1. The central atom of all 20 standard amino acids is what is termed the α-carbon that has four covalent bonds. Which of these would NOT be considered to be bonded to the α-carbon:

   A. a carbon atom
   B. an amino group
   C. a methyl group
   D. a side chain (R- group)
   E. a carboxyl group

2. The level of protein structure that describes the relative three-dimensional arrangements of a polypeptide is referred to as the

A. quaternary structure.

B. Ramachandran plot.

C. secondary structure.

D. primary structure.

E**. tertiary structure.**

3. To determine the **primary** amino-acid sequence in a protein, a useful technique is:

A. Mass Spectrometry

B. Edman degradation

C. Molecular Modelling

D. Nuclear Magnetic Resonance (NMR) Spectroscopy

E. Circular Dichroism (CD) Spectroscopy

4. Which amino acid has an R-group which contains only hydrogens and carbons?

   A. Glutamic acid (Glu)
   B. Isoleucine (Ile)
   C. Tyrosine (Tyr)
   D. Cysteine (Cys)
   E. Histidine (His)

5. Because proteins can absorb light maximally at 280 nm, they can be identified and quantified in solution by using a spectrophotometer. Which of the following is true about the absorption of light by proteins?

A. Proteins absorb infrared light.

B. All amino acids absorb light equally.

C. The greater the concentration of protein in a solution, the more 280 nm transmitted

D. light will be detected by a spectrophotometer.

E. Absorbance of 280 nm light by proteins increases with the concentration of the protein.

6. The Protein Data Bank (PDB)

A. is a computer generated representation of a protein structure

B. contains only the three-dimensional structures of proteins determined by X-ray crystallography and not nmr spectroscopy

C. ensures that any protein structure can be prediction by calculation

D. is the major database of the three-dimensional structures of proteins

E. is not available for use in undergraduate student workshops

7. In the β-structure of proteins

A. The hydrogen bonds when drawn are relatively parallel in anti-parallel structure

B. The hydrogen bonds when drawn are not parallel in anti-parallel structure

C. The hydrogen bonds when drawn are not parallel in anti-parallel structure

D. There are no hydrogen bonds

E. None of the above

8. In the titration curves of amino acids with ionisable sidechains

A. there is only one pKa evident

B. whether or not the pKa values are close or not is not relevant to measuring them

C. there are three(3) pKa that are relevant

D. their complexity is only the same as other amino acids

E. None of the above

9. A type 3 receptor *e.g*. adrenoreceptor has as its couple (effector):

A. nothing, drug action is direct.

B. DNA.

C. a G-protein.

D. both DNA and a G-protein.

E. None of the above.

10. In the presence of alcohol dehydrogenase, the rate of reduction of acetaldehyde to ethanol increases as you increase the concentration of acetaldehyde. Eventually the rate of the reaction reaches a maximum, where further increases in the concentration of acetaldehyde have no effect. Why?

A. **Free active sites are not available for acetaldehyde**

B. The competitive inhibitor ethylene glycol is a present

C. At high concentrations of acetaldehyde, the activation energy of the reaction decreases

D. The enzyme is no longer specific for acetaldehyde

E. At high concentrations of acetaldehyde, the change in free energy of the reaction decreases

11. It is stated that agonists and antagonists may bind in an analogous manner, but part of the binding site for the antagonist need not be shared with the binding site. Which statements are CORRECT?

A. a more extensive binding site is considered consistent with a higher affinity of the antagonist

B. the theory is incorrect because agonist binding sites are always larger than antagonist binding sites

C. the theory is incorrect as the agonist and antagonist always bind in a different location

D. A and C are correct

E. B and C are correct

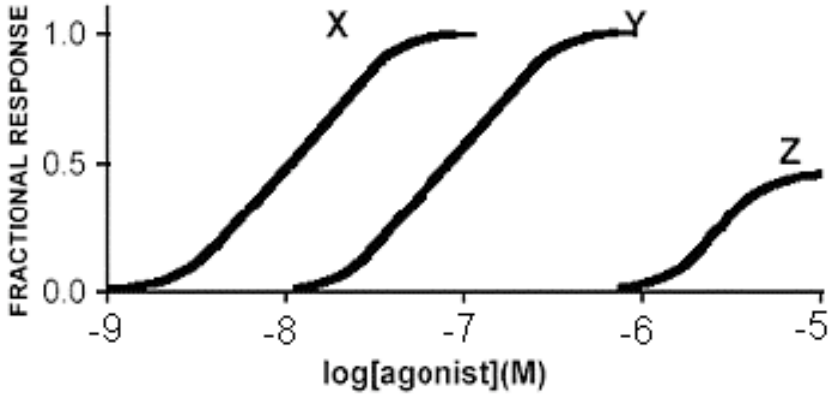
12. Evidence that a drug is being used out of its *selectivity* window is:

A. the intrinsic activity of the drug is not that for a full agonist
B. the receptor interaction is known to be with a single receptor
C. side effects associated with responses from the target receptor are observed
D. side effects associated with inhibiting receptors other than the targeted receptor are observed
E. All of the above

13. Evidence that *intrinsic activity* and *affinity* need not be proportionally related is:

A. a ligand can have high affinity and no intrinsic activity
B. a set of ligands for a single receptor are seen to bind with the same affinity and intrinsic activity
C. antagonist binding can be reversible or irreversible
D. both A and C are correct
E. both B and C are correct

The diagram below is used for the following 2 Questions (Questions 14 and15). The vertical axis is relative biological activity. The curves are labelled X,Y and Z, but they may represent different situations in each question.



14. If curve Y represents the dose-response curve for an agonist, the EC_{50} value of the agonist is closest to:

A. 10^{-8}
B. 8.0
C. 7.0
D. 10^{-7}
E. $10^{-5.5}$

15. If curve X represents the dose-response curve for agonist X, and curve Z represents the dose-response curve for agonist X in the presence of an antagonist Z, compound Z:

A. demonstrates an intrinsic activity of approximately 0.5
B. is an irreversible competitive antagonist of X
C. is a reversible competitive antagonist of X
D. must also be a partial agonist
E. answers A and B are correct

16. Agonist and antagonist interaction with receptors generally differs in the following ways:

A. agonists bind more tightly to receptors than antagonists as they are more specific.

B. agonists bind less tightly than antagonists so that they can dissociate from the receptor quite rapidly once bound.

C. agonists induce a specific conformational change in the receptor leading to generation of a stimulus while antagonists do not.

D. answers A and C are correct.

E. answers B and C are correct.

17. An inverse agonist is a ligand that:

A. produces a response lower than basal.

B. requires an allosteric model of drug action to explain its activity.

C. is an antagonist.

D. answers A and C are correct.

E. answers B and C are correct.

18. If maximal response results from less than maximal receptor occupation (spare receptors), relative to an ideal dose-effect curve:

A. the dose response curve will coincide at the K_D concentration.

B. the half maximal effect will be seen to occur at lower concentrations.

C. the 75% maximal effect will be seen to occur at higher concentrations.

D. A and B are correct.

E. A and C are correct.

19. The "two-state allosteric model" of drug action has the following features:

A. an agonist binds preferentially to the "closed" (T) state of receptor compared to the "open" (R) state, thereby stabilising this state.

B. an agonist binds preferentially to the "open" (R) state of receptor compared to the "closed" (T) state, thereby stabilising this state.

C. both "open" and "closed" states of the receptor bind an agonist equally well.

D. the “closed” (T) and “open” (R) state of the receptor can not take part in an equilibrium that shifts the predominating state.

E. B and D are correct.

20. Which of the following BEST describes a characteristic of a reversible enzyme inhibitor?

A. The inhibitor will permanently alter the enzyme, and the enzyme can no longer catalyse the conversion of substrate to product.

B. The inhibitor binds tightly to the enzyme via non-covalent bonds and does not dissociate from the active site even with dialysis.

C. The inhibitor will covalently bind to the enzyme via a nonhydrolysable bond.

D. The inhibitor with temporarily tie up the enzyme, during which time the substrate cannot be converted to product.

E. All of the above.

21. Which of the following is NOT a characteristic of a suicide substrate or mechanism-based irreversible inhibitor?

A. The normal catalytic machinery of the enzyme is required for its activation.

B. Irreversibly alkylates an electrophilic amino acid residue.

C. Contains a latent reactive functionality.

D. Irreversibly alkyates a nucleophilic amino acid residue.

E. C. and D.

22. Which of the following statements is CORRECT?
When a reaction is performed in zero-order kinetics:

A. The substrate concentration is very low.

B. The rate of reaction is directly proportional to the substrate concentration.

C. **The rate of the reaction is independent of the substrate concentration.**

D. The enzyme level is always high.

E. None of the above.

23. Which of the following statements is CORRECT?
Activation energy is:

A. The energy needed for an enzyme reaction to stop.

B. Increased by enzymes.

C. Very high in catalysed reactions.

D. **Decreased by enzymes**.

E. A. and B.

24. Which of the following statements is CORRECT?
In an enzymatic reaction with a low substrate concentration, a competitive inhibitor binds:

A. The enzyme at a site other than the active site, thereby decreasing the Vmax of the reaction.

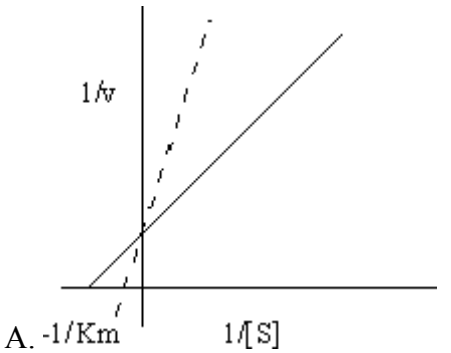
B. To the active site of the enzyme, with no effect on the Vmax of the reaction.

C. To the entire enzyme-substrate complex, thereby decreasing the Km.

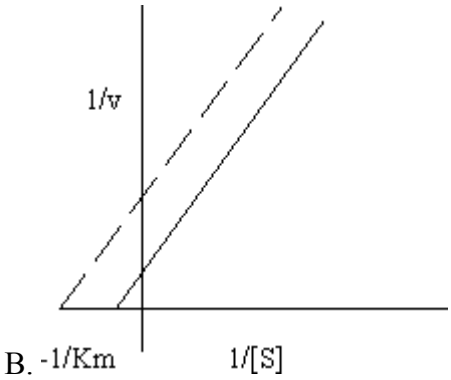
D. To the active site of the enzyme, thereby causing the Km to increase.

E. B and C.

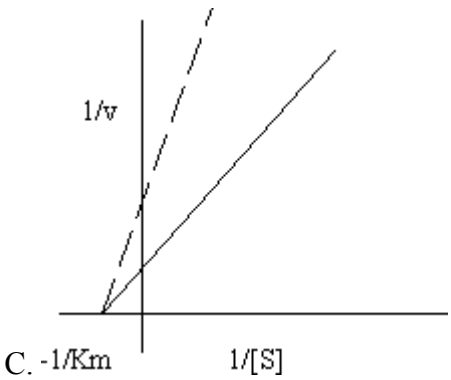
25. Use the following Lineweaver-Burk plots to answer this question. The solid line represents a normal plot (no inhibition). Which one of the plots illustrates the effect of *noncompetitive* inhibition?



A.



B.



C.

A. Plot A.

B. Plot B.

C. Plot C.

D. None of these plots illustrate this effect.

E. Noncompetitive inhibition cannot be determined using Lineweaver-Burk plots.

26. G_q

A. inhibits adenylyl cyclase
B. activates adenylyl cyclase
C. **causes the release of calcium ions**
D. activates phosphodiesterases
E. inhibits phospholipase C-β

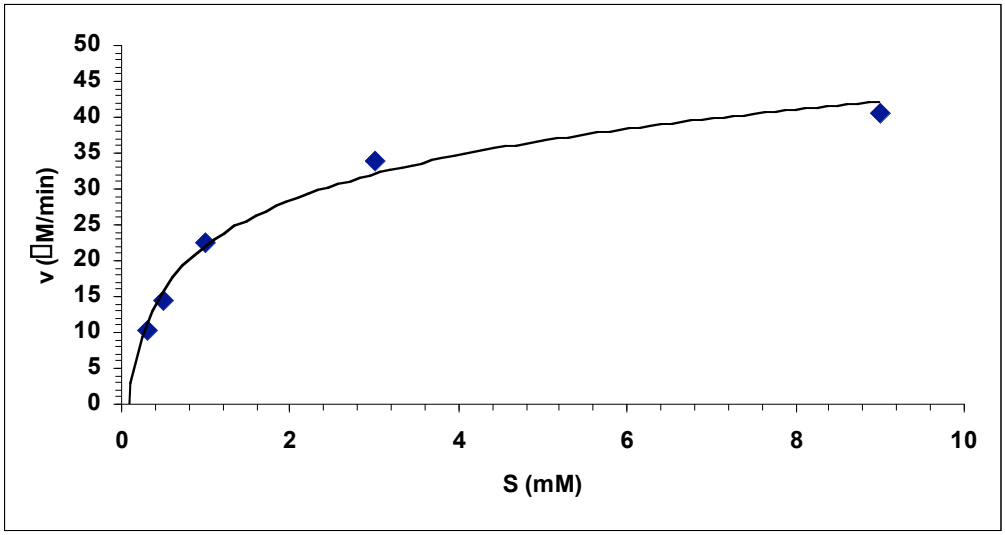
27. Which of the following statements are INCORRECT? Enzyme-linked receptors

A. are transmembrane proteins with their ligand-binding domain on the outer surface of the plasma membrane
B. are characterised as having a cytosolic domain that either has an intrinsic enzyme activity or associates directly with an enzyme
C. **include receptor-like tyrosine phosphatases, receptor serine/threonine** kinases, but not receptor tyrosine kinases
D. includes the receptors for epidermal growth factor and vascular endothelial growth factor
E. Both B and D

Short answer questions

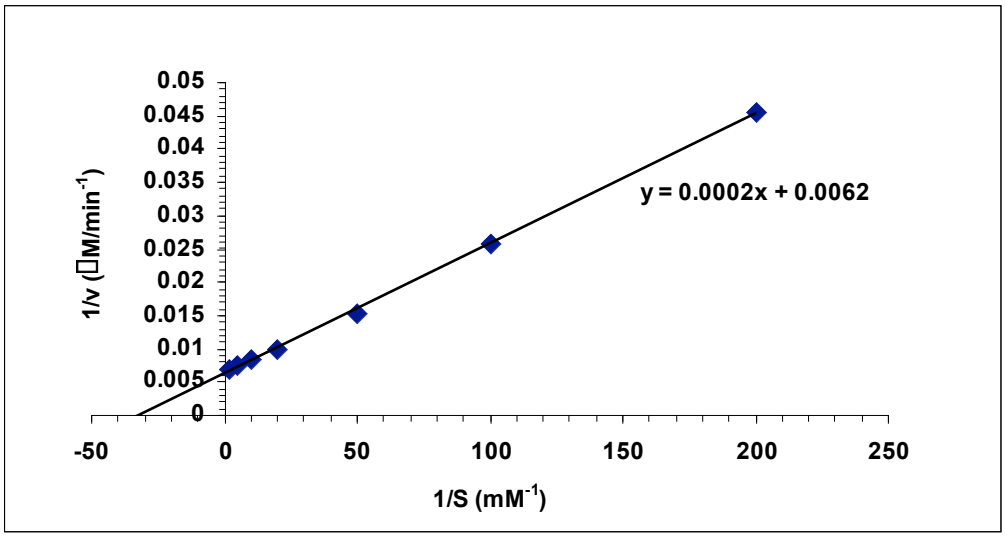
1. Use oxygen-binding curves to explain how myoglobin and haemoglobin each perform their different functions.

2.
(a) **Estimate** Vmax and Km from the graph below. Show your working and units. Part marks will be awarded.



(b) **Calculate** Vmax and Km from the graph below. Show your working and units (to 4 d.p.). Part marks will be awarded.

Note: $1/v$ = Km/Vmax . 1/S + 1/Vmax



3. Discuss the different factors affecting the rate of an enzymatic reaction.

4. Outline the molecular mechanism by which bronchospasm can be alleviated by β_2-agonists AND the mechanism of action of phosphodiesterase inhibitors.