the type of mutation what would be the likely hair color for Individuals 1-4.

c) Although the active site of MR-1 is composed of only a few amino acids, the MR-1 protein as a whole is composed of many amino acids. **Explain** how the amino acids outside of the active site of MR-1 may contribute to its function.

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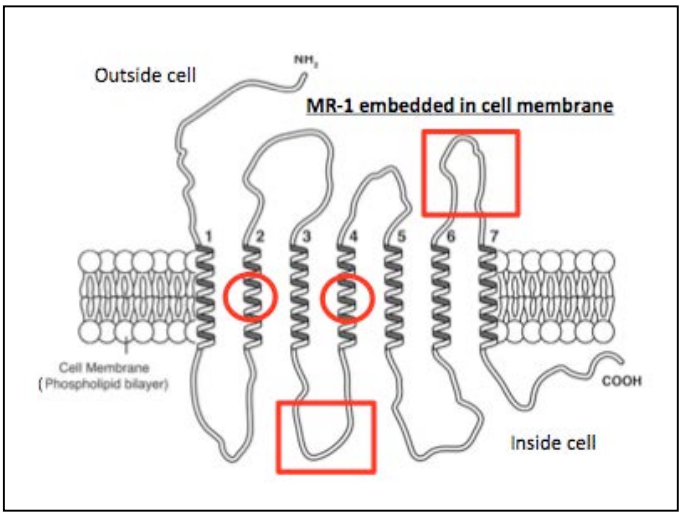
Question 5

The schematic below shows MR-1 receptor embedded in the cell membrane. This receptor has 7 transmembrane domains labeled 1-7 in the schematic.



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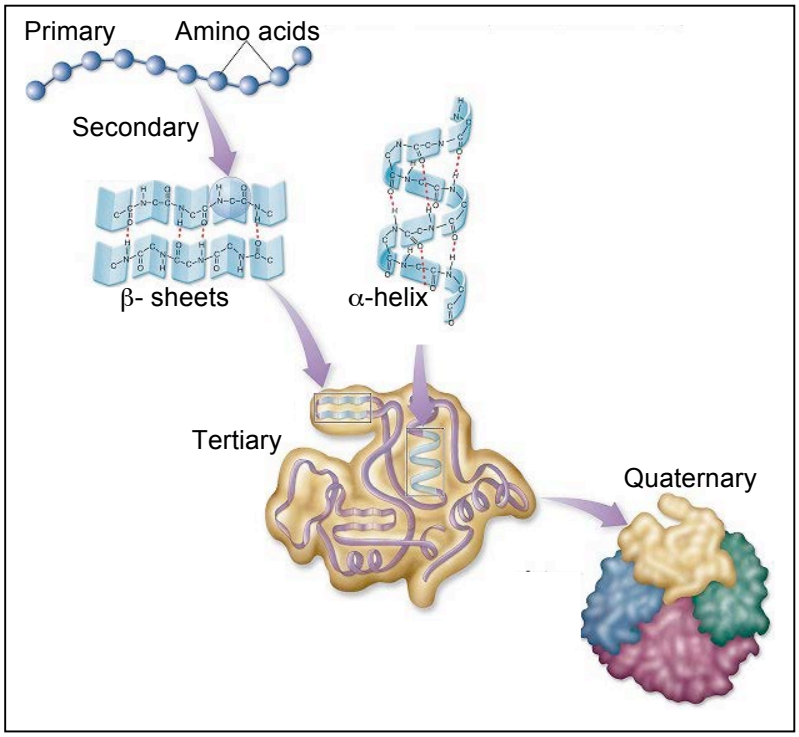
a) Does the nature/ characteristics of amino acids inside **the circled region** of MR-1 differ from the nature of amino acids inside **the boxed regions**? If so, **why**?

b) Would the sequence of amino acids in both circled regions ALWAYS be the same? **Why or why not?**

c) The following schematic depicts different levels of structure for the MR-1 receptor that functions at pH 7.4. Answer the questions below by choosing from: **primary/ secondary/ tertiary/ quaternary.** Select **All** that apply**.**



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i. Which level of MR-1 structure is stabilized only by hydrogen bonding?

ii. Which level of MR-1 structure shows only the covalent amide/peptide bonds?

iii. If MR-1 is exposed to an acidic pH, which level of protein structure remains unchanged even when the protein is denatured?

iv. Which level(s) of MR-1 structure is stabilized by **INTRA** molecular non-covalent interactions?

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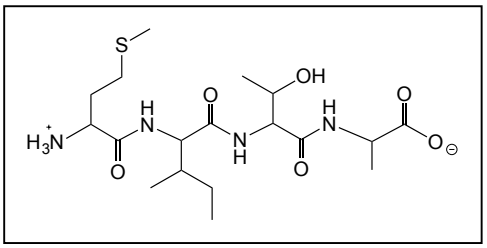
Question 5 continued

d) The first four amino acids of MR-1 are shown in the diagram below.



i. On the diagram, show the direction of synthesis of MR-1 by an arrow and box the **first amino acid**.

ii. On the diagram, circle **ALL** the peptide bonds between the amino acids.

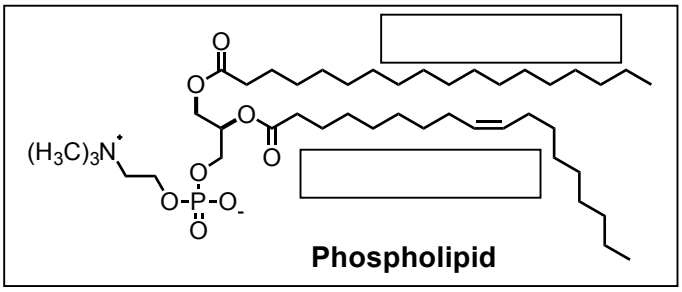
iii. Give the **byproduct** of a peptide (amide) bond synthesis reaction and classify the reaction as **condensation** or **hydrolysis**.

iv. Which amino acid(s) in the sequence above is **hydrophilic**? ***Note:*** *An amino acid table is provided on the last page of this problem set.* _____

v. Which of the following did you consider that you considered while answering part (iv) above?

- Amino group ($-NH_2$ group)
- Carboxyl group (-COOH group)
- Side-chain group (R group)
- H atom attached to α-C

e) MR-1 is localized to and functions in the cell membrane. This membrane is made up of phospholipid molecules.



i. On the schematic, identify the saturated and unsaturated fatty acid chains by filling in the boxes.

ii. **Circle** the best option: The phospholipids that make up the plasma membrane are **hydrophilic/ hydrophobic/ amphipathic.** How does your choice allow them to arrange to form the lipid bilayer in water?

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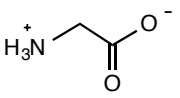
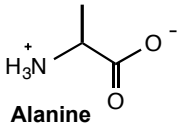
Amino acids table

TWENTY ENCODED
α-AMINO ACIDS
at pH 7

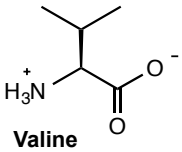
NO side chain



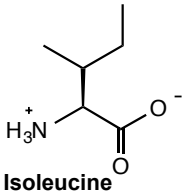
Glycine
Gly (G)



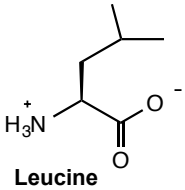
Alanine
Ala (A)



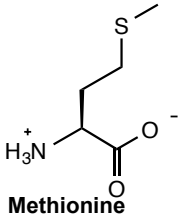
Valine
Val (V)



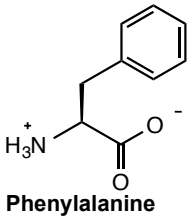
Isoleucine
Ile (I)



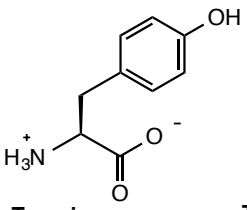
Leucine
Leu(L)



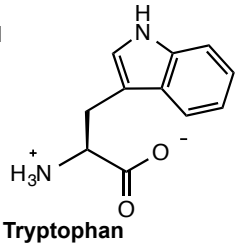
Methionine
Met (M)



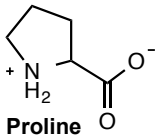
Phenylalanine
Phe (F)



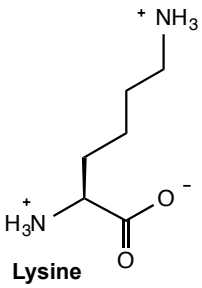
Tyrosine
Tyr (Y)



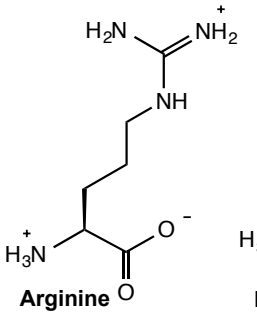
Tryptophan
Trp (W)



Proline
Pro (P)

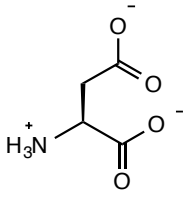


Lysine
Lys (K)

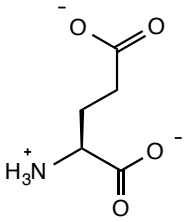


Arginine
Arg (R)

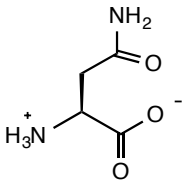
Histidine
His (H)



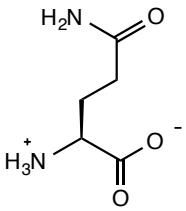
Aspartic acid
Asp (D)



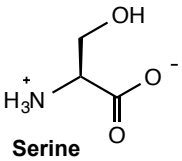
Glutamic acid
Glu (E)



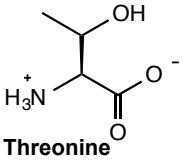
Asparagine
Asn (N)



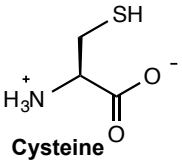
Glutamine
Gln (Q)



Serine
Ser (S)



Threonine
Thr (T)



Cysteine
Cys (C)

Cystine
AA-S-S-AA

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