The exam will cover concepts, experimental procedures, and expected outcomes that we discussed in lab since the last practical. All material in the lab manual is fair game. For more review: go over your quizzes, the questions that you answered in your lab reports, and my power point lectures (they are saved on the server, location: IPHY folder-Public folder-Zoe’s labs)

**Physiology of Skeletal Muscle**

reference pages in the text: 257-276, 283-288, 297

**BIG IDEA:** Muscle contractions occur in groups called motor units, comprised of a motor-neuron and all of the muscle fibers (muscle cells) that it innervates. There is an optimal muscle (and sarcomere) length for maximal tension production. This Length-Tension relation of muscle is explained by the sliding filament theory. *In vivo*, muscle contractions are generally tetanic in nature, achieved through summation of graded twitch responses.

**KEY POINTS**

- **Muscle structure** (know from cell to whole muscle level)
  - some key parts: sarcolemma
  - ♣ sarcomere (I band, A band, Z line, H zone, M line)
  - ♣ fasiculi
  - ♣ motor unit
- **Excitation-Contraction (EC) coupling:**
  - Nerve sends impulse to neuromuscular junction. The neurotransmitter acetycholine (Ach) is released and travels across the synaptic crease and onto receptors on the sarcolemma. The resulting AP depolarizes T tubules at the A-I junction of the sarcomere, causing Ca++ release from the sarcoplasmic reticulum (SR). Ca++ binds to actin filaments (troponin-tropomyosin component) causing a conformational change that allow actin-myosin cross bridges to form.
  - ATP breaks the bond allowing sliding of filaments, **muscle shortens**. Ca++ moves back into the lateral sacs of the SR. In the presence of ATP inhibitory troponin-tropomyosin conformation is restored, muscle relaxes.

- **Sliding Filament Theory of Muscle Contraction** (see text for review)
  - Know the relation of muscle length to this theory- optimal muscle length reflects the point at which there is ideal amount of overlap in actin/myosin filaments

- **Isometric (same length) and isotonic (same force) muscle contractions.**

- **All or None?**

- Motor Units- act in all or none fashion but entire muscle shows graded response due to recruitment of motor units. At threshold stimulus, at least one motor unit is activated.
- Increase strength of contraction by muscle fiber recruitment

- **Twitch (single contraction) vs. Tetanic (fused contractions)**
  - Know about difference in force for these two types of contractions. Why can a titanic contraction occur (hint- action potentials are shorter then contractions) ? Know about the role of Ca++ in tetanic contractions
• **Muscle fatigue**: 4 major theories discussed
  - Nutrient fatigue (low glycogen levels)
  - Intramuscular fatigue (lactate increase causes decrease in pH)
  - Calcium fatigue (alterations in Ca++ distribution)
  - Neural fatigue (AP does not cross neuromuscular junction)

• **Work calculation**
  \[ \text{Work} = \text{force} \times \text{distance} \]
  \[ \text{Force} = \text{Mass} \times \text{acceleration} \text{ or } \text{Mass} \times \text{Gravity} \]
  Mass and weight are not the same thing
  \[ \text{Force} = (\text{kg}) \times (\text{m/s}^2) = \text{Mass} \times (9.8 \text{ m/s}^2) = \text{Newton or N} \]
  \[ \text{Work} = \text{force} \times \text{distance} = \text{Newton} \times \text{meters} = \text{Nm} = \text{Joule} \]
  Or \[ \text{Mass} \times \text{gravity} \times \text{distance} \]

**MORE QUESTIONS TO THINK ABOUT**

- Draw a sarcomere and label the various lines/bands/filaments. How does the structure of the sarcomere relate to its function? What ion is directly involved in muscle contraction at the level of the sarcomere?
- What causes rigor mortis?

**Physiology of Isolated Peripheral Nerve**

**BIG IDEA:** *Nerves are composed of many neurons.* Each neuron’s action potential occurs in all or none manner. The characteristics of threshold, refractory period and conductance velocity of a nerve depend on the size and number of neurons within that nerve.

**KEY POINTS:**

• **Neurons**
  - *Neuron structure*: cell body, dendrites, axon hillock, axon, axon terminals, myelin sheath, nodes of Ranvier
  - Neurons: obey the “All or None” Law, meaning that if a supra-threshold stimulus is delivered, an action potential will result. The amplitude of a neuronal action potential is fixed.
  - With sub-threshold stimuli, neurons exhibit graded potentials. Graded potentials can be excitatory post synaptic potentials (EPSPs) or inhibitory post synaptic potentials (IPSPs). Graded potentials degrade with propagation distance.

• **Nerves**
  - If a the stimulus does not activate the entire population of neurons, a nerve will exhibit a graded response. Thus, compound action potentials (CAPs) produced by nerves can vary in amplitude.

• **Refractory period**
  - Absolute refractory period- no amount of stimulation will produce a second AP
  - Relative refractory period- stimulation at higher then normal levels can produce a second AP
  - The refractory period of a given nerve is dependent on the refractory periods of the
individual neurons within that nerve. Know when and why refractory period occur.

- **Summation:** occurs *in vivo.*
  Stimuli from dendrites sum to produce an AP at the axon hillock where the concentration of voltage gated Na channels is highest
- Temporal summation: neurons may reach threshold in response to successive sub-threshold stimuli provided that the stimuli are applied within a given time period.
- Spatial summation: neurons may reach threshold in response to stimuli from multiple sites of stimulation.

- **Axon diameter**
  - In comparison to small diameter axons, large diameter axons have lower thresholds, higher conduction velocities and shorter refractory periods.
- **Conduction velocity**
  change in distance/ t2-t1

MORE QUESTIONS TO THINK ABOUT
What factors contribute to the resting membrane potential?

Define threshold

Given a Chart trace of a single action potential, could you identify the phases of depolarization and re-/hyperl polarization? Which ion contributes to depolarization, is it moving into or out of the cell, and through what type of channel does it travel during an action potential? Which ion contributes to repolarization, is it moving into or out of the cell, and through what type of channel does it travel during an action potential?

What factors affect conduction velocity? How? If you were asked to calculate conduction velocity for a nerve, what information would you need?

Why did we use Frog Ringers in this experiment, as opposed to cat Ringers? Why not water?

**Lab 4: Ventilation Physiology**
Big Idea: Breathing rate is primarily determined by CO2 levels in the blood (PCO2), not PO2.

Concepts/Terms:

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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<tbody>
<tr>
<td>PCO₂</td>
<td></td>
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<tr>
<td>PO₂</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td></td>
</tr>
<tr>
<td>Hyperventilation</td>
<td></td>
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<tr>
<td>Hypoxia</td>
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<tr>
<td>Bicarb. Buffering System</td>
<td></td>
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<tr>
<td>Hypercapnia</td>
<td></td>
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<tr>
<td>CNS control of respiration</td>
<td></td>
</tr>
<tr>
<td>Hypoxia</td>
<td></td>
</tr>
<tr>
<td>Peripheral and Central chemoreceptors</td>
<td></td>
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<tr>
<td>O₂-Hb dissociation curve</td>
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</tbody>
</table>

Tidal Volume (Vₜ) volume of inspired air per breath

Minute Ventilation (VₑATP) = Vₜ x BPM (units = mL/min)
• Anatomical Dead Space: inspired air not participating in diffusion (gas exchange); primarily found in lungs and trachea; Dead Space volume in milliliters is ~ equal to subjects weight in lbs.

Muscles involved in ventilation: know which contract/which relax with inspiration/exhalation:
  *Diaphragm: most important
    ♠ innervated by phrenic nerve (cervical spinal region)
    ♠ contraction = inspiration; relaxation = expiration

External intercostals
Internal intercostals
remember that most exhalation is passive!

• Control of Ventilation:
  • Neural control:
  • Hering Breuer Reflex: response to over-inflation of the lungs
    ♠ review in lab manual

CNS centers involved in control:
  • Medulla: Groups of neurons in the medullary respiratory center generate central pattern; receive afferent input from central and peripheral chemoreceptors, hypothalamus, other brainstem regions associated with respiration, and cerebral cortex; send efferent input to spinal motor neurons that innervate diaphragm and intercostals
  • Pons: pneumotaxic center: modifies respiratory pattern by sending inhibitory inputs that terminate inspiration and initiate expiration
    apneustic center: modifies respiratory pattern by promoting inspiration
    both centers send inputs to medulla
  • Cerebral Cortex: motor cortex modifies breathing pattern for voluntary control of breathing during speaking, singing.
  • Hypothalamus: modifies pattern of inspiration/expiration; emotional and pain responses activate sympathetic centers in hypothalamus, which result in modulation of pattern.

Humoral (blood) control of ventilation:
  • Main internal stimuli for regulation of breathing are PCO₂ and pH of arterial blood and cerebrospinal fluid. The ventilatory system protects the extracellular fluid from metabolic acidosis (due to increase in CO₂ produced from intracellular respiration). Ventilatory response is an immediate compensatory mechanism for alterations in pH.

  • Arterial CO₂ (PₐCO₂):
    ♠ CO₂ transport in the blood: 7% dissolved in plasma, 20% bound to hemoglobin, 73% as H₂CO₃/HCO₃⁻
    ♠ Remember: CO₂ production alters acid-base balance within the body
    ♠ Bicarb. Buffering System:
      ♠ CO₂+H₂O ↔ H₂CO₃ ↔ HCO₃⁻ + H⁺
      ♠ Increasing ventilatory rate results in a reduction of PCO₂, and thus, a reduction in [H⁺]

  • pH:
    ♠ central chemoreceptors - most important sensors of PCO₂ are in the medulla; they do not DIRECTLY sense PaCO₂, rather, they respond to
changed in [H+] in medullary intercerebral fluid.

Therefore: the increase in [H+] is a direct stimulus for ventilation (and PCO2 is the indirect).

• peripheral chemoreceptors - unlike central chemoreceptors, the peripheral receptors are in direct contact with arterial blood; aortic and carotid bodies (aortic in aortic arch / carotid at bifurcation of central carotid and internal/external carotids); send afferent input to medulla via vagal and glossopharyngeal nerves; sense PO2 and changes in pH and, thus, PaCO2.

• Arterial O₂ (PₐO₂):
  ♣ Although PaCO2 is responsible for the majority of respiratory drive (~75%), the respiratory centers also respond to changes in PaO2.
  ♣ Oxygen-Hemoglobin Saturation Curve: Significance of sigmoidal shape?

• PO2 remains saturated at venous levels of PO2. PO2 must drop to extremely low levels to effectively reduce the amount of O2 carried by Hgb. PO2 doesn’t drive respiration until ~60 mmHg, 40mmHg-danger!

• Shift to right - increased temperature & CO2/decreased pH causes a shift of curve to right (at least in humans) decreasing the %Hgb saturation;
  ♣ _ Shift to left: decreased temperature, CO2/pH can cause a shift of the curve to the left increasing %Hgb saturation, we also see this in fetal hemoglobin
  ♣ Know how to draw a graph of the curve and the shifts to the curve

• Altitude:
  ○ Review O2 and CO2 % present in ambient air
  • remember that as altitude increases % of gasses in air is CONSTANT but atmospheric pressure (mmHG) and thus partial pressure of gasses DOES change.
  • Partial pressure of a gas:
    • (Atmospheric pressure) x (% gas)
  • Review lab manual: What is the cause of altitude illness? What are some methods of preventing altitude illness? What are AMS, HACE and HAPE?

• Review results and methods used in the experiment:
  Based on a spirometer trace in Chart, could you calculate the minute ventilation (Veₐṭp)?
  What about alveolar ventilation? Which is a more accurate measure?
  For most measurements (tidal volume, Veₐṭp, Alveolar ventilation, heart rate)
    Hypercapnic air (6%) > Hypoxic (15%) > Hypoxic (10%) > Ambient air
    Why would we expect to see a greater response to hypercapnic than hypoxic air?
  What happened to our breath holding time as after we exercised or hyperventilated?

EKG and Phonocardiogram Lab
some reference pages in the text 289-319

BIG IDEA: The EKG, heart Asculation and peripheral pulse recording allow us to see visual images of the different stages of contraction and relaxation in the heart. In a clinical setting these recordings can be used to identify the
Three major components of a closed system cardiovascular system: heart, blood vessels, blood. Path of blood flow through heart & lungs: R. atrium ◊ tricuspid valve ◊ R. ventricle ◊ pulmonary semilunar valve ◊ pulmonary artery ◊ pulmonary vein ◊ L. atrium ◊ bicuspid valve ◊ L. ventricle ◊ aortic semilunar valve ◊ aorta; Left ventricular mass is greater than right because left ventricle pumps blood out to systemic circulation.

Systole: contraction phase of heart / Systolic Blood Pressure: peak pressure exerted in the arteries during ventricular systole

Frank Starling Law - review

Diastole: relaxation phase of heart / Diastolic Blood Pressure: lowest pressure exerted in the arteries.

EKG: An EKG is a recording of myocardial electrical activity. It shows electrical conduction of the heart NOT contraction. You should be able to identify the following portions of an EKG trace and describe the electrical events (depolarization/repolarization) occurring at each portion:

- P wave
- P-R interval
- QRS complex
- ST segment
- T wave
- Q-T interval
- T-P interval

Einthoven’s triangle - what is a lead? Which lead did we use in this lab? What is the difference between the 3 lead (limb lead) and 12 lead systems?

Phonocardiogram: Represent the sounds in the heart due

- S1-(lub)
- S2-(dub)
- What do S3 and S4 represent? Remember that we did not see these sounds in our recordings

Murmurs: a murmur is any abnormal sound represented in the phonocardiogram. Typically this is turbulent blood low due to stenotic values (cannot fully open) or regurgitation (values don’t fully close and blood leaks back)

The two main groups of murmurs are diastolic and systolic murmurs (look at your handout for some examples). Systolic murmurs should appear between S1 and S2, while diastolic murmurs should appear after S2.

Arterial Pulse Wave: demonstrates the differences in pressure between systole and diastole in the arteries. The peak of the pressure wave represents the systolic peak in pressure. Sometimes we can observe a dicrotic notch - a small decrease in the peak that occurs when the aortic semilunar valve shuts.

Combination of the three recordings:

A representative trace is shown below. Make sure you understand that the EKG for any particular component (i.e. ventricular contraction) will appear first because it represents the change in electrical potential, while the other recordings demonstrate changes due to the actually changes in contraction of the atria and/or ventricles. For example: for systolic changes - The QRS complex will appear first followed by S1 and then S2. Usually the arterial pulse wave will appear between the two heart sounds.
Exercise: Look over your HW- what aspect(s) of the three traces changed with exercise. Why?

Regulation of Heart Function in the Rat
BIG IDEA: The heart is myogenic, but its rhythmicity and contractile force are modulated by the parasympathetic and sympathetic branches of the autonomic nervous system.

KEY POINTS:
Review anatomy of heart, including cardiac tissue anatomy
- (endocardium, endothelium, myocardium, epicardium)

- Vertebrate hearts are myogenic, (cardiac muscle can generate its own rhythmic contraction, independent of neural input)
- The inherent rate of cardiac autorhythmicity is set by the sino-atrial (SA) node, which is located in the right atrium. The cells of the SA node have the fastest rate of depolarization in the heart and, in healthy hearts, cardiac action potentials are generated at the SA node.
- The specialized muscle cells of the SA node are also called “pacemaker cells” and the action potentials generated within these cells are called “pacemaker potentials.” Pacemaker cells have “leaky Na+” channels which transmit Na+ ions into the cell, causing the membrane potential to slowly depolarize to threshold. Unlike neurons, there is not a steady resting potential
- Cardiac cells have specializations for enhanced conductance. Resistance to ion flow is greatly reduced at intercalated discs (gap junctions), allowing electrical signals to spread rapidly from one cell to another at these areas, this allows for synchronized contraction.
- Action potentials are propagated from the SA node through the atrial tissue. Once the atrial tissue depolarizes, the atria contract and blood is ejected into the ventricle. The wave of depolarization through the atria reaches the AV node (between the atria and
ventricles), where the signal experiences a very small delay. This delay is important for atrial filling.

- **Electrical conduction system of the heart**: SA node → AV node → Bundle of His (right and left bundle branches) → Purkinje Fibers

- **Parasympathetic Nervous System Modulation**: Parasympathetic neural input decreases rate of SA depolarization, HR, excitability of AV node and atrial contractility. The Vagus nerve supplies parasympathetic innervation to heart, neurotransmitter = acetylcholine (Ach), Ach binds receptors on cardiac cells

- **Sympathetic Nervous System Modulation**: Sympathetic neural input increases rate of SA node depolarization, excitability of AV node, HR, and contractile force in ventricles. Also leads to an increase in venous return and increase in strength of contraction (via Frank Starling)
  
  Sympathetic cardiac nerves supply sympathetic innervations to heart, neurotransmitter = norepinephrine (NE), NE binds adrenergic receptors on cardiac cells. Sympathetic nervous activation of the adrenal medulla causes the release of epinephrine (a hormone NOT a neurotransmitter) Once released, EPI circulates through the blood and binds to adrenergic receptors in the heart, again resulting in increased HR and contractile force.

**Hypoxia**: Cardiac muscle is highly aerobic, primarily relying on oxidative-phosphorylation for ATP production. Exposure to hypoxia has an immediate effect to increase sympathetic stimulation, increasing heart rate

**MORE QUESTIONS TO THINK ABOUT**

Which component of the ANS is more “active” when we are at rest? What about in “fight or flight” situations.

What happens with stimulation or cutting of the vagus nerve?

How does the “pacemaker potential” in cardiac cells differ from the “action potential” seen in the sciatic nerve?