Bio 240 Neurobiology  
Chapter 2 Neurons and Glia

I. Introduction
   A. The brain is the most sophisticated and complex organ.
   B. There are two primary types of cells in the brain: Neurons and Glia
      1. Neurons
         a. 100 billion in brain
         b. Neurons are the basic functional unit of the brain
         c. Perform the bulk of the information processing.
            (1) Sense the environment, communicate with other neurons and command the
                body’s response to sensation.
      2. Glia
         a. 10X as many Glia compared to neurons
         b. Play a supportive role to Neurons
            (1) Insulate, support and nourish neighboring neurons.
         c. The role of Glia in the brain is just beginning to emerge.

II. The Neuron Doctrine
   A. Obstacles to studying the brain
      1. Small size (10 to 50 um in diameter)
         a. Almost no progress was made until the development of the compound microscope
      2. Thin slices necessary to use microscope
         a. Brain is like slicing Jello: not firm enough to make thin slices
         b. *Brain fixation techniques* had to be developed.
            (1) *ie.* Formaldehyde
         c. *Microtome* had to be developed.
      3. Introduction of Stains
         a. Franz Nissl (Nissl Stain)
            (1) Stained nuclei and nissl bodies (RER)
            (2) Distinguished neurons from Glia
            (3) Enabled the study of cytoarchitecture.
               (a) Identification of specialized regions in the brain.
         b. Limitation - only shows the soma of the neuron.
   B. The Golgi Stain
      1. Developed by Camillo Golgi (1873)
      2. Uses a silver chromate solution
      3. Stains a small percentage of neurons in their entirety.
      4. Revealed that the cell body is only a small part of the neuron.
      5. Golgi stain revealed neurons have at least two parts
         a. Cell body or soma (pl. somata) or perikaryon (pl. Perikarya)
         b. Neurites: two types
            (1) Axons
               (a) Single
               (b) uniform in diameter
               (c) branches at right angles
               (d) may extend over great distance.
            (2) Dendrites
(a) rarely extend more than 2 mm.
(b) receive input.
(c)  

C. Cajal’s contribution
1. Santiago Ramon y Cajal used the Golgi method to produce a remarkable series of publications
   a. Golgi argued for the reticular theory that neurons are continuous
   b. Cajal that neurons communicate by contact not continuity (neuron doctrine)
2. Cajal and Golgi remained rival although they share a Nobel prize in 1906.
3. Final proof of the neuron doctrine wasn’t discovered until the advent of the electron microscope in the 1950's.

III. The Prototypical Neuron
A. Soma
1. Most ~ 20 um in diameter
2. Surrounded by a neuronal membrane
   a. selectively permiable
   b. Separates internal structures from the extracellular environment
   c. Participates in intercellular communication.
3. Cytosol
   a. aqueous content between nucleus and cell membrane -
   b. high in potassium
4. Contains organelles
   a. subcellular structures within the cytoplasm
B. Nucleus
1. Stores genetic information determining structure/function of cells by regulating sequences of amino acids.
2. Structures
   a. Nucleus is a prominent structure within the cell (diameter of about 5 μm).
      (1) Large membrane bound structure.
      (2) Usually located near the center of the cell.
   b. Nuclear envelope is a double membrane that separates nucleoplasm from cytoplasm.
   c. Nuclear pores (100 nm) fusion of inner and outer nuclear envelope which permit passage of molecules into or out of the nucleus.
   d. Nucleoplasm is semifluid medium of nucleus; has a different pH from cytosol.
   e. Deoxyribonucleic acid (DNA) and associated proteins are dispersed throughout the nucleus.
      (1) DNA content of each cell in the body is the same.
      (2) Genes are expressed differently in each cell.
         (a) DNA in each gene codes for a specific protein.
         (b) DNA never leaves the nucleus-
         (c) DNA - RNA - protein (Transcription / translation)
         (d) Proteins are made of amino acids
   f. DNA is found in one of two forms:
      (1) Chromatin is a threadlike material made up of DNA, proteins called histones, and some RNA
Chromosomes are rod-like structures formed during cell division; made up of coiled or folded chromatin.

Nucleolus are dark-staining spherical body in nucleus;

The subunits of ribosomes are manufactured within the nucleolus.

Ribosomal RNA joins proteins to form ribosomes (ribosomes are important components in protein production.)

Endoplasmic Reticulum (ER)

1. **Structure:**
   a. broad flattened interconnected system of membranous channels.
   b. continuous with outer membrane of the nuclear envelope.
   c. interior space is called cisternae and is isolated from the rest of the cytoplasm.

2. **Two types:** Rough ER and Smooth ER
   a. **Rough ER** (Nissl bodies)
      1. **Structure:**
         a) studded with ribosomes;
      2. **Function:**
         a) protein synthesis and modification
         i) for secretion or internal use
         ii) Free and polyribosomes.
            a) - destination of proteins
         b) Cells with abundant rough ER generally synthesize large amounts of proteins.
            i) neurons have vast amounts of RER
   b. **Smooth ER**
      1. **Structure**
         a) lacks ribosomes and is continuous with rough ER
      2. **Functions:**
         a) Site of protein folding into membranes.
         b) lipid and carbohydrate synthesis (ie. Phospholipids, steroids, cholesterol, -- glycogen)
            i) cells that produce large amounts of lipids generally have an extensive sooth ER.
         c) detoxification
            i) - enzymes within the SER act on chemical sand drugs to change their structure and reduce toxicity,
         d) storage
            i) - calcium in muscle cells, excess proteins/lipids
         e) Forms transport vesicles.
            i) transport vesicles carry proteins etc to either the Golgi apparatus or the plasma membrane

Golgi apparatus

1. Named for Camillo Golgi who discovered it in cells in 1898.
2. **Structure:**
   a. Flattened membranous saccules containing cisternae
   b. Stacked like dinner plates (3-20 deep).
3. **Function:**
a. Receives protein-filled or lipid filled vesicles that bud from the ER.
b. Modification of proteins and lipids
   (1) Carbohydrates are added making glycoproteins and glycolipids
c. Concentration and packaging of molecules into vesicles.
   (1) Vesicles pinch off from the margins of the outer face of the Golgi apparatus
d. Delivery of Vesicles containing modified proteins and lipids to:
   (1) Plasma membrane where proteins are secreted via exocytosis or incorporated into the plasma membrane.
   (2) Lysosomes - filled with enzymes that are used with the cell.
e. The golgi apparatuses are most numerous in cells that secrete large amounts of protein and glycoproteins.

E. Mitochondrion (pl. Mitochondria)

1. Structure
   (1) Double membrane organelle
      (a) membranes are separated by an intermembranous space.
      (b) outer is membrane is smooth
      (c) inner has numerous folds called cristaee
   b. Function: Major sites of ATP production
      (1) Energy source for most endergonic (energy requiring) chemical reactions within the cell.
      (2) Two major enzyme systems are responsible for ATP synthesis
         (a) Citric acid cycle (Kreb’s cycle)
             i) enzymes found in matrix (space inside the inner membrane).
         (b) Electron transport chain
             i) enzymes are embedded within the inner membrane.
      (3) Cells with high energy requirements have a higher number of mitochondria.
         (a) Mitochondria can divide as need increase
         (b) eg. muscle cells enlarge and need more ATP for contraction - increase in mitochondria number.
      (4) Mitochondria have their own DNA.

F. Neuronal membrane

1. The plasma membrane is the outermost component of the cell.
   a. Forms a barrier to prevent the loss of cellular material
   b. Extracellular - substances outside membrane
   c. Intracellular - substances within the cell or inside the cell membrane.

2. Functions:
   a. To enclose and support the cell contents.
   b. Determine what moves in and out of the cell.
   c. Recognition and communication with other cells.

3. Structure:
   a. 45-50% lipid; 45-50% proteins and 4-8% carbohydrates
   b. Lipid
      (1) Predominantly phospholipids and cholesterol
      (2) Phospholipids readily assemble to form a lipid bilayer
         (a) Polar (hydrophilic) head face outward
         (b) non-polar (hydrophobic) tail face inward.
(3) Cholesterol
(a) interspersed among the phospholipid bilayer
(b) makes up approx. 1/3 of lipid.
(c) lies within the hydrophobic region of bilayer
(d) determines the fluid nature of the membrane
   i) critical to its nature.

c. Fluid-mosaic model
   (1) The plasma membrane is neither rigid or static in structure
   (2) Cell membrane is highly flexible
   (3) Can change its shape and composition.
   (4) The lipid bilayer is a liquid in which proteins float.
   (5) Fluid nature important
      (a) slight damage is easily repaired. - phospholipids tend to reassemble.
      (b) means of distributing molecules in the membrane

d. Functions of plasma membrane are determined by its proteins
   (1) While structure comes mostly from lipid bilayer
   (2) Two types of membrane proteins
      (a) integral or intrinsic - extend from one surface to the other
         i) regions of hydrophobic a.a. - located within the hydrophobic
            region of the membrane
         ii) hydrophilic regions of a.a. - located at the inner or outer surface.
      (b) peripheral or extrinsic - attached to either the inner or outer surfaces of
         the lipid bilayer.
         i) usually attached to integral proteins.
   (3) Functions of membrane Proteins
      (a) Channel proteins
         i) integral proteins arranged to form a tiny channel through the
            membrane
      (b) Receptor molecules
         i) have an exposed binding site on the outer surface
         ii) bind to a specific ligand
         iii) part of an intercellular communications system
            a) ie. Nerves release chemical messages which travel to other
               nerves or muscles.
            b) binding of the chemical signal to the receptor acts as a
               signal that triggers a response.
      (c) Marker molecules
         i) mostly glycoproteins - proteins with carbohydrates attached.
         ii) allows cells to identify and attach to each other.
            a) cells must function together - communication is important.
   (4) Function of membrane proteins is dependent on 3 dimensional shape.
      (a) Channel can be opened or closed depending on the shape of the
          protein.
          i) ligand-gated channels - ligand binds to a specific site causing a
             change in the 3D structure of the channel protein causing it to
             open.
          ii) voltage-gated channels: open with a change in the voltage across
the cell membrane.

G. Cytosol
1. Consists of fluid portion, cytoskeleton, and cytoplasmic inclusions.
2. Fluid portion of cytosol
   a. Dissolves ion and molecules
   b. Forms a colloid with suspended molecules especially proteins.
   c. Many of these proteins are enzymes.

H. Cytoskeleton
   a. Cytoskeleton is a network of connected filaments and tubules; extends from
      nucleus to plasma membrane.
   b. Elements of cytoskeleton maintain cell shape, holds nucleus in place allow
      organelles to move.
   c. Elements can disassemble and reassemble in life of a cell.
   d. Three groups of proteins: microtubules, microfilaments, intermediate filaments

2. Microtubules
   a. Microtubules are small hollow cylinders (25 nm in diameter and from 200 nm-25
      μm in length).
   b. Microtubules are composed of a globular protein tubulin
      (1) alpha and beta tubulin form a dimer.
   c. Tubulin dimers assembly into tubes (13 tubulin dimers in circumference).
   d. Microtubule Associated Proteins
      (1) kinesin and dynein are motor molecules associated with microtubules.
         (a) kinesin proteins specialize to move vesicles or organelles
         (b) dynein is a protein that moves pairs of microtubules
      (2) tau
         (a) implicated in the plaques associated with Alzheimer’s disease.

3. Neurofilaments (Intermediate filaments)
   a. Intermediate filaments are 8-11 nm in diameter, between actin filaments and
      microtubules in size.
   b. They are rope-like assemblies of fibrous polypeptides.
   c. Provide mechanical support to cells.
      (1) Some support nuclear envelope, others support plasma membrane (eg. Nerve
          cells-thin and meter long.,
   d. form cell-to-cell junctions in desmosomes (eg. Keratin)

4. Microfilaments (Actin Filaments)
   a. Actin filaments are long, thin fibers (about 7 nm in diameter)
   b. Occur in bundles, sheets or mesh like networks.
   c. Actin filament consists of two chains of globular actin monomers twisted to form
      a helix.
   d. Actin filaments play a structural role,
      (1) forming a dense complex web just under the plasma membrane.
      (2) support the cell and determine the shape of the cell.
      (3) Changes in cell shape involve the breakdown and reconstruction of actin
           filaments.
   e. Muscle fibers have large numbers of highly organized actin filaments and myosin
      which are responsible for the contraction of muscle cells.
I. The Axon

1. Highly specialized for the transfer of information over the distances of the nervous system.

2. Two features distinguish it from the soma
   a. No RER, with few ribosomes (no protein synthesis)
   b. Membrane protein composition is very different

3. Structure
   a. Axon Hillock
   b. Axon may extend from less than 1 mm to over 1 meter.
   c. May branch in collaterals
      (1) sometimes return to communicate with the same cell forming a recurrent circuit.
   d. Diameter is variable
      (1) 1 um to 25 um
      (2) variation is size is important because size affects the speed of impulse conduction.
         (a) The thicker the axon the faster the conduction.

4. The axon terminal (terminal bouton, synaptic bouton)
   a. Site where the axon contacts other neurons
   b. Synapse (gk to fasten together)
      (1) point of contact between axon terminal and the post synaptic dendrite
   c. Axons often terminate in a terminal arbor
   d. Innervation - synaptic contact.
   e. Differences between axon and bouton
      (1) microtubules do not extend into terminal
      (2) synaptic vesicles are found in the bouton.(50 nm in diameter)
      (3) inner surface of synaptic bouton contains a dense covering of proteins
      (4) mitochondria - indicating high energy demand.

5. Synapse
   a. Structure
   b. Two sides
      (1) presynaptic (axon terminal) and postsynaptic (dendrite or soma of another neuron)
   c. Synaptic cleft - transfer of information across the synapse is called synaptic transmission.
   d. Electrical impulses are converted to the release of a chemical (neurotransmitter) which binds to post synaptic receptors
   e. Binding to the post synaptic receptors generates a new electric signal in the next neuron.
   f. Electrical to chemical to electrical transmission of information makes the brains computational properties possible.
      (1) modification of these processes makes memory and learning possible.
      (2) it also may account for many dysfunctions associated with mental disorders
      (3) site of most psychoactive drugs.

6. Axoplasmic transport
   a. Proteins are produced primarily in the soma.
   b. Must be transported along the axon
c. If cut the axon will degenerate (Wallerian degeneration)
   (1) used to trace axonal connections.
   (2) occurs because the normal flow of proteins is disrupted.

d. Paul Weiss demonstrated axonal transport
   (1) tied string around axon
   (2) observed accumulation of material at site
   (3) release string - material moved at 1 - 10 mm / day.
   (4) longest axon may require ½ year. (Slow axonal transport)
e. Protein transport
   (1) 1960s - labeled proteins with radiactivity
   (2) Bernice Grafstein - discovered fast axonal transport (1000 mm / day)
   (3) How does it work
      (a) anterograde trans - soma to terminal (kinesin - uses ATP to transport vesicles)
      (b) retrograde trans - terminal to soma. (Uses dynein)
   (4) Both mechanisms are used to trace connections in the brain.
      (a) Horseradish peroxidase (retrograde tracer)
      (b) many viruses are retrogradely transported.

J. Dendrites (gk tree)
   1. May be highly branched.
   2. Dendritic tree and dendritic branches
   3. Covered with thousands of synapses.
      a. Synapses contain receptors that detect neurotransmitters.
   4. Dendritic spines
      a. Thought to isolate chemical reaction that are triggered by synaptic activity
      b. Spine structure is sensitive to the type and amount of synaptic activation
      c. Unusual spine structures have been associated with cognitive impairments.
      d. Content is much like the cytoplasm
         (1) Oswald Stewart ( U of Virginia) showed that protein synthesis can take place in dendrites and can be altered by synaptic activity.

IV. Classifying Neurons
   A. There are billions of neurons in the brain. Each with a unique structure and function.
      Neurons can be categorized in an attempt to help us understand the unique nature of neurons.
   B. Classification Based on the Number of Neurites
      1. Unipolar
      2. Bipolar
      3. Multipolar
      4. Pseudounipolar
   C. Classification Based on Dendrites
      1. Dendritic trees / arborization vary dramatically
         a. Neurons are distinguished by the branching pattern of their dendrites
         b. In cortex – Pyramidal cells vs stellate cells.
      2. Classified by spine density
         a. Spiny (pyramidal cells an stellate)
         b. Aspinous (stellate)
   D. Classification Based on Connections
      1. Sensory - Primary vs secondary
2. Motor

E. Classification Based on Axon Length
   1. Long axons - Golgi type I or projection neurons (pyramidal cells)
   2. Short axons - local or Golgi type II axons (stellate)

F. Classification Based on Neurotransmitter
   1. Based on chemistry of neuron
   2. Ie. Type of neurotransmitters

V. Glia

A. Astrocytes
   1. Most numerous
   2. Regulate the chemical content of the extracellular space
      a. Restrict the spread of neurotransmitters
      b. Actively remove some neurotransmitters
      c. May supply neurotransmitters to the neuron or into the synapse
      d. Regulate the ion concentration
   3. Contain receptors for some neurotransmitters
      a. May trigger electrical or biochemical events in glia

B. Myelinating Glia
   1. Provide layers of membrane that insulate and speed conduction in the neuron.
      a. Layers of cell membrane wrap around the axon.
   2. Oligodendrocytes vs Schwann cells
   3. Nodes of Ranvier

C. Ependymal Cells
   1. Lining of fluid filled ventricles
   2. Produce CSF
   3. May play a role in directing cell migration during development.

D. Microglia
   1. Phagocytes of the brain

VI. Conclusion