Answer the following questions before using the online tools to verify your answers. This exercise should help you develop an intuitive understanding for ion movement, the effect on V_m, and thus the predicted outcome for neuronal and muscle activity.

There is no answer key for this self-test as many of your predictions can be immediately verified with the online tools. Make sure you understand the physiological reason behind each change! If there are problems, contact me (tostrowski@atsu.edu; or in person: 5th floor TBR, Office 508).

Important: The below questions do not reflect examples of questions I would ask in the exam. They should merely help you understand a difficult concept.

Ion concentrations and their effect on the *resting* membrane potential:

('Membrane Potential App', reset concentrations before each question)

1. Increasing the extracellular K^+ concentration $[K]_{out}$ to 30 mM:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. Move towards 0 mV
  C. E = 0 mV
  D. No change

- The outward ionic current for K^+ through leak channels will:
  A. Increase and make the inside more negative
  B. Decrease and make the inside more positive
  C. Remain the same as before

- What is the effect on the membrane potential (V_m)?
  A. Depolarize
  B. Hyperpolarize
  C. No change

2. Increasing the intracellular Na^+ concentration $[Na]_{in}$ to 30 mM:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. move towards 0 mV
  C. E = 0 mV
  D. No change

- What is the effect on the membrane potential (V_m) **and why**?
  A. Depolarize
  B. Hyperpolarize
  C. No change

3. Increasing the intracellular Cl^- concentration $[Cl]_{in}$ to 30 mM:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. move towards 0 mV
  C. E = 0 mV
  D. No change

- What is the effect on the membrane potential (V_m) **and why**?
  A. Depolarize
  B. Hyperpolarize
  C. No change

4. Which of the above changes (Q1-3) had the greatest effect on V_m **and why**?

5. Increasing the extracellular Cl^- concentration $[Cl]_{out}$ to 150 mM:

- Which equilibrium potential(s) will be affected?
    A. E_K
    B. E_{Na}
    C. E_{Cl}
    D. For all three ion species
    E. Only those for cations (K^+, Na^+)
    F. None

- What is the predicted change for that equilibrium potential?
    A. Move away from 0 mV
    B. Move towards 0 mV
    C. E = 0 mV
    D. No change

- What is the effect on the membrane potential (V_m) **and why**?
    A. Depolarize
    B. Hyperpolarize
    C. No change

6. Increasing the extracellular K^+ concentration $[K]_{in}$ to 140 mM (same as intracellular):

- Which equilibrium potential(s) will be affected?
    A. E_K
    B. E_{Na}
    C. E_{Cl}
    D. For all three ion species
    E. Only those for cations (K^+, Na^+)
    F. None

- What is the predicted change for that equilibrium potential?
    A. Move away from 0 mV
    B. Move towards 0 mV
    C. E = 0 mV
    D. No change

- What is the effect on the membrane potential (V_m) **and why**?
  A. Depolarize
  B. Hyperpolarize
  C. No change

<u>Ion permeability and their effect on the resting membrane potential:</u>

('Membrane Potential App', reset concentrations and permeabilities before each question)
(note: permeabilities are expressed as fraction from K^+ permeability)

7. Increasing membrane permeability for K^+ (i.e., opening K-channels) to 3:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. Move towards 0 mV
  C. E = 0 mV
  D. No change

- More K^+ ions will:
  A. Leave the cell and make the inside more negative
  B. Remain in the cell and make the inside more positive
  C. Do nothing (no change)

- What is the effect on the membrane potential (V_m)?
  A. Depolarize
  B. Hyperpolarize
  C. No change

8. Decreasing membrane permeability for K^+ (i.e., closing K-channels) to 0:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. Move towards 0 mV
  C. E = 0 mV
  D. No change

- More K^+ ions will:
  A. Leave the cell and make the inside more negative
  B. Remain in the cell and make the inside more positive
  C. Do nothing (no change)

- What is the effect on the membrane potential (V_m)?
  A. Depolarize
  B. Hyperpolarize
  C. No change

9. Increasing membrane permeability for Na^+ (i.e., opening Na-channels) to 3:

- Which equilibrium potential(s) will be affected?
  A. E_K
  B. E_{Na}
  C. E_{Cl}
  D. For all three ion species
  E. Only those for cations (K^+, Na^+)
  F. None

- What is the predicted change for that equilibrium potential?
  A. Move away from 0 mV
  B. Move towards 0 mV
  C. E = 0 mV
  D. No change

- More Na^+ ions will:
    A. Enter the cell and make the inside more positive
    B. Remain on the outside of the cell and make the inside more negative
    C. Do nothing (no change)

- What is the effect on the membrane potential (V_m)?
    A. Depolarize
    B. Hyperpolarize
    C. No change

10. Decreasing membrane permeability for Na^+ (i.e., closing Na-channels) to 0:

- Which equilibrium potential(s) will be affected?
    A. E_K
    B. E_{Na}
    C. E_{Cl}
    D. For all three ion species
    E. Only those for cations (K^+, Na^+)
    F. None

- What is the predicted change for that equilibrium potential?
    A. Move away from 0 mV
    B. Move towards 0 mV
    C. E = 0 mV
    D. No change

- More Na^+ ions will:
    A. Enter the cell and make the inside more positive
    B. Remain on the outside of the cell and make the inside more negative
    C. Do nothing (no change)

- What is the effect on the membrane potential (V_m)?
    A. Depolarize
    B. Hyperpolarize
    C. No change

11. Increasing membrane permeability for Cl^- (i.e., opening Cl-channels) to 3:

- What is the effect on the membrane potential (V_m) **and why**?
    A. Depolarize
    B. Hyperpolarize
    C. No change

- When opening even more Cl^- channels (P_{Cl} to 15), will V_m ever surpass E_{Cl}?
    A. Yes
    B. No
    C. Briefly

12. Completely closing channels for Na and K (P_{Na} and $P_K = 0$):

- V_m will be at:
    A. E_{Na}
    B. E_K
    C. E_{Cl}
    D. At 0 mV
    E. Previous resting potential (no change)

- In this state, increasing P_{Cl} to 15 will:
    A. Depolarize V_m
    B. Hyperpolarize V_m
    C. Shift V_m to 0 mV
    D. Do nothing

13. Close all K channels ($P_K = 0$, V_m goes to -41 mV). Now change the <u>extra</u>cellular K^+ concentration to 50 mM:

- In this state, which equilibrium potential(s) will be affected?
    A. E_K
    B. E_{Na}
    C. E_{Cl}
    D. For all three ion species
    E. Only those for cations (K^+, Na^+)
    F. None

- What is the predicted change for that equilibrium potential?
    A. Move away from 0 mV
    B. Move towards 0 mV
    C. E = 0 mV
    D. No change

- What is the effect on the membrane potential (V_m) **and why**?
  A. Depolarize
  B. Hyperpolarize
  C. No change

Nernst and Goldman-Hodgkin-Katz equations:

('Membrane Potential App', reset concentrations and permeabilities)

Equations are Ideas that can help you get a better understanding of the physiological principle. Use above questions to change ion concentrations and permeabilities to see the change on the equilibrium potentials and V_m. Every change in the graphical window is based on these equations.

Action potential discharge:

('MetaNeuron', Lesson 4: Action potential)
(restore all lesson defaults before each question – Ctrl+L)

14. Drag the 'knob' next to E_{Na} (grey box) and increase to 70 mV:

- How does this change affect the AP amplitude (measured from resting V_m to AP peak) (know why)?
  A. increases
  B. decreases
  C. no change
  D. no AP elicited

15. (Ctrl+L). Now set sweep duration to 50 ms (bigger time frame) and increase the width of 'Stimulus 1' to 20 ms:

- What happened to the number of action potentials?
  A. increase
  B. decrease
  C. no change

- From this condition, increasing the width of 'stimulus 1' to 30 ms:
  A. Increases the number of APs
  B. Decreases the number of APs
  C. Does not change AP number

- The AP frequency is:
    A. Increased
    B. Decreased
    C. Did not change

- From this condition, increasing the amplitude of ‘stimulus 1’ to 120 µA (by dragging the knob):
    A. Increases the number of APs
    B. Decreases the number of APs
    C. Does not change AP number

- The AP frequency is now:
    A. Increased
    B. Decreased
    C. Did not change

- The amplitudes of subsequent Aps is:
    A. Increased
    B. Decreased
    C. Did not change

- Switch on the ‘Ionic conductance’ (to show open channels). The amplitude of the Na^+ conductance (green trace) for subsequent APs is _________. **Why**?
    A. bigger
    B. smaller
    C. Did not change

- Subsequent APs occur:
    A. In the relative refractory period
    B. In the absolute refractory period
    C. Outside of the refractory period

15. (Ctrl+L). Set sweep duration to 20 ms and turn on ‘Stimulus 2’ (same amplitude as ‘Stimulus 1’ and with the current delay of 2 ms):

- The new stimulus:
    A. Elicited a second AP
    B. Did not do anything
    C. Cancelled all spikes

- Change the delay of ‘stimulus 2’ until you see an AP. Now you are:
    A. In the relative refractory period
    B. In the absolute refractory period
    C. Outside of the refractory period

- Reduce the delay of ‘stimulus 2’ to 4 ms and change the amplitude to 140 µA. Now you are:
    A. In the relative refractory period
    B. In the absolute refractory period
    C. Outside of the refractory period

- Reduce the delay of ‘stimulus 2’ back to 2 ms and change the amplitude to 1000 µA. Now you are:
    A. In the relative refractory period
    B. In the absolute refractory period
    C. Outside of the refractory period