Chapter 1

Cellular Components of the nervous system
Neurons
- Dendrites and axon's are wrapped with myelin
- Synapse - Communication point
CNS - Myelin sheath- Oligodendrocytes
PNS - Myelin Sheath - Schwann Cells
Cajal- Neurons are polarized establishing directional flow reflected by molecular specializations.
Neurons
- Protein synthesis occurs in the soma
- Long axon with a terminal where synaptic vesicles release neurotransmitters <- presynaptic cells
-Postsynaptic cells have receptors
Divergence - Few to many
Convergence - Many to few
Glia Cells
CNS - Brain + Spinal Cord
- Astrocytes - blood-brain barrier + buffer ions/neurotransmitters
- Oligodendrocytes - myelinate neuronal axons
-Microglia - macrophage activity + secrete cytokines
PNS - Extension of CNS
- Schwann cells - myelinate neuronal axons + participate in recovery of function resulting from neuronal damage
Afferent - towards the CNS Efferent- Away from the CNS
Signals can be excitatory, Inhibitory or Modulatory
Input-output geometry
- tap - Sensory neuron excites and inhibits motor neuron - Motor conducts action potential causing contraction - Flexor relaxes due to inhibition - Leg extends
Optogenetics - Genes introduced, monitor and control activity to light signals by chemical signals
Organization by type of info - Unity of function
Topographic Maps - Parallel Pathways
Computational Map - Time/order of input
Lesion Studies - direction of information flow
- Transgenic reporter - specific genes
- Aintibody labeling - specific proteins
- In Situ hybridization - localizing mRNA - particular protein
Receptive Field - region in sensory space where a neuron will respond
Organization of HNS

Chapter 1 (cont)

- Visceral Motor Neurons - synapse with peripheral motor neurons in autonomic ganglion
- Sympathetic division: originate at Sympathetic trunk at thoracic and lumbar levels
- Parasympathetic division - orig @ brainstem and sacral levels
- Enteric division: Gastrointestinal tract
- Gray Matter : Cell Bodies
- White Matter : Myelin-covered axon tracts BRAIN - Commissures SPINAL CORD - Columns
Genomics - analysis of the complete DNA seq of species/individual
Homozygosity Mapping - Identify multiple genes associated with disorders - Individual/family
Genome-wide association studies - Analysis in inheritance of large cohorts
Transgenic animals - introduce novel gene into stem/zygote cells
Knock-in/out
-Homologous recombination - Recombining DNA sequence into genome
-Conditional Mutations - preventing mRNA becoming protein
- Gene Editing - CRISPER-Cas9 - Specific mutations into gene

Chapter 2

Electrical Signals of a Neve Cells
Concentration gradients from charged protein molecules and ions create a measurable electrical gradient.
electrical gradient - potential difference across the cell membrane.
Resting membrane - constant voltage at cell rest (-40_-90)
Synaptic potential - Change in potential one neuron stimulates another via synapses using a neurotransmitter
Action Potential - Nerve impulse/spike travels along an axon
Passive electrical response - no response to the membrane potential
Hyperpolarization - stimulus casing the membrane to go negative than the resting potential
Active electrical response - stimulus causing the membrane potential to increase past threshold - depolarizing action potential
Stimilus intensity - Action potential frequency
Requirements for Generating Cellular electrical signals
1. Concentration gradient
2. Membrane semipermeability through ion channels
Nerst equation linear relationship between transmembrane concentration gradient + membrane potential
- predicts the electrical potential at electrochemical equilibrium for 1 ion.
Resting membrane is more permeable to K+ than any other ion
During depolarization - membrane potential becomes more positive

Chapter 2 (cont)

During repolarization - membrane potential becomes more negative
Rising phase, overshoot phase, falling phase, undershoot phase

Chapter 3

Chapter 3 - Voltage-Dependent Membrane Permeability
At rest, neuronal membranes are more permeable to K+, than to Na+, the resting membrane potential is negative and approaches the equilibrium potential for K+.
During an AP, the membrane becomes permeable to Na+, the MP becomes positive and approaches the equilibrium potential for Na+
MP and Permeability change affect each other
axon membrane permeability is voltage-dependent
By examining how the inward and outward currents changed, it is possible to measure ion permeability as the membrane potential varied.

Chapter 4

Chapter 4 - Ion Channels and Transporters
Measurement of currents flowing through single ion channels
Ion channels and the currents flowing through them should have several properties :
- capable of allowing ions to move across the membranes at high rates
- make use of the electrochemical gradients of various ions
- channels selectivity
- sense changes in membrane potential
The Patch Clamp Method
Four configurations in patch clamp measurements of ion currents
Cell-attached recording.
Whole-cell recording.
Inside-out recording.
Outside-out recording
Patch clamp measurements of ion currents can separate currents through individual channels (microscopic currents) or many channels (macroscopic currents) representing relatively large surfaces of membrane.
Microscopic and macroscopic currents have also been shown for single K+ channels
Channels for both Na+ and K+ are voltage-gated
- They open during depolarization, but at different times
- They close during a hyperpolarization
- The gates of both channels are closed when the membrane potential is hyperpolarized
Tetrodotoxin, saxitoxin, μ-Conotoxin – block Na+ channels; inhibit depolarization.

Chapter 4 (cont)

α-Toxins – prolong the action potentials, scrambling information flow.
β-Toxins – Cause Na+ channels to open at lower-than-normal potentials, causing uncontrolled action potential firing.
Batrachotoxin – removes inactivation and shifts activation of Na+ channels.
Dendrotoxin, apamin, charybdotoxin block K+ channels
Voltage-gated ion channels:
SCN - Na+ channel genes.
KCN – K+ channel genes.
CACNA – Ca2+ channel genes.
CLCN – Cl- channel genes
Ligand-gated ion channels genes:
Neurotransmitter-gated.
Cyclic nucleotide-gated.
Transient receptor potential family of genes.
Thermosensitive channel.
Mechanosensitive channel.

Chapter 5

Chapter 5 - Synaptic Transmission
- Chemical synapses.
Use neurotransmitters and their receptors.
Ca2+-dependent neurotransmitter release
Unidirectional.
Slower.
- Electrical synapses
Uses gap junctions as ion channels.
Bidirectional.
Faster.
A presynaptic terminal button (top) forms a synapse with a postsynaptic dendrite (bottom).
Generation of action potentials in one neuron results in the synchronized firing of action potentials in the adjacent neuron
Hippocampal interneurons – one of the few places in the CNS that use electrical synapses
Entails electrical (action potential in presynaptic neuron), chemical (neurotransmitter diffusing across the synaptic cleft), and then resumption of electrical (action potential in postsynaptic neuron) transmission
Ultimately, action potential in the postsynaptic neuron is generated by the opening of ion channels, thereby changing the membrane potential.

Chapter 5 (cont)

- Achieved through either ionotropic or metabotropic receptors
Presynaptic structures:
filamentous structures help guide vesicles to active zone.
Several pools of vesicles exist: only those at the active zone are ready for exocytosis.
Postsynaptic structures:
Postsynaptic Density (PSD)
helps anchor postsynaptic receptors in postsynaptic membrane: prevents lateral diffusion of receptors.
Contains many proteins involved in plasticity-dependent processes, such as learning, memory, health, and disease
Quantal* release of neurotransmitters.
Synaptic transmission at the neuromuscular junction (nmj) results in end-plate potentials (EPP) in the muscle cell.
Acetylcholine is released in discrete packets, each leads to a miniature EPP (MEPP).
Spontaneous firings in the muscle cell manifested in MEPPs (Fatt and Katz, 1952).A quantum (plural: quanta) is the smallest discrete unit of a phenomenon
Ligand-gated ion channels.
Receptor itself is also the ion channel.
Also called ionotropic receptors.
Fast: postsynaptic potentials responses range: 1-2 msec after an action potential reached the presynaptic terminal.
Metabotropic receptors.
G-protein-coupled receptors: G-protein complex activated by ligand binding to the receptor.
Slow: postsynaptic potentials responses range: hundreds of msec to 1-2 minutes.
Cascade of phosphorylation events and second-messenger production
Release of transmitters from synaptic vesicles.
Individual quanta of neurotransmitter released are caused by the fusion of the vesicle membrane with the plasma membrane.
Number of quanta released positively correlated with the number of vesicles fusing.
The average synaptic vesicle has a diameter of ~ 50 nm, corresponding to about 100 mM acetylcholine
Local recycling of synaptic vesicles.
Following neurotransmitter exocytosis, fusion of synaptic vesicles with the plasma membrane is temporary.
Retrieved vesicular membrane passes through several intracellular compartments, such as endosomes.
Vesicles are loaded with neurotransmitter in an ATP-dependent/proton antiporter process.

Chapter 5 (cont)

Vesicles are stored in the presynaptic reserve pool until needed again to participate in neurotransmitter release.
SNARE Complex at Work to Exocytose Neurotransmitter.
Key Proteins:
Vesicular (V-SNARE) proteins: synaptobrevin, synaptotagmin.
Target (T-SNARE) proteins: syntaxin, SNAP-25.
Synaptobrevin coils around syntaxin and SNAP-25.
Synaptotagmin binds Ca2+ ✉ conformational change to pull vesicle closer to plasma membrane, which protrudes towards the former, bringing the 2 membranes closer together.
Fusion of the 2 membranes leads to exocytosis of neurotransmitter
Myasthenic Syndromes – abnormal transmission at neuromuscular synapses.
Concepts 5.3, 5.4, 5.6, and 5.7 will not be covered in this course.

Chapter 6

Chapter 6 - Neurotransmitters and Their Receptors
Neurotransmitters :
- In the presynaptic neuron
- Must be released during synaptic activity
- binds to receptors on the post synaptic neuron
Types - Neuropeptides or peptide neurotransmitters, Small molecule neurotransmitters - acetylcholine, amino acids, purines, and biogenic amines.