Fundamentals of Biomedical Sciences (INTD 5000)
Energetics and Endocrinology
Test P1

Name:_____

Student I.D._____

Please check that there are 10 pages in your copy of the exam.
Please put your name on every page as each question will be graded by different Professors.

If there is not enough room in the space provided to answer your question please use the back of **that** question page to complete your answers. Pages will be separated and given to each of the Professors to grade, so the answers to a particular QUESTION must be on that QUESTION page.

Test is 65 points should take no more than 80 minutes. Please answer **QUESTION 1 and choose 4 from the remaining 5 questions (2-6).** Please note some questions offer you choices of different components. Do **NOT** answer all of these choices or you will run out of time and we will only grade the number of components asked for, in the order given.

Please indicate below which 4 questions (other than question 1) that you have answered:-

Question 1: Compulsory	Grade____
Question 2:___	Grade____
Question 3:___	Grade____
Question 4:___	Grade____
Question 5:___	Grade____
Question 6:___	Grade____

When you have completed this test, please fill in the course assessment.

Question 1: Compulsory (25 points)

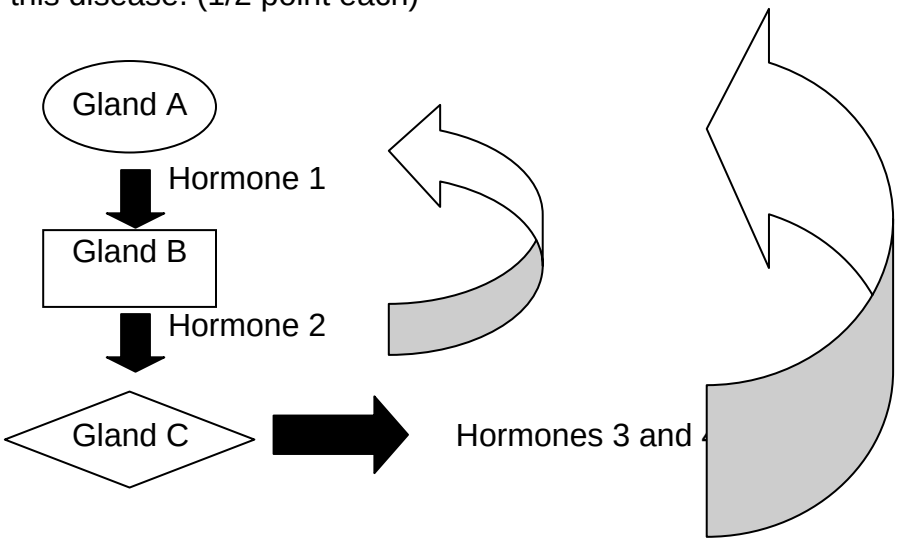
Case Study:

A 25 year-old male complains that he has put on a lot of weight in the last 6 months even though his appetite has decreased and he claims he eats much less than he used to, so much so that now in order to maintain his weight eats only once a day. He also mentions he is always tired and feels constantly cold. The doctor measures the patient's resting metabolic rate in the examination room and skin and oral temperature. The room temperature during measurement was 18 ^{o}C. The thermoneutral zone for people lies between 25 and 32^{o}C.

The data are presented in the table below.

		Normal range
Oral temperature (^{o}C)	35.8	36.8-37.5
Peripheral skin temperature (^{o}C)	20.0	
Blood pressure (mmHg)	100/65	120/80
Heart rate (BPM)	45	50-80
T_4 (nmol/l)	45	60-200
T_3 (nmol/l)	0.4	0.3-4.0
TRH (mU/l)	2	0.1-1.5
TSH (mU/l)	10	1.5-7.0
RMR (ml O_2/min)	150	

A. On the diagram below identify the three glands (A, and C) and "hormone 2" that may be involved in this disease. (1/2 point each)



i) Gland A _____

ii) Gland C _____

iii) Hormone 2 _____

iv) What do the curved arrows represent? _____

v) Is this considered a hyposecretory or hypersecretory endocrine disorder? (1 point) _____

vi) Is this a primary, or secondary disorder? Explain briefly (2 points)

B. Giving reasons for your answer, explain whether the following statements are **True Or False. <u>Choose four of the statements (I-IV)</u> (5 points each)**

I. The patients metabolic rate would be higher in the TNZ than the measured RMR.

II. The patient's change in appetite is due to lower than normal leptin levels.

III. The patient has a goiter.

IV. The patient will have higher rates of gluconeogenesis than normal.

V. His feeding regime will induce greater diet induced thermogenesis than if he ate three meals a day.

Choose 4 Questions (2-6)

Question 2: (10 points)

a) List two chemical mediators that regulate satiety.

b) Briefly describe the changes you would expect in chemical mediators that regulate appetite following prolonged caloric restriction.

Question 3: (10 points)

AMP-activated protein kinase is activated during fasting. Explain how this could be beneficial and unbeneficial/detrimental in respect to metabolic adjustments to fasting that must occur in muscle, liver, red blood cells, adipose tissue, and brain. (10)

Question 4: (10 points)

a) Explain why activation of the AMP-activated protein kinase is a good treatment for type 2 diabetes mellitus.

b) Would it be a good therapy for type 1 diabetes mellitus? Why or why not?

Question 5: (10)

In mammalian organisms, growth of cells, tissues and organs does not occur directly as a response to increased availability of nutrients.

Explain

a) why the response to nutrients needs to be different in single-cell organisms versus mammals;

b) why most cells in the adult mammalian body at any instant of time are not dividing, rather than dividing;

c) why hormones (as opposed to other kinds of signals) are needed in the mammalian body to control the growth of cells in tissues and organs. [Note, this last section of the question does not need an answer that mentions any specific hormone, but if you want to give a specific hormone as an example within your answer that is OK, but not necessary. In all 3 parts of this question, please focus entirely on a direct answer to the question. Also, please only give answers as full sentences, without drawings].

Question 6: (10 points)

Insulin affects cellular function in mammals through two signaling pathways. Calorie restriction increases insulin sensitivity, compared to that observed in humans eating ad libitum.

If you were to conduct an experiment in which calorie restricted and “ad libitum” fed individuals were exposed to the same blood concentrations of insulin,

a) how would these dietary regimes affect the two insulin signaling pathways?

b) Describe and give a rationale for

i) what tissue you might choose for taking your measurements;

ii) what you would measure to ascertain the response of these pathways to insulin;

iii) any differences you might observe in the responses to insulin of these two pathways between ad libitum fed and calorie restricted individuals.

ASSESSMENT OF THIS SECTION AND THIS TEST

1. **Strongly agree**
2. **Agree**
3. **Neutral**
4. **Disagree**
5. **Strongly disagree**

If you wish to explain your answer please do so in the space below the question

1. The material selected for this topic was interesting. __

2. This material and approach brought the material to life.__

3. This course covered the right amount of material. __

4. This course emphasized concepts rather than facts. __

5. The interactive approach in lectures made me stay alert in class. ___

7. The test was easy.__

8. The test was in a format similar to what I had expected. ___

9. The following questions were ambiguous._____

10. The test was a fair assessment of my knowledge.___

11. What did you like the most about this section?

12. What did you like the least about this section?

13. Suggest ways we may improve this section

Name:_____

Fundamentals of Biomedical Sciences (INTD 5000)
Exam 7 - Physiology

Cardiovascular & Renal: Drs. Toney and Stockand
Neurophysiology: Drs. Shapiro, Macleod, & Eaton

Name:_____

Student I.D._____

INSTRUCTIONS

1) Please check that there are 13 pages in your copy of the exam.

2) **Please put your name on every page**. Questions will be graded by different Professors.

3) Your answers must fit in the space provided for each question or must be limited to the number of sentences specified by each question.

4) This test is worth 10.5% of your final grade and should take about 90 minutes or less to complete.

5) When you have completed this test, please fill in the section assessment on page 13.

6) Please remember to return the course evaluation to Ms. Kelley Fuhrbach in the Graduate Dean's Office by 5:00 PM on Friday, Dec. 12th.

Name:_____

Dr. Toney

1. Briefly describe the concept of homeostasis and the role played by negative feedback control mechanisms. (3.5 points)

2. The only biological action of drug ZETA is to decrease aortic compliance. Briefly explain how treatment with drug ZETA alone would affect each of the variables listed below. Also explain how each variable would change if treatment with drug ZETA were combined with a -adrenoceptor blocker (beta blocker), which interrupts the action of sympathetic nerves on the heart. (8 points)

a) Systolic Arterial Pressure

b) Diastolic Arterial Pressure

3. Which would be a more effective way to lower the mean arterial pressure in a patient with high blood pressure, treatment with drug ZETA alone or with drug ZETA combined with a -adrenoceptor blocker? Briefly explain the rationale for your answer. (5 points)

Name:_____

4. An accident victim is determined to have low mean arterial pressure (MAP) and to have lost 30% of her blood volume. One hour later, her blood volume is measured again and has increased by 0.75 L. Another hour passes and her blood volume has again risen by another 0.25 L. Assuming that no fluid resuscitation was given, what mechanisms could account for the increase of blood volume? Briefly explain how this would occur. (7 points)

5. A person arrives in hospital with very low mean arterial pressure (MAP: ~65 mmHg). Also, their sympathetic nerve activity and arterial baroreceptor nerve activity are both below normal. To raise blood pressure a vasoconstrictor drug is given, which caused baroreceptor nerve activity to rise in pace with the increase of MAP. However, you notice that sympathetic nerve activity failed to change. What is a likely cause of these symptoms? Briefly explain the rationale for your answer. (7 points)

Name:_____

Dr. Stockand

1. Jake is given a drug that constricts both the afferent and efferent arterioles, but has a substantially larger effect on the afferent arteriole. Explain the consequences of this drug on GFR, RBF and MAP. In your explanation, describe how the changes in these vascular effectors relate to the three variables. (5.0 points)

2. Long-term use of drug E destroys the glomerular basement membrane (basal lamina). Describe the consequences of this on filtration. (2 points)

3. What would be the result of a loss of function mutation in the Na/K/2Cl transporter (tri-transporter) in the thick ascending limb? (3 points)

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Name:_____

4. Draw and label a typical epithelial cell within a renal epithelium. Describe the properties of this cell and epithelium that allow vectorial transport and separation of fluid compartments. (5.5 points)

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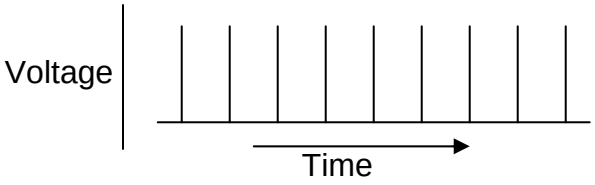
Name:_____

Dr. Shapiro

1. A certain stimulus of a neuronal cell soma (not axon) produces the pattern of action potentials shown below: (7.5 points)



Assume physiological concentrations of ions inside and outside of the cell.

a. Draw the pattern of firing of action potentials that could be expected to result from a doubling of the stimulus intensity. Briefly explain your logic. (2.5 points)

b. Then, a ground-up *Xanax* pill is dissolved in the extracellular solution, resulting in the opening of many $GABA_A$-type Cl^- channels. Draw the firing pattern resulting from the same stimulus that you might expect now. Briefly explain your logic. (2.5 points)

c. Finally, a robust concentration of the fish toxin, tetrodotoxin (TTX) (a voltage-gated Na^+-channel blocker), is then added to the extracellular solution. Draw the firing pattern expected from the stimulus now. Briefly explain your logic. (2.5 points)

Name:_____

2. In class, we discussed that the resting membrane potential of excitable cells is relatively negative (approximately -80 mV). Within the space of a paragraph, explain the mechanism by which this negative resting potential exists. Be sure to include the actions of ions, ion channels, diffusion and permeability in your answer. (8 points)

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Name:_____

Dr. Macleod

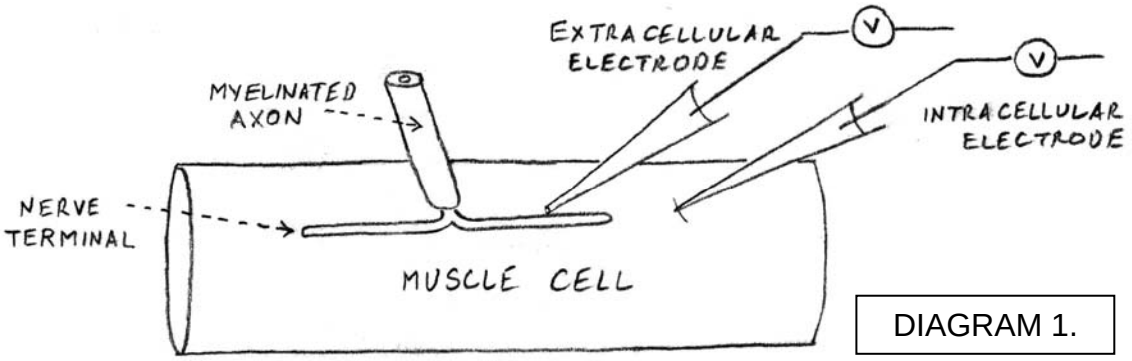

DIAGRAM 1.

A synapse between a motor-nerve terminal and a muscle cell (neuromuscular junction) is represented in Diagram 1 directly above. The terminal forms an excitatory synapse, releasing Acetylcholine onto ionotropic Acetylcholine receptors on the muscle surface. The tip of an electrode inside the muscle (intra-cellular) records the potential across the muscle membrane and can detect release from the entire nerve terminal. The tip of another electrode outside the muscle cell (extra-cellular) can only detect release from less than one half of the nerve terminal.

Use the information above to assist you in responding to the following 5 questions. (8 points)

1. Describe, or preferably sketch, the muscle membrane potential (a trace) recorded by the intracellular electrode while the motor-neuron is quiescent, i.e. in the absence of any action potentials in the motor-neuron. (2 point)

2. Describe, or indicate in Diagram 1 above, the morphological/structural distribution of Acetylcholine release along the nerve terminal. What is the term used to describe the physical site of release? (2 points)

3. Describe or sketch the potentials (traces) recorded by <u>each</u> electrode when the terminal releases a single quantum of Acetylcholine. Clearly indicate the polarity of the signals, and name the ionic species that flow(s) through the receptor channels. (4 points)

Name:_____

4. Make an estimate of the total number of Acetylcholine molecules released if the nerve is stimulated once to initiate an action potential and ten quanta are released. (1 point)

5. Describe or sketch the muscle membrane potential (trace) recorded by the intracellular electrode when the nerve is stimulated once to initiate an action potential when there are no extracellular calcium ions (Ca^{2+}). (2 point)

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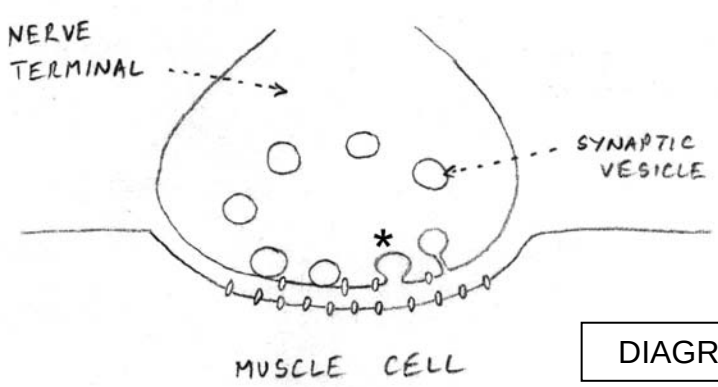

DIAGRAM 2.

A nerve terminal opposite a muscle cell membrane is represented in Diagram 2 directly above. Synaptic vesicles cycle past the site of neurotransmitter release in the nerve terminal. Neurotransmitter receptors are shown in the muscle membrane, while just 4 channels are shown in the terminal membrane.

Use the information above to assist you in responding to the following 5 questions. (10 points)

1. What types of channels are found in the terminal membrane closely associated with the site of the synaptic vesicle undergoing fusion (indicated by the asterisk)? What activates the opening of these channels? (2 points)

Name:_____

2. What does the SNARE hypothesis propose? On what basis are the three SNARE proteins classified? What role does synaptotagmin play in the SNARE hypothesis? (4 points)

3. Name the pinchase that mediates endocytosis. Indicate its site of action on Diagram 2 above. (2 points)

4. How soon after the start of an action potential does Ca^{2+} enter the nerve terminal? For what period of time does its entry persist? (2 point)

5. To what degree may the Ca^{2+} concentration in a microdomain exceed the Ca^{2+} concentration in the bulk of the cytosol in the terminal? Indicate the location of the Ca^{2+} microdomain on Diagram 2 above. (2 points)

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Name:_____

Dr. Eaton

1. Graduate student Leo has developed an in vitro myotube culture system from mouse skeletal muscle cells that allows him to grow myotubes in culture dishes. Using fluorescent Bungaro toxin to visualize ACh receptor clusters (AChRs), Leo has found that addition of recombinant agrin to the culture medium can stimulate AChR clustering on the myotubes. Leo has collected a freezer box full of antibodies from various sources that recognize the cell surface protein MuSK and he would like to determine whether any of these antibodies **activate** MuSK signaling. Design a testing protocol using Leo's myotube culture system to help determine whether a particular antibody **activates** MuSK activity. Please be specific about how your assay will determine MuSK activity and limit response to the space provided below (i.e. be concise). (9 points)

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Name:_____

2. Leo finds that if he raises the K+ concentration in the culture media of his myotube cultures, the myotubes begin to contract in the dish! Leo looks in the freezer and finds a general kinase inhibitor, and thinking that this would block the contractions, he adds it to the culture media containing high K+. To his surprise, the cells continued to contract. He then tried the same kinase inhibitor on a myotube culture he derived from blood vessel muscle cells, and found that the contractions induced by high K+ stopped in these cultures when he added the inhibitor. Explain why you think Leo observed these differences in the response of his two cultures to the kinase inhibitor (please limit your response to the space below). (6.5 points)

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Name:_____

ASSESSMENT OF THIS SECTION AND THIS TEST

1. **Strongly agree**
2. **Agree**
3. **Neutral**
4. **Disagree**
5. **Strongly disagree**

If you wish to explain your answer please do so in the space below the question

1. The material taught for this section was interesting. ____
2. This course covered the right amount of material. ____
3. This course emphasized concepts rather than facts. ____
4. Approaches used by lecturers made me stay alert in class. _____
5. The test was in a format similar to what I had expected. _____
6. The following questions seemed ambiguous._____
7. The test was a fair assessment of my knowledge._____
8. What did you like the most about this section?

9. What did you like the least about this section?

10. Suggest ways to improve this section