Multiple Choice Questions

1. The resting membrane potential is
   (a) much closer to the equilibrium potential for Na\(^+\) than to the equilibrium potential for K\(^+\).
   (b) much closer to the equilibrium potential for K\(^+\) than to the equilibrium potential for Na\(^+\).
   (c) the same as the equilibrium potential for Cl\(^-\).
   (d) Both (a) and (c) above.
   (e) Both (b) and (c) above.

2. Graded potentials
   (a) are local changes in membrane potential that occur in varying degrees of magnitude.
   (b) serve as short-distance signals.
   (c) serve as long-distance signals.
   (d) Both (a) and (b).
   (e) Both (a) and (c).

3. When chemically-gated Na\(^+\) channels open
   (a) the membrane hyperpolarizes.
   (b) the membrane repolarizes.
   (c) the membrane depolarizes.
   (d) the membrane becomes more negative.
   (e) the membrane is inhibited.

4. Spatial summation occurs in a postsynaptic neuron
   (a) when several EPSPs from a single presynaptic input sum to reach threshold.
   (b) when EPSPs from several presynaptic inputs sum to reach threshold.
   (c) upon simultaneous interaction of an EPSP and an IPSP.
   (d) when several IPSPs from a single presynaptic input sum to hyperpolarize the membrane.
   (e) None of these answers.

5. Which of the following statements concerning the brain stem is incorrect?
   (a) the medulla is part of the brain stem.
   (b) the brain stem is a critical connecting link through which all fibers traversing between the periphery and higher brain centers must pass.
   (c) the brain stem controls sociosexual behaviors conducive to mating.
   (d) the brain stem contains the reticular activating system.
   (e) the brain stem contains centers that control respiration, blood vessel and heart function, and digestive activities.

6. Which is not a function of the basal nuclei?
   (a) inhibition of muscle tone.
   (b) coordinate impulses related to posture.
   (c) suppression of unnecessary motor activity.
   (d) autonomic control activity.
   (e) All of these answers.
7. The left cerebral hemisphere normally excels in all of the following except
(a) musical ability.
(b) verbal tasks.
(c) math skills.
(d) logical and analytical tasks.
(e) language ability.

8. Which of the following structures normally controls the amount of light entering the eye?
(a) ciliary muscle.
(b) suspensory ligaments.  
(c) iris.  
(d) cornea.  
(e) lens.

9. Cones
(a) are most abundant in the periphery of the retina.
(b) are more numerous than rods.
(c) have high sensitivity to light.
(d) are responsible for color vision.
(e) More than one of these.

10. Transmission of sound through the middle ear results in
(a) amplification of the pressure vibrations.
(b) stimulation of middle ear receptor cells.
(c) opening of the eustachian tube.
(d) increased firing rate in sensory axons associated with the tympanic membrane.
(e) None of these answers.

11. The sympathetic nervous system
(a) is always excitatory.
(b) innervates only tissues concerned with protecting the body against challenges from the outside environment.
(c) dominates in fight-or-flight situations.
(d) is part of the somatic nervous system.
(e) is part of the afferent division of the peripheral nervous system.

12. Acetylcholinesterase
(a) has enhanced activity from organophosphates.
(b) inactivates a neurotransmitter.
(c) is a neurotransmitter.
(d) stimulates an excitatory postsynaptic potential.
(e) triggers the release of sodium into postsynaptic cells.

13. Which of the following statements concerning cross bridges is not correct?
(a) cross bridges bind to actin during muscle contraction.
(b) cross bridges are formed by the globular heads of the myosin molecules.
(c) cross bridges consist of troponin and tropomyosin protruding from the actin helix.
(d) cross bridges bend during muscle contraction.
(e) cross bridges protrude from the thick filaments.
14. The T tubules
(a) store Ca$^{2+}$.  
(b) provide a means of rapidly transmitting the action potential from the surface into the central portions of the muscle fiber.  
(c) store ATP.  
(d) run longitudinally between the myofibrils.  
(e) have expanded lateral sacs.

15. Muscular fatigue is caused by
(a) depletion of lactic acid.  
(b) depletion of ATP.  
(c) accumulation of ACh.  
(d) Acetylcholinesterase.  
(e) All these answers.
1. The venom of certain poisonous snakes contains alpha bungarotoxin, which binds tenaciously to acetylcholine receptor sites on the motor end-plate membrane and blocks the action of ACh. What would the resultant symptoms be? How would they differ from the symptoms of an ACh agonist?

The symptom of bungarotoxin would be flaccid paralysis. In the case of an agonist the symptoms would be first muscle spasms followed by fatigue and paralysis.

2. The refractory period of a nerve cell’s electrical response to an input signal is an important parameter in determining the frequency of a nerve cell’s response. What is the refractory period, and what are the underlying molecular mechanisms? What role does the refractory period have in setting the frequency of AP firings in a nerve cell?

The refractory period of a nerve cell’s electrical response can be divided into
- Absolute refractory period (during an AP) when no APs can be triggered. In this case the Na+ channels are already open and the K+ channels are in the processes of opening so no new APs can be triggered.
- Relative refractory period (after an AP) when some APs can be triggered. The Na+ channels are mostly inactive and the K+ channels are slow to close. After an AP a second AP can be triggered only by exceedingly strong signals

The refractory period sets an upper limit to the frequency of APs.

3. What are the main reasons people do not fall down when they pick up one foot by flexion of leg muscles? What kinds of connections are involved, in addition to those from the vestibular system?

The reason is a spinal reflex which causes extension of the opposite site. The connections involved are: sensors of the flexed legs → interneurons → motor neurons of the opposite leg (extension).
**Case Studies (with solutions)**
(Not required. These problems are given for your reading pleasure only!)

**Case 1 – Dancing in ecstasy**

Dancing Dottie and Boogying Betty went off to a rave (wild dance party) together. Dottie consumed an Ecstasy tablet before the rave began but Betty did not. The rave was crowded and hot, and the drug made Dottie feel like she could dance all night. Betty also danced wildly, but she took occasional breaks to rest and drink water. After about 5 hours of non-stop wild dancing, Dottie collapsed. Betty noted that Dottie’s skin was hot and dry, and that her pulse was racing. When an ambulance arrived, Dottie’s body temperature was found to be 105°F (>40°C).

MDMA (3,4-methylenedioxymethamphetamine), most commonly known by the street names ecstasy or XTC, is a synthetic entactogen of the phenethylamine family, whose primary effect is believed to be the stimulation of secretion as well as inhibition of re-uptake of large amounts of serotonin as well as dopamine and norepinephrine in the brain, inducing a general sense of openness, empathy, energy, euphoria, and well-being. Serotonin is a neurotransmitter believed to play a role in the regulation of mood and pleasure. MDMA causes serotonin vesicles in the neurons to release quantities of serotonin into the synapses. The effects of ecstasy depend on the strength of the dose, the physiology of the user and their state of mind at the time of taking the drug. Generally some of the immediate effects of ecstasy include: Feelings of confidence, happiness and benevolence, Accelerated heart rate and breathing, Rise in blood pressure, Sweating and dehydration, Nausea, Jaw clenching and teeth grinding, Loss of appetite, Hallucinations, An increased urge for sex, Loss of inhibitions. Acute dehydration is a risk among users who are highly physically active and forget to drink water, as the drug may mask one’s normal sense of exhaustion and thirst. In high doses, ecstasy can cause seizures and vomiting. The symptoms of overdose include a sharp rise in body temperature and blood pressure, dizziness, cramps, heart palpitations and vomiting. Ecstasy can cause death in a number of ways, including: Cardiac arrest, Stroke, Kidney failure, Overheating (hyperthermia) and dehydration, Dilutional hyponatremia, when the user ‘drowns’ their brain by drinking too much water.

1. Dancing in a warm room increases heat production, and thereby challenges the body’s thermoregulatory system. Draw a negative feedback loop to illustrate how Betty's body copes with this thermal stress without allowing her body temperature to rise. Include at least 3 effectors that help to increase heat loss. (Hint: you can include behavioral effectors as well as physiologic ones)

The following figure is a negative feedback control loop of body temperature. Physiologic factors of temperature control are sweating and vasodilation of skin blood vessels, leading to excess heat released to the environment. Behavioral factors are cessation of activities which lead to heat production (e.g. exercise, etc.) and reduction of the ambient body temperature (e.g. removing clothes, finding a cooler place, etc.)
2. The use of Ecstasy altered Dottie's ability to regulate her body temperature. Briefly describe two ways that Ecstasy alters the body's ability to thermoregulate. On the diagram that you drew in part A, indicate how each of these alterations influences this negative feedback system. (again, consider behavioral effects as well as physiologic ones)

Ecstasy affects the hypothalamus causing brain hyperthermia. In addition, the adrenergic effects of ecstasy cause vasoconstriction of the blood vessels of the skin and vasodilation of vessels to the muscles. Also, the increase in heart rate increases the heat produced by the heart muscle. Ecstasy can impair judgment and also mask the symptoms of hyperthermia. This leads to engagement in increased physical activity and disregard of behavioral patterns leading to reduction of body heat. In addition, the impairment in judgment can lead to reduced water intake, dehydration, reduction of seating and therefore further increase in body temperature.
3. Based on the information given above, what do you think is wrong with Dottie? What kind of treatment would you recommend for her? How could the club owners prevent this kind of health emergency?

Based on the information given above Dottie is suffering from hyperthermia (which will become malignant hyperpyrexia if the temperature exceeds 107°F) and dehydration.

While still at the club, her friends and/or the club personnel should
a. Seek medical health immediately
b. Make sure that she is still breathing and administer CPR (cardiopulmonary resuscitation) if needed and if someone there is trained to perform CPR
c. Reduce Dottie’s body temperature by moving her to a cooler, well ventilated place, removing excess clothing and using cold water or icepacks.
d. If she is unconscious (which she is) they should NOT attempt to give her anything by mouth.

The medical personnel (on the ambulance and the hospital) will also probably
e. Administer oxygen
f. Re-hydrate with IV (intravenous) fluids
g. Run tests to exclude other causes of hyperthermia
h. Monitor kidney function (kidney failure is a major consequence)
i. Counsel and educate the patient regard the use of illegal drugs

The club owners could adopt policies to reduce the use of illegal drugs on their premises and take steps to minimize the health risks of such drugs. Actions might include:
j. Provide free and accessible cold drinking water.
k. Have adequate ventilation and/or air conditioning.
l. Have a separate chill-out room with comfortable seating.
m. Don’t overcrowd your venues. Take steps if areas get too crowded.
n. For indoor events, provide secure and efficient coat check services (coats increase heat stroke potential).
o. Have at least one staff member present who is trained and qualified in basic first aid.
p. For parties over 500 people, have present a licensed and equipped EMT or paramedic on duty.
q. Have a private medical room or tent where emergency cases can be dealt with.
r. Make available free harm reduction literature about drug use, safer sex, driving home safely, preventing heat stroke, and other safety issues. (You can order literature directly from DanceSafe.)
s. Allow harm reduction organizations free entry to distribute literature and provide drug abuse prevention services.
t. Have a clearly displayed policy about searching.
u. Maintain the right to search patrons’ outside clothing, pockets and bags.
v. Don’t allow entry to any patron who refuses to be searched.
w. Enforce age limits when applicable.

4. If Dottie and Betty had decided to skip the rave and rent a video instead, do you think that Dottie’s body temperature would have been higher than normal (assuming that Dottie still took the Ecstasy tablet). Why or why not?

Since ecstasy causes brain hyperthermia, skin vessel constriction and increased heart rate, it is most likely that Dottie’s temperature would have been higher even in the setting of watching a DVD. However, it is unlikely that it would have reached the same levels as at the rave party, since the other aggravating factors would have been absent (i.e. dancing, hot room, lack of hydration, etc)

Case 2 – Grandma can't hear you

An 81 year old woman was admitted to the Royal Gwent Hospital with severe shortness of breath. She had a history of chronic obstructive pulmonary disease (COPD), angina, hypertension, and a
previous cerebrovascular accident. She was sensitive to penicillin. She was diagnosed with pneumonia and was started on nebulisers and clarithromycin (a macrolide antibiotic). On day 3 of her admission she complained of new onset deafness in her right ear. She stated that she had been deaf, in her left ear, for many years but had had no prior problems with her right. Her testimony was supported by her family who reported a subjective reduction in her hearing over the first two days of her admission, so much that they had to shout to be heard.

Clarithromycin is one of the advanced generation macrolides. It is used commonly as a broad spectrum antibiotic, often in conjunction with a penicillin type antibiotic, for community acquired pneumonia or for patients who are penicillin sensitive (as in this case). It is an erythromycin derivative with slightly greater activity than its parent compound and achieves high tissue concentrations. Macrolides have been investigated for ototoxicity. The conclusion was that there is the possibility of mainly reversible sensorineural deafness which is dose related. Interestingly, in cases of macrolide induced deafness, the deafness occurs around the frequencies used for everyday speech, hence making it easier for patients to detect changes in hearing.

1. **Describe the sensation of sound from the outer ear to the cortex.**

   External Ear (Sound enters the meatus) → Tympanic membrane (Vibrates when struck by sound waves) → Middle ear (Transfers vibrations through ossicles (malleus, incus, stapes) to oval window) → Cochlea (Sound dissipates) → Organ of Corti (Mechanically gated channels convert sound to graded potentials and then chemical signals at the synapse) → Neurons of the auditory nerve → Brain stem (Signals cross over to opposite site and create reflex synapses) → Thalamus (Sorts and relays signals to cortical regions) → Cortex (Higher processing)

2. **Which parts of the sensorineural pathway could these antibiotics affect? List all possible locations you think might be involved!**

   There many possible mechanisms which are postulated to explain this phenomenon. Elevated levels of antibiotic could affect
   - Organ of Corti (Interfere with function or destroy the hair cells (cell death))
   - Auditory nerve (Inhibit normal AP initiation and transmission)
   - Central auditory pathways in the central nervous system (Inhibit neuronal activity or synapses (probably the least likely))

3. **Given that the hearing impairment is mainly at higher frequencies which part of the Organ of Corti should be most involved?**

   Narrow, stiff end of the basilar membrane near the oval window.

4. **If the ototoxicity is a result of neuronal effects of the antibiotic, what mechanisms might affect the creation of action potentials by the auditory nerve?**

   - Interfere with mechanically-gated channels (block, destroy, cross-link to adjacent membranes, etc)
   - Block synaptic transmission (block synthesis or release of neurotransmitter, enzymatic metabolize neurotransmitter, block receptor, etc)
   - Block initiation of APs in the postsynaptic neuron (block ion channels)

5. **What possible interventions could help a patient with permanent sensorineural hearing impairment?**

   Hearing aids may have some effect (if some hair cells are still functioning) but it will, most likely, be limited. Cochlear implants, which are electrical devices stimulating the auditory nerve directly, might help. Social interventions (e.g. lip reading and lifestyle adjustments) also help cope with sudden hearing loss.
Case 3 – A stiff baby

Baby boy Borne Steeff was a full-term healthy baby born in a rural region of a developing country. He was delivered at home after a short and uneventful labor. The woman assisting the delivery cut the baby’s umbilical cord with an unsterilized instrument and, as was customary in the area, dressed the cord with a paste made of clay. Borne was vigorous and nursed well. On his sixth day of life, however, he became unusually irritable. He cried a lot. He had trouble sucking from the breast and swallowing milk. Over the next few days, he became stiff. He suffered spasms that contracted muscles all over his body. His alarmed parents took Borne to the nearest health clinic. By then his body was completely rigid and his back was arched. He was so stiff he could be supported by one hand under his head and another under his feet. His grieving parents were told that nothing could be done. Soon, Borne stopped breathing and died.

Although no formal diagnosis was made in this case, the signs were quite consistent with neonatal tetanus, a familiar disease in developing countries, and one that is completely preventable with good medical care. The bacterium which causes tetanus, Clostridium tetani, enters the body through a cut or wound. Once in the body, it grows and produces a potent and deadly toxin which travels along peripheral nerves to the central nervous system. There it interferes with normal synaptic transmission to the motor neurons resulting in skeletal muscle spasms.

1. **What process characteristic of neurons could transport tetanus toxin to the CNS?**
   Transport of the tetanus toxin is by reverse axonal transport from the motor axon terminals to the spinal cord.

2. **What is the significance of the concept of the "final common pathway" as it relates to somatic motor neurons?**
   Somatic motor neurons are called the "final common pathway" because all neuronal input to the skeletal muscles must be conducted along these neurons. The pattern of action potentials transmitted along the motor neurons is determined by the net effect of stimulatory and inhibitory synaptic input to these neurons. In effect, these neurons sum all their synaptic input to determine the final output in the form of action potentials to the muscles.

3. **Considering the muscle spasms characteristic of tetanus, how is the toxin likely to affect neurotransmitters acting on the motor neurons?**
   The spasms indicate that the muscles are somehow being over-stimulated. If the effect is at the synapses converging on the spinal motor neurons, it is likely that the toxin either causes too much and uncontrolled release of stimulatory neurotransmitters or blocks release of inhibitory neurotransmitters. In fact, it is known that tetanus toxin blocks the release of inhibitory neurotransmitters (namely glycine and/or GABA) so there remains an over-balance of stimulatory input causing the uncontrolled tetanic contractions.

4. **What finally causes death in tetanus?**
   Death is finally caused by paralysis of the respiratory muscles (intercostals and diaphragm).

5. **What is the difference in the use of the word "tetanus" as a disease, and as a phenomenon associated with normal muscle physiology?**
   The word tetanus can be used for the disease discussed here, and it can also describe a normal phenomenon of muscle contraction. In the latter case, it is a sustained, smooth contraction caused by the fusion of individual twitches. It occurs when a muscle is stimulated so rapidly that it is not able to relax at all before the next stimulus. Because widespread and uncontrolled tetanic contractions are characteristic of the disease, the name "tetanus" was used.