ONTOGENETIC DEVELOPMENT OF THE NERVOUS SYSTEM

Ontogenetic development

= individual development of
the organism from the fertilized egg
to its mature form and finally death

The human heart begins to beat late in the third week after fertilization. Before the heart begins to beat, the nervous system commences to differentiate and change in shape.

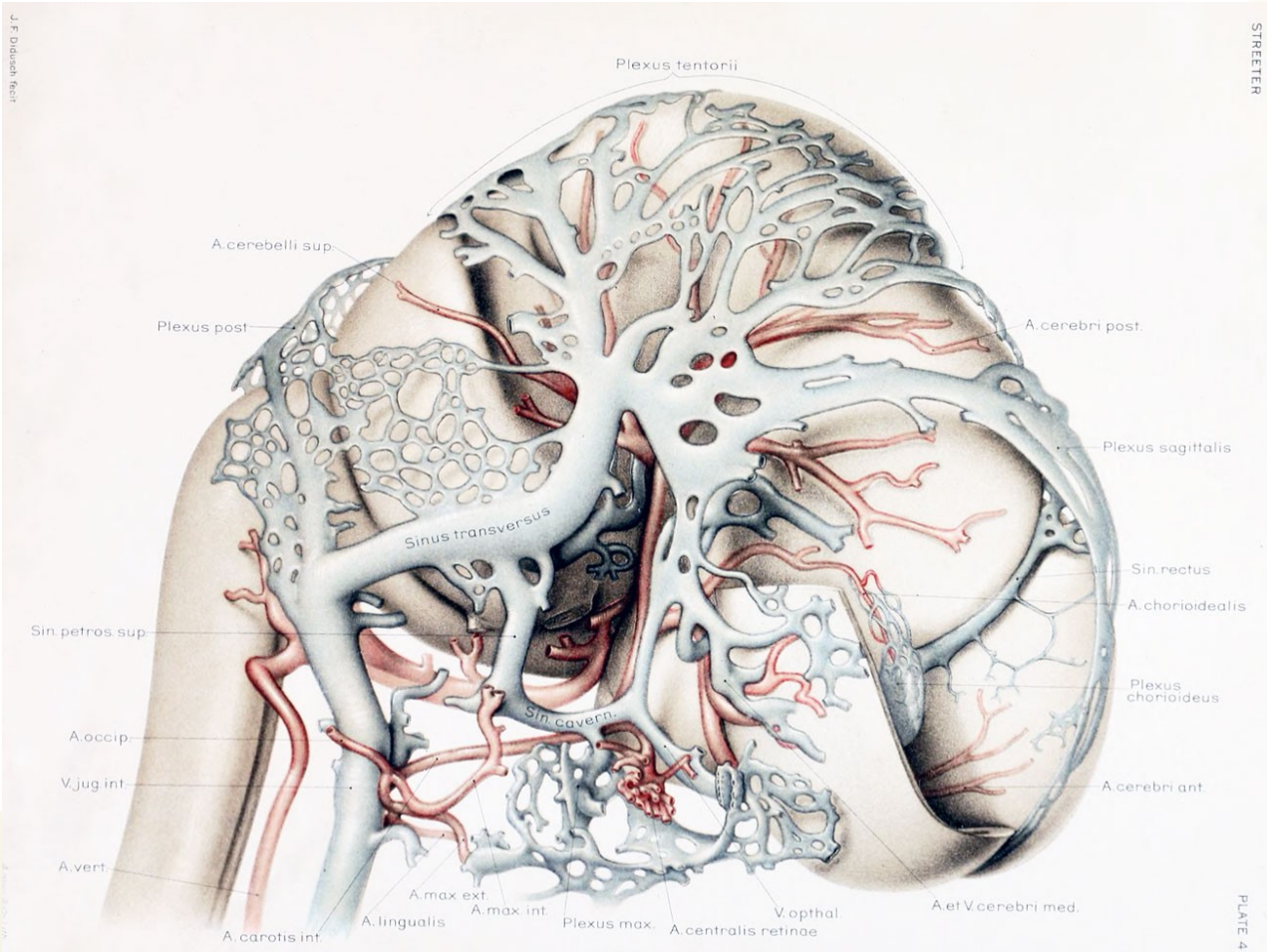
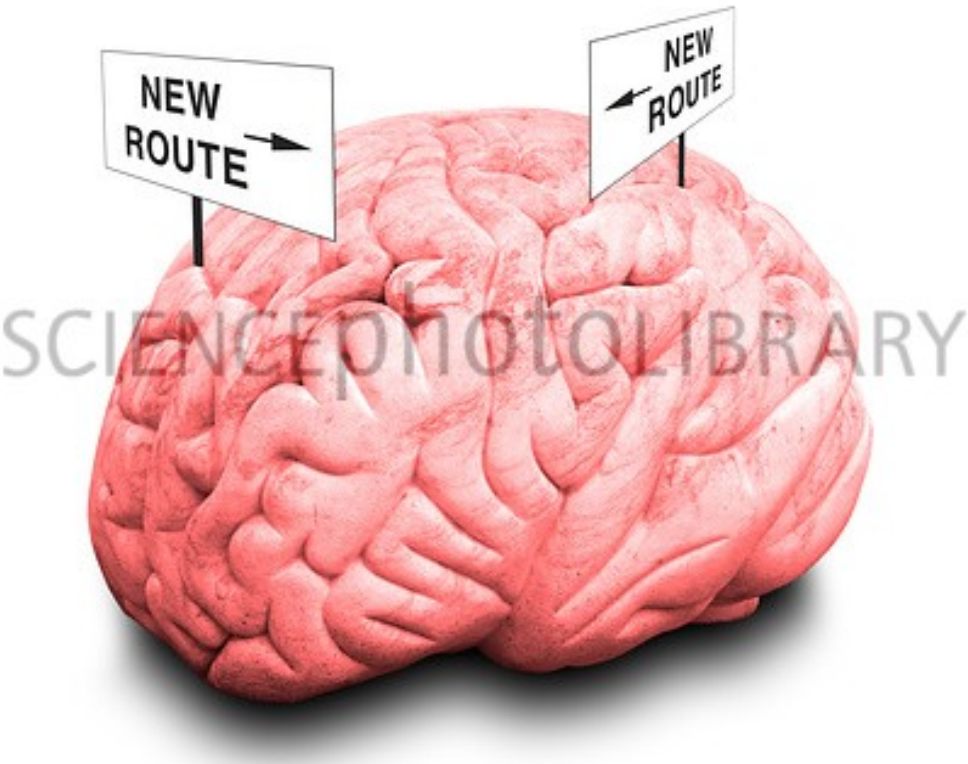


Fig. 26

Differentiation and growth continue postnatally throughout life as the nervous system is remodeled through plasticity.



Development of a neuron:

1) genetic level

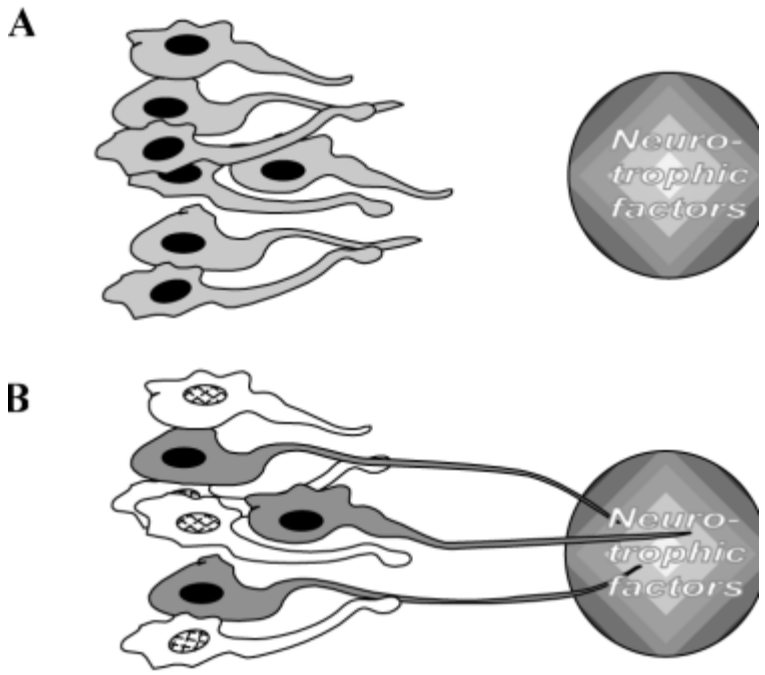
a) transciption (DNA → RNA)

b) translation (RNA → polypeptides)

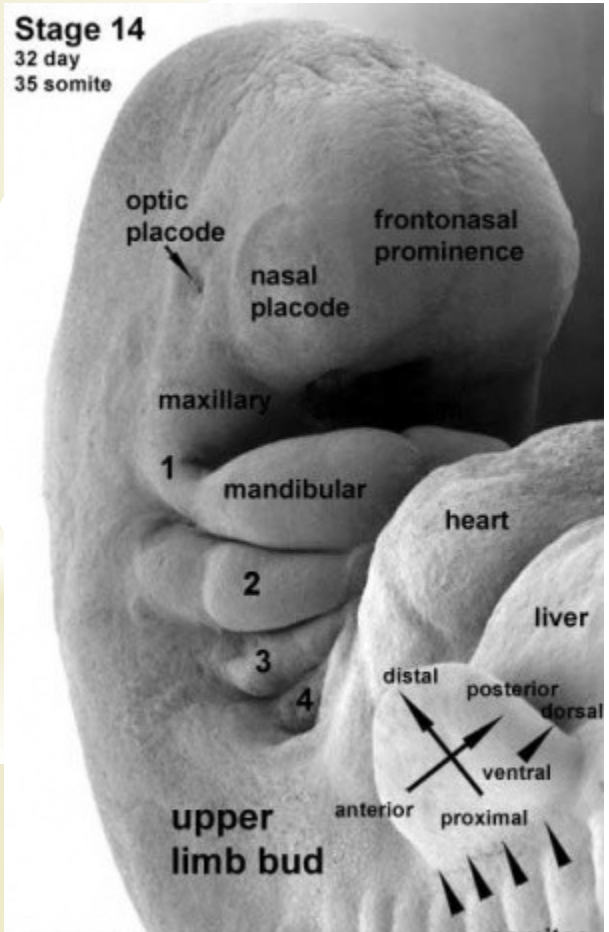
2) epigenetic level

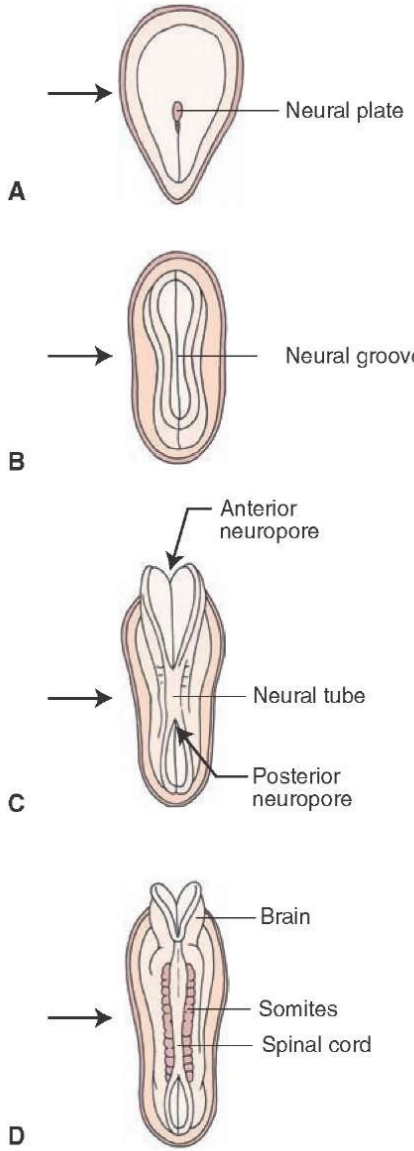
neurotropic and neurotrophic molecules

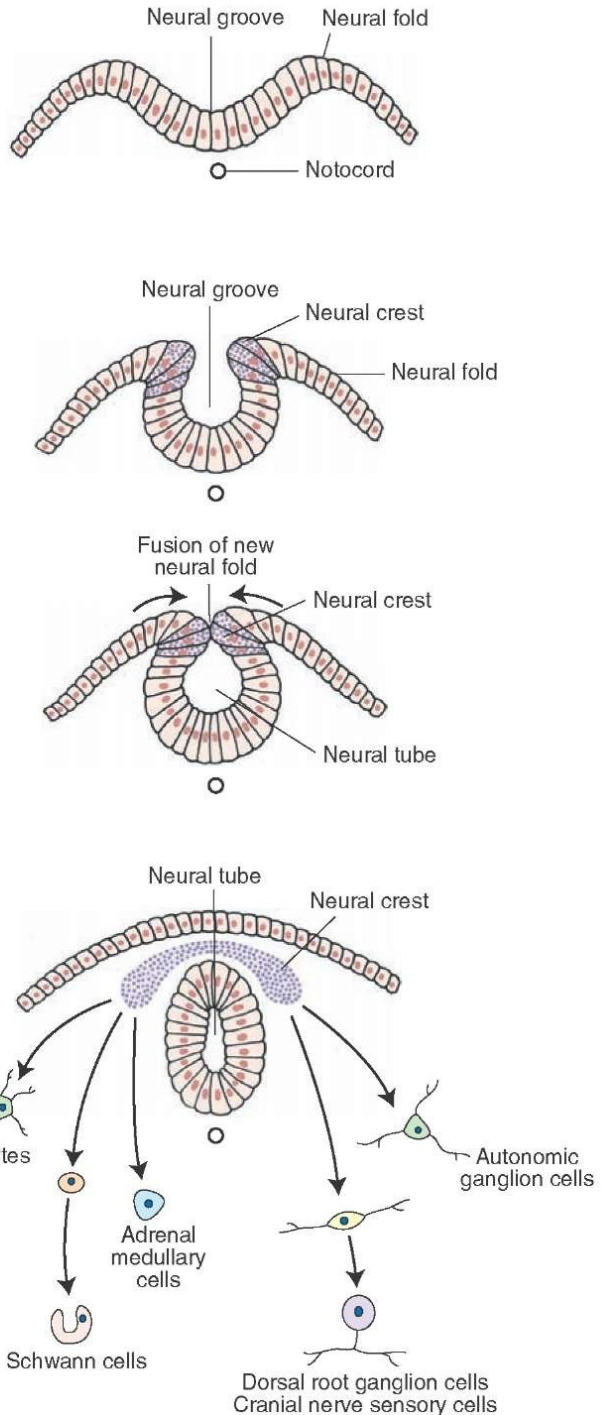
Target field theory



Development of the NS







Contributions of the Cranial Neural Crest to Craniofacial Tissues

Ectodermal Derivatives

Epithelium of mouth/nose

SKIN
Keratinocytes
Melanocytes

NERVOUS SYSTEM
Brain
Spinal Cord
Cranial nerve sensory ganglia (V, VII, IX, X)
Schwann cells

TEETH
Ameloblasts (Enamel)
Odontoblasts (Dentin)
Fibroblasts (Pulp)

EYE
Retina
Lens
Cornea
Sclera
Ciliary Muscle
Pigment of Iris

Mesodermal Derivatives

BONE/CARTILAGE
Cranial Vault
*(except Parietal)
Facial Bones
Mandible
Inner ear (incus, malleus, stapes)
Hyoid bone
*Parietal bone
Laryngeal cartilages
Ribs
Spine
Extremities

FAT
Face
Trunk
Extremities

MUSCLE
Somitic Mesoderm:
- Tongue
- Anterior neck
- Trunk
- Extremities

Pharyngeal Arch Mesoderm:
- Mastication
- Facial expression

Anterior Paraxial and Prechordal Mesoderm:
- Extraocular

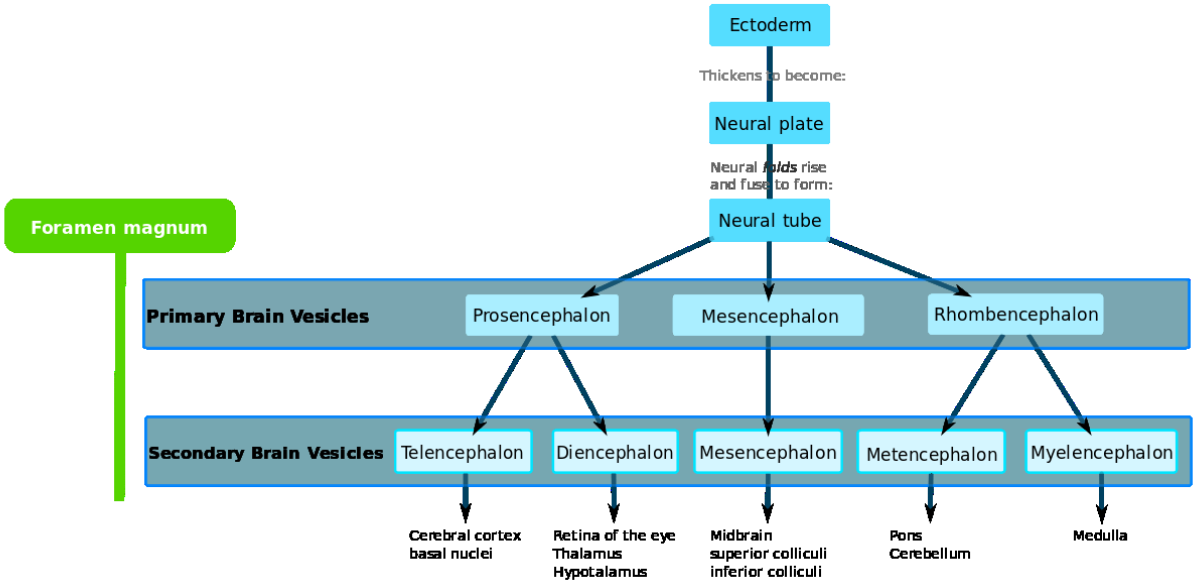
Endodermal Derivatives

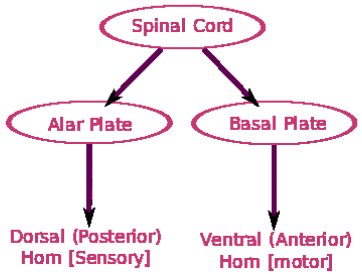
Respiratory tract

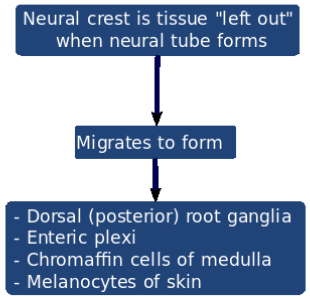
GI tract: esophagus to rectum

THYROID GLAND
Follicular cells
Parafollicular cells (C cells)

Development of the NS

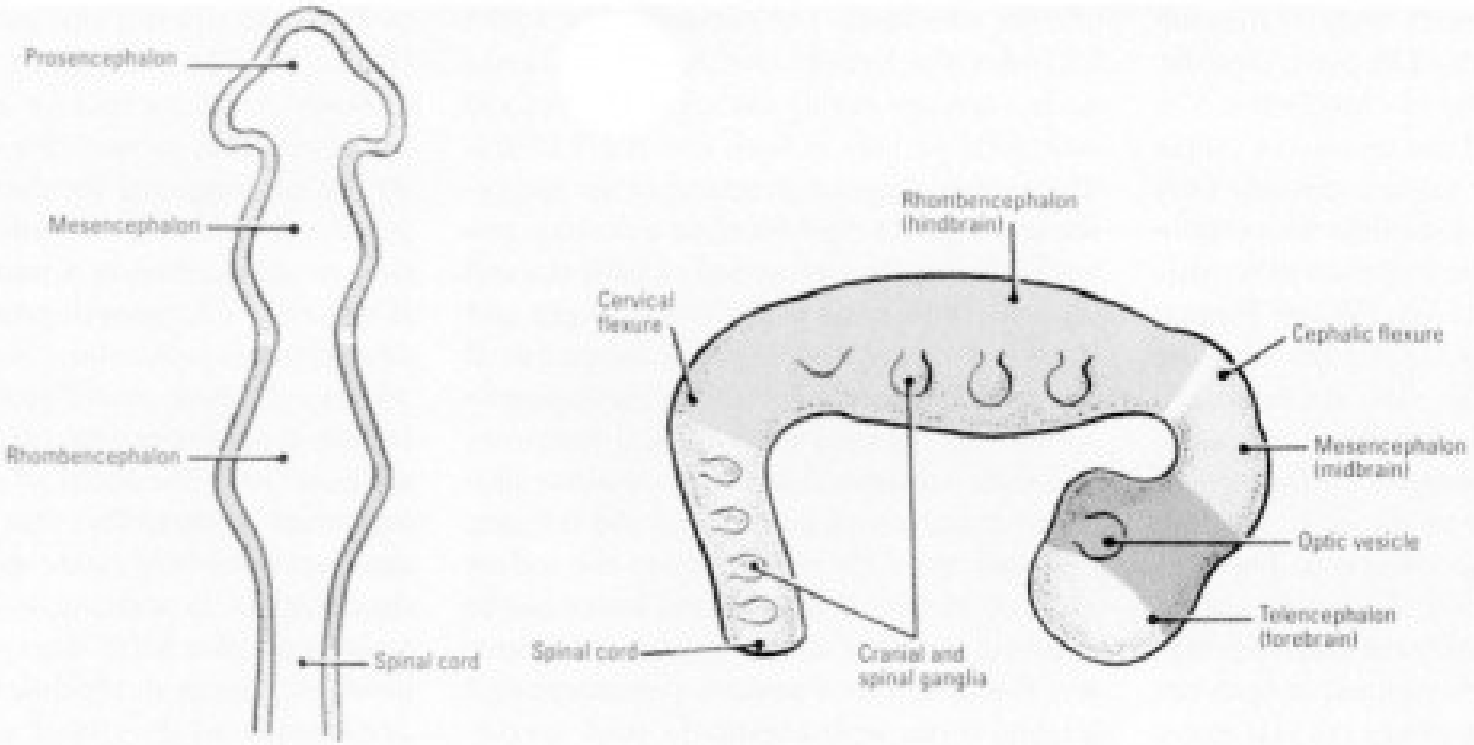






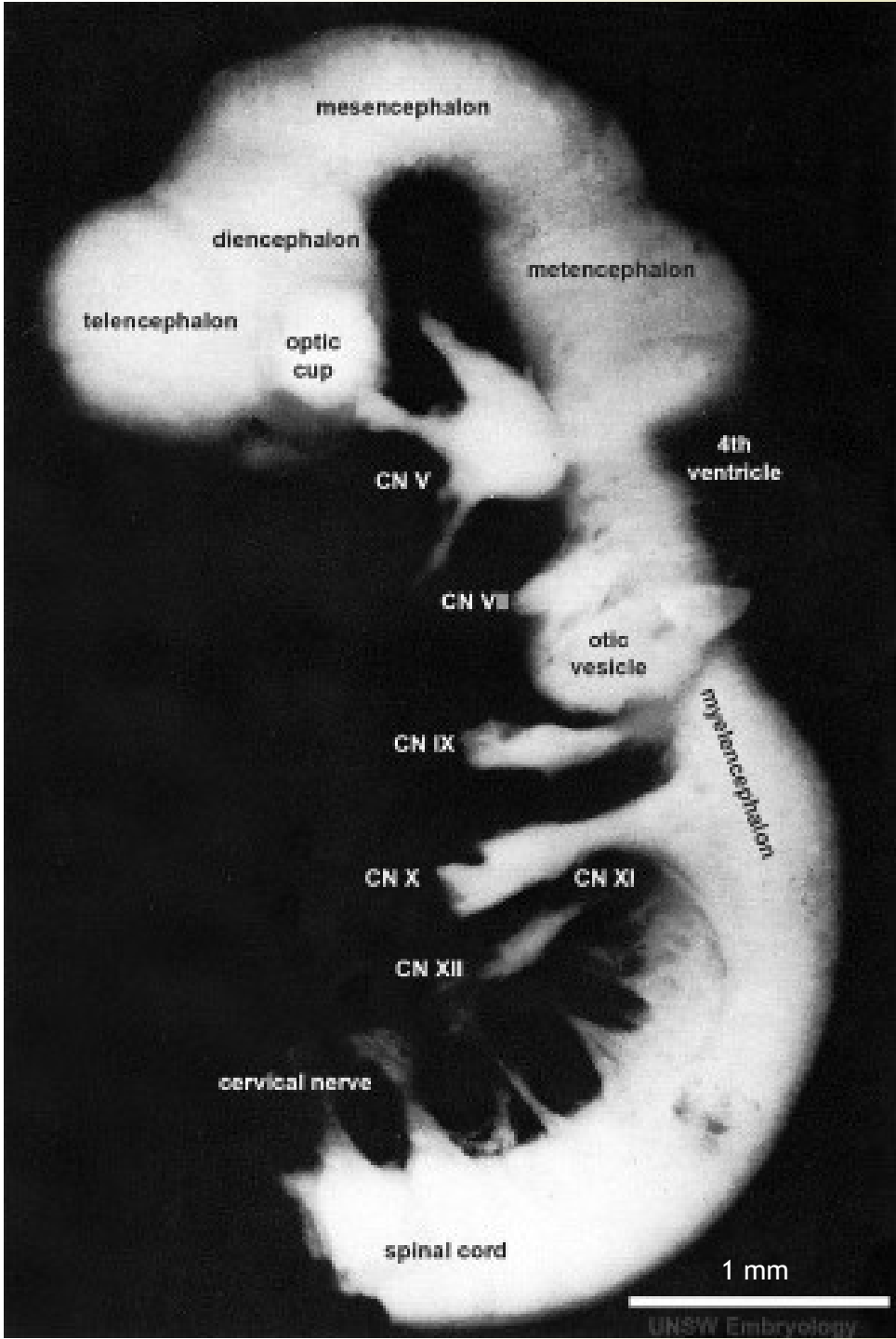
neurons and glia of sensory, symp. and parasymp nerves

Primary brain vesicles

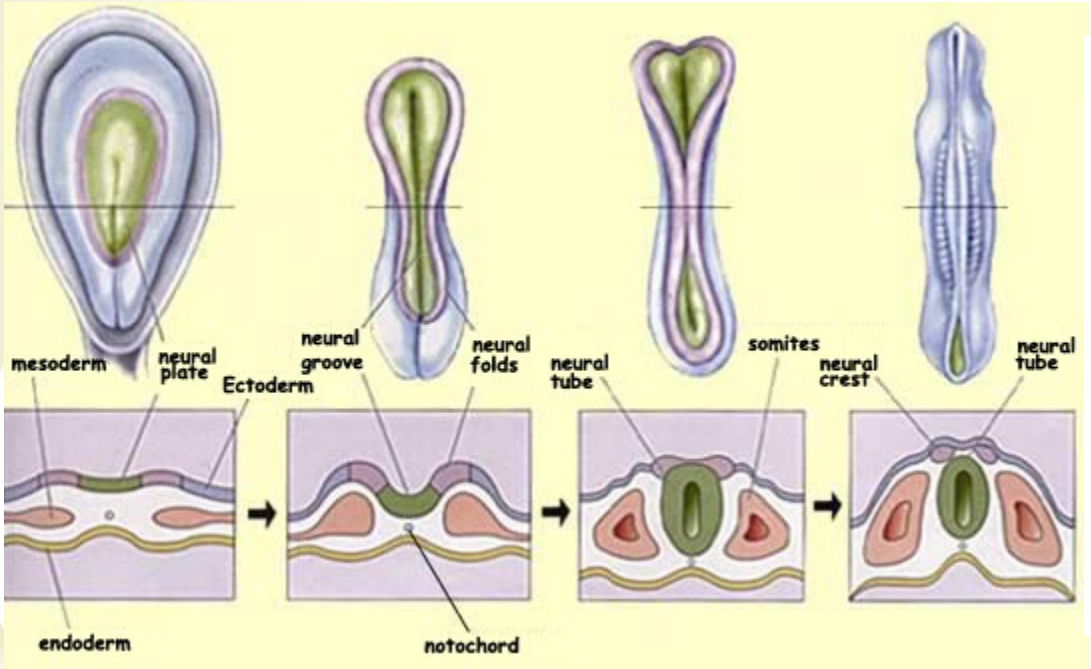


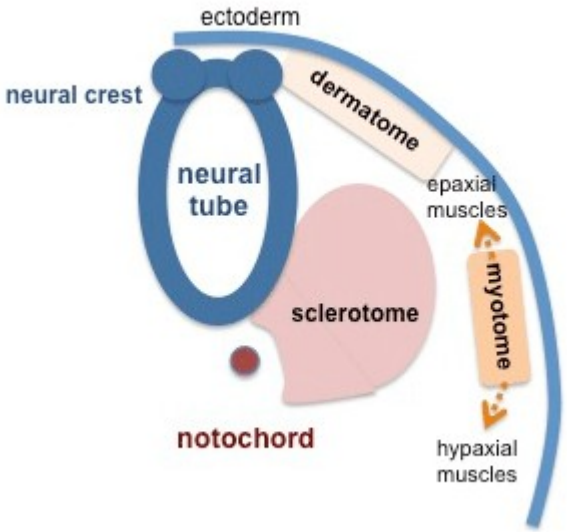
Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Rice D, Barone S Jr. Environ Health Perspect. 2000 Jun;108 Suppl 3:511-33. Review. PMID: 10852851

Secondary vesicles and cranial nerves



Differentiation of the neural tube in the anterior-posterior axis pattern (rostrocaudal axis) and dorsal-ventral axis pattern is linked to different transcription factors.





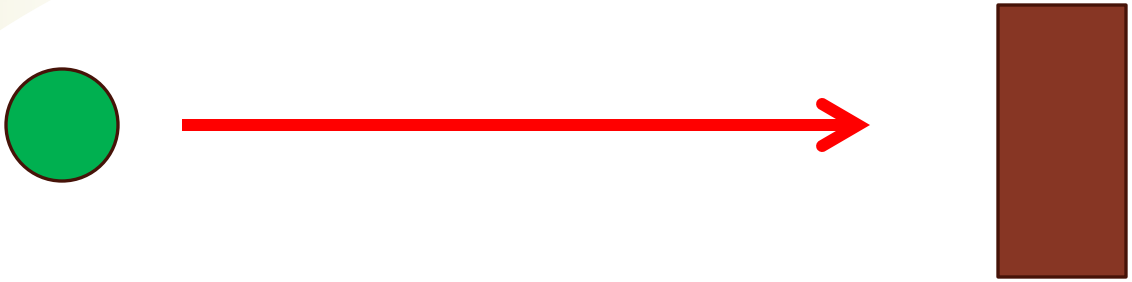
Each somite and its associated spinal cord segment is integrated into a structural and functional unit consisting of a spinal nerve, its sensory dermatomal distribution, and its myotome.

General principles of the ontogenetic development of the CNS

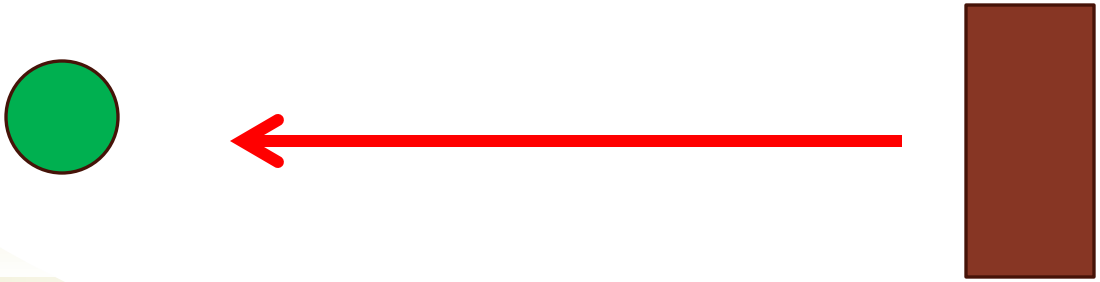
- segmentation of NS (somitogenesis)
  - control by genes
- fate of neurons (death or survival) based on epigenetic factors, migration and interaction of neurons – neurotrophic molecules
  - neuronal differentiation and survival molecules
- navigation of neurons towards the target structures – neurotropism
- end-differentiation of neurons

Trophic relationships in the NS

Neurons have trophic effect on periferal tissues



Periferal tissues have trophic effect on neurons



Neurotrophic factor families

Neurotrophins

- Nerve Growth Factor (NGF)
- Brain Derived Neurotrophic Factor (BDNF)
- Neurotrophin 3 (NT3)
- Neurotrophin 4/5 (NT4/5)

Neuropoietins

- Ciliary Neurotrophic Factor (CNTF)
- Leukemia Inhibitory Factor (LIF)

Insulin-like Growth Factors 1-2 (IGF-1, IGF-2)

Transforming Growth Factors

- Transforming Growth Factor α (TGFα)
- Transforming Growth Factor β 1-3 (TGFβ 1, TGFβ 2, TGFβ 3)
- Glial Cell Line-Derived Neurotrophic Factor (GDNF)
- Neurturin (NTN)
- Persephin (PSP)

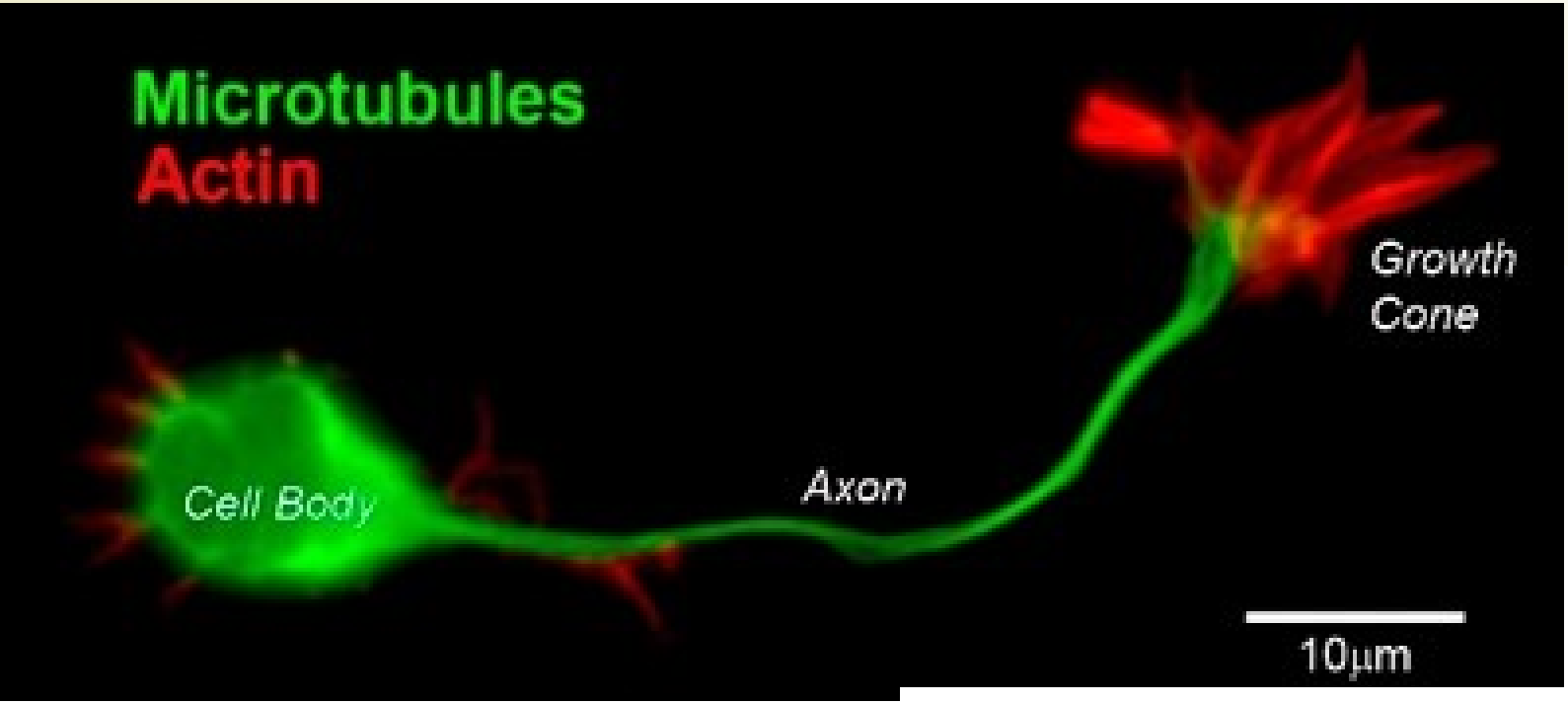
Fibroblast Growth Factors

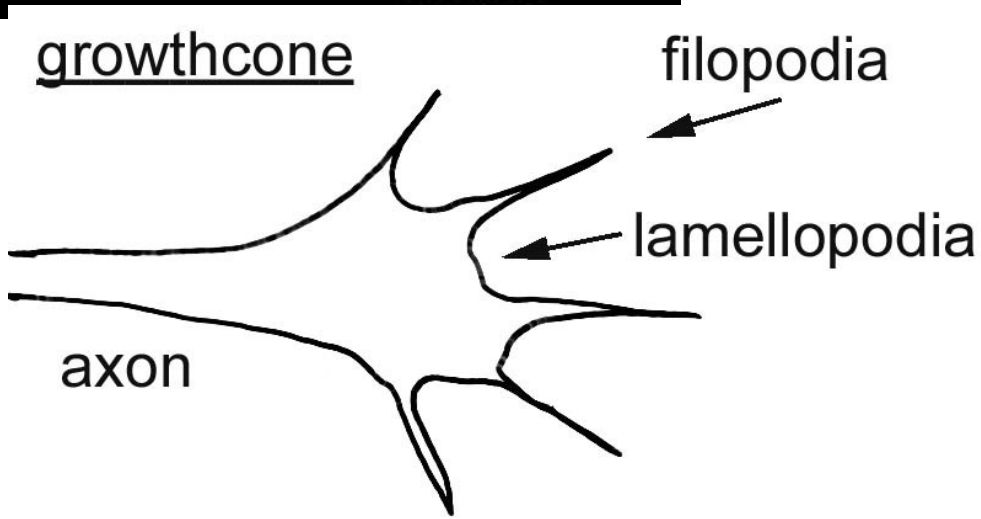
- Acidic Fibroblast Growth Factor (FGF-1)
- Basic Fibroblast Growth Factor (FGF-2)
- Fibroblast Growth Factor-5 (FGF-5)

Other factors

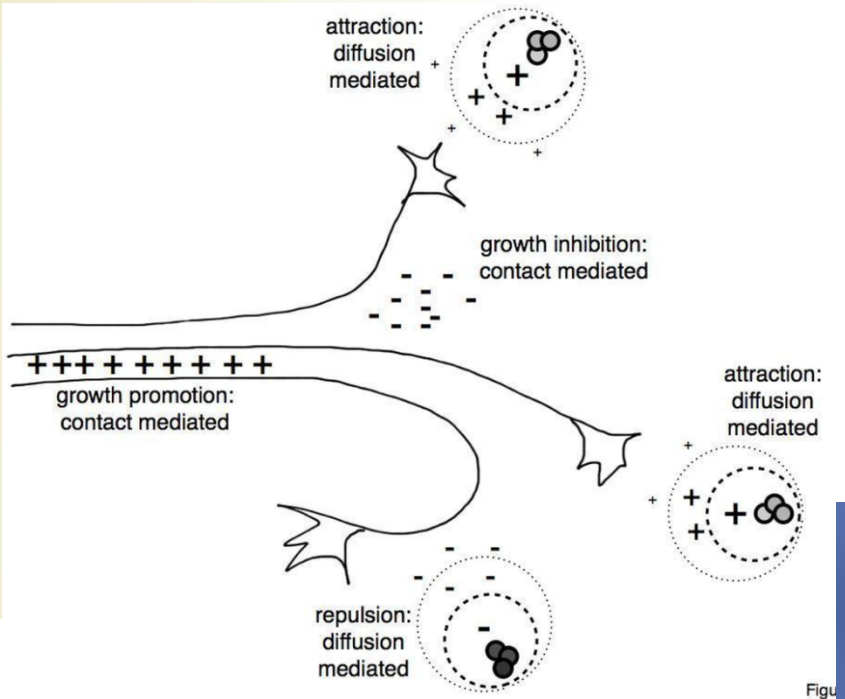
- Platelet-Derived Growth Factor (PDGF)
- Stem Cell Factor (SCF)

Growth cone


Microtubules
Actin
Growth
Cone
Cell Body
Axon
10μm

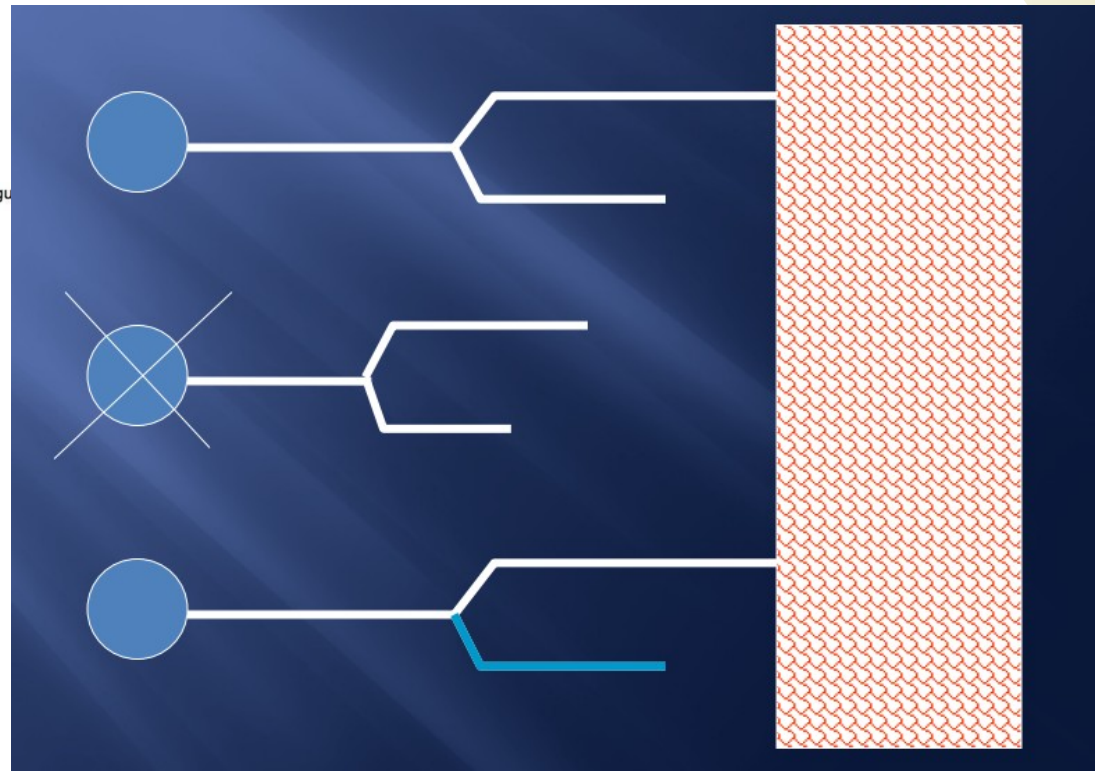

growthcone
filopodia
lamellopodia
axon

Axon guidance

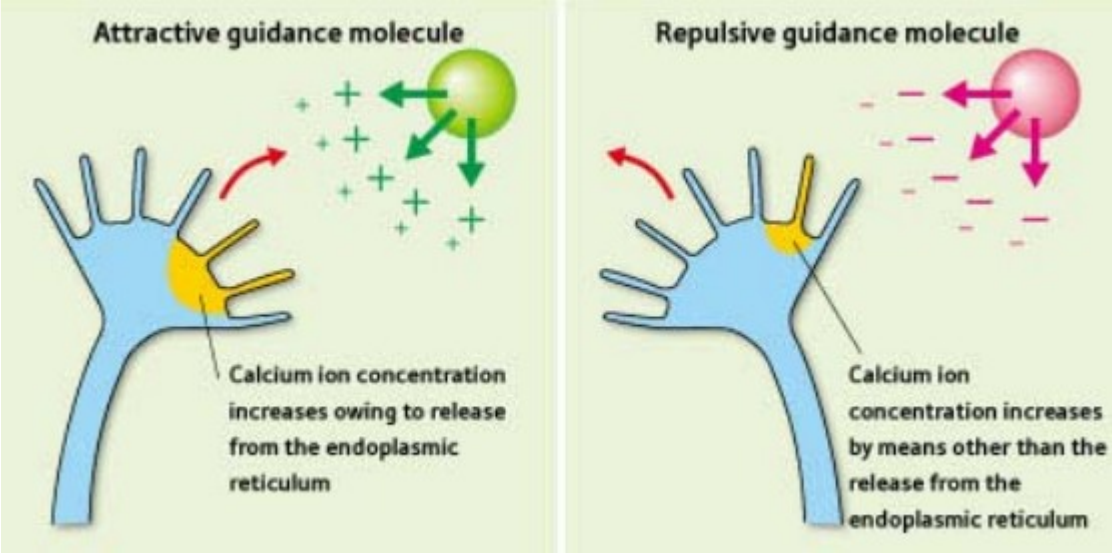


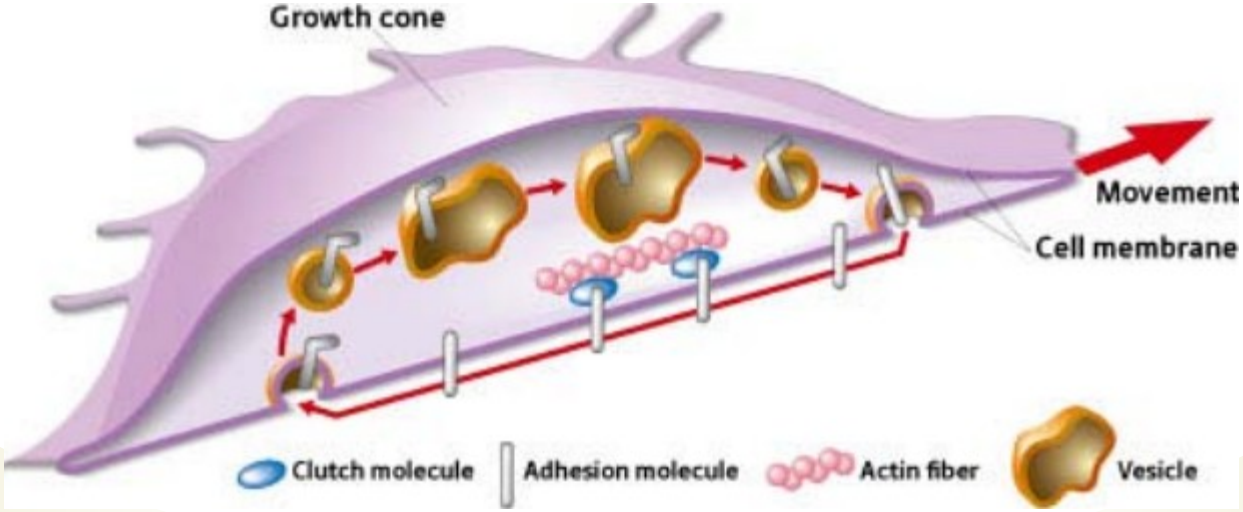
Figu

Reduction of redundant axons



Axon guidance

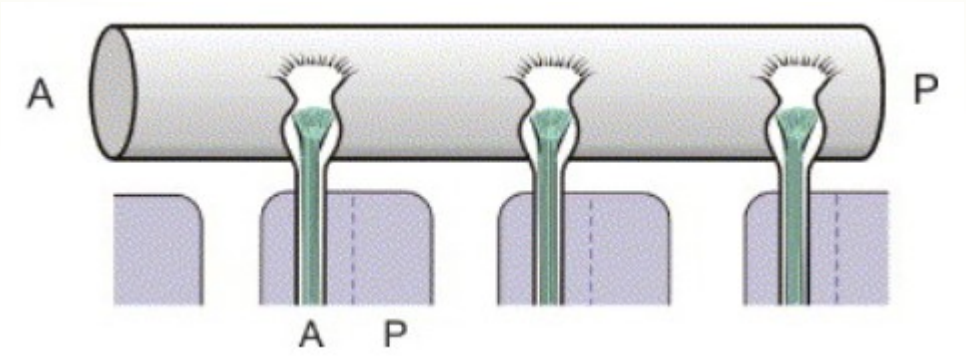


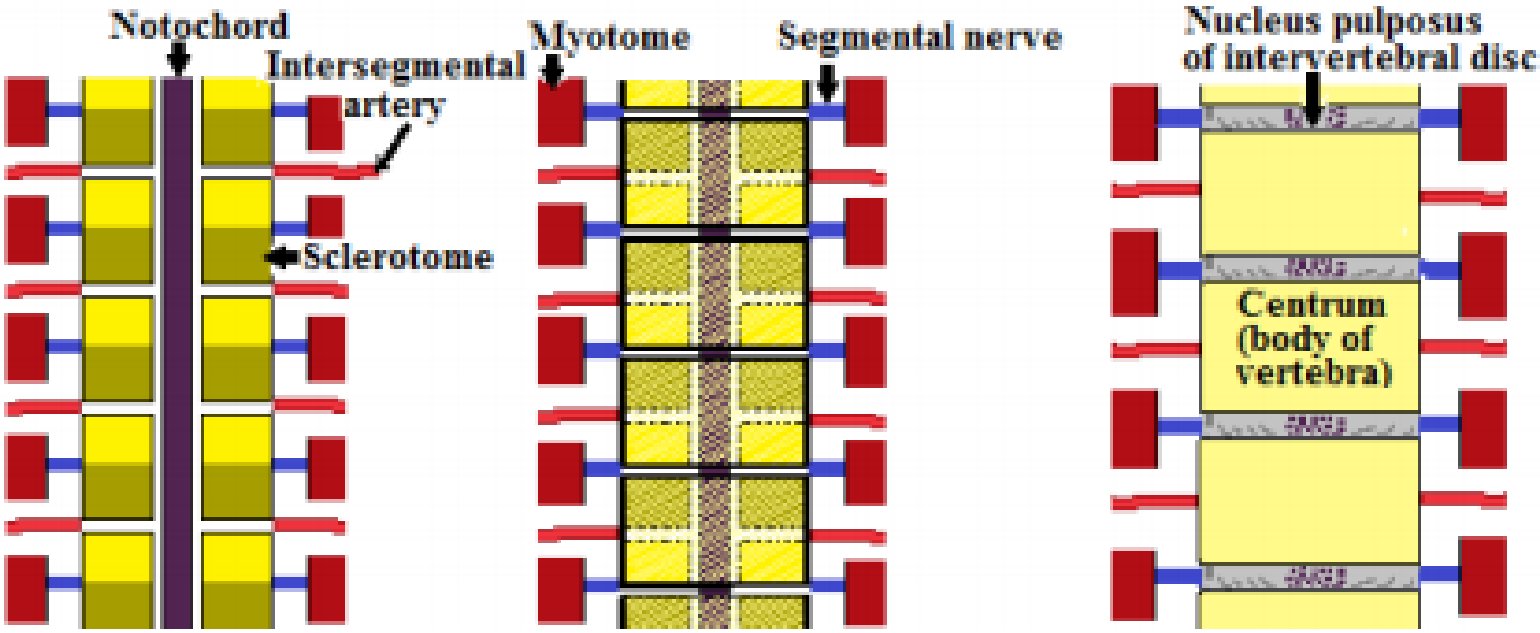


Molecular mechanisms of axonal guidance

- contact adhesion
  - permissive surface (laminin, fibronectin, cell-adhesion molecules)
- contact inhibition
  - non-permissive surface
- fasciculation
- chemotropism – attractive molecules

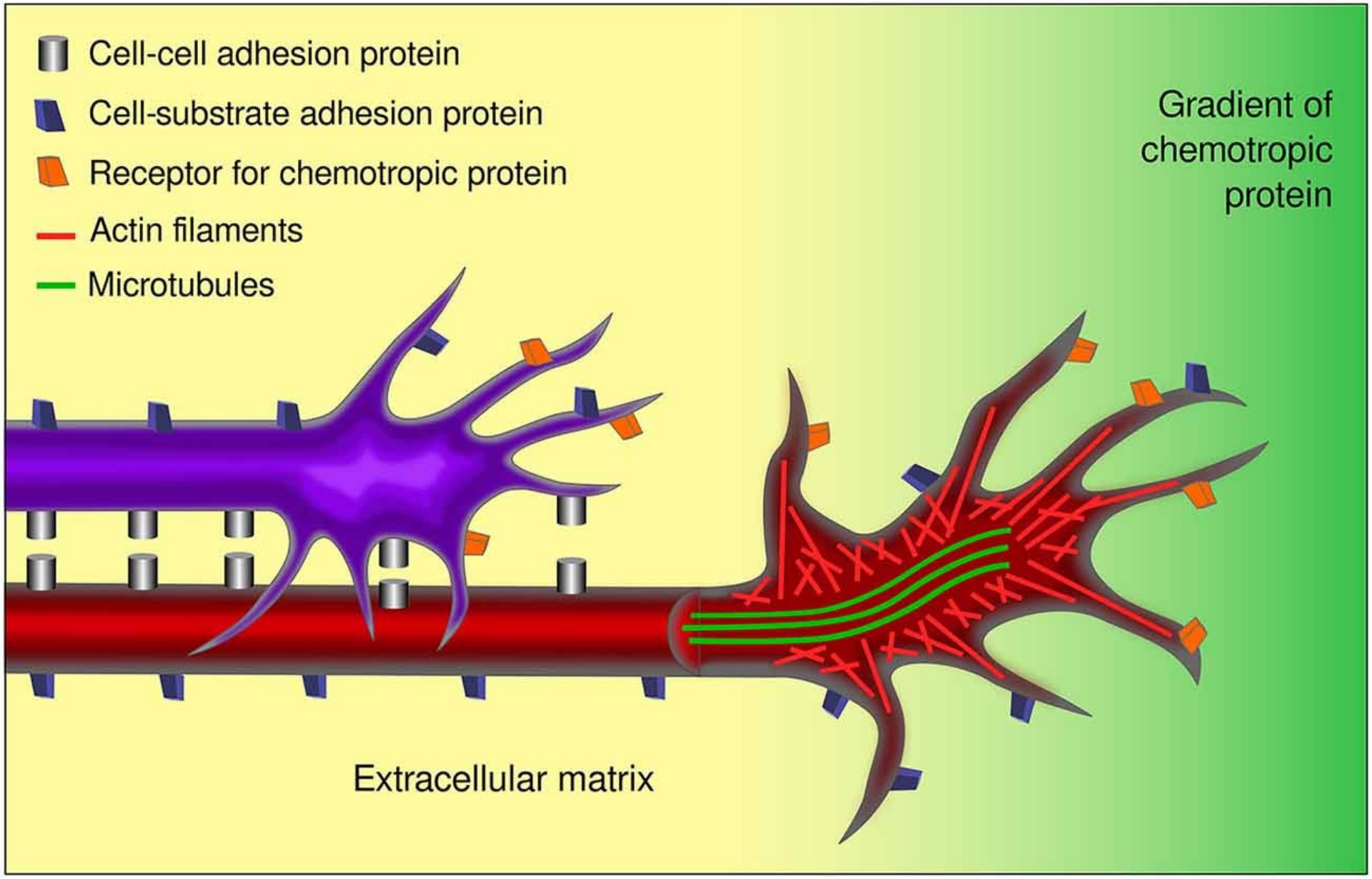
Contact adhesion and inhibition



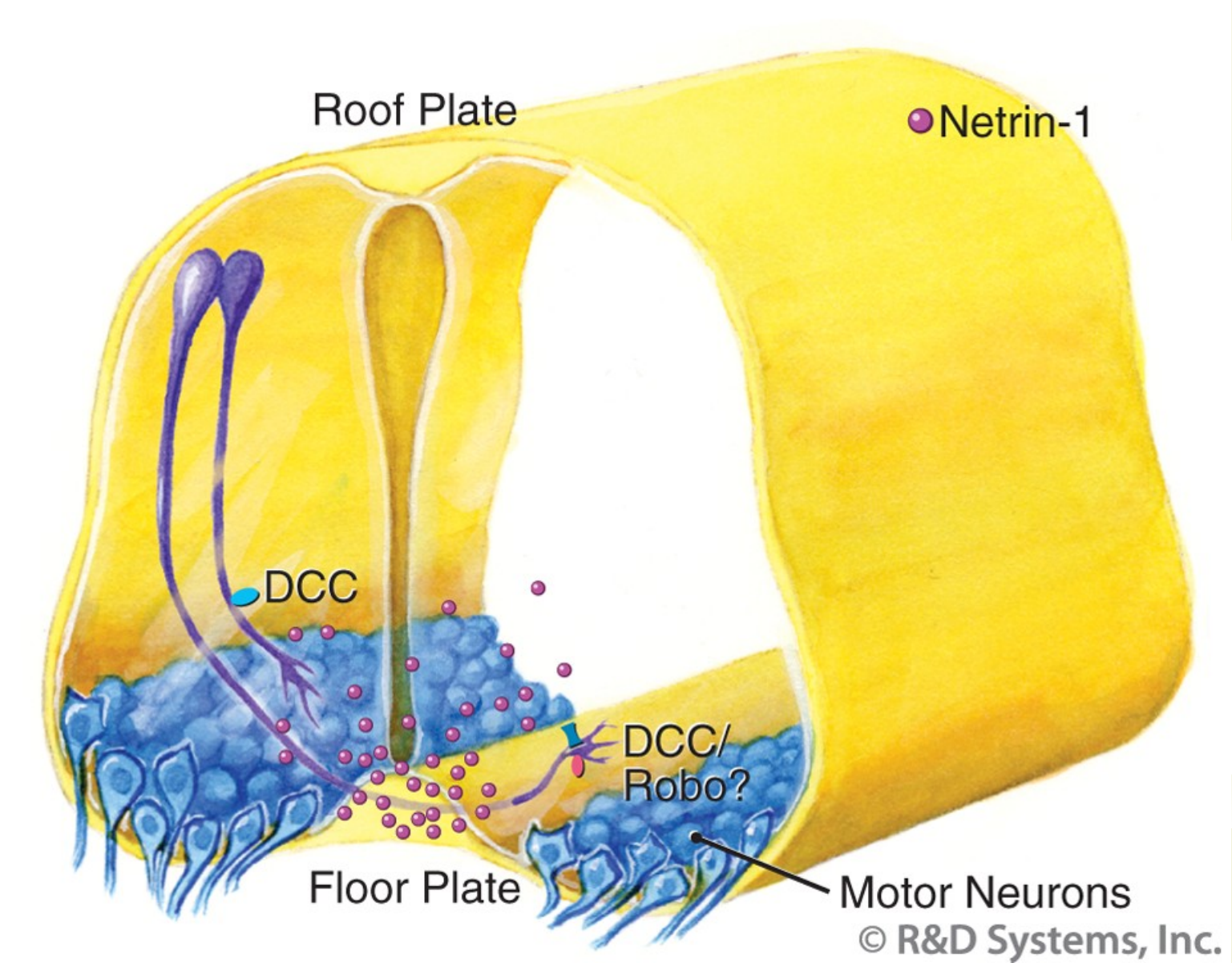


Vertebral column Development (Coronal section)

Fasciculation



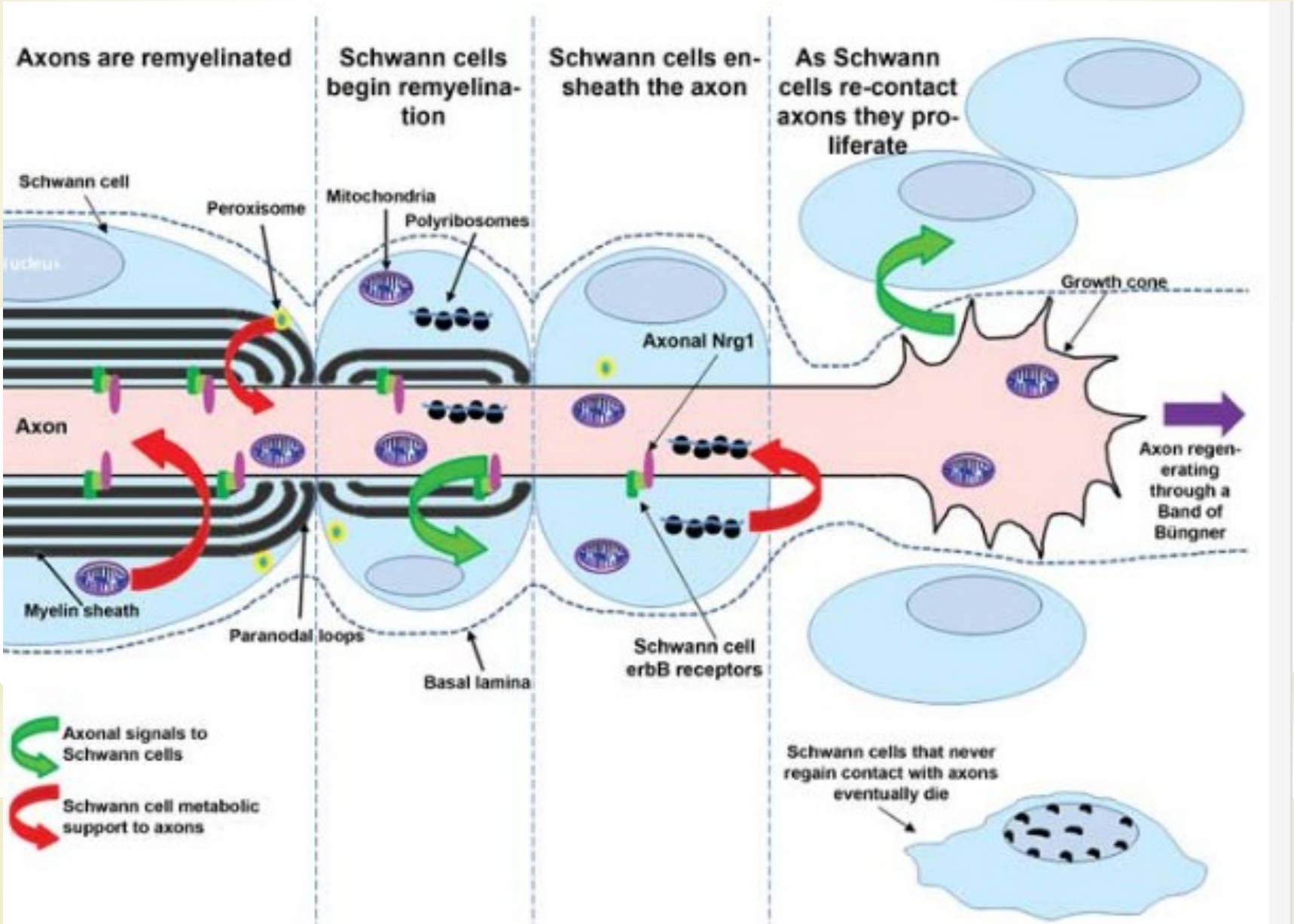
Chemotropism



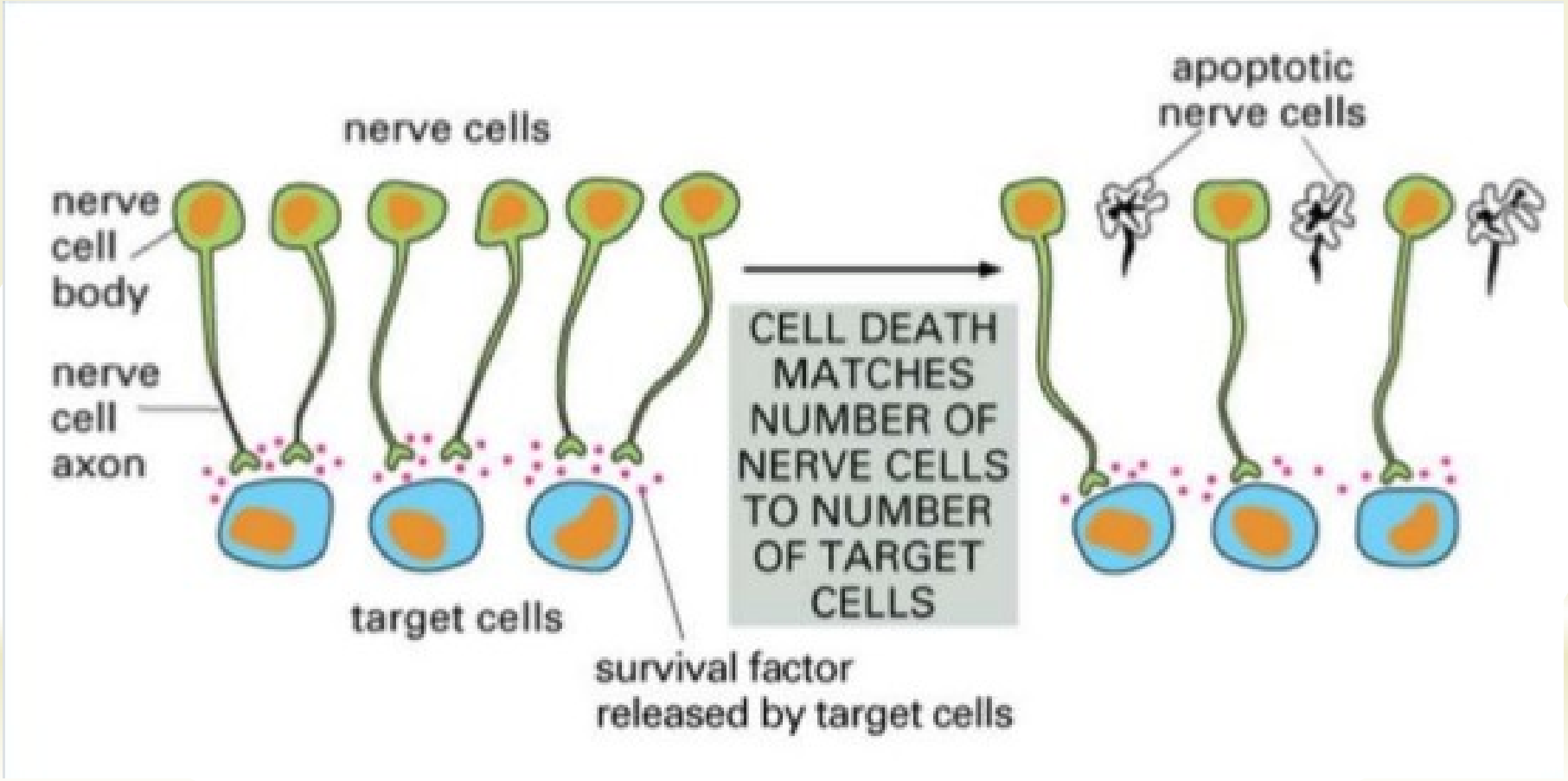
Neural plasticity

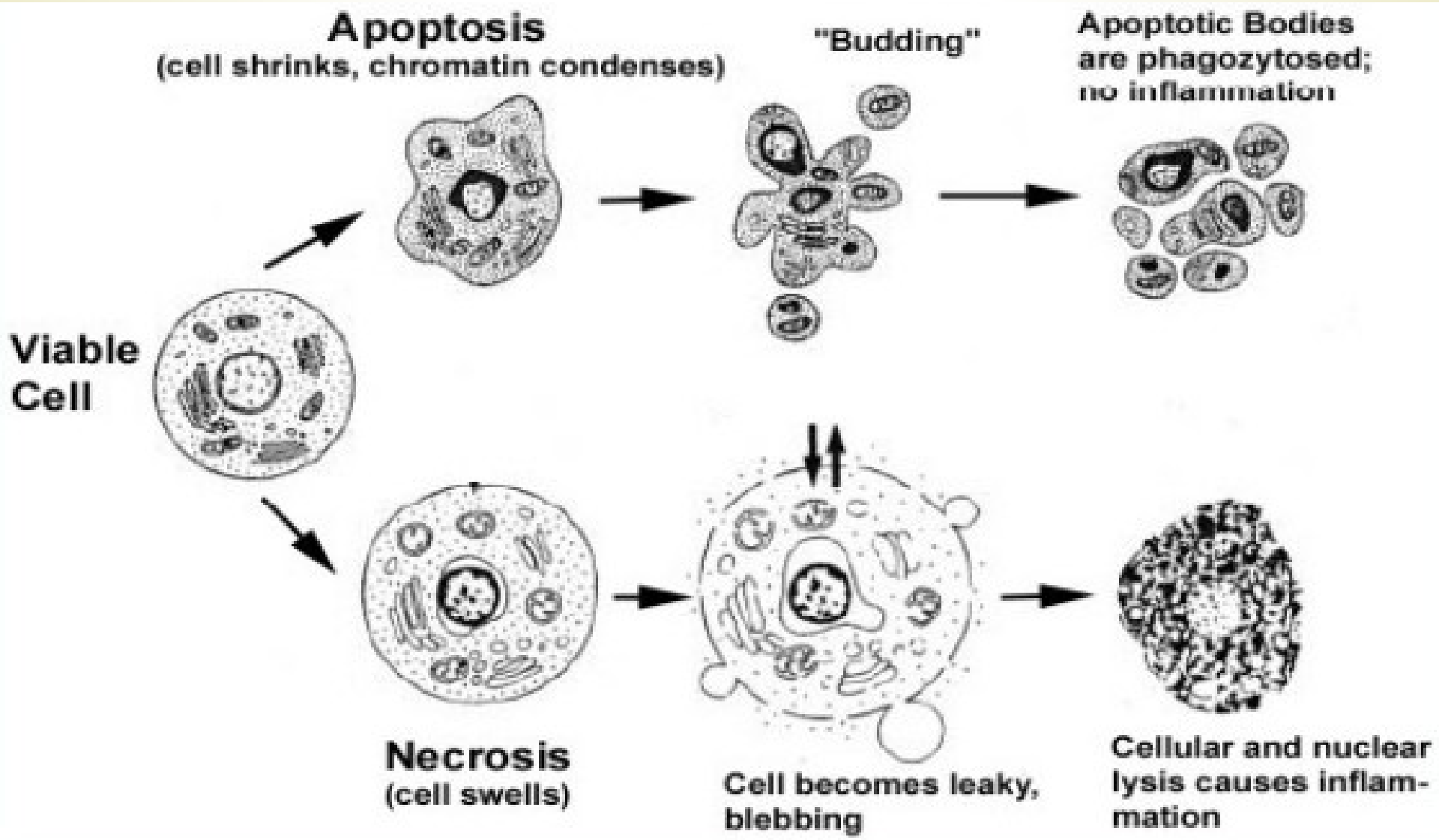
- *developmental plasticity*
  - neuroanatomical and neurophysiological changes
- *chemical plasticity*
  - fast or slow turnover
- *neurotrophic-derived plasticity*
  - neurons are not irrevocably genetically programmed to produce one transmitter
- *neuronal plasticity*
  - capability of generating new branches and synapses
- *synaptic plasticity*
  - strengthening or weakening of synapses

Reciprocal Schwann cell-axon interactions



Apoptosis


nerve cells
apoptotic nerve cells
nerve cell body
nerve cell axon
CELL DEATH MATCHES NUMBER OF NERVE CELLS TO NUMBER OF TARGET CELLS
target cells
survival factor released by target cells


Apoptosis
(cell shrinks, chromatin condenses)
"Budding"
Apoptotic Bodies
are phagozytosed;
no inflammation
Viable
Cell
Necrosis
(cell swells)
Cell becomes leaky,
blebbing
Cellular and nuclear
lysis causes inflam-
mation

Critical factors and periods in development of the CNS

- critical period in development of the CNS
  - influence of the proper factors is necessary for the next development of the structure
- genetic factors (initial period of development)
- nutritive factors
  - critical period – the 2nd trimester – 1st year
- hormonal factors
- factors of afferent pathways

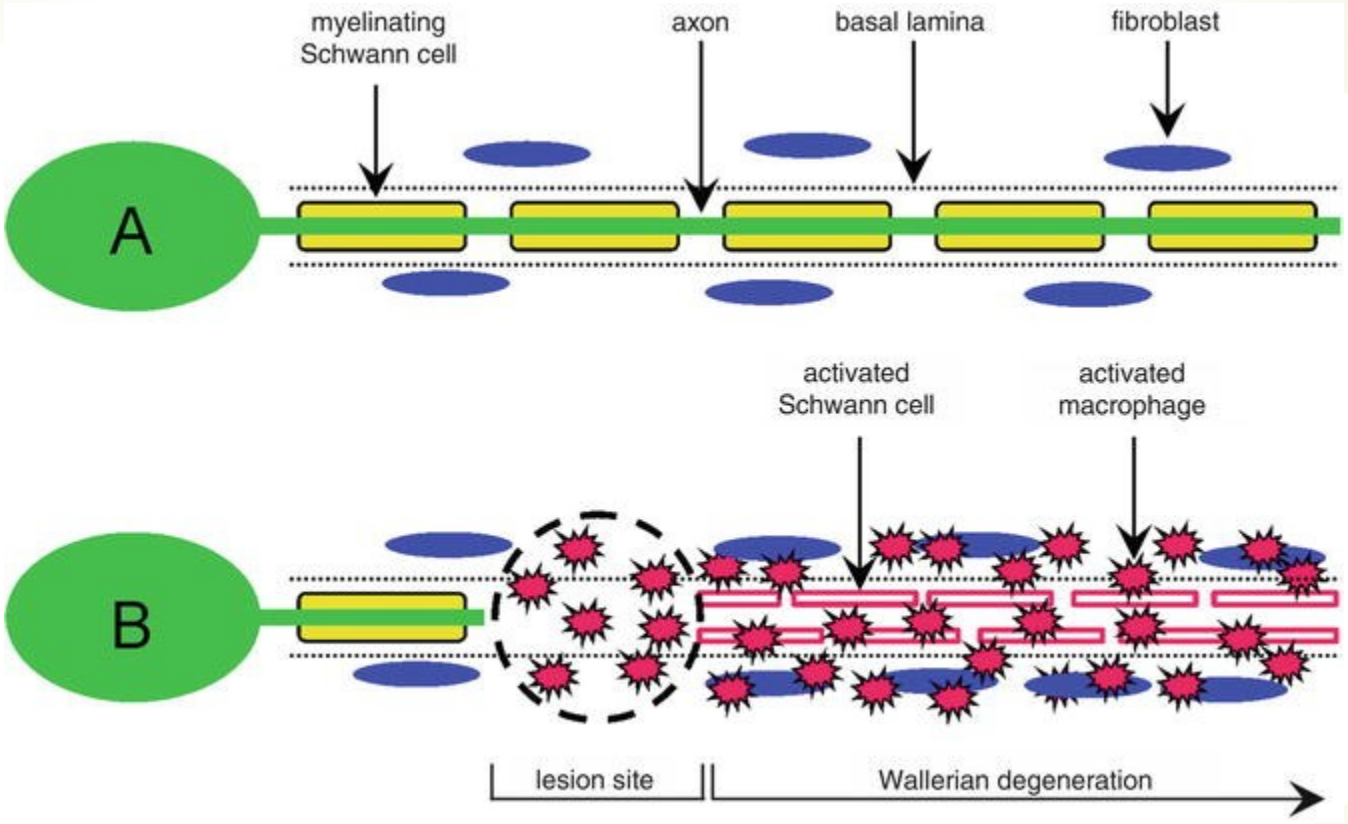
Reaction of neurons to injury

- loss of function
- influence of duration of the damaging agent
- reaction to injury of processes differs in neurons of CNS and PNS
- CNS neurons - atrophy and death due to great decline of RNA synthesis
- PNS neurons – anabolic processes depending on
  - type of injury
  - distance of the injury site from the body
  - age of the organism
  - localization and function of neurons

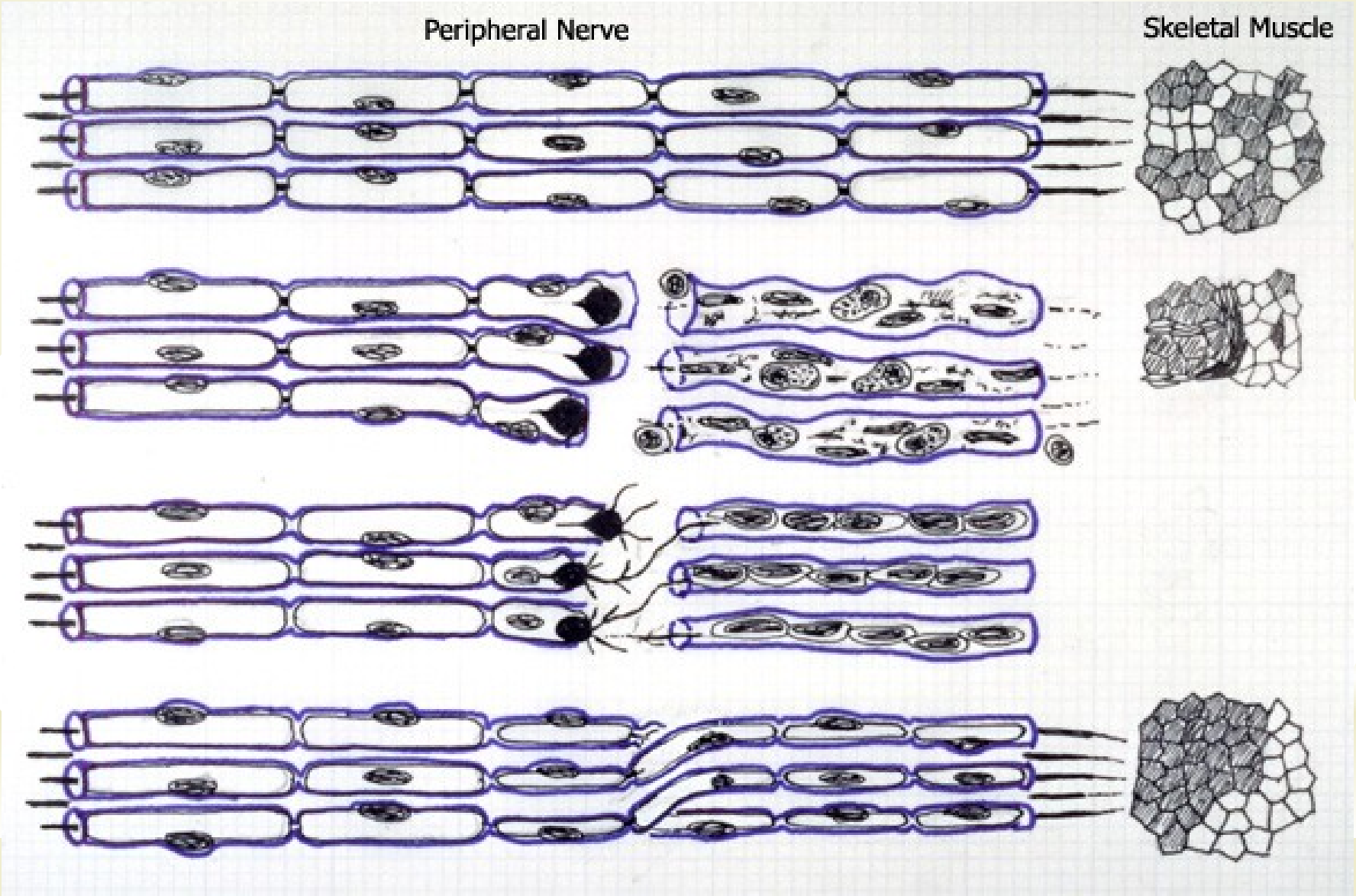
Wallerian Degeneration

In less than 24 hours	Neurofilaments break up; axons break up into short lengths
Within 10 days	Myelin sheath breaks down into lipid droplets around the axon
Within a month	Myelin gets denatured chemically
Within three months	Macrophages from the endoneurium invade the degenerating myelin sheath and axis cylinder and phagocytose the debris

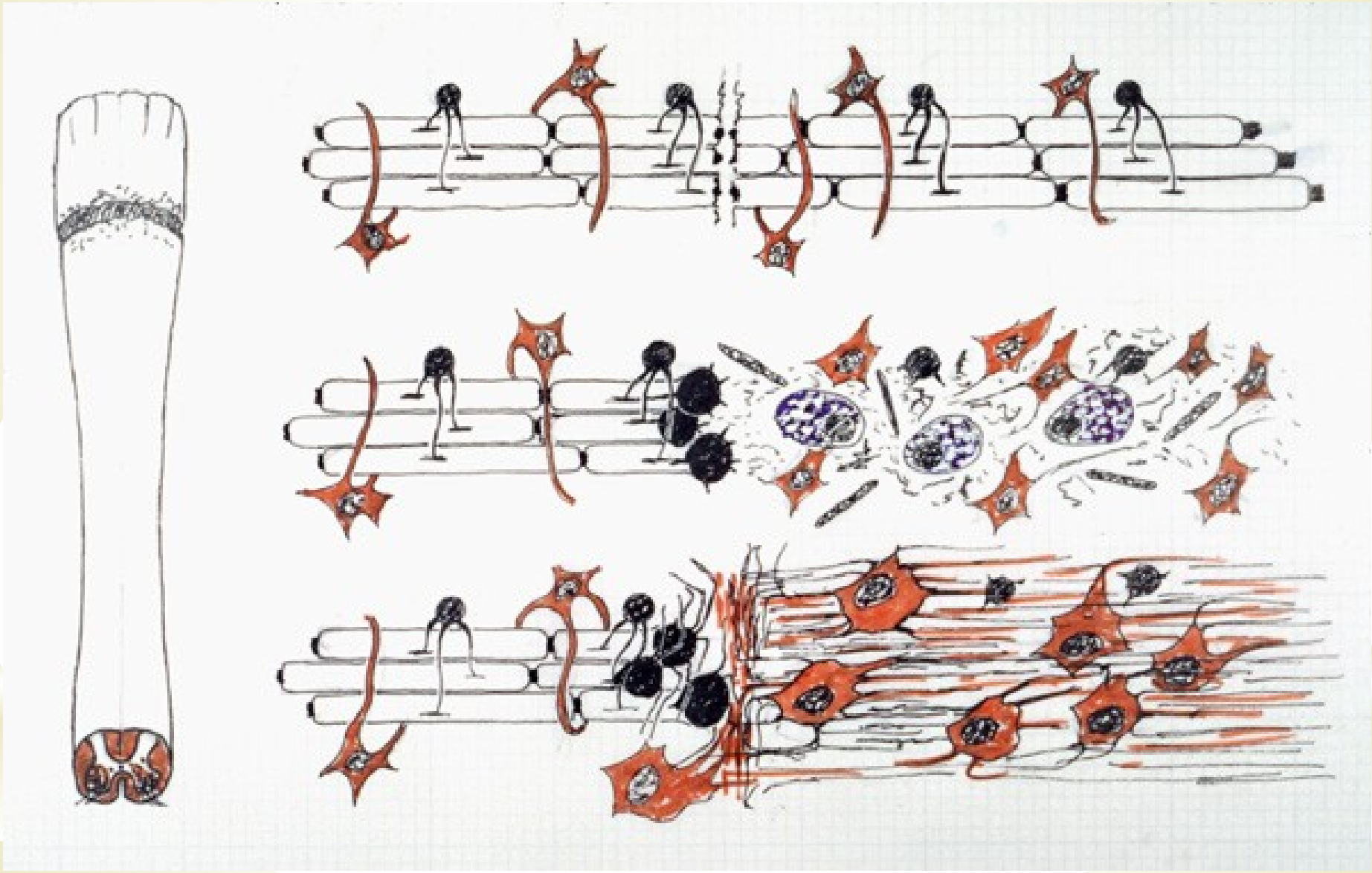
Wallerian degeneration



Peripheral nerve transection



Spinal cord trauma



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