ORENBURG STATE MEDICAL UNIVERSITY
Ministry of Health of the Russian Federation
Department of Normal Physiology

WORKBOOK FOR PRACTICAL CLASSES ON CELLULAR PHYSIOLOGY

Full name_____

Group_____

Orenburg, 2017

Lesson 1, 2. Cell structure. Transport across Cell Membranes

Issues for consideration

1. Volume and composition of body fluids. Distribution of water in the body fluid compartments. Composition of body fluid compartments.
2. Characteristics of cell membranes. Phospholipid component of cell membranes. Protein component of cell membranes.
3. Transport across cell membranes. Simple diffusion. Facilitated diffusion. Primary active transport. Secondary active transport. Osmosis.

Homework (writing)

1. List the major body fluid compartments.

_____
_____
_____
_____
_____

2. Fill in the table: Approximate Compositions of Extracellular and Intracellular Fluids.

Substance and Units	Extracellular Fluid	Intracellular Fluid*
Na^+ (mEq/L)		
K^+ (mEq/L)		
Ca^{2+}, ionized (mEq/L)		
Cl^- (mEq/L)		
HCO_3^- (mEq/L)		
pH‡		
Osmolality (mOsm/L)		

3. Draw the cytoplasmic membrane and mark its basic elements.

4. List types of mechanisms are responsible for transport of substances across cell membranes.

_____
_____
_____
_____
_____
_____
_____

5. Explain the term "simple diffusion".

_____
_____

_____
_____

6. List variables that affect the rate of diffusion of non-electrolytes.

_____
_____
_____
_____
_____
_____
_____

7. Explain the meaning of "facilitated diffusion".

_____
_____
_____
_____
_____

8. Explain the meaning of "primary active transport". Give examples.

_____
_____
_____
_____
_____
_____

9. Explain the meaning of "secondary active transport". Give examples.

_____
_____
_____
_____
_____
_____

10. Give a definition of osmosis.

_____
_____
_____
_____
_____

Teacher's signature: _____

Exercise 1: Cell Transport Mechanisms and Permeability

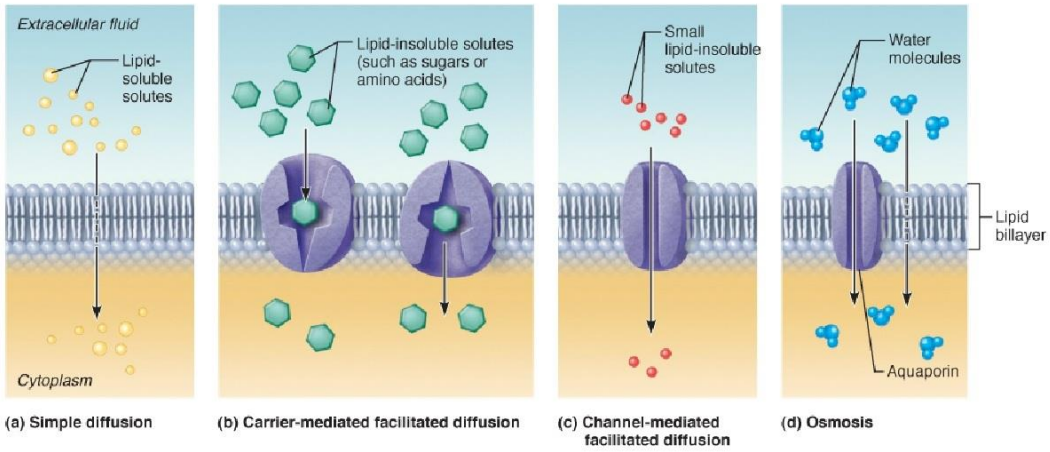
Exercise Overview

The molecular composition of the plasma membrane allows it to be selective about what passes through it. It allows nutrients and appropriate amounts of ions to enter the cell and keeps out undesirable substances. For that reason, we say the plasma membrane is **selectively permeable.** Valuable cell proteins and other substances are kept within the cell, and metabolic wastes pass to the exterior.

Transport through the plasma membrane occurs in two basic ways: either passively or actively. In **passive processes,** the transport process is driven by concentration or pressure differences (*gradients*) between the interior and exterior of the cell. In **active processes,** the cell provides energy (ATP) to power the transport.

Two key passive processes of membrane transport are **diffusion** and **filtration.** Diffusion is an important transport process for every cell in the body. **Simple diffusion** occurs without the assistance of membrane proteins, and **facilitated diffusion** requires a membrane-bound carrier protein that assists in the transport (view Figure 1.1).

In both simple and facilitated diffusion, the substance being transported moves *with* (or *along* or *down)* the *concentration gradient* of the solute (from a region of its higher concentration to a region of its lower concentration). The process does not require energy from the cell. Instead, energy in the form of **kinetic energy** comes from the constant motion of the molecules. The movement of solutes continues until the solutes are evenly dispersed throughout the solution. At this point, the solution has reached **equilibrium.**



A special type of diffusion across a membrane is **osmosis.** In osmosis, water moves with its concentration gradient, from a higher concentration of water to a lower concentration of water. It moves in response to a higher concentration of solutes on the other side of a membrane.

In the body, the other key passive process, **filtration,** usually occurs only across capillary walls. Filtration depends upon a *pressure gradient* as its driving force. It is not a selective process. It is dependent upon the size of the pores in the filter.

The two key active processes (recall that active processes require energy) are **active transport** and **vesicular transport.** Like facilitated diffusion, active transport uses a membrane-bound carrier protein. Active transport differs from facilitated diffusion because the solutes move *against their* concentration gradient and because ATP is used to power the transport. Vesicular transport includes phagocytosis, endocytosis, pinocytosis, and exocytosis. These processes are not covered in this exercise.

The activities in this exercise will explore the cell transport mechanisms individually

Exercise 1. Activity 1: Simulating dialysis (Simple diffusion)

Objectives

1. To understand that diffusion is a passive process dependent upon a solute concentration gradient.
2. To understand the relationship between molecular weight and molecular size.
3. To understand how solute concentration affects the rate of diffusion.
4. To understand how molecular weight affects the rate of diffusion.

Introduction

Recall that all molecules possess *kinetic energy* and are in constant motion. As molecules move about randomly at high speeds, they collide and bounce off one another, changing direction with each collision. For a given temperature, all matter has about the same average kinetic energy. Smaller molecules tend to move faster than larger molecules because kinetic energy is directly related to both mass and velocity (KE = 1/2 mv^2).

When a **concentration gradient** (difference in concentration) exists, the net effect of this random molecular movement is that the molecules eventually become evenly distributed throughout the environment—in other words, diffusion occurs. **Diffusion** is the movement of molecules from a region of their higher concentration to a region of their lower concentration. The driving force behind diffusion is the kinetic energy of the molecules themselves.

The diffusion of particles into and out of cells is modified by the plasma membrane, which is a physical barrier. In general, molecules diffuse passively through the plasma membrane if they are small enough to pass through its pores (and are aided by an electrical and/or concentration gradient) or if they can dissolve in the lipid portion of the membrane (as in the case of CO_2 and O_2). A membrane is called *selectively permeable, differentially permeable,* or *semipermeable* if it allows some solute particles (molecules) to pass but not others.

The diffusion of *solute particles* dissolved in water through a selectively permeable membrane is called **simple diffusion.** The diffusion of *water* through a differentially permeable membrane is called osmosis. Both simple diffusion and osmosis involve movement of a substance from an area of its higher concentration to an area of its lower concentration, that is, *with* (or *along* or *down*) its concentration gradient.

This activity provides information on the passage of water and solutes through selectively permeable membranes. You can apply what you learn to the study of transport mechanisms in living membrane-bounded cells. The dialysis membranes used each have a different *molecular weight cutoff (MWCO),* indicated by the number below it. You can think of MWCO in terms of pore size: the larger the MWCO number, the larger the pores in the membrane. The molecular weight of a solute is the number of grams per mole, where a mole is the constant Avogadro's number 6.02 x 10^{23}molecules/mole. The larger the molecular weight, the larger the mass of the molecule. The term molecular mass is sometimes used instead of molecular weight.

Equipment Used:

- Left and right beakers—used for diffusion of solutes
- Dialysis membranes with various molecular weight cutoffs (MWCOs)

Experiment data:

Solute	MWCO	Solute concentration	Average diffusion weight

Review Sheet:

1. Describe two variables that affect the rate of diffusion.

_____
_____
_____

2. Why do you think the urea was not able to diffuse through the 20 MWCO membrane? How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

The molecular weight of urea is 60.07. Do you think urea will diffuse through the 20 MWCO membrane?

_____
_____
_____

3. Describe the results of the attempts to diffuse glucose and albumin through the 200 MWCO membrane. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

Recall that glucose is a monosaccharide, albumin is a protein with 607 amino acids, and the average molecular weight of a single amino acid is 135 g/mole.

_____
_____
_____

4. Which of the following will be able to diffuse through the 200 MWCO membrane?

Put the following in order from smallest to largest molecular weight: glucose, sodium chloride, albumin, and urea.

_____
_____
_____

Exercise 1. Activity 2: Simulated facilitated diffusion

Objectives

1. To understand that some solutes require a carrier protein to pass through a membrane because of size or solubility limitations.
2. To observe how the concentration of solutes affects the rate of facilitated diffusion.
3. To observe how the number of transport proteins affects the rate of facilitated diffusion.
4. To understand how transport proteins can become saturated

Introduction

Some molecules are lipid insoluble or too large to pass through pores in the cell's plasma membrane. Instead, they pass through the membrane by a passive transport process called **facilitated diffusion.** For example, sugars, amino acids, and ions are transported by facilitated diffusion. In this form of transport, solutes combine with carrier-protein molecules in the membrane and are then transported *with* (or *along ox down)* their concentration gradient. The carrier-protein molecules in the membrane might have to change shape slightly to accommodate the solute, but the cell does not have to expend the energy of ATP.

Because facilitated diffusion relies on carrier proteins, solute transport varies with the number of available carrier-protein molecules in the membrane. The carrier proteins can become saturated if too much solute is present and the maximum transport rate is reached. The carrier proteins are embedded in the plasma membrane and act like a shield, protecting the hydrophilic solute from the lipid portions of the membrane.

Facilitated diffusion typically occurs in one direction for a given solute. The greater the concentration difference between one side of the membrane and the other, the greater the rate of facilitated diffusion.

Equipment Used

- Left and right beakers—used for diffusion of solutes
- Dialysis membranes with various molecular weight cutoffs (MWCOs)
- Membrane builder—used to build membranes with different numbers of glucose protein carriers.

Experiment data:

Run number	Solute	Start conc. L	Start conc. R	Carriers	Rate

Review sheet:

1. Explain one way in which facilitated diffusion is the same as simple diffusion and one way in which it is different from simple diffusion.

_____
_____
_____
_____

2. The larger value obtained when more glucose carriers were present corresponds to an increase in the rate of glucose transport. Explain why the rate increased. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

What effect do you think increasing the number of protein carriers will have on the glucose transport rate?

_____
_____
_____
_____

3. Explain your prediction for the effect Na^+ Cl' might have on glucose transport. In other words, explain why you picked the choice that you did. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

What effect do you think adding Na^+ Cl' will have on the glucose transport rate?

_____
_____
_____

Exercise 1. Activity3: Simulating osmotic pressure

Objectives

1. To explain how osmosis is a special type of diffusion.
2. To understand that osmosis is a passive process that depends upon the concentration gradient of water.
3. To explain how tonicity of a solution relates to changes in cell volume.
4. To understand conditions that affect osmotic pressure.

Introduction

A special form of diffusion, called **osmosis,** is the diffusion of water through a selectively permeable membrane. (A membrane is called *selectively permeable, differentially permeable,* or *semipermeable* if it allows some molecules to pass but not others.) Because water can pass through the pores of most membranes, it can move from one side of a membrane to the other relatively freely. Osmosis takes place whenever there is a difference in water concentration between the two sides of a membrane.

If we place distilled water on both sides of a membrane, /^movement of water does not occur. Remember, however, that water molecules would still move between the two sides of the membrane. In such a situation, we would say that there is no *net* osmosis.

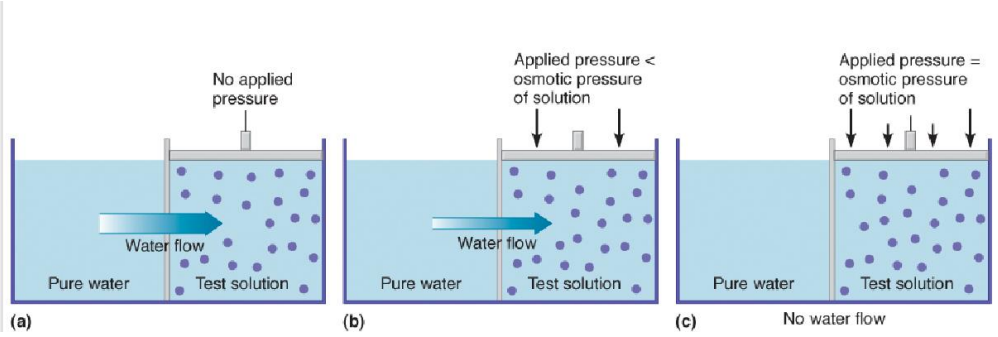
The concentration of water in a solution depends on the number of solute particles present. For this reason, increasing the solute concentration coincides with decreasing the water concentration. Because water moves down its concentration gradient (from an area of its higher concentration to an area of its lower concentration), it always moves *toward* the solution with the highest concentration of solutes. Similarly, solutes also move down their concentration gradients.

If we position a *fully* permeable membrane (permeable to solutes and water) between two solutions of differing concentrations, then all substances—solutes and water—diffuse freely, and an equilibrium will be reached between the two sides of the membrane. However, if we use a selectively permeable membrane that is impermeable to the solutes, then we have established a condition where water moves but solutes do not. Consequently, water moves toward the more concentrated solution, resulting in a *volume increase* on that side of the membrane.

By applying this concept to a closed system where volumes cannot change, we can predict that *the pressure\n* the more concentrated solution will rise. The force that would need to be applied to oppose the osmosis in a closed system is the **osmotic pressure** (view Figure 1.2).

Osmotic pressure is measured in *millimeters of mercury [mm Hg).*In general, the more impermeable the solutes, the higher the osmotic pressure.

Osmotic changes can affect the volume of a cell when it is placed in various solutions. The concept of **tonicity** refers to the way a solution affects the volume of a cell. The tonicity of a solution tells us whether or not a cell will shrink or swell. If the concentration of impermeable solutes is the *same* inside and outside of the cell, the solution is **isotonic.** If there is a *higher* concentration of impermeable solutes *outside* the cell than in the cell's interior, the solution is **hypertonic.** Because the net movement of water would be out of the cell, the cell would *shrink* in a hypertonic solution. Conversely, if the concentration of impermeable solutes is *lower* outside of the cell than in the cell's interior, then the solution is **hypotonic.** The net movement of water would be into the cell, and the cell would *swell and* possibly burst



Equipment Used

- **Left and right beakers—used for diffusion of solutes**
- Dialysis membranes with various molecular weight cutoffs (MWCOs)

Experiment data:

Run number	Solute	MWCO	Start conc. L	Pres. L	Start conc. R	Pres. R	Rate

Review sheet:

1. Explain the effect that increasing the Na^+Cl^- concentration had on osmotic pressure and why it has this effect. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

What effect do you think increasing the Na^+ Cl^- concentration will have?

_____
_____
_____
_____

2. Describe one way in which osmosis is similar to simple diffusion and one way in which it is different.

_____
_____
_____
_____

3. Solutes are sometimes measured in milliosmoles. Explain the statement: "Water chases milliosmoles".

_____
_____
_____
_____

Exercise 1. Activity 4: Simulating filtration

Objectives

1. To understand that filtration is a passive process dependent upon a pressure gradient.
2. To understand that filtration is not a selective process.
3. To explain that the size of the membrane pores will determine what passes through.
4. To explain the effect that increasing the hydrostatic pressure has on the filtration rate and how this correlates to events in the body.
5. To understand the relationship between molecular weight and molecular size.

Introduction

Filtration is the process by which water and solutes pass through a membrane (such as a dialysis membrane) from an area of higher hydrostatic (fluid) pressure into an area of lower hydrostatic pressure. Like diffusion, filtration is a passive process. For example, fluids and solutes filter out of the capillaries in the kidneys into the kidney tubules because blood pressure in the capillaries is greater than the fluid pressure in the tubules. So, if blood pressure increases, the rate of filtration increases.

Filtration is not a selective process. The amount of *filtrate* – the fluids and solutes that pass through the membrane – depends almost entirely on the *pressure gradient (the* difference in pressure between the solutions on the two sides of the membrane) and on the size of the *membrane pores.* Solutes that are too large to pass through are retained by the capillaries. These solutes usually include blood cells and proteins. Ions and smaller molecules, such as glucose and urea, can pass through.

In this activity, the pore size is measured as a *molecular weight cutoff (MWCO),* which is indicated by the number below the filtration membrane. You can think of MWCO in terms of pore size: the larger the MWCO number, the larger the pores in the filtration membrane. The molecular weight of a solute is the number of grams per mole, where a mole is the constant Avogadro's number 6.02×10^{23} molecules/mole. You will also analyze the filtration membrane for the presence or absence of solutes that might be left sticking to the membrane.

Equipment Used:

- Top and bottom beakers—used for filtration of solutes
- Dialysis membranes with various molecular weight cutoffs (MWCOs)

Membrane residue analysis station—used to analyze the filtration membrane.

Experiment data:

Run number	Solute	MWCO	Pressure	Filter rate	Residue	Start conc.	Filter conc.

Review sheet:

1. Explain in your own words why increasing the pore size increased the filtration rate. Use an analogy to support your statement. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

What effect will increasing the pore size of the filter have on the filtration rate?

_____

_____

_____

_____

_____

_____

2. Which solute did not appear in the filtrate using any of the membranes? Explain why.

_____

_____

_____

_____

3. Why did increasing the pressure increase the filtration rate but not the concentration of solutes?

Recall that, during the experiment you were asked:
What will happen if you increase the pressure above the beaker (the driving pressure)?

_____
_____
_____
_____
_____

Exercise 1. Activity 5: Simulating active transport

Objectives

1. To understand that active transport requires cellular energy in the form of ATP.
2. To explain how the balance of sodium and potassium is maintained by the Na^+K^+ pump, which moves both ions against their concentration gradients.
3. To understand coupled transport and be able to explain how the movement of sodium and potassium is independent of other solutes, such as glucose.

Introduction

Whenever a cell uses cellular energy (ATP) to move substances across its membrane, the process is an *active transport process.* Substances moved across cell membranes by an active transport process are generally unable to pass by diffusion. There are several reasons why a substance might not be able to pass through a membrane by diffusion: it might be too large to pass through the membrane pores, it might not be lipid soluble, or it might have to move *against,* rather than with, a concentration gradient.

In one type of active transport, substances move across the membrane by combining with a carrier-protein molecule. This kind of process resembles an enzyme-substrate interaction. ATP hydrolysis provides the driving force, and, in many cases, the substances move *against* concentration gradients or electrochemical gradients or both. The carrier proteins are commonly called **solute pumps.** Substances that are moved into cells by solute pumps include amino acids and some sugars. Both of these kinds of solutes are necessary for the life of the cell, but they are lipid insoluble and too large to pass through membrane pores.

In contrast, sodium ions (Na^+) are ejected from the cells by active transport. There is more Na^+ outside the cell than inside the cell, so Na^+ tends to remain in the cell unless actively transported out. In the body, the most common type of solute pump is the Na^+-K^+(sodium-potassium) pump, which moves Na^+ and K^+ in opposite directions across cellular membranes. Three Na^+ ions are ejected from the cell for every two K^+ ions entering the cell. Note that there is more K^+ inside the cell than outside the cell, so K^+ tends to remain outside the cell unless actively transported in.

Membrane carrier proteins that move more than one substance, such as the Na^+-K^+ pump, participate in *coupled transport.* If the solutes move in the same direction, the carrier is a s*ymporter.* If the solutes move in opposite directions, the carrier is an *antiporter.* A carrier that transports only a single solute is a *uniporter.*

Equipment Used:
• Simulated cell inside a large beaker

Experiment data:

Run number	Solute	ATP	Start conc. L	Start conc. R	Pumps	Carriers	Rate

Review sheet:

1. Describe the significance of using 9 m/W sodium chloride inside the cell and 6 m/W potassium chloride outside the cell, instead of other concentration ratios.

_____
_____
_____
_____

2. Explain why there was no sodium transport even though ATP was present. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

What do you think will result from these experimental conditions?

_____
_____
_____
_____

3. Explain why the addition of glucose carriers had no effect on sodium or potassium transport. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

Do you think the addition of glucose carriers will affect the transport of sodium or potassium?

_____
_____
_____
_____

Teacher's signature: _____

Computer tests: RESIDUAL KNOWLEDGE

1. All of the following hormones are involved in the menstrual cycle EXCEPT:
1. estrogen
2. LH
3. prolactin
4. progesterone
5. FSH

2. DNA contains all the following molecules EXCEPT:
1. uracil
2. guanine
3. adenine
4. deoxyribose
5. phosphate

3. In aerobic respiration, the final electron acceptor in the electron transport chain is:
1. NAD^+
2. O_2
3. H_2O
4. $NADP^+$
5. H_2

4. All of the following statements are correct regarding alleles EXCEPT:
1. one gene can have more than one allele.
2. two identical alleles are said to be heterozygous with respect to that gene.
3. alleles are found on corresponding loci of homologous chromosomes.
4. alleles are alternative forms of the same gene.
5. one allele can be dominant and the other can be recessive.

5. The Krebs cycle in humans occurs in the
1. intermembrane phase
2. inner mitochondrial membrane
3. outer mitochondrial membrane
4. cytoplasm
5. mitochondrial matrix

6. The part of the brain that controls involuntary actions is known as the
1. thalamus
2. cerebrum
3. medulla
4. cerebellum
5. hypothalamus

7. A researcher performs a cross between 2 mice, both having black fur. Black for is dominant over white for. 75% of the offspring have black coats and 25% have white coats. The researcher can assume that the parents genotypes were most likely:
1. BB x BB
2. BB x Bb
3. BB x bb
4. Bb x Bb
5. bb x bb

8. A feature of amino acids not found in carbohydrates is the presence of
1. nitrogen
2. hydrogen
3. oxygen
4. carbon
5. phosphorous

9. Which of the following are characteristics of both bacteria and fungi?
1. cell wall, unicellularity, and mitochondria
2. cell wall, DNA, and plasma membrane
3. nucleus, organelles, and unicellularity
4. plasma membrane, multicellularity, and Golgi apparatus
5. nucleus, RNA, and cell wall

10. The major difference between cartilage and bone is that cartilage
1. is a type of connective tissue
2. lacks blood vessels and nerves
3. secretes a rubbery matrix
4. is composed of collagen and salts
5. is part of the skeletal system

11. A macromolecule which consists of a polymer of amino acids.
1. glycogen
2. cellulose
3. protein
4. triglyceride
5. nucleic Acid

12. The stored form of carbohydrates in humans.
1. glycogen
2. cellulose
3. protein
4. triglyceride
5. nucleic Acid

13. Lipid which consists of three fatty acids covalently bonded to glycerol.
1. glycogen
2. cellulose
3. protein
4. triglyceride
5. nucleic acid

14. The lung of a reptile and the air bladder of a fish.
1. analogous structures
2. homologous structures
3. divergent evolution
4. convergent evolution
5. vestigial Structures

15. All of the following are stimulated by the sympathetic nervous system EXCEPT:
1. increased heart rate.
2. increase secretion of the sweat glands.
3. dilation of the pupil.
4. constriction of blood vessels
5. increased peristalsis in the gastrointestinal tract.

16. Which of the following is a characteristic of arteries?
1. they contain valves which prevent backflow.
2. they carry blood away from the heart.
3. blood is kept moving by the contraction of voluntary muscles.
4. they or thin-walled blood vessels.
5. they always carry oxygenated blood.

17. Vitamins are essential to the human diet because they act as
1. neurotransmitters
2. enzymes
3. cofactors
4. hormones

18. When the chromosomes line up in mitosis this is known as which phase?
1. telophase
2. anaphase
3. metaphase
4. prophase

19. Which cellular organelle contains enzymes that are considered digestive?
1. Golgi Apparatus
2. lysosomes
3. nucleus
4. ribosomes

20. Organs repair themselves through a process of?
1. meiosis
2. mitosis
3. cellular differentiation
4. transformation

21. Which of the following is considered a model for enzyme action?
1. lock and Key model
2. enzyme interaction model
3. transformation model
4. transcription model

22. Which of the following statements about enzymes is not true?
1. enzymes are catalysts.
2. almost all enzymes are proteins.
3. enzymes operate most efficiently at optimum pH.
4. enzymes are destroyed during chemical reactions.

23. Which of the following statements about prostaglandins is not true?
1. prostaglandins promote inflammation.
2. prostaglandins can only constrict blood vessels.
3. prostaglandins are made in the renal medulla.
4. prostaglandins can lead to pain and fever.

24. Cholesterol that is known as (LDL) stands for:
1. low-density lipoproteins
2. low-density lysosomes
3. level-density lipoproteins
4. level-density lysosomes

25. Hardening of the arteries is known as:
1. atherosclerosis
2. venous narrowing
3. micro-circulation
4. hypertension

26. Breathing properly requires the presence of what compound that affects surface tension of alveoli in the lungs?
1. potassium
2. plasma
3. surfactant
4. sodium Chloride

27. Which of the following is not considered a function of the kidneys?
1. secretion
2. reabsorption
3. transport
4. filtration

28. The functional unit of the kidney is known as?
1. medulla
2. glomerulus
3. pyramid
4. nephron

29. What anatomical structure connects the stomach and the mouth?
1. trachea
2. spinal column
3. hepatic duct
4. esophagus

30. The_____system consists of the brain, spinal cord, peripheral nerves, ganglia and special sense organs.
1. circulatory
2. reproductive
3. nervous
4. immune
5. urinary

31. _____tissue provides physical protection, controls permeability, and produces specialized secretions
1. epithelium
2. connective
3. nervous
4. muscle

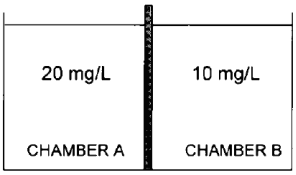
32. The foramen magnum is found in which bone?
1. frontal
2. sphenoid
3. ethmoid
4. occipital
5. none of the above

33. There are_____cervical vertebrae in the vertebral column.
1. seven
2. five

3. twelve
4. nine
5. six

Computer tests: CELL STRUCTURE
TRANSPORT ACROSS CELL MEMBRANES

1. The diagram below illustrates the concentration of a substance in two chambers. If the concentration of the substance in chamber A doubles, the diffusion of the substance will change from 10 mg/h to



1. 5 mg/h
2. 10 mg/h
3. 15 mg/h
4. 20 mg/h
5. 30 mg/h

2. Which of the following statements best characterizes a molecule whose reflection coefficient to a membrane is zero?
1. it will not permeate the membrane
2. it can only cross the membrane through the lipid bilayer
3. it causes water to flow across the membrane
4. it is as diffusible through the membrane as water
5. it is transported across the membrane by a carrier

3. The characteristic of a water-insoluble substance most important in governing its diffusibility through a cell membrane is its
1. hydrated diameter
2. molecular weight
3. electrical charge
4. lipid solubility
5. three-dimensional shape

4. The movement of water across a plasma membrane occurs by
1. active transport.
2. facilitated diffusion.
3. simple diffusion (osmosis).
4. all of these.

5. Which of these statements about the facilitated diffusion of glucose is true?
1. there is a net movement from the region of lower
2. carrier proteins in the cell membrane are required for this transport.
3. this transport requires energy obtained from ATP.
4. it is an example of cotransport.

6. If a poison such as cyanide stopped the production of ATP, which of the following transport processes would cease?
1. the movement of Na^+ out of a cell
2. osmosis
3. the movement of K^+ out of a cell
4. all of these

7. Red blood cells crenate in
1. hypotonic solution.
2. isotonic solution.
3. hypertonic solution.

8. Plasma has an osmolality of about 300 mOsm. The osmolality of isotonic saline is equal to
1. 150 mOsm.
2. 300 mOsm.
3. 600 mOsm.
4. none of these.

9. Which of these statements comparing a 0.5m NaCl solution and a 1.0m glucose solution is true?
1. they have the same osmolality.
2. they have the same osmotic pressure.
3. they are isotonic to each other.
4. all of these are true.

10. The most important diffusible ion in the establishment of the rest membrane potential is
1. K^+
2. Na^+
3. Ca^{2+}
4. Cl^-
5. Mg^{2+}

11. Which of these statements regarding an increase in blood osmolality is true?
1. it can occur as a result of dehydration.
2. it causes a decrease in blood osmotic pressure.
3. it is accompanied by a decrease in ADH secretion.
4. all of these are true.

12. Which of these statements about the Na^+/K^+ pump is true?
1. Na^+ is actively transported into the cell.
2. $K^+$is actively transported out of the cell.
3. equal number of Na^+ and K^+ ions are transported with each cycle of the pump.
4. the pumps are constantly active in all cells.

13. Which of these statements about carrier mediated facilitated diffusion is true?
1. it uses cellular ATP
2. it is used for cellular uptake of blood glucose
3. it is a form of active transport
4. none of these are true

14. Which of these is not an example of cotransport?
1. movement of glucose and Na^+ through the apical epithelial membrane in the intestinal epithelium
2. movement of Na^+ and K^+ through the action of the Na^+/K^+ pumps
3. movement of Na^+ and glucose across the kidney tubules
4. movement of Na^+ into a cell while Ca^{2+} moves out

15. Interstitial fluid
1. is an ultrafiltrate of plasma, formed by filtration processes across the capillary wall
2. the fluid circulating in the blood vessels and is the smaller of the two ECF subcompartments
3. is contained within the cells and is two thirds of total body water
4. the fluid that actually bathes the cells and is the larger of the two sub compartments

16. What is the major cation and the balancing anions in ECF?
1. sodium (Na^+) and chloride (Cl^-) and bicarbonate (HCO^{3-})
2. potassium (K^+), magnesium (Mg^{2+}) and proteins and organic phosphates
3. calcium (Ca^{2+}) and hydrogen (H^+)
4. sodium (Na^+), magnesium (Mg^{2+}) and proteins and organic phosphates

17. What is the major cation and the balancing anions in ICF?
1. sodium (Na^+) and chloride (Cl^-) and bicarbonate (HCO^{3-})
2. potassium (K^+), magnesium (Mg^{2+}) and proteins and organic phosphates
3. calcium (Ca^{2+}) and hydrogen (H^+)
4. sodium (Na^+), magnesium (Mg^{2+}) and proteins and organic phosphates

18. The main property of the cell membrane is:
1. differential permeability
2. immobility
3. invariability
4. variability

19. The absorption of large particles by cells is called:
1. phagocytosis
2. diffusion
3. pinocytosis
4. exocytosis

20. The absorption of globules of fluid by cells is called:
1. water delivery
2. nutrition
3. diffusion
4. pinocytosis

21. Bothe phagocytosis and pinocytosis are joined under a common term:

1. exocytosis
2. endocytosis
3. diffusion
4. coupled transport

22. The transport of particles and globules of solute from the cell to outside is called:

1. excision
2. endocytosis
3. outflow
4. exocytosis

23. The transport of substances across cell membranes from the larger concentration to the less concentration is called:

1. downhill transport (transport down the concentration gradient)
2. transport not depending on the concentration gradient
3. transport against the concentration gradient

24. Transport across cell membranes without using carriers and energy of ATP is called:

1. simple diffusion
2. facilitated diffusion
3. occlusion
4. active diffusion

25. Transport across cell membranes against the concentration gradient using carriers and energy of ATP is called:

1. active transport (uphill)
2. passive transport (downhill)
3. exocytosis
4. endocytosis

26. Active transport is a way for molecules to move across the plasma membrane. When active transport is used to move molecules, what is required?

1. concentration gradient
2. very small molecules
3. energy that the cell provides
4. osmosis

Lesson 3. General physiology of excitable cells. Resting Membrane Potential. Action Potentials. Issues for consideration

1. Diffusion potentials and equilibrium potentials. Ion channels. Diffusion potentials. Equilibrium potentials. Nernst equation.
2. Resting membrane potential.
3. Action potentials. Terminology. Characteristics of action potentials.
4. Ionic basis of the action potential. The nerve Na+ channel .
5. Refractory periods. Absolute refractory period. Relative refractory period. Accommodation
6. Propagation of action potentials. Conduction velocity. Changes in conduction velocity

Home work (writing)

1. Name and describe the types of ion channels.

_____
_____
_____
_____
_____
_____

2. Give a definition of the diffusion potential?

_____
_____
_____
_____

3. Give a definition the equilibrium potential?

_____
_____
_____
_____

4. Write the Nernst equation and typical values for equilibrium potential for common ions (Na^+,Ca^{2+}, K^+, Cl^-), calculated and assuming typical concentration gradients across cell membranes.

_____
_____

5. Give a definition of the resting membrane potential? What is the average resting membrane potential of excitable cells?

6. Give a definition of the action potential.

7. List characteristics of action potentials.

8. Draw and label the action potential Time course of voltage and conductance changes (Na^+, K^+) during the action potential of nerve.

9. Draw voltage-gated Na+ channel and draw how the state of the channel gate in the generation of an action potential.

10. Give a definition of absolute refractory period, relative refractory period and accommodation.

_____
_____
_____
_____
_____

Teacher's signature: _____

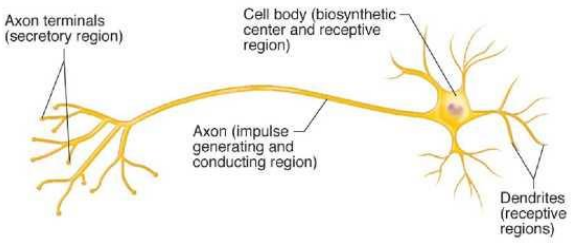
Exercise 3: Neurophysiology of Nerve Impulses

Exercise Overview

Neurophysiology of Nerve Impulses

The nervous system contains two general types of cells: **neurons** and neuroglia (or glial cells). This exercise focuses on neurons. Neurons respond to their local environment by generating an electrical signal. For example, sensory neurons in the nose generate a signal (called a **receptor potential)** when odor molecules interact with receptor proteins on the membrane of these olfactory sensory neurons. Thus, sensory neurons can respond directly to sensory stimuli. The receptor potential can trigger another electrical signal (called an **action potential),** which travels along the membrane of the sensory neuron's axon to the brain—you could say that the action potential is conducted to the brain.

The action potential causes the release of **chemical neurotransmitters** onto neurons in olfactory regions of the brain. These chemical neurotransmitters bind to receptor proteins on the membrane of these brain **interneurons.** In general, interneurons respond to chemical neurotransmitters released by other neurons. In the nose the odor molecules are sensed by sensory neurons. In the brain the odor is perceived by the activity of interneurons responding to neurotransmitters. Any resulting action or behavior is caused by the subsequent activity of **motor neurons,** which can stimulate muscles to contract (see Exercise 2).



In general each neuron has three functional regions for signal transmission: a receiving region, a conducting region, and an output region, or secretory region. Sensory neurons often have a receptive ending specialized to detect a specific sensory stimulus, such as odor, light, sound, or touch. The **cell body** and **dendrites** of interneurons receive stimulation by neurotransmitters at structures called **chemical synapses** and produce **synaptic potentials.** The conducting region is usually an **axon,** which ends in an output region (the axon terminal) where neurotransmitter is released (view Figure 3.1). Although the neuron is a single cell surrounded by a continuous plasma membrane, each region contains distinct membrane proteins that provide the basis for the functional differences. Thus, the receiving end has receptor proteins and proteins that generate the receptor potential, the conducting region has proteins that generate and conduct action potentials, and the output region has proteins to package and release neurotransmitters. Membrane proteins are found throughout the neuronal membrane—many of these proteins transport ions (see Exercise 1).

The signals generated and conducted by neurons are electrical. In ordinary household devices, electric current is carried by electrons. In biological systems, currents are carried by positively or negatively charged **ions.** Like charges repel each other and opposite charges attract. In general, ions cannot easily pass through the lipid bilayer of the plasma membrane and must pass through **ion channels** formed by integral membrane proteins. Some channels are usually open (leak channels) and others are gated, meaning that the channel can be in an open or closed configuration. Channels can also be selective for which ions are allowed to pass. For example, sodium channels are mostly permeable to sodium ions when open, and potassium channels are mostly permeable to potassium ions when open. The term **conductance** is often is used to describe **permeability.** In general, ions will flow through an open channel from a region of higher concentration to a region of lower concentration (see Exercise 1). In this exercise you will explore some of these characteristics applied to neurons.

Although it is possible to measure the ionic currents through the membrane (even the currents passing through single ion channels), it is more common to measure the potential difference, or voltage, across the membrane. This membrane voltage is usually called the **membrane potential,** and the units are **millivolts (mV).** One can think of the membrane as a battery, a device which separates and stores charge. A typical household battery has a positive and negative pole so that when it is connected, for example, through a light bulb in a flashlight, current flows through the bulb. Similarly, the plasma membrane can store charge and has a relatively positive side and a relatively negative side. Thus, the membrane is said to be **polarized.** When these two sides (intracellular and extracellular) are connected through open ion channels, current in the form of ions can flow in or out across the membrane and thus change the membrane voltage.

Exercise 3. Activity 1: The Resting Membrane Potential

Objectives

1. To define the term resting membrane potential.
2. To measure the resting membrane potential in different parts of a neuron.
3. To determine how the resting membrane potential depends on the concentrations of potassium and sodium.
4. To understand the ion conductances/ion channels involved in the resting membrane potential.

Introduction

The receptor potential, synaptic potentials, and action potentials are important signals in the nervous system. These potentials refer to changes in the membrane potential from its resting level. In this activity you will explore the nature of the resting potential. The **resting membrane potential** is really a potential difference between the inside of the cell (intracellular) and the outside of the cell (extracellular) across the membrane. It is a steady-state condition that depends on the resting permeability of the membrane to ions and on the intracellular and extracellular concentrations of those ions to which the membrane is permeable.

For many neurons, Na^+ and K^+ are the most important ions, and the concentrations of these ions are established by transport proteins, such as the Na^+-K^+ pump, so that the intracellular Na^+ concentration is low and the intracellular K^+ concentration is high. Inside a typical cell, the concentration of K^+ is ~150 mM and the concentration of Na^+ is ~5 mM. Outside a typical cell, the concentration of K^+ is ~5 mM and the concentration of Na^+ is ~150 mM. If the membrane is permeable to a particular ion, that ion will diffuse down its concentration gradient from a region of higher concentration to a region of lower concentration. In the generation of the resting membrane potential, K^+ ions diffuse out across the membrane leaving behind a net negative charge—large anions that cannot cross the membrane.

The membrane potential can be measured with an amplifier. In the experiment the extracellular solution is connected to a ground (literally, the earth) which is defined as 0 mV. To record the voltage across the membrane, a microelectrode is inserted through the membrane without significantly damaging it. Typically, the microelectrode is made by pulling a thin glass pipette to a fine hollow point and filling the pulled pipette with a salt solution. The salt solution conducts electricity like a wire, and the glass insulates it. Only the tip of the microelectrode is inserted through the membrane, and the filled tip of the microelectrode makes electrical contact with the intracellular solution. A wire connects the microelectrode to the input of the amplifier so that the amplifier records the membrane potential, the voltage across the membrane between the intracellular and grounded extracellular solutions.

The membrane potential and the various signals can be observed on an oscilloscope. An electron beam is pulled up or down according to the voltage as it sweeps across a phosphorescent screen. Voltages below 0 mV are negative and voltages above 0 mV are positive. For this first activity, the time of the sweep is set for 1 second per division, and the sensitivity is set to 10 mV per division; a division is the distance between gridlines on the oscilloscope.

Equipment Used

- Neuron (in vitro)—a large, dissociated (or cultured) neuron
- Three extracellular solutions—control, high potassium, and low sodium
- Microelectrode—a probe with a very small tip that can impale a single neuron (In an actual wet lab, a microelectrode manipulator is used to position the microelectrode. For simplicity, the microelectrode manipulator will not be depicted in this activity.)
- Microelectrode manipulator controller—controls movement of the manipulator Microelectrode amplifier—used to measure the voltage between the microelectrode and a reference
- Oscilloscope—used to observe voltage changes

Experiment Data:

Extracellular Fluid (ECF)	Microelectrode Position	Voltage (mV)
Control	Cell body extracellular	
Control	Cell body intracellular	
Control	Axon extracellular	
Control	Axon intracellular	
High K+	Axon intracellular	
High K+	Axon extracellular	
High K+	Cell body extracellular	
High K+	Cell body intracellular	
Low Na+	Cell body intracellular	
Low Na+	Cell body extracellular	
Low Na+	Axon extracellular	
Low Na+	Axon intracellular	

Review sheet:

1. Explain why increasing extracellular K^+ reduces the net diffusion of K^+ out of the neuron

through the K^+ leak channels.

_____
_____
_____
_____
_____

2. Explain why increasing extracellular K+ causes the membrane potential to change to a less negative value. How well did the results compare with your prediction?

_____
_____
_____
_____

3. Explain why a change in extracellular Na+ did not significantly alter the membrane potential in the resting neuron?

_____
_____
_____
_____

4. Discuss the relative permeability of the membrane to Na+ and K+ in a resting neuron.

_____
_____
_____
_____

5. Discuss how a change in Na^+ or K^+ conductance would affect the resting membrane potential.

_____
_____
_____
_____

Exercise 3. Activity 3: The Action Potential: Threshold

Objectives

1. To define the terms action potential, nerve, axon hillock, trigger zone, and threshold.
2. To predict how an increase in extracellular K^+ could trigger an action potential.

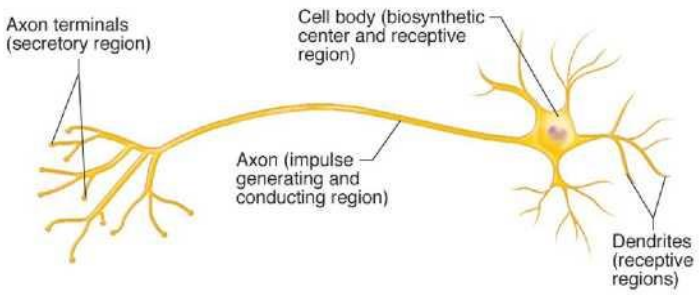
Introduction

In this activity you will explore changes in potential that occur in the axon. Axons are long, thin structures that conduct a signal called the **action potential.** A **nerve** is a bundle of axons.

Axons are typically studied in a nerve chamber. In this activity the axon will be draped over wires that make electrical contact with the axon and can therefore record the electrical activity in the axon. Because the axon is so thin, it is very difficult to insert an electrode across the membrane into the axon. However, some of the charge (ions) that cross the membrane to generate the action potential can be recorded from outside the membrane (extracellular recording) as you will do in this activity. The molecular mechanisms underlying the action potential were explored more than 50 years ago with intracellular recording using the giant axons of the squid, which are about 1 millimeter in diameter.

In this activity the axon will be artificially disconnected from the cell body and dendrites. In a typical multipolar neuron (view Figure 3.1). the axon extends from the cell body at a region called the **axon hillock** In a myelinated axon, this first region is called the initial segment. An action potential is usually initiated at the junction of the axon hillock and the initial segment; therefore, this region is also referred to as the **trigger zone.**

You will use an electrical stimulator to explore the properties of the action potential. Current passes from the stimulator to one of the stimulation wires, then across the axon, and then back to the stimulator through a second wire. This current will depolarize the axon. Normally, in a



sensory neuron, the depolarizing receptor potential spreads passively to the axon hillock and produces the depolarization needed to evoke the action potential. Once an action potential is generated, it is regenerated down the membrane of the axon. In other words, the action potential is **propagated,** or *conducted,* down the axon (see Activity 6).

You will now generate an action potential at one end of the axon by stimulating it electrically and record the action potential that is propagated down the axon. The extracellular action potential that you record is similar to one that would be recorded across the membrane with an intracellular microelectrode, but much smaller. For simplicity, only one axon is depicted in this activity.

Equipment Used:

- Nerve chamber
- Axon
- Oscilloscope—used to observe timing of stimuli and voltage changes in the axon
- Stimulator—used to set the stimulus voltage and to deliver pulses that depolarize the axon
- Stimulation wires (S)

Recording electrodes (wires R1 and R2)—used to record voltage changes in the axon (The first set of recording electrodes, R1, is 2 centimeters from the stimulation wires, and the second set of recording electrodes, R2, is 2 centimeters from R1.)

Experiment Data:

Stimulus Voltage (mV)	Peak Value at R1 (μV)	Peak Value at R2 (μV)	Action Potential (yes/no)
10			
20			
30			
40			
50			

Review Sheet:

1. Define the term threshold as it applies to an action potential.

_____
_____
_____
_____

2. What change in membrane potential (depolarization or hyperpolarization) triggers an action potential?

_____
_____
_____
_____

3. How did the action potential at R1 (or R2) change as you increased the stimulus voltage above the threshold voltage? How well did the results compare with your prediction?

_____
_____
_____
_____

4. An action potential is an "all-or-nothing" event. Explain what is meant by this phrase

_____
_____
_____
_____

5. What part of a neuron was investigated in this activity?

_____
_____
_____
_____

Exercise3. Activity 4: The Action Potential: Importance of Voltage-Gated Na^+ channels

Objectives

1. To define the term voltage-gated channel.
2. To describe the effect of tetrodotoxin on the voltage-gated Na^+ channel.
3. To describe the effect of lidocaine on the voltage-gated Na^+ channel.
4. To examine the effects of tetrodotoxin and lidocaine on the action potential.
5. To predict the effect of lidocaine on pain perception and to predict the site of action in the sensory neurons (nociceptors) that sense pain.

Introduction

The action potential (as seen in Activity 3) is generated when voltage-gated sodium channels open in sufficient numbers. **Voltage-gated sodium channels** open when the membrane depolarizes. Each sodium channel that opens allows Na^+ ions to diffuse into the cell down their electrochemical gradient. When enough sodium channels open so that the amount of sodium ions that enters via these voltage-gated channels overcomes the leak of potassium ions (recall that the potassium leak via passive channels establishes and maintains the negative resting membrane potential), threshold for the action potential is reached, and an action potential is generated.

In this activity you will observe what happens when these voltage-gated sodium channels are blocked with chemicals. One such chemical is tetrodotoxin (TTX), a toxin found in pufferfish, which is extremely poisonous. Another such chemical is lidocaine, which is typically used to block pain in dentistry and minor surgery.

Equipment Used:

- Nerve chamber
- Axon
- Oscilloscope—used to observe timing of stimuli and voltage changes in the axon
- Stimulator—used to set the stimulus voltage and the interval between stimuli and to deliver pulses that depolarize the axon Stimulation wires (S)
- Recording electrodes (wires R1 and R2)—used to record voltage changes in the axon (The first set of recording electrodes, R1, is 2 centimeters from the stimulation wires, and the second set of recording electrodes, R2, is 2 centimeters from R1.)
- Tetrodotoxin (TTX)
- Lidocaine

Experiment Data:

Condition	Stimulus Voltage (mV)	Electrode	Peak Value of Response (µV) 2 sec	Peak Value of Response (µV) 4 sec	Peak Value of Response (µV) 6 sec	Peak Value of Response (µV) 8 sec	Peak Value of Response (µV) 10 sec
Control	30	R1					
Control	30	R2					
TTX	30	R1					
TTX	30	R2					
Lidocaine	30	R1					
Lidocaine	30	R2					

Review Sheet:

1. What does TTX do to voltage-gated Na^+ channels?

_____
_____
_____
_____

2. What does lidocaine do to voltage-gated Na^+ channels? How does the effect of lidocaine differ from the effect of TTX?

_____
_____
_____
_____

3. A nerve is a bundle of axons, and some nerves are less sensitive to lidocaine. If a nerve, rather than an axon, had been used in the lidocaine experiment, the responses recorded at R1 and R2 would be the sum of all the action potentials (called a compound action potential). Would the response at R2 after lidocaine application necessarily be zero? Why or why not?

_____
_____
_____
_____

4. Why are fewer action potentials recorded at recording electrodes R2 when TTX is applied between R1 and R2? How well did the results compare with your prediction?

_____
_____
_____
_____

5. Why are fewer action potentials recorded at recording electrodes R2 when lidocaine is applied between R1 and R2? How well did the results compare with your prediction?

_____
_____
_____
_____

6. Pain-sensitive neurons (called nociceptors) conduct action potentials from the skin or teeth to sites in the brain involved in pain perception. Where should a dentist inject the lidocaine to block pain perception?

_____
_____
_____
_____

Exercise 3. Activity 5: The Action Potential: Measuring Its Absolute and Relative Refractory Periods

Objectives

1. To define inactivation as it applies to a voltage-gated sodium channel.
2. To define the absolute refractory period and relative refractory period of an action potential.

Introduction

To define the relationship between stimulus frequency and the generation of action potentials. Voltage-gated sodium channels in the plasma membrane of an excitable cell open when the membrane depolarizes. About 1 -2 milliseconds later, these same channels inactivate, meaning they no longer allow sodium to go through the channel. These inactivated channels cannot be reopened by depolarization for an additional period of time (at least a few milliseconds). Thus, during this time, fewer sodium channels can be opened. There are also voltage-gated potassium channels that open during the action potential. These potassium channels open more slowly. They contribute to the repolarization of the action potential from its peak, as more potassium flows out through this second type of potassium channel (recall there are also passive potassium channels that let potassium leak out, and these leakage channels are always open). The flux through extra voltage-gated potassium channels opposes the depolarization of the membrane to threshold, and it also causes the membrane potential to become transiently more negative than the resting potential at the end of an action potential. This phase is called after-hyperpolarization, or the undershoot.

In this activity you will explore the consequences the conformation states of the voltage-gated channels have for the

generation of subsequent action potentials.

Equipment Used:

- Nerve chamber
- Axon
- Oscilloscope—used to observe timing of stimuli and voltage changes in the axon
- Stimulator—used to set the stimulus voltage and the interval between stimuli and to deliver pulses that depolarize the axon
- Stimulationwires (S)
- Recording electrode (wires R1)—used to record voltage changes in the axon (The recording electrode is 2 centimeters from the stimulation wires.)

Experiment Data:

Interval Between Stimuli (msec)	Stimulus Voltage (mV)	Second Action Potential (Yes/No)
250	20	
125	20	
60	20	
60	25	
60	30	
30	30	
30	35	
30	40	
30	45	
15	60	
7.5	60	
3.75	60	

Review Sheet:

1. Define inactivation as it applies to a voltage-gated sodium channel.

_____
_____
_____

2. Define the absolute refractory period.

_____
_____
_____
_____

3. How did the threshold for the second action potential change as you further decreased the interval between the stimuli? How well did the results compare with your prediction?

_____
_____
_____
_____

4. Why is it harder to generate a second action potential during the relative refractory period?

_____
_____
_____
_____

Teacher's signature _____

Computer tests: GENERAL PHYSIOLOGY OF EXCITABLE CELLS
RESTING MEMBRANE POTENTIAL

ACTION POTENTIALS

1. Depolarization of an axon is produced by

1. inward diffusion of Na^+
2. active extrusion of K^+
3. outward diffusion of K^+
4. inward active transport of Na^+

2. Repolarization of an axon during an action potential is produced by
1. inward diffusion of Na^+
2. active extrusion of K^+
3. outward diffusion of K^+
4. inward active transport of Na^+

3. As the intensity of a depolarizing stimulus to an axon is increased,
1. the amplitude of action potentials increases
2. the duration of action potentials increases
3. the speed with which action potentials are conducted increases
4. the frequency with which action potentials are produced increases

4. The conduction of action potentials in a myelinated nerve fiber is
1. saltatory
2. without decrement.
3. faster than in an unmyelinated fiber
4. all of the these

5. Which of these is not a characteristic of action potential?
1. they are produced by voltage-gated channels
2. they are conducted without decrement.
3. Na^+ and K^+ gates open at the same time.
4. the membrane potential reverses polarity during depolarization.

6. The absolute refractory period of a neuron
1. occurs due to the high negative polarity of the inside of the neuron
2. occurs only during the repolarization phase
3. occurs only during the depolarization phase
4. occurs during depolarization and the first part of the repolarization phase

7. A pharmacological or physiological perturbation that increases the resting PK^+/PNa^+ ratio for the plasma membrane of a neuron would
1. lead to depolarization of the cell
2. lead to hyperpolarization of the cell
3. produce no change in the value of the resting membrane potential

8. The afterhyperpolarization phase of the action potential is caused by
1. outward calcium current
2. inward sodium current
3. outward potassium current
4. outward sodium current

9. If the extracellular K^+ concentration is increased from 4 meq/L to 10 meq/L,
1. the membrane potential will become more negative
2. the sodium conductance will increase
3. the potassium conductance will increase
4. the membrane will become more excitable
5. the Na^+/K^+ pump will become inactivated

10. Inactivation of the sodium-potassium pump will cause
1. increase in the intracellular volume
2. increase in the intracellular potassium concentration
3. hyperpolarization of the membrane potential
4. increase in the excitability of nerve cells
5. increase in the flow of sodium out of the cell

11. Membrane excitability will be increased by the greatest amount of
1. increasing extracellular Na^+
2. increasing extracellular K^+
3. decreasing extracellular Cl^-
4. decreasing extracellular Ca^{2+}
5. decreasing extracellular H^+

12. The resting potential of a nerve membrane is primarily dependent on the concentration gradient of
1. potassium
2. sodium
3. calcium
4. chloride
5. bicarbonate

13. In a nerve, the magnitude of the action potential overshoot depends on
1. magnitude of the stimulus
2. intracellular potassium concentration
3. extracellular sodium concentration
4. resting membrane potential
5. diameter of the axon

14. The membrane potential will depolarize with the greatest amount if the membrane permeability increases for
1. potassium
2. sodium and potassium
3. chloride
4. potassium and chloride
5. sodium

15. Which of the following during the overshoot of action potential will be less than during the resting state?
1. membrane conductance for sodium
2. membrane conductance for potassium
3. transference for sodium
4. transference for potassium
5. total membrane conductance

16. The preventing inactivation of sodium channels will cause the decrease of
1. the relative refractory period of nerve cells
2. the upstroke velocity of action potentials
3. the downstroke velocity of action potentials
4. the magnitude of the overshoot in action potentials
5. the duration of action potentials

17. Which of the following statements are true for the equilibrium and steady states?
1. the sum of all fluxes across the membrane is zero in both
2. both are maintained by the consumption of free energy
3. the concentration gradient across the membrane is zero in both
4. both are maintained by homeostatic processes
5. the membrane potential is zero in both

18. Voltage-gated channels are normally involved in
1. the depolarization of the end-plate membrane by ACh
2. hyperpolarization of the rods by light
3. release of calcium from ventricular muscle sarcoplasmic reticulum
4. transport of glucose into cells by a sodium-dependent, secondary active transport system
5. increase in nerve cell potassium conductance caused by an increase in extracellular potassium

19. The sodium gradient across the nerve cell membrane is
1. a result of the Donnan equilibrium
2. significantly changed during an action potential
3. **used as a source of energy for the transport of other ions**
4. an important determinant of the resting membrane potential
5. maintained by a Na^+/Ca^{2+} exchanger

20. Increase in extracellular potassium concentration will
1. increase the threshold for eliciting an action potential
2. hyperpolarize the membrane potential
3. decrease potassium permeability
4. decrease the activity of the sodium-potassium pump
5. make the equilibrium potential for potassium more negative

21. Which of the following would immediately reduce in the amount of potassium leaking out of a cell?
1. increasing the permeability of the membrane to potassium
2. increasing the intracellular potassium concentration
3. increasing (hyperpolarizing) the membrane potential
4. reducing the activity of the sodium-potassium pump

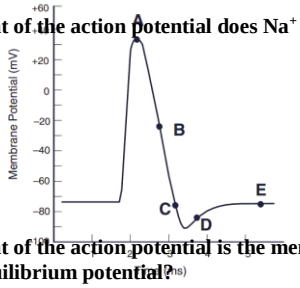
5. decreasing the potassium equilibrium potential

22. In which one of the following transport processes is the substance moving down its electrochemical gradient?

1. Sodium out of nerve cells
2. calcium into the sarcoplasmic reticulum
3. hydrogen into the lumen of the distal nephron
4. glucose into adipose tissue
5. potassium into striated muscle cells

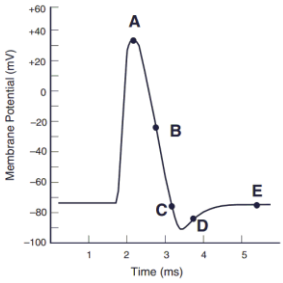
23. At which point of the action potential does Na^+ current exceed K^+ current?

1. at point A
2. at point B
3. at point C
4. at point D
5. at point E



24. At which point of the action potential is the membrane closest to the Na^+ equilibrium potential?

1. at point A
2. at point B
3. at point C
4. at point D
5. at point E



25. A typical neuron has a resting membrane potential of about:

1. +70 mV
2. +70 V
3. -70 mV
4. -70 V
5. All of the above are observed at rest

26. At the peak of the action potential the membrane potential is:

1. exactly at the Na^+ equilibrium potential (VNa)
2. close to but more positive than the Na^+ equilibrium potential (VNa)
3. close to but less positive than the Na^+ equilibrium potential (VNa)
4. exactly at 0 mV
5. the same as the resting membrane potential (Vrest)

27. At what membrane voltage do neuronal voltage-gated Na^+ channels become activated?

1. -70 mV
2. -50 mV
3. 0 mV
4. +50 mV
5. None of the above

28. At what membrane voltage do neuronal voltage-gated K^+ channels become activated?

1. -70 mV
2. -50 mV
3. 0 mV
4. +50 mV
5. None of the above

29. The spike phase of action potential occurs due to:

1. the opening of voltage-gated Na^+ channels
2. the opening of voltage-gated K^+ channels
3. the closure of resting K^+ channels
4. the opening of voltage-gated Cl^- channels
5. none of the above

30. In the nervous system, the intensity of the stimulus is coded into:

1. The frequency of action potentials generated
2. the amplitude of action potentials generated
3. both the frequency and amplitude of action potentials generated

31. What is the assumed resting intracellular and extracellular concentrations of Na^+, determine the Na^+ equilibrium potential (V Na^+)?

1. 0 mV
2. +61 mV
3. -61 mV
4. +96 mV
5. -96 mV

32. What is the assumed resting intracellular and extracellular concentrations of K^+, determine the K^+ equilibrium potential (VK^+)?

1. 0 mV
2. +61 mV
3. -61 mV
4. +96 mV
5. -96 mV

33. Let's assume that in a cell at rest, only K^+ channels are open in the plasma membrane. This situation could arise if all other ion channels are blocked by the addition of pharmacological agents (i.e., blockers or inhibitors). What is the value of the membrane potential (Vm) under this condition in this cell?

1. the membrane potential is the same as the equilibrium potential for K^+ (Vm = VK^+)
2. the membrane potential is the same as the equilibrium potential for Na^+ (Vm = VNa^+)
3. the membrane potential is the same as the equilibrium potential for Cl^- (Vm = VCl^-)
4. none of the above is correct
5. all of the above are possible

34. Let's assume that in a cell at rest, only Na^+ channels are open in the plasma membrane. This situation could happen if all other ion channels are blocked by the addition of pharmacological agents (i.e., blockers or inhibitors). What is the value of the membrane potential (Vm) under this condition in this cell?

1. the membrane potential is the same as the equilibrium potential for K^+ (Vm = VK^+)
2. the membrane potential is the same as the equilibrium potential for Na^+ (Vm = VNa^+)
3. the membrane potential is the same as the equilibrium potential for Cl^- (Vm = VCl^-)
4. none of the above is correct
5. all of the above are possible

35. A change in the membrane potential (Vm) from the resting value of -50 mV to a new value of -90 mV is known as:

1. depolarization
2. hyperpolarization

36. Change in the membrane potential (Vm) from the resting value of -50 mV to the new value of -10 mV is known as:

1. depolarization
2. hyperpolarization

37. "All-or-none" response is usual for:

1. postsynaptic potential
2. local potential
3. action potential
4. membrane potential
5. receptor potential

38. Adaptation of excitable tissues to slowly increasing intensity of stimuli is called:

1. lability
2. functional mobility
3. sensitization
4. stabilization
5. accommodation

39. Excitable tissues are:

1. epithelial, muscle
2. nerve, muscle, epithelial
3. nervous, muscular
4. bone, connective

40. Tissues that respond with the excitability to the stimulus are called

1. irritable

2. excitable
3. conducted
4. contractile

41. The basic process of accommodation is:
1. the increase of the sodium permeability
2. the lowering of potassium permeability
3. the inactivation of potassium and an increase of sodium permeability
4. the inactivation of sodium and an increase potassium permeability

42. Electric current is the _____ stimulus to the excitable membrane
1. adequate
2. nonspecific
3. threshold
4. inadequate

43. Decreased excitability of a cell during relative refractory period is determined by:
1. the phased reactivation of sodium channels
2. the significant decrease of potassium current
3. the decrease of the value of threshold potential
4. the inactivation of sodium channel

44. The period of a decreased excitability during the repolarization of the action potential is called:
1. relative refractory period
2. Reversion
3. exaltation
4. absolute refractory period

45. The period of a complete non-excitability of a cell is called:
1. relative refractory period
2. subnormal excitability period
3. absolute refractory period
4. exaltation

46. Which of the following phenomena characterizes absolute refractory period:
1. the inactivation of K+ voltage-gated channels
2. the inactivation of Ca2+ voltage-gated channels;
3. the inactivation of Na+ voltage-gated channels;
4. the inactivation of Mg2+ voltage-gated channels

47. In neurons:
1. stimuli can alter the potential difference by closing sodium channels in the membrane.
2. stimuli can alter the potential difference by opening sodium channels in the membrane
3. stimuli has no affect on potentials
4. stimuli is only affective when tissue temperature is above 31 degrees Celsius

48. Protein molecular mechanism that let sodium ions go out of cytoplasm and potassium ions go into cytoplasm is called:
1. voltage-gated sodium channel
2. nonspecific sodium potassium channel
3. sodium-potassium pump
4. ligand-gated sodium channel

49. The potential difference that exists across the membrane of excitable cells is called:
1. action potential
2. prepotential
3. membrane potential
4. reversion

50. For what ion the value of the resting potential is close to the equilibrium potential?
1. potassium
2. chlorine
3. calcium
4. sodium
5. magnesium

51. Every action potential is formed by two successive processes:
1. hyperpolarization-repolarization
2. repolarization-depolarization
3. depolarization-repolarization
4. depolarization-hyperpolarization

Lesson 4. Cell signaling. Synaptic and Neuromuscular Transmission Issues for consideration

1. Cell receptors and their properties. Classification of cell receptors (for localization and mechanism). Regulation of the amount of cellular receptors (up- and down-regulation)
2. Primary and second messengers. G proteins. Adenylate cyclase mechanism. Phospholipase C mechanism. Steroid and thyroid hormone mechanism
3. Synaptic and neuromuscular transmission. Types of synapses.
4. Neuromuscular junction-example of a chemical synapse.
5. Types of synaptic arrangements.
6. Synaptic input-excitatory and inhibitory postsynaptic potentials.
7. Integration of synaptic information. Neurotransmitters.

Home work (writing)

1. Ways of Signals relayed between cells

_____
_____
_____
_____
_____
_____

2. Stages of Cell Signaling

_____
_____

3. Cell Communication Systems with Surface Receptors

4. Cell Communication Systems. Intracellular Receptors

5. Give the definition of the concept of a cellular receptor

6. List types of Receptors in the Plasma Membrane

7. Give the definition of primary and secondary messengers

8. List the second messengers

9. Draw a diagram of the transmission signal of G-receptor.

10. Give the definition of synapse.

_____

_____

_____

11. Give the classification of synapses.

_____

_____

_____

_____

_____

_____

_____

12. Draw a chemical synapse, and show the main steps of synaptic transmission.

13. Draw graphics EPSP and IPSP

14. List the excitatory and inhibitory neurotransmitters

_____

_____

_____

_____

_____

Computer tests: CELL SIGNALING

1. Which of the following is a secondary mediator?
1 acetylcholine
2 noradrenaline

3 cAMP
4 somatostatin

2. Adenylate cyclase is activated by:
1 cAMP
2. G-protein
3 Ca^{2+}
4 protein kinase
5 membrane receptors

3. Inositol triphosphate (IP3) activates:
1 adenylate cyclase
2 guanylate cyclase
3 Ca^{2+} channels of EPR
4 calcium ATPase
5 protein kinase

4. The activation of adenylate cyclase triggers the synthesis of:
1 ATP
2 cGMP
3 cAMP
4 tyrosine kinase
5. G-protein

5. Which of the G-protein subunits generates an activation of the effector protein?
1 alpha
2 beta
3 gamma
4 delta
5 kappa

6. Which of the G-protein subunits is capable to detach from the receptor and bind to an effector-protein?
1 alpha
2 beta
3 gamma
4 delta
5 kappa

7. A fatigue occurs first:
1 at synapse
2 in skeletal muscle
3 in the nerve trunk
4 in neuronal cells

8. A mediator in the neuromuscular junctions of skeletal muscles of man is:
1 acetylcholine
2 noradrenaline
3 GABA
4 adrenaline

9. The structural formation providing the propagation of excitation from one cell to another is called:
1 nerve
2 axonal hillock
3 synapse
4 Ranvier's node

10. What kind of the potential occurs on the postsynaptic membrane of the neuromuscular synapse:
1 inhibitory postsynaptic potential
2 actions
3 end plate potential (EPP)

11. What happens to the mediator released from the presynaptic terminals?
1 It diffuses through the postsynaptic membrane
2: It binds the postsynaptic membrane receptors
3 It carries through the postsynaptic membrane by an active transport
4 It binds proteins of synaptic fluid
5 It accumulates in the synaptic cleft, thereby reducing the electrical resistance

12. What determines a value of the end-plate potential?
1 the intensity of the synthesis of acetylcholine in the motoneurons
2 a number of receptors that unbound to acetylcholine
3 a concentration of calcium ions in the presynaptic terminal
4 a concentration neurotransmitter in the synaptic cleft
5 a number of cholinergic receptors bound to mediator

13. What ion current mainly generates the endplate potential?
1 Calcium
2 chlorine
3 Sodium
4 Magnesium
5 all answers are correct

14. What is the function of acetylcholinesterase in the neuromuscular junction?
1 to increase a value of the end-plate potential
2 to increase duration of the end plate potential
3 to stimulate the synthesis of the mediator
4 to ensure the timely closing of ligand-gated channels
5 to split the mediator bound to acetylcholine receptors

15. Which of the following is typical for generating of the endplate potential?
1 it is formed by using ligand-gated channels
2 it is formed by using voltage-gated channels
3 it has an amplitude equal to the action potential
4 it is formed by the rule of "all or non response"
5 it has an duration equal to the action potential

16. What is the result of the effect of curare on the nerve-muscle synapse?
1 acetylcholinesterase is inactivated
2 the synthesis of acetylcholine is inhibited
3 the release of acetylcholine is blocked
4 **cholinergic receptors are blocked**
5 acetylcholine is split

17. What triggers releasing of mediator from presynaptic terminal?
1 current of potassium ions into the presynaptic terminal
2 current of chlorine ions into the presynaptic terminal
3 current of calcium ions out of the presynaptic terminal
4 **current of calcium ions into the presynaptic terminal**
5 current of chlorine ions out of the presynaptic terminal

18. Which of ion channels may be involved in forming of IPSP?
1 sodium
2 potassium
3 calcium
4 magnesium
5 all of the above

19. Choose the way mediator releases from the presynaptic terminal:
1 exocytosis
2 pinocytosis
3 by a specific carriers
4 diffusion
5. filtration

20. Which of the following mediators more often than others play the role of inhibitory mediator:
1 acetylcholine
2 GABA
3 norepinephrine
4 dopamine
5 glutamate

21. What ion channels may be used in inhibitory synapses?
1 Potassium;
2 Magnesium;
3 Sodium;
4 Calcium;
5 all cations.

22. Which of these events must occur before the others during metabotropic control?

1 building of c-AMP;
2 activation of protein kinase;
3 activation of adenylate cyclase;
4 activation of G-protein:

23. Ligand-gated channels of the postsynaptic membrane during formation of the EPSP are permeable to:

1 sodium ions
2 potassium ions
3. potassium ions and sodium ions
4. sodium ions and calcium ions

24. What electric process leads to the formation of EPSP?

1 **depolarization of the presynaptic membrane**
2 hyperpolarization of the postsynaptic membrane
3 depolarization of the postsynaptic membrane
4 all the answers are correct

25. If the enzyme system splitting the mediator in the synapse cleft is completely inactivated efficiency of synaptic transmission will:

1 increase
2 not change
3 be equal to zero
4 all the answers are wrong

Lesson 5. Nerve cell physiology. Propagation of action potentials.

Issues for consideration.

1. Morphofunctional characteristic of nerve cells.
2. Propagation of action potentials. Spread of depolarization down a nerve fiber by local currents.
3. Conduction velocity. Cable properties. Time constant. Membrane resistance. Membrane capacitance. Length constant
4. Changes in conduction velocity from nerve diameter, myelination. Saltatory conduction

Integration of synaptic information. Spatial summation. Temporal summation.

Home work (writing)

1. Draw a neuron, specify the major structural elements, list the physiological properties of the neuron.

_____
_____
_____
_____

2. What is time constant (τ)?

_____
_____
_____
_____

3. What is length constant (λ)?

_____
_____
_____

4. Draw a spread of depolarization down a nerve fiber by local currents.

5. Explain the terms: spatial summation, temporal summation.

_____
_____
_____
_____
_____
_____
_____

Teacher's signature _____

Exercise3. Activity 7: The Action Potential: Conduction Velocity

Objectives

1. To define and measure conduction velocity for an action potential.
2. To examine the effect of myelination on conduction velocity.

Introduction

To examine the effect of axon diameter on conduction velocity. Once generated, the action potential is propagated, or conducted, down the axon. In other words, all-or-none action potentials are regenerated along the entire length of the axon. This propagation ensures that the amplitude of the action potential does not diminish as it is conducted along the axon. In some cases, such as the sensory neuron traveling from your toe to the spinal cord, the axon can be quite long (in this case, up to 1 meter). Propagation/conduction occurs because there are voltage-gated sodium and potassium channels located along the axon and because the large depolarization that constitutes the action potential (once generated at the trigger zone) easily brings the next region of the axon to threshold. The conduction velocity can be easily calculated by knowing both the distance the action potential travels and the amount of time it takes. Velocity has the units of distance per time, typically meters/second. An experimental stimulus artifact (see Activity 3) provides a convenient marker of the stimulus time because it travels very quickly (for our purposes, instantaneously) along the axon.

Several parameters influence the conduction velocity in an axon, including the axon diameter and the amount of myelination. Myelination refers to a special wrapping of the membrane from glial cells (or neuroglia) around the axon. In the central nervous system, oligodendrocytes are the glia that wrap around the axon. In the peripheral nervous system, the Schwann cells are the glia that wrap around the axon. Many glial cells along the axon contribute a myelin sheath, and the myelin sheaths are separated by gaps called nodes of Ranvier. Introduction

In this activity you will compare the conduction velocities of three axons: (1) a large-diameter, heavily myelinated axon, often called an A fiber (the terms axon and fiber are synonymous), (2) a medium-diameter, lightly myelinated axon (called the Bfiber), and (3) a thin, unmyelinated fiber (called the C fiber). Examples of these axon types in the body include the axon of the sensory Pacinian corpuscle (an A fiber), a visceral sensory fiber (a Bfiber), and the axon of both the olfactory sensory neuron and a free nerve ending (C fibers).

Equipment Used:

- Nerve chamber
- Three axons—A fiber, Bfiber, and C fiber
- Oscilloscope—used to observe timing of stimuli and voltage changes in the axon
- Stimulator—used to set the stimulus voltage and to deliver pulses that depolarize the axon
- Stimulationwires (S)
- Recording electrodes (wires R1 and R2)—used to record voltage changes in the axon (The first set of recording electrodes, R1, is 2 centimeters from the stimulation wires, and the second set of recording electrodes, R2, is 2 centimeters from R1.)

Experiment Data:

Axon Type	Myelination	Stimulus Voltage (mV)	Distance From R1 to R2 (m)	Time Between APs (msec)	Time Between APs (sec)	Conduction Velocity (m/sec)
A fiber		30	0.1			
B fiber		30	0.1			
C fiber		30	0.1			

Review Sheet:

1. How did the conduction velocity in the B fiber compare with that in the A Fiber? How well did the results compare with your prediction?

2. How did the conduction velocity in the C fiber compare with that in the B Fiber? How well did the results compare with your prediction?

3. What is the effect of axon diameter on conduction velocity?

4. What is the effect of the amount of myelination on conduction velocity?

5. Why did the time between the stimulation and the action potential at R1 differ for each axon?

6. Why did you need to change the timescale on the oscilloscope for each axon?

Exercise 3. Activity 8: Chemical Synaptic Transmission and Neurotransmitter Release

Objectives

1. To define neurotransmitter, chemical synapse, synaptic vesicle, and postsynaptic potential,
2. To determine the role of calcium ions in neurotransmitter release.

Introduction

A major function of the nervous system is communication. The axon conducts the action potential from one place to another. Often, the axon has branches so that the action potential is conducted to several places at about the same time. At the end of each branch, there is a region called the axon terminal that is specialized to release packets of chemical neurotransmitters from small (~30 nm diameter) intracellular membrane-bound vesicles, called synaptic vesicles. Neurotransmitters are extracellular signal molecules that act on local targets as paracrine agents, on the neuron releasing the chemical as autocrine agents, and sometimes as hormones (endocrine agents) that reach their target(s) via the circulation. These chemicals are released by exocytosis and diffuse across a small extracellular space (called the synaptic gap, or synaptic cleft) to the target (most often the receiving end of another neuron or a muscle or gland). The neurotransmitter molecules often bind to membrane receptor proteins on the target, setting in motion a sequence of molecular events that can open or close membrane ion channels and cause the membrane potential in the target cell to change. This region where the neurotransmitter is released from one neuron and binds to a receptor on a target cell is called a chemical synapse, and

the change in membrane potential of the target is called a synaptic potential, or postsynaptic potential.

In this activity you will explore some of the steps in neurotransmitter release from the axon terminal. Exocytosis of synaptic vesicles is normally triggered by an increase in calcium ions in the axon terminal. The calcium enters from outside the cell through membrane calcium channels that are opened by the depolarization of the action potential. The axon terminal has been greatly magnified in this activity so that you can visualize the release of neurotransmitter. Different from the other activities in this exercise, however, this procedure of directly seeing neurotransmitter release is not easily done in the lab; rather, neurotransmitter is usually detected by the postsynaptic potentials it triggers or by collecting and analyzing chemicals at the synapse after robust stimulation of the neurons.

Equipment Used:

- Neuron (in vitro)—a large, dissociated (or cultured) neuron with magnified axon terminal
- Four extracellular solutions—control Ca^{2+}, no Ca^{2+}, low Ca^{2+}, and Mg^{2+}

Review Sheet:

1. When the stimulus intensity is increased, what changes: the number of synaptic vesicles released or the amount of neurotransmitter per vesicle?

_____
_____
_____
_____
__

2. What happened to the amount of neurotransmitter release when you switched from the control extracellular fluid to the extracellular fluid with no Ca^{2+} ? How well did the results compare with your prediction?

_____
_____
_____
_____
_____
__

3. What happened to the amount of neurotransmitter release when you switched from the extracellular fluid with no Ca^{2+} to the extracellular fluid with low Ca^{2+} ? How well did the results compare with your prediction?

_____
_____
_____
_____
_____
__

4. How did neurotransmitter release in the Mg^{2+} extracellular fluid compare to that in the control extracellular fluid? How well did the result compare with your prediction?

_____
_____
_____
_____
_____
__

5. How does Mg^{2+} block the effect of extracellular calcium on neurotransmitter release?

_____
_____
_____
_____
_____
__

Exercise 3. Activity 9: The Action Potential: Putting It All Together

Objectives

1. To identify the functional areas (for example, the sensory ending, axon, and postsynaptic membrane) of a two-neuron

circuit.

2. To predict and test the responses in each functional area to a very weak, subthreshold stimulus.
3. To predict and test the responses in each functional area to a moderate stimulus.

Introduction

To predict and test the responses in each functional area to an intense stimulus. In the nervous system, sensory neurons respond to adequate sensory stimuli, generating action potentials in the axon if the stimulus is strong enough to reach threshold (the action potential is an "all-or-nothing" event). Via chemical synapses, these sensory neurons communicate with interneurons that process the information. Interneurons also communicate with motor neurons that stimulate muscles and glands, again, usually via chemical synapses.

After performing Activities 1-8 you should have a better understanding of how neurons function by generating changes from their resting membrane potential. If threshold is reached, an action potential is generated and propagated. If the stimulus is more intense, then action potentials are generated at a higher frequency, causing the release of more neurotransmitter at the next synapse. At an excitatory synapse the chemical neurotransmitter binds to receptors at the receiving end of the next cell (usually the cell body or dendrites of an interneuron), causing ion channels to open, resulting in a depolarization toward threshold for an action potential in the interneuron's axon. This depolarizing synaptic potential (called an excitatory postsynaptic potential) is graded in amplitude, depending on the amount of neurotransmitter and the number of channels that open. In the axon, the amplitude of this synaptic potential is coded as the frequency of action potentials. Neurotransmitters can also cause inhibition, which will not be covered in this activity.

In this activity you will stimulate a sensory neuron, predict the response of that cell and its target, and then test those predictions.

Equipment Used:

- Sensory neuron (in vitro)—a large, dissociated (or cultured) neuron
- Interneuron (in vitro)—a large, dissociated (or cultured) interneuron
- Microelectrodes—small probes with very small tips that can impale a single neuron (In an actual wet lab, a microelectrode manipulator is used to position the microelectrodes. For simplicity, the microelectrode manipulator will not be depicted in this activity.)
- Hook electrodes—used to record extracellular voltage changes in the axon.
- Oscilloscope - used to observe the changes in voltage across the membrane of the neuron and interneuron
- Stimulator—used to set the stimulus intensity (low or high) and to deliver pulses to the neuron

Experiment Data:

Stimulus	Sensory Neuron Membrane Potential (mV) Receptor	Sensory Neuron AP Frequency (Hz) in Axon	Sensory Neuron Vesicles Released from Axon Terminal	Interneuron Membrane Potential (mV) Receiving End	Interneuron AP Frequency (Hz) in Axon
None					
Weak					
Moderate					
Strong					

Review Sheet:

1. Why is the resting membrane potential the same value in both the sensory neuron and the interneuron?

_____
_____
_____
_____
___

2. Describe what happened when you applied a very weak stimulus to the sensory receptor. How well did the results compare with your prediction?

_____
_____
_____
_____
_____
___

3. Describe what happened when you applied a moderate stimulus was to the sensory receptor. How well did the results compare with your prediction?

_____
_____
_____
_____
_____
___

4. Identify the type of membrane potential (graded receptor potential or action potential) that occurred at R1, R2, R3, and R4 when you applied a moderate stimulus (view Experiment Results to view the response to this stimulus).

_____
_____
_____
_____
_____
___

5. Describe what happened when you applied a strong stimulus to the sensory receptor. How well did the results compare with your prediction?

_____
_____
_____
_____
_____
___

Teacher's signature _____

Computer tests: SYNAPTIC AND NEUROMUSCULAR TRANSMISSION

1. A fatigue occurs first:
1. at synapse
2. in skeletal muscle
3. in the nerve trunk
4. in neuronal cells

2. A mediator in the neuromuscular junctions of skeletal muscles of man is:
1. acetylcholine
2. noradrenaline
3. GABA
4. adrenaline

3. The structural formations providing the transmission of excitation from one cell to another is called:
1. nerve
2. axonal hillock
3. synapse
4. Ranvier's nodes

4. What kind of the potential occurs on the postsynaptic membrane of the neuromuscular synapse?
1. inhibitory postsynaptic
2. actions
3. end plate potential (EPP)

5. What happens to the mediator released from the presynaptic terminals?
1. it diffuses through the postsynaptic membrane
2. it binds to the postsynaptic membrane receptors
3. it carries through the postsynaptic membrane by an active transport
4. it binds proteins of synaptic fluid
5. it accumulates in the synaptic cleft, thereby reducing the electrical resistance

6. What determines a value of the end-plate potential?
1. the intensity of the synthesis of acetylcholine in the motoneurons;
2. a number of receptors that unbound to acetylcholine
3. a concentration of calcium ions in the presynaptic terminal;
4. a concentration neurotransmitter in the synaptic cleft;
5. a number of cholinergic receptors bound to mediator

7. What ion current mainly generates the endplate potential?
1. calcium
2. chlorine
3. sodium
4. magnesium
5. all cations

8. What function does acetylcholinesterase have to do in the neuromuscular junction?
1. it increases a value of the end-plate potential
2. it increases duration of the end plate potential
3. it stimulates the synthesis of the mediator
4. it ensures the timely closing of ligand-gated channels
5. it splits the mediator bound to acetylcholine receptors

9. Which of the following is typical for generating of endplate potential?
1. it is formed by using ligand-gated channels
2. it is formed by using voltage-gated channels
3. it has an amplitude equal to the action potential
4. it is formed by the rule of "all or non response"
5. it has an duration equal to the action potential

10. What is the result of the effect of curare on the nerve-muscle synapse?
1. acetylcholinesterase is inactivated
2. the synthesis of acetylcholine is inhibited
3. the release of acetylcholine is blocked
4. cholinergic receptors are blocked
5. acetylcholine is split

11. What is a trigger for outflow of mediator from presynaptic terminal?
1. current of potassium ions into the presynaptic terminal

2. current of chlorine ions into the presynaptic terminal
3. current of calcium ions out of the presynaptic terminal
4. current of calcium ions into the presynaptic terminal
5. current of chlorine ions out of the presynaptic terminal

12. Which of ion channels may be involved in forming of IPSP?
1. sodium
2. potassium
3. calcium
4. magnesium
5. all of the above

13. Choose the way that mediator is released from the presynaptic terminal:
1. exocytosis
2. pinocytosis
3. by a specific carriers
4. diffusion
5. filtration

14. Which of the following mediators more often than others plays the role of inhibitory mediator:
1. acetylcholine
2. GABA
3. norepinephrine
4. dopamine
5. glutamate

15. What ion channels may be used in inhibitory synapses?
1. potassium
2. magnesium
3. sodium
4. calcium
5. all cations

16. Ligand-gated channels of the postsynaptic membrane during formation of the EPSP are permeable to:
1. sodium ions
2. potassium ions
3. potassium ions and sodium ions
4. sodium ions and calcium ions

17. What electric process leads to the formation of EPSP?
1. depolarization of the presynaptic membrane
2. hyperpolarization of the postsynaptic membrane
3. depolarization of the postsynaptic membrane
4. all the answers are correct

18. If enzyme system that splits mediators in the synaptic cleft is completely inactivated, efficiency of synaptic transmission will:
1. increase
2. not change
3. be equal to zero
4. all the answers are wrong

Computer tests: NERVE CELL PHYSIOLOGY
PROPAGATION OF ACTION POTENTIALS

1. The open site of the axon membrane with width of about 1 mm, where myelin sheath is interrupted, is called
1. axon terminal
2. node of Ranvier
3. presynaptic terminal
4. axonal hillock

2. What of the following structures perform isolate and trophic function in myelinated nerve fibers?
1. neurofibrils
2. myelin sheath
3. axon membrane
4. microtubule

3. How does the propagation of action potential along the unmyelinated nerve fibers spread?
?
1. saltatory, "jumping" across the fiber sections covered by myelin sheath
2. in the direction of axoplasm
3. continuously along the entire area of the membrane from the excited section to the adjacent unexcited one

4. How does the propagation of action potential along the myelinated nerve fibers spread?
1. continuously along the entire area of the membrane from the excited section to the adjacent unexcited one
2. in both directions from the place of formation
3. in the direction of axoplasm
4. saltatory, "jumping" across the fiber sections covered by myelin sheath

5. The fatigue comes first
1. in synapse
2. in skeletal muscle
3. in the nerve trunk
4. in neuronal cells

6. Velocity of conduction along nerves depends on:
1. diameter of nerve
2. presence or absence of the myelin sheath
3. all the answers are correct

7. What relationship is between the diameter of nerve fibers and the velocity of conduction:
1. direct
2. reverse
3. it does not exist

8. The signal transduction along the axon is directly provided by
1. stimulus;
2. neurotransmitter release;
3. presence of the myelin sheath
4. local electric current
5. absence of the myelin sheath;

9. The different sizes of the diameter of the axons are indicated by numbers 1-5. Which of them propagate the excitation faster?
1. 0.5 microns
2. 1 micron
3. 3 microns
4. 6 microns
5. 9 microns

10. What neurons are called afferent?
1. peripheral
2. somatic
3. vegetative
4. carrying the information to the working organ
5. carrying the information to the CNS

11. What part of a neuron contains the most number of synaptic contacts?
1. soma
2. axon
3. dendrites
4. perikaryonic
5. axonal hillock

12. What is the function of myelin?
1. envelopes neurons, providing them the mechanical protection
2. envelopes blood vessels, creating a blood-brain barrier
3. absorbs the excess of potassium ions and thereby acts as a buffer
4. is an electrical insulator for the axons
5. is a conductor of electrical signals

13. What neurons have one process?
1. pseudo unipolar neurons
2. bipolar neurons
3. multipolar neurons

14. Final branches of axons are called
1. terminals
2. collaterals

15. Laterals branches of axons are called

1. collaterals
2. terminals

16. Where does the action potential occur first?
1. dendrites
2. dendro-dendritic synapses
3. neuron soma
4. axonal hillock
5. all the answers are correct

17. Integrative activity of neuron consists in
1. the summation of postsynaptic potentials generating on the membrane of the neuron
2. generation of the resting potential
3. encoding and storage of information.
4. post-tetanic potentiation

18. What process provides the generation of action potential in the trigger zone of a neuron when rhythmic synaptic potentials occur on the postsynaptic membrane, which separately are not able to cause the generation of action potential
1. occlusion
2. convergence
3. spatial summation
4. temporal summation
5. multiplication

19. Which cells provide the myelin insulation of axons of the central nervous system?
1. all glial cells
2. microglia
3. oligodendrocytes
4. astrocytes

20. The phenomenon characterizing by the increase of EPSPs' amplitude during rhythmical occurrence of them is called
1. spatial summation
2. multiplication
3. occlusion
4. tetanic potentiation
5. post-tetanic potentiation

21. What is the property of excitatory postsynaptic potential?
1. spreading
2. summation
3. a local increase in excitability
4. graduality
5. all the answers are correct

22. What change of the resting potential can occur in the trigger zone of a neuron, if equidistant synapses generate EPSP and IPSP of equal amplitudes at the same time:
1. two-phase local response
2. resting potential will not change
3. hyperpolarisation
4. depolarization
5. posttetanic depolarization

23. What is the process that provides the excitation of neuron getting impulses coming from other neurons:
1. aftereffect
2. transformation of rhythm
3. spatial summation
4. temporal summation
5. occlusion

Lesson 6. Skeletal Muscle

Issues for consideration.

1. Muscle filaments. Structure of thick and thin filaments of skeletal muscle. Transverse Tubules and the Sarcoplasmic Reticulum
2. Excitation-contraction coupling in skeletal muscle. Temporal sequence of events in excitation-contraction coupling in skeletal muscle. Steps of excitation-contraction
3. Mechanism of tetanus. Length-tension relationship in skeletal muscle. Passive tension. Total tension. Active tension. Force-velocity relationship.

Home work (writing)

1. List the types of muscles and their basic physiological properties.

_____
_____
_____
_____

2. List the types of muscle contractions and define it.

_____
_____
_____
_____
_____

3. Draw a sarcomere and label its major parts

4. List the steps involved in excitation-contraction coupling in skeletal muscle

5. Define tetanus and draw its main types

6. Explain the mechanism of tetanus

7. Draw a graph Length-tension relationship in skeletal muscle

8. Define motor unit

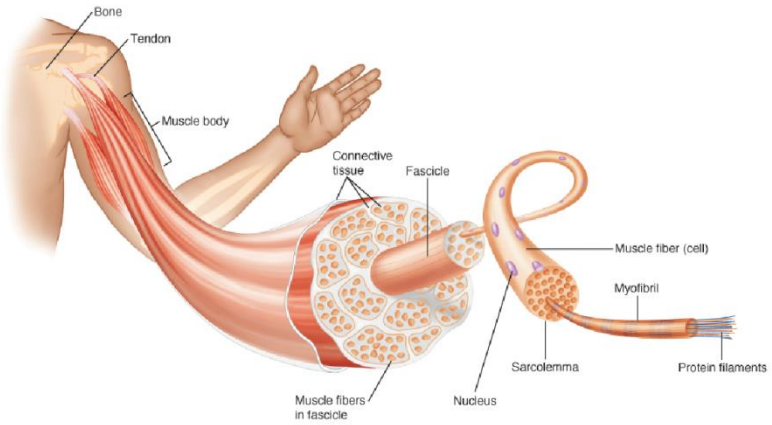
Teacher's signature _____

Exercise 2. Skeletal Muscle Physiology

Overview

Humans make voluntary decisions to walk, talk, stand up, and sit down. Skeletal muscles, which are usually attached to the skeleton, make these actions possible (view Figure 2.1).

Skeletal muscles characteristically span two joints and attach to the skeleton via **tendons,** which attach to the periosteum of a bone. Skeletal muscles are composed of hundreds to thousands of individual cells called **muscle fibers,** which produce **muscle tension** (also referred to as **muscle force).** Skeletal muscles are remarkable machines. They provide us with the manual dexterity to create magnificent works of art and can generate the brute force needed to lift a 45-kilogram sack of



concrete.

When a skeletal muscle is isolated from an experimental animal and mounted on a **force transducer,** you can generate **muscle contractions** with controlled **electrical stimulation.**

Importantly, the contractions of this isolated muscle are known to mimic those of working muscles in the body. That is, *in vitro* experiments reproduce *in vivo* functions. Therefore, the activities you perform in this exercise will give you valuable insight into skeletal muscle physiology.

Exercise 2. Activity 1:The muscle twitch and the latent period

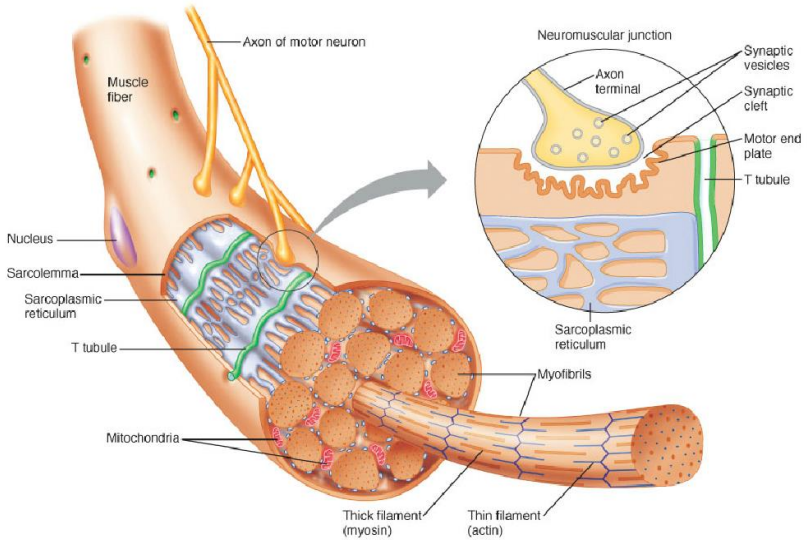
Objectives

1. To understand the terms excitation-contraction coupling, electrical stimulus, muscle twitch, latent period, contraction phase, and relaxation phase.
2. To initiate muscle twitches with electrical stimuli of varying intensity.
3. To identify and measure the duration of the latent period.

Introduction

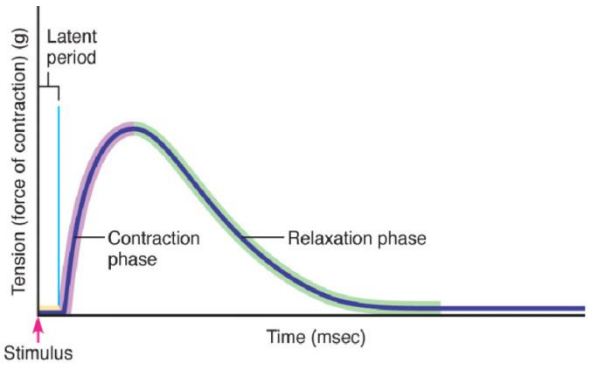
A motor unit consists of a **motor neuron** and all of the **muscle fibers** it innervates. The motor neuron and a muscle fiber intersect at the **neuromuscular junction** (view Figure 2.2).

Specifically, the neuromuscular junction is the location where the axon terminal of the neuron meets a specialized region of the muscle fiber's plasma membrane. This specialized region is called the **motor end plate.**



The events that occur at the neuromuscular junction lead to the **end-plate potential.** An action potential in a motor neuron triggers the release of acetylcholine from its terminal. Acetylcholine then diffuses onto the muscle fiber's plasma membrane (or **sarcolemma)** and binds to receptors in the motor end plate, initiating a change in ion permeability that results in a *graded depolarization* of the muscle plasma membrane (the end-plate potential). The end-plate potential triggers a series of events that results in the contraction of a muscle cell. This entire process is called **excitation-contraction coupling.**

You will be simulating excitation-contraction coupling in this and subsequent activities, but you will be using electrical pulses, rather than acetylcholine, to trigger action potentials. The pulses will be administered by an electrical stimulator that can be set for the precise voltage, frequency, and duration of shock desired. When applied to a muscle that has been surgically removed from an animal, a single electrical stimulus will result in a **muscle twitch –** the mechanical response to a single action potential. A muscle twitch has three phases: the latent period, the contraction phase, and the relaxation phase (view Figure 2.3).



1. The **latent period** is the period of time that elapses between the generation of an action potential in a muscle cell and the start of muscle contraction. Although no force is generated during the latent period, chemical changes (including the release of calcium from the sarcoplasmic reticulum) occur intracellularly in preparation for contraction.
2. The **contraction phase** starts at the end of the latent period and ends when muscle tension peaks.

3. The **relaxation phase** is the period of time from peak tension until the end of the muscle contraction

Equipment Used:

- Intact, viable skeletal muscle dissected off the leg of a frog.
- Electrical stimulator—delivers the desired amount and duration of stimulating voltage to the muscle via electrodes resting on the muscle.
- Mounting stand—includes a force transducer to measure the amount of force, or tension, developed by the muscle.
- Oscilloscope—displays the stimulated muscle twitch and the amount of active, passive, and total force developed by the muscle.

Experiment data:

Voltage	Length	Active force	Passive force	Total force	Latent period

Review sheet:

1. Define the terms skeletal muscle fiber, motor unit, skeletal muscle twitch, electrical stimulus, and latent period.

2. What is the role of acetylcholine in a skeletal muscle contraction?

3. Describe the process of excitation-contraction coupling in skeletal muscle fibers.

4. Describe the three phases of a skeletal muscle twitch.

5. Does the duration of the latent period change with different stimulus voltages? How well did the results compare

with your prediction?

Recall that, during the experiment, you were asked:

Will changes to the stimulus voltage alter the duration of the latent period?

_____

_____

_____

6. At the threshold stimulus, do sodium ions start to move into or out of the cell to bring about the membrane depolarization?

_____

_____

_____

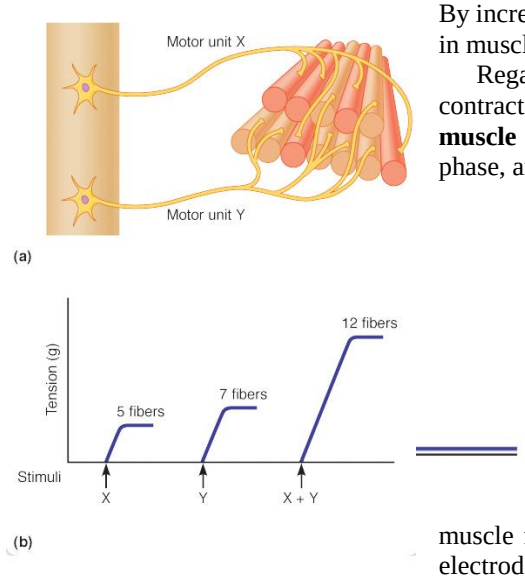
Exercise 2. Activity 2: The effect of stimulus voltage on skeletal muscle contraction

Objectives

1. To understand the terms motor neuron, muscle twitch, motor unit, recruitment, stimulus voltage, threshold stimulus, and maximal stimulus.
2. To understand how motor unit recruitment can increase the tension a whole muscle develops.
3. To identify a threshold stimulus voltage.
4. To observe the effect of increases in stimulus voltage on a whole muscle.
5. To understand how increasing stimulus voltage to an isolated muscle in an experiment mimics motor unit recruitment in the body.

Introduction

A skeletal muscle produces **tension** (also known as **muscle force)** when nervous or electrical stimulation is applied. The force generated by a whole muscle reflects the number of active **motor units** at a given moment. A strong muscle contraction implies that many motor units are activated, with each unit developing its maximal tension, or force. A weak muscle contraction implies that fewer motor units are activated, but each motor unit still develops its maximal tension. By increasing the number of active motor units, we can produce a steady increase in muscle force, a process called **motor unit recruitment** (view Figure 2.4).



Regardless of the number of **motor units** activated, a single stimulated contraction of whole skeletal muscle is called a **muscle twitch.** A tracing of a **muscle twitch** is divided into three phases: the latent period, the contraction phase, and the relaxation phase (view Figure 2.3).

The latent period is a short period between the time of muscle stimulation and the beginning of a muscle response. Although no force is generated during this interval, chemical changes occur intracellularly in preparation for contraction (including the release of calcium from the sarcoplasmic reticulum). During the contraction phase, the myofilaments utilize the cross-bridge cycle and the muscle develops tension. Relaxation takes place when the contraction has ended and the muscle returns to its normal resting state and length.

In this activity you will stimulate an isometric, or fixed-length, contraction of an isolated skeletal muscle. This activity allows you to investigate how the strength of an electrical stimulus affects whole-muscle function. Note that these simulations involve indirect stimulation by an electrode placed on the surface of the muscle. Indirect stimulation differs from the situation in vivo, where each fiber in the muscle receives direct stimulation via a nerve ending. Nevertheless, increasing the intensity of the electrical stimulation mimics how the nervous system increases the number of activated motor units.

The **threshold voltage** is the smallest stimulus required to induce an action potential in a muscle fiber's plasma membrane, or sarcolemma. As the **stimulus voltage** to a muscle is increased beyond the threshold voltage, the amount of force produced by the whole muscle also increases. This result occurs because, as more voltage is delivered to the whole muscle, more muscle fibers are activated and, thus, the total force produced by the muscle increases. Maximal tension in the whole muscle occurs when all the muscle fibers have been activated by a sufficiently strong stimulus (referred to as the **maximal voltage).** Stimulation with voltages greater than the maximal voltage will not increase the force of contraction. This experiment is analogous to, and accurately mimics, muscle activity *in vivo,* where the recruitment of additional motor units increases the total muscle force produced. This phenomenon is called *motor unit recruitment.*

Equipment Used:

- Intact, viable skeletal muscle dissected off the leg of a frog

Electrical stimulator—delivers the desired amount and duration of stimulating voltage to the muscle via electrodes

resting on the muscle

- Mounting stand—includes a force transducer to measure the amount of force, or tension, developed by the muscle
- Oscilloscope—displays the stimulated muscle twitch and the amount of active, passive, and total force developed by the muscle

Experiment data:

Voltage	Length	Active force	Passive force	Total force

Review sheet:

1. Describe the effect of increasing stimulus voltage on isolated skeletal muscle. Specifically, what happened to the muscle force generated with stronger electrical stimulations and why did this change occur? How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

As the stimulus voltage is increased from 1.0 volt up to 10 volts, what will happen to the amount of active force generated with each stimulus?

_____
_____
_____
_____

2. How is this change in whole-muscle force achieved *in vivo*?

_____
_____
_____
_____

3. What happened in the isolated skeletal muscle when the maximal voltage was applied?

_____
_____
_____

Exercise 2. Activity 3: The effect of stimulus frequency on skeletal muscle contraction

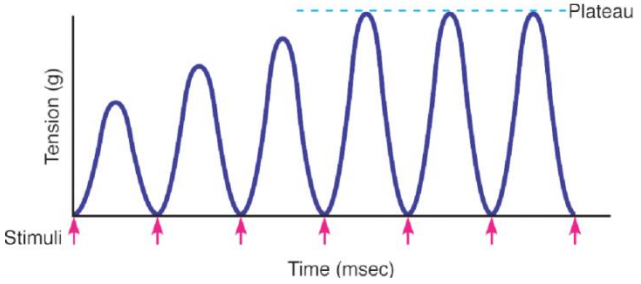
Objectives

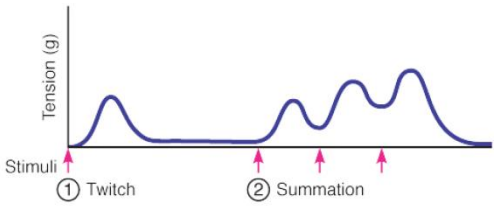
1. To understand the terms stimulus frequency, wave summation, and treppe.
2. To observe the effect of an increasing stimulus frequency on the force developed by an isolated skeletal muscle.
3. To understand how increasing stimulus frequency to an isolated skeletal muscle induces the summation of twitch force.

Introduction

As demonstrated in Activity 2, increasing the stimulus voltage to an isolated skeletal muscle (up to a maximal value) results in an increase of force produced by the whole muscle. This experimental result is analogous to motor unit recruitment in the body. Importantly, this result relies on being able to increase the single stimulus intensity in the experiment. You will now explore another way to increase the force produced by an isolated skeletal muscle.

When a muscle first contracts, the force it is able to produce is less than the force it is able to produce with subsequent stimulations within a relatively short time span. **Treppe** is the progressive increase in force generated when a muscle is stimulated in succession, such that muscle twitches follow one another closely, with each successive twitch peaking slightly higher than the one before (view Figure 2.5). This step-like increase in force is why treppe is also known as the staircase effect. For the first few twitches, each successive twitch produces slightly more force than the previous twitch as long as the muscle is allowed to fully relax between stimuli and the stimuli are delivered relatively close together.





When a skeletal muscle is stimulated repeatedly, such that the stimuli arrive one after another within a short period of time, muscle twitches can overlap with each other and result in a stronger muscle contraction than a stand-alone twitch (view Figure 2.6). This phenomenon is known as wave summation. **Wave summation** occurs when muscle fibers that are developing tension are stimulated again before the fibers have relaxed. Thus, wave summation is achieved by increasing the **stimulus frequency,** or rate of stimulus delivery to the muscle. Wave summation occurs because the muscle fibers are already in a partially contracted state when subsequent stimuli are delivered.

Equipment Used:

- An intact, viable skeletal muscle dissected off the leg of a frog
- An electrical stimulator—delivers the desired amount and duration of stimulating voltage to the muscle via electrodes resting on the muscle
- A mounting stand—includes a force transducer to measure the amount of force, or tension, developed by the muscle
- An oscilloscope—displays the stimulated muscle twitch and the amount of active, passive, and total force developed by the muscle.

Experiment data:

Voltage	Length	Stimulus	Active force	Passive force	Total force

Review sheet:

1. What is the difference between stimulus intensity and stimulus frequency?

_____

_____

2. In this experiment you observed the effect of stimulating the isolated skeletal muscle multiple times in a short

period with complete relaxation between the stimuli. Describe the force of contraction with each subsequent stimulus. Are these results called treppe or wave summation?

_____
_____
_____
_____
_____

3. How did the frequency of stimulation affect the amount of force generated by the isolated skeletal muscle when the frequency of stimulation was increased such that the muscle twitches did not fully relax between subsequent stimuli? Are these results called treppe or wave summation? How well did the results compare with your prediction? Recall that, during the experiment, you were asked: As the stimulus frequency increases, what will happen to the muscle force generated with each successive stimulus? Will there be a limit to this response?

_____
_____
_____
_____
_____
_____

4. To achieve an active force of 5.2g, did you have to increase the stimulus voltage above 8.5 volts? If not, how did you achieve an active force of 5.2g? How well did the results compare with your prediction? Recall that, during the experiment, you were asked:

In order to produce sustained muscle contractions with an active force value of 5.2 grams, do you think you will need to increase the stimulus voltage?

_____
_____
_____
_____
_____

5. Compare and contrast frequency-dependent wave summation with motor unit recruitment (previously observed by increasing the stimulus voltage). How are they similar? How was each achieved in the experiment? Explain how each is achieved *in vivo*

_____
_____
_____
_____
_____
_____

Teacher's signature: _____

Computer tests: PHYSIOLOGY OF SKELETAL MUSCLES

1. Which one of the following muscle proteins plays the important role in
contraction of both smooth and skeletal muscles?
1. calmodulin
2. troponin
3. tropomyosin
4. actin
5. myosin light chains

2. During the process of excitation-contraction coupling in skeletal muscle calcium is released from the sarcoplasmic reticulum by
1. inositol triphosphate (IP3)
2. protein kinase A
3. the increase in intracellular calcium concentration
4. membrane depolarization
5. the increase in intracellular sodium concentration

3. Which of the following words or phrases is most closely associated with the end-plate potential at the neuromuscular junction?
1. "all-or-none response"
2. depolarization
3. hyperpolarization
4. action potential
5. voltage-gated channels

4. Which of the following statements about synaptic transmission at the
neuromuscular junction is true?
1. it is enhanced by the high level of cholinesterase
2. it is caused by the influx of potassium ions through the muscle membrane
3. it is depressed by abnormally low levels of magnesium
4. it is depressed by increased parasympathetic nerve activity
5. it is produced by the release of acetylcholine from the alpha motoneuron

5. What ions release from the sarcoplasmic reticulum during excitation of membrane?
1. potassium
2. calcium
3. sodium
4. chlorine

5. magnesium

6. The amount of force produced by a skeletal muscle can be increased by
1. increasing extracellular Mg^{2+}
2. decreasing extracellular Ca^{2+}
3. increasing the activity of acetylcholine esterase
4. **decreasing the interval between contractions**
5. increasing the preload beyond 2.2 μm

7. A contraction of the muscle when both ends of it are fixed is called
1. isometric
2. aucsotonic
3. pessimal
4. isotonic

8. When skeletal muscle is at rest myosin heads are prevented from binding to actin filaments by
1. calmodulin
2. troponin and tropomyosin
3. tropomyosin
4. titin
5. phospholamban

9. A muscle contraction occurs during the stimulation by series of impulses, where the intervals between the impulses are longer than the duration of one muscle contraction is called
1. unfused tetanus
2. fused tetanus
3. pessimum tetanus
4. optimum tetanus
5. a single twitch

10. The muscle fibers innervated by the single motor neuron are called
1. motor area of muscle
2. touch-sensitive area of muscle
3. muscle nerve center
4. motor unit
5. receptor field muscles

11. Disconnection of myosin heads from actin filaments is caused by its binding to
1. calcium ions
2. sodium ions
3. ATP
4. Troponin
5. Tropomyosin

12. Initiation of muscle contraction is done by:
1. calcium ions
2. ATP
3. primary mediators
4. sodium ions

13. Muscle fibers of skeletal muscles are innervated by:
1. motor neurons of the spinal cord
2. neurons of the sympathetic system
3. neurons in the higher brain

14. What happens during the latent period of a single twitch of skeletal muscle:
1. propagation of AP down the sarcoplasm and sarcoplasmic reticulum
2. outflow of Ca^{2+} from T system of SPR
3. activation of a number of enzyme systems
4. all the answers are correct

15. Describe the main skeletal muscle function:
1. the movement of the body in space
2. ensure the discharge function of the heart
3. implementation of intestinal motility
4. all the answers are correct

16. What are the characteristics (physiological properties) of skeletal muscle:
1. excitability
2. conductivity
3. contractility
4. all the answers are correct

17. What is the isometric contraction?
1. increase of muscle tension without change of length
2. change of length without change of tension
3. change of tension and length

18. Which of the skeletal muscle protein may have the most ATP-ase activity
1. actin
2. myoglobin
3. hemoglobin
4. myosin
5. calmodulin

19. Which proteins of muscles involved in contraction:
1. actin
2. myosin
3. tropomyosin
4. troponin
5. all the answers are correct

20. What are the characteristics of isotonic contraction?
1. increase of muscle tension without change of length
2. change of length without increase of tension
3. change of tension and length

21. The ATP in muscle is used for...
1. Na^{+}-K^{+} - pump
2. cross bridge cycling between the actin and myosin
3. calcium pump
4. all of above

22. What causes muscle relaxation ?
1. outflow of Ca^{2+} from the sarcoplasmic reticulum
2. blocking of Na^{+}-K^{+} ATPase
3. active Ca^{2+} transport into the sarcoplasmic reticulum
4. formation of a cross bridge between the actin and myosin

23. A motor unit is
1. a group of fast-twitch muscle fibers
2. a group of fast and slow twitch muscle fibers
3. made up of a motor neuron and the skeletal muscle fibers innervated by that motor neuron's axonal terminals

24. In what case the amplitude of single twitch will be higher, if isolated muscle fiber is irritated by a threshold or a suprathreshold stimulus
1. amplitude is higher when suprathreshold stimulus are exposed
2. amplitude will be lower under the influence of the threshold stimulus
3. the amplitude is the same in both cases

25. What ions release from the sarcoplasmic reticulum during the excitation of membrane?
1. calcium
2. potassium
3. chlorine
4. sodium
5. all the answers are correct

26. The mediator of neuromuscular synapses is ...
1. adrenaline
2. acetylcholine
3. norepinephrine
4. gamma-aminobutyric acid (GABA)
5. all the answers are correct

27. When the inflow of calcium into the sarcoplasm is completely blocked the muscle contraction :
1. increases
2. does not change
3. is not performed
4. slightly reduced

Lesson 7. Smooth Muscle.

Issues for consideration.

1. Types of smooth muscle. Unitary smooth muscle. Multiunit smooth muscle
2. Excitation-contraction coupling in smooth muscle. Steps in excitation-contraction coupling in smooth muscle
3. Mechanisms that increase intracellular Ca^{2+} concentration in smooth muscle

Home work (writing)

1. List and describe the types of smooth muscle

2. List and describe the steps in excitation-contraction coupling in smooth muscle

3. List the mechanisms that increase intracellular Ca^{2+} concentration in smooth muscle

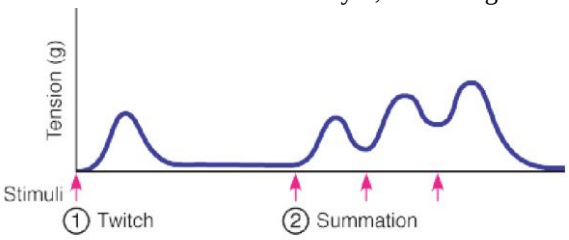
Exercise 2. Activity 4:Tetanus in isolated skeletal muscle

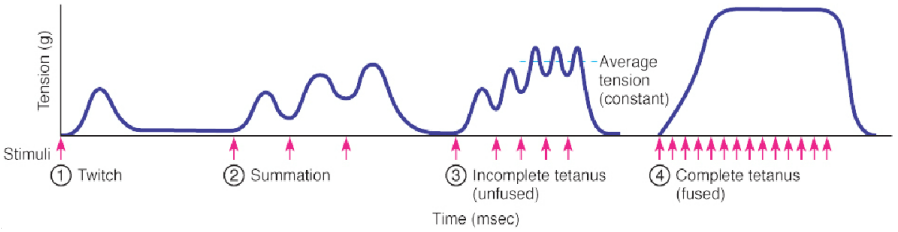
Objectives

1. To understand the terms stimulus frequency, unfused tetanus, fused tetanus, and maximal tetanic tension.
2. To observe the effect of an increasing stimulus frequency on an isolated skeletal muscle.
3. To understand how increasing the stimulus frequency to an isolated skeletal muscle leads to unfused or fused tetanus.

Introduction

As demonstrated in Activity 3, increasing the **stimulus frequency** to an isolated skeletal muscle results in an increase in force produced by the whole muscle. Specifically, you observed that, if electrical stimuli are applied to a skeletal muscle in quick succession, the overlapping twitches generated more force with each successive stimulus (view Figure 2.6). However, if stimuli continue to be applied frequently to a muscle over a prolonged period of time, the maximum possible muscle force from each stimulus will eventually reach a plateau—a state known as **unfused tetanus.** If stimuli are then applied with even greater frequency, the twitches will begin to fuse so that the peaks and valleys of each twitch become indistinguishable from one another—this state is known as **complete (fused) tetanus** (view Figure 2.7). When the stimulus frequency reaches a value beyond which no further increases in force are generated by the muscle, the muscle has reached its **maximal tetanic tension.**





Equipment Used:

- An intact, viable skeletal muscle dissected off the leg of a frog
- An electrical stimulator – delivers the desired amount and duration of stimulating voltage to the muscle via electrodes resting on the muscle
- A mounting stand – includes a force transducer to measure the amount of force, or tension, developed by the muscle
- An oscilloscope – displays the stimulated muscle twitch and the amount of active, passive, and total force developed by the muscle.

Experiment data:

Voltage	Length	Stimulus/sec	Active force	Passive force	Total force

Review sheet:

1. Describe how increasing the stimulus frequency affected the force developed by the isolated whole skeletal muscle in this activity. How well did the results compare with your prediction?

Recall that, during the experiment, you were asked:

As the stimulus frequency increases further, what will happen to the muscle tension and twitch appearance with each successive stimulus? Will there be a limit to this response?

_____

_____

_____
_____
_____
_____

2. Indicate what type of force was developed by the isolated skeletal muscle in this activity at the following stimulus frequencies: at 50 stimuli/sec, at 140 stimuli/sec, and above 146 stimuli/sec.

_____
_____
_____
_____

3. Beyond what stimulus frequency is there no further increase in the peak force? What is the muscle tension called at this frequency?

_____
_____
_____
_____

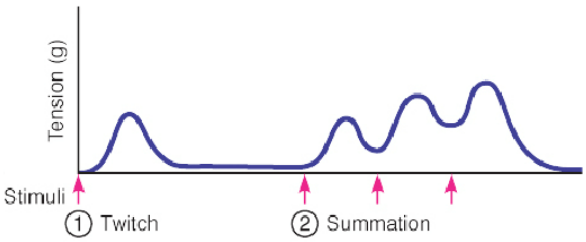
Exercise 2. Activity 5: Fatigue in Isolated Skeletal Muscle

Objectives

1. To understand the terms stimulus frequency, complete (fused) tetanus, fatigue, and rest period.
2. To observe the development of skeletal muscle fatigue.
3. To understand how the length of intervening rest periods determines the onset of fatigue.

Introduction

As demonstrated in Activities 3 and 4, increasing the stimulus frequency to an isolated skeletal muscle induces an increase of force produced by the whole muscle. Specifically, if voltage stimuli are applied to a muscle frequently in quick succession, the skeletal muscle generates more force with each successive stimulus (view Figure 2.6).

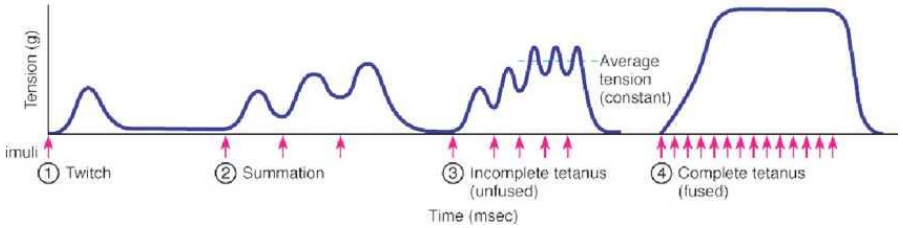


However, if stimuli continue to be applied frequently to a muscle over a prolonged period of time, the maximum force of each twitch eventually reaches a plateau—a state known as *unfused tetanus.* If stimuli are then applied with even greater frequency, the twitches begin to fuse so that the peaks and valleys of each twitch become indistinguishable from one another—this state is known as **complete (fused) tetanus** (view Figure 2.7). When the **stimulus frequency** reaches a value beyond which no further increase in force is generated by the muscle, the muscle has reached its **maximal tetanic tension.**

In this activity you will observe the phenomena of skeletal muscle fatigue. Fatigue refers to a decline in a skeletal muscle's ability to maintain a constant level of force or tension after prolonged, repetitive stimulation (view Figure 2.8).

You will also demonstrate how intervening **rest periods** alter the onset of fatigue in skeletal muscle. The causes of fatigue are still being investigated and multiple molecular events are thought to be involved, though the accumulations of lactic acid, ADP, and Pi in muscles are thought to be the major factors causing.

Common definitions for **fatigue** are:



- the failure of a muscle fiber to produce tension because of previous contractile activity.
- a decline in the muscle's ability to maintain a constant force of contraction after prolonged repetitive stimulation.

Equipment Used:

- An intact, viable skeletal muscle dissected off the leg of a frog
- An electrical stimulator—delivers the desired amount and duration of stimulating voltage to the muscle via electrodes resting on the muscle

•A mounting stand—includes a force transducer to measure the amount of force, or tension, developed by the muscle

• An oscilloscope—displays the stimulated muscle twitch and the amount of active, passive, and total force developed by the muscle

Voltage	Stimuli/sec	Rest Period (sec)	Active Force (g)	Sustained Maximal Force
8.5	**120**			
8.5	**120**			
8.5	**120**			
8.5	**120**			

Review Sheet:

1. When a skeletal muscle fatigues, what happens to the contractile force over time?

_____
_____
_____
_____
_

2. What are some proposed causes of skeletal muscle fatigue?

_____
_____
_____
_____
__

3. Turning the stimulator off allows a small measure of muscle recovery. Thus, the muscle will produce more force for a longer time period if the stimulator is briefly turned off than if the stimuli were allowed to continue without interruption. Explain why this might occur. How well did the results compare with your prediction?

_____
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4. List a few ways that humans could delay the onset of fatigue when they are vigorously using their skeletal muscles.

_____
_____
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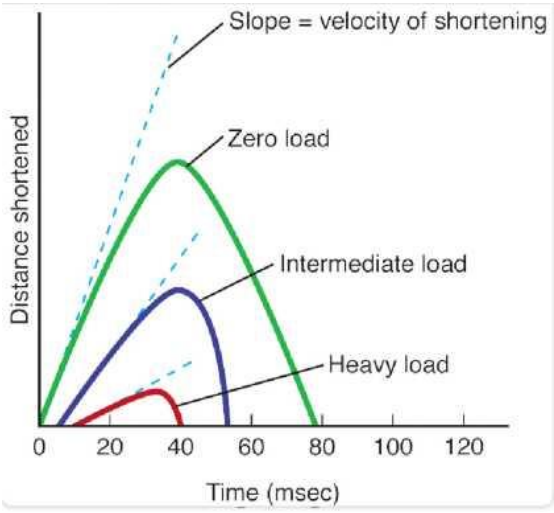
Exercise 2. Activity 7: Isotonic Contractions and the Load-Velocity Relationship

Objectives:

1. To understand the terms isotonic concentric contraction, load, latent period, shortening velocity, and load-velocity relationship.
2. To understand the effect that increasing load (that is, weight) has on an isolated skeletal muscle when the muscle is stimulated in an isotonic contraction experiment.
3. To understand the load-velocity relationship in isolated skeletal muscle

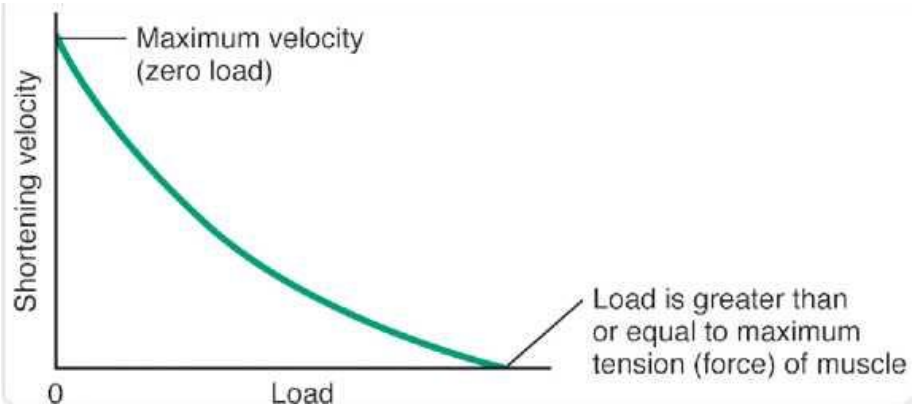
Introduction

Skeletal muscle contractions can be described as either isometric or isotonic. When a muscle attempts to move an object (the **load)** that is equal in weight to the force generated by the muscle, the muscle is observed to contract isometrically. In an isometric contraction, the muscle stays at a fixed length (isometric means same length).



During an **isotonic contraction,** the skeletal muscle length changes and, thus, the load moves a measurable distance. If the muscle length shortens as the load moves, the contraction is called an **isotonic** *concentric* **contraction.** An isotonic concentric contraction occurs when a muscle generates a force greater than the load attached to the muscle's end. In this type of contraction, there is a **latent period** during which there is a rise in muscle tension but no observable movement of the weight. After the muscle tension exceeds the weight of the load, an isotonic concentric contraction can begin. Thus, the latent period gets longer as the weight of the load gets larger. When the building muscle force exceeds the load, the muscle shortens and the weight moves (view Figure 2.10). Eventually, the force of the muscle contraction will decrease as the muscle twitch begins the relaxation phase, and the load will therefore start to return to its original position.

An isotonic twitch is not an all-or-nothing event. If the load is increased, the muscle must generate more force to move it and the latent period will therefore get longer because it will take more time for the necessary force to be generated by the muscle. The speed of the contraction (muscle **shortening velocity)** also depends on the load that the muscle is attempting to move (view Figure 2.11). Maximal shortening velocity is attained with minimal load attached to the muscle. Conversely, the heavier the load, the slower the muscle twitch. You can think of lifting an object from the floor as an example. A light object can be lifted quickly (high velocity), whereas a heavier object will be lifted with a slower velocity for a shorter duration.



In an isotonic muscle contraction experiment, one end of the muscle remains free (unlike in an isometric contraction experiment, where both ends of the muscle are held in a fixed position). Different weights (loads) can then be attached to the free end of the isolated muscle, while the other end is held in a fixed position by the force transducer. If the weight (the load) is less than the tension generated by the whole muscle, then the muscle will be able to lift it with a measurable distance, velocity, and duration (view Figure 2.10). In this activity, you will change the weight (load) that the muscle will try to move as it shortens.

Equipment Used:

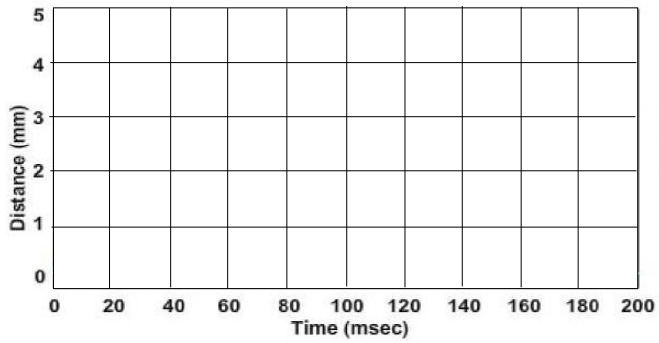
- An intact, viable skeletal muscle dissected off the leg of a frog
- An electrical stimulator—delivers the desired amount and duration of stimulating voltage to the muscle via electrodes resting on the muscle
- Several weights (in grams)—can be interchangeably attached to the hook on the free lower tendon of the mounted skeletal muscle
- An oscilloscope—displays the stimulated isotonic concentric contraction, the duration of the contraction, and the distance that muscle lifts the weight (load)A mounting stand – includes a ruler that allows a rapid measurement of the distance (cm) that the weight (load) is lifted by the isolated muscle

Experiment Data:

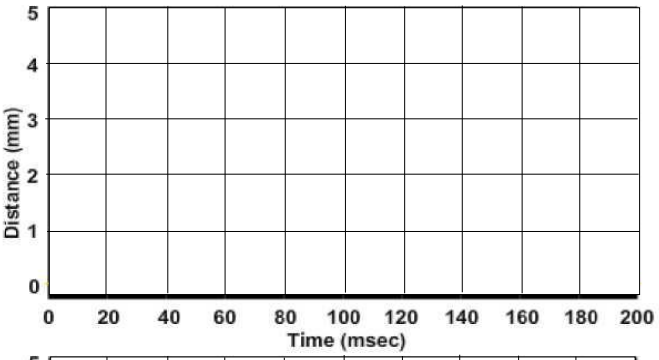
Voltage	Length	Weight	Velocity (mm/msec)	Twitch Duration (msec)	Distance Lifted (mm)
8.5	75	0.5			

8.5	75	1.0			
8.5	75	1.5			
8.5	75	2.0			

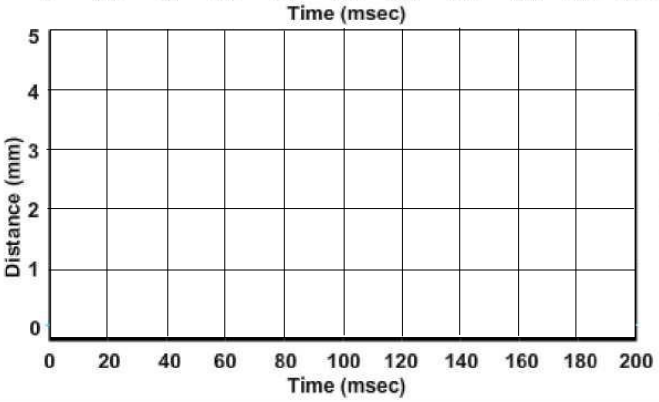
Draw a graph of muscle contractions



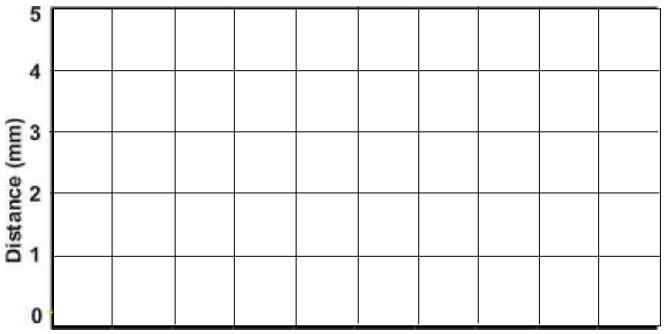
weight = 0.5 g
duration of twitch = 78.00 msec
velocity = 0.100 mm/msec
distance lifted = 4.0 mm



weight = 1.0 g
duration of twitch = 49.00 msec
velocity = 0.057 mm/msec
distance lifted = 2.0 mm



weight = 1.5 g
duration of twitch = 30.00 msec
velocity = 0.022 mm/msec
distance lifted = 0.5 mm



weigt= 2.0 g
duration of twitch = 0.00 msec
velocity = 0.000 mm/msec
distance lifted = 0.0 mm

1. If you were using your bicep muscles to curl a 7-kg dumbbell, when would your muscles be contracting isotonically?

_____

_____

_____

_____

___

2. Explain why the latent period became longer as the load became heavier in the experiment. How well did the results compare with your prediction?

_____
_____
_____
_____

___

3. Explain why the shortening velocity became slower as the load became heavier in this experiment. How well did the results compare with your prediction?

_____
_____
_____
_____

___

4. Describe how the shortening distance changed as the load became heavier in this experiment. How well did the results compare with your prediction?

_____
_____
_____
_____

_____

5. Explain why it would take you longer to perform 10 repetitions lifting a 10-kg weight than it would to perform the same number of repetitions with a 5-kg weight.

_____
_____
_____
_____

_____

6. Describe what would happen in the following experiment: A 2.5-g weight is attached to the end of the isolated whole skeletal muscle used in these experiments. Simultaneously, the muscle is maximally stimulated by 8.5 volts *and* the platform supporting the weight is removed. Will the muscle generate force? Will the muscle change length? What is the name for this type of contraction?

_____
_____
_____
_____

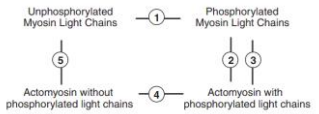
Teacher's signature _____

Computer tests: PHYSIOLOGY OF SMOOTH MUSCLE

1. Excitation-contraction coupling in smooth muscle is initiated when calcium binds to
1. myosin light chains
2. calmodulin
3. troponin
4. tropomyosin
5. protein kinase A

2. Which one of the following enzymes is responsible for step 1 in the diagram?
1. calmodulin
2. protein kinase A
3. myosin light chain kinase
4. phospholipase C
5. actomyosin ATPase

3. When comparing the contractile responses in smooth and skeletal muscle, which of the following is most different?
1. the source of activator calcium
2. the role of calcium in initiating contraction
3. the mechanism of force generation



4. the source of energy used during contraction
5. the nature of the contractile proteins

4. Property of smooth muscle that skeletal muscle doesn't have is called
1. excitability
2. conductivity
3. contractility
4. automaticity

5. Which is characteristic of skeletal muscle VS smooth one:
1. rapid contraction and relaxation
2. slow contraction and relaxation
3. little spending of energy
4. automaticity

6. Which is characteristic of smooth muscle cells:
1. slow contraction and relaxation

2. automaticity
3. low spending of energy
4. high plasticity
5. all the answers are correct

7. Thick myofilaments are made mostly of:
1. actin
2. troponin
3. myosin
4. tropomyosin
5. myoglobin

8. Calmodulin is found in:
1. smooth
2. cardiac
3. skeletal

9. The autonomic nervous system stimulates _____ muscle:
1. smooth
2. cardiac
3. skeletal
4. smooth and cardiac

5. none of them

10. Which of muscle types is stimulated by hormones, neurons and self-excitation?
1. cardiac
2. smooth
3. skeletal

11. Alpha motor neurons stimulate _____ muscle:
1. skeletal
2. smooth
3. cardiac

12. Sarcomeres are lacking in _____ muscle:
1. smooth
2. skeletal
3. cardiac

13. Actin, myosin and cross-bridges operate in:
1. smooth muscle
2. cardiac muscle
3. skeletal muscle
4. all of them

Lesson 8. Exam on the Cellular Physiology

Stages:
1.PC testing (50 questions)
2. Written work (10 questions)
the minimum passing result is 70% for the PC test and 70% for the written work