

# **ONTOGENETIC DEVELOPMENT OF THE NERVOUS SYSTEM**

# Ontogenetic development

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

# Development of a neuron:

## 1) genetic level

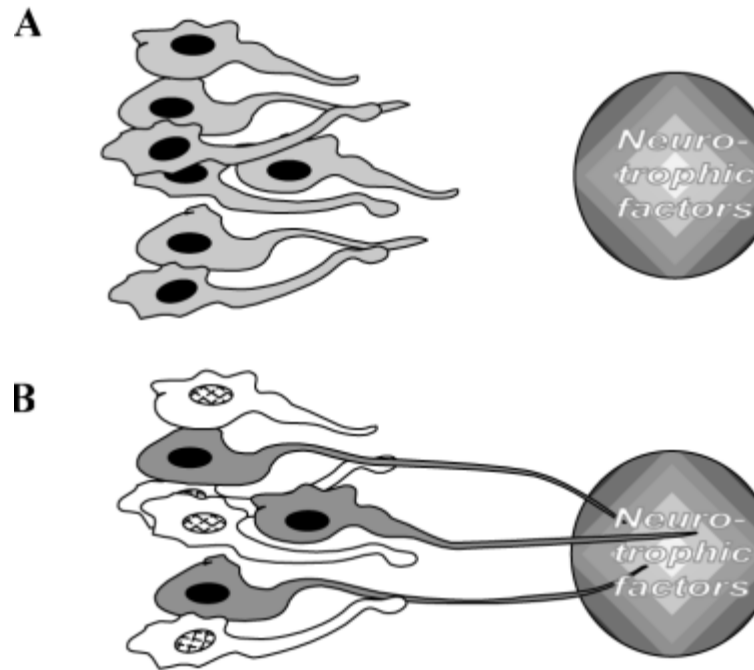
a) transcription (DNA  $\rightarrow$  RNA)

b) translation (RNA  $\rightarrow$  polypeptides)

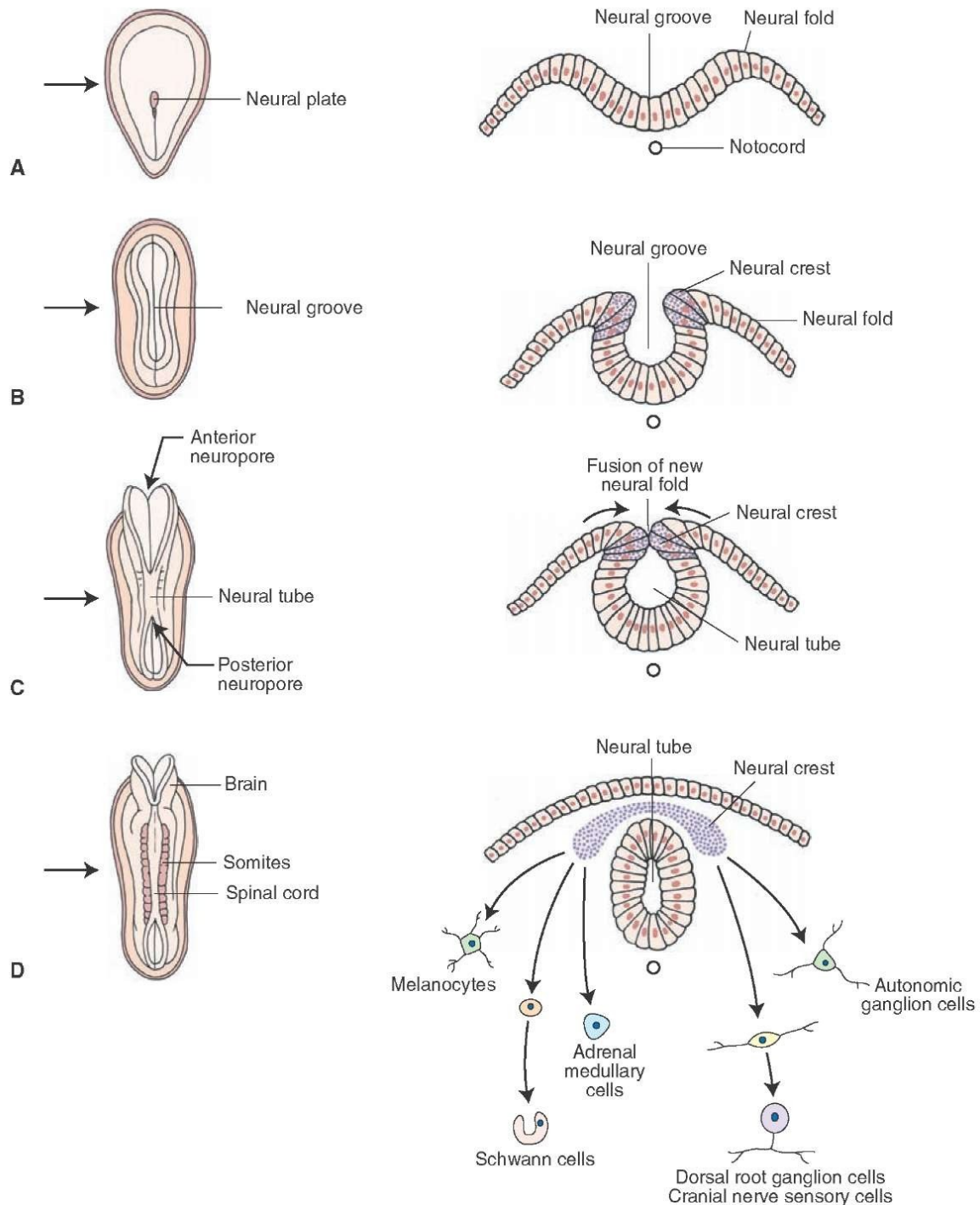
## 2) epigenetic level

neurotropic and neurotrophic molecules

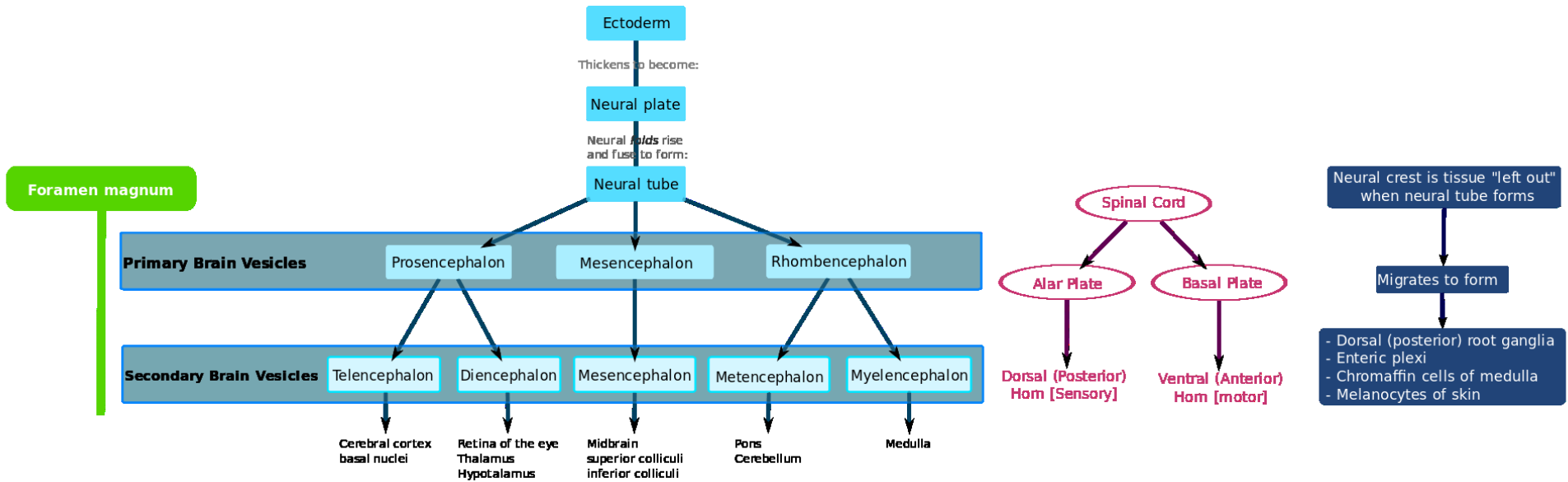
# Target field theory



# Development of the NS



# Development of the NS



# 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

# 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  $\alpha$  (TGF $\alpha$ )
- Transforming Growth Factor  $\beta$  1-3 (TGF $\beta$  1, TGF $\beta$  2, TGF $\beta$  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)

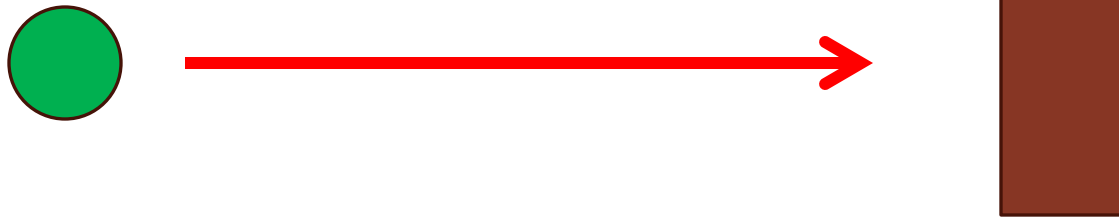
## Other factors

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



# Trophic relationships in the NS

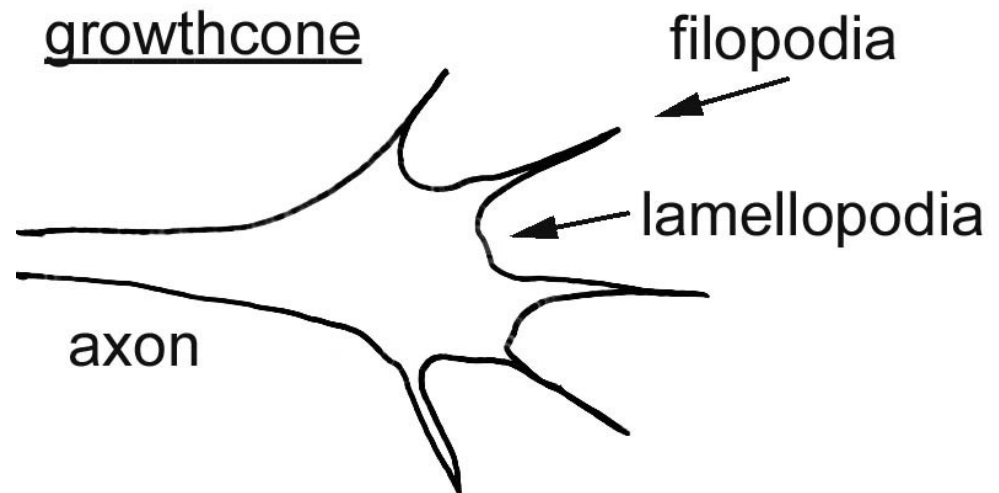
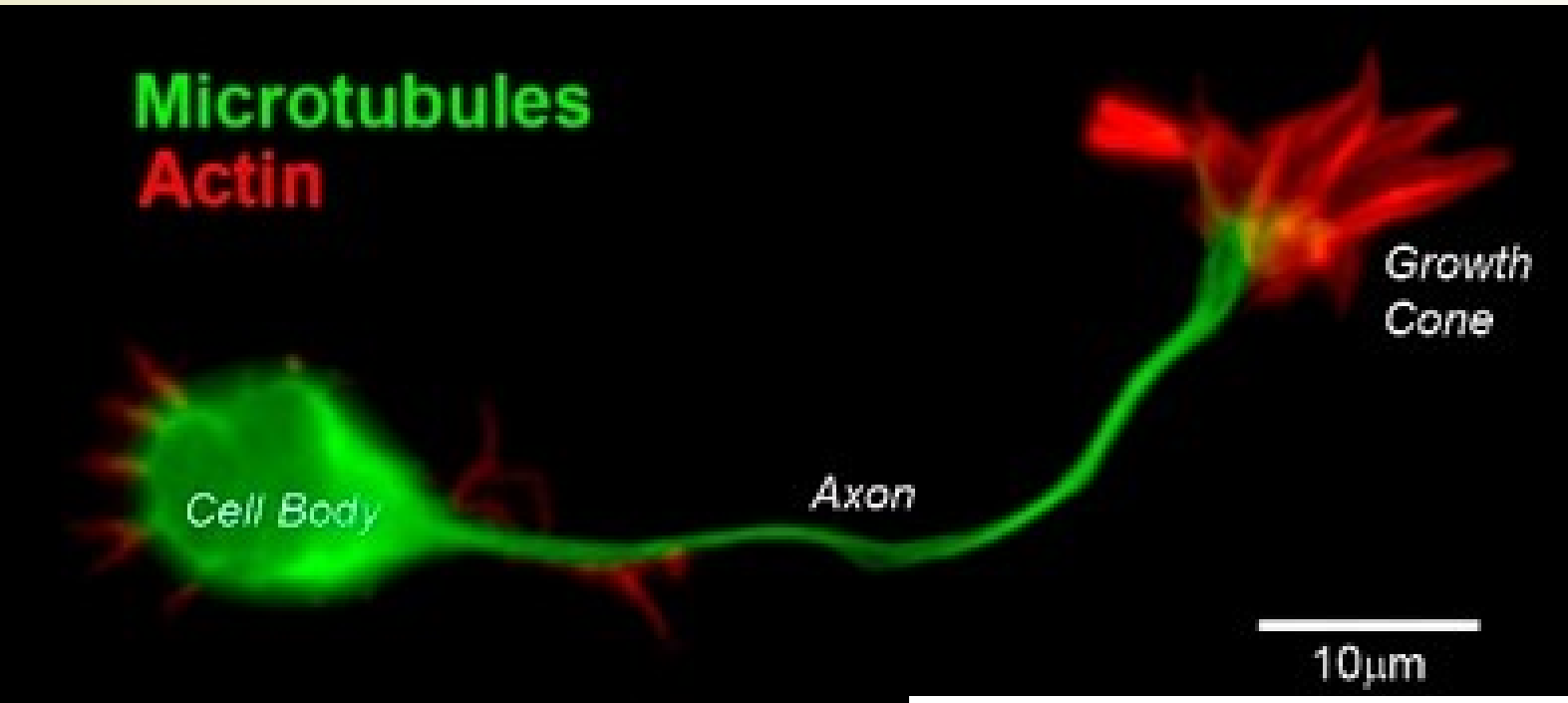
Neurons have trophic effect on periferal tissues



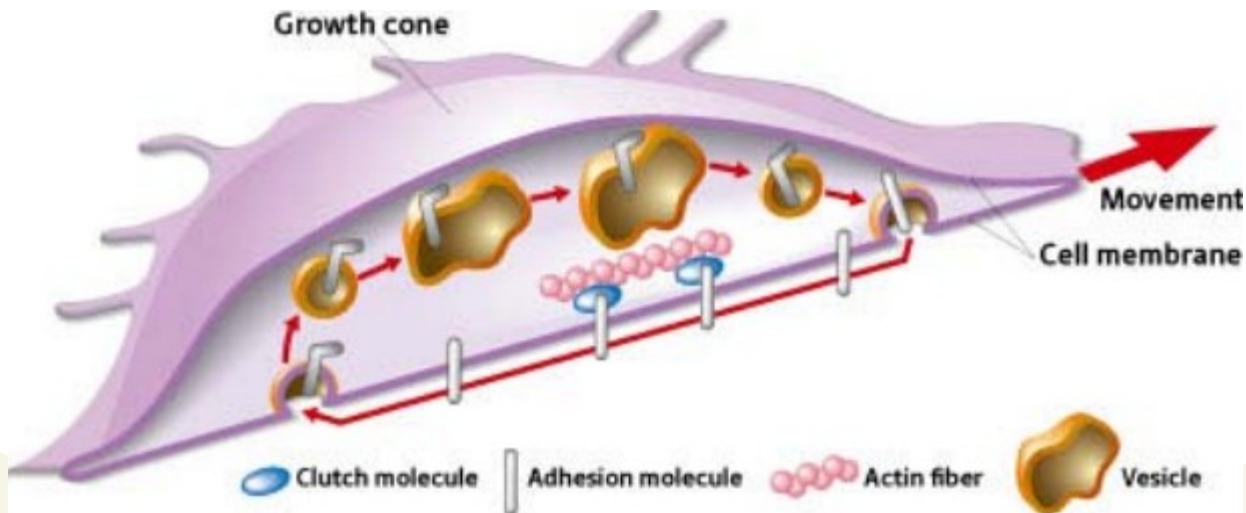
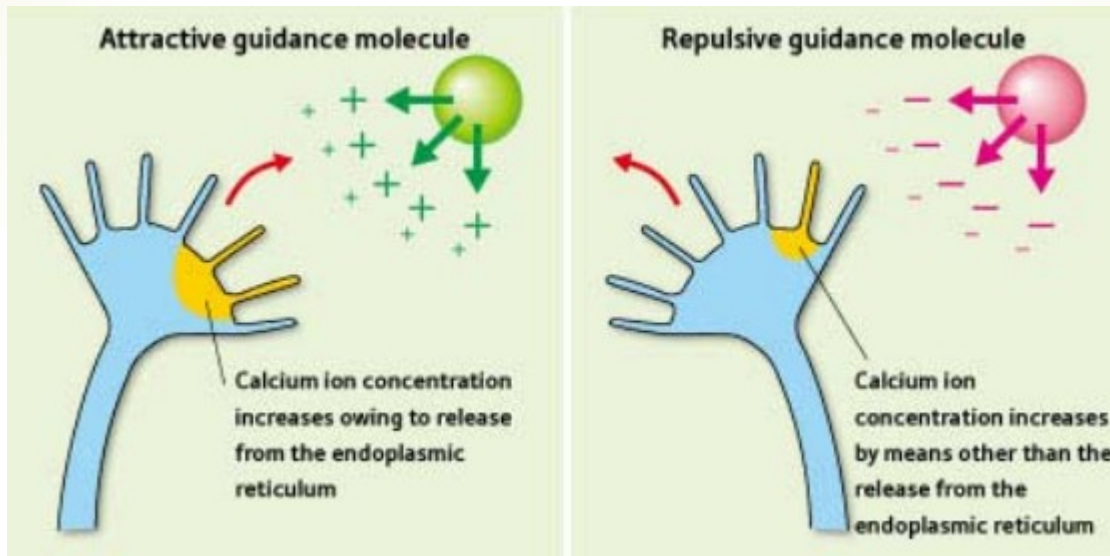
Periferal tissues have trophic effect on neurons



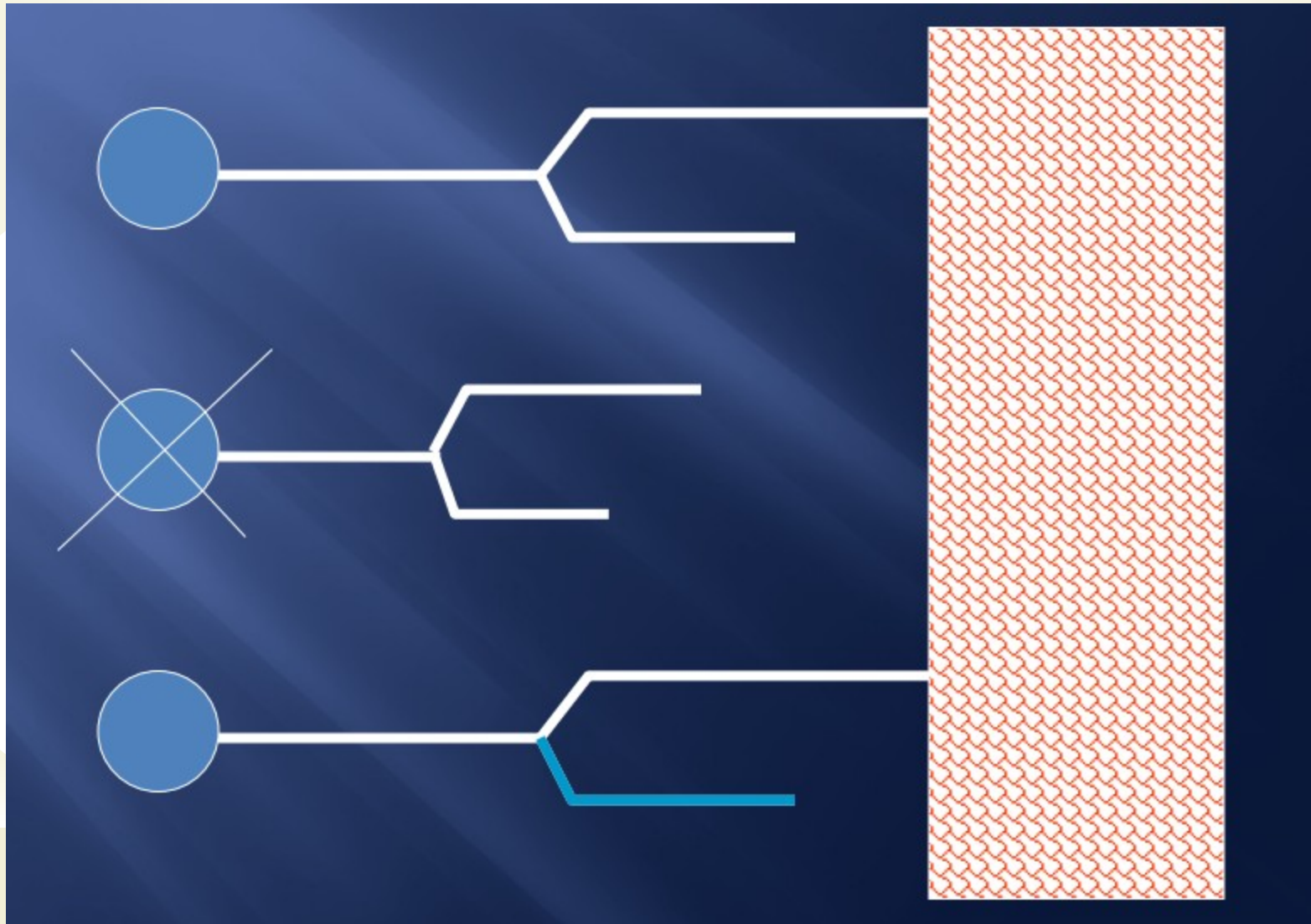
# Growth cone



# Axon guidance



# Reduction of redundant axons



# Molecular mechanisms of axonal guidance

- ❑ contact adhesion
  - permissive surface
  
- ❑ contact inhibition
  - non-permissive surface
  
- ❑ fasciculation
  
- ❑ chemotropism - attractive molecules

# Axon guidance

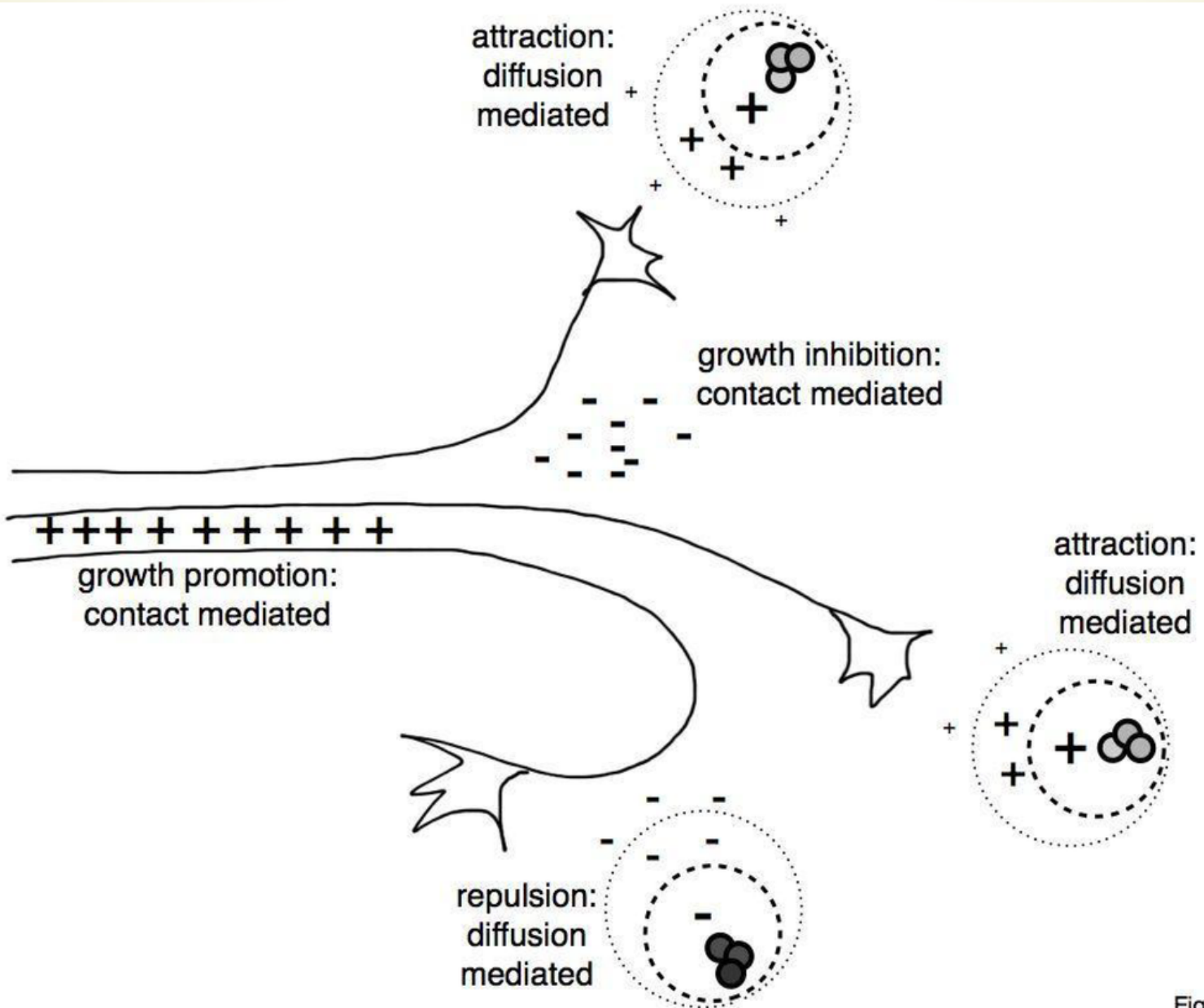
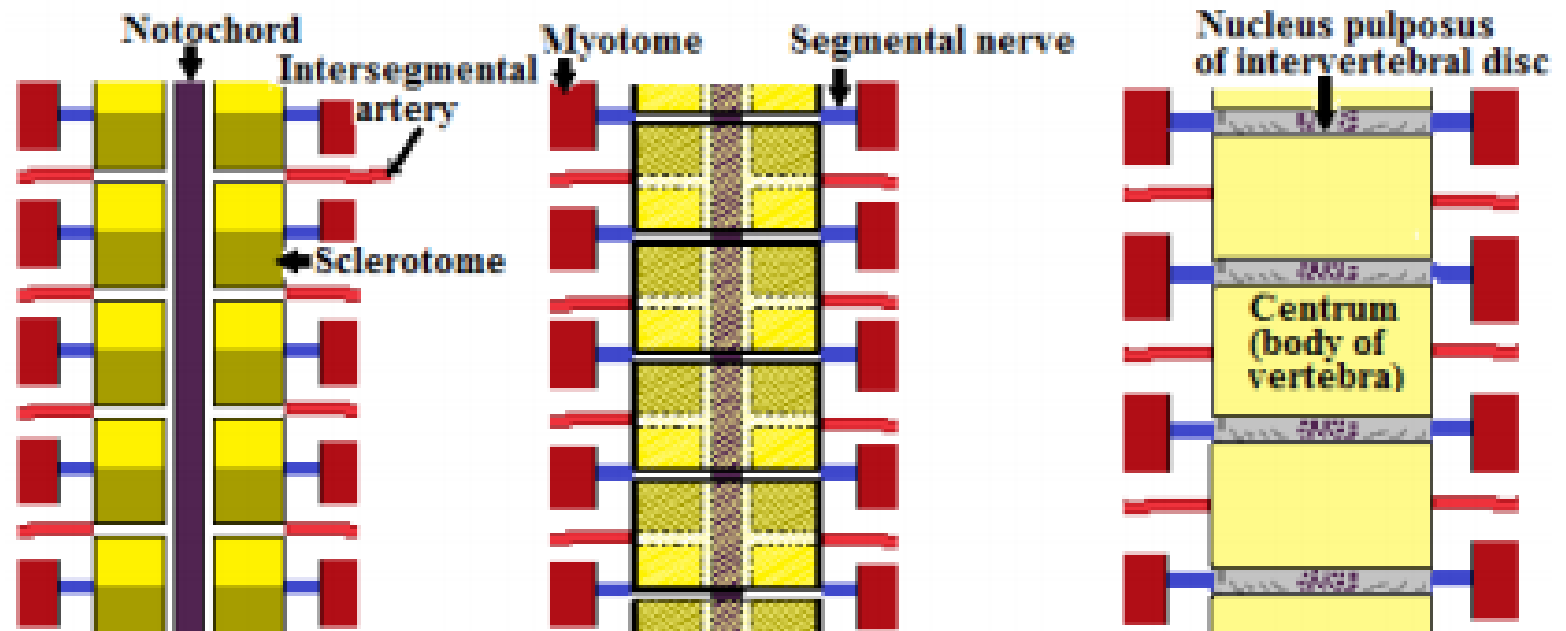


Figure 1

# Contact adhesion and inhibition

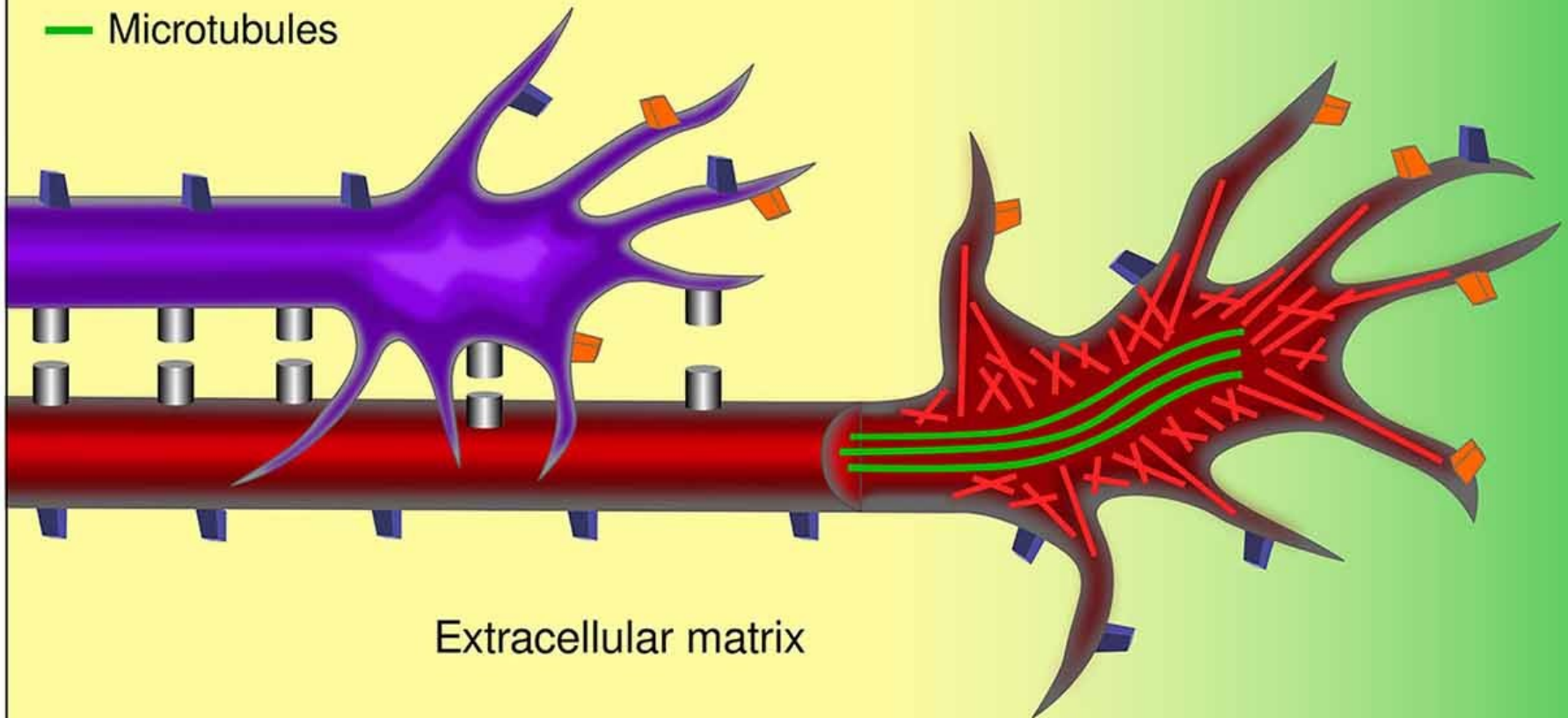


*Vertebral column Development (Coronal section)*

# Fasciculation

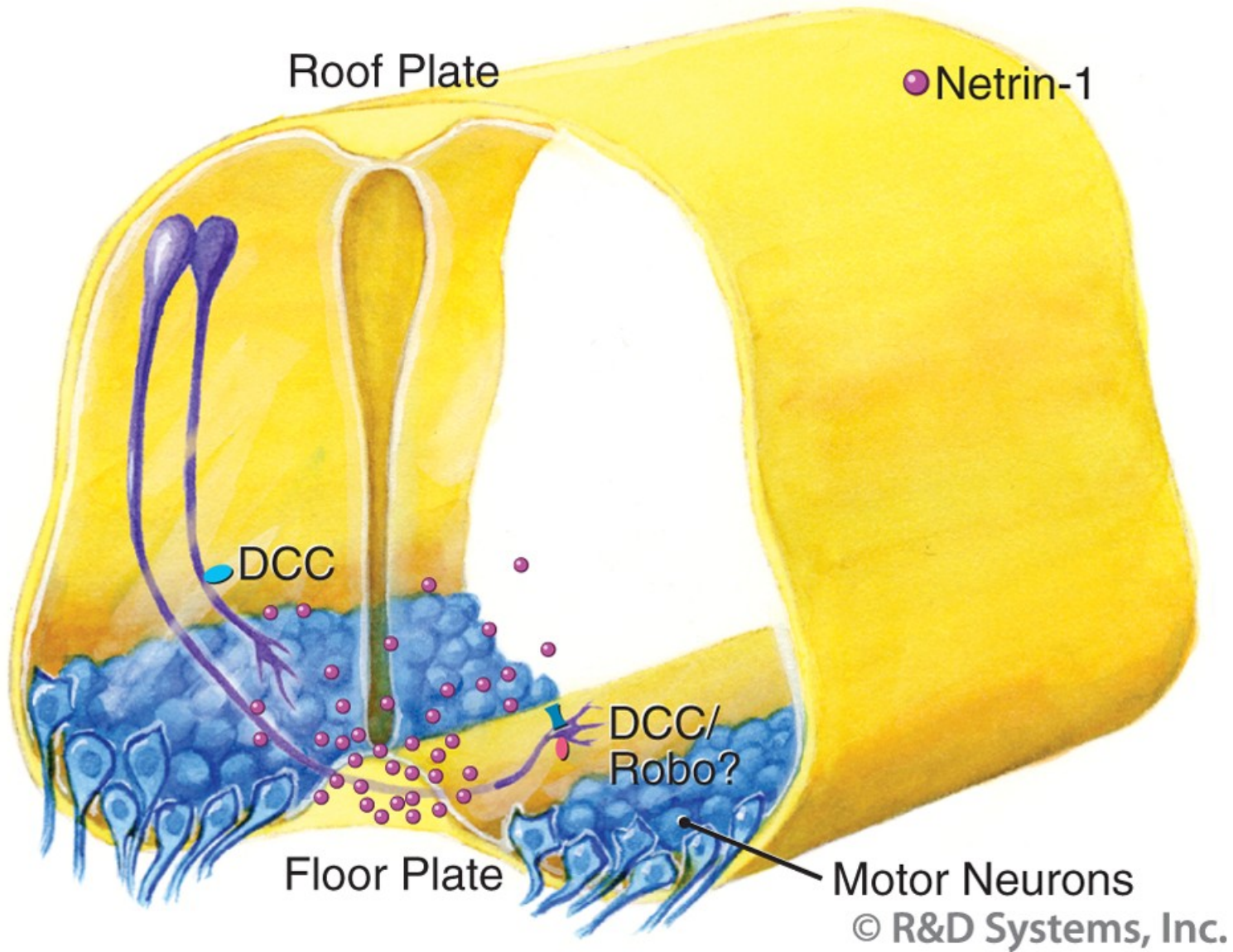
- Cell-cell adhesion protein
- Cell-substrate adhesion protein
- Receptor for chemotropic protein
- Actin filaments
- Microtubules

Gradient of chemotropic protein





# 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

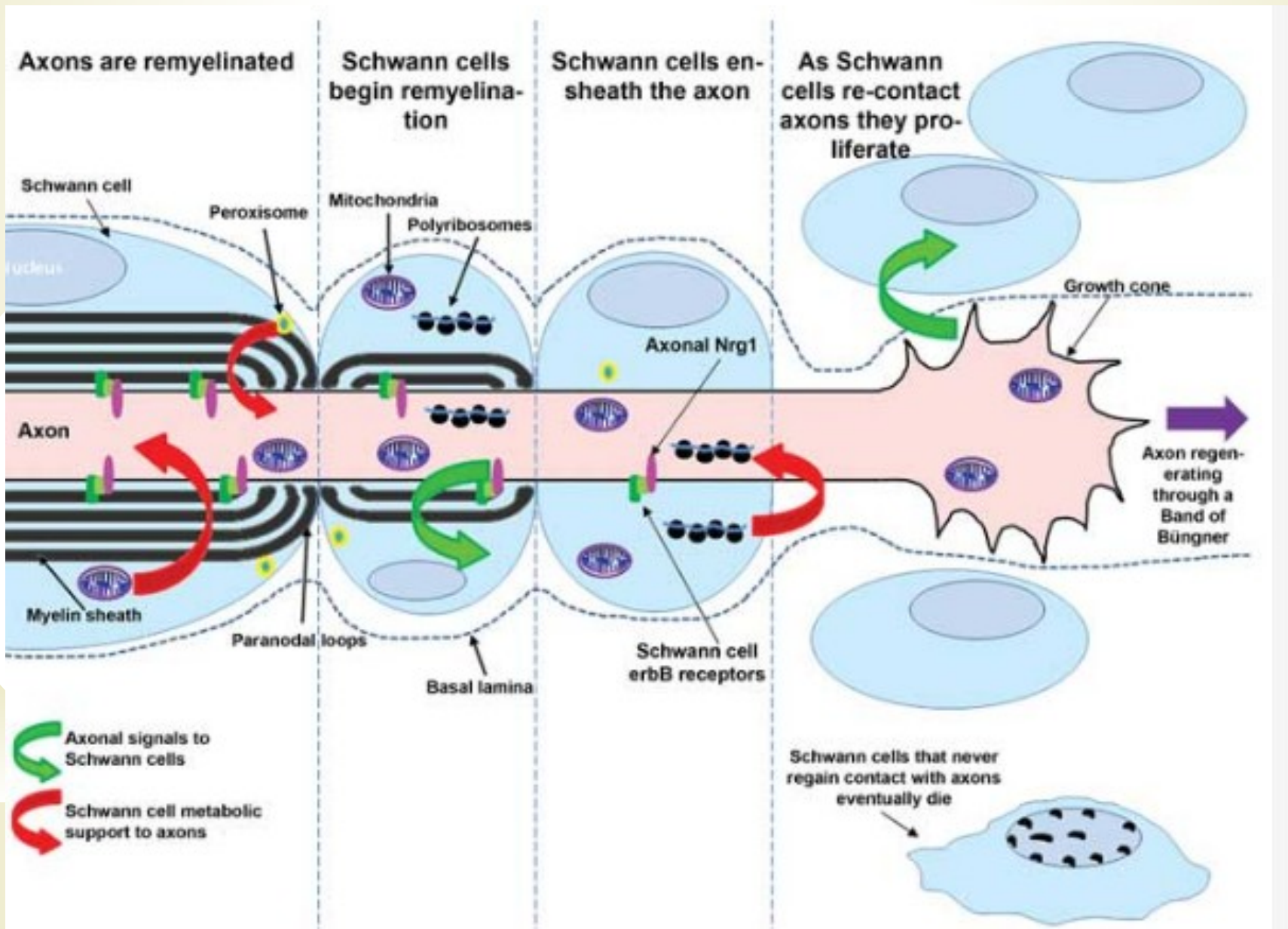
## ❑ *neuronal plasticity*

- capability of generating new branches and synapses

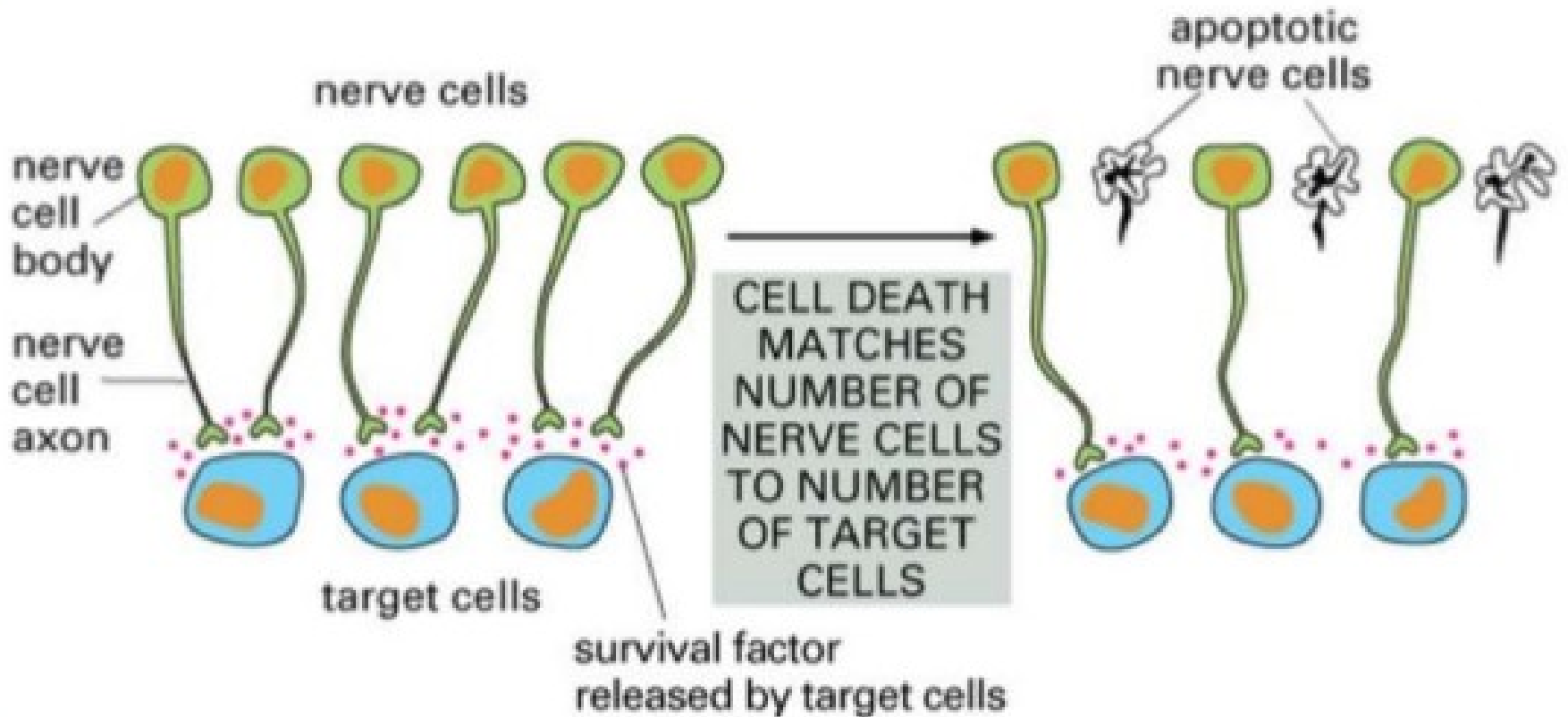
## ❑ *synaptic plasticity*

- strengthening or weakening of synapses

# Reciprocal Schwann cell-axon interactions



# Apoptosis

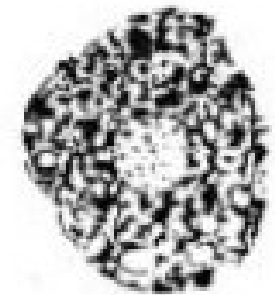
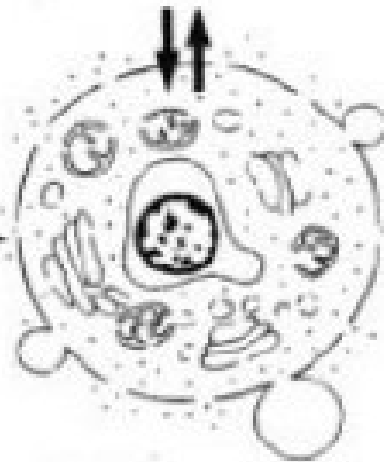
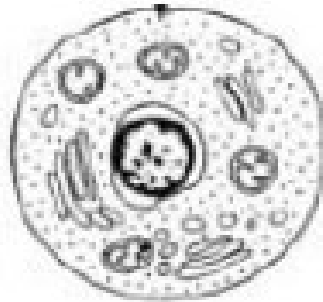
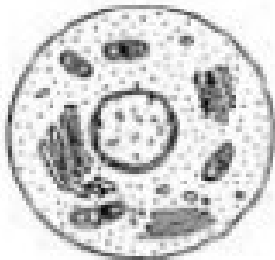
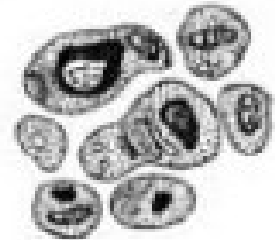
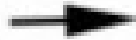
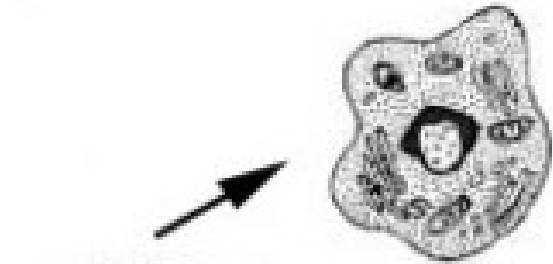


**Apoptosis**  
(cell shrinks, chromatin condenses)

"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 developmental factors is necessary for the next development of the structure
- ❑ genetic factors (initial period of development)
- ❑ nutritive factors
  - critical period - the 3rd trimester - reduction in amount of neurons
- ❑ hormonal factors
- ❑ factors of afferent pathways

# Reaction of neurons to injury

- ❑ loss of function
- ❑ influence of duration of the damaging agent
- ❑ reaction 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*

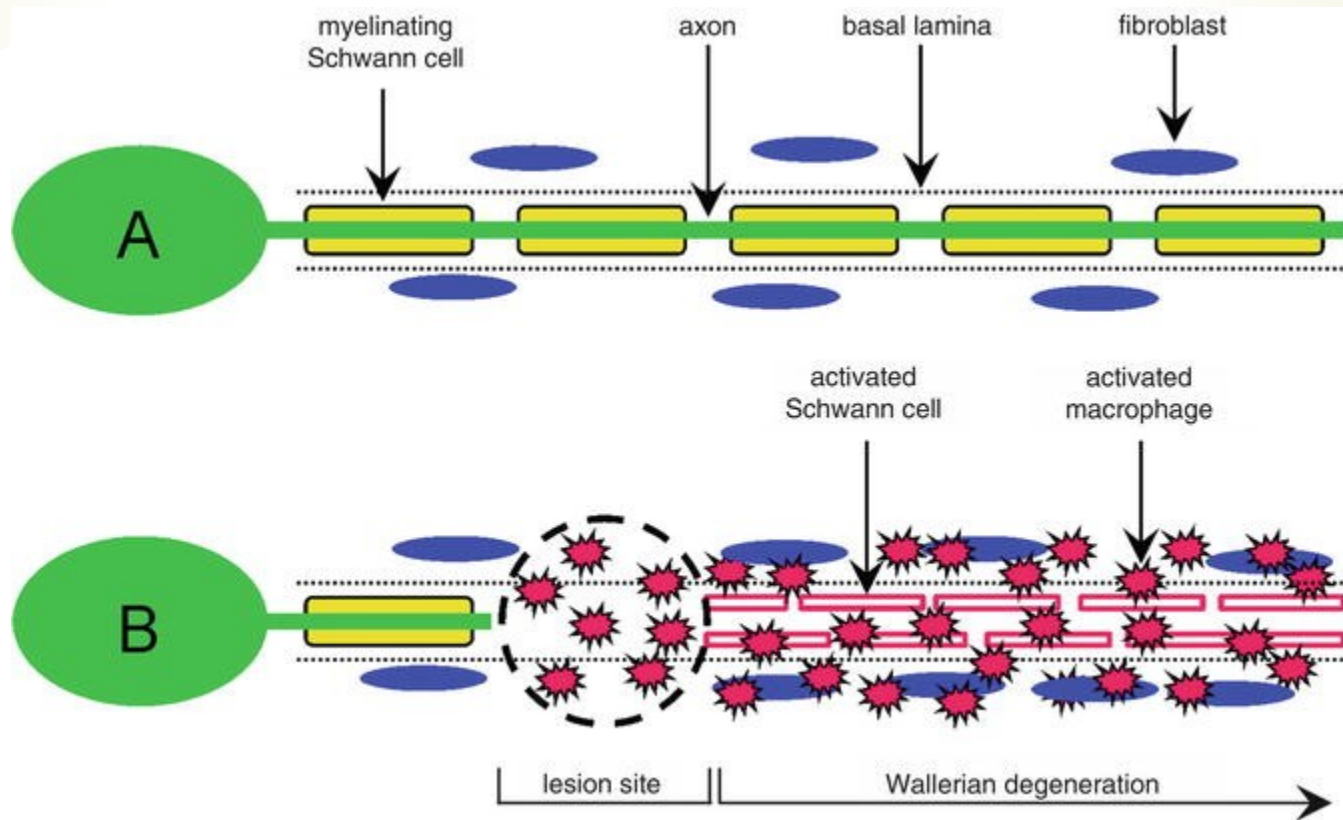
*Myelin gets denatured chemically*

*Within three months*

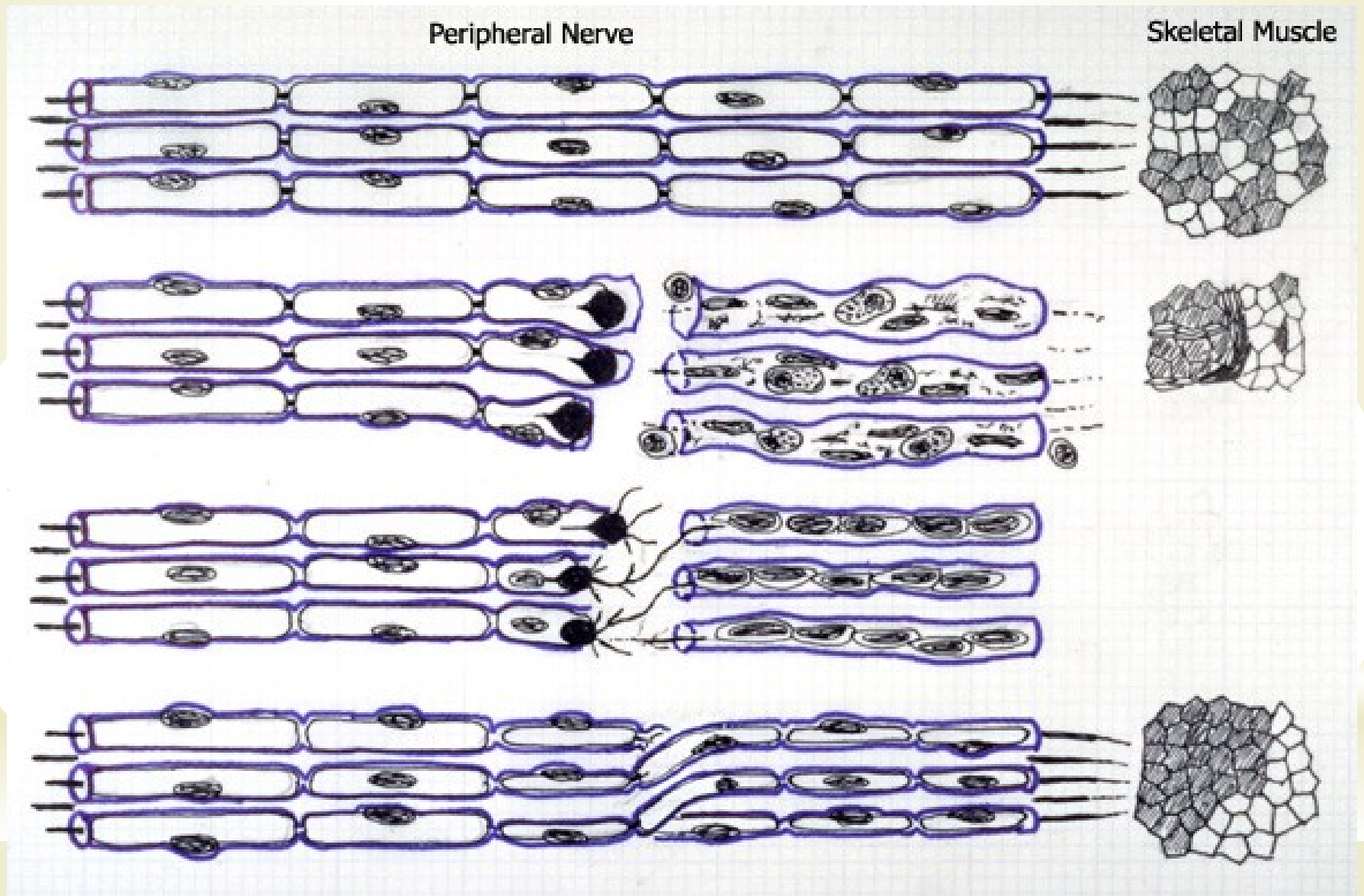
*Macrophages from the endoneurium invade the degenerating myelin sheath and axis cylinder and phagocytose the debris*



# Wallerian degeneration



# Peripheral nerve transection



# Spinal cord trauma



Illustrations were copied from:

**Neuroscience Online, the Open-Access Neuroscience  
Electronic Textbook**

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