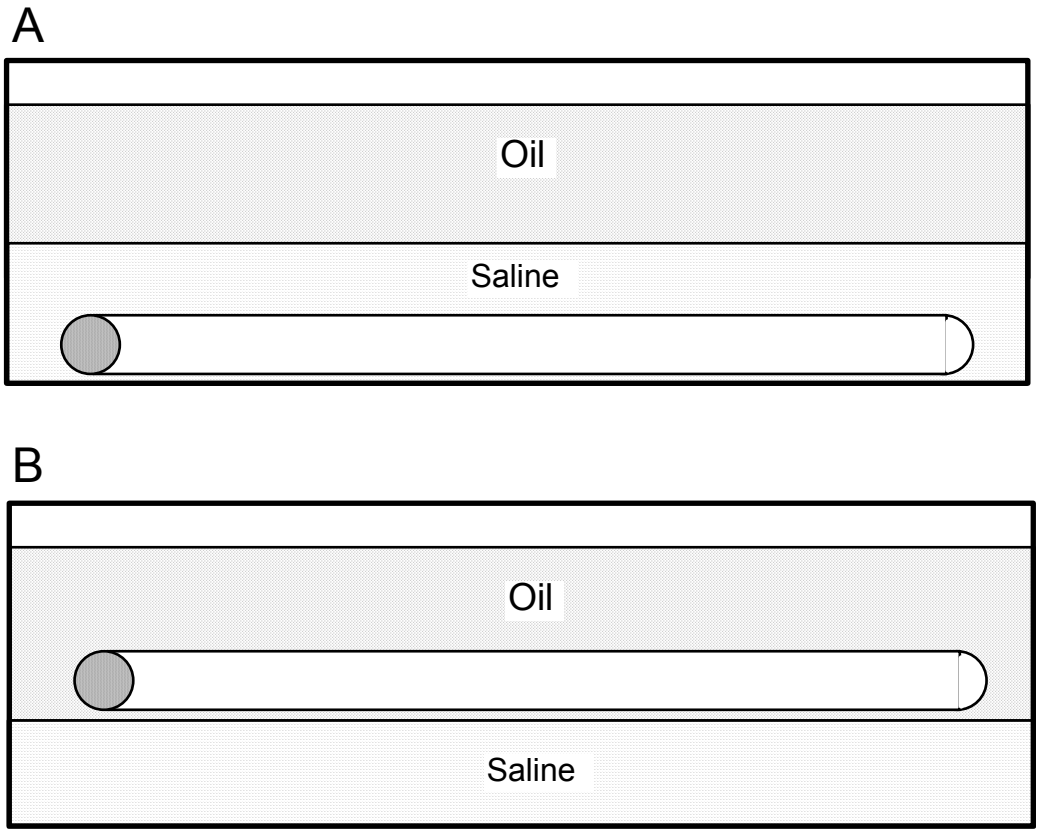
MEDICAL & GRADUATE STUDENTS ONLY

Neuroscience Course Conference – 2003

Please read these questions and think about them before the conference on "Cellular Neurophysiology". *Do not get upset* if you cannot answer some of the questions. They are meant to serve as discussion points that will lead you to a better understanding of the material.

1. When an isolated (non-myelinated) axon was placed in bath of saline and stimulated, it conducted action potentials at 90 m/sec (A). When the same nerve was then placed in mineral oil (B), only a thin film of saline clung to the hydrophilic sheath of



connective tissue surrounding the nerve. Under these conditions, conduction velocity was reduced to 50 m/sec.

a. What might have caused this slowing?

b. The passive spread of current that propagates the action potential flows not only ahead of the axon, but also behind it. Why doesn't it re-excite the axon and trigger repetitive firing?

2. In demyelinating syndromes such as multiple sclerosis, an action potential propagating into a demyelinated zone from a normally-myelinated zone may fail.
   a. What could cause this failure?
   b. What type of drug might you try to overcome this conduction failure?
   c. What might be the side effects of such a drug?

3. Although g_{Na} increases as a graded function of membrane depolarization (Fig. 9-6 of textbook), the action potential has a discrete voltage threshold. Why?

4. When we inject current into the cell with an electrode to cause a depolarization, we say we are passing an **outward** membrane current. On the other hand, during the rising phase of the action potential, we say that the **inward** current that flows through the voltage-gated Na^+ channels is depolarizing. In both cases we are depolarizing the cell, so why do we call one current inward and one outward?

5. During epileptic seizures, massive synchronous bursts of activity in cortical neurons cause changes in the extracellular concentrations of K^+.
   a. Why is the $[K^+]_o$ concentration more likely to change significantly than the concentrations of $[Na^+]_0$ and $[Cl^-]_o$.
   b. What effects might changes in $[K^+]_0$ concentration have on the excitability of cortical neurons?

6. You examined a patient who exhibited neuromuscular weakness. A small sample of intercostal muscle with the attached nerve trunk was removed for biopsy. You found that the end-plate potentials were sub-normal in amplitude but the miniature end-plate potentials were normal in amplitude.
   a. Do you think the primary defect in neuromuscular transmission has a presynaptic or a postsynaptic locus?
   b. What physiological or biochemical tests would you perform to determine the precise cause of the deficit in transmission?
   c. What general type of pharmacological agent might you try to generate symptomatic relief of this syndrome? Why?

d. How would you expect the electromyogram (EMG) of such a person to behave in response to tetanic stimulation of a motor nerve? (The EMG is an extracellular recording of the entire population of individual muscle fiber action potentials.)

7. You have discovered a new neurotransmitter that causes depolarization of motoneurons. You found that application of the transmitter causes Ca^{++} elevation in the neuron. Using a voltage clamp and an intracellularly-injected dye that fluoresces when it binds Ca^{++} ions, how could you localize the source of this Ca^{++}.

8. A dominant mutation in the gene that encodes the α-subunit of the voltage gated Na^{+} channel in skeletal muscle has been shown to cause the mutant channels to have defective inactivation gates. In a heterozygote, approximately half of the channels are normal and the other half are in the mutant form. The mutant channels are normal, except that at any given time about 6% of them will not inactivate as quickly as they should. As a result, they will stay open longer during and following an action potential. Although only 3% of all the sodium channels (mutant plus wild type) are defective in gating, people expressing the mutant genes may have severe clinical symptoms. How can such a tiny minority of channels have such a large effect?

9. Skeletal muscle myotonia caused by Cl^{-} channel mutations generally has more severe symptoms in recessively-inherited homozygotes than in dominantly-inherited heterozygotes. Can you speculate as to why that might be so?

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http://www.neuro.wustl.edu/neuromuscular/