Electrical Engineering 3BB3: Cellular Bioelectricity (2013)

Solutions to Midterm Quiz #1

1. In a typical excitable cell, the ion species with the *most positive* Nernst equilibrium potential is:

a. potassium,
b. sodium,
c. calcium, or
d. chloride. **(5 pts)**

The answer is **c. calcium**. This is due to the substantial buffering of intracellular calcium, greatly reducing the free calcium in the intracellular space (see slide 14 of Lecture #4).

2. Currents through single ionic channels are stochastic predominantly because of:

a. the "random walk" of ions in the diffusion process,
b. random fluctuations in the transmembrane potential,
c. random changes in the membrane capacitance due to movement of lipids in the bilayer, or
d. thermal noise affecting the opening and closing of gating particles. **(5 pts)**

The answer is **d. thermal noise affecting the opening and closing of gating particles**. See slides 10–12 of Lecture #7 and slides 2–4 of Lecture #8.

3. The intracellular and extracellular electrolytes of excitable cells have a primarily linear conductivity that arises because of phenomena described by:

a. Fick's law of diffusion,
b. Ohm's law of drift,
c. Einstein's equation, or
d. the Goldman–Hodgkin–Katz Equation. **(5 pts)**

The answer is **b. Ohm's law of drift**. Eqn. (3.2), Ohm's law of drift, states that the ionic flux in an electrolyte is proportional to the potential gradient ($\nabla\Phi$). The resulting current will therefore be proportional to the potential gradient, such that the electrolyte's conductance is linear (see slides 13 & 14 of Lecture #3).

4. When the membrane is *hyperpolarized*, the Hodgkin–Huxley sodium channel *h* particle:

a. activates,
b. deactivates,
c. inactivates, or
d. deinactivates. **(5 pts)**

The answer is **d. deinactivates**. This was discussed in Lecture #10. (See also slide 13 of Lecture #11.)

5. The selectivity of an ion channel for *anions* versus *cations* is due primarily to:

a. whether or not it has an inactivation particle,

b. whether it is voltage-gated or ligand-gated,

c. the sign of the charge of the protein residues in the narrowest part of the channel pore, or

d. the diameter of the narrowest part of the channel pore. (5 pts)

The answer is **c. the sign of the charge of the protein residues in the narrowest part of the channel pore**. This was discussed in Lecture #7.

6. The experimental technique physiologists use to measure ionic currents while removing the effects of the membrane's capacitive current is:

a. capacitance-clamp recording,

b. current-clamp recording,

c. inductance-clamp recording, or

d. voltage-clamp recording. (5 pts)

The answer is **d. voltage-clamp recording**. This was discussed in Lecture #10 (see slide 3 of Lecture #10).

7. The sodium-potassium pump:

a. pumps 3 moles of Na out of a cell for every 2 moles of K that it pumps in,

b. pumps 2 moles of K out of a cell for every 3 moles of Na that it pumps in,

c. generates action potentials, or

d. is a form of passive membrane transport. (5 pts)

The answer is **a. pumps 3 moles of Na out of a cell for every 2 moles of K that it pumps in**. See slide 8 of Lecture #12.

8. The phenomenon in which an excitable cell does *not* fire an action potential if its membrane is depolarized too slowly from rest is referred to as :

a. facilitation,

b. accommodation,

c. sleepiness, or

d. refractoriness. (5 pts)

The answer is **b. accommodation**. See slides 10–12 of Lecture #11.

9. Describe the typical *strength-duration* tradeoff for a pulse of stimulating current to generate an action potential in an excitable cell and briefly explain the cause of this tradeoff. (15 pts)

The strength-duration tradeoff refers to the fact that shorter current pulses need a larger current amplitude to reach the threshold for action potential generation. As the pulse duration increases, the threshold current drops until it approaches the asymptotic threshold current, referred to the rheobase current.

The major cause of the tradeoff is the fact that it takes some time for the membrane to charge up in response to a current pulse (due to the parallel RC-circuit nature of the membrane and typically quantified by the membrane time-constant $\tau = RC$). Therefore, the threshold current will depend on how much the membrane is depolarized by the time the current pulse is turned off. Consequently, shorter pulses need a larger current amplitude to produce sufficient depolarization, and thus sodium channel activation, while the pulse is still on. The rates of ion channel activation and inactivation are secondary factors.

10. Explain the cause of the shape of a stereotypical action potential (AP) waveform. In your explanation, include a discussion of why an excitable cell always tends to fire APs with similar waveforms but different *types* of excitable cells can have vastly different AP waveform shapes and durations. (15 pts)

A stereotypical AP waveform is illustrated below.

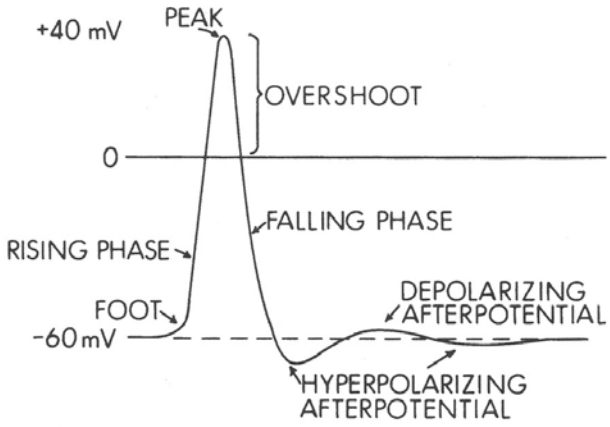


Figure 5.4. Diagram to show the nomenclature applied to an action potential and the afterpotentials that may follow it.

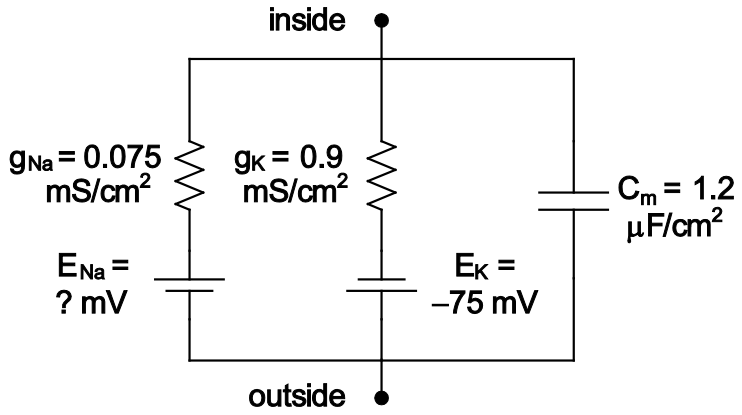
An AP is initiated by sufficient opening of voltage-gated sodium channels due to activation of sodium activation (*m*) particles. This causes an increase in the influx of sodium, which depolarizes the membrane, leading the further opening of *m* particles. The onset of this positive feedback loop gives rise to the foot of the AP waveform, followed by the rising phase during which there is a massive influx of sodium through voltage-gating sodium channels as practically all these channels open. The peak of the AP approaches (but does not exceed) the sodium Nernst equilibrium potential. The falling phase is caused by closing of sodium inactivation (*h*) particles (reducing the inward sodium current) and opening of potassium activation (*n*) particles (increasing the outward potassium current), both of which lag behind sodium activation because

of their slower time constants. Because of the slow dynamics of the *n* and *h* particles, in some cells the potassium current remains higher than the sodium current as the membrane repolarizes, such that it overshoots the resting potential and approaches (but does not exceed) the potassium Nernst equilibrium potential. One or more afterpotentials may occur as the membrane potential and the gating particles eventually return to their resting values.

During the AP, the sodium and potassium currents grow so large that the changes in the membrane potential are driven only by the gating particle dynamics, which are dependent in turn only on the membrane potential, not the stimulus that initiated the AP. The AP waveform is consequently determined by the ion channel conductances, the gating particle dynamics, and the Nernst equilibrium potentials, which are properties of the cell not the stimulus. Thus the waveform remains fairly consistently the same for all APs fired by an excitable cell.

Different excitable cell types can have different AP waveforms, however, because they may have different Nernst equilibrium potentials (see slide 14 of Lecture #4), conductances (see slide 14 of Lecture #7), gating particle dynamics (see slides 3 & 4 of Lecture #12), or a range of different ionic channel types (slides 10–15 of Lecture #12).

11. Consider a patch of membrane described by the parallel conductance model shown below.



a. If the resting transmembrane potential $V_{\text{rest}} = -65\ \text{mV}$, what is the sodium Nernst equilibrium potential E_{Na}?

b. If the intracellular potassium concentration $[\text{K}]_i = 400\ \text{mM}$ and the temperature is 37°C, what is the extracellular potassium concentration $[\text{K}]_e$? (15 pts)

a. For the given circuit, the resting membrane potential will be determined by:

$$V_{\text{rest}} = \frac{g_{\text{Na}}E_{\text{Na}} + g_{\text{K}}E_{\text{K}}}{g_{\text{Na}} + g_{\text{K}}} = \frac{0.075\cdot(E_{\text{Na}}) + 0.9\cdot(-75)}{0.075 + 0.9} = -65\ \text{mV}.$$

Thus, the sodium Nernst equilibrium potential is given by:

$$0.075\cdot(E_{\text{Na}}) + 0.9\cdot(-75) = -65\cdot 0.975$$

$$\Rightarrow E_{\text{Na}} = \frac{-65\cdot 0.975 + 75\cdot 0.9}{0.075} = 55\ \text{mV}.$$

b. The potassium Nernst equilibrium potential is determined by:

$$E_{\mathrm{K}} = -\frac{RT}{Z_{\mathrm{K}}F}\ln\left(\frac{[\mathrm{K}]_i}{[\mathrm{K}]_e}\right) = -\frac{8.314\cdot 310}{1\cdot 96487}\ln\left(\frac{400}{[\mathrm{K}]_e}\right) = -75\times 10^{-3}\ \mathrm{V}.$$

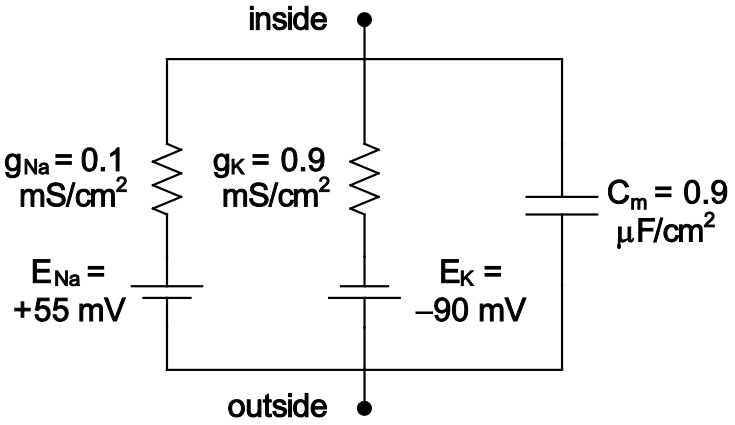
Therefore, the extracellular potassium concentration $[\mathrm{K}]_e$ is given by:

$$\ln\left(\frac{400}{[\mathrm{K}]_e}\right) = \frac{96487\cdot 75\times 10^{-3}}{8.314\cdot 310}$$

$$\Rightarrow \frac{400}{[\mathrm{K}]_e} = \mathrm{e}^{\frac{96487\cdot 75\times 10^{-3}}{8.314\cdot 310}}$$

$$\Rightarrow [\mathrm{K}]_e = 400\,\mathrm{e}^{\frac{-96487\cdot 75\times 10^{-3}}{8.314\cdot 310}}\ \mathrm{mM} = 24.1\ \mathrm{mM}$$

12. Consider a spherical cell with diameter $d = 7\ \mu\mathrm{m}$ and the parallel-conductance model for a membrane patch shown below. Note that the potential between the inside and the outside of the membrane in the given circuit is the *absolute* transmembrane potential V_m.



If the membrane is at rest for time $t < 0$ and for time $t \geq 0$ a current of density $I_{\mathrm{inj}} = 10\ \mu\mathrm{A}/\mathrm{cm}^2$ is injected into the intracellular space, determine an expression for the *relative* transmembrane potential $v_m(t)$ for all times $t \geq 0$. (15 pts)

For the given circuit, the net resistance for a square centimetre of membrane is:

$$R_m = \frac{1}{G_m} = \frac{1}{g_{\mathrm{Na}} + g_{\mathrm{K}}} = \frac{1}{0.1 + 0.9}\ \mathrm{k\Omega\cdot cm^2} = 1\ \mathrm{k\Omega\cdot cm^2},$$

and the membrane time constant is thus:

$$\tau = R_m C_m = \left(1\ \mathrm{k\Omega\cdot cm^2}\right)\cdot\left(0.9\ \mu\mathrm{F}/\mathrm{cm^2}\right) = 0.9\ \mathrm{ms}.$$

As given in the equation sheet, the response of the *absolute* membrane potential will be of the form:

$$V_m(t) = I_0 R_m \left[1 - \mathrm{e}^{-t/\tau}\right] + V_{\text{rest}}.$$

Consequently, the *relative* membrane potential, which is defined as $v_m = V_m - V_{\text{rest}}$, will be equal to:

$$v_m(t) = I_0 R_m \left[1 - \mathrm{e}^{-t/\tau}\right] = 10 \cdot 1 \left[1 - \mathrm{e}^{-t/0.9}\right] \text{mV} = 10 \left[1 - \mathrm{e}^{-t/0.9}\right] \text{mV}, \text{ for } t \geq 0,$$

where t is in units of millisecond.

Note that because the injected current is given as a density (i.e., per square centimetre) and the membrane circuit is given for a unit area of membrane (i.e., for a square centimetre of membrane), it is not necessary to work out the membrane surface area. However, knowing that the cell is small indicates that the entire cell membrane should be isopotential.