Physiology of the nerve

Objectives

Transmembrane potential

Action potential

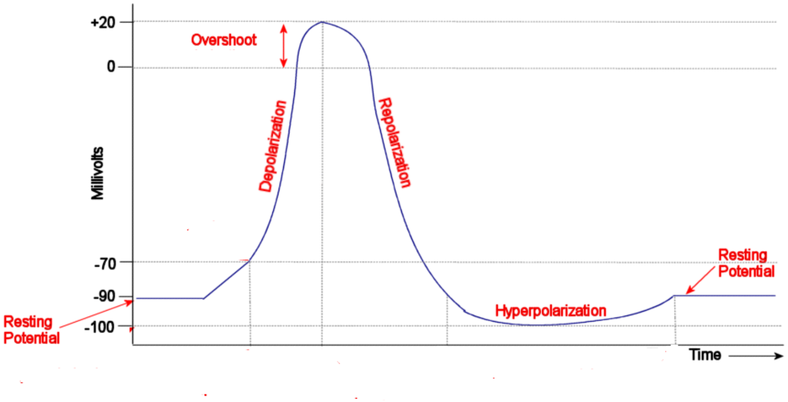
Relative and absolute refractory period

The all-or-none law

Hoorweg – Weiss curve

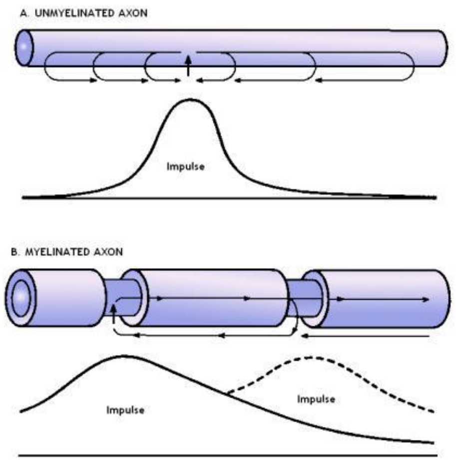
Du Bois – Reymond principle

Types of nerve fibres

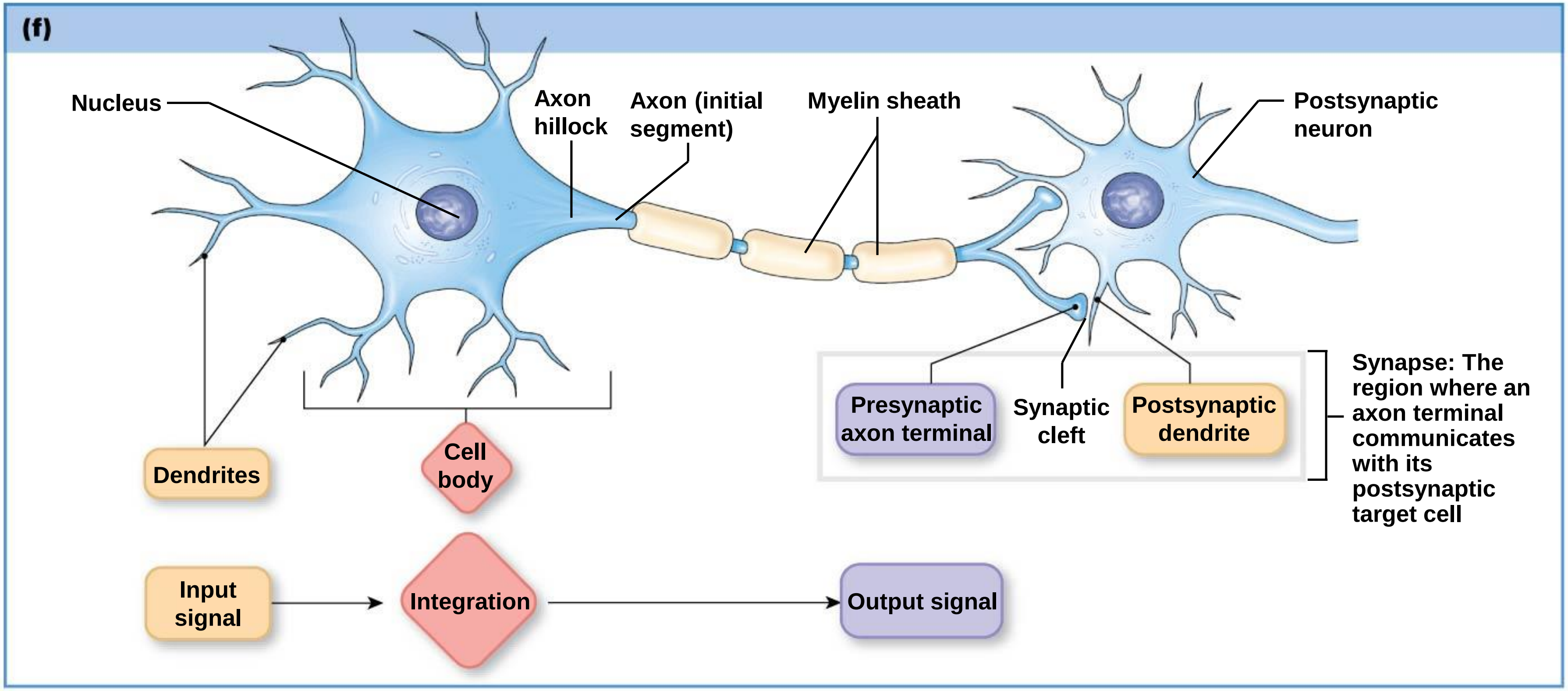


Practical tasks

Virtual physiology of the nerve (PC programme)



Parts of a neuron

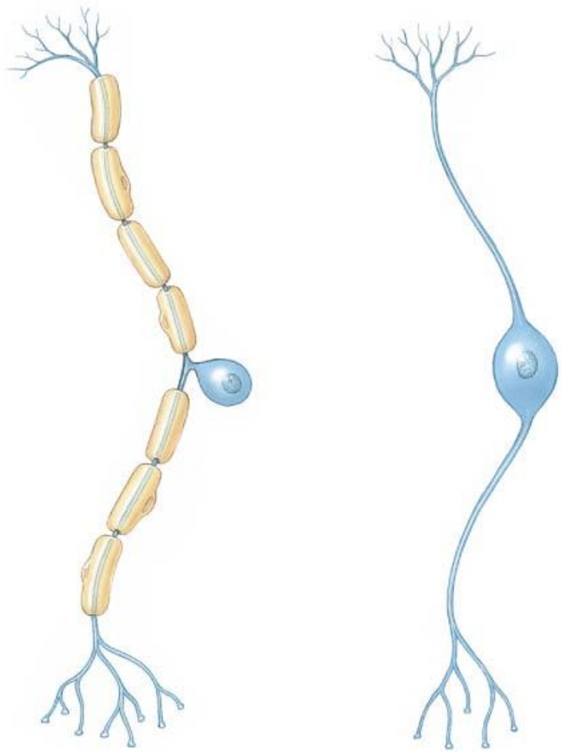


Synapse

- connection: neuron-neuron or or neuron - effector (muscle, gland)
- transmits signals from a neuron to another neuron or to the effector

Draw a scheme of a neuron and indicate its parts

Types of neurons

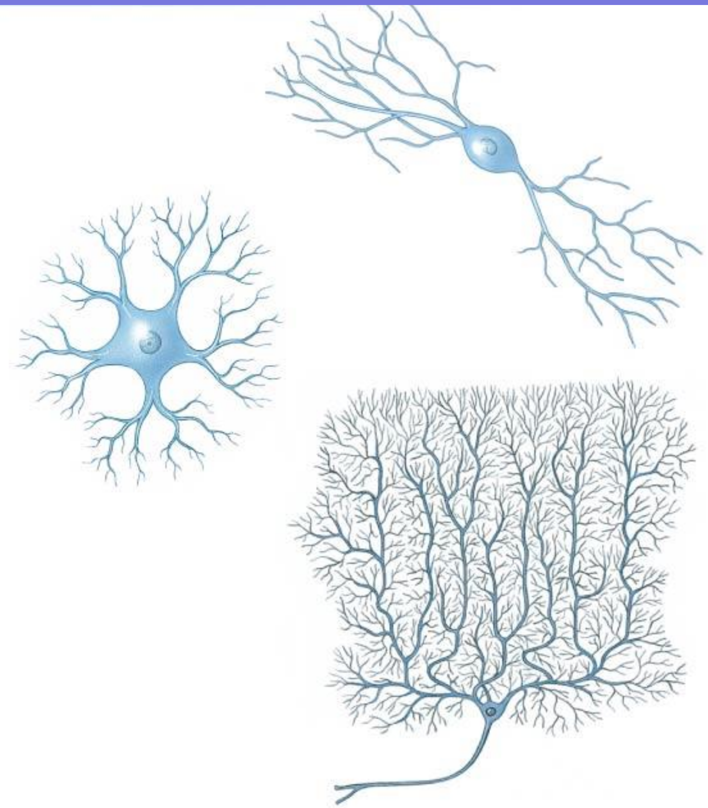


Pseudounipolar

(a) Pseudounipolar neurons have a single process called the axon. During development, the dendrite fused with the axon.

Bipolar

(b) Bipolar neurons have two relatively equal fibers extending off the central cell body.



Anaxonic

(c) Anaxonic CNS interneurons have no apparent axon.

Multipolar

(d) Multipolar CNS interneurons are highly branched but lack long extensions.

Receptive and conductive membranes

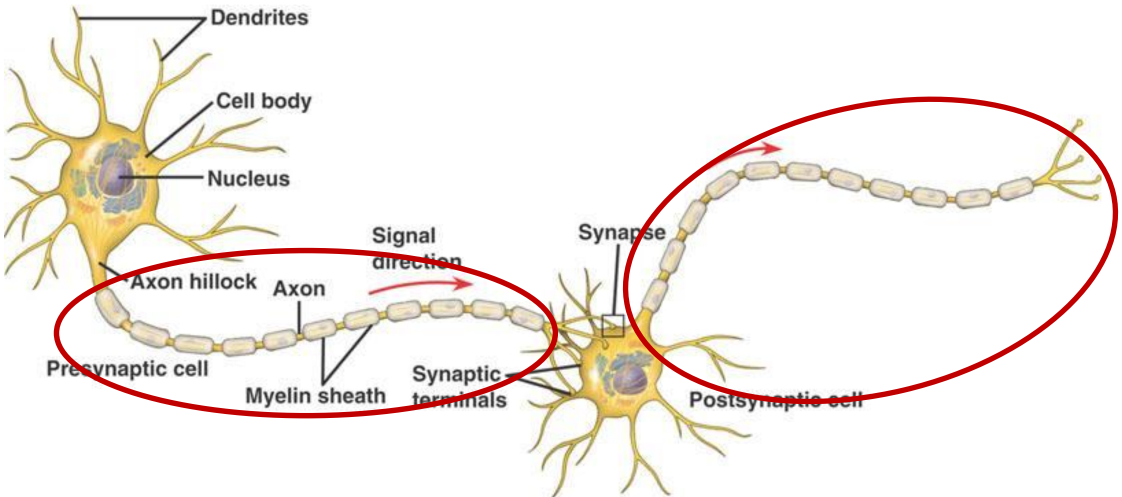
Dendrites and the cell body

- receptive and integrative region of the neuron
- **receptive membrane**
    - receives incoming signals
    - detects/codes the intensity of a stimulus (amplitude coding)
    - sums up (spatial and temporal summation) the incoming signals
    - send them towards the axon

Axon

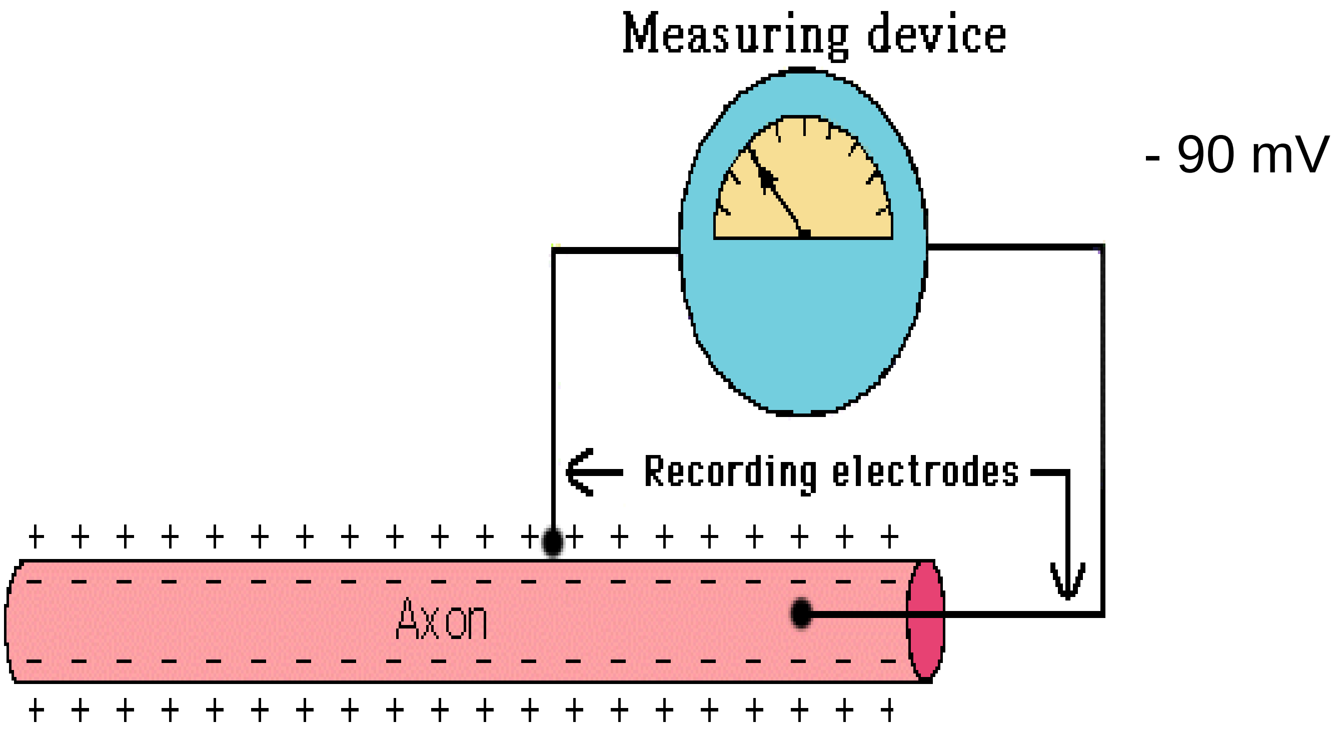
- **axon hillock -** generates an action potential (an outgoing signal /a nerve impulse)
- **axon (conductive membrane) -** conducts the action potential to the next cell

- the receptive and conductive membranes differ in their properties



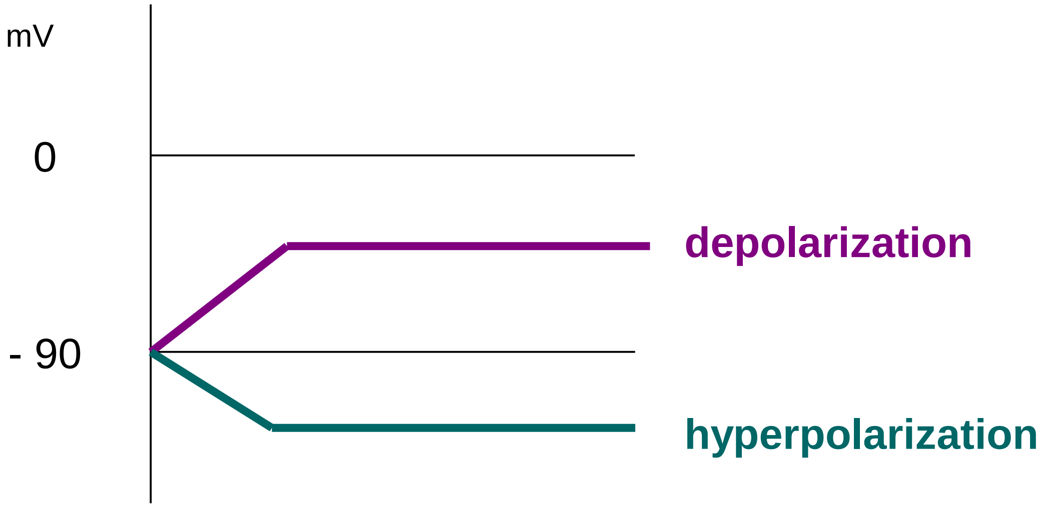
Membrane (transmembrane) potential

- is **the voltage difference between the interior and exterior of a cell** (can be masured by electrodes – one INSIDE/ one OUTSIDE the cell)
- electrical potential exists across the membranes of **all** cells in the body
- the **interior of the cell** is **more negative** than the exterior
- typical values of transmembrane potential are -30 mV to -90 mV
- changes in the transmembrane potential – basis og the funvtion of excitable tissues



Excitable tissues

- **nerve (and muscle) = excitable tissues**
  - they **react to stimulation** by a change of the membrane potential
    - **depolarization** – membrane potential becomes less negative (or even positive)
    - **hyperpolarization** - potential becomes more negative
  - change in membrane potential is the principle of their function
    - nerve – signal transmission
    - muscle – contraction



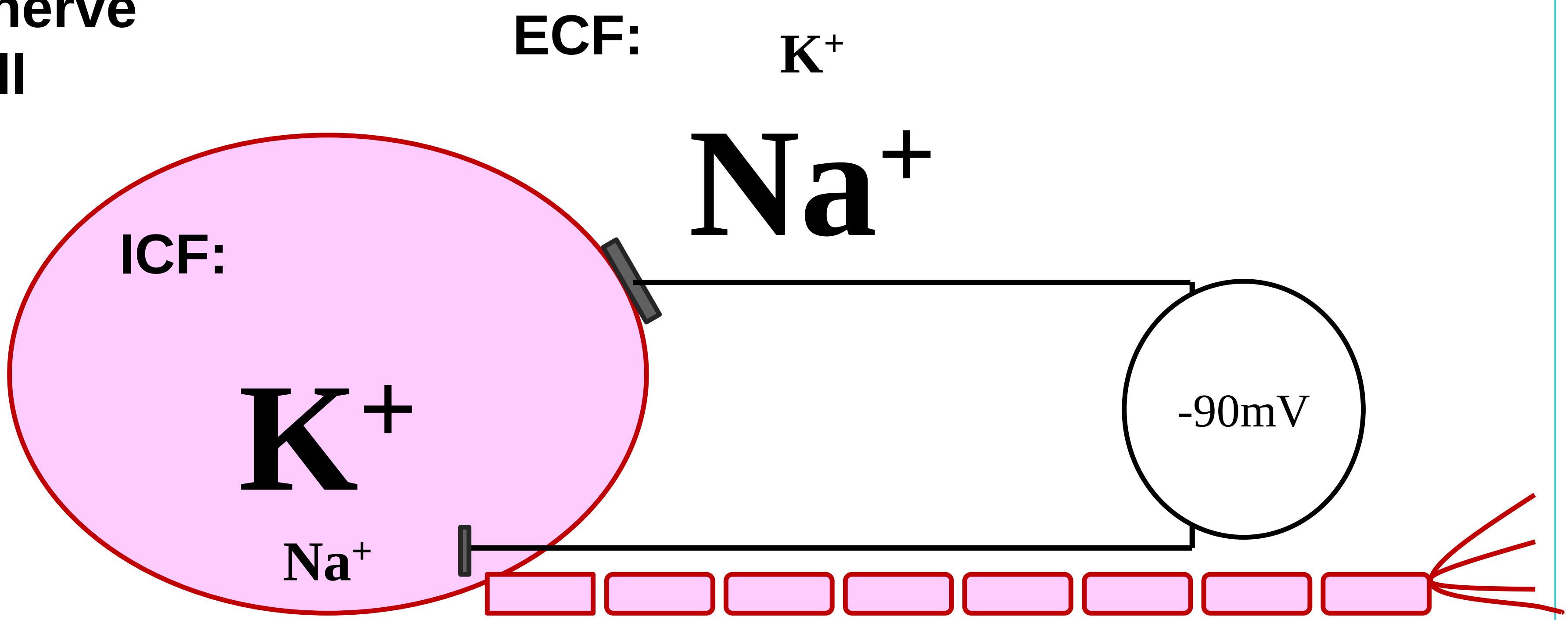
RESTING MEMBRANE POTENTIAL of nerves

- is the **membrane potential of nerves when they are not transmitting** nerve signals (they are at rest)

- **normal value -90 mV**: due to **unequal concentration of Na^+ and K^+ in intracellular fluid (ICF) and extracellular fluid (ECF)**

ECF	Na^+ 142 mmol/l	K^+ 4 mmol/l
ICF	Na^+ 14 mmol/l	K^+ 140 mmol/l

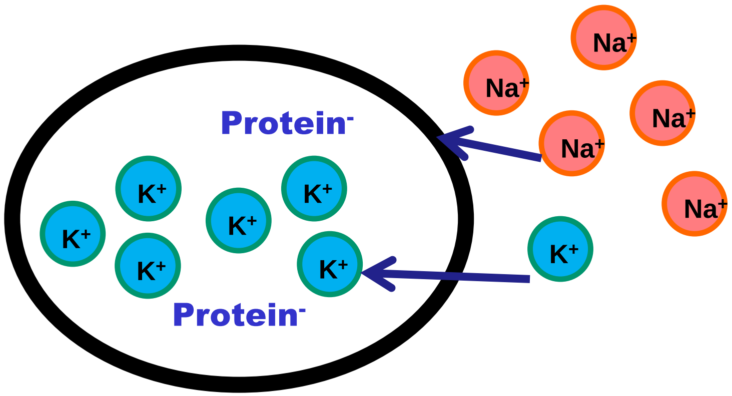
A nerve cell

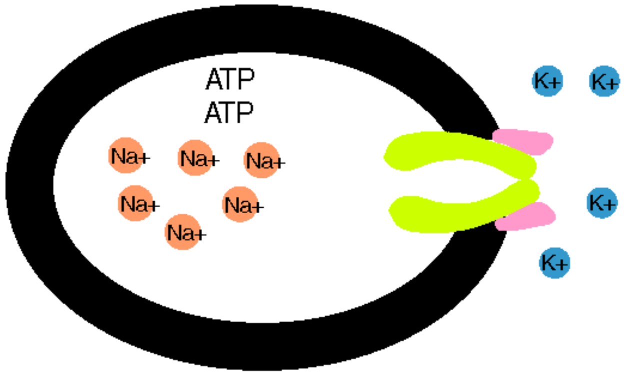


RESTING MEMBRANE POTENTIAL of nerves

- **unequal ion distribution is generated by**:

1. **activity of Na^+- K^+ pump** (3 Na^+ pumped out of the cell for 2 K^+ into the cell)
2. large negatively charged **protein molecules** inside the neuron - cannot cross the membrane (attract positively charged ions)
3. **different permeability** of the cell membrane for ions
   - **permeable for K^+**
     - K^+ is attracted inside by the negative protein ions
     - K^+ tends to leak in the concentration gradient – outwards
     - until a balance between chemical and electric gradient is established
   - **impermeable for Na^+** (leaks through the membrane only in very small amounts)



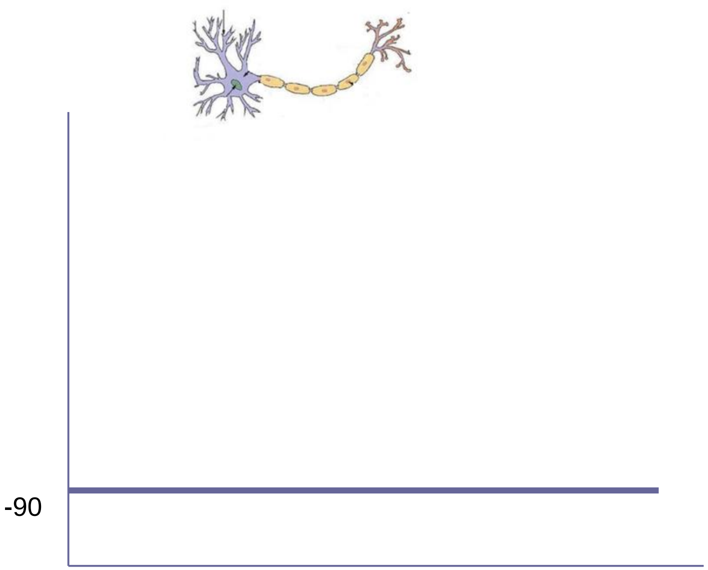


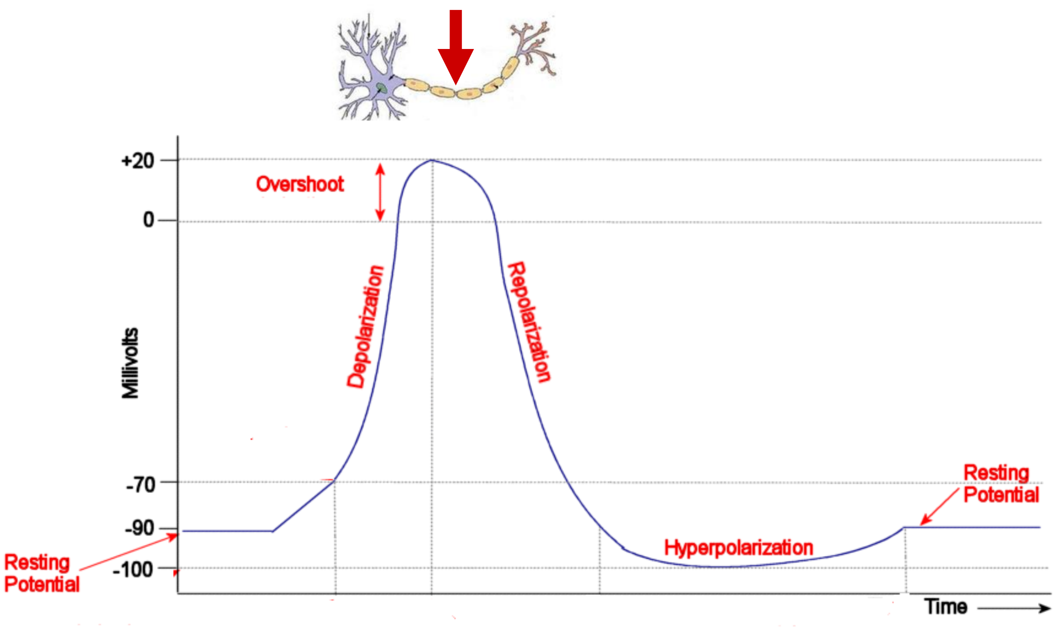
ACTION POTENTIAL of a nerve

- a stimulus (e.g. electric current) - may cause a change of membrane potential and elicit the **action potential (AP)**
- **AP are transmitted along the nerve fibres (axons)**

When transmembrane potential is measured:

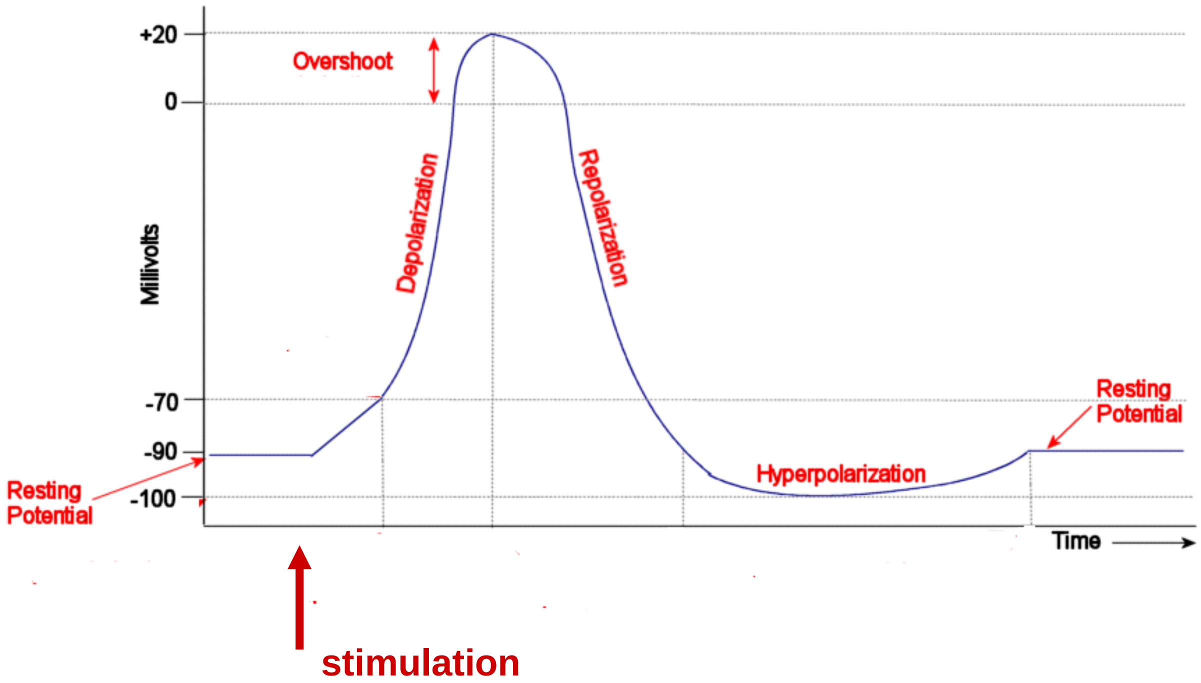
- unstimulated nerve – resting membrane potential – shows a straight line
- after stimulation – action potential – shows a curve with a typical shape:





ACTION POTENTIAL of a nerve – the curve and its parts

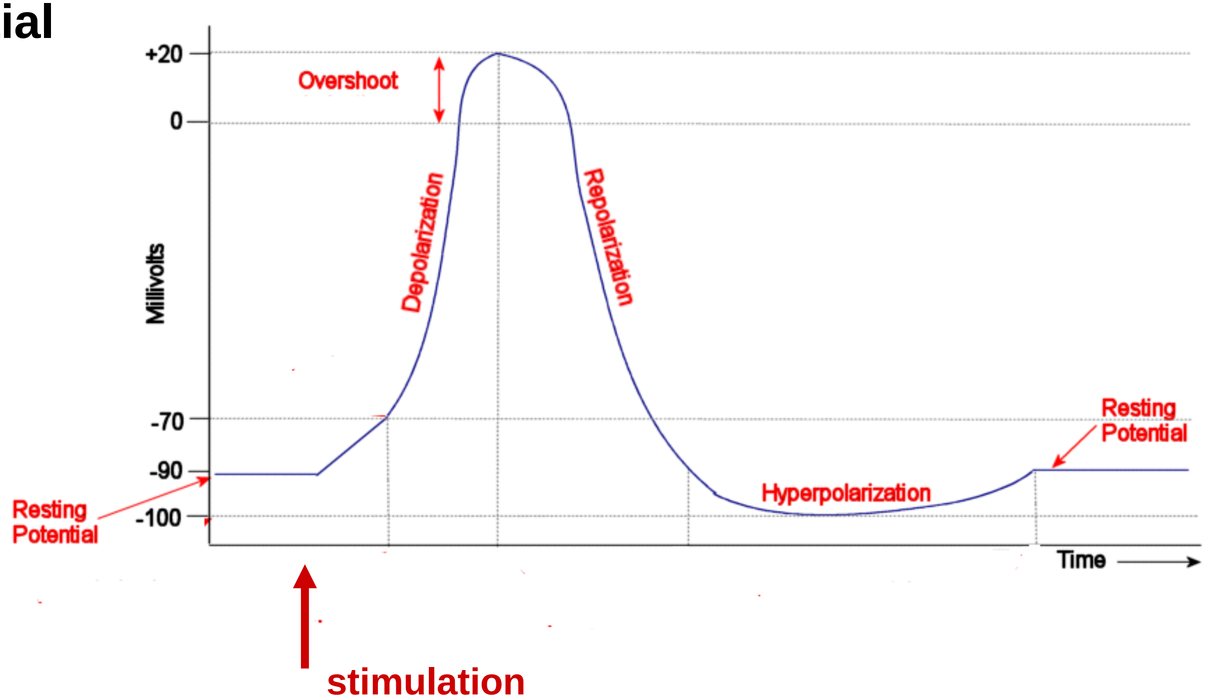
- curve of action potential has a typical shape and involves following parts:
  1. **depolarisation** (comes after stimulation)
     - quick increase of the membrane potential - **overshoot (transpolarization)** to positive values
  2. **repolarisation**
     - the membrane potential decreases
  3. **hyperpolarisation** (after-potential)
     - the membrane potential becomes more negative than in resting state
  4. **resting membrane potential**



What is the cause of the voltage changes?

- changes of membrane potential are caused by opening or closing of membrane voltage-gated Na^+ and K^+ channels, that cause changes in permeability for Na^+, K^+

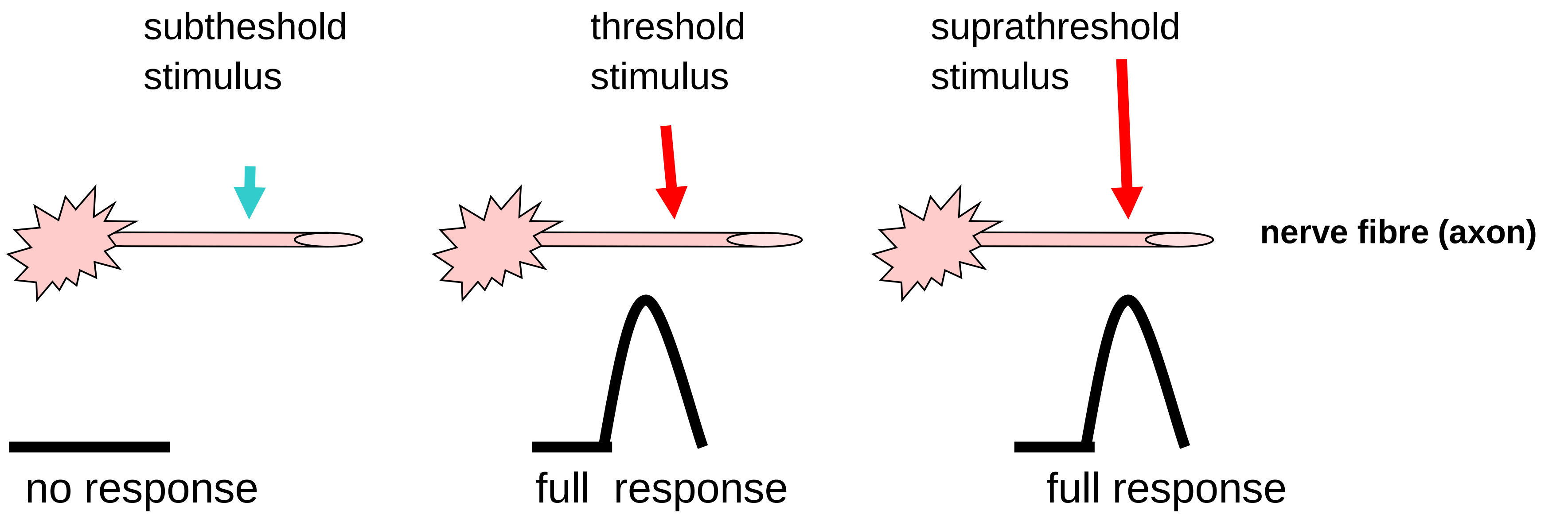
1. **depolarisation** - Na^+ voltage-gated channels open causing flow of Na^+ into the cell
2. **repolarisation** - the Na^+ channels get inactivated – Na^+ influx stops
   - voltage-gated K^+ channels open - K^+ ions exit out of the the cell
3. **after-hyperpolarisation**
   - **K^+ channels** are **inactivated slowly** and **only gradually**
   - this allows prolonged efflux of small amounts of K^+ that causes hyperpolarization
4. **resting membrane potential**



Response of a SINGLE NERVE FIBRE to a stimulus
All or nothing principle (law)

- only a stimulus with sufficient intensity can elicit an action potential (AP)
- **threshold stimulus** – stimulus with minimum intensity that elicits action potential
- **subthreshold stimulus** – stimulus with too low intensity – does not elicit AP

- **All or nothing principle:** the stimulus may elicit either
  - full response of the nerve fibre (action potential)
  - no response of the nerve fibre (no action potential)
  - no graded response (i.e. stronger stimulus – stronger response) of the nerve fibre is possible

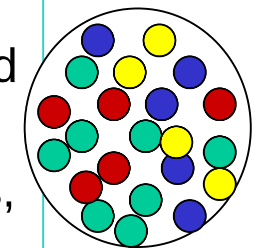


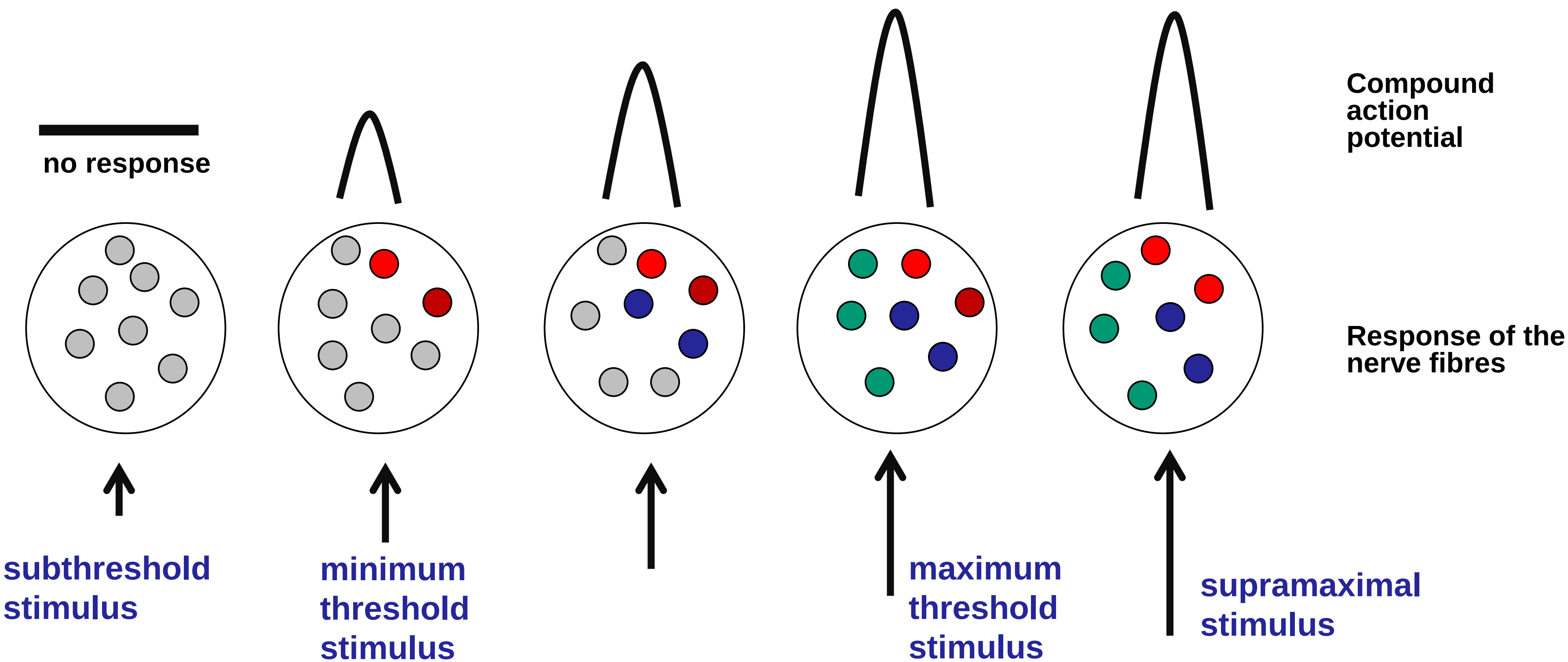
Response of a NERVE to stimulation – the compound AP

- a nerve = a bundle of nerve fibres (axons)
- individual fibres differ in sensitivity to stimuli = they have different threshold

(more sensitive respond to a weaker stimulus, less sensitive to a stronger stimulus)

- a nerve displays graded response - the higher the intensity of the stimulus, the higher the response (progressively more fibres respond)
- the amplitude of AP is composed of responses of several individual fibres = **compound AP**



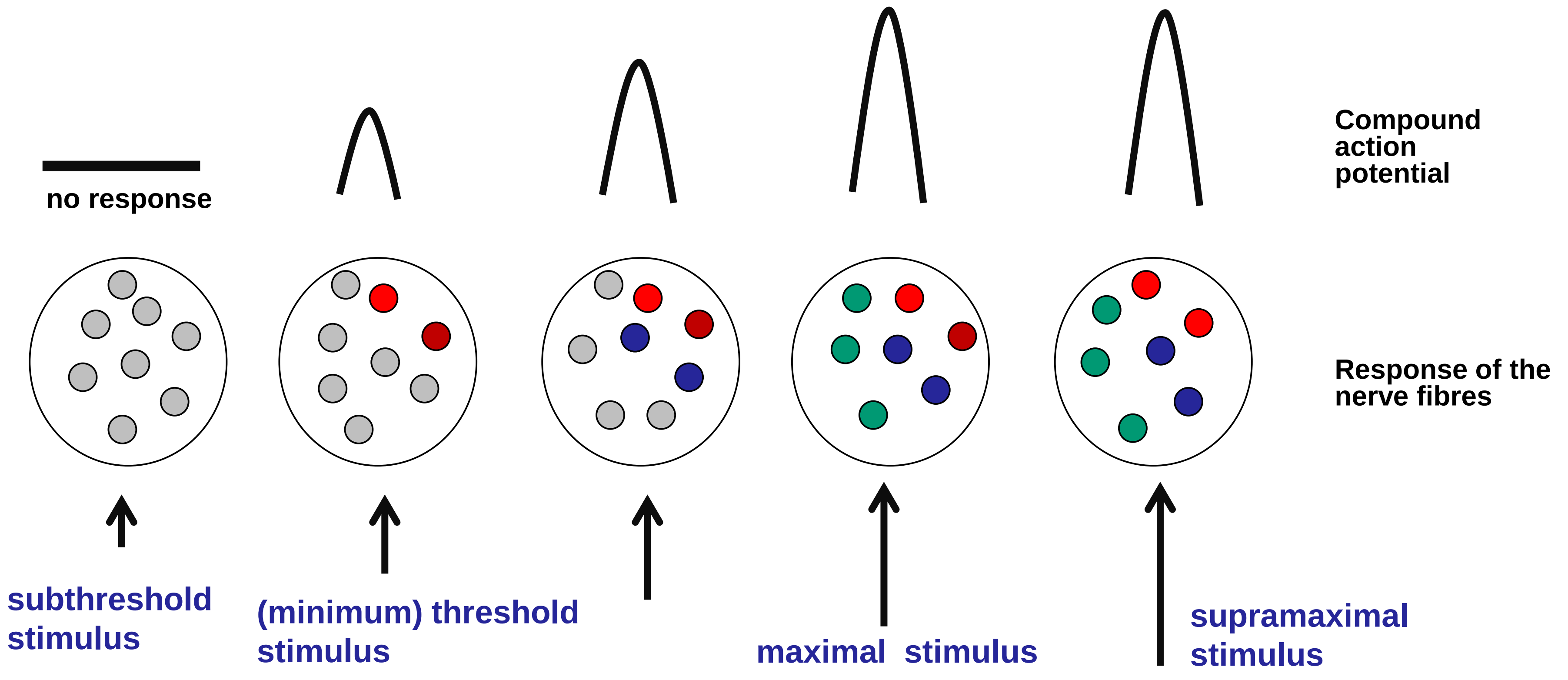


Minimum threshold stimulus - minimum intensity of stimulus that initiates the response of the **most sensitive nerve fibres**

Maximum threshold stimulus - intensity of stimulus that initiates also the response of the least sensitive fibres, i.e. of **all fibres**

A nerve fibre - responds according to all or nothing law

A nerve (bundle of nerve fibres) - does not respond according to the all or nothing law, it shows a graded response

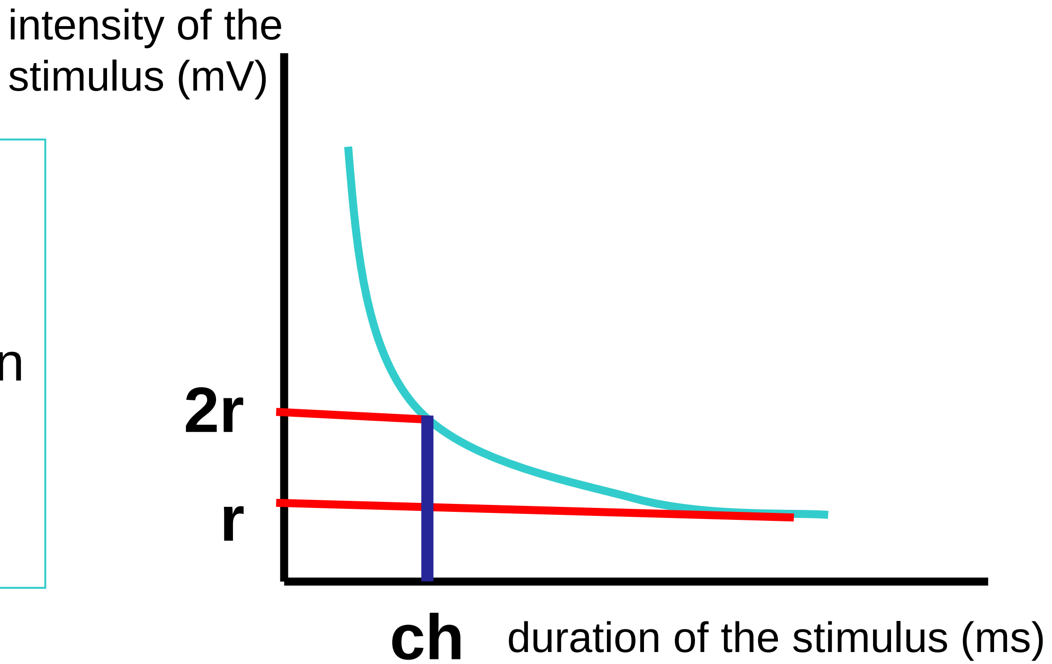


Hoorweg – Weiss curve

- the term **rheobase** is used for the minimum threshold stimulus
- a stimulus can elicit an action potential if it has sufficient duration
- **intensity** and **duration** of the electric stimulus and have an inverse relation
- **chronaxy** is defined as: the minimum interval of time necessary to electrically stimulate a muscle or nerve fiber, using twice the minimum current (rheobase) needed to elicit a threshold response

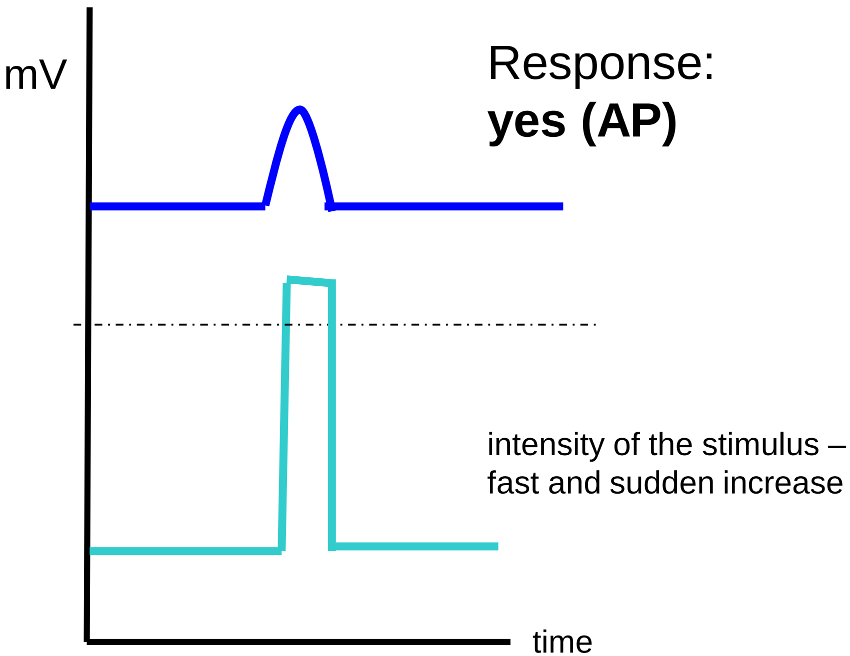
Hoorweg – Weiss curve

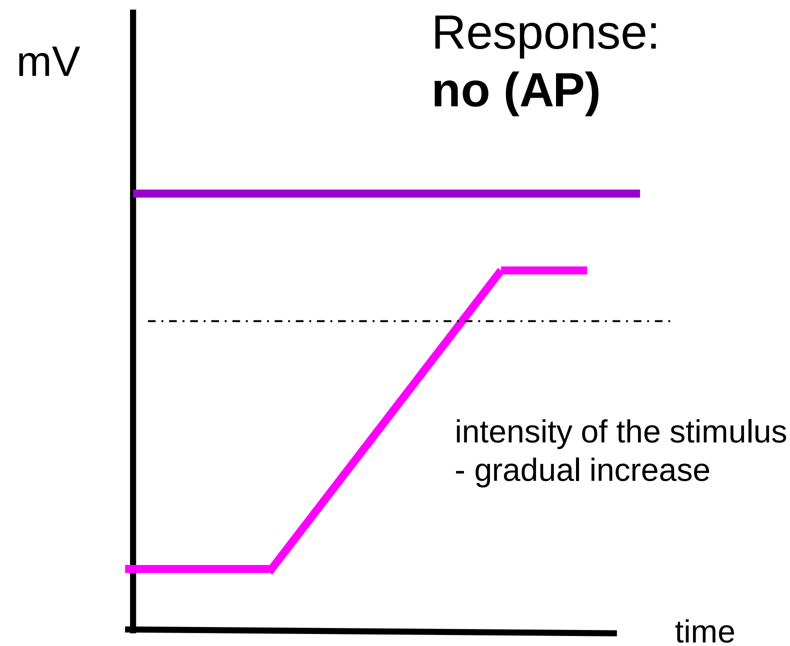
- shows the inverse relationship between intensity and duration of an electric stimulus



Du Bois – Reymond principle

- **initiation of action potential** requires a **fast and sudden change** (stimulus)
- if the intensity of stimulus is **increasing slowly - no action potential** is initiated
- the membrane gets accomodated to slowly increasing change (Na channels are inactivated)





Absolute and relative refractory period

- during the period of action potential the ability of nerve to respond to next stimulus is diminished
- due to change in ion distribution

- **absolute refractory period**

  (immediately after depolarization)

  – no response to the next stimulus

  – the Na channels are inactive after previous depolarization

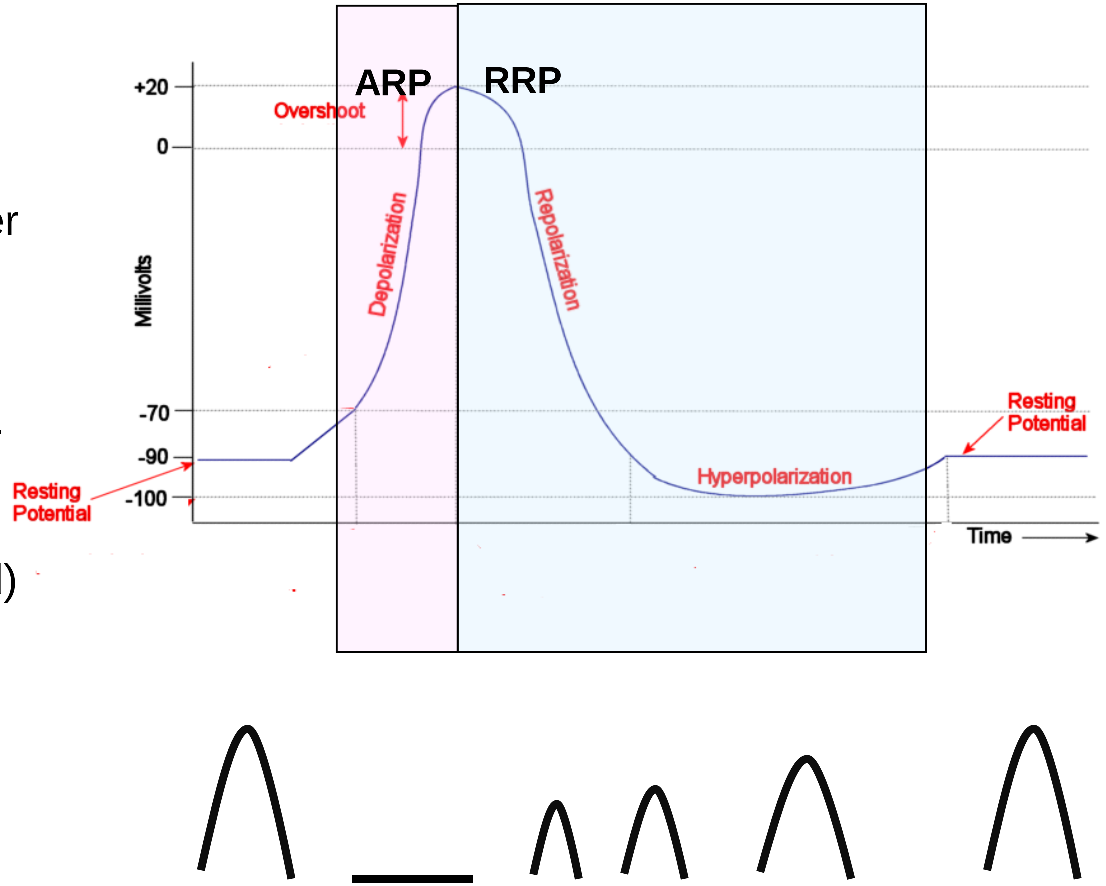
- **relative refractory period** – the nerve responds to the next stimu-lus, but is more difficult to excite

  (follows the absolute refractory period)

  – requires a stronger stimulus

  – the response may be weaker

  – some of the Na channels are recovered and already active



Types of nerve fibres in nerves of mammals

	Type	Function	Diameter (mm)	Speed of AP propagation (m/s)
A	α	proprioception, motor functions	12 – 20	70-120
	β	touch, pressure	5 – 12	30-70
	γ		3 – 6	15-30
	δ	pain, heat	2 – 5	12-30
B		preganglionic autonomic fibres	3	3-15
C	dorsal roots	pain	0,4 -1,2	0,5-2
	sympa-thetic	postganglionic sympathetic fibres	0,3 -1,3	0,7-2,3

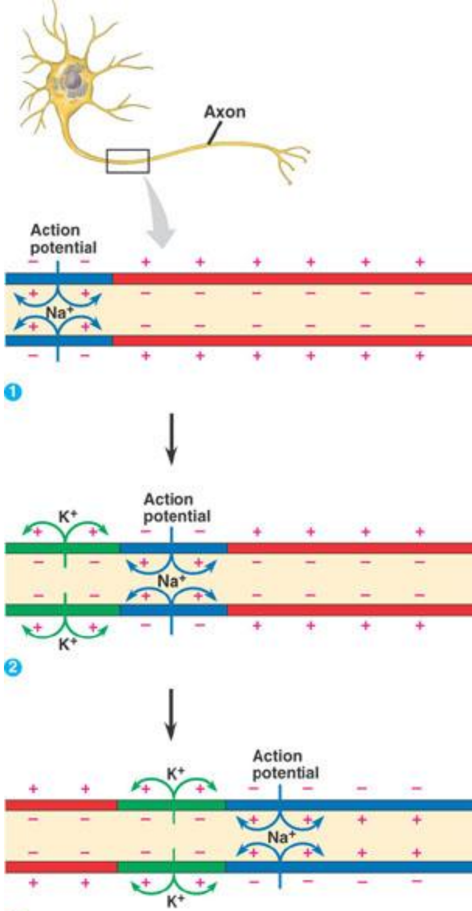
The fibres differ in myelinization, diameter and speed of transmission

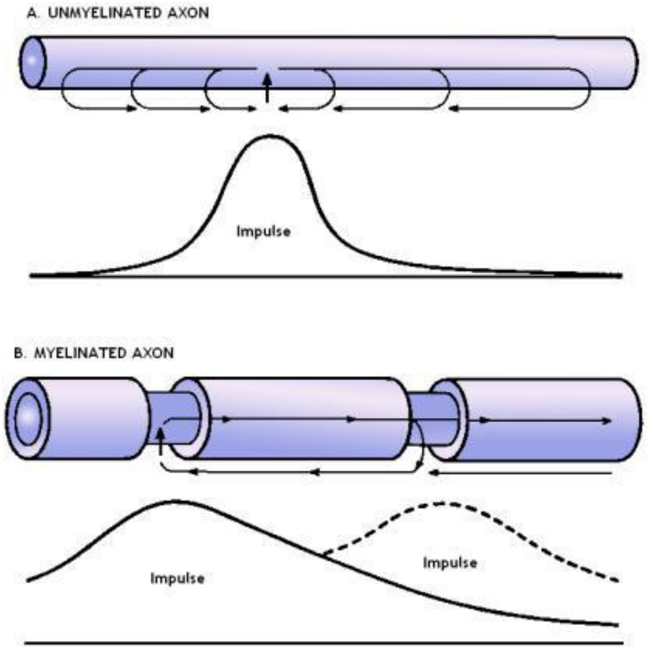
- the thicker the fibre, the faster the transmission
- velocity of nerve impulse transmission – higher in myelinated nerve fibres (A, B) than unmyelinated (C fibres) -

Conduction of the action potential

Unmyelinated axons

- AP at one spot excites adjacent portions of the membrane resulting in propagation of AP (local currents)
- the depolarization process travels along the membrane





Myelinated axons - Saltatory transmission of AP

- propagation from one node of Ranvier to another
- in myelinated nerve fibres

Advantages

- increases velocity of transmission
- energy needs for AP propagation are reduced

Physiological properties of a nerve

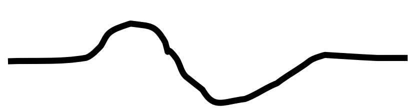
- experiments on a frog nerve – musculus ischiadicus
- (please test only one nerve)

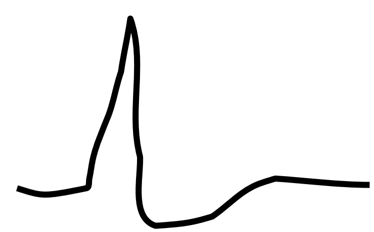
Dissection

- a short video showing the preparation of a frog nerve
- 6 steps (see in the right)
- each step is manually started by the button

Experiments

- a virtual laboratory is available for experiments with the frog nerve
- electric current will be used for stimulation
- if the nerve responds – biphasic curve is seen on the screen
- (electrodes are placed in the membrane, none is inside the nerve)

biphasic 

monophasic 

stimulator

- serves for stimulation of the nerve
- quality of the stimulus must be preset

- **intensity** of the stimulus = amplitude
- **duration** of the stimulus
- **single/twin** mode

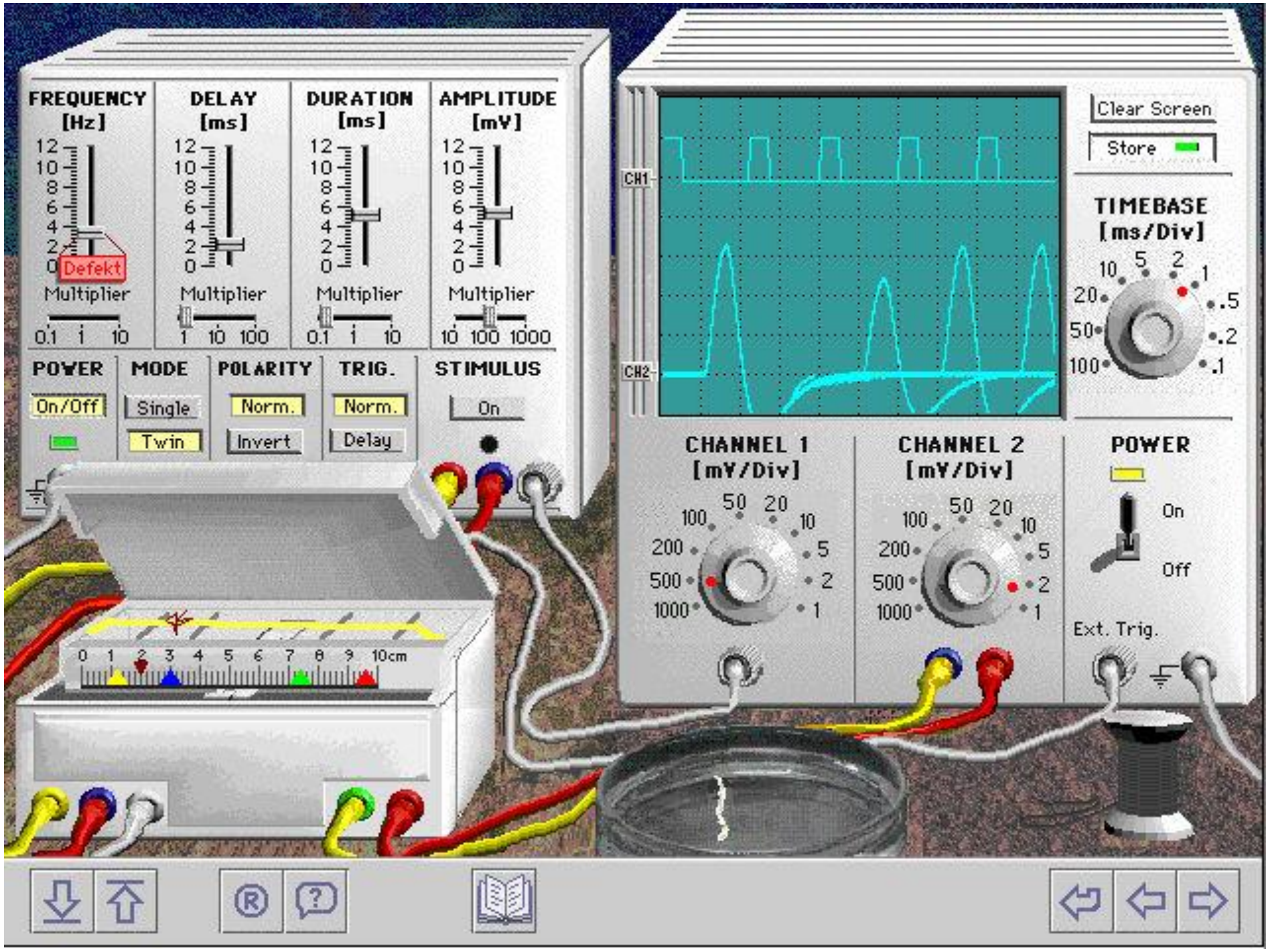
(1 pushing of button gives 1 or 2 stimuli)

- **delay** - time between 2 stimuli

- **multiplier** – allows to modify quality of the stimulus within a broader range

oscilloscope - screen for viewing the results

- **timebase, channel 1, channel 2** - must be preset properly in order to see the results (AP) in proper size
- **store** – switch on to store the results on screen
- **clear screen** – push to remove previous results



experimental chamber

- the nerve is put inside

Procedure

- turn on the stimulator and oscilloscope (click on the ON/OFF)
- open the experimental chamber
- place one nerve to the experimental chamber (drag-and-drop)

- **preset the devices:**
- by moving the appropriate knob to desired value (click with mouse on the value)
- channel 1: 100 mV/div (or 200 mV/div)
- channel 2: to value 5 mV/div
- timebase: 1 ms/div
- mode: single
- duration: 20 ms
- delay : 1 ms

A/ Compound action potential and stimulus intensity

- preset a stimulus with long duration (20 ms)
- stimulate the nerve with a low intensity stimulus (10 mV) – if there is no response (straight line), continue the stimulation with stimuli of increasing intensity (20, 30....mV)
- intensity that causes action potential ( on the oscilloscope) is the **minimum (threshold) stimulus**

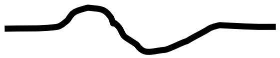
- switch on the „store“ button – presets the oscilloscope for saving the results
- stimulate the nerve further with increasing intensity – it is presumed that the response will also increase
- record the last intensity (in mV) when an increase was observed, i.e. **maximum threshold intensity** stimulus

Result: value of minimum and maximum threshold intensity

Conclusion: explain what is minimum and maximum threshold intensity

B/ Chronaxy and rheobase of the frog nerve

- the **minimum (threshold) stimulus** = **rheobase** (result of part A)

- set the intensity of stimulus (amplitude) to the value equal to 2x rheobase
- start to stimulate the nerve with a stimulus of short duration (0,1 ms)
- if you observe no action potential continue the stimulation with gradually increasing stimulus (0,2 ms – 0,3 ms ....)
- record the minimum duration of stimulus that causes response 

  = **chronaxy**

Result: value of rheobase and chronaxy

C. Determination of the absolute and relative refractory period of the frog nerve

• change settings	mode – twin	delay 10 ms
	duration 1 ms	amplitude 200 mV
	CH1 200 (500)	CH2 5
	timebase 2	store: OFF

Procedure

- stimulate the nerve with twin stimuli
- stepwise decrease the delay between 2 stimuli
- record the time when you first time observe a decrease of the second response (=end of RRF)
- continue with stimulation, further decrease the delay
- record the time when no 2nd response occurs (=end of ARF)
- Beginning of the ARF = beginning of the stimulation

Result: determine the duration of ARF and RRF

D. The Hoorweg-Weiss curve

Change the settings:

timebase: 5 ms/div

channel 1: 100

Channel 2: 5

delay: 1 ms

trig: off

Store: off

- preset a short duration of the stimulus (0,2 ms)
- by increasing the intensity of stimulus find the minimum strength of stimulus that causes action potential
- repeat the measurement for a series of stimuli with increasing duration (the duration time is indicated in the table)

Result:

0,2	0,3	0,5	1	2	3	4	5	(ms)
								(mV)

Conclusion:

- draw the Hoorweg – Weiss curve