Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

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BASICS OF NEUROBIOLOGY

Neurobiológia alapjai

SYNAPTIC COMMUNICATION

(Szinaptikus kommunikáció)

ZSOLT LIPOSITS

SYNAPTIC COMMUNICATION

NEURONAL SIGNALS ARE TRANSMITTED FROM ONE NEURON TO THE NEXT THROUGH INTERNEURONAL JUNCTIONS CALLED SYNAPSES

THE TERM OF SYNAPSE WAS GIVEN BY CHARLES SHERRINGTON

NEURONAL STRUCTURES APPROACH EACH OTHER AND ESTABLISH CLOSE CONNECTIONS BY THE JUXTAPOSITION OF THEIR CELL MEMBRANE-COVERED PARTS. THE INTERACTING ELEMENTS ARE IN CONTIGUITY

THERE ARE TWO DIFFERENT TYPES OF SYNAPSES: THE CHEMICAL SYNAPSE AND THE ELECTRICAL SYNAPSE

THE CHEMICAL SYNAPSE IS THE DOMINANT FORM OF COMMUNICATION IN THE CNS OF HUMANS. CHEMICAL SUBSTANCES CALLED NEUROTRANSMITTERS MEDIATE THE INFORMATION FROM ONE CELL TO THE OTHER. THE SYNAPSING ELEMENTS ARE SEPARATED BY THE SYNAPTIC CLEFT

IN CASE OF ELECTRICAL SYNAPSES THE EXTRACELLULAR SPACE NARROWS AND THE INTERACTING MEMBRANES GET COUPLED BY GAP JUNCTIONS. AT THE GAPS, THE INTERACTING ELEMENTS ARE IN CONTINUITY, ALTHOUGH THE OPENING OF THE PORES IS REGULATED.

CHEMICAL SYNAPSE

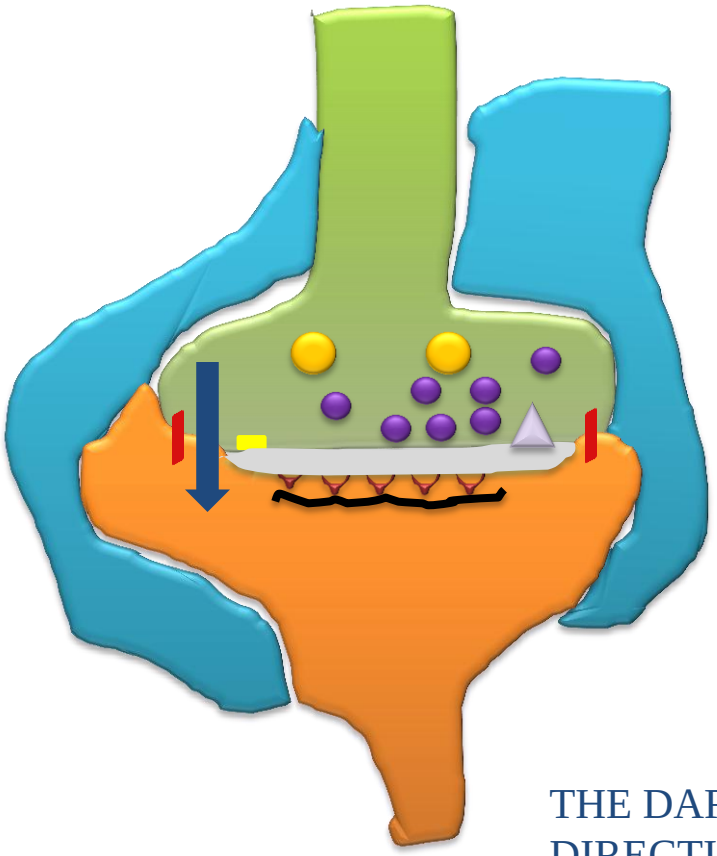
PRINCIPAL OF ONE WAY CONDUCTION. IT MEANS THAT THE INFORMATION TRANSFER BETWEEN THE SYNAPSING ELEMENTS OCCURS IN ONE DIRECTION SPREADING EXCLUSIVELY FROM THE PRESYNAPTIC STRUCTURE TO THE POSTSYNAPTIC ELEMENT

THE HUMAN BRAIN POSSESSES ABOUT 10^{14} TO 5×10^{14} SYNAPSES

MAIN CHARACTERISTICS OF CHEMICAL NEUROTRANSMISSION INCLUDE:

1. THE SYNTHESIS OF THE CLASSIC NEUROTRANSMITTERS TAKES PLACE IN THE PRESYNAPTIC AXON TERMINAL
2. THE CLASSIC AND PEPTIDE NEUROTRANSMITTERS ARE STORED IN SYNAPTIC VESICLES AND GRANULES FORMING A RELEASABLE POOL OF BIOACTIVE MESSENGER SUBSTANCES
3. UPON ACTIVATION OF THE PRESYNAPTIC ELEMENT, THE NEUROTRANSMITTERS ARE RELEASED INTO THE SYNAPTIC CLEFT
4. BINDING AND RECOGNITION OF NEUROMESSENGERS BY SPECIFIC RECEPTORS OF TARGET STRUCTURES
5. TERMINATION OF THE SYNAPTIC EVENTS, INACTIVATION OF TRANSMITTERS

SCHEMATIC STRUCTURE OF THE CHEMICAL SYNAPSE



PRESYNAPTIC ELEMENT
POSTSYNAPTIC STRUCTURE
GLIAL PROCESS
TIGHT JUNCTION
CALCIUM CHANNEL
SYNAPTIC VESICLE
PEPTIDERGIC GRANULE
RE-UPTAKE PUMP
SYNAPTIC CLEFT
TRANSMITTER RECEPTORS
POSTSYNAPTIC PROTEINS

THE DARK BLUE ARROW INDICATES THE DIRECTION OF ONE-WAY CONDUCTION

CELLULAR EVENTS OF SYNAPTIC INFORMATION TRANSFER

- THOUSANDS OF AXON BOUTONS TERMINATE ON THE DENDRITIC TREE AND SOMATA OF TARGET NEURONS CARRYING EXCITATORY AND INHIBITORY SIGNALS
- THE INTEGRATED MEMBRANE POTENTIAL REACHING THE THRESHOLD EVOKES AN ACTION POTENTIAL IN THE PRESYNAPTIC CELL WHICH IS PROPAGATED TOWARD ITS AXON TERMINAL
- THE ACTION POTENTIAL OPENS THE VOLTAGE-GATED CALCIUM CHANNELS IN THE TERMINAL ALLOWING THE INFLUX OF CALCIUM
- CALCIUM ACTIVATES THE PROTEIN MACHINERIES OF SYNAPTIC VESICLE DOCKING RESULTING IN THE EXOCYTOSIS OF VESICLES
- THE NEUROTRANSMITTER IS RELEASED INTO THE SYNAPTIC CLEFT
- THE NEUROTRANSMITTER ACTS ON THE POSTSYNAPTIC MEMBRANE ACTIVATING ION CHANNELS AND RECEPTOR-COUPLED INTRACELLULAR MESSENGER SYSTEMS
- AFTER THE ACTION, THE NEUROTRANSMITTER GETS INACTIVATED IN THE SYNAPTIC CLEFT BY BREAKDOWN OR UNDERGOES RE-UPTAKE

STRUCTURAL CLASSIFICATION OF CHEMICAL SYNAPSES

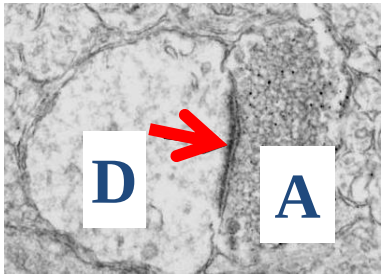
THE INTERACTING NEURONAL ELEMENTS ESTABLISH A WIDE VARIETY OF SYNAPSES UTILIZING ALMOST ALL FORMS OF COMBINATION

THE MOST FREQUENT TYPES OF SYNAPTIC COMMUNICATION INCLUDE:

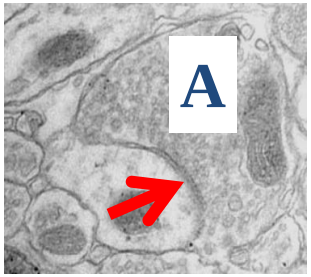
1. AXO-DENDRITIC SYNAPSE: AXON TERMINATING ON THE DENDRITIC SHAFT
2. AXO-SPINOUS SYNAPSE: AXON TERMINATING ON DENDRITIC SPINE
3. AXO-SOMATIC SYNAPSE: AXON TERMINATING ON CELL BODY
4. AXO-AXONIC SYNAPSE: AXON TERMINATING ON PRESYNAPTIC AXON
5. DENDRO-DENDRITIC SYNAPSE: DENDRITE COMMUNICATING WITH DENDRITE

BASED UPON THE CHARACTERISTICS OF THE PRE- AND POSTSYNAPTIC MEMBRANES SYNAPSES ARE CLASSIFIED INTO TWO CATEGORIES:

I. ASYMMETRIC SYNAPSE
(GRAY TYPE 1)



II. SYMMETRIC SYNAPSE
(GRAY TYPE 2)



EXCITATORY SYNAPSES

THEY RELEASE EXCITATORY NEUROTRANSMITTERS LIKE ACETYLCHOLINE, SEROTONIN, DOPAMINE, NORADRENALINE AND HISTAMINE

EXCITATORY TRANSMITTERS INCREASE THE MEMBRANE'S PERMEABILITYY TO Na^+

THE SODIUM INFLUX RESULTS IN THE INCREASE OF THE RESTING MEMBRANE POTENTIAL: EXCITATORY POSTSYNAPTIC POTENTIAL (EPSP)

THE EXCITATORY POSTSYNAPTIC POTENTIALS ARE GRADED

THE EPSP-S ARE SUBJECT OF SPATIAL AND TEMPORAL SUMMATION MECHANISMS THAT INCREASE THE PROBABILITY OF EVOKING ACTION POTENTIAL FIRING IN THE POSTSYNAPTIC NEURON

EXCITATORY SYNAPSES GENERALLY CARRY SPHERICAL SYNAPTIC VESICLES WITH 30-40 nm DIAMETER

THE FORMED SYNAPTIC SPECIALIZATIONS ARE ASYMMETRIC IN NATURE WITH PROMINENT THICKENING OF THE POSTSYNAPTIC MEMBRANE

THE INHIBITORY SYNAPSE

THE AXONS RELEASE INHIBITORY NEUROTRANSMITTERS LIKE GAMMA-AMINOBUTYRIC ACID (GABA) AND GLYCINE. IN CERTAIN SYSTEMS AND DEVELOPMENTAL PERIODS, SOME NEUROTRANSMITTERS CAN ALSO ACT IN AN OPPOSITE MANNER

INHIBITORY TRANSMITTERS OPEN POTASSIUM AND/OR CHLORIDE CHANNELS

THE EFFLUX OF POTASSIUM AND/OR THE INFLUX OF CHLORIDE IONS RESULT IN THE DECREASE OF THE RESTING MEMBRANE (HYPERPOLARIZATION). THE VOLTAGE IS CALLED INHIBITORY POSTSYNAPTIC POTENTIAL (IPSP)

THE INHIBITORY POSTSYNAPTIC POTENTIALS ARE ALSO GRADED

THE IPSP-S ARE SUBJECT TO SPATIAL AND TEMPORAL SUMMATION MECHANISMS WITH OTHER IPSP-s AND WITH EPSP-s

INHIBITORY SYNAPSES GENERALLY CARRY FLATTENED SYNAPTIC VESICLES

THE FORMED SYNAPTIC SPECIALIZATIONS ARE SYMMETRIC IN NATURE. THE PRE- AND POSTSYNAPTIC MEMBRANE REGIONS ARE EQUAL IN THICKNESS

SPECIAL FEATURES OF SYNAPTIC COMMUNICATION

SYNAPTIC DELAY. DELAY IN THE TRANSFER OF INFORMATION FROM ONE NEURON TO THE OTHER. IT IS ABOUT 0.5 MILLISECOND. PRIMARILY DUE TO THE DURATION OF ACTIONS IN THE SYNAPTIC CLEFT AND AT THE POSTSYNAPTIC MEMBRANE

SYNAPTIC STRENGTH. IT IS DEFINED BY THE CHANGE IN TRANSMEMBRANE POTENTIAL RESULTING FROM ACTIVATION OF THE POSTSYNAPTIC NEUROTRANS-MITTER RECEPTORS

FATIGUE OF SYNAPTIC TRANSMISSION. OVERSTIMULATION OF EXCITATORY SYNAPSES REPETITIVELY AT A RAPID RATE INDUCES A COMPENSATORY MECHANISM MANIFESTED IN A GRADUAL DECLINE OF DISCHARGES OF THE POSTSYNAPTIC NEURON

POST-TETANIC FACILITATION. IN THE REST PERIOD AFTER A REPETITIVE, TETANIC STIMULATION THE SYNAPSE MIGHT BECOME EVEN MORE RESPONSIVE TO SUBSEQUENT STIMULATION THAN NORMALLY. IT MAY LAST FOR SECONDS OR MINUTES. THIS MECHANISM CONTRIBUTES TO SHORT TERM MEMORY STORAGE

SYNAPTIC TYPES IN SOME SPECIAL NETWORKS OF THE CNS

BOUTON-TYPE SYNAPSE. THE AXON EXHIBITS SIGNIFICANTLY ENLARGED, SPHERICAL AXON TERMINALS, SO CALLED BOUTONS. INNERVATION OF SPINAL MOTONEURONS REPRESENTS THIS CONNECTION TYPE

EN PASSANT SYNAPSE. THE AXON ESTABLISHES SEVERAL SYNAPSES ALONG ITS COURSE WITHOUT BRANCHING INTO AXON TERMINALS. DENDRITIC SPINES OF PURKINJE CELLS RECEIVE INFORMATION FORM GRANULE CELLS THIS WAY

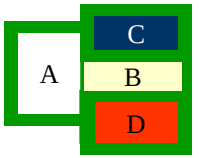
BASKET-LIKE SYNAPSE. THE TERMINATING AXONS FORM BASKET LIKE STRUCTURES AROUND THE BASE OF THE CELL AT THE AXON HILLOCK REGION. INNERVATION OF PURKINJE CELLS BY BASKET NEURONS

PARALLEL CONTACTS. THE AXONS CLIMB AND WIND AROUND THE INNERVATED CELL. CLIMBING FIBERS TERMINATE THIS WAY ON PURKINJE CELLS

GLOMERULAR SYNAPSE. HAS A COMPLEX ARCHITECTURE IN WHICH MULTIPLE DENDRITES RECEIVE INFORMATION FROM THE SAME, TERMINATING LARGE-SIZED AXON. THE INTERACTING STRUCTURES FIT EACH OTHER LIKE COGWHEELS. SYNAPSES FORMED BY MOSSY FIBERS AND GRANULE CELL DENDRITES IN CEREBELLUM

ELECTRICAL SYNAPSE

AT ELECTRICAL SYNAPSE SITES, THE INTERACTING NEURAL ELEMENTS ARE COUPLED BY GAP JUNCTIONS WITH EACH OTHER



THE INTERCELLULAR SPACE (20 nm) REDUCES CONSIDERABLY IN SIZE AT THE GAPS (2.7 nm)

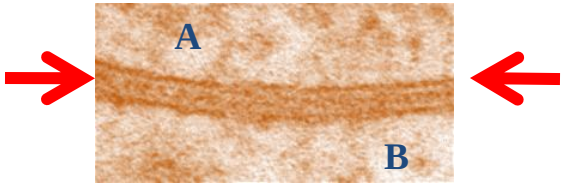
GAP JUNCTIONS ARE COMPOSED OF CONNEXONS. THE INTERACTING MEMBRANES PROVIDE HEMI-CONNEXONS FOR ESTABLISHING THE CHANNELS

THE ELECTRICAL SYNAPSES TRANSMIT SIGNALS IN A BIDIRECTIONAL MANNER

THERE IS NO SYNAPTIC DELAY IN THE INFORMATION TRANSFER

THE OPENING OF THE PORE OF CONNEXONS IS REGULATED BY THE INTRACELLULAR CALCIUM LEVEL. HIGH CALCIUM CONCENTRATION CLOSES THE PORES

CELLS COUPLED BY ELECTRICAL SYNAPSES CAN BE DETECTED BY INTRACELLULAR DELIVERY OF THE DYE, LUCIFER YELLOW. IT PASSES THROUGH THE PORES



CELLS (A, B) ESTABLISHING AN ELECTRICAL SYNAPSE (ARROW)

COMPARISON OF CHEMICAL AND ELECTRICAL SYNAPSES

FEATURE	ELECTRICAL SYNAPSES	CHEMICAL SYNAPSES
➢ Distance between pre- and postsynaptic cell membranes	3.5 nm	30-50 nm
➢ Cytoplasmic continuity between pre- and postsynaptic cells	Yes	No
➢ Ultrastructural components	Gap junction channels	Presynaptic active zones and vesicles; postsynaptic receptors
➢ Agent of transmission	Ionic current	Chemical transmitter
➢ Synaptic delay	Virtually absent	Significant: at least 0.3 ms, usually 1-5 ms or longer
➢ Direction of transmission	Usually bidirectional	Unidirectional