Introduction to Biopotentials and the BioRadio

Introduction

The human body is beautifully complex consisting of mechanical, electrical, and chemical systems that allow us to live and function. An example of a mechanical system in the body is the actin and myosin filaments found in muscles that allow them to contract. Chemical systems include the neurotransmitters that are released by neurons for communication with other cells. Finally, electrical systems include the electrical potentials that propagate down nerve cells and muscle fibers. These potentials are responsible for brain function, muscle movement, cardiac function, eye movement, sensory function, and many other events in the body (Fig 1). These electrical potentials are created by the flow of ions in and out of cells. The flow of these charged ions creates potential differences between the inside and outside of cells. These potential differences are called biopotentials. Biopotentials can be measured with electrodes and electronic instrumentation to provide insight into the functioning of various biological systems.
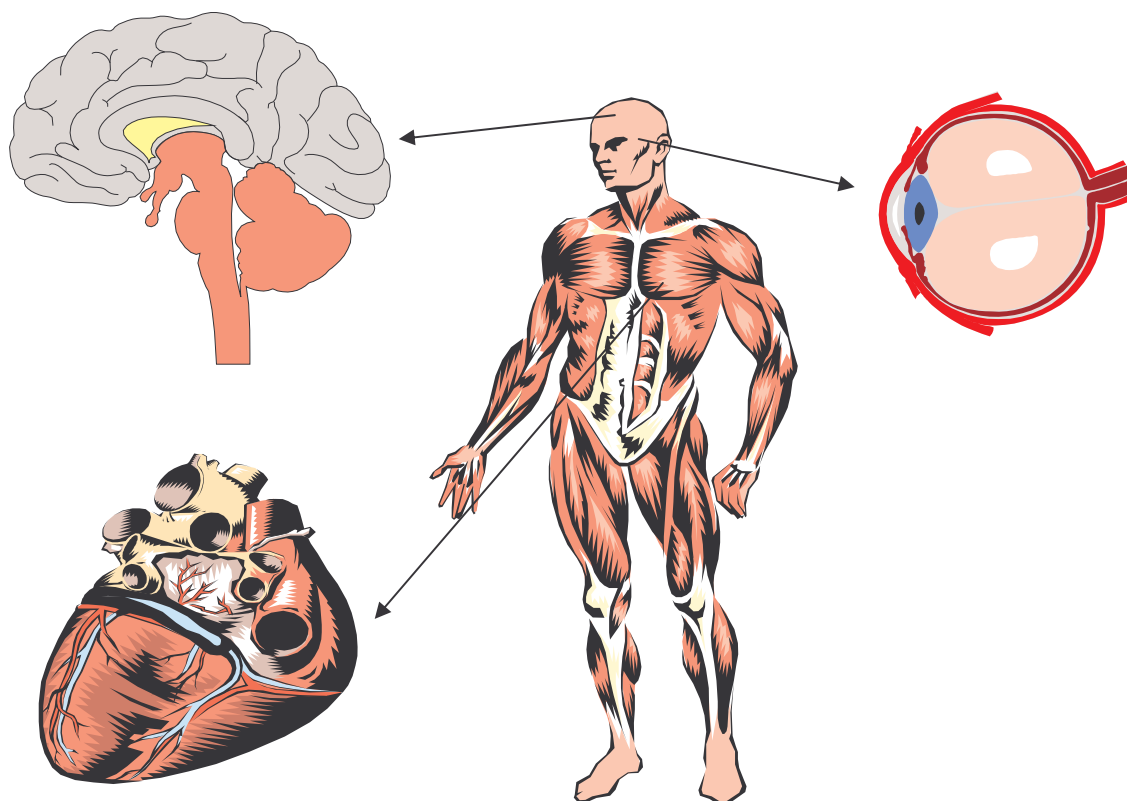

Figure 1: The body produces many different types of biopotentials. Sources of this potential include skeletal muscle, the brain, the heart, and the eye. Each of these organs produce electrical activity that can be recorded on the surface of the skin.

Background

Human Biopotentials

A typical nerve cell is made up of a cell body, an axon, and dendrites (Fig 2A). The cell body contains the nucleus or command center of the cell, the axon, which is responsible for transmitting the action potential along the cell, and the dendrites, which are responsible for receiving inputs to the cell in the form of neurotransmitters. Nerve and muscle cells in the body communicate with each other via action potentials. Action potentials are voltage impulses that propagate along a nerve or muscle and may cause neurotransmitter release when the action potential reaches a specific area of the nerve cell. A typical action potential recorded from a muscle is shown in Fig 2B. These voltage impulses arise from tiny currents in the nerve or muscle cells. These currents are a result of charged ions flowing in and out of voltage-gated channels in the membrane of the cells. Kirchoff's Law from basic circuits tells us that V=IR, where V is a measured voltage, I is a current, and R is a resistance. The cell membrane has a specific resistance. Therefore, the ionic currents flowing across the membrane of the cell create a voltage, i.e., a biopotential.
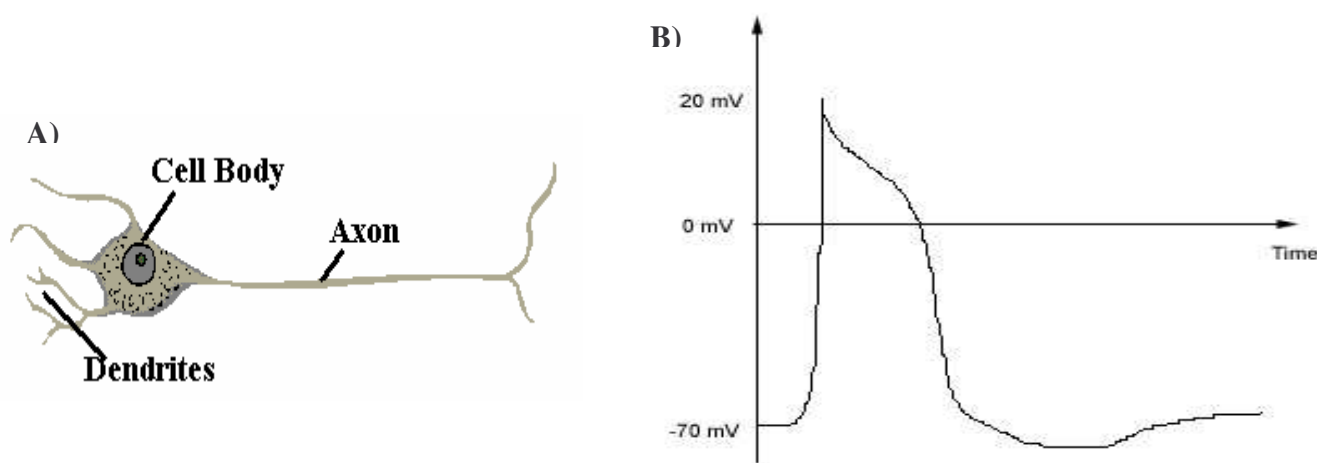

Figure 2: A) A typical nerve cell. B) A typical muscle action potential, with resting potential at -70 mV.

The membrane of a cell is a layer of lipids. The lipid membrane separates the inner structures of the cell from the rest of the body. There are specific concentrations of ions inside and outside of the cell including sodium (Na+), potassium (K+), and chloride (Cl-). These ions are either positively or negatively charged. Therefore, a separation of charge exists across a cell membrane. The standard convention used in neurology is that the potential of the cell is the relative potential inside the cell with respect to the outside of the cell. All along the cell membrane there are openings or channels made of proteins. These channels allow ions to flow in and out of the cell. Each channel is specific to a specific ion. For example, there are sodium ion channels, potassium ion channels, etc. There are two types of channels that transverse the

cell membrane, resting channels and gated channels. Resting channels are open all of the time and, along with active ion pumps, are responsible for maintaining the resting membrane potential of a cell. The gated channels will be discussed later in this laboratory.

Two major forces determine how ions will flow in and out of a cell at rest. One is a chemical force and the other is an electrical force. When a cell is at rest there is a high concentration of sodium outside of the cell and a low concentration of sodium inside the cell (Fig 3). On the other hand, there is a high concentration of potassium inside the cell and a low concentration outside of the cell. Therefore, a chemical concentration gradient exists for each ion. For example, consider the potassium ion. Since there is a high concentration inside the cell and a low concentration outside, the potassium ions inside the cell begin to move through the resting potassium channels to the outside of the cell. These ions are positively charged. Therefore, as they move out of the cell, the outside of the cell becomes more positive than the inside and a potential difference develops across the cell membrane. This separation of charge across the membrane creates the second major force involved in the resting potential, the electrical force. When this electrical force is equal to the chemical force of the concentration gradient, a steady state potential will be reached. However, sodium is also important in the nerve cell. The same process occurs with sodium as with potassium. Sodium ions flow into the cell due to the concentration gradient. The flow of positively charged sodium flowing into the cell balances the flow of positively charged potassium out of the cell and a steady state potential is maintained.
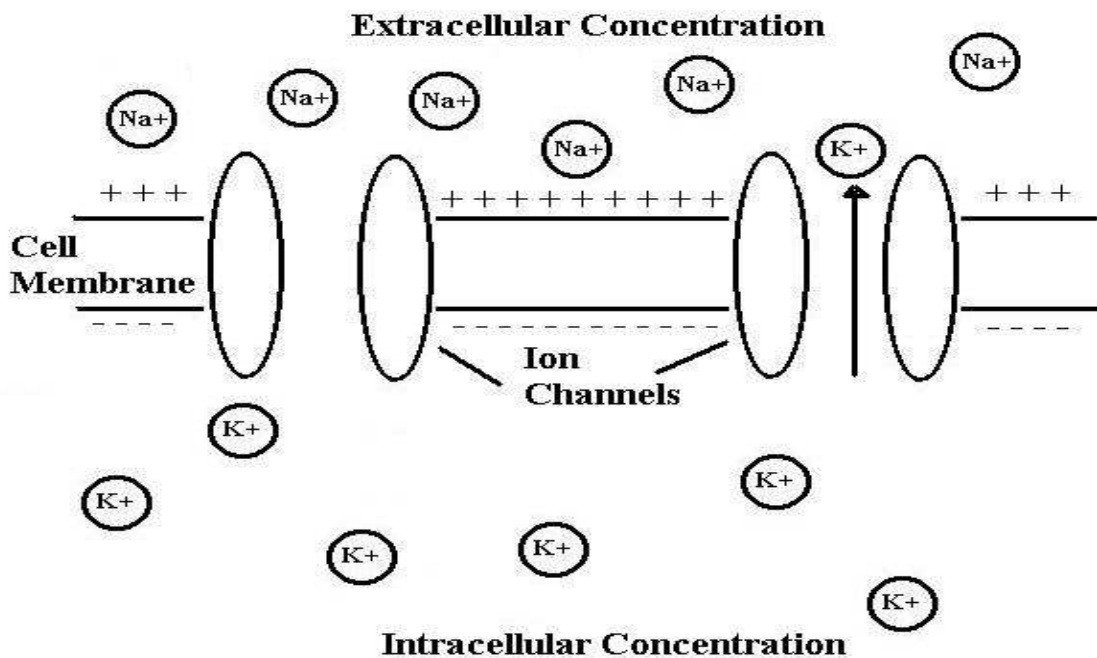

Figure 3: The resting potential of a cell is determined by the resting ion channels, the concentration of ions inside and outside of a cell, and the potential difference across the cell membrane. The concentration gradient causes positively charged potassium to flow out of the cell and causes the outside of the cell to become more positive.

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The potential that is created is governed by Nernst's equation. Nernst's equation describes the relationship between the concentration of an ion outside and inside of a cell and the cellular potential (V). Nernst's equation is:

$$V = \frac{RT}{zF} \ln \frac{[X_{ext}]}{[X_{int}]}$$

Where R is the gas constant, T is temperature in Kelvin, F is Faraday's constant, z is the valence of the ion, and [X] is the ionic concentration, externally and internally.

In addition to the passive process described above, there is an active process that occurs in the cell to maintain its steady state potential. If the passive process were allowed to continue with no intervention, the ionic concentrations would begin to dissipate, i.e. most of the potassium would eventually flow out of the cell and a large amount of sodium would flow into the cell. Therefore, a sodium-potassium pump also exists in the cell. This pump acts to force sodium and potassium ions against their concentration gradients and hence maintain proper concentration of ions in the cell without disturbing the steady state resting potential. A cell at rest is therefore not really at rest, but the potential difference across the membrane is in a steady state condition.

The cell membrane is not always at rest. During the action potential, the membrane of a cell is very active. Voltage-gated channels begin to open and allow large fluxes of ions in and out of the cell. This causes a large change in the potential difference across the membrane of the cell. An action potential can occur when dendrites receive neurotransmitters from another cell. These neurotransmitters cause voltage-gated channels to open and ions to start flowing. If the neurotransmitter release was strong enough, an action potential can result. The following will explain voltage gated ion channels and how the action potential arises.

In the early 1950's, two scientists from Britain, Alan Hodgkin and Andrew Huxley discovered how the action potential was generated using a giant squid axon and later received the Nobel Prize for their work. This giant squid axon is a very large nerve cell that they manipulated using a voltage clamp instrument. A voltage clamp instrument uses feedback circuitry to fix the potential of a cell or neuron at a desired potential. As stated earlier, the membrane of nerve cells also contains voltage gated ion channels. As the potential of the inside of the cell changes with respect to the outside of the cell, it causes these gates to open and ions to flow. As ions flow in and out, it further depolarizes the cell and causes more gates to open. This in turn causes a greater change in potential and even more channels to open. As you can see, this process would keep occurring until all the possible channels were opened. However, since the voltage clamp instrument uses feedback circuitry to apply sufficient current in the opposite polarity, the voltage on the cell does not change and is therefore "clamped". Researchers determined the membrane ionic current through ion channels at specific potentials by measuring the amount of current required by the voltage clamp to maintain the cell at a specific potential.

Hodgkin and Huxley concluded that the depolarization (the inside of the cell becoming more positive with respect to the outside) associated with the action potential was related to the

permeability of Na+ and the repolarization (the inside of the cell returning to its original potential with respect to the outside of the cell) with the permeability of K+. To test this, Hodgkin and Huxley used the voltage clamp to create various step potentials and measured the current of the various ionic channels through the cell membrane. In order to record one specific type of ion channel (either K+ or Na+), drugs were used to block the other channels.

Hodgkin and Huxley discovered that sodium channels created a sharp inward current during the beginning action potential while later in the action potential, potassium channels created a current that flowed out of the cell. At the start of the action potential the voltage-gated sodium channels quickly open and sodium ions flow into the cell. These ions are positively charged, therefore, the inside of the cell becomes more positive. Since the potential increases, more sodium channels open and the cell is further depolarized. This cycle continues until the peak of the action potential is reached. At this point, the slower potassium channels open, allowing positively charged potassium ions to flow back out to the extracellular solution, causing the repolarization of the cell. The currents and conductances of sodium and potassium can be seen in Fig 4 as a function of a step change in the membrane potential.
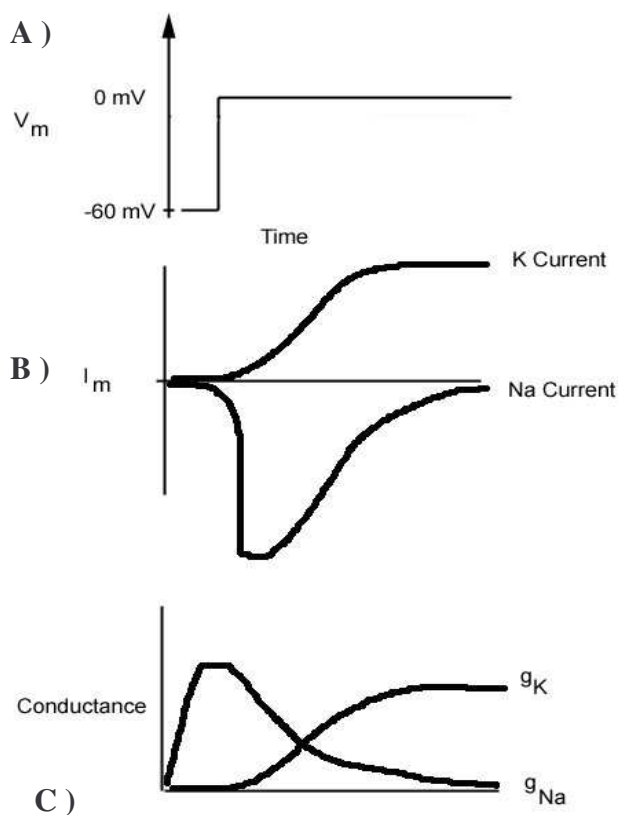

Figure 4: A) A step change in membrane potential to depolarize the cell will cause ions to flow in and out of the cell. B) As a result of the change in potential, first the sodium channels open, creating a sharp inward Na+ current to the cell. The potassium gates open much more slowly, therefore, after the Na+ current has reached its peak, the K+ gates open and potassium begins to flow out of the cell. C) The currents that are produced are a result of the conductance of the cell to the two ions.

Another way to understand the membrane voltage and ionic current from the action potential is to look at an equivalent circuit of a nerve cell (Fig 5). Part of the cell membrane can be modeled as a capacitor since it separates charges on the inside and outside of the cell. At the same time, there are gates in the membrane that control the conductance of various ions. This conductance can be directly translated to resistance, since conductance is simply the inverse of resistance. So, the cell membrane is modeled as a resistor and capacitor in parallel. In addition, the cytoplasm inside the cell represents another source of resistance. The extracellular fluids and tissues present a finite resistance to the flow of action currents, creating the extracellular potential gradients that form the basis of most electrophysiological methods. However for most models, the outside of the membrane is usually represented as a shorted wire. Researchers have used this model to better understand how an action potential propagates down a nerve cell.
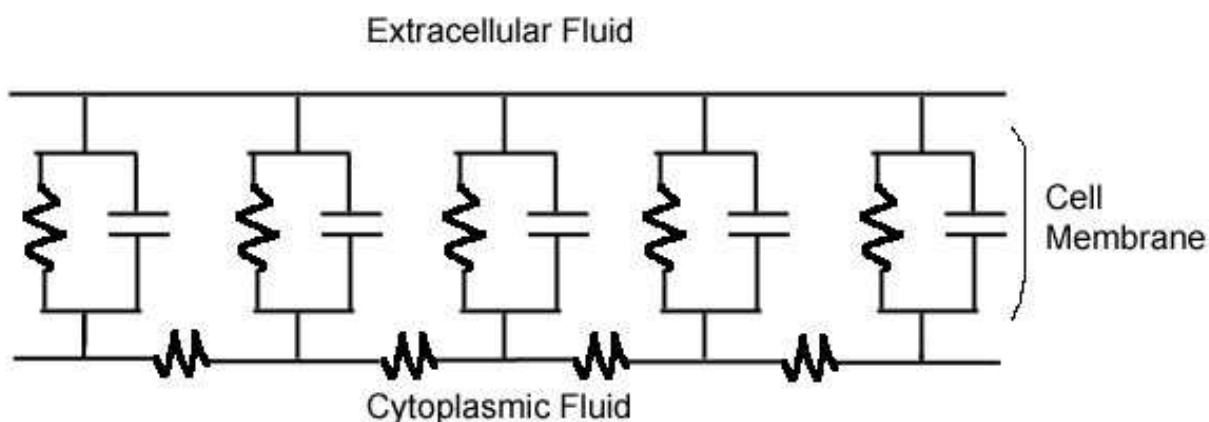

Figure 5: Equivalent Circuit Model for the Cell.

Examples of Biopotentials

In order to measure the potentials from a single cell, invasive recording instruments are necessary. For the purposes of the laboratories in this lab book we will be measuring electrical potentials on the surface of the skin. Electrical potentials measured on the skin are not the result of a single cell, but are the combination of a large number of cells firing together. These cells may be firing synchronously or asynchronously.

There are many different sources of biopotentials. One of the most popular electrophysiological measurements is the electrocardiogram (ECG) (Fig 6). As the heart pumps blood, different chambers of cardiac muscle are activated in a specific order. The ECG waveform represents the rhythmical depolarization and repolarization of each chamber of the heart. The ECG can be used to determine whether the heart is functioning properly or if conduction problems exist.
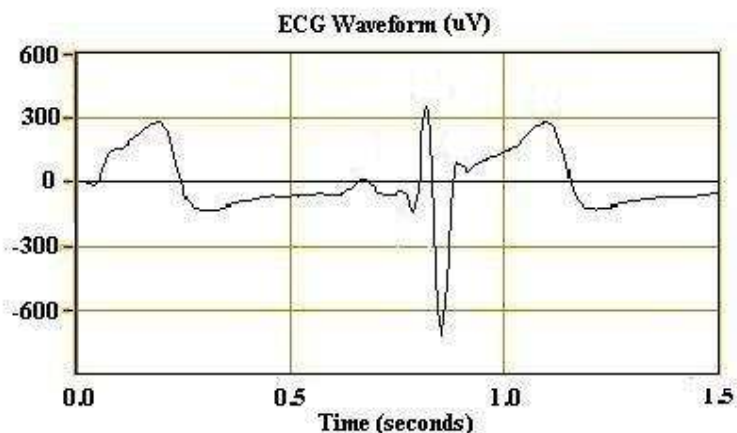
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Figure 6: Typical ECG recording illustrating the beating of the heart.

Another source of human biopotentials is the electroencephalogram (EEG). EEG signals measure the electrical activity of neurons in the brain. Surface EEG from the scalp is extremely low voltage, ranging from 5 - 200 microvolts. Unlike the ECG signal, EEG recordings do not have a discernable pattern during normal waking activity. The EEG can be used to detect states of sleep and awareness. It can also be used to detect neurological disorders such as epilepsy. Shown below in Table 1 are the typical rhythms monitored by an EEG.

Common EEG Activity		
Alpha Rhythm	8 - 13 Hz	Quiet Resting Activity, eyes closed
Beta Rhythm	13 - 22 Hz	Awake, Attentive state
Delta Rhythm	0.5 - 4 Hz	Stressful activity or some brain disorders
Theta Rhythm	4 - 8 Hz	Deep Sleep, brain disorders

Table 1: Common frequencies found in EEG recordings and their associated conditions.

Electromyograms (EMG) are recordings of skeletal muscle potential. Just as the nerves that innervate them, skeletal muscle tissue carries action potentials. The EMG signal can be on the order of millivolts. EMG measurements are an indicator of muscle force. The amplitude of the recording is related to the amount of force generated from the muscle contraction. EMG potentials can be used to diagnose muscle disorders and also have applications in sports medicine, where muscle potentials could be recorded and analyzed to help increase an athlete's performance.

Biopotentials can also be recorded from the eye. One popular biopotential recorded from the eye is the electro-oculogram (EOG). The eye can be modeled as a dipole with the retina and cornea acting as the two ends. To measure an EOG, surface electrodes are placed next to the eyes. As the eye moves back and forth the field generated by the dipole changes direction and hence the potential measured by the electrode changes. The EOG can effectively measure the eye's horizontal deflection up to approximately ±30 degrees.

Electrodes

As discussed above, physiological potentials arise from ionic currents flowing in and out of a nerve or muscle cell. This creates the measurable potential difference on the surface of the skin. There are several types of electrodes that are used to record biopotentials. The type of electrode that is used depends on the biopotential that is being measured and the application. An electrode provides the interface between the ionic currents in the body and the electrical currents in the measuring device.

Two types of electrodes exist theoretically, polarizable and nonpolarizable. Electrode polarization is a function of three components. These components include an ohmic overvoltage, a concentration overvoltage, and an activation overvoltage. The ohmic overvoltage refers to the voltage potential that arises from the current flowing through the electrode-electrolyte interface. The concentration overvoltage is a result of the alterations in the local ionic concentrations around the electrode. Finally, the activation overvoltage is a function of the electrode structure changing over time. When current is passed through the electrode deposition, dissolution can occur on the electrode surface changing the electrode properties for passing current. The goal in fabricating an electrode is to minimize all of these components so that the electrode has the same characteristics over time. A perfectly nonpolarizable electrode is not possible in the real world, therefore, electrodes are designed as close to this as possible.

There are several different types of electrodes that are suited for particular biomedical applications. One of the most common types is the metal plate snap electrode (Fig 7). This electrode consists of a small metal disc, generally silver or silver plated with silver chloride, surrounded by foam padding with an adhesive. There is a metal snap on the other side of the electrode that connects to a snap lead. These leads are then connected to an instrumentation amplifier. The silver-silver chloride electrode is considered nonpolarizable. It provides a stable output over time, it can perform DC recording, has low noise, and a small amount of drift. These snap electrodes are frequently used for ECG and EMG recordings. For EMG, the electrodes may have a less reactive metal, such as stainless steel, gold or platinum to avoid any reaction between the metal and perspiration coming from the skin. Other variations on the metal plate snap electrodes are long curved rectangular plates that can be placed flush on a limb, or metal discs that are attached with surgical tape.

Another modification to the metal plate electrode is the suction electrode. This electrode has a bell-shaped metal surface with a small rubber bulb above it. The electrode is attached by coating gel on the metal contact surface, squeezing the rubber bulb, pushing the electrode against the chest, and releasing the bulb. The suction electrode gives a better connection between the skin and the electrode. However, these types of electrodes can only be used for brief amounts of time since the suction would eventually cause some irritation on the skin of the patient.

Gold cup electrodes are frequently used for EEG recordings (Fig 7). They may also be used to record EOG and EMG from facial muscles. These electrodes are smaller than metal disc electrodes and are shaped like a cup. The small size of these electrodes allow easier placement on the head, since the hair would interfere with a larger metal disc electrode. Unlike the snap electrodes, which have an adhesive backing, these cup electrodes require a paste to adhere the electrodes to the skin. These electrodes are filled with a conductive paste, pressed against the scalp, and then taped to the head. Gauze may also be used to wrap the head to hold these electrodes in place.
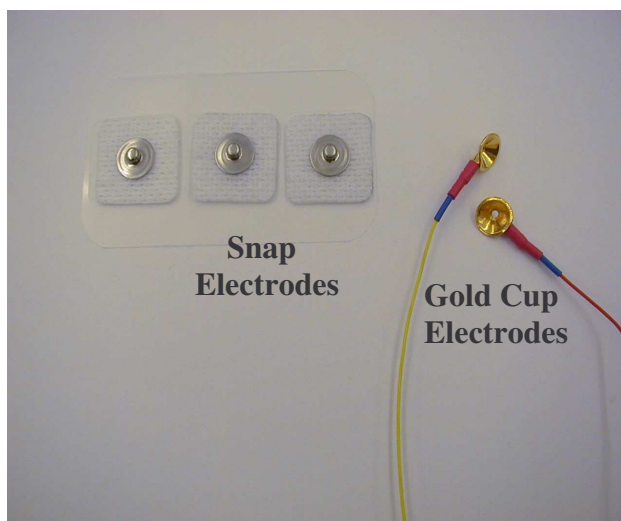

Figure 7. Snap leads can be used to measure EMG, ECG, and EOG, while the gold cup electrodes can be used for EEG recordings.

Since some locations on the body are not flat, electrodes are needed that can be deformed to fit flush against the skin. For these cases, flexible electrodes can be used. These electrodes are constructed with either a fabric that is impregnated with silver particles or a conducting rubber pad. Sometimes measurements need to be conducted below the skin. Percutaneous electrodes are used for these applications. Percutaneous electrodes usually have a deinsulated end and are inserted through the skin and into the target muscle or next to the target nerve to be monitored. These types of electrodes are often used for monitoring EMG from deep muscles. These electrodes allow for a highly localized recording. Since these electrodes are placed directly in the tissue to be recorded, fewer artifacts are likely and the recordings are of higher amplitude due to the proximity of the signal source. The laboratories in this book will not require the use of percutaneous electrodes.

Electrodes are not always passive devices. Electrodes may also be used to electrically stimulate tissues and nerves. Stimulating electrodes deliver a current to tissue and nerves. One application of stimulating electrodes is cardiac pacing. During cardiac pacing an implanted electronic device delivers stimulating pulses to the heart to regulate the heartbeat. In addition to cardiac pacemakers, stimulating electrodes have been used in functional electrical stimulation of paralyzed skeletal muscles in spinal cord injury patients to restore motor function. Current research also focuses on using electrical stimulation to treat neurological disorders, such as Parkinson's disease and epilepsy, by stimulating areas of the deep brain.

Skin Preparation for Surface Electrodes

For most laboratories you complete in this course, the surface of the skin needs to be properly prepared before placing recording electrodes. Properly preparing the skin allows for better conductance of the signal that is to be measured. The dead layer of skin on the surface of the skin creates a large resistance for the physiological signal to travel through and hence decreases the amplitude of the signal to be recorded. The skin surface should be abraded with a lightly abrasive scrub to remove the dead layer of skin on the surface and improve conductance. Simply use the provided cotton tipped applicators to apply the skin prep and gently rub over the surface of the skin where the electrode is to be placed with the applicator. The fine granules will act to abrade the skin and remove the dead outer layer. Do not rub the skin intensely with the abrasive material so that it turns red, just lightly rub the location a few times in order to remove the dead skin cells. In addition to using an abrasive, alcohol is often used to clean the skin before electrode application. However, the surface electrodes that we are including with this kit recommend using soap and water instead. In some instances it may even be necessary to shave hair off the skin before applying an electrode. However, you should not shave anyone for these labs. For example, before recording ECG from a patient certain areas of their chest may need to be shaved before surface electrodes are applied. In addition to preparing the skin, a conductive gel may need to be placed between the electrode and the skin to further improve signal conductance. You will use a conductive gel during the EEG lab later in this course.

Experimental Methods

Experimental Setup

1. Read the BioRadio User's Guide that is included with your lab kit to learn how to use the BioRadio and BioCapture software. You will use both the BioCapture Lite software and the BioRadio Lab Course software to complete the exercises in this course.
2. After reading the BioRadio User's Guide, open the BioRadio Lab Kit and examine the contents. First examine the BioRadio transmitter and receiver. Look at the connections and make sure you understand how to connect the transmitter and receiver for both configurations and running in real-time.
3. Examine the electrodes included with the kit. The BioRadio includes positive and negative inputs for eight channels and a ground. Each input is labeled. Snap leads and gold cup electrode leads can be connected to the inputs. The snap leads connect to snap electrodes for monitoring potentials on the surface of the skin (Fig 8). In addition, other sensors such as piezo-electric respiratory effort belts and nasal/oral airflow thermistors can be connected to the inputs.

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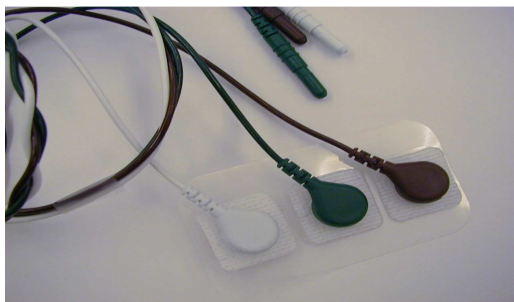
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Figure 8: The snap leads can then be connected to snap electrodes for monitoring EMG, ECG, EOG, and other physiological signals.

4. Install the BioRadio Capture Lite software on your computer. Read the instruction manual.

5. Follow the User's Guide to setup the BioRadio for an eight channel recording and collect data from the BioRadio Test Pack.

Discussion Questions

1. Given the table below of various ionic concentrations inside and outside the cell, find the Nernst potential of each of these ions at room temperature (25C). Assume that for a temperature of 25 C, RT/F simplifies to 26mV. The valence of Na and K are 1, while Cl is –1.

Ion	External	Internal
Potassium	120 mM	400 mM
Sodium	440 mM	50 mM
Chloride	400 mM	60 mM

2. The Nernst potential for a certain single valence ion is at –60 mV. Assuming this measurement is being done within the body (i.e. normal body temperature), find the ratio of the concentration of this ion.

3. Which ion is most responsible for the depolarization of the nerve cell? And for repolarization?

4. Sodium ion channels open much more quickly than the potassium ion channels. Why is this important? Can you hypothesize what the action potential would look like if the potassium channels opened much more quickly than the sodium channels?

5. Notice that the ionic currents for both the potassium and sodium channels don't respond immediately to the step command from the voltage clamp. Why do you think that the

response is not immediate? Hint: Think about how you would calculate current across each element in the membrane in Figure 5 from basic circuits.

6. What is the purpose of the voltage clamp? Explain how it is able to keep the cell at a given potential and measure the ionic current of a specific type of channel.

7. List several types of biopotentials that can be measured with surface electrodes. Give applications that each of these biopotentials could be used for.

8. The nerve cell can be modeled as an electrical circuit as shown in Figure 5. Explain what each of the components in the circuit represents.

9. Why are gold cup electrodes used to monitor an EEG signal instead of snap electrodes?

10. Why is it important that the electrode location on the skin is properly cleaned before electrodes are placed there? Explain the proper procedure for preparing and cleaning these electrode sites..

11. The Nernst potential for a single ion is given by Nernst equation. However, as we have seen, the resting membrane potential for a typical nerve cell is governed not just one ion, but by sodium and potassium ions. The equation that governs a resting potential for more than one ion is the Goldman Equation:

$$V = \frac{RT}{F} \ln[\frac{Px[X_{ext}] + Py[Y_{ext}]}{Px[X_{int}] + Py[Y_{int}]}]$$

Calculate the resting potential for a cell that has both sodium and potassium ions flowing through channels in the membrane. Px and Py represent the membrane permeability to the specific ion. Assume a Pna of 0.02 and a Pk of 1.00. Assume the same concentrations as shown under question 1.

12. Why does repolarization occur slower than depolarization in the cell?

13. In addition to placing surface electrodes on the skin in order to record biopotentials, reference electrodes also need to be placed on the body. Describe what you would consider a "good" location on the body to place a reference electrode.

14. The electrical equivalent circuit shown in Figure 5 can be used to represent a nerve fiber. Researchers use this model to determine how action potentials propagate down a nerve fiber. Notice how the extracellular fluid side of the model is just shorted together, while a resistance is used on the intracellular side. Is this accurate in real life? Why or why not and what consequences does this have on measuring biopotentials on the surface of the skin?

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