

ES/RP 531
Fundamentals of Environmental Toxicology

Lecture 12
Neurotoxicity
Part I

Context: Why Study Neurotoxicity?

- The pharmacodynamic action of most insecticides is at the level of nerve function
- The ultimate biochemical receptors are at different sites of the nerve cell
- Some insecticides are extremely persistent in environment and in tissues
 - These are banned from commercial use but residues still bioaccumulate in the food web
- Modern insecticides are easily biodegradable in the environment and easily metabolized
 - But a number of commonly used insecticides have very high acute toxicities against nontarget invertebrates, aquatic and terrestrial vertebrates

Context: Why Study Neurotoxicity

- In addition to the historical issues of neurotoxic insecticides and acute toxicity to birds and fish, concerns about neurodevelopmental toxicity have grown
 - Indeed, these have been addressed for humans in the Food Quality Protection Act of 1996, a major amendment to the Federal Insecticide Fungicide Rodenticide Act (FIFRA)
- Historical concerns over neurotoxicological effects of lead and mercury
- New concerns over potential neurodevelopmental effects of PCBs and PBDEs

Nerve Physiology

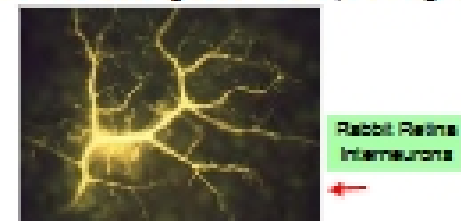
- Nerve function is remarkably conserved across both invertebrates and vertebrates
 - Earliest knowledge of how nerves work came from experiments using the squid giant axon, which was several mm in thickness
- Thus, toxicants that act at the level of the nerve can potentially have adverse effects across a wide spectrum of organisms

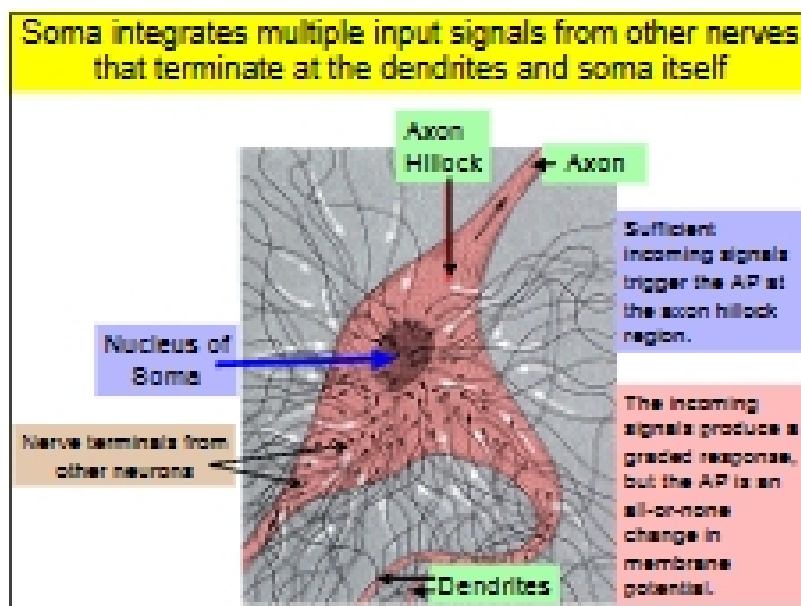
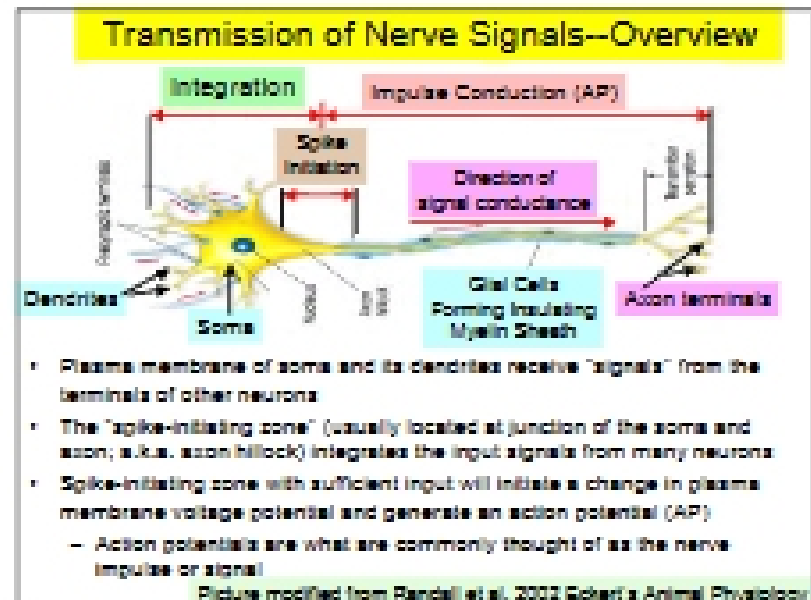
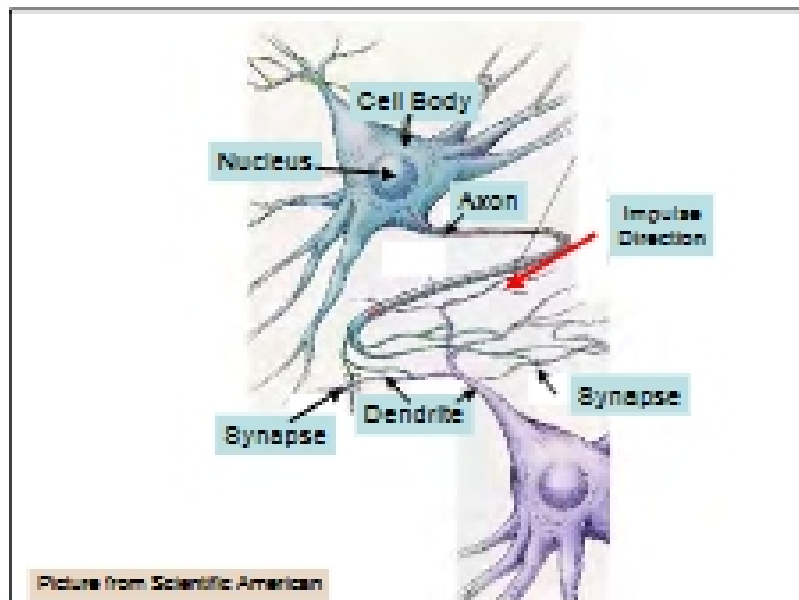
Introduction to Nervous System & Nerve Physiology

- Rapid coordination in the body
- Electrically excitable cells (neurons)
- Generate electrical signals long distances without degrading strength of signal
- Function similarly among all animals
- Basic structure
 - Soma (cell body; contains nucleus; metabolic maintenance of cell)
 - Dendrites (receive & carry signal toward soma)
 - Axons (carry signal away from soma)
 - Supporting cells (for ex., myelin sheath)

Organization of Nervous System

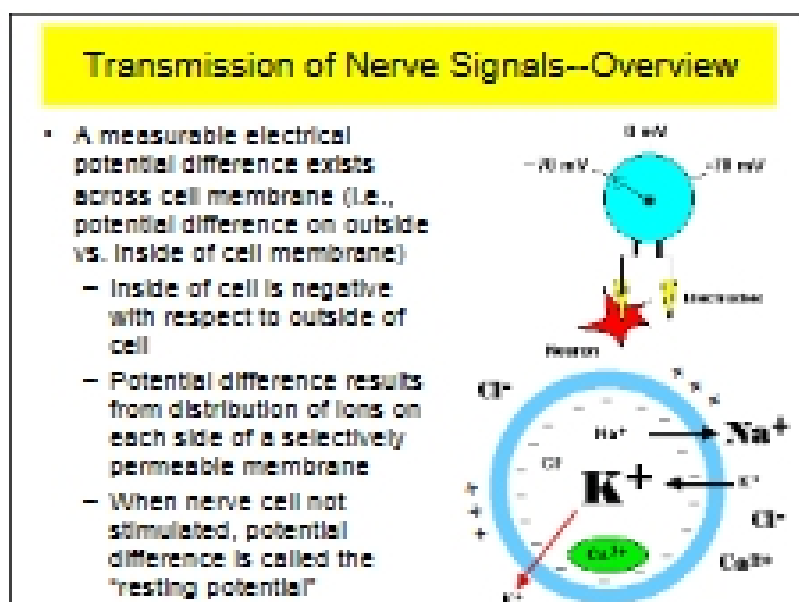
- Sensory neurons
 - Transmit information collected from external stimuli
 - Respond to stimuli inside body
 - For ex., blood oxygen level, position of a joint, orientation of the head
- Interneurons
 - Link other neurons within the central nervous system
 - Networked to exchange information and perform complex "computations" leading to behavior (or thought)





Nerve Signal (Impulse) Conduction

- Because of the synapse, nerve signals only travel one direction down the axon
 - Nerve signal is actually an electric current that moves along the axon until it reaches the synapse, which separates the axon and the dendrite
- Ability to conduct electrical current is due to two factors:
 - Membrane electrical potential
 - Permeability of the membrane to ions



Membrane Potential

- Charge separation or potential difference across the membrane inside surface (the cytoplasm or axoplasm side) and the outside surface (actually the space in between the cell membrane and the myelin or the cell membrane and the blood)
- Inside is negative with respect to the outside
 - The electrical potential prior to nerve signal conduction is called the membrane resting potential
 - Resting potential value: ~ -70 mV