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

RELEASE OF NEUROTRANSMITTERS

(Neurotranszmitter felszabadulás)

ZSOLT LIPOSITS

QUANTAL RELEASE OF NEUROTRANSMITTERS

THE EXPERIMENTS PERFORMED BY HEUSER (1977) AND HEUSER AND REESE (1981) ON FROG NEUROMUSCULAR JUNCTION

SPONTANEOUS RELEASE OF TRANSMITTERS FROM SYNAPTIC VESICLES OCCURS IN PACKETS (QUANTA) IN THE ABSENCE OF ACTION POTENTIAL

THE RELEASED QUANTA EVOKE MINIATURE POSTSYNAPTIC POTENTIALS: EXCITATORY (mEPSPs) AND INHIBITORY (mIPSPs) TYPES

THE ACTION POTENTIAL INCREASES, ACCELERATES AND SYNCHRONIZES THE RELEASE OF QUANTA IN ORDER TO EVOKE A POSTSYNAPTIC POTENTIAL

THE SIZE OF THE QUANTUM IS INDEPENDENT OF THE ACTION POTENTIAL AND THE CYTOPLASMIC CONCENTRATION OF THE TRANSMITTER

INTERFERING WITH FILLING OF SYNAPTIC VESICLES WITH TRANSMITTERS CAUSES A REDUCTION IN THE mEPSPs

THE NUMBER OF TRANSMITTER MOLECULES IN A VESICLE EQUALS THAT OF THE RELEASED QUANTUM

RECYCLING OF SYNAPTIC VESICLES

DURING TRANSMITTER RELEASE, THE SYNAPTIC VESICLES FUSE WITH THE PLASMA MEMBRANE AND EMPTY THEIR CONTENT INTO THE SYNAPTIC CLEFT

IN ORDER TO ENSURE THE PROPER RELEASABLE POOL OF VESICLES IN THE TERMINAL BOTH THE SYNAPTIC VESICLE MEMBRANE AND THE TRANSMITTER SUBSTANCE UNDERGO RECYCLING

THE SYNAPTIC MEMBRANE IS RETRIEVED BY ENDOCYTOSIS. THE CLATHRIN-COATED RECOVERED MEMBRANE APPEARS IN ENDOSOMES THAT ARE USED FOR THE PRODUCTION OF NEW VESICLES

THE PRESYNAPTIC MEMBRANE OF THE AXON TERMINAL CONTAINS TRANSMITTER TRANSPORTERS (FOR CHOLINE, DOPAMINE, NORADRENALINE, GABA, GLUTAMATE, SEROTONIN) THAT ALLOW THE UPTAKE OF THE TRANSMITTER OR ITS BREAKDOWN PRODUCT FROM THE SYNAPTIC CLEFT FOR RECYCLING

DRUGS ACTING ON MEMBRANE TRANSPORTERS ARE POWERFUL MODULATORS OF SYNAPTIC FUNCTIONS AND PERFORMANCE OF NEURONAL NETWORKS

EXCITATION-COUPLED SECRETION OF VESICLES

ACTION POTENTIALS OPEN VOLTAGE GATED CALCIUM CHANNELS IN THE TERMINALS THAT ALLOW THE INFLUX OF CALCIUM

THE CALCIUM CHANNELS ARE SITUATED IN THE MEMBRANE FACING THE ACTIVE ZONE OF THE SYNAPSE WHERE THE DOCKED AND PRIMED VESICLES ARE WAITING FOR RELEASE

THE ELEVATION OF THE INTRACELLULAR CALCIUM CONCENTRATION ACCELERA-TES THE QUANTAL RELEASE

DECREASING THE CALCIUM CONCENTRATION OF THE EXTRACELLULAR BATH RESULTS IN AN ATTENUATED RESPONSE

HIGH CALCIUM CONCENTRATION AND FUNCTIONAL CALCIUM CHANNELS CAN EVOKE TRANSMITTER RELEASE EVEN UNDER BLOCKED SODIUM ACTION POTENTIAL AND POTASSIUM CHANNELS

DIVALENT CATIONS THAT BLOCK CALCIUM CHANNELS ARREST THE VESICULAR RELEASE OF TRANSMITTERS

THE SYNAPTIC VESICLE

CLASSIC NEUROTRANSMITTERS ARE PACKED INTO SMALL SIZED (40-50 nm), ELECTRON LUCENT VESICLES POSSESSING EITHER ROUND OR FLATTENED SHAPE

THE BIOCHEMICAL PURIFICATION OF SYNAPTIC VESICLES REVELED IMPORTANT PROTEIN STRUCTURES BUILT IN THE SYNAPTIC MEMBRANE

VESICULAR TRANSMITTER TRANSPORTERS. UPTAKE AND ACCUMULATION OF TRANSMITTERS

PROTON PUMP. GENERATION OF ELECTROCHEMICAL GRADIENT

SYNAPTOBREVIN. VESICULAR FUSION

SYNAPTOTAGMIN. BINDING OF CALCIUM IONS

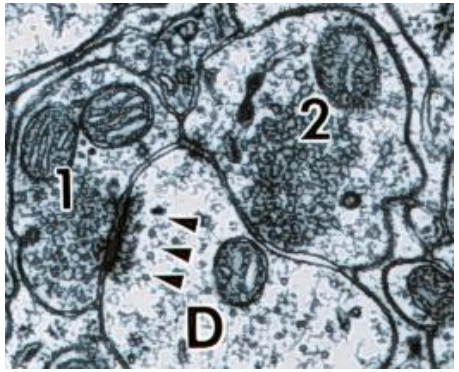
SYNAPSIN. BINDING TO ACTIN

RAB3. REGULATION OF VESICLE TARGETING

CYSTEINE STRING PROTEIN. REGULATION OF Ca CHANNELS

SYNAPTOPHYSIN. FUNCTION IS UNKNOWN

SV2. FUNCTION IS UNKNOWN



AXON TERMINALS (1,2) FILLED WITH SYNAPTIC VESICLES. BOUTON 1 FORMS AN ASYMMETRIC SYNAPSE (ARROWHEADS) WITH A NEIGHBORING DENDRITE (D)

UPTAKE OF TRANSMITTERS INTO SYNAPTIC VESICLES

THE SYNAPTIC VESICLES CONTAIN PROTON PUMP, A MULTI-SUBUNIT ATPase WHICH CATALYZES THE TRANSLOCATION OF PROTONS FROM CYTOPLASM TO THE ORGANELLE

THE ESTABLISHED ELECTROCHEMICAL GRADIENT IS USED FOR THE UPTAKE OF NEUROTRANSMITTERS INTO THE VESICLES

THE PROCESS RESULTS IN AN EXTREME ACCUMULATION OF THE TRANSMITTER IN THE VESICLES IN COMPARISON WITH ITS ORIGINAL CYTOPLASMIC CONCENTRATION

THE DIFFERENCE MIGHT BE 1000-FOLD GREATER

THE NEUROTRANSMITTER TRANSPORTERS ARE PROTEINS WITH 12 MEMBRANE SPANNING DOMAINS

VESICULAR MEMBRANE TRANSPORTERS HAVE BEEN CLONED FOR GLUTAMATE, ACETYLCHOLINE, GABA, SEROTONIN, DOPAMINE, NOREPINEPHRINE AND GLYCINE

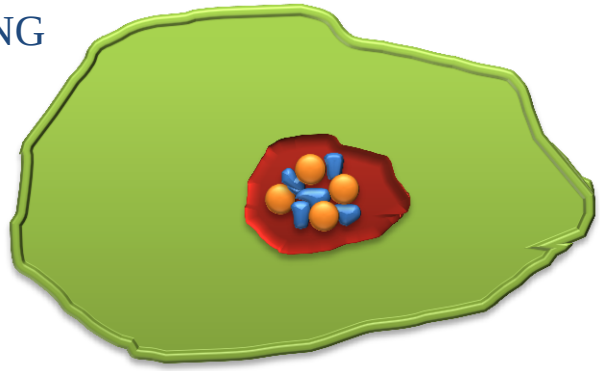
THE PRESYNAPTIC ACTIVE ZONE

CALCIUM RUSHED IN THE TERMINAL LIBERATES THE SYNAPTIC VESICLES FROM ACTIN FILAMENTS OF THE CYTOSKELETON

VESICLES GET INSERTED IN THE PRE-SYNAPTIC GRID WHICH IS A HEXAGONAL ARRAY OF ELECTRON DENSE PARTICLES ATTACHED TO THE CYTOPLASMIC FACE OF THE PRESYNAPTIC MEMBRANE. IT CAN BE REVEALED BY STAINING WITH ETHANO-LIC PHOSPHOTUNGSTIC ACID

THE PRESYNAPTIC GRID (WEB) CONSISTS OF 50 nm PYRAMID-SHAPED PARTICLES BEING INTERCONNECTED BY 100 nm SPACED FIBRILS

THE PROCESS OF INSERTION OF SYNAPTIC VESICLES INTO THE PRESYNAPTIC GRID AND ESTABLISHING CONTACT WITH THE PRESYNAPTIC MEMBRANE IS CALLED DOCKING



SCHEMATIC ILLUSTRATION OF THE PRESYNAPTIC WEB. SYNAPTIC VESICLES ARE ATTACHED TO THE ACTIVE ZONE OF THE PRESYNAPTIC MEMBRANE. THE VESICLES FIT THE HOLES OF THE PRESYNAPTIC WEB (GRID) AND GET CLOSE TO THE FUSION SITE

MEMBRANE FUSION

THE SNARE PROTEIN SUPERFAMILY (**SNA**P-(SOLUBLE NSF ATTACHMENT PROTEIN) **RE**CEPTORS) IS COMPOSED OF DOZENS OF PEPTIDES

A PIVOTAL ROLE OF SNARE PROTEINS IS TO ASSIST THE DOCKING, FUSING AND EMPTYING OF SYNAPTIC VESICLES

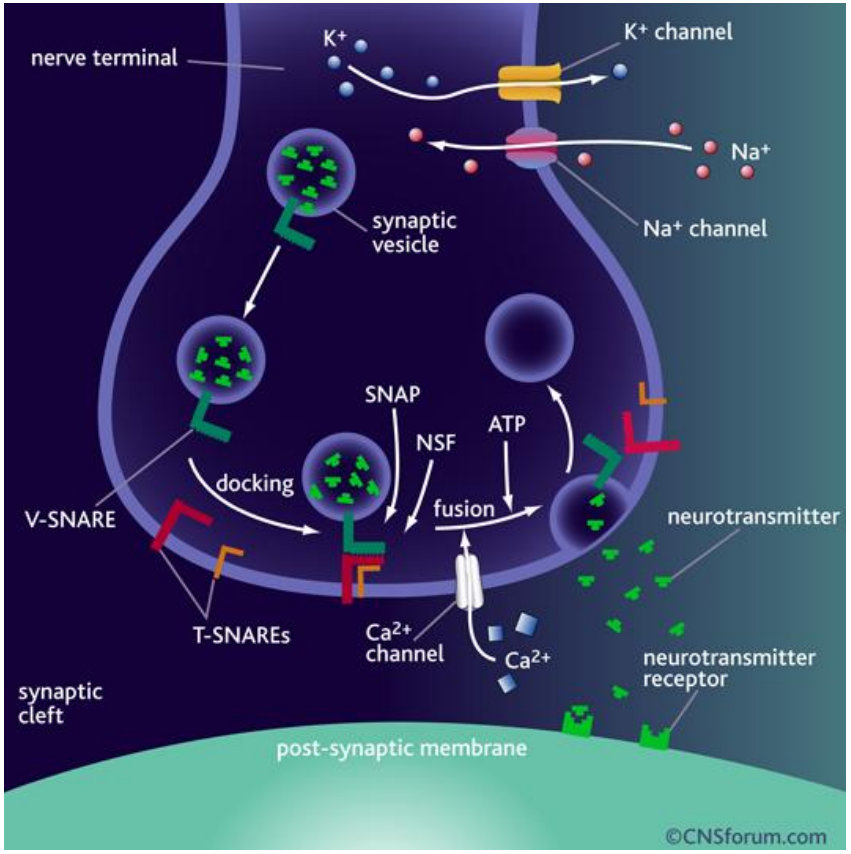
IN ADDITION TO THE SYNAPTIC MEMBRANE PROTEIN SYNAPTOBREVIN, PROTEINS SYNTAXIN AND SNAP 25 CONTRIBUTE TO THE FORMATION OF THE SNARE OR PORE COMPLEX. SYNTAXIN AND SNAP-25 ARE PRIMARILY ASSOCIATED WITH THE CELL MEMBRANE

THE VESICULAR COMPONENTS OF THE COMPLEX ARE REFERRED TO AS V-SNARE, WHILE THE MEMBRANE-ASSOCIATED UNIT IS CALLED T-SNARE

THE TIGHT SNARE COMPLEX BRINGS TOGETHER THE TWO MEMBRANES

THE CALCIUM INFLUX TRIGGERS THE FORMATION OF AN INITIAL MEMBRANE PORE SIMILAR TO A GAP JUNCTION THAT GRADUALLY ENLARGES AND LEADS TO THE COLLAPSE OF THE EXOCYTOTIC VESICLE. SYNAPTOTAGMIN SERVES AS CALCIUM SENSOR IN THE PROCESS

SCHEMATIC ILLUSTRATION OF DOCKING AND FUSION OF SYNAPTIC VESICLES



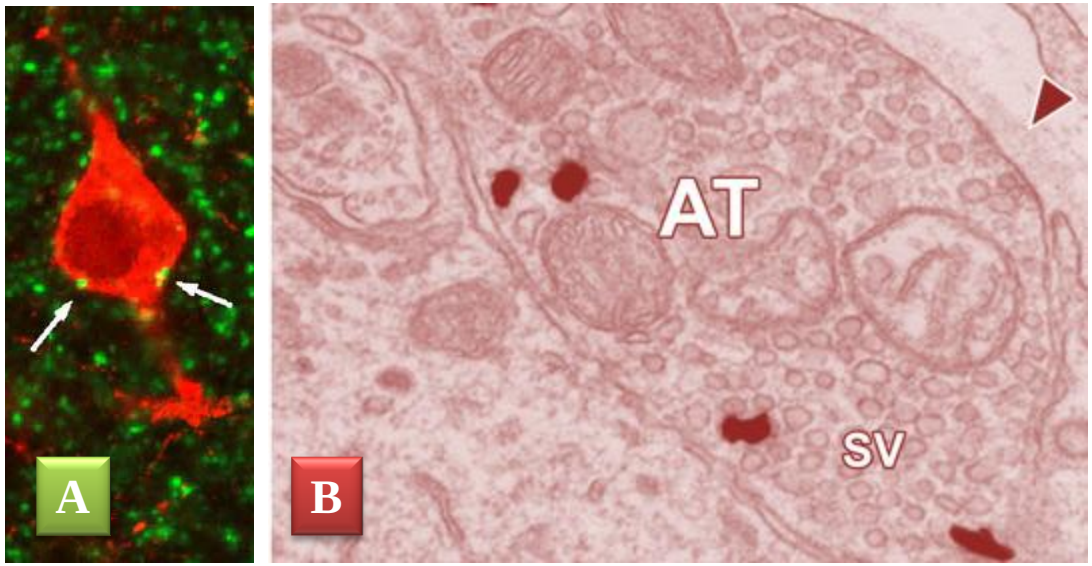
COURTESY OF LUNDBECK INSTITUTE, DENMARK

NOTE THE INTERACTION OF VESICULAR AND TARGET MEMBRANE-ASSOCIATED PROTEINS (V-SNARE AND T-SNARE). THE PROTEIN COMPLEX ATTACHES THE VESICLE TO THE MEMBRANE. NSF AND SNAP PROTEINS ALSO CONTRIBUTE TO THE FORMATION OF THE FUSION COMPLEX. THE FUSION AND FISSION OF THE VESICLE IS TRIGGERED BY CALCIUM AND THE DISASSEMBLY OF THE FUSION COMPLEX BY ATP HYDROLYSIS (NSF). THE TRANSMITTER GETS RELEASED AND THE VESICULAR MEMBRANE RECYCLED. BOTULINUM AND TETANUS TOXINS CLEAVE THE SNARE PROTEINS AND PREVENT THE RELEASE OF THE TRANSMITTERS. BOTH INFECTIONS MAY BE LETHAL

USE OF VESICULAR MEMBRANE TRANSPORTERS IN RESEARCH

VESICULAR MEMBRANE TRANSPORTERS ARE GENUINE PHENOTYPICAL MARKERS OF TRANSMITTERERGIC NEURONS

THE IMMNUNOCYTOCHEMICAL DETECTION OF THE SPECIFIC VESICULAR TRANSPORTERS UNAMBIGUOUSLY IDENTIFIES THE TRANSMITTER CHARACTER OF NEURONS



IN FIG. A. VESICULAR GLUTAMATE TRANSPORTER 2 (VGLUT 2)-CONTAINING AXONS (ARROWS) INNERVATE A TRH NEURON. IN FIG. B. COLLOIDAL GOLD PARTICLES LABEL VGLUT 2 IMMUNOREACTIVE SYNAPTIC VESICLES (SV) IN A GLUTAMATERGIC AXON TERMINAL (AT)