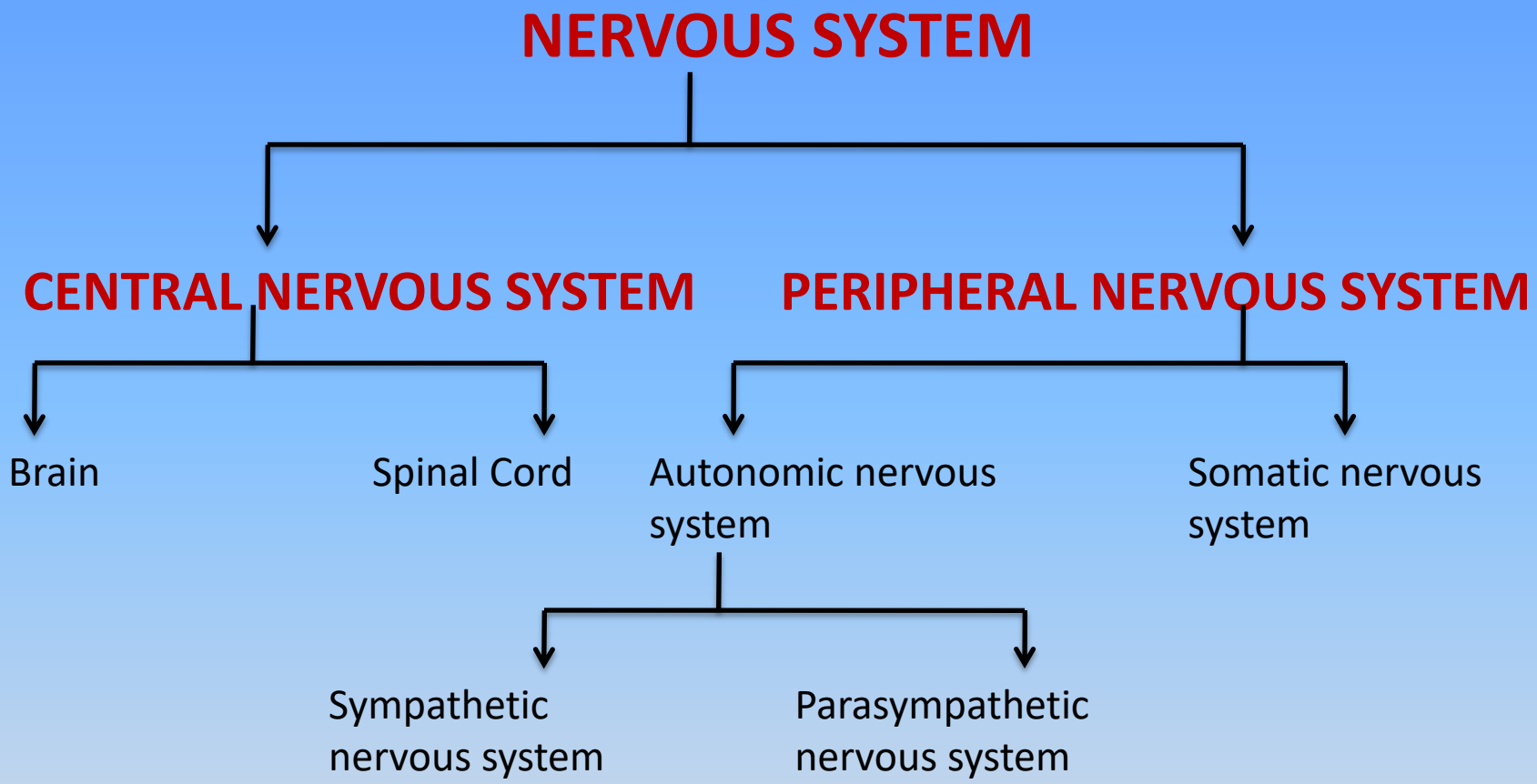
NERVE MUSCLE PHYSIOLOGY

LECTURE 1

- INTRODUCTION
- STRUCTURE & FUNCTION OF NEURON
- MYELINOGENESIS

Introduction

- Human CNS contain >100 billion neurons
- 50-100 times this number glial cells
- About 40% human genes participating its formation
- Specialized function of muscle – contraction
- Specialized function of neurons – integration & transmission of nerve impulse
- Along with endocrine, nervous system forms the major control system for body functions


NERVOUS SYSTEM
CENTRAL NERVOUS SYSTEM
PERIPHERAL NERVOUS SYSTEM
Brain
Spinal Cord
Autonomic nervous system
Somatic nervous system
Sympathetic nervous system
Parasympathetic nervous system

NEURON

- Structural and functional unit of nervous system
- Similar to other cell in body having nucleus and most organelles in cytoplasm
- **Different from other cells:**
  I. Neurons has branches or processes- dendrites and Axon
  II. Have nissl granules and neurofibrillae
  III. No centrosome- loss power of division
  IV. Contain and secrete neurotransmitter

Classification of Neuron

1. Depending upon the number of poles
2. Depending upon the function
3. Depending upon the length of axon

1. Depending upon the number of poles

a. Unipolar:

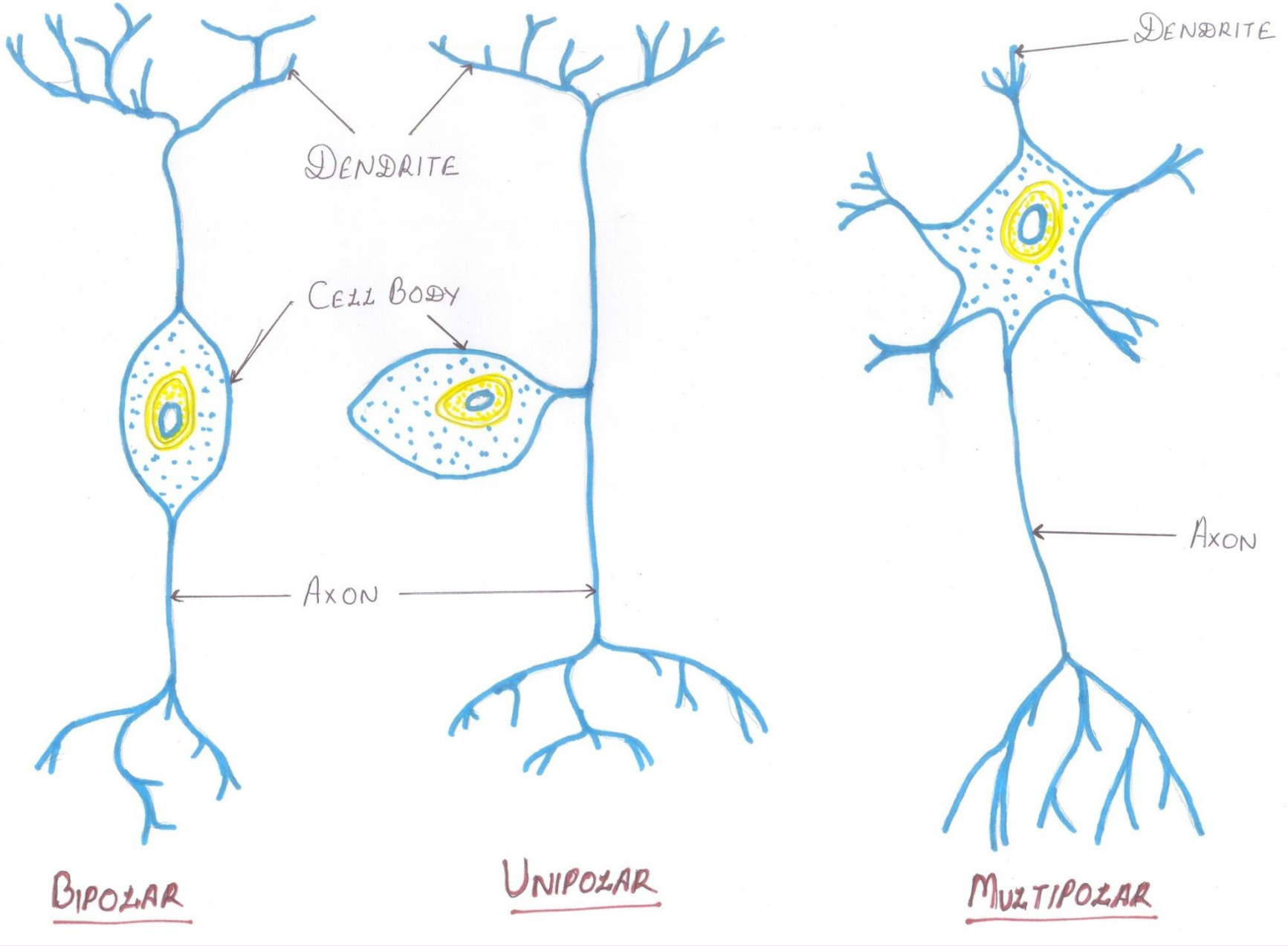
- Having only one pole
- From single pole both axon and dendrites arise
- Present in embryonic stage in human being

b. Bipolar:

- Having two poles
- Axon arises one pole and dendrites other pole

c. Multipolar:

- Nucleus having multipoles
- Axon arise one pole & all other pole give rise dendrites


DENDRITE
CELL BODY
AXON
DENDRITE
AXON
BIPOLAR
UNIPOLAR
MULTIPOLAR

2. Depending upon the functions

- **Motor or efferent neurons:**
  - Carry impulses from CNS to peripheral effector organs e.g., muscles/glands/blood vessels
  - Generally each motor neurons has **long axon and short dendrites**
- **Sensory or afferent neurons:**
  - Carry impulses from periphery to CNS
  - Generally each neuron has **short axon a long dendrites**

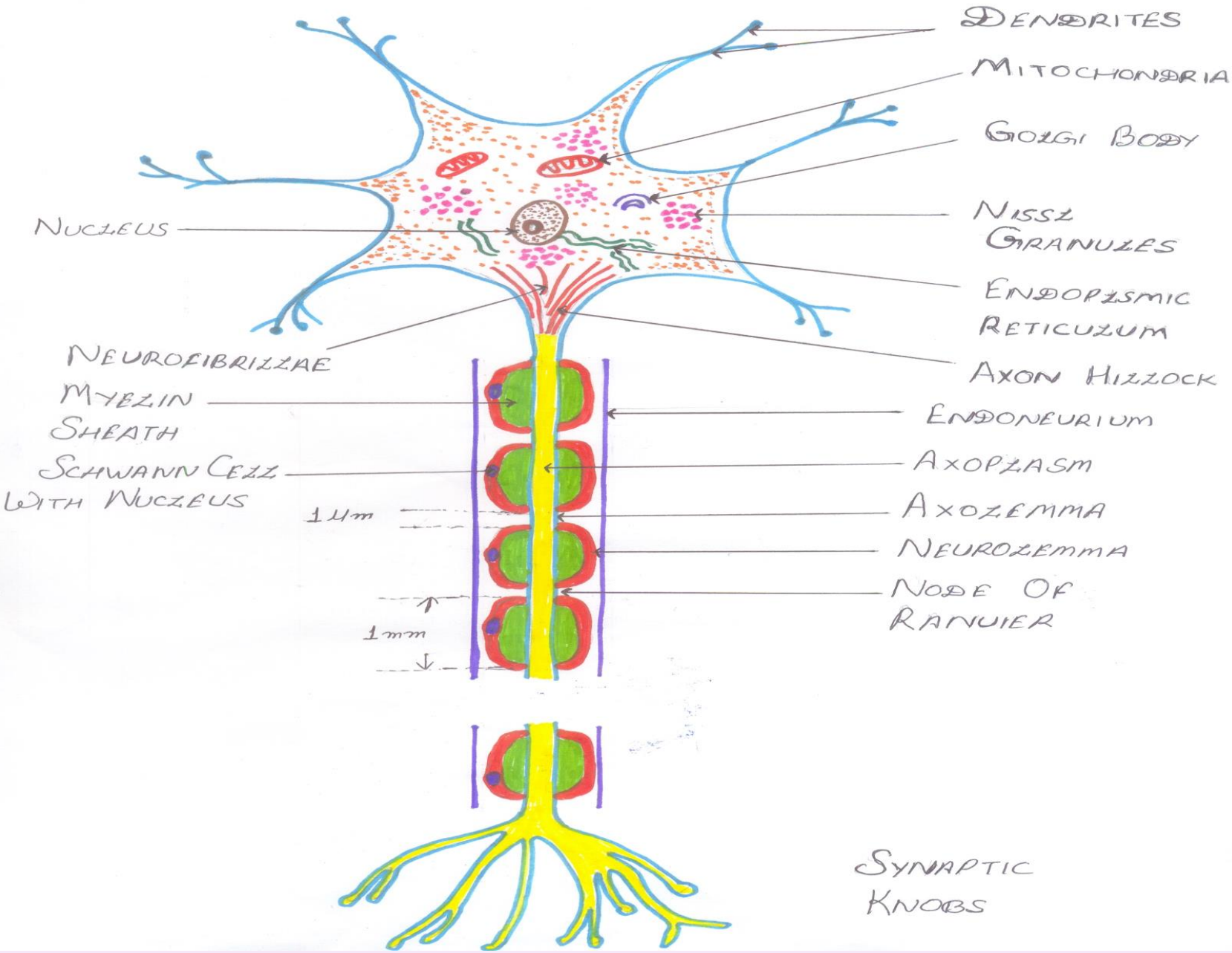
3. Depending upon the length of axon

- **Golgi Type I neurons:**
  - Have long axons
  - Cell body situated in CNS and their axon reaches remote peripheral organs
- **Golgi type II neurons:**
  - Have short axons
  - Present in cerebral cortex and spinal cord

Structure of Neuron

- Structural and functional unit of nervous system
- Consists of nerve cell body with all its processes axon and dendrites
- All neurons contain one and only one axon
- But dendrites may be absent one or many
- Axon carries impulses from the soma towards a centrifugal directions (away from soma)
- Dendrites brings impulse from distance centripetally (towards the soma)
- Nerve cell means a neuron where as nerve cell body means soma

Structure Of Neuron



- **Neuron can be divided in to:**
  - Cell body (nerve cell body)
  - Dendrites
  - Axon
  - Nerve terminals

i. Nerve cell body:

- AKA soma, perikaryon
- Various size and forms – stellate, round, pyramidal
- It maintains the functional and anatomical integrity of axon cut part distal to cut degenerate
- **Cytoplasm contains:**
  - Nucleus
  - Nissl bodies or Nissl granules
  - Neurofibrillae
  - Mitochondria
  - Golgi apparatus
- Nissl granules and neurofibrillae found only in nerve cell not in other cells

CONTI

- **Soma are present in** :
  - Grey matter of CNS
  - Nuclei of brain e.g., cranial N. Nuclei/Basal ganglia/Ganglia of CNS
  - All neurons contain soma
  - All processes do not survive without soma

CONTI

i. Nucleus:

- Each neuron has centrally placed one nucleus in soma
- Prominent nucleoli which contains ribose nucleic acid
- No centrosome – loss power of division

CONTI

ii. Nissl granules or bodies:

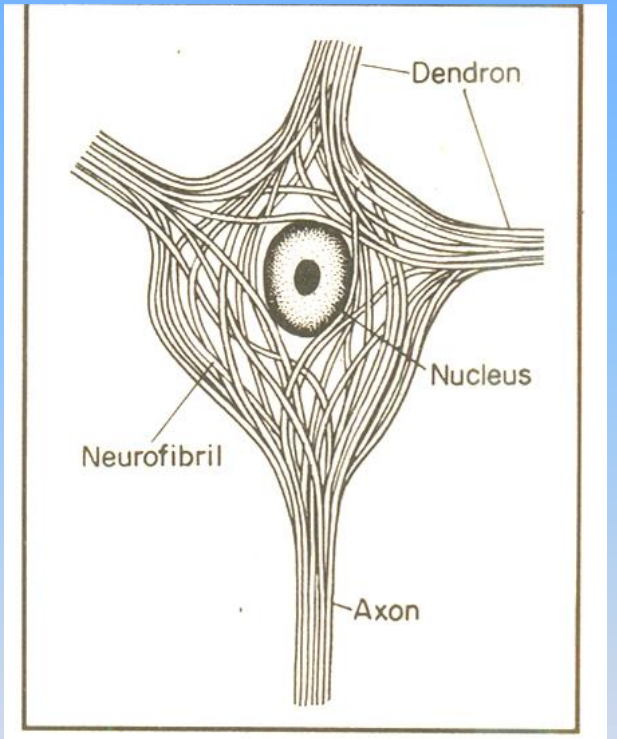
- Named after discoverer FRANZ NISSL in 19th century
- Also called tigroid substance (spotted appearance when properly stained)
- Small basophilic granules or membrane bound cavities found in clusters or clumps in soma
- Present in cell body and dendrites but absent in axon and axon hillock

CONTI

- Composed of ribonucleoprotein (RNA + Protein)
  Ribosome= RNA+ protein
- Synthesize proteins of neurons which transported to axon by axonal flow
- When demand of protein synthesis great nissl granules over work and may altogether disappear (chromatolysis) e.g, fatigue, anoxic, injured
- Reappear following recovery of neurons from fatigue or after regeneration

CONTI

- Neurofibrillae (Microtubules & microfilaments):
  - Thread like structure present all over cell
  - Consists of microtubules and microfilament
- Mitochondria:
  - Present in soma and axon
  - Form the power house of the nerve cell where ATP produced
- Golgi Apparatus
  - Same of Golgi Apparatus other cells
  - Concerned with processing and packing of proteins into granules



DENDRITES:

- Tapering and branching extension of soma
- Dendrites of cerebral cortex and cerebellar cortex show knobby projections called dendritic spine
- May be absent if present may be one or many in number
- Conduct impulses towards the cell body
- Generate local potential **not action potential** as well as integrate activity
- Has Nissl granules and neurofibrils
- Dendrites and soma constitute input zone

AXON

- Each axon has only one axon
- Arises from axon hillock of soma
- Carry impulses away from cell body
- Cannot synthesize own protein depends upon soma
- Branched only at its terminal end called synaptic knobe, terminal button, axon telodendria

CONTI

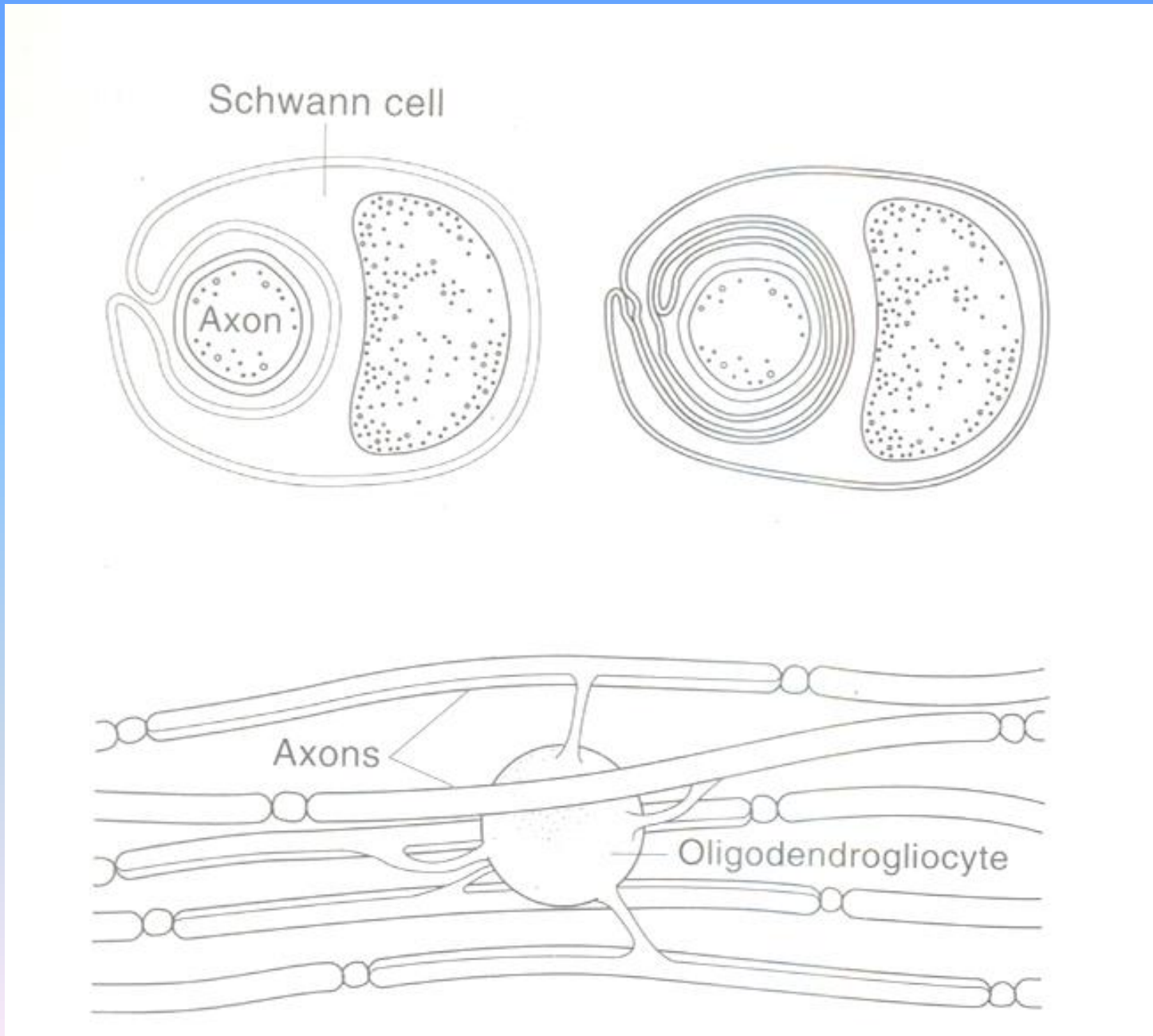
- Axon may be medullary or non medullary
- Synaptic knobs Terminal buttons or Axon Telodendria
- Axon divides into terminal branches and each ending in numbers of synaptic knobs
- Contain granules or vesicles which contain synaptic transmittors
- Specialized to convert electrical signal (AP) to chemical signal

Axis cylinder

- Has long central core of cytoplasm- axoplasm
- Axoplasm covered by membrane – axolemma continuation of cell membrane of soma
- Axoplasm along with axolemma- axis cylinder
- Contain mitochondria, neurofibrils and axoplasm, vesicles
- Axis cylinder covered by neurilemma in non myelinated nerve fiber
- Nerve fiber insulated by myelin sheath – myelinated nerve fiber

MYELIN SHEATH

- Concentric layers of protein alternating with lipid
- Nerve fiber insulated by myelin sheath- myelinated nerve fiber
- Protein lipid complex wrapped around axon >100 times
- Outside the CNS (peripheral nerve) myelin produced by Schwann cells
- Inside the CNS myelin sheath produced by oligodendrogliocytes


Schwann cell
Axon
Axons
Oligodendrogliocyte

CONTI

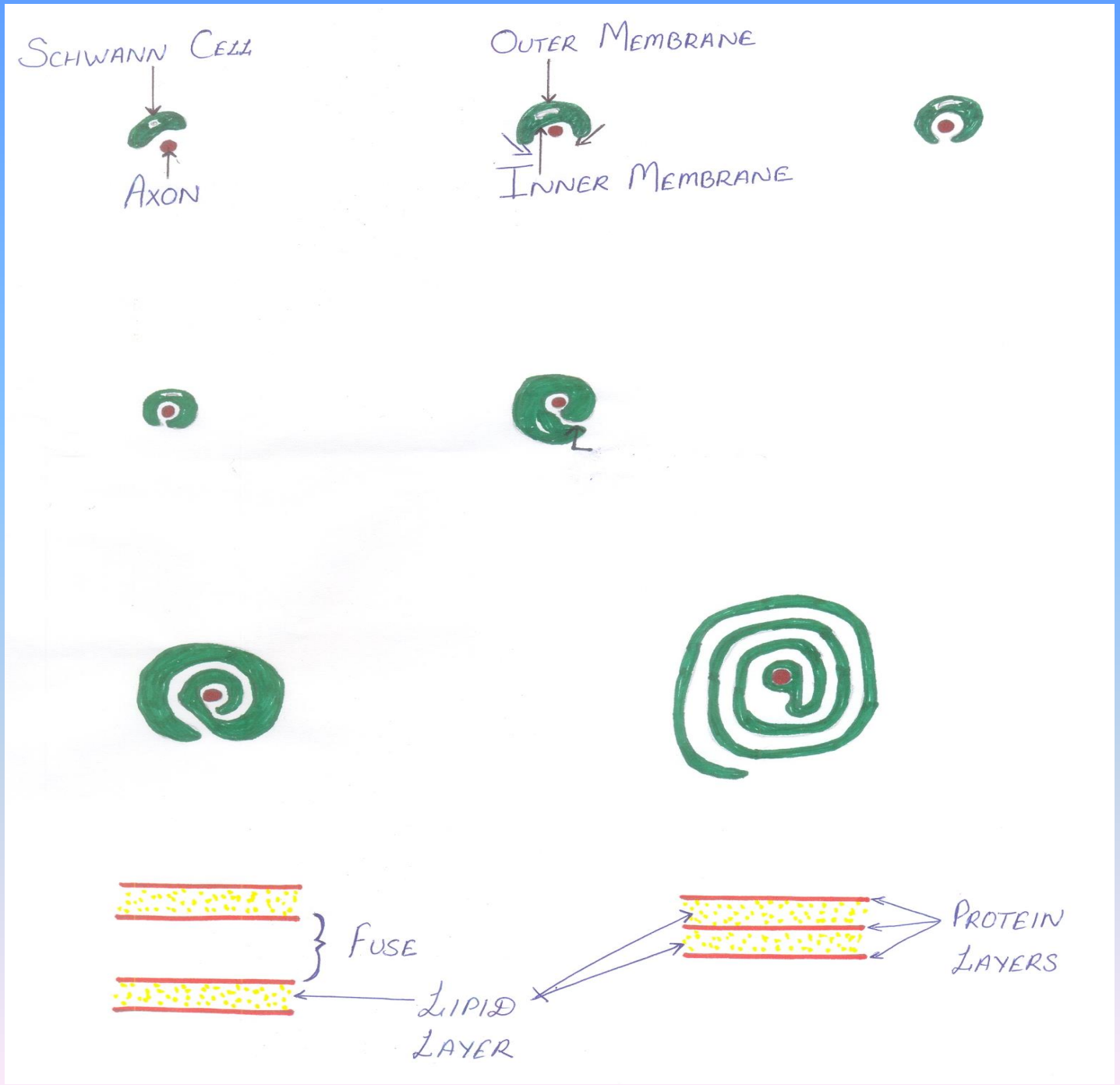
- Myelin is compacted when extracellular membrane protein (Po) locked extracellular portion of Po apposing membrane
- Not continuous sheath absent at regular intervals
- Where sheath absent – node of Ranvier (1µm)
- Segment between two node- internode (1mm)

MYELINOGENESIS

- Formation of myelin sheath around the axon
- Peripheral nerve started 4th month of IUL and completed few years after birth
- Pyramidal tract remain unmyelinated at birth and completed around end of 2nd year of life
- Outside its CNS myelin sheath formed by Schwann cells
- Before myelinogenesis Schwann cells (Double layer) close to axolemma as in non myelinated nerve fiber

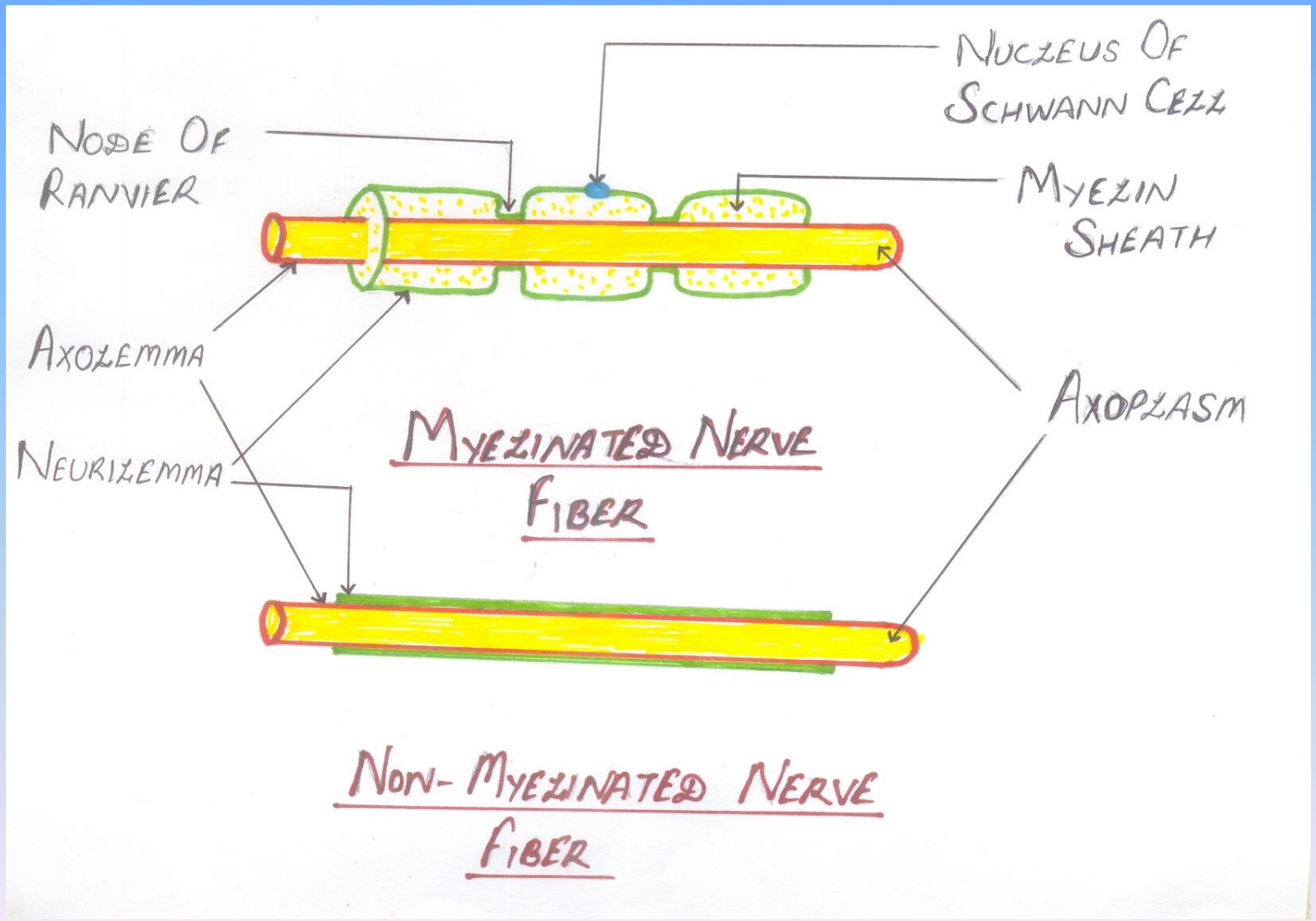
CONTI

- Membrane of Schwann cells wrappe up and rotate around the axon many concentric layer but not cytoplasm
- These concentric layer compacted – produce myelin sheath
- Cytoplasm of cell not deposited in myelin sheath
- Nucleus of cell remain in between myelin sheath and neurilemma
- Myelinogenosis in CNS occurs by oligodendrogeocytes


Schwann Cell
Axon
Outer Membrane
Inner Membrane
Fuse
Lipid Layer
Protein Layers

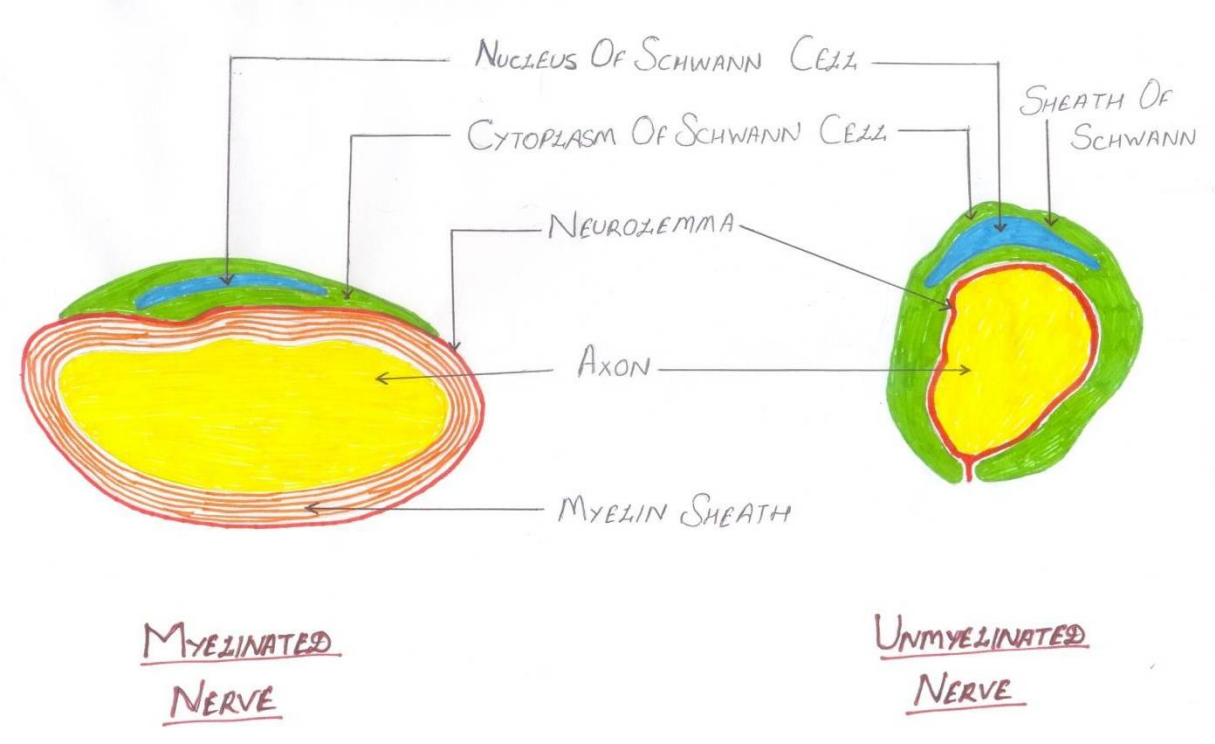
NON MYELINATED NERVE

- No myelin sheath formation
- Nerve fiber simply covered by Schwann cells, no wrapping
- No internode and node of Ranvier
- Neurilemma and axis cylinder close to each other
- In CNS no neurilemma
- Myelinogenosis in CNS by oligodenogliocytes not by Schwann cells


NUCLEUS OF SCHWANN CELL
NODE OF RANVIER
MYELIN SHEATH
AXOLEMMA
AXOPLASM
NEURILEMMA
MYELINATED NERVE FIBER
NON-MYELINATED NERVE FIBER

IMPORTANCE AND MYELIN SHEATH

- Propagation of AP very fast d/t saltatory conduction (possible only in myelinated nerve fiber)
- Myelination results quicker mobility in higher animals
- Have high insulating capacity so prevents cross stimulation



NEURILEMMA

- AKA sheath of schwann
- This membrane which surrounds axis cylinder
- Contain schwann cells which have flattend and elongated nuclei
- One nucleus is present in each internode of axon
- Nucleus situated between myelin sheath and neurilemma
- Non myelinated nerve fiber neurilemma surrounds axolemma continuously
- At node of ranvier neurilemma invaginates upto axolemma

FUNCTIONS OF NEURILEMMA

- Non myelinated nerve fiber – serve as covering membrane
- In myelinated nerve fiber necessory for myelinogenesis
- Neurilemma absent in CNS
- Oligodendrogliocytes are responsible for myelinogenesis in CNS

FUNCTIONAL DIVISION OF NEURON

- **Divided in to four zone:**

1. Receptor or dendritic zone:

  – Multiple local potential generated by synaptic connection are integrated

2. Origin of conducted impulse:

  – Propagated action potential generated (Initial of segment of spinal motor neuron)

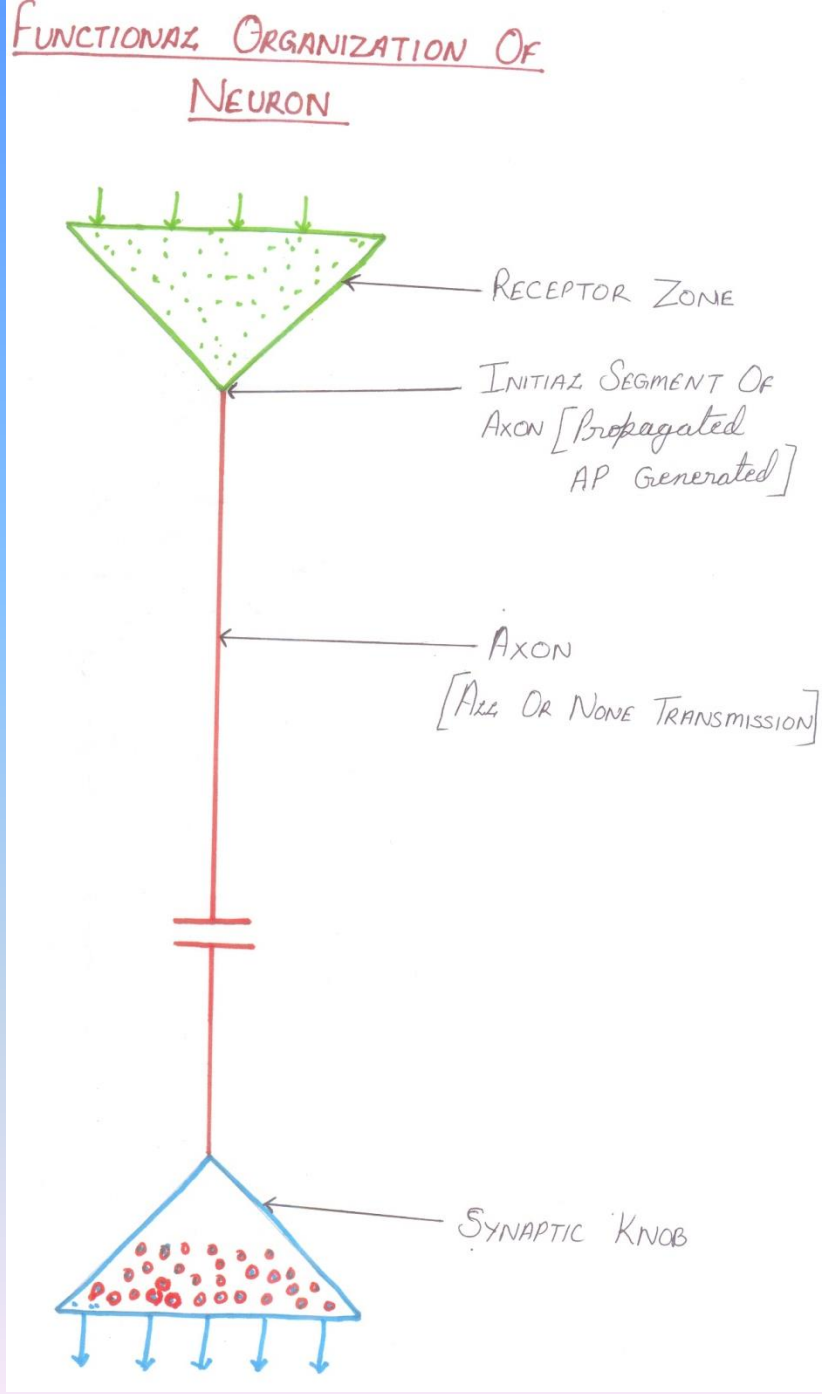
  – Initial node of Ranvier in sensory neuron

3. Conductive zone:

- Axonal process transmits Propogated impulse to the nerve ending
- All or none transmission

4. Secretory zone:

- Nerve ending where AP cause release of neurotransmitters



Axonal Transport

- Transport sub^{s} from soma to synaptic ending
- **Fast axonal transport-** Membrane bound organelles & mitochondria (400 mm/ day)
- **Slow axonal transport-** Sub^{s} dissolved in cytoplasm- Proteins (1mm/ day)
- Requires ATP/ Ca^{++} & microtubules for guide
- Occurs in both direction anterograde & retrograde
- **Anterograde transport-** Synaptic vesicles/ proteins
- **Retrograde transport-** Neurotrophins /viruses

Question 1

Nissl bodies are composed of

a. DNA
b. RNA with protein
c. Lipoprotein
d. Fine granules composed of uracil

Question 2

Development of myelin sheath in peripheral nervous system depends on

a. Astrocytes
b. Microglia
c. Oligodendrocytes
d. Schwann cells

Question 3

All or None phenomenon in a nerve is applicable to

a. Mixed nerve
b. Only a sensory nerve
c. Only a motor nerve
d. A single nerve fiber

Question 4

Which of the following may show antidromic conduction

a. Synapse
b. Axons
c. Both a & b
d. Cell body

Question 5

Myelin is

a. Usually ensheaths the axon hillock

b. Usually forms an uninterrupted coating around axons

c. Cover the dendrites, cell bodies and axon endings

d. Is found in greater concentration in the white matter of the spinal cord then in the grey matter

Lecture 2

- Neurotrophins
- Glial cells (Neuroglia)
- Classification of nerve fiber

Neurotrophins – Neurotrophic Factors

- Protein substances
- Play important role in growth and functioning of nervous tissue
- Secreted by many tissue in body e.g., muscles/ neurons/ astrocytes
- Functions:
  - Facilitate initial growth and development of nerve cells in CNS & PNS

CONTI

- Promote survival and repair of nerve cell
- Maintenance of nerve tissue and neural transmission
- Recently – neurotrophins capable of making damaged neuron regrow
- Used reversing devastating symptoms of nervous disorders like Parkinson disease, Alzheimer's disease,
- Commercial preparation for treatment of some neural diseases

TYPE

- 1st protein identified as neurotrophin- nerve growth factor (NGF)
- Now many numbers neurotrophin identified

1. Nerve growth factors (NGF)

  - Promote early growth and development in neurons
  - Major action on sympathetic and sensory neurons especially neurons concerned with pain
  - AKA sympathetic NGF (major actions on sympathetic neurons

CONTI

- Commercial preparation of NGF extracted from snake venoms and submaxillary gland of male mouse
- Used in sympathetic neurons disease as well as many neurons disorders:
  - Alzeimer’s disease
  - Neuron degeneration in aging

Other Neurotrophins:

2. Brain derived neurotrophic growth factor (BDGF)

- 1st discovered in pig brain now found in human brain and sperm
- Promotes survival of sensory and motor neurons
- Enhances growth of cholinergic, dopaminergic neurons and optic nerve
- Also regulate synaptic transmission
- Commercial preparation used to treat motor neuron disease

CONTI

3. Ciliary Neurotrophic factor (CNTF)

- Found in neurological cells/ astrocytes and Schwann cells
- Potent protective action on dopaminergic neurons
- Used for treatment of Parkinson’s disease
- 4. Fibroblast growth factors:
- Promoting fibroblastic growth

CONTI

5. **Glial cell line- derived neurotrophic factor (GDNF)**
   - Maintains mid bran dopaminergic neurons
6. **Leukemia inhibitory factors (LIF)**
   - Enhances the growth of neurons
7. **Insulin like growth factor I (IGF-I)**
8. **Transforming growth factor**
9. **Fibroblast growth factor**
10. **Platelet – derived growth factors**

NEUROTROPHIN 3 (NT-3)

- Act on motor sympathetic and sensory organs neurons
- Regulates release of neurotransmitter from NMJ
- Useful for treatment of motor neuron neuropathy and diabetic neuropathy
- Others sub belong to neurotrophin family NT-4, NT-5 α leukemia inhibitory factors
- NT-4 & NT-5 act on sympathetic and sensory and motor neurons

NEUROGLIA

- Neuroglia or glia (glia- glue) supporting cells of nervous system
- Non excitable and do not transmit nerve impulse
- 10-50 time as many glial cells as neurons
- Capable of multiplying by mitosis
- Schwann cells invest axon also glial cells

CLASSIFICATION OF NEUROGLIAL CELLS

1. Central Neuroglial cells

- Astrocytes:
  - Fibrous astrocytes
  - Protoplasmic astrocytes
- Microglia
- Oligodendrocytes

2. Peripheral neuroglial cells

- Schwann cells
- Satellite cells

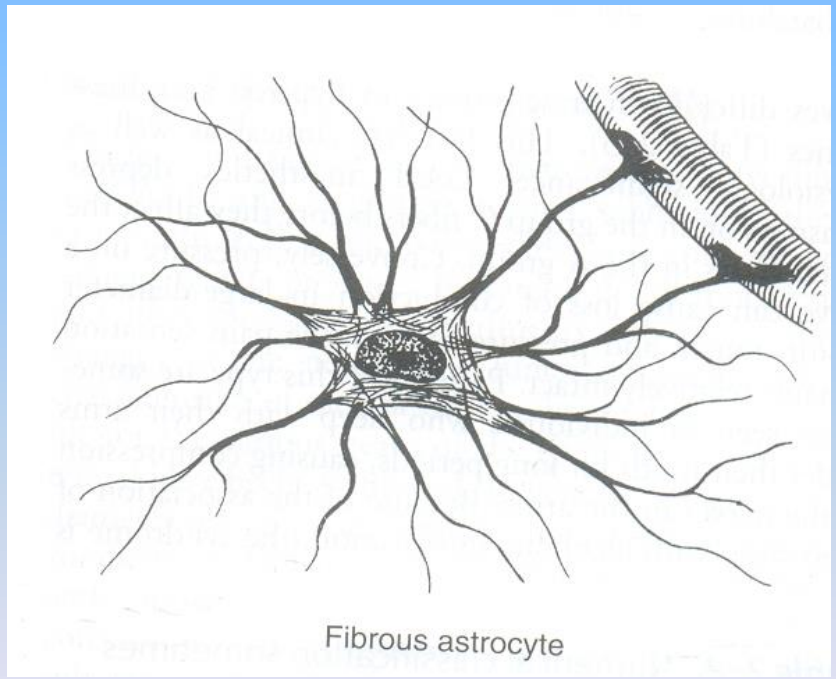
Astrocytes:

- Star shaped found throughout the brain joining to blood vessels
- Investing synaptic structures neuronal bodies and neuronal process
- **Two types:**
  - **i. Fibrous astrocytes**
  - **ii. Protoplasmic Astrocytes:**

CONTI

i. Fibrous astrocytes

- Found mainly in white matter
- Process of cells cover nerve cells and synapses
- Play important role in formation of blood brain barrier by sending process to blood vessels of brain

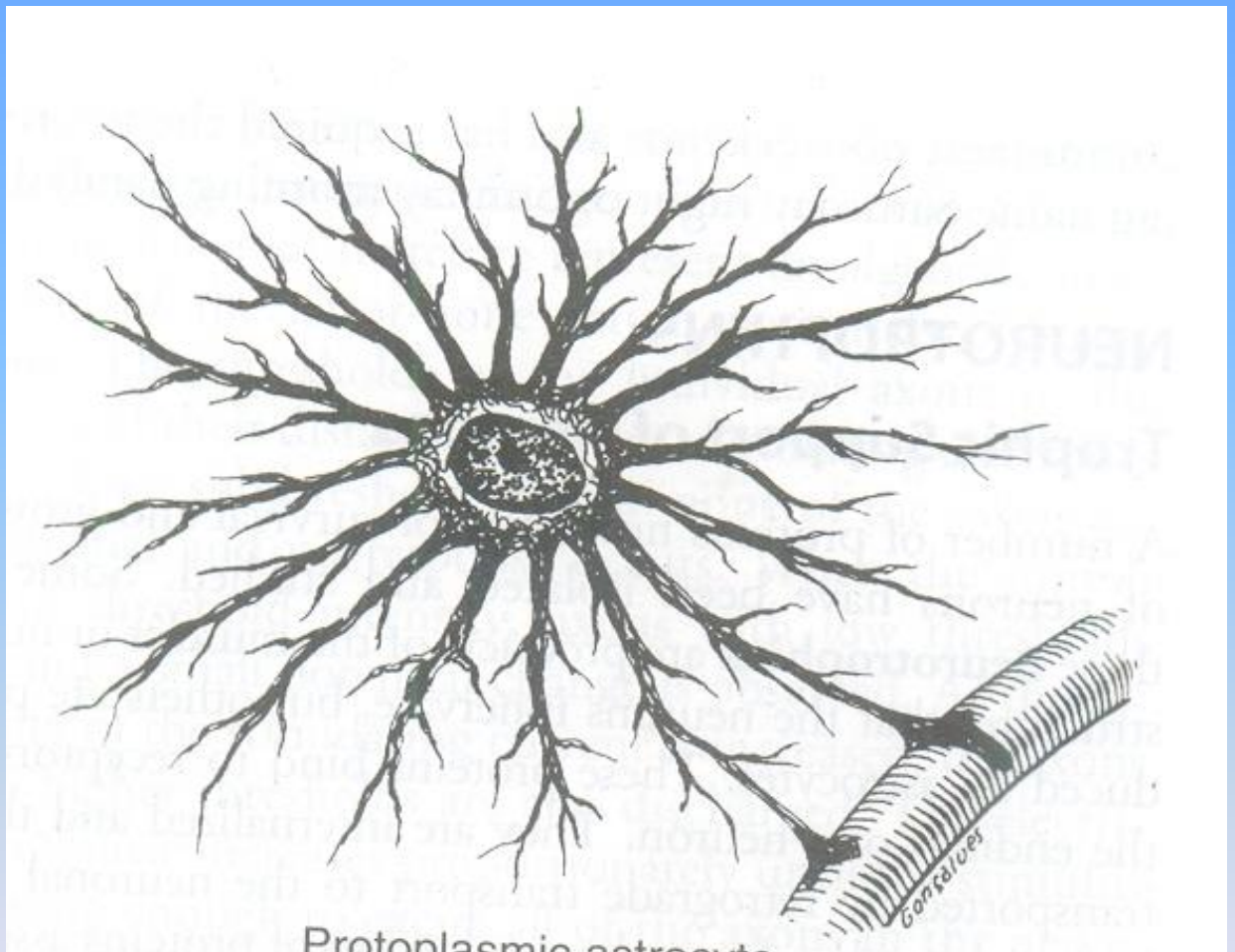


ii. Protoplasmic Astrocytes:

- Present mainly in grey matter
- Process of neuroglia run between nerve cell bodies

Functions:

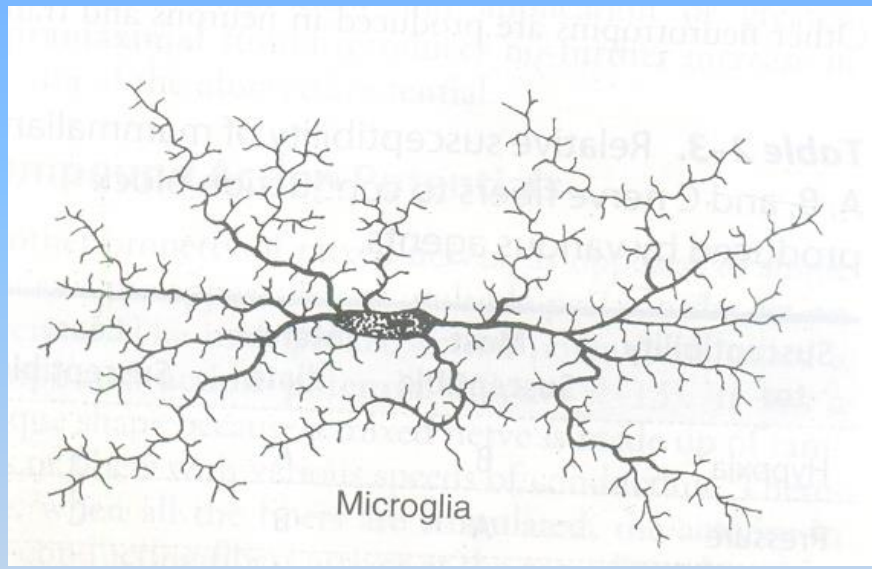
- Form blood brain barrier so regulate the entry of sub^{s} from blood to brain tissue
- Twist around the nerve cells and form supporting network in brain and spinal cord
- Maintain chemical environment of ECF around CNS neurons
- Provides Ca+ and potassium and regulate neurotransmitter level in synapses
- Regulate recycling and neurotransmitter during synaptic transmission



Protoplasmic astrocyte

MICROGLIA

- Derived from monocytes and enter the CNS from blood
- Phagocytic cells migrate to the site of infection or injury after called macrophages of CNS
- Smallest neuroglial cells



Functions:

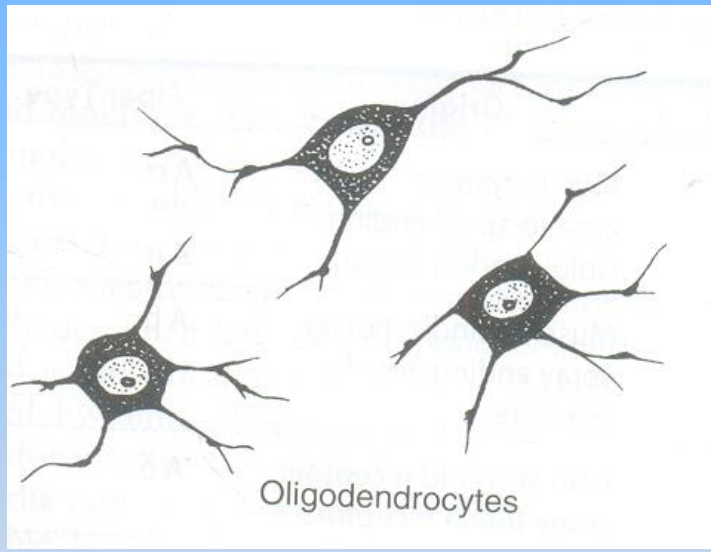
- Engulf and destroy microorganism and cells as debris
- Migrate to injured or infected area of CNS and act as mature macrophages

OLIGODENDROCYTES

- Produced myelin sheath around nerve fiber in CNS
- Nerve only few process which are short

Functions:

- Provide myelination
- Provide support to CNS neurons by forming semi still connective tissue between neurons



PERIPHERAL NEUROGLIAL CELLS

1. Schwann cells:

- Major glial cells in PNS
- Play important role in nerve regeneration
- Remove celluler debris during regeneration by their phagocytic activity

CONTI

2. Satellite cells:

- Present on extensor surface of PNS neurons

Functions:

- Provide physical support to PNS neurons
- Help in regulation of chemical environment of ECF around PNS neurons

Classification of Nerve fiber

- **General features of nerve:**
- Greater the diameter of nerve fiber
  - Greater speed of conduction
  - Greater magnitude of spike potential
  - Smaller duration of spike
  - Lesser threshold of excitation

CONTI

- **Speed of conduction**
- **Myelinated fibers**
  - Approximately **6 times** fiber diameter
  - Myelinated fiber diameter ranges from $1–20$μ m
  - Therefore conduction velocity varies from 6-120 mts/sec

- **Nonmyelinated fibers:**
  - Speed of conduction proportional to square root of diameter
  - Largest unmyelinated fiber approxi 1µm in diameter
  - Therefore max conduction velocity 1 mt/sec
- Long axon mainly concerned with proprioceptive, pressure and touch sensation and somatic motor functions
- Small axons concerned with pain and temp sensation and autonomic functions

CLASSIFICATION OF NERVE FIBERS

1. **Depending upon structure**
   - Myelinated nerve fibers
   - Non myelinated nerve fibers
2. **Depending upon distribution**
   - Somatic nerve fibers (supply skeletal muscles)
   - Visceral or autonomic (supply internal organs)
- **Depending upon origin**
   - Cranial nerve (arising from brain)
   - Spinal nerve (arising from spinal cord)

- **Depending upon functions:**
  - Sensory nerve fibers (afferent nerve fiber)
  - Motor nerve fibers (efferent nerve fibers)
- **Depending upon secretion of neurotransmitter**
  - Adrenergic nerve fibers
  - Cholinergic nerve fibers
- **Depending upon diameter and conductions of impulse (Erlanger- gasser classification)**
- **Classified into three major groups:**
  - Type A nerve fibers
  - Type B nerve fibers
  - Type C nerve fibers

- Among these type A thickest fibers
- Type c thinnest fibers
- Except type C fibers all fibers are myelinated
- Type A nerve fibers further subdivided four groups:
  - Aα or Type I nerve fibers
  - Aβ or Type II nerve fibers
  - Aγ or Type III nerve fibers
  - Aδ

Fiber type	Functions	Fiber diameter (µm)	Conduction velocity (mt/sec)
α	Proprioception, somatic motor	12-20	70-120
β	Touch, pressure, motor	5-12	30-70
γ	Motor to muscle spindles	3-6	15-30
δ	Pain cold touch	2-5	12-30
B	Preganglionic autonomic	<3	3-15
C	Pain temperature some mechanoreceptor	0.4-1.2	0.5-2
Dorsal root	Reflex response		
Sympathetic	Post ganglionic sympathetic	0.3-1.3	0.7-2.3

NUMERICAL CLASSIFICATION

Number	Origin	Fiber type
Ia	Muscle spindle Annulo-spiral ending	Aα
Ib	Golgi Tendon organ	Aα
II	Muscle spindle flower spray ending, Touch, Pressure	Aβ
III	Pain and cold receptor some touch receptors	Aδ
IV	Pain, Temp and other receptors	Dorsal roots

PHYSIO-CLINICAL CLASSIFICATION

Susceptibility	Most susceptible	Intermediate	Least suitable
Hypoxia	B	A	C
Pressure	A	B	C
Local Anesthesia	C	B	A

Question 1

Which is not a CNS glial cell

a. Schwann cell
b. Microglia
c. Astrocyte
d. Oligodendroglia

Question 2

The most susceptible nerve fiber to local anesthetics

a. C type fiber
b. B type fiber
c. Parasympathetic
d. A type Fiber

Question 3

The conduction velocity in a myelinated fiber is directly related to

a. The amount of axon branching
b. Length of the fiber
c. Diameter of the fiber
d. Diameter of the dendrites

Question 4

Non-myelinated fiber differ from myelinated once in that they

a. Lack nodes of ranvier
b. Are more excitable
c. Have higher conduction velocity
d. Are not associated with schwann cells

Question 5

Not true of an astrocyte

a. Found throughout the brain joined to the blood vessels
b. Help forming blood brain barrier
c. Forms myelin around the axons within CNS
d. Helps in maintaining optimal conc^{n} of ions in the brain neurons