考生注意事項：所有考題務必在答案卷上作答，在問題卷上作答者不計分。

I. 選擇題（1-10 題，每題二分，答錯倒扣 0.5 分，均為單選）

Answer the following questions using the key outlined below:

A. if 1, 2, and 3 are correct
B. if 1 and 3 are correct
C. if 2 and 4 are correct
D. if only 4 is correct
E. if all four are correct

1. The major substrates for gluconeogenesis are
   1. pyruvate
   2. most amino acids.
   3. all TCA intermediates.
   4. fatty acids.

2. Glycogen synthase is covalently inactivated by
   1. synthase-phosphorylase kinase.
   2. phosphoprotein phosphatase.
   3. active protein kinase.
   4. cAMP-dependent protein phosphatase.

3. Glycosaminoglycans
   1. are bound to protein by electrostatic interaction.
   2. contain large segments of repeating disaccharide unit typically of a hexosamine and a uronic acid.
   3. are components of bacterial cell wall.
   4. are high molecular weight polyanionic substances.

4. A characteristic of the dihydroxyacetone phosphate/glycerol-3-phosphate shuttle is that
   1. the mitochondrial glycerol-3-phosphate dehydrogenase is a flavoprotein.
   2. it shuttles NADH across the mitochondrial membrane to yield 2.5 ATP/NADH.
   3. it transfers two reducing equivalents from cytosolic NADH to mitochondrial $FADH_2$.
   4. it requires the aspartate aminotransferase activity.

5. Uncoupling of mitochondrial oxidative phosphorylation
   1. allows continued ATP formation, but inhibits O_2 consumption.
   2. slows down all mitochondrial metabolism.
   3. inhibits both ATP formation and O_2 consumption.
   4. allows continued O_2 consumption, but inhibits ATP formation.

6. Which of the following statements is correct for pentose phosphate pathway?
   1. In the oxidative phase, glucose-6-phosphate is converted to ribulose-5-phosphate and CO_2.
   2. NADPH is produced in the nonoxidative phase.
   3. Three pentoses can be converted to two hexoses and one glyceraldehyde-3-phosphate.
   4. It generates CO_2 from C-6 of glucose.

7. Three carbon sugars resulting from the splitting of fructose-1,6-bisphosphate are
   1. 3-phosphoglycerate
   2. glyceraldehyde-3-phosphate
   3. 2-phosphoglycerate
   4. dihydroxyacetone phosphate

8. Which of the following is accomplished by the citric acid cycle in mammals?
   1. generation of NADH and $FADH_2$.
   2. formation of α-keotglutarate for amino acid synthesis.
   3. oxidation of acetyl-CoA.
   4. net synthesis of oxaloacetate from acetyl-CoA.

9. Which of the following cofactors is required in the oxidative decarboxylation of α-ketoglutarate to succinyl-CoA?
   1. Lipoic acid
   2. Thiamine pyrophosphate
   3. NAD^+
   4. Coenzyme A

10. Glycogen phosphorylase
   1. is activated by phosphorylation.
   2. removes glucose residues from the reducing ends of the glycogen chains.
   3. catalyzes phosphorolysis of the α(1→4) bonds of glycogen.
   4. uses UDP-glucose as a substrate

II. 選擇題（**11-56** 題，每題一分，答錯倒扣 **0.25** 分，均為單選）

11. The cholesterol in LDL(low density lipoprotein):
   A. binds to a cell receptor and diffuses across the cell membrane.
   B. when it enters a cell, suppresses the activity of ACAT (AcylCoA:cholesterol acyltransferase).
   C. once in the cell is converted to cholesterol ester by LCAT (lecithin:cholesterol acyltransferase).
   D. once it has accumulated in the cell, inhibits the replenishment of LDL receptors.

12. Structural features that are common to all prostaglandins include:
   A. 20 carbon atoms.
   B. an oxygen-containing internal heterocyclic ring.
   C. a peroxide group at C-15.
   D. two double bonds.
   E. a ketone group.

13. The enzyme catalyzed the regulatory step in cholesterol biosynthesis is:

A. HMG-CoA synthase.
B. mevalonate kinase.
C. sequalene monooxygenase.
D. HMG-CoA reductase.
E. none of the above.

14. The α-glycerol-3-phosphate, an important intermediate in the triacylglycerol biosynthesis in adipose tissue is mainly derived from

A. the glycolysis pathway.
B. the action of glycerol kinase.
C. the citric cycle.
D. the pentose cycle.
E. none of the above.

15. Which of the following compounds is an important intermediate for both triacylglycerol and phospholipid biosynthesis?

A. Diacylglycerol.
B. Phosphatidic acid.
C. CDP-diacylglycerol.
D. α-glycerol-3-phosphate.
E. None of the above.

16. In well-fed state, not only glucose uptake is increased. Fat deposition is also increased, because:

A. NADH is increased.
B. activity of Kreb's cycle is slowed down due to high NADH.
C. formation of α-glycerol-3-phosphate in the adipose tissue is increased.
D. citrate is accumulated.
E. all of the above.

17. The largest energy reserve in humans is :

A. blood glucose.
B. liver glycogen.
C. muscle glycogen.
D. adipose tissue triacylglycerol.
E. Muscle protein.

18. Adipose tissue responds to low insulin/glucagon ratio by:

A. dephosphorylation the interconvertible enzymes.
B. stimulating the deposition of fat.
C. increaseing the amount of pyruvate kinase.
D. stimulating hormone-sensitive lipase.
E. none of the above.

19. Fatty acids are activated to acyl-CoAs and the acyl group is further transferred to carnitine because:

A. acyl-CoAs easily cross the mitochondrial membrane, but the fatty acids themselves will not.
B. fatty acids cannot be oxidized by FAD unless they are in the acyl-carnitine form.
C. carnitine is required to oxidize NAD^+ to NADH.
D. acyl-carnitines readily cross the mitochondrial inner membrane, but acyl-CoAs do not.
E. none of the above.

20. The fatty acid, $^{14}CH_3(CH_2)_9COOH$ in which the indicated carbon is labeled with ^{14}C, is fed to an animal, After allowing 30 minutes for fatty acid β oxidation, the label would most likely be recovered in:

A. acetyl-CoA.
B. propionyl-CoA.
C. palmitoyl-CoA.
D. both acetyl-CoA and propionyl-CoA.
E. none of the above.

21. The major site of formation of acetoacetate from fatty acids is the:

A. intestinal mucosa.
B. adipose tissue.
C. liver.
D. muscle.
E. kidney.

22. The rate-limiting step in fatty acid synthesis is:

A. formation of acetyl-CoA from acetate.
B. the reaction catalyzed by acetyl-CoA carboxylase.
C. condensation of acetyl-CoA and malonyl-CoA.
D. the reduction of the acetoacetyl group to a β-hydroxybutyryl group.
E. formation of malonyl-CoA from malonate and coenzyme A.

23. Which of the following can be synthesized by plants not by humans?

A. Palmitate.
B. Stearate.
C. Linoleate.
D. Pyruvate.
E. Phosphatidylcholine.

24. When blood glucose is abnormally high, the pancreas releases:

A. insulin.
B. glucagon.
C. epinepherine.
D. trypsin.
E. glucose.

25. What sequence of events take place, when hepatocytes are incubated with epinepherine?

1. GTP replaces GDP on Gs.
2. Adenylate cyclase is activated.
3. Epinepherine binds to its receptor on the cell surface.
4. Gs associates with adenylate cyclase.
5. CAMP-dependent protein kinase is activated.

A. 2,4,1,3,5.
B. 3,1,4,2,5.
C. 3,2,1,4,5.
D. 3,5,4,2,1.
E. 5,2,3,1,4.

26. When inositol-1,4,5-triphosphate (IP_3) binds to its specific intracellular receptor:

A. A phospholipase in the plasma membrane is activated.
B. Ca^{2+} is released from the endoplasmic reticulum into the cytosol.
C. GTP replaces GDP on a Gs protein.
D. The intracellular concentration of cAMP rises.
E. There is no intracellular receptor for IP3.

27. What is the net charge of a tetrapeptide EEKY at pH 7.0?

A. 2
B. 1
C. 0
D. -1
E. -2

28. The pI (isoelectric pH) of the protein means that

A. the amino and carboxy termini of the protein are not charged.
B. the internal amino acids of the protein do not have ionizable side chains.
C. the total net charge of protein is zero.
D. there are one positive ionic charge.
E. there are one negative ionic charge

29. A nonapeptide was determined to have the following amino acid composition: 2K, 2G, 2F, H, L. M. The following observations are made:

a. The native peptide was incubated with 1-fluoro-2,4-dinitrobenzene(FDNB) and then hydrolyzed: 2,4-dinitrophenylhistidine was identified by HPLC.
b. When the native peptide was exposed to cyanogens bromide (CNBr), an octapeptide and free glycine were found.
c. Incubation of the native peptide with trypsin gave a petapeptide, a tripeptide, a free lysine. 2, 4-Dinitrophenylhistidine was recovered from the pentapeptide and 2, 4-Dinitrophenylalanine was recovered from the tripeptide
d. Digested with the enzyme pepsin produced a dipeptide, a tripeptide, and tetrapeptide. The tetrapeptide was composed of 2K, F and G.

The native sequence was determined to be

A. GFKKGLMFH
B. MLFKFGGKH
C. HFLGKKFMG
D. HLFGKKFMG
E. HLGKKFFGM

30. Which interaction or force plays the most important role in the formation of protein secondary structures?

A. covalent bond
B. hydrogen bond
C. van der Waals interaction
D. electrostatic interaction
E. hydrophobic interaction

31. Which of the following atom is associated for determining the dihedral angles (phi, psi) of the peptide bonds?

A. N_H
B. C_O
C. C_α
D. H_N
E. C_β

32. In an α helix, the R groups on the amino acid residues ?

A. are found on the outside of the helix spiral.
B. generate the hydrogen bonds that form the helix.
C. stack within the interior of the helix.
D. cause only right-handed helices to form.
E. alternate between the outside and inside of the helix.

33. Which of the following statements about oligomeric proteins is false?

A. All subunits are identical.
B. Some subunits may have nonprotein prosthetic groups.
C. A subunit may be very similar to other protein.
D. Some oligomeric proteins can further associate into large fiber.
E. Subunit may be modular protein.

34. Myoglobin, but not hemoglobin, when it binds oxygen, exhibits:?

A. a hyperbolic saturation curve
B. a sgmoidal saturation curve
C. a Hill coefficient of 2.8
D. linear with a positive slope
E. linear with a negative slope

35. The E6V mutation in the β-subunit of Hemoglobin (Hb) S results in aggregation of the protein because of _____ interactions between Hb S.

A. covalent bond
B. hydrogen bond
C. van der Waals interaction
D. electrostatic interaction
E. hydrophobic interaction

36. What is the tertiary fold of antibody?; which of the following part of antibody is involved in antigen recognition?

A. All α; Fab
B. All β: Fab
C. α+β; Fc
D. α/β; Fc
E. None of them

37. The proteins of the Major Histocompatibility Complex (MHC) bind and display

A. immunoglobin fragment
B. antigen fragments
C. T cell fragment
D. B cell fragment
E. macrophage fragment

38. Which of the following protein or complex aids the protein folding and assembly in vivo?

A. ribosome
B. ER
C. mRNA
D. Chaperonin.
E. tRNA.

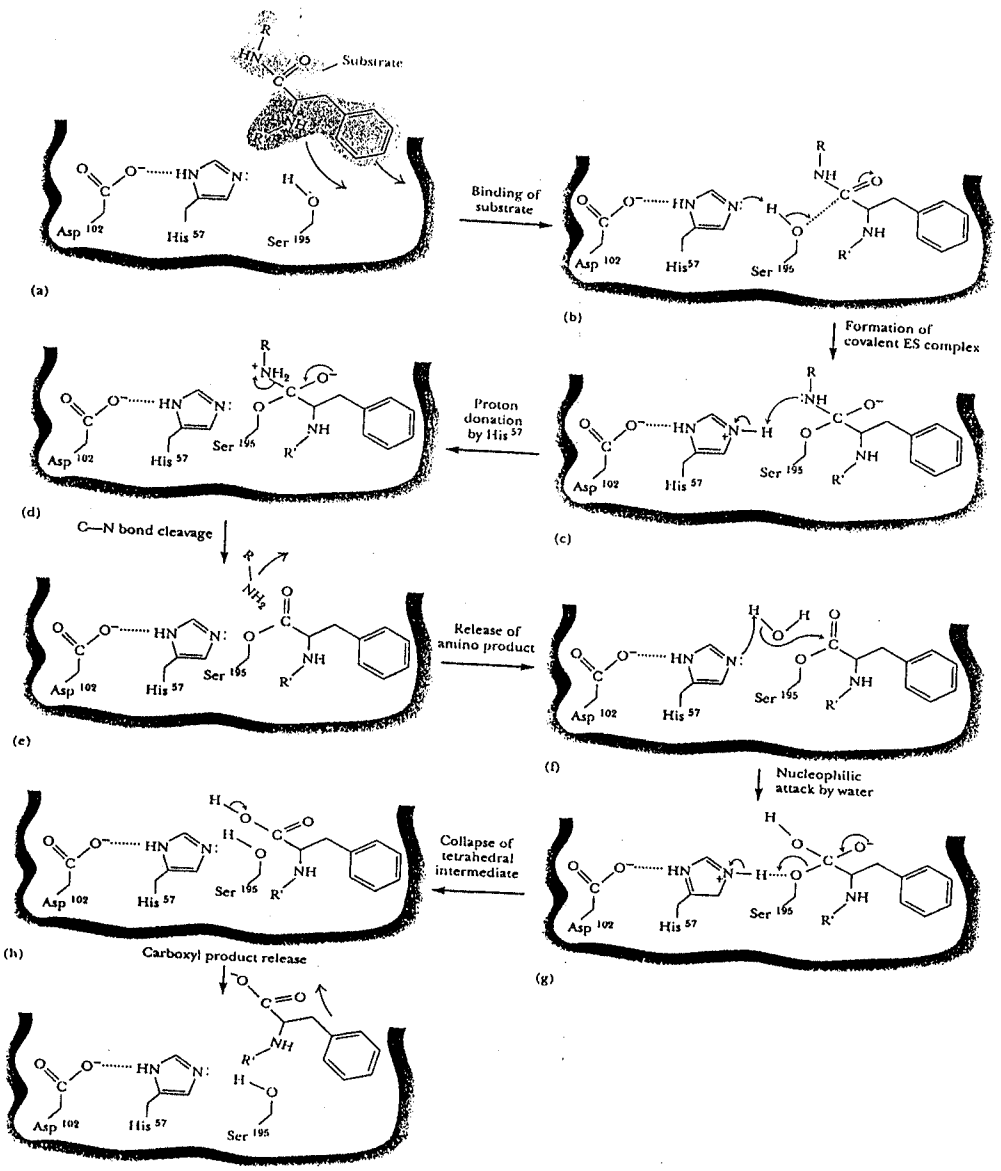
39. Which of the following statements about protein is false?

A. Primary structure determines tertiary structure.
B. Globular proteins are generally very compact.
C. Proteins are sometimes conjugated with carbohydrate or fats.
D. Nonpolar amino acid side chains generally are arranged on the surface where they interact with water.
E. Proteins consist of amino acids linked by peptide bonds.

40. Which the following techniques can be used to determine 3-dimensional structures of proteins?

A. X-ray diffraction and Circular dichroism spectroscopy
B. Circular dichriosim and absorption spectroscopy
C. Infrared and absorption spectroscopy
D. X-ray diffraction and nuclear magnetic resonance spectroscopy
E. Circular dichriosim and nuclear magnetic resonance spectroscopy

A detailed mechanism for the HCV protease (15-28).



41. Your "genius" professor found an important enzyme which could cleave the polyprotein products of the HCV genome. Which of the following names is classfied for it?

A. Oxidoreductase
B. Transferase
C. Hydrolase
D. Lyase
E. Isomerase or Ligase

42. After 3 years studying, they figured out that this enzyme is a serine protease which uses the "catalytic triad" for catalytic mechanism. The mechanism of this enzyme in detail is showing on introduction figure. Which of the following residue is the general base in this mechanism?

A. Aspartic acid
B. Histidine
C. Serine
D. H_2O
E. OH^-

43. Which of the following residue is the general base?

A. Aspartic acid
B. Histidine
C. Serine
D. H_2O
E. OH^-

44. If this enzyme involves general acid/base catalysis, which of the following parameters are pH-dependent?

1. kcat, 2. Km, 3. kcat/Km, and 4. Vmax

A. 1, 2, 3, and 4
B. 1 and 4
C. 1, 2, and 4
D. 1, 3, and 4
E. None of them.

45. The reaction mechanism is

A. Bi Bi single displacement reaction.
B. Bi Bi double displacement reaction.
C. Uni Uni Uni Uni order single displacement reaction.
D. Uni Uni Uni Uni random single displacement reaction.
E. Uni Uni Uni Uni double displacement reaction.

46. Since this enzyme is so important for us, we want to calculate the Kcat, Km of the substrate (Phe-Phe) and the K_I of two different inhibitors. The following kinetic data were obtained for in the absence of any inhibitor (1), and in the presence of two different inhibitors (2) and (3) at 5 μM concentration. Assume $[E]_o$ is 5 μM in these experiments.

[S], μM	ν(substrate), μM/Sec	ν(substrate + inhibitor I), μM/Sec	ν (substrate + inhibitor II), μM/Sec
1	12	4.3	5.5
4	29	14	13
8	35	21	16
12	40	26	18

What is kcat value?

A. 50 μM/sec.
B. 50 sec^{-1}.
C. 5.0 mM/sec.
D. 5.0 sec^{-1}.
E. 10 sec^{-1}.

47. What is Km value?

A. 3.1 mM.
B. 1.0 mM.
C. 3.1 μM.
D. 1.0 μM.
E. 0.3 μM.

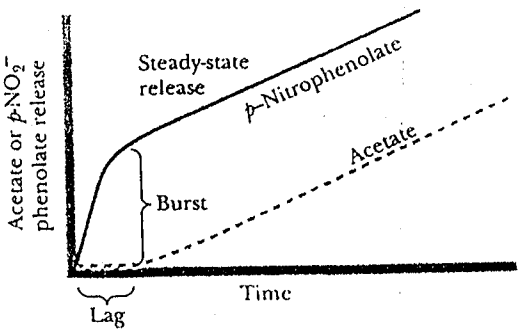
48. What kind of inhibitor I is and K_I value of inhibitor I is?

A. a competitive inhibitor, and K_I is 10.2 μM.
B. a noncompetitive inhibitor, and K_I is 10.2 μM.
C. a competitive inhibitor, and K_I is 2.2 μM.
D. a noncompetitive inhibitor, and K_I is 2.2 μM.
E. a competitive inhibitor, and K_I is 10.2 nM.

49. What kind of inhibitor II is and K_I value of inhibitor II is?

A. a competitive inhibitor, and K_I is 4.2 μM.
B. a noncompetitive inhibitor, and K_I is 4.2 μM.
C. a competitive inhibitor, and K_I is 3.1 μM.
D. a noncompetitive inhibitor, and K_I is 3.1 μM.
E. a competitive inhibitor, and K_I is 4.2 nM.

50. When they use *p*-Nitrophenylactate as substrate, they found burst kinetics showing in the following figure.

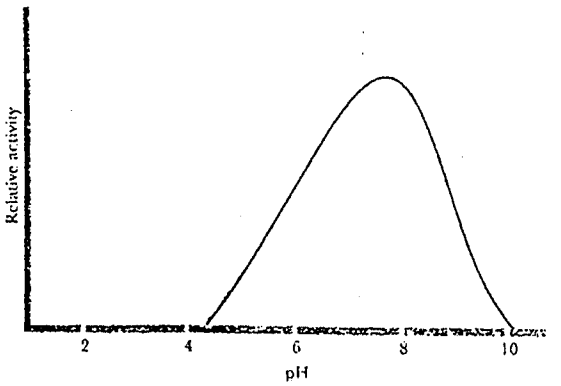


Which of the statements are required for burst kinetics.

1. The concentration of substrate must be greater than the concentration of enzyme.
2. The concentration of enzyme must be greater than the concentration of substrate.
3. The substrate addition is the rate determining step.
4. The first product release is the rate determining step.
5. The final product release is the rate determining step.

A. 1 and 3.
B. 1 and 4.
C. 2 and 3.
D. 2 and 4.
E. 1 and 5.

51. The optimal pH of this enzymatic reaction is 7.7 and two pKa of the general acid and general base are 6.2 and 8.5, respectively. The pH profile of this enzyme is showing on the below.



Supposing the general acid in this reaction mechanism is "Histidine" and the normal pKa of Histidine is about 6.0. What kind of environment can increase the pKa of Histidine?

A. hydrophobic.
B. hydrophilic.
C. neutral.
D. high temperature.
E. none of them.

52. In order to design a potent and "money making" inhibitor, they studied this enzyme by using X-ray diffraction. They found that this enzyme involves a tetrahedral oxyanion transition state as showing in front page. Which of the following interactions will help to stabilize the transition state?

1. hydrophobic interaction.
2. positive charge.
3. negative charge.
4. NH of the amino acids.

A. 1 and 2.
B. 1 and 3.
C. 2 and 3.
D. 2 and 4.
E. none of them.

53. There are a limited number of catalytic mechanisms or factors that contribute to the rate accelerations.

1. entropy loss in ES formation.
2. stabilization of ES complex.
3. stabilization of transition-state complex.
4. covalent catalysis.
5. general acid/base catalysis.
6. specific acid/base catalysis.
7. metal ion catalysis.
8. proximity and orientation.

Please choose the mechanism and factors which of them can explain this enzymatic mechanism.

A. all
B. all except 3, 5, and 7.
C. all except 2, 6, and 7.
D. all except 2, 4, 5, and 7.
E. all except 3, 4, 6, and 7.

54. There are several ways to regulate enzyme activity. Which of the following ways are true for serine protease?

1. Zymogen (proenzyme).
2. The concentration of substrate is greater than 10 Km.
3. Allosteric regulation.
4. Kinetic control.

A. 1
B. 1 and 2.
C. 2 and 3.
D. all.
E. none of them.

55. Which of the following can **NOT** be used to regulate enzymes?

A. end product inhibition.
B. feedback inhibition.
C. allosteric regulation.
D. covalent modification.
E. None of them.

56. Allosteric enzymes

A. usually have only one active site.
B. are regulated primarily by covalent modification..
C. usually have more than one peptide chain..
D. usually show strict Michaelis-Menten kinetics.
E. usually catalyze several different reactions within a metabolic pathway.

III. 問答題

57. Some bacteria require *p*-aminobenzoate in the culture medium for normal growth, and their growth is severely inhibited by the addition of sulfanilamide, one of the earliest sulfa drugs. Moreover, in the presence of this drug, 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) accumulates in the culture medium. These effects are reversed by addition of excess *p*-aminobenzoate. (a) What is the role of p-aminobenzoate in these bacteria ? (b) Why does AICAR accumulate in the presence of sulfanilamide ? (c) Why are the inhibition and accumulation reversed by addition of excess *p*-aminobenzoate ? (14%)

58. Please describe in detail about the relationship between urea cycle, citric acid cycle and mitochondria, as well as their contribution to the *de novo* biosynthesis of pyrimidine nucleotides in mammals. (10%)

59. Please describe the methodology of DNA sequencing used in human genome project and their reaction mechanisms in detail. (10%)