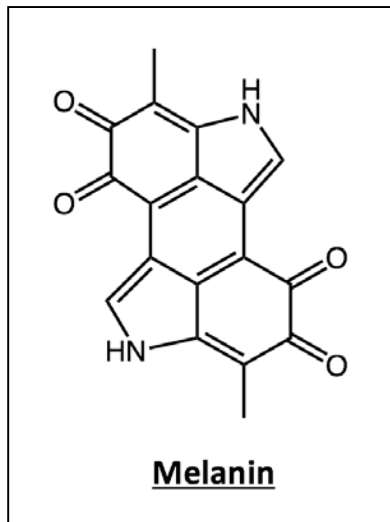


# 7.016 Problem Set 1- 2018

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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.



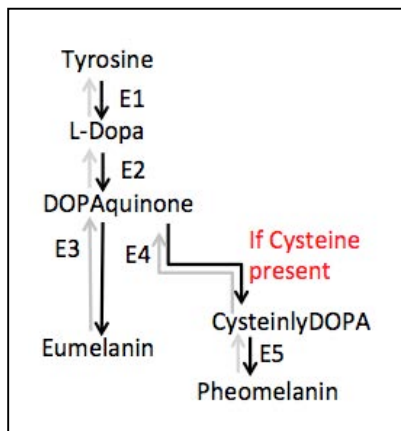
a) Clearly label **ALL** C and H atoms on the line angle drawing and write the **molecular formula** of melanin in the space below.

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

c) Do you think melanin would dissolve in acid? **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  $\rightarrow$ ) and NOT in the reverse direction (shown by  $\rightarrow$ ) 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.

**Question 2 continued**

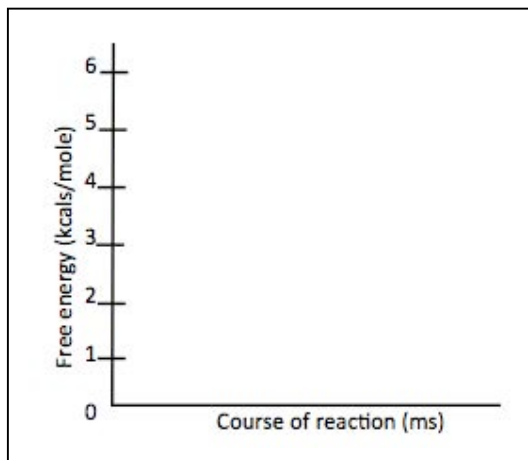
c) Which class of macromolecules is cysteine a monomer of: **carbohydrates/ lipids/ nucleic acids/ proteins**? Briefly **explain** why cysteine is different from other monomers that make the class of macromolecules that you chose.

**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 ( $\Delta G$ ) = **-1.8 kcal/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),  $\Delta G$  and activation energy ( $E_{AC}$ ) of the reaction.

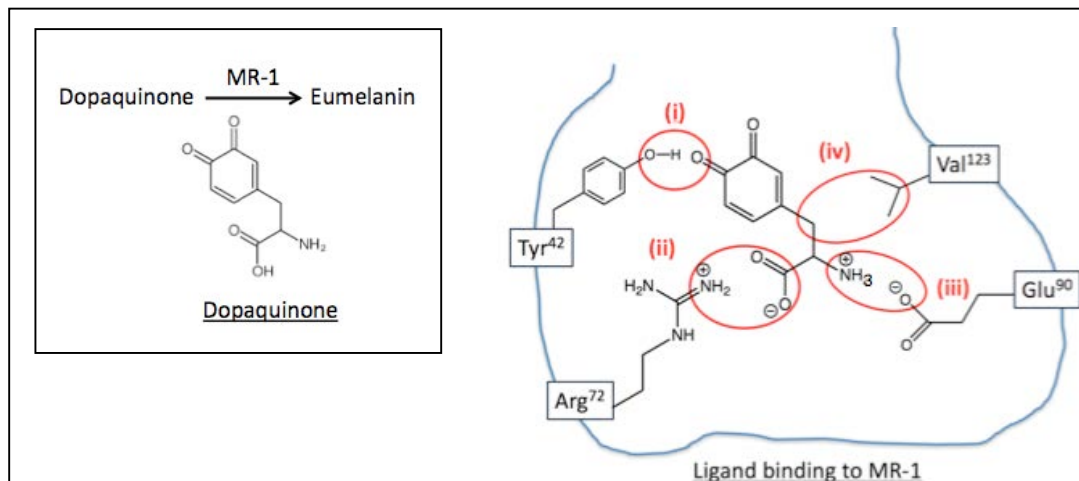
c) E3 is optimally active at pH 7.4 and 37°C. If the same E3-catalyzed reaction were conducted *in vitro* (in a test tube) at pH 7.4 and 50°C, would you expect to see **more/ less/ the same level** of melanin synthesis? **Explain why. Note:** Provide an explanation with respect to the three dimensional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

**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.

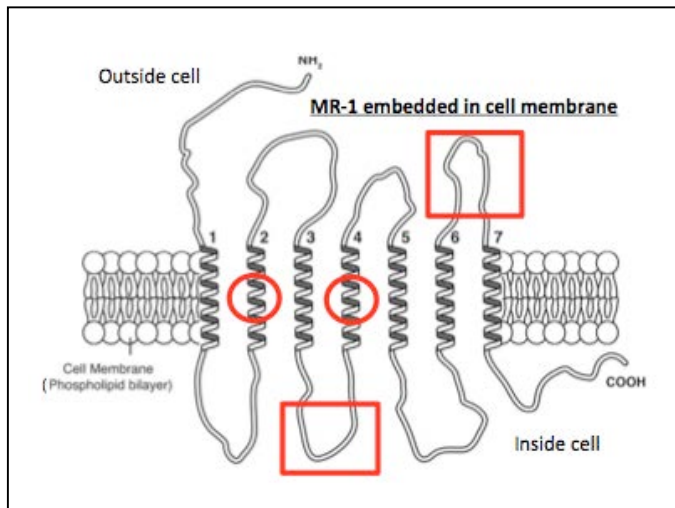
Individuals	Amino acid substitutions
1	Tyr <sup>42</sup> → Ile <sup>42</sup> at position (i)
2	Arg <sup>72</sup> → Asp <sup>72</sup> at position (ii)
3	Glu <sup>90</sup> → Asp <sup>90</sup> at position (iii)
4	Val <sup>123</sup> → Ala <sup>123</sup> at position (iv)

**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.

**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.

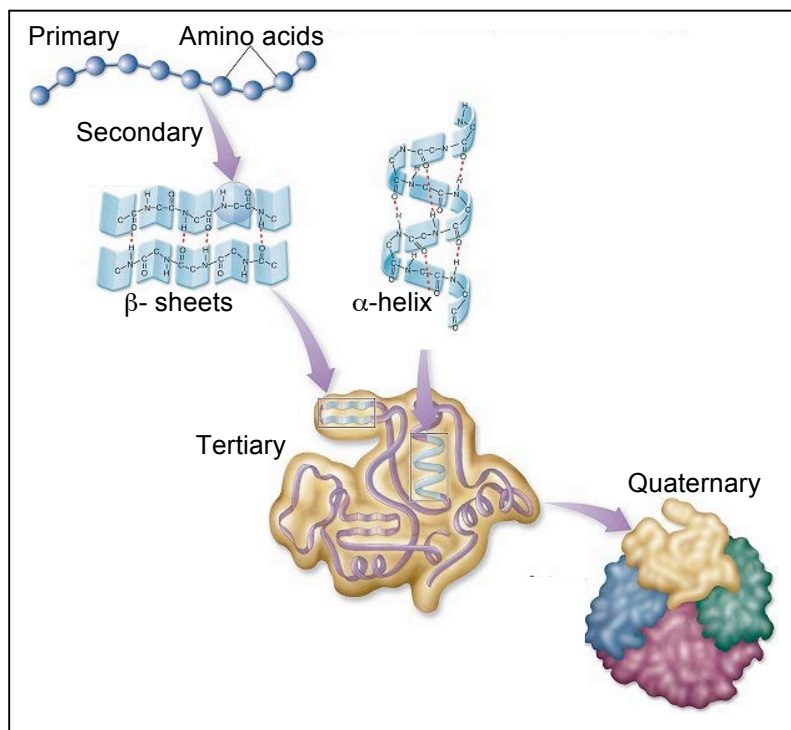


a) Does the nature/ characteristics of amino acids inside **the circled region** of MR-1 differ from the nature of amino acids inside **the boxed regions**? If so, **why**?

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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.

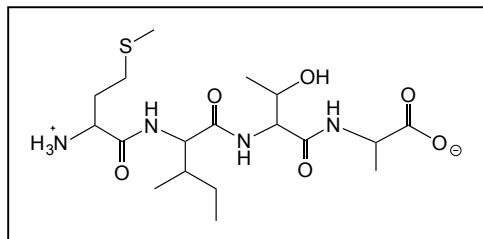


- i. Which level of MR-1 structure is stabilized only by hydrogen bonding?
- ii. Which level of MR-1 structure shows only the covalent amide/peptide bonds?
- iii. If MR-1 is exposed to an acidic pH, which level of protein structure remains unchanged even when the protein is denatured?
- iv. Which level(s) 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.

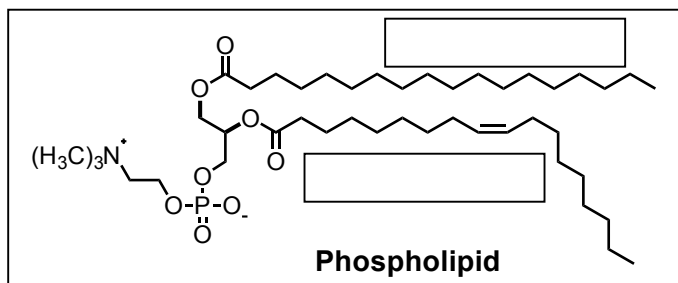
iii. Give the **byproduct** of a peptide (amide) bond synthesis reaction and classify the reaction as **condensation** or **hydrolysis**.

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?

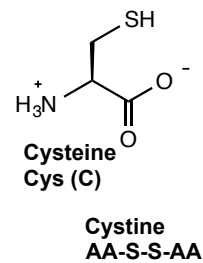
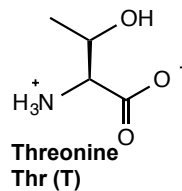
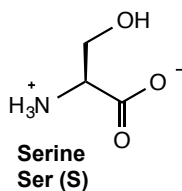
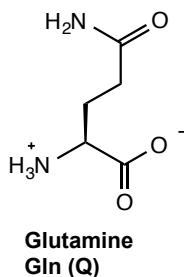
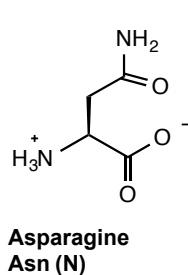
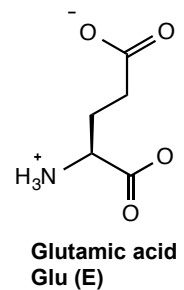
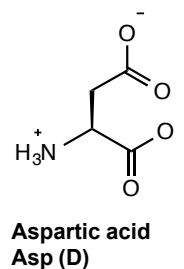
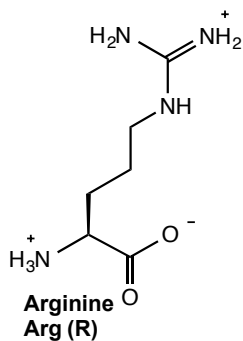
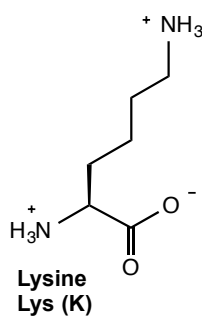
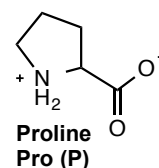
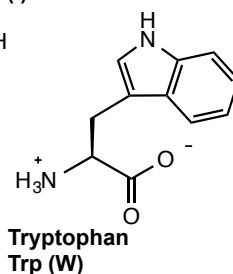
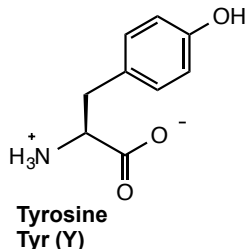
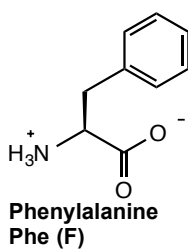
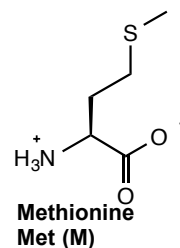
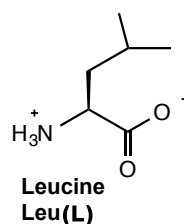
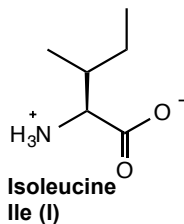
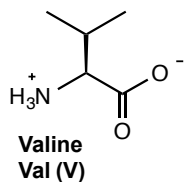
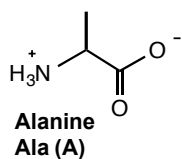
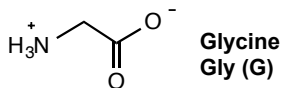
- Amino group (-NH<sub>2</sub> group)
- Carboxyl group (-COOH group)
- Side-chain group (R group)
- H atom attached to α-C

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 acid?

**Amino acids table****TWENTY ENCODED  
 $\alpha$ -AMINO ACIDS  
at pH 7****NO side chain**

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