Lesson (6)

Inside the neuron II

The synapse: history, morphology and molecular composition of different types of synapses

What is the main function of a neuronal cell ?

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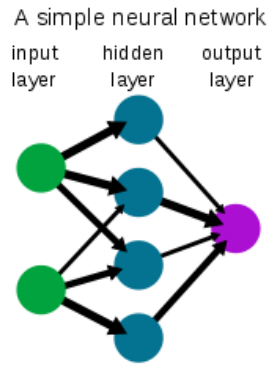
Neuronal network



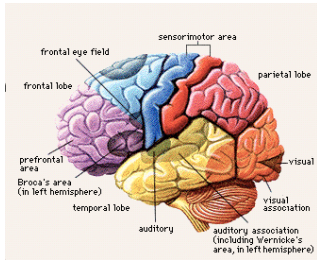
Signals integration : Short term and persistent changes

Synaptic plasticity

The Brain as an Information Processing System

	processing elements	element size	energy use	processing speed	style of computation	fault tolerant	learns	intelligent, conscious
	10^{14} synapses	10^{-6} m	30 W	100 Hz	parallel, distributed	yes	yes	usually
	10^{8} transistors	10^{-6} m	30 W (CPU)	10^{9} Hz	serial, centralized	no	a little	not (yet)

Neural Networks in the Brain



It requires

Axon

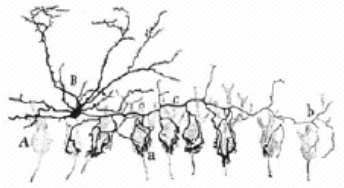
Dendrites

Synapses

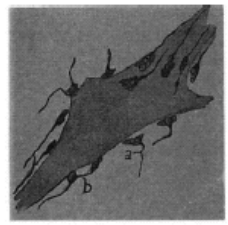
Synaptic Transmission: *historic view*

1. Histologist *Golgi* and *Ramon Cajal*: neuronal connection via "Synapse"
2. *Oliver, Shafer, Langley* and *Elliot* (1890): Chemical transmission *Discovery: noradrenaline as neurotrasmitter*
3. Experimental biology by *Otto Loewi*: electrical stimulation on vagus n. decrease heart contraction

CAJAL: NERVE ENDINGS ARE NOT CONTINUOUS WITH THE CELLS ON WHICH THEY IMPINGE



Endings of cerebellar basket cells in the mouse (Golgi method)



Terminal boutons surrounding a funicular neuron in the spinal cord

The Nobel Prize in Physiology or Medicine 1906

"in recognition of their work on the structure of the nervous system"

Camillo Golgi

Santiago Ramón y Cajal

Baskets surrounding the empty spaces previously occupied by Purkinje cells that are now destroyed

Evidence at the end of the 19th century that nerve terminals are not in continuity with the cells on which they impinge.

Sir Charles Scott Sherrington (1858 –1952)
The Nobel Prize in Physiology or Medicine 1932

Nobel Lecture
Nobel Lecture, December 12, 1932

Inhibition as a Coordinative Factor

The word "synapse" comes from "synaptein", which Sherrington adopted following the suggestion from his colleagues Foster and Verrall who coined it from the Greek "syn-" ("together") and "haptein" ("to clasp").

In Foster's textbook of 1897 he describes the nervous impulse 'sweeping along' the axon of one neuron until it is:

. . . brought to bear through the terminal arborisation on the dendrites of another neuron where 'the lack of continuity between the material of the arborisation of the one cell and that of the dendrite (or body) of the other cell offers an opportunity for some change in the nature of the nervous impulse as it passes from one cell to the other'.

Sir Charles Scott Sherrington (1858 –1952)
The Nobel Prize in Physiology or Medicine 1932

Nobel Lecture
Nobel Lecture, December 12, 1932

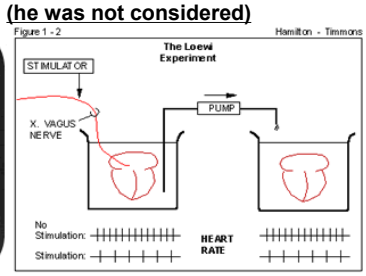
Inhibition as a Coordinative Factor

As a consequence of his work on spinal reflexes in frogs in the 1890s, **Sherrington** reached the conclusion that the transmission of the peripheral stimuli to spinal cord neurons involved **only electrical principles**.

...but he was wrong on this last point..

Discovery of the chemical synapse

- T.R. Elliott (young British scientist) in 1905:
  - **Increase of frog heart beat by direct incubation with Adrenalin (he was not considered)**



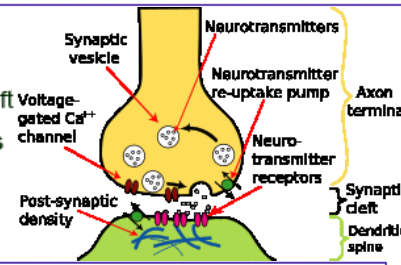
- Otto Lewi (German scientist)
- Nobel Prize for medicine in 1936:
  - **Decrease of frog heart beat by stimulation of vagus nerve (parasympathetic function due to release of Acethylcholine)**
  - **Collection of fluid from stimulated heart and incubation of a second heart with this fluid: decrease of heart beat also in the second.**

The synapse: definition

Information from one neuron flows to another neuron across a synapse.
The synapse is a small gap separating neurons

Action potentials **cannot** cross the synaptic cleft

Nerve impulse is carried by **neurotransmitters**



The synapse consists of:

- **presynaptic ending** (where neurotransmitters are made) also contains mitochondria and other cell organelles,

- **postsynaptic ending** (contains neuroreceptors on the membrane)

- **synaptic cleft** between the presynaptic and postsynaptic endings (20nm)

The adult human brain has been estimated to contain from 10^{14} to $5X10^{14}$ (100-500 trillion) synapses.

- Synapses are functional connections between neurons, or between neurons and other types of cells.
- A typical neuron gives rise to several thousand synapses, although there are some types that make far fewer.

Criteria for Chemical transmission

1. the neurotransmitter is **synthesized** in the presynaptic terminals

2. The neurotransmitter is **stored** in secretory vesicles.

3. The release is **regulated,** neurotransmitter is released in the synaptic cleft, between the pre- /post-synaptic neurons.

4. Presence of **receptors on the postsynaptic** membrane

5. The action of the neurotransmitter is tightly controlled by "**termination" steps (**degradation, diffusion, uptake)

Different types of synapses

● **Excitatory** synapses (Na+ / Ca2+ ion channels). After opening, local **depolarisation occurs**, when/if threshold is reached, action potential is initiated. Neurotransmitters are: glutamate, ATP, acetylcholine.

● **Inhibitory** synapses (Cl- ion channels). After opening, influx of (-) charges **evoke hyperpolarisation** , making action potential less likely. Neurotransmitters are: GABA , Glycine.

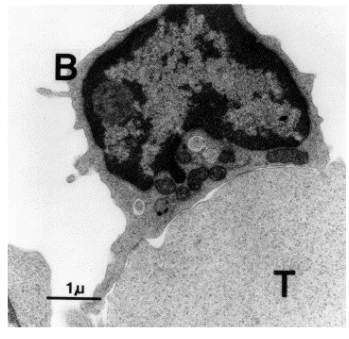
● **Non channel synapses :** neuroreceptors / metabotropic receptors, G-protein-coupled receptors, with enzymatic activity. When activated, they **catalyse the ' chemical messenger '**, which in turn affect the sensitivity of ion channels in the cell. Neurotransmitters are: adrenaline, noradrenaline (called epinephrine in USA), dopamine, serotonin, endorphin, angiotensin, and acetylcholine.

● **Neuromuscular junctions** - synapses formed between motor neurones and muscle cells. Always use the neurotransmitter acetylcholine, always excitatory

● **Electrical synapses** -(gap juctions) close contact of membranes of the two cells, composed of hexamers of connexin proteins. The action potential can pass directly from one membrane to the next, BIDIRECTIONAL effect

Also other cell types communicate via membrane specialization

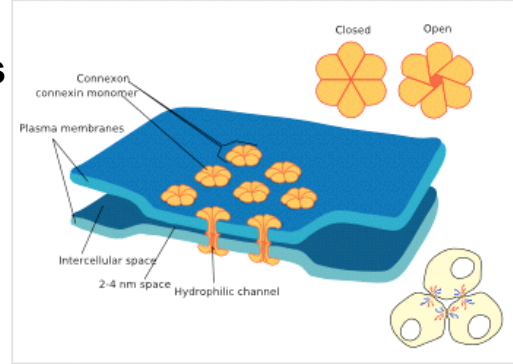
Immunological Synapse



Also other cell types communicate via membrane specialization

GAP junctions
Electrical synapses

BIDIRECTIONAL !!!

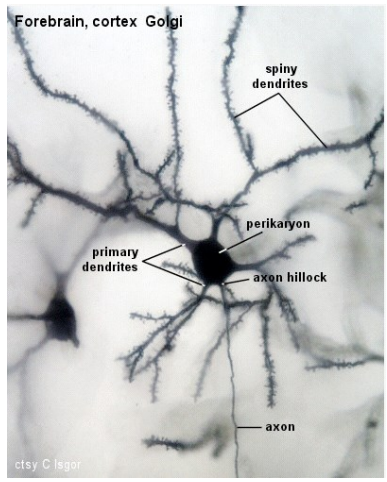


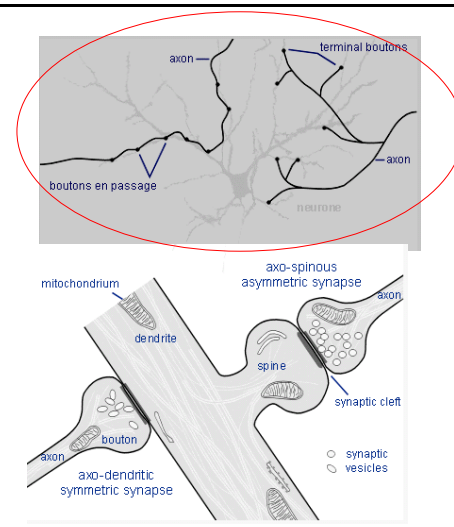
gap junction

The neuronal chemical synapse

The neuronal chemical synapse is UNIDIRECTIONAL

Donor of information (synaptic vesicle release)
Acceptor of information (receptor activation)



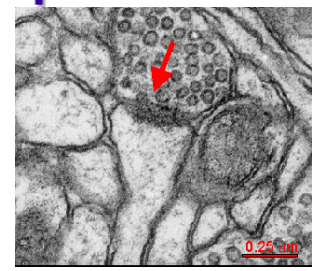


Symmetric synapses : between an axon and neuronal cell bodies

A-Symmetric synapses : between an axon and a dendrite

Classification of synapses

Gray classified two types of synapses within the brain based on the ultrastructural characteristics of the presynaptic (vesicle-bearing) and postsynaptic partners (length of apposed membrane, membrane thickenings and synaptic cleft):



Type 1 = Excitatory(glutamate)

Type 1 synapses on dendritic spines and dendrite shafts (**asymmetric synapse***)

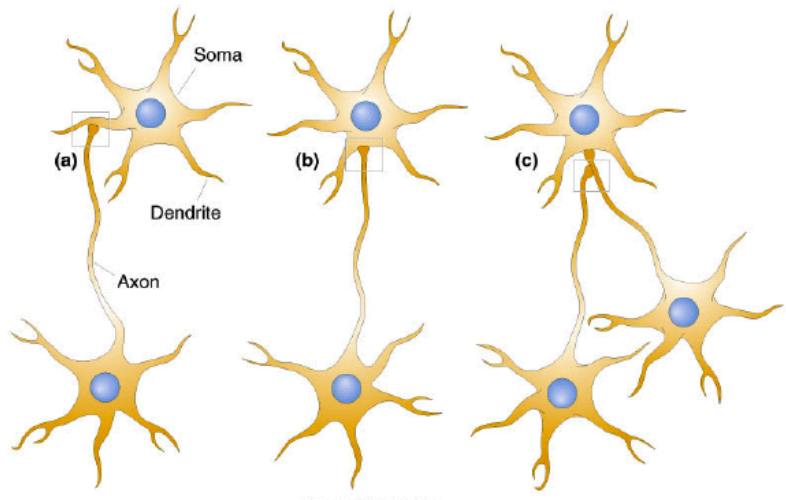
Type 2 synapses on dendrite shafts and neuronal cell bodies (**symmetric synapse*)**

***described by Colonnier**

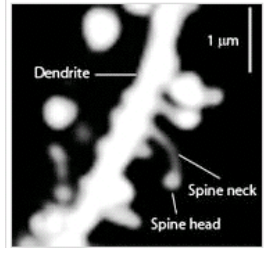
Type 2 = Inhibitory(GABA)

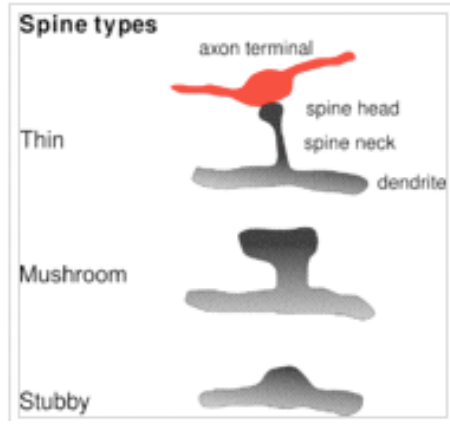
Classification of synapses

- Cytoarchitectural classification
  - Axo-dendritic synapse
  - Axo-somatic synapse
  - Axo-axonic synapse
  - Dendro-dendritic synapse
  - Soma-somatic synapse
  - Neuromuscular synapse (skel m.: NM junction)
  - Neuroglandular synapse



DENDRITIC SPINE



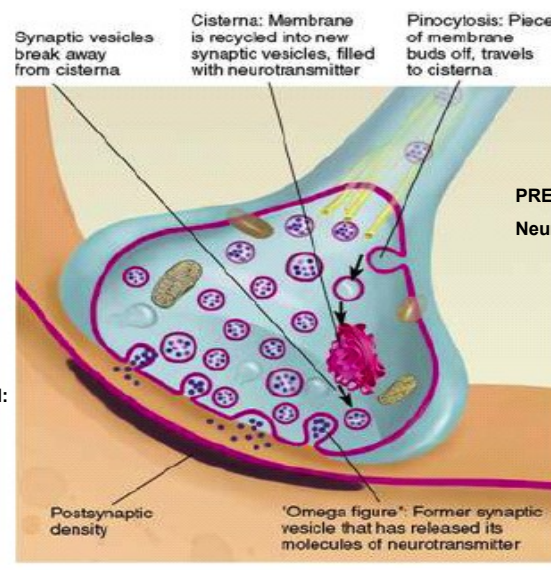


Dendritic spine : A dendritic spine (or spine) is a small protrusion from a neuron's dendrite that receives input from a single synapse of an axon

Classification of synapses by:

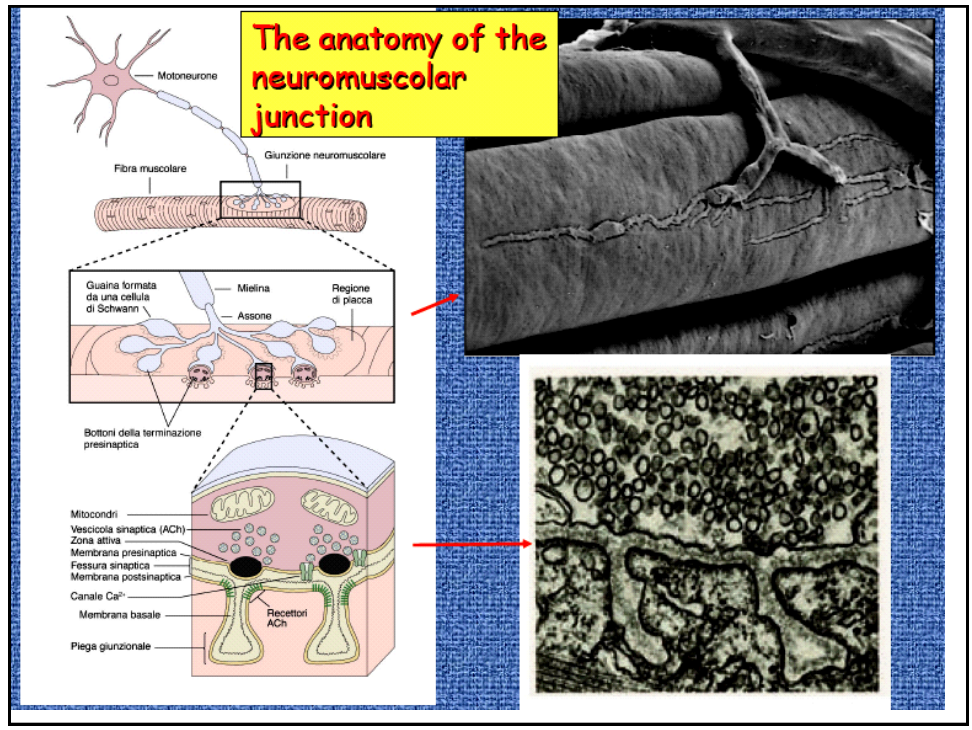
- Cytoarchitectural classification
- Based on method of signal conduction (electrical/chemical)
- Based on conductance of postsynaptic membrane to selective ion species (excitatory/inhibitory)

The synaptic bouton

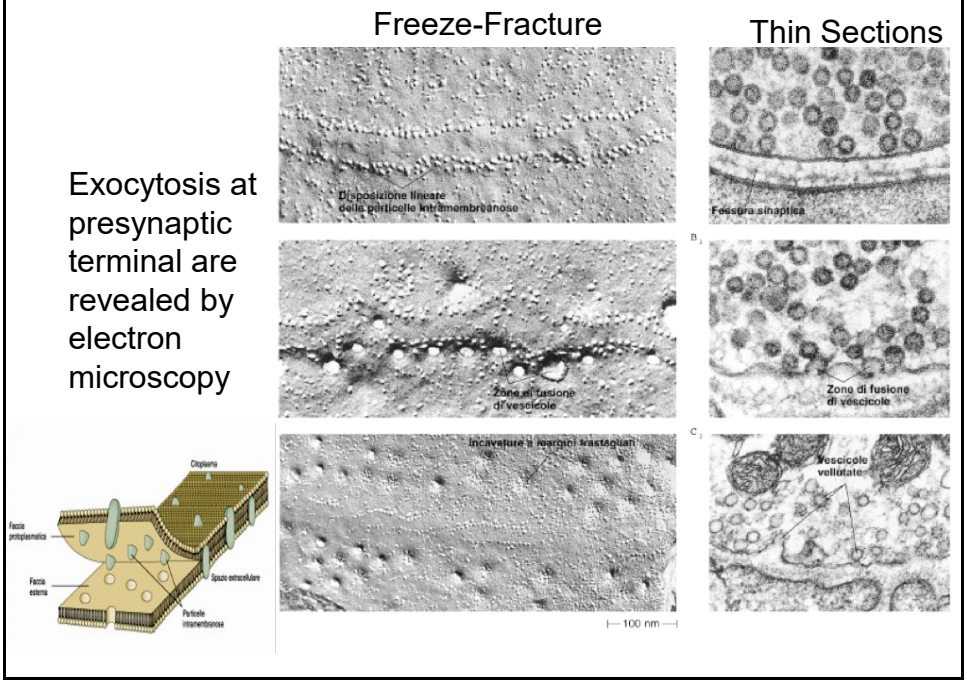


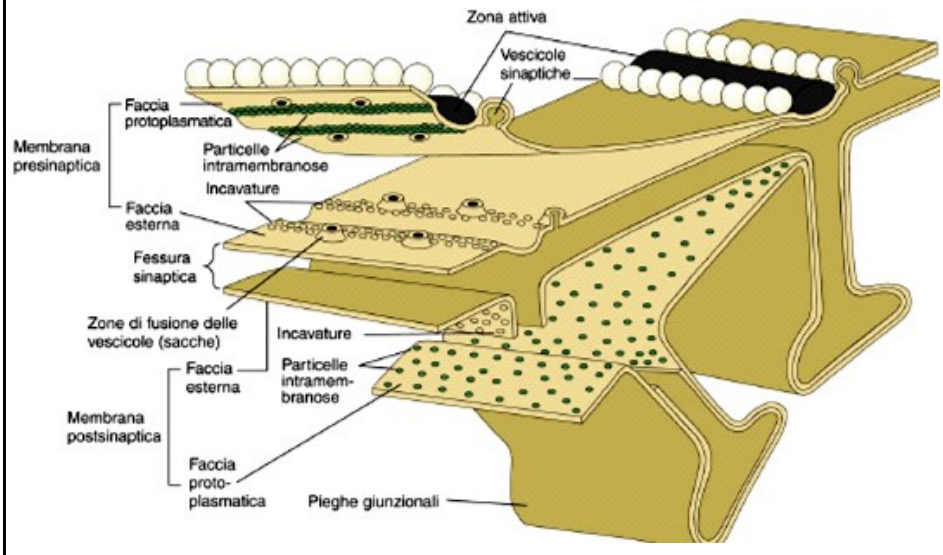
PRE-synaptic cell: Neurotrasmitter Vesicles

POST-synaptic cell: Neurotrasmitter receptors



Exocytosis at presynaptic terminal are revealed by electron microscopy





The neuron is a secretory cell

Neurotrasmitters

Neurotransmitters are **endogenous chemicals** which relay, amplify, and modulate signals between a neuron and another cell.

Neurotransmitters are packaged into **synaptic vesicles** that cluster beneath the membrane on the presynaptic side of a synapse, and are **released** into the synaptic cleft, where they bind to receptors in the membrane on the postsynaptic side of the synapse.

Release of neurotransmitters usually follows arrival of an **action potential** at the synapse,

Major neurotransmitters:

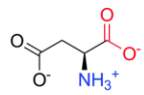
* **Amino acids**: glutamate, aspartate, serine, γ-aminobutyric acid (GABA), glycine

* **Monoamines**: dopamine (DA), norepinephrine (noradrenaline; NE, NA), epinephrine (adrenaline), serotonin (SE, 5-HT), melatonin

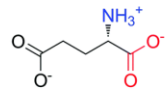
* **Others**: acetylcholine (ACh), adenosine, anandamide, histamine, nitric oxide, ATP, etc.

* over 50 **neuroactive peptides** : CGRP, SP, PY

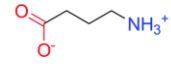
Amino acids



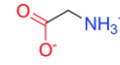
L-aspartate (Asp)



L-glutamate (Glu)

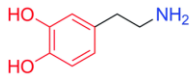


γ-aminobutyric acid (GABA)

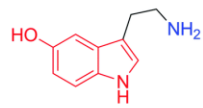


Glycine (Gly)

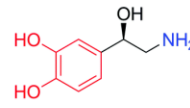
Monoamines



Dopamine (DA)

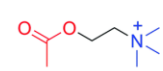


Serotonin (5HT)



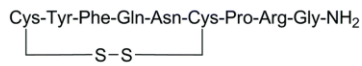
Noradrenaline (NA)

Other amines

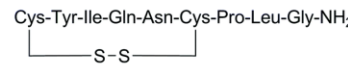


Acetylcholine (Ach)

Peptides



Arginine vasopressin or argipressin (AVP)



Oxytocin (OXT)

Tyr-Gly-Gly-Phe-Leu

Leucine-enkephalin (LE)

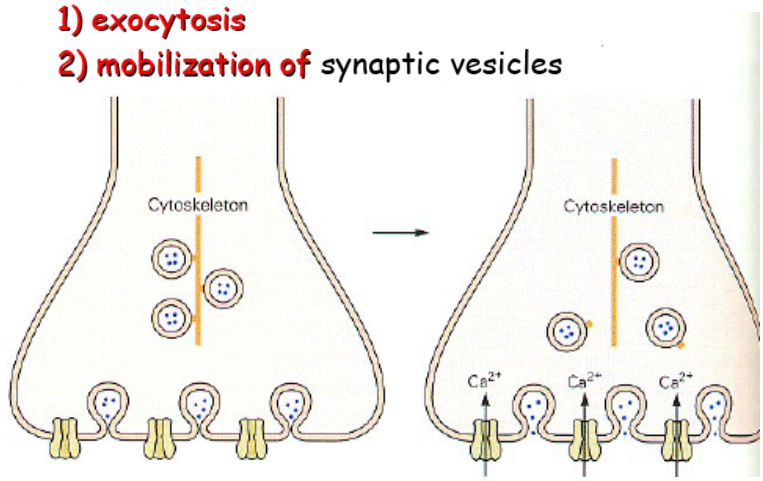
Tyr-Gly-Gly-Phe-Met

Methionine-enkephalin (ME)

Neurotransmitter secretion is very fast (~100 times faster than insulin secretion by pancreatic β-cells) and is **induced by Ca^{++} increase in the presynaptic terminal**

Calcium controls:

1) **exocytosis**
2) **mobilization of** synaptic vesicles



Vesicle cycle and turn-over

Budding
Trafficking
Filling
Docking
Priming
Fusion pore
Full fusion
Endocytosis
Recycling
or degradation