

Name: _____

Student #: _____

University of Toronto
Faculty of Applied Science and Engineering
Division of Engineering Science
Midterm Examination

BME205S

Monday Mar 3, 2014, 9:00 – 10:50 am

Duration: 110 minutes

Examiners: J. Rocheleau and P. Gilbert

ANSWER ALL QUESTIONS ON THESE SHEETS

1. No cell phones are allowed.
 2. Type A: Closed book examination, no aids permitted.
 3. Part 1 Multiple Choice Questions. Your answers are to be submitted on the scantron sheet provided.
 4. Part 2 Questions have the mark available in the square brackets []; each portion of a question also shows how many marks are allocated to it. **Each question has a strict sentence limit restriction, each sentence written above the limit will be deducted half a mark.**
 5. There are two extra blank pages at the end of the test for rough work.
 6. Please note that a help sheet has been provided with the test.
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Last Name: _____ **Solutions and Marking Scheme** _____

First Name: _____

Student Number: _____

Tutorial section:

[]	TUT 01	1	Tue	13:00	14:00	BA2195
[]	TUT 02	1	Tue	13:00	14:00	BA3116
[]	TUT 03	1	Thu	16:00	17:00	BA3008
[]	TUT 04	1	Thu	16:00	17:00	BA2135
[]	TUT 05	1	Fri	12:00	13:00	BA2135
[]	TUT 06	1	Fri	12:00	13:00	BA3008
[]	TUT 07	1	Fri	10:00	11:00	BA2159
[]	TUT 08	1	Fri	10:00	11:00	BA2135

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PART I: Multiple Choice

_____ out of 40

PART 2: Short Answer Questions

Question	1	2	3	4	5	6	7	8
Marks Available	2	4	3	3	3	4	4	7
Marks Achieved								

PART 2 _____ out of 30

TOTAL MARKS _____ out of 70

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PART 1: Multiple Choice
ANSWERS TO BE FILLED OUT ON ANSWER SHEET

- (1) The first culture of human cells was begun by George and Martha Gey of Johns Hopkins University in 1951). The cells were obtained from a malignant tumor and named _____ cells after the donor, _____.
- a) HeLa, Herbert Lane
 - b) HeLa, Henrietta Lacks**
 - c) Roberts, John Roberts
 - d) MaLe, Martin Lewis
 - e) HeLa, Helen Lassiter
- (2) The process by which a relatively unspecialized cell becomes highly specialized is called **a or b** accepted.
- a) differentiation**
 - b) determination**
 - c) degeneracy
 - d) denaturation
 - e) renaturation
- (3) In some cases, an infecting virus does not lead to the death of the host cell, but instead integrates its DNA into the DNA of the host cell's chromosomes. Integration of the viral DNA can have different effects like exhibiting normal behavior until exposure to a stimulus that activates the dormant viral DNA, production of viral progeny that bud off of the infected cell or a loss of control over growth and division leading to malignancy. Such an infection is referred to as a(n) _____ infection.
- a) lytic
 - b) proviral**
 - c) elutable
 - d) virulent
 - e) avirulent
- (4) What kind of noncovalent interaction is typified by interactions between two molecules that are so close together that they can experience weak attractive forces bonding them together?
- a) H bonds
 - b) ionic bonds
 - c) hydrophobic interactions
 - d) polar covalent bonds
 - e) van der Waals forces**
- (5) A molecule that is capable of releasing or donating a hydrogen ion is termed a(n) _____.
- a) base
 - b) hydron
 - c) acid**
 - d) anachronism
 - e) pain

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(6) Why do sugars tend to be highly water soluble?

- a) because they have only a few hydroxyl groups
- b) because of their large numbers of hydroxyl groups**
- c) because of their large numbers of sulfhydryl groups
- d) because of their large numbers of methyl groups
- e) because of their small molecular weights

(7) Proteins are often composed of two or more distinct modules that fold up independently of one another. They often represent parts of a protein that function in a semi-independent manner. These modules are called _____.

- a) protein motifs
- b) functionals
- c) domains**
- d) dominoes

(8) Tertiary structure in DNA is also known as _____.

- a) primary structure
- b) supercoiling**
- c) double helix
- d) α -helix

(9) What kind of membrane protein is found entirely outside the bilayer on either the extracellular or cytoplasmic surface? These proteins are covalently linked to a membrane lipid situated within the bilayer.

- a) integral protein
- b) lipid-anchored protein**
- c) peripheral proteins
- d) carbohydrate-anchored protein
- e) transmembrane

(10) Integral membrane proteins have been engineered to lack the portion that normally projects into the extracellular space. When the gene is inserted in cells, what happens to the mobility of this protein in the membrane?

- a) They move at a much greater rate than the wild type protein.**
- b) They move at a much smaller rate than the intact protein.
- c) They do not move at all.
- d) They are not inserted into the membrane so nothing can be learned about their mobility.
- e) They flip to the opposite leaflet.

(11) In the Na⁺/glucose cotransporter, _____ moving down its gradient drives the transport of _____ against its gradient.

- a) Na⁺ ions, K⁺ ions
- b) Na⁺ ions, glucose**
- c) glucose, Na⁺ ions
- d) glucose, K⁺ ions
- e) K⁺ ions, glucose

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(12) Which site in a neuron receives incoming information from external sources?

- a) Dendrites
- b) Axon
- c) Axon hillock
- d) Terminal knob
- e) Cell body

(13) What causes the membrane potential to return to the normal negative value after an action potential has occurred?

- a) opening of a voltage-gated K⁺ channel
- b) opening of a voltage-gated Na⁺ channel
- c) closing of a voltage-gated K⁺ channel
- d) opening of a ligand-gated Na⁺ channel
- e) opening of a voltage-gated K⁺ facilitated transporter

(14) Where in a myelinated axon are nearly all of the ion channels concentrated?

- a) the cell body
- b) nodes of Ranvier
- c) dendrites
- d) axon terminals
- e) neuron nucleus

(15) The backbone of a DNA molecule is _____.

- a) made up of sugars alone
- b) made up of nitrogenous bases alone
- c) made up of phosphate groups alone
- d) made up of alternating phosphate and sugar groups
- e) made up of alternating sugars and nitrogenous bases

(16) You isolate DNA from a particular organism and analyze it. The amount of adenine was 6 μ moles and the A+T/G+C ratio is 4.0. How much guanine should be in the sample?

- a) 6 μ moles
- b) 3 μ moles
- c) 1.5 μ moles
- d) 4 μ moles
- e) 12 μ moles

(17) Different versions of a gene are called _____.

- a) heterologues
- b) homologues
- c) allogues
- d) alleles
- e) mutoids

(18) Hemoglobin molecules analyzed at various times during an animal's life seem to be highly

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variable. What is the explanation?

- a) Contaminants at various points in an organism's life cause the variation in data.
- b) Hemoglobin denatures when isolated from older embryos.
- c) The combinations of α -family and β -family globin polypeptides differ with developmental stage.
- d) Hemoglobins are chemically altered as they age.
- e) Hemoglobins bind copper ions instead of iron ions.

(19) DNA sequences in bacteria that on rare occasions moved from one place in the genome to another are called _____.

- a) movers
- b) jumpons
- c) transposons
- d) transpodons
- e) jumpsons

(20) The most common type of genetic variability in humans occurs at sites in the genome where single nucleotide differences are found among different members of the population. What are these sites called? (a, b or c was accepted)

- a) single nucleotide polymorphisms
- b) SNPs
- c) "snaps"
- d) single nucleotide polymathisms
- e) single nucleotide polymorphisms and SNPs

(21) What could be defined as an organized network of extracellular materials found beyond the immediate vicinity of the plasma membrane?

- a) intracellular matrix
- b) extracellular matrix
- c) extracellular netrax
- d) intercellular material
- e) epicellular matrix

(22) All collagen family members consist of _____ chains arranged in a _____.

- a) 2, double helix
- b) 3, double helix
- c) 3, triple helix
- d) 3, triple lattice
- e) 2, triple helix

(23) What substance joins proteoglycans together into gigantic complexes called proteoglycan aggregates? These complexes can occupy very large volumes.

- a) hyaluronidase
- b) hyaluronic acid
- c) proteoglycase
- d) fibronectin
- e) laminin

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(24) The degradation of the extracellular matrix, along with cell surface proteins, is accomplished mostly by a zinc-containing enzyme family called _____.

- a) TIMPs
- b) MTPs
- c) matrix metalloproteinases
- d) matrix metallophosphatases
- e) TRIMPs

(25) Evidence strongly suggests that the bent conformation of an integrin is _____ and unable to bind its ligand.

- a) loose
- b) active
- c) tight
- d) stretched
- e) inactive

(26) You coat a Petri dish with fibronectin and proteoglycans and culture cells on the dish. The cells adhere to the dish. You repeat the experiment but this time add RGD tripeptides to the culture dish as the cells are added. The result of this experiment is an example of what biochemical process?

- a) competitive inhibition
- b) noncompetitive inhibition
- c) enzymatic activation
- d) feedback inhibition
- e) allosterism

(27) To what is the cytoplasmic domain of integrins in the region of a focal contact connected via various adaptors?

- a) tubulins of the cytoskeleton
- b) actinin of the cytoskeleton
- c) actin of the cytoskeleton
- d) dynein of the cytoskeleton
- e) band III protein of the membrane

(28) If the receptor is degraded along with its ligand after internalization, what is the effect on the cell's ability to respond to a hormone?

- 1) The response is enhanced.
- 2) The cell has increased sensitivity to subsequent stimuli.
- 3) The cell has decreased sensitivity to subsequent stimuli.
- 4) The cell exhibits no change in responsiveness to subsequent stimuli.

- a) 1
- b) 2
- c) 3
- d) 4
- e) 1 and 2

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(29) Which amino acids are known to be phosphorylated by protein kinases?

- a) tyrosine, threonine, glycine
- b) threonine, serine, tryptophan
- c) serine, threonine, tyrosine
- d) phenylalanine, serine, tyrosine
- e) serine, leucine, tyrosine

(30) Why are G-protein coupled receptors often known as 7TM receptors?

- a) They have 7 tyrosine-methionine dipeptides in their structure.
- b) They have 7 transmembrane β -pleated sheets.
- c) They have 7 transmembrane α -helices.
- d) They have 7 methionine-tryptophan dipeptides in their structure.
- e) They have 7 nucleotides attached to their structure.

(31) Place the following events in the proper order.

- 1) Activation of one or more cellular signaling proteins.
- 2) Dissociation of G_α from the G protein complex.
- 3) Production of a second messenger, like cAMP.
- 4) Replacement of GDP by GTP on the G_α after interaction with an activated GPCR.
- 5) Conformational change in the G_α subunit causing a decreased affinity for the $G_{\beta\gamma}$ subunit.
- 6) G_α -subunit with its attached GTP activates an effector like adenylyl cyclase.

- a) 4 – 5 – 2 – 6 – 3 – 1
- b) 5 – 4 – 2 – 6 – 3 – 1
- c) 4 – 6 – 2 – 5 – 3 – 1
- d) 4 – 5 – 2 – 3 – 1 – 6
- e) 1 – 5 – 2 – 4 – 3 – 6

(32) What does the interaction between arrestin and clathrin promote?

- a) the uptake of free hormone
- b) the uptake of phosphorylated GPCRs into the cell by exocytosis
- c) the uptake of phosphorylated GPCRs into the cell by endocytosis
- d) the expulsion of phosphorylated GPCRs from the cell by exocytosis
- e) the secretion of GPCRs

(33) How is signaling by an activated G_α subunit terminated?

- a) The bound GTP is hydrolyzed to GMP.
- b) The bound GDP is hydrolyzed to GTP.
- c) The bound GTP is hydrolyzed to GDP.
- d) The bound GDP is phosphorylated to GTP.
- e) The G_α subunit releases GDP and binds GTP.

(34) _____ are enzymes that phosphorylate specific tyrosine residues on protein substrates.

- a) Protein tyrosinases
- b) Protein-tyrosine kinases

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- c) Tyrosine pronases
- d) Proteokinases
- e) Tyrokinases

(35) Which of the following features would be a requirement for a receptor that exhibits ligand-mediated dimerization?

- a) The ligand has only one binding site for receptors.
- b) The ligand has two binding sites for receptors.**
- c) The receptor must have a phenylalanine residue in a specific location.
- d) The receptor must have a molecular weight of 50,000 daltons.
- e) Ligand binding causes a conformational shift that reveals a binding site for another receptor.

(36) Once the kinase domain of receptor protein-tyrosine kinase has been activated, what does the activated receptor protein-tyrosine kinase do?

- a) The receptor subunits denature.
- b) Each receptor subunit phosphorylates its partner on tyrosine residues found in regions adjacent to the kinase domain.**
- c) Each receptor subunit phosphorylates itself on tyrosine residues found in regions adjacent to the kinase domain.
- d) The receptor subunits dephosphorylate each other.
- e) The receptor subunits refold into a more effective conformation.

(37) Specificity in MAP kinase pathways is sometimes achieved by spatial localization of the pathway's component proteins. Spatial localization of these components is done by structural (i.e., nonenzymatic) proteins called _____.

- a) sequestration proteins
- b) partitioning proteins
- c) scaffolding proteins**
- d) framework proteins
- e) spatial organization proteins

(38) What is the name of a calcium-binding protein that acts in conjunction with calcium to bring about the responses associated with cytoplasmic rises in calcium ion concentration?

- a) calpectin
- b) calmodulin**
- c) calcariain
- d) callistin
- e) modulocalcin

(39) The activation of a common effector by signals from a variety of unrelated receptors, each of which binds to its own ligand, is called _____.

- a) divergence
- b) convergence**
- c) crosstalk
- d) transvergence
- e) coherence

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(40) Once activated, what does caspase-9 itself activate?

- a) phospholipase C
- b) protein kinase A
- c) other initiator caspases
- d) downstream executioner caspases
- e) downstream caspase-8

PART 2: Short Answer Questions

(1) [2 marks] Unlike eukaryotic cells, prokaryotic cells have no membrane-bound organelles, which act to transport some materials around the cell and compartmentalize certain cellular processes. In 2 or less sentences, describe why do prokaryotic cells not require such membrane-bound organelles?

Solution: Prokaryotic cells are smaller, and simple diffusion is sufficient to move things around the cell.

(2) [4 marks] You treat a partially purified preparation of protein with a reagent that breaks bonds between sulfur atoms. In three or less sentences, which level(s) of protein structure are likely to be affected the most?

Solution: Both the **tertiary and quaternary** (3 marks – minus 1 mark if they give more) levels of structure would be affected since those levels are the only ones in which **disulfide bonds** (1 mark) are prominent.

(3) [3 marks] Which of the following tripeptides would be most likely to be soluble in an organic (hydrophobic) solvent like benzene: N - phenylalanine - alanine - glutamine - C, N - leucine - alanine - lysine - C, N - proline - phenylalanine - leucine - C, N - arginine - lysine - proline - C, N - glutamate - aspartate - glycine - C? Explain your answer in three or fewer sentences.

Solution: N - proline - phenylalanine - leucine - C would be most soluble in a hydrophobic solvent. All three amino acids are classed as nonpolar amino acids and could be soluble in benzene. In the other tripeptides, at least one of the amino acids does not belong to the nonpolar class.

(4) [3 marks] If mice are maintained on very strict diets with reduced caloric intake, what happens to their life span as compared to littermates fed diets with normal caloric content? In 2 or less sentences, what is a possible explanation for the effect of this diet on these animals?

Solution: The mice on restricted calorie diets live 30 – 40% longer. The animals exhibit a marked decrease in superoxide free radical and hydrogen peroxide production, which could explain their increased longevity.

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- (5) [3 marks] A membrane's transition temperature is determined and found to stretch over a wide range of temperatures. The membrane also exhibits high stability and a reduced permeability similar to that in most mammals. In two or less sentences, what membrane component is responsible for these traits and how does it do it?

Solution: Cholesterol alters the way hydrocarbon chains pack together and is responsible for these traits.

- (6) [4 marks] Why is flip-flop of membrane phospholipids so rare? In what cell process do cells actively move the phospholipid phosphatidylserine from the inner (inside) leaflet to the outer (outside) leaflet of the plasma membrane? Once on the outside, what does the phosphatidylserine do? (Your answer should be contained in 5 or fewer sentences)

Solution: For flip-flop to occur, it would be necessary for the hydrophilic head of a phospholipid to move through the hydrophobic part of the bilayer, an extremely unlikely event. PS is flipped to the outer membrane during apoptosis. Once on the outside it is recognized as an "eat me" signal by macrophages (i.e. it acts as a signal for the cell to be cleared by phagocytosis)

- (7) [4 marks] Signaling by soluble extracellular molecules can be classified as endocrine, paracrine, or autocrine. Describe how these three types of cellular signalling differ. Growth hormone is secreted from the pituitary, which is located at the base of the brain and acts through growth hormone receptors located on the liver. Is this an example of endocrine, paracrine or autocrine signalling? Why?

Solution: endocrine is secretion of a factor that enters the blood stream to act on other tissues [1 mark]. Paracrine involves diffusion of the factor a short distance to act on neighboring cells [1 mark]. Autocrine signalling the factor acts on the cell that secreted it [1 mark]. The example given is endocrine signalling because the factor is secreted to act on another tissue (brain to liver) [1 mark].

- (8) [7 marks] Epithelial cadherin is a single pass transmembrane protein, which means that only one segment of the protein is embedded in the plasma membrane of the cell. The part of the protein that is N-terminal to the transmembrane segment is on the outside of the cell and the part that is C-terminal is on the inside.

- a. (1 mark) The transmembrane segment adopts the secondary structure of an alpha helix. In the structure of an alpha helix, there are 3.6 amino acids per turn and each turn is the 5.4 Å (or 5.4 nm) in length. Given that the thickness of the plasma membrane is 40.5 Å (or 40.5 nm). How many amino acids are in the transmembrane segment?

ANSWER:

$(40.5/5.4) \times 3.6 = 27$ amino acids

Marking scheme:

1 marks for above solution

0 marks otherwise

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- b. (4 marks) Below is a segment of the sequence of epithelial cadherin containing the transmembrane segment, circle the region that is the most likely the transmembrane segment. In three sentences or less, state the reason for your selection.

QVTTLDVHVCDCEGTVNNCMKAGIVAAGL**QVPAILGILGGILALLILLLLLLFLRR**RTVV
KEPLLPPDDDT

ANSWER:

Looked for a sequence with consecutive amino acids with **hydrophobic R-groups** around 27 aa long (in this case 25 aa) that interact with **the fatty acyl tails of the phospholipids**. The transmembrane space also includes **hydrophilic amino acids** flanking the hydrophobic portion (at the ends) that interact with the **hydrophilic head group of the phospholipids**. The selected sequence is therefore 27 amino acids long, with one hydrophilic amino acid on each side (flanking) the 25 hydrophobic amino acids.

Marking scheme:

- + 2 mark for selecting the exact region, +1 for mostly correct
- + 1 marks for mentioning fatty acyl tails interact with hydrophobic R-groups (or amino acids)
- + 1 marks for mentioning the hydrophilic head group of the phospholipid interact with hydrophilic aa

- c. (2 marks) What is the membrane thickness due to the fatty acyl tails of one phospholipid?

Recognition that 25 hydrophobic aa acids interact with the phospholipid tails – which works to

+ 1 Mark: $x/5.4 \times 3.6 = 25$ $x = 37.5$ Å

+ 1 Mark: This thickness is the phospholipid bilayer, so one phospholipid tail would add $37.5/2 = \sim 19$ Å