Instructor's notes

Title: "The Biomedical Blunder"

Appropriate course: General Physiology

Degree of difficulty: Introductory – moderately difficult

Students will apply equations and interpret results from the Goldman-Katz equation.

Resources needed: A computer with spreadsheet software. Data set was prepared in Microsoft Excel, but other similar applications that can perform similar functions may be used.

Duration of project: The project in current form should require one 50-minute class period and one-two weeks for students to complete. However, drugs "A" and/or "B" can be omitted to suit needs of the instructor. Questions should be edited to reflect changes. To further reduce time demands of students this can be converted to an in-class assignment. The write up would be omitted in this case, and data analysis would be limited.

Timeline of events

- **Project as designed: 1-2 weeks**
    - Go through the case study together as a class
    - Generate hypothesis as group
    - Introduce students to the spreadsheet in class: 50-minute class period
        - Explain important variables
        - Explain general layout of spreadsheet
        - Introduce calculations that will need to be carried out
        - Go over lab report requirements
- **Reduced project: (few days to 1 week)**
    - Alteration suggested:
        - Reduce the number of drugs
    - Project carried out as designed.
        - Students will perform less analysis and be required less response toward discussion
- **In class (1-2 50-minute periods)**
    - Alteration suggested:
        - Write up is omitted
    - Go through the case study together as a class
    - Break into small groups:
        - Students generate hypothesis: 5-10 minutes
            - Discuss as group
        - Students calculate membrane potential and averages for variables of interest: 30 minutes
        - Conclude with discussion of the significance of the data: 10 minutes

Guidelines on evaluation:

A rubric is provided in the student version to guide instructor grading. To encourage students to work together cooperatively:

- Have students determine roles when they are initially formed into group.
  - Allowing students to determine this promotes ownership and provides another opportunity to engage students.
- Gather input from both group members regarding work investment.
- Reflective statement:
  - Potential items to address:
    - Did role affect your understanding of the topic?
    - Did this project increase your understanding of membrane potential?

Write up:

Introduction: Include the following questions and components in your write up.

1. What is membrane potential and why is it important for the application stated in the development of the drug?
   a. Students should explain resting membrane potential. The drug targets resting membrane potential. It is designed to reduce nerve excitability that produces muscle spasms.
2. How is membrane potential different from membrane ion equilibrium? How is resting membrane potential generated?
   a. Students should demonstrate a clear understanding of how these two measurements differ and their uses.
3. How does the neuronal resting membrane potential lead to increased excitation of skeletal muscle?
   a. Neuron resting membrane potential if reduced (less negative) is closer to threshold and the neuron can more easily be stimulated.
4. How could the drug potentially act to correct neuronal excitability?
   a. Responses must include that the drug reduces nerve excitation by:
      i. The impact the drug has on channels and their impact on membrane potential of neurons.

      OR

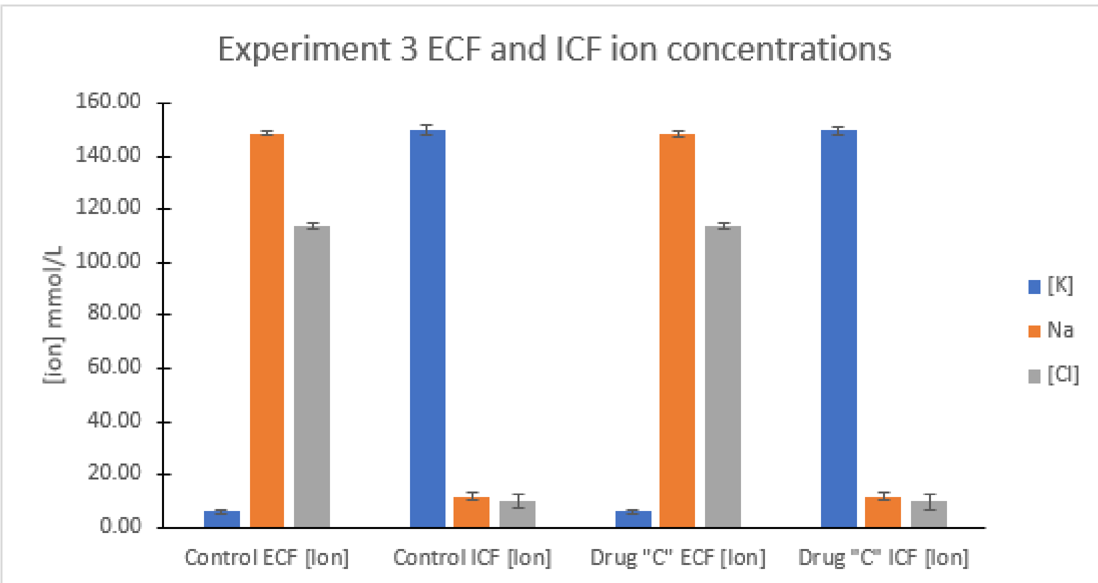
      ii. The impact the drug has on intracellular or extracellular fluid.
5. Hypothesize the response to the drug.

Results:

1. Present averages for ECF and ICF ion concentrations, ion membrane permeability, and membrane potential in bar charts.

a. Each figure needs to have the following:
   i. Error bars
   ii. Figure caption
   iii. Legend
   iv. Properly labeled axes

Example figure:



2. Explanation of figures.
   a. Summarize the effect of each drug on membrane potential in text.
      i. How each drug affected membrane potential.
      ii. Figures referenced in text.

Example responses:

- Drug "A": Reduced membrane potential, less negative, by reducing permeability to K+ ions.
- Drug "B": Reduced membrane potential, less negative, by increasing permeability to Na+ ions.
- Drug "C": Increased membrane potential, more negative, by increasing permeability to Cl- ions.

Discussion:

Instructor version

1. Identify which of the drug samples was the drug you have been developing. Explain how the results support your conclusion.
    - The effect on membrane potential should indicate this.

Example responses:

- The drug you have been developing is drug C.
- Explanation: Membrane potential becomes hyperpolarized (More negative), making the neuron more difficult to excite.

2. How does your drug reduce somatic nerve excitation?
    - You need to integrate information from fluid concentrations, membrane permeability, and membrane potential in order to do this.

Example responses:

- The drug increases membrane potential (more negative) by increasing permeability to chloride, hyperpolarizing the neuronal cell. Results to be included that support the question.
    i. Membrane potential will be more negative
    ii. Cl permeability increases
    iii. Hyperkalemic ECF allows slight depolarization, increasing chances of sporadic depolarization.

3. What did the other drugs do? How did they carry this out?

Example responses:

- Drug “A” depolarizes the cell by decreasing permeability to K+
- Drug “B” depolarizes the cell by increasing permeability Na+
- Drug “C” hyperpolarizes the cell by increasing permeability to Cl-
    i. This is the drug that the researcher has been developing to reduce muscle spasms.

4. Why did you use an elevated $[K]_{ECF}$ and how did this affect resting membrane potential?

Example responses:

- Hyperkalemia depolarizes the cell by reducing the K^+ concentration gradient.
    i. Reduction of the K^+ concentration gradient reduces efflux of K^+ out of cell, increasing the amount of intracellular cations.

5. Why does the resting membrane potential lead to increased excitation of skeletal muscle?

Example responses:

- The resting membrane potential sets the baseline for cell excitability for neurons, if the RMP is depolarized, the neuron could be more easily stimulated causing a signal to be relayed to the target (skeletal muscle).

6. How else could a drug reduce the excitability of a neuron?

Example responses:

- The drug could increase K^+ excretion from the body, increasing the concentration gradient in the process.
- The drug could reduce permeability to Na^+
- The drug could reduce excretion of Cl from the body

Evaluation:

Students will be evaluated based on the completeness and accuracy of their project. All projects must be polished and well written. If errors are present in the analysis or write up, the evaluation of your project will be negatively affected. Refer to the provided rubric for more detail regarding grading.