4.1 Problem Set
Nerve Conduction

1. Renshaw (*J. Neurophys.* 3:373–387, 1940) provided an ingenious method for estimating the time of synaptic delay in the spinal cord. He stimulated the intermediate gray of the spinal cord with successively larger stimuli and recorded the output of the ventral root. A schematic of his experimental set-up and results are shown in Figure 4.PS1.1. *Recordings were performed using extracellular electrodes*. A postulated schematic of the neuronal "wiring diagram" is provided to help you think about this. With successively larger stimuli, more and more of the cord interneurons, and eventually the motoneurons, were excited, as indicated by the dashed lines in the neuronal wiring diagram.
   A. Explain the origins of peaks S, T, and M in the record.
   B. Why does S decline as M increase?
   C. Estimate the synaptic delay from the traces.

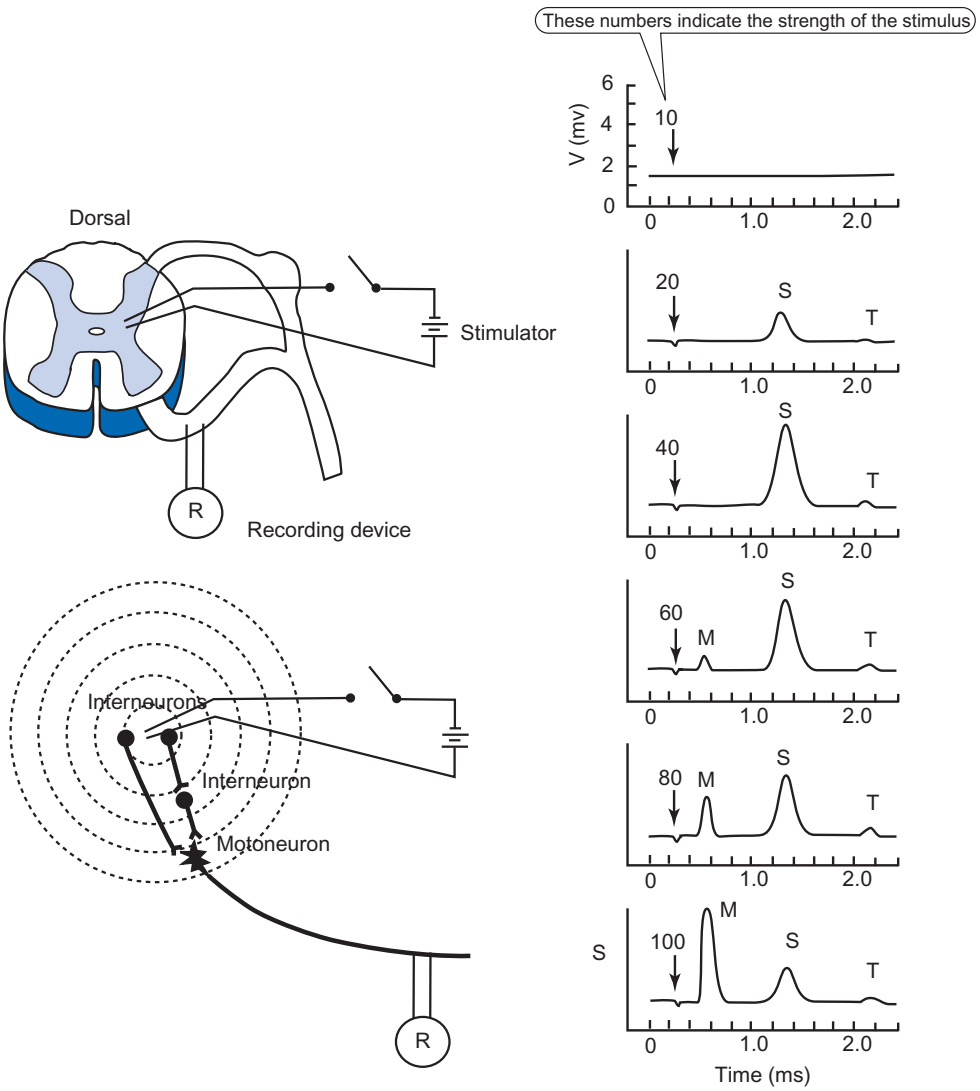

FIGURE 4.PS1.1

DOI: http://dx.doi.org/10.1016/B978-0-12-800883-6.00038-0

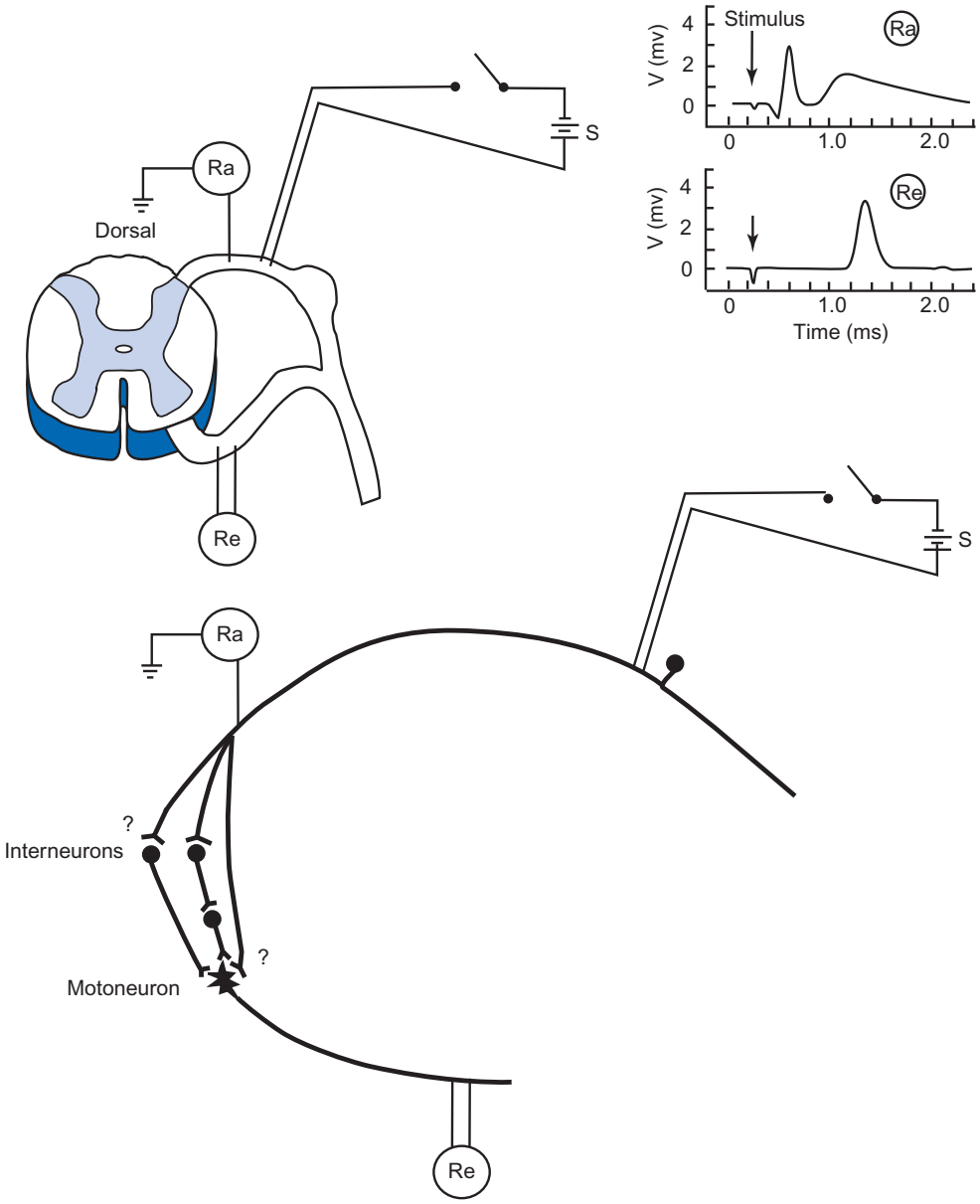

FIGURE 4.PS1.2

2. Renshaw also set up the experiment shown in Figure 4.PS1.2, in which the dorsal root was stimulated weakly (which stimulates the Ia afferents) and the resulting electrical activity was recorded in the dorsal root entry zone and in the ventral root. The results are shown at the top right of the figure, where Ra represents the afferent root (sensory) and Re indicates the efferent root (motor). Explain how this result, coupled with that of problem 1, allowed Renshaw to conclude that the Ia afferent reflex was monosynaptic.
3. The **Hoffman reflex** refers to the reflex contraction of a muscle caused by stimulation of the nerve. The experimental set-up is shown in Figure 4.PS1.3. The muscle contraction is monitored by electromyography (EMG). An example of the EMG response is given. The Ia fibers in the nerve have a lower threshold for activation than do the motor axons, and so the EMG recording depends on the magnitude of the stimulus. At low stimulus strengths a pure H-reflex is recorded, with no M-wave. As the strength of stimulus increases, motor axons supplying the muscle are excited and two distinct responses are recorded, the H-reflex and the M-wave. As the stimulus strength increases still further, the H-reflex progressively is extinguished. From the "wiring diagram", deduce why the H-wave disappears at high stimulus strength. Hint: stimulation of a nerve in its middle conducts **orthodromically** (toward its normal terminal) *and* **antidromically**—in the opposite direction toward the cell body.
4. The International Olympic Committee has approached you for help in making sprint races fair. In these races, sprinters are started by three commands: "On your marks," "Get set," and

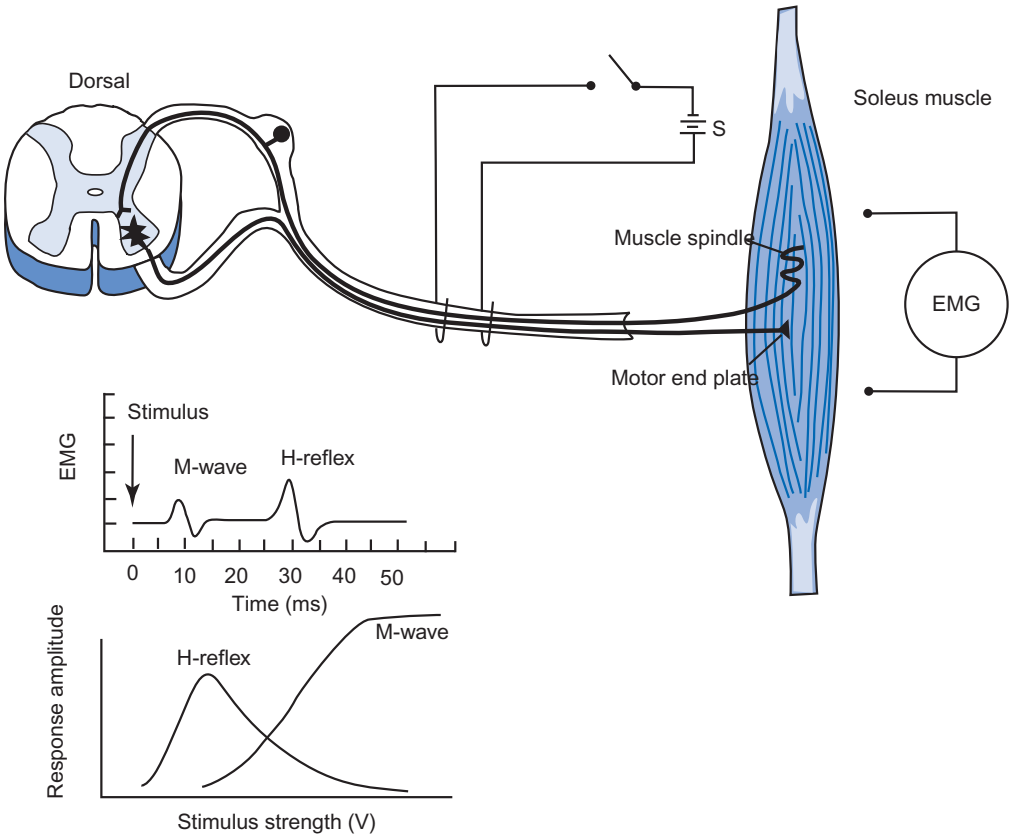

FIGURE 4.PS1.3

"Blam!" A blank pistol report starts the runners. Winners of these races are often determined by a scant hundredth of a second, or 10 ms, over the course of 100 m. The slightest advantage by a sprinter can mean victory. If a sprinter anticipates the gun, just slightly, he can win the race. In an unfair race, when a runner starts before the gun, the race is stopped by a second blank pistol report. The field is allowed one false start, and the next false start results in the disqualification of the runner who first begins. The IOC wants an automatic determination of when a false start occurs, and their question to you is: what is the minimum reaction time for a sprinter to come off the blocks *after* hearing the pistol report? How would you determine this reaction time? Knowing what you do about the pathways involved, synaptic delays, and propagation velocities, estimate the minimum reaction time.

5. Estimate the time of diffusion for a neurotransmitter across a 100-nm synaptic gap using the equations developed in Chapter 1.6.
6. A typical standard for military hikes is about 4 miles per hour with 30 in. strides. This is *not* double-time, but it is a rigorous pace. It may not seem like much, but it is harder than it sounds.
   A. Estimate the frequency of foot strikes.
   B. The definition of walking as opposed to running is that there is always contact with the ground. Estimate the duty cycle (the fraction of time that is active) for the gastrocnemius muscle (the calf muscle) during the hike.
   C. Based on your answer to 6A and 6B, what do you suppose the action potential train to the gastrocnemius muscle looks like?
7. Suppose that a vesicle 100 nm in external diameter, with 10 nm wall thickness, contains 10,000 molecules of neurotransmitter. It dumps its neurotransmitter into a cleft 50 nm wide and 500 nm in diameter.
   A. What is the concentration, in molar, of neurotransmitter inside the synaptic vesicle?
   B. What is the concentration, in molar, of neurotransmitter in the synaptic cleft assuming that it becomes evenly distributed and there is no degradation?
8. When you roll down a long hill, and then try to stand immediately upon reaching the bottom, you discover that you are dizzy. Why?
9. You are seated on a rotating chair, and your pals quickly rotate you to your right for about 20 s, and then stop you. They get a chuckle out of watching your eyes move slowly to one side and then being rapidly reset, a condition called **nystagmus** (from the Greek "nod" because it resembles the nod when one falls asleep, the slow phase as the head drops and a quick phase as it is snapped back to an erect position). The slow phase is part of the vestibulo-ocular reflex and brain stem circuits generate the quick phase. What causes this slow phase, and in what direction does it occur?
10. A diagram of the dermatomes is shown in Figure 4.PS1.4. These are areas of the skin that

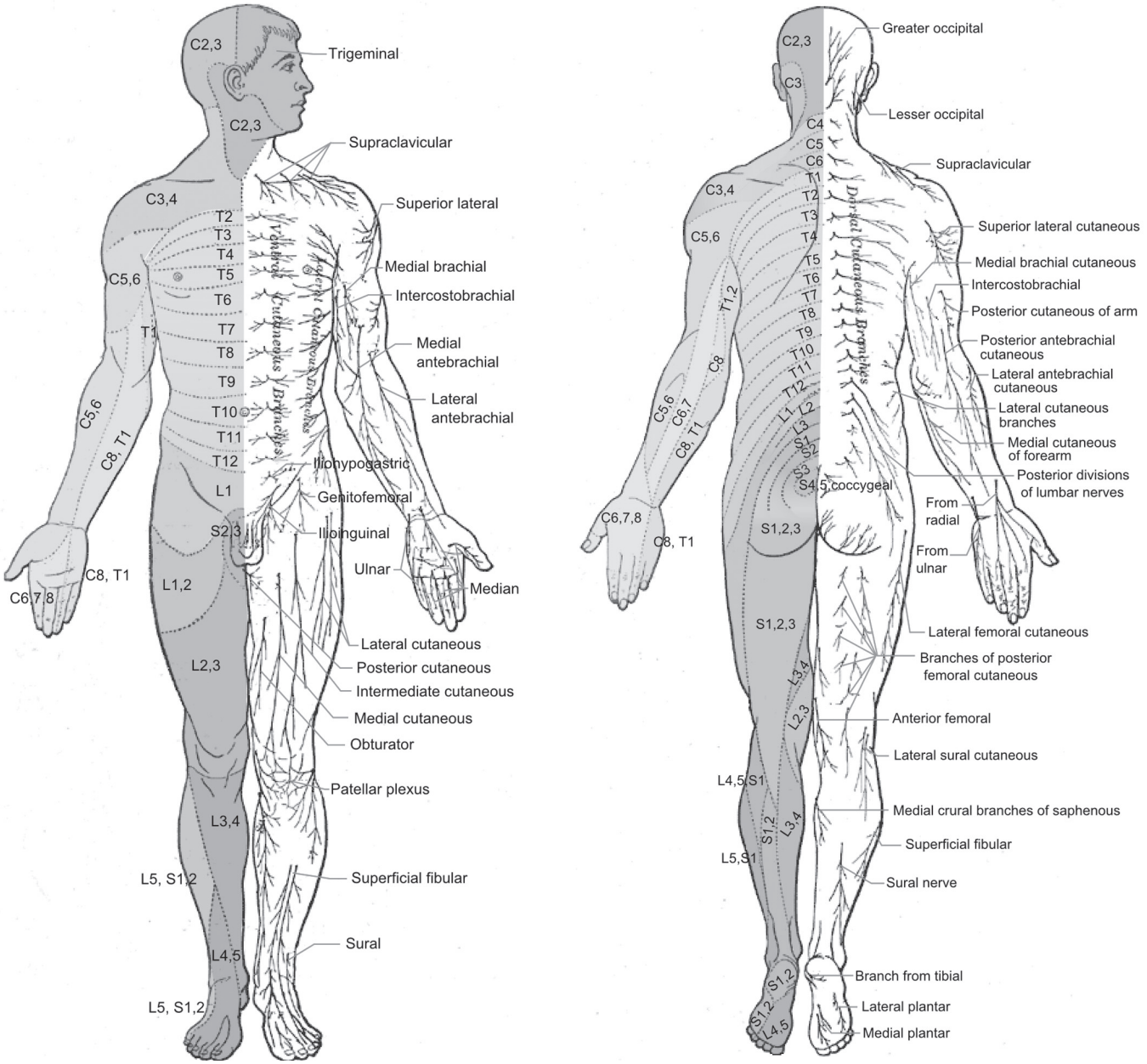

FIGURE 4.PS1.4 Dermatomes.

are innervated by the indicated spinal nerves. The myotomes are muscles that generally lie under the corresponding dermatomes.

A. Your friend took a nasty spill playing intramural soccer and now complains of loss of sensation in his left shoulder. What might cause this?

B. Another friend noticed the other day that his left foot sort of flaps along when he walks and he has trouble lifting the foot and cannot walk on his heels, but only on his left foot. What might cause this problem?

11. The Weber–Fechner Law uses what are called "just noticeable differences", or jnd. Persons were asked to determine the jnd for various sensory modalities. The just noticeable difference was the one that was identified 50% of the time. In this sense, it describes a threshold for sensory perception. The Stevens power law, on the other hand, asked people to rate the intensity of a their perception relative to some standard. The standard stimulus was assigned a number, the modulus, and all perceptions were given a number in proportion to that modulus. Thus, if a subject reported that the stimulus was twice the standard, its assigned number was twice the modulus.

A. For weight lifting, Stevens reports an exponent of 1.45 in his power law. Given an initial weight of 1 kg, at what mass would the perceived stimulus double?

B. At what weight would it double again (be four times as great as the 1 kg mass)?
C. What additional information is needed to compare the Weber–Fechner law to the Stevens power law?

12. Nerve conduction studies are performed to distinguish among several causes of sensory or motor deficits. These can take multiple forms. Motor nerve conduction studies stimulate motor nerves and record from the muscle innervated by the nerve. Sensory nerve conduction studies stimulate purely sensory portions of a nerve and record from proximal sections of the nerve.

    In the F-wave study, supramaximal stimulation of a nerve sends action potentials antidromically towards the ventral horn where a small population of motor neurons backfire towards the muscle, and the second small peak is measured at the site of stimulation. The distance is measured from the site of stimulation to the spinal cord and doubled because the nerve is conducted both ways, and this is divided by the latency, with 1 ms subtracted.
    A. The measured distance between the site of stimulation on the arm and the spinal cord was 85 cm, and the latency in the F-wave study was 30 ms. Calculate the nerve conduction velocity. Is this normal?
    B. The measured distance between the site of stimulation on the calf and the spinal cord was 145 cm, and the latency in the F-wave study was 50 ms. Calculate the nerve conduction velocity. Is this normal?
13. Botulinum toxin is produced by *Clostridium botulinum*, a gram-negative bacterium. The toxin actually consists of seven related toxins, types A, B, C1, D, E, F, and G. The toxin is synthesized as a protoxin of 150 kDa, which is proteolytically cleaved to a light (L) and a heavy (H) chain that remain linked by a disulfide bond. Nerve terminals have receptors for both L and H chains. The L-chain is transported across the nerve terminal membrane by endocytosis. These L chains are metalloproteinases—proteases that require metal ions for activity. The L-chain binds Zn^{2+}, and it proteolytically degrades several proteins that make up the SNARE complex.

    What do you suppose happens when botulinum toxin is injected near neuromuscular junctions?

    From this conclusion, what do you suppose is the basis for botox injections?
14. The two-point discrimination test generally gives a discrimination of 2–4 mm on the lips and finger pads, 8–15 mm on the palms, and 30–40 mm on the shins or on the back. What are the approximate relative densities of cutaneous touch receptors in these regions?
15. A muscle strain is a tear in the muscle fiber or associated tendons. The tear or damage to ligaments is called a sprain. It is usually caused by stretching of the muscle while it is contracted through the antagonistic muscles.
    A. Would you expect the Golgi tendon organ to prevent muscle strains?
    B. Given that the distance from the hamstring neuromuscular junction to the spinal cord is 50 cm, what is the expected delay in response of the Golgi tendon organ?