Synaptic transmission

- Synapses– functional contacts between neurons
- Two general classes– chemical and electrical synapses
- Chemical– neurons talk to each other by release of neurotransmitters
- Electrical– **direct** flow of current between neurons

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Speaker notes

Thus far we've discussed how neurons generate action potentials that propagate down axons with high fidelity over cm's to to meters of space and the ion channels in the membrane that underly voltage dependent excitability.

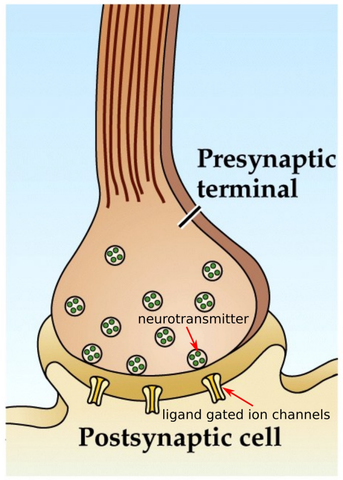
But is through synapses that neurons actually talk with one another and it is also through synapses that the nervous system effects behavior function enabling us to interact with the world around us– in other words there are synapses between pairs of neurons that form the basis of inter-neuronal communication as well as synapses on muscle fibers that neurons use to get our muscles to contract.

Now there are two general classes of synapses, chemical... and electrical...

todo: motor neuron - muscle fiber model

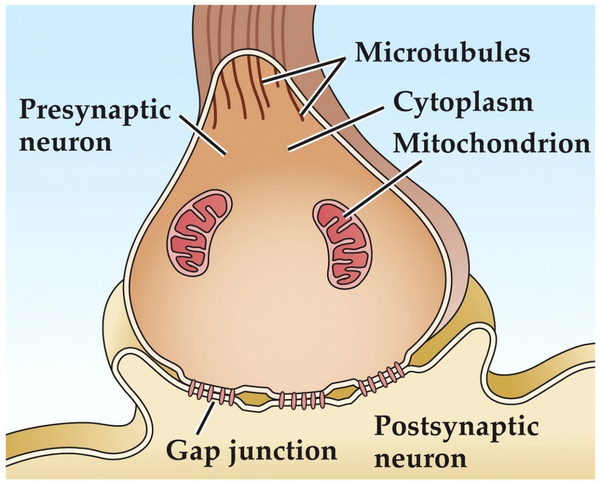
Electrical and chemical synapses have different mechanisms for transmission

chemical synapse



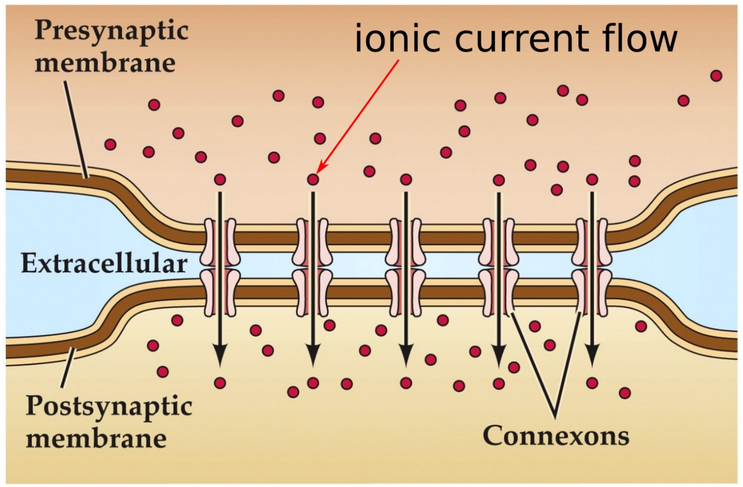
Neuroscience 6e Fig. 5.1

electrical synapse



Neuroscience 6e Fig. 5.1

electrical synapse



Neuroscience 6e Fig. 5.1

Speaker notes

No notes on this slide.

Electrical synapses

- Less common than chemical synapses
- The cell membranes of two cells are linked together via **gap junctions**
- Current flows **directly** from one neuron to another via gap junctions– form large pores (compared to ion channels) between cells made up of connexin proteins
- The signal is very fast– the only limit is diffusion
- Signals can go in both directions
- Function to **synchronize** electrical activity among populations of neurons

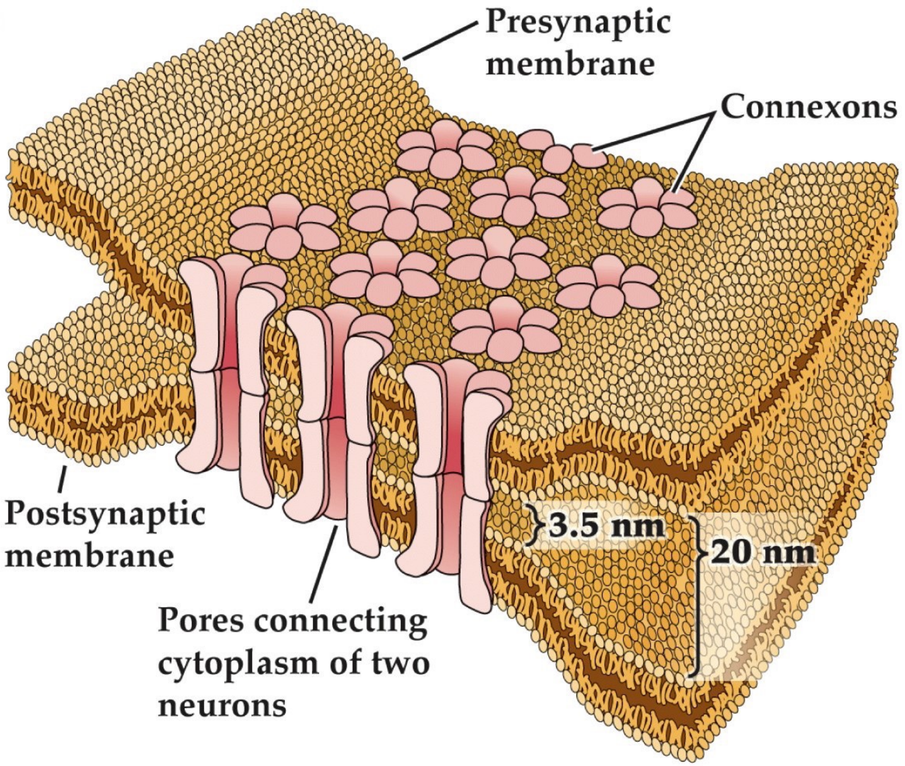
Speaker notes

We have a quadrillion synapses, 10^15 in our nervous system. A tiny fraction are electrical synapses.

These electrical synapse or gap junction synapses are thought to be more common among inhibitory interneurons in the brain—

Pore is approx 1 nm in diameter. Allows passage of small molecular weight substances like intracellular metabolites (a few hundred daltons), but not proteins (typically 5-500 kilodaltons in diameter)

Gap junctions allow current to flow from one cell to the next



6e Fig. 5.2

Speaker notes

- connexins— extracellular loops and disulfide bridges
- 3.5nm separating the apposed lipid bilayers connected through connexon hemichannels
  - versus 20-40nm separation at a chemical synaptic cleft
- passive ionic current flow, small substances like ATP and second messengers can pass through

In contrast to gap junctions/electrical synapses, for chemical synapses current flow does not occur directly from the presynaptic cell to postsynaptic cell.

gap junction proteins: connexins (chordates), innexins (invertebrates), and also pannexins. Similar topologies but dissimilar gene/amino acid sequences.

connexins : 20 isoforms in humans and mice. 40 connecxin orthologues across species. Cx36 36kDa protein, hexamer possibly only forming hemichannels homotypically, specific to neurons. [^Connors:2004]. Cx36 KO mouse has no obvious behavioral phenotype other than retinal deficits[^Connors:2004].

50% of mammalian connexins widely expressed in CNS. Some strong in astrocytes (Cx26,30,43) or oligodendrocytes (Cx29,32,47) [^Connors:2004]

gap junctions first found and studied in invertebrates. Innexins for gap junctions in drosophila, c elegans molluscs, annelids, playhelminthes. Mammalian pannexin genes are similar to innexins and Px1 and Px2 mRNA is present in pyramidal neurons and interneurons of the hippocampus.

c elegans: 959 total cells in adult hermaphrodite. 302 are neurons, 58 are glia. Every cell in worm expresses innexins, most of the 20+ isoforms are expressed in nervous system and every neuron is believed to form gap junctions. 7000 synapses. 6393, 890 electrical junctions. 1410 NMJ.

Electrical Synapses: putative functions

- Synchronization of the electrical activity of large populations of neurons
  - the large populations of neurosecretory neurons that synthesize and release biologically active peptide neurotransmitters and hormones are extensively connected by electrical synapses
  - brainstem neurons involved in breathing
- Synchronization may be required for neuronal development, including the development of chemical synapses
- Synchronization may be important in functions that require instantaneous responses, such as reflexes and pacemakers

Speaker notes

Electrical synapses could play an important role in diseases of pathological oscillations/synchrony like childhood epilepsy.

Electrical synapses and synchronization of activity is characteristic of cells that stimulate pulses of pituitary hormones (e.g oxytocin/vasopressin secretion).

Important for neuronal networks in the pons, medulla: nucleus ambiguous, pre-botzinger complex, solitary nucleus

Inferior olivary nucleus: source of climbing fiber input to cerebellar cortex. ultrastructure and electrophysiology (Llinas 1974) found electrical coupling between pairs of neurons in cat inferior olive. Same thing demonstrated later in guinea pig, rat, mouse. Also dye coupling evidence between neurons. 2-8Hz synchronous oscillations. ^Connors:2004

Thalamic reticular nucleus (thin interneuron layer) of dorsal thalamus. Spatially localized electrical coupling (cells 40 um apart). ^Connors:2004

Hippocampus. between pyramidal neurons and also interneurons. ^Connors:2004

In neocortex only rarely found between pyramidal neurons, often between interneurons. 'Late spiking' L1 interneurons make electrical synapse with other neurons of the same class 83% of time but with other interneuron types only 2% of time. Maybe necessary for gamma frequency rhthyms.

The retina has widespread electrical coupling. Extensive between the amacrine cells (interneurons) that synthesize GABA, acetylcholine as neurotransmitter), scoptopic vision impaired in Cx36 KO mice from loss in rods and cones and between amacrine cells and bipolar cells.

Cx36 in both olfactory epithelium and olfactory bulb. between granule cells. between mitral cells in same glomerulus.

Early in development, first postnatal week in rat electrical coupling extensive between motor neurons in spinal cord. Declines during first postnatal week but still present in adult.

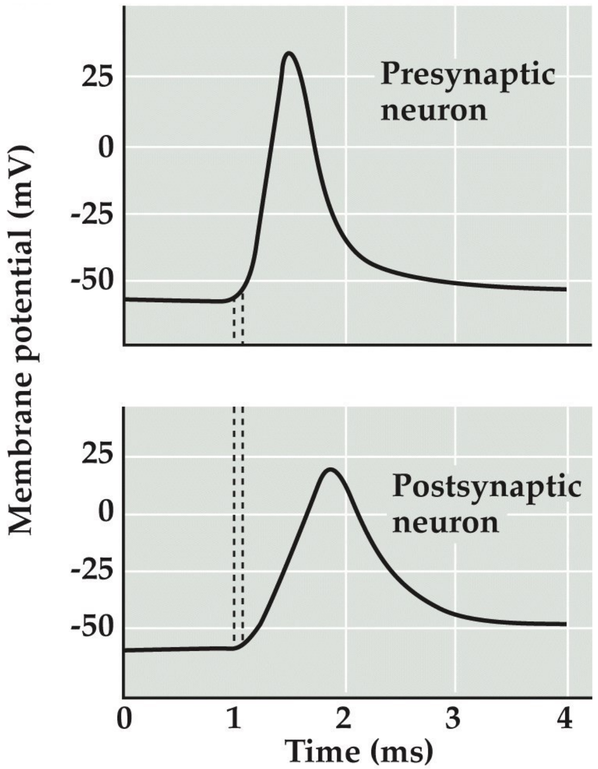
Gap junctions may be sensitive to Ca2+ influx, at least at high concentrations. But are very sensitive to small intracellular (but not extracellular) pH changes and intracellular pH changes occur doing neuronal activity.

Carbenoxolone (from licorice root) not very specific for Cx36.

Quinine selectively blocks Cx36,50,45. Mefloquine is a derivative that is 100x more potent.

Electrical synapses

Synchronous spikes between two crayfish neurons



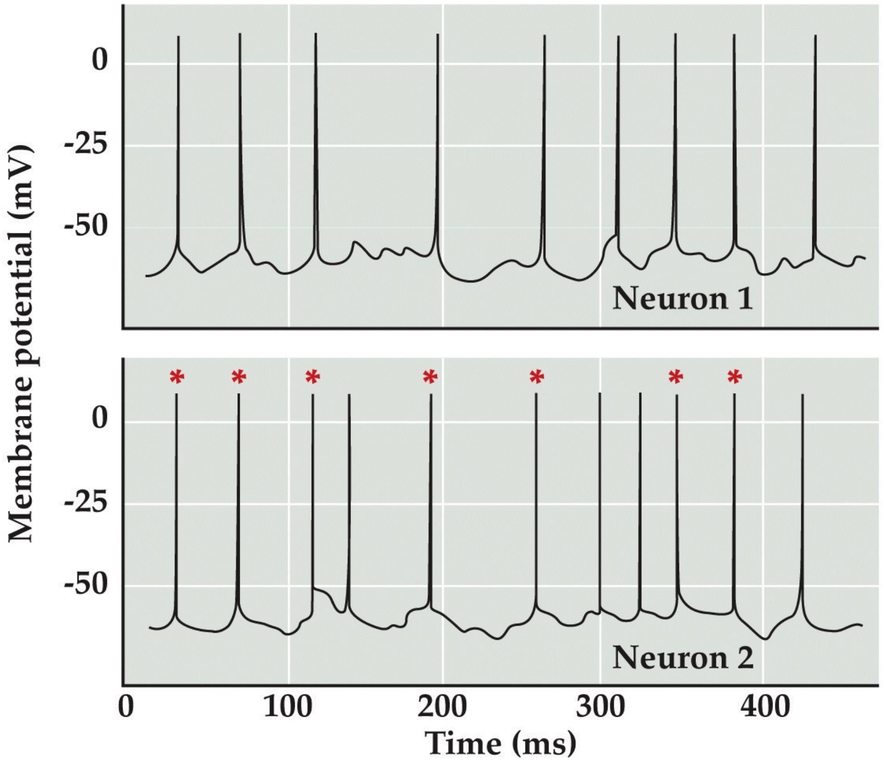
Neuroscience 6e Fig. 5.3, 5e Fig. 5.2; from Fushpan and Potter, 1959

Speaker notes

In Crayfish an action potential in one neuron can spread quickly to the next in fraction of a millisecond.

Electrical synapses

Synchronous spikes between a pair of mammalian hippocampal neurons



Neuroscience 6e Fig. 5.3, 5e Fig. 5.2; from Beierlein et al. 2000

Speaker notes

In hippocampal neurons, gap junctions can make neurons fire in synchrony

Chemical synapses

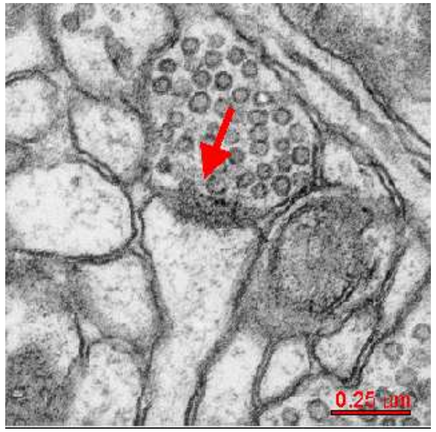
- Majority of connections use chemical synapses
- Form at the synaptic cleft
- Presynaptic cells have synaptic vesicles that have neurotransmitters in them
- Post-synaptic cells have neurotransmitter receptors on the plasma membrane

Speaker notes

No notes on this slide.

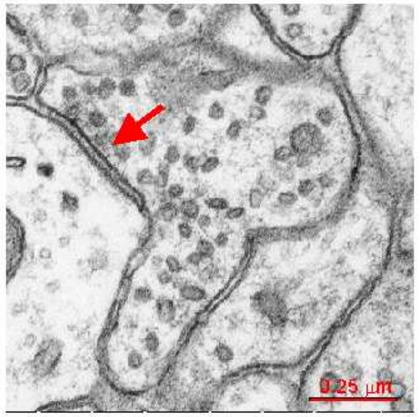
Synapse structure as seen by electron microscopy

chemical synapse, type 1



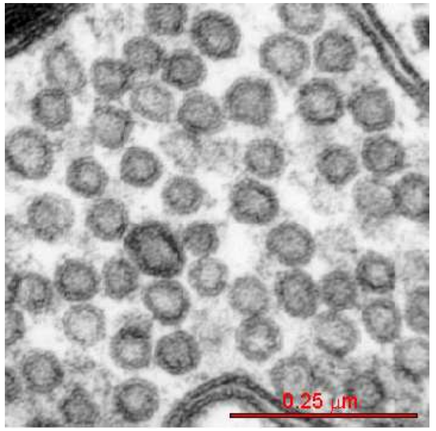
SynapseWeb, Kristen M. Harris, PI

chemical synapse, type 2



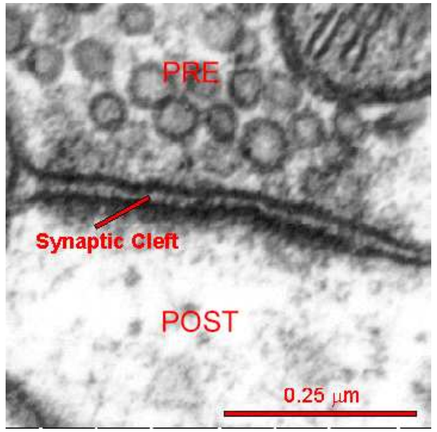
SynapseWeb, Kristen M. Harris, PI

synaptic vesicles



SynapseWeb, Kristen M. Harris, PI

synaptic cleft

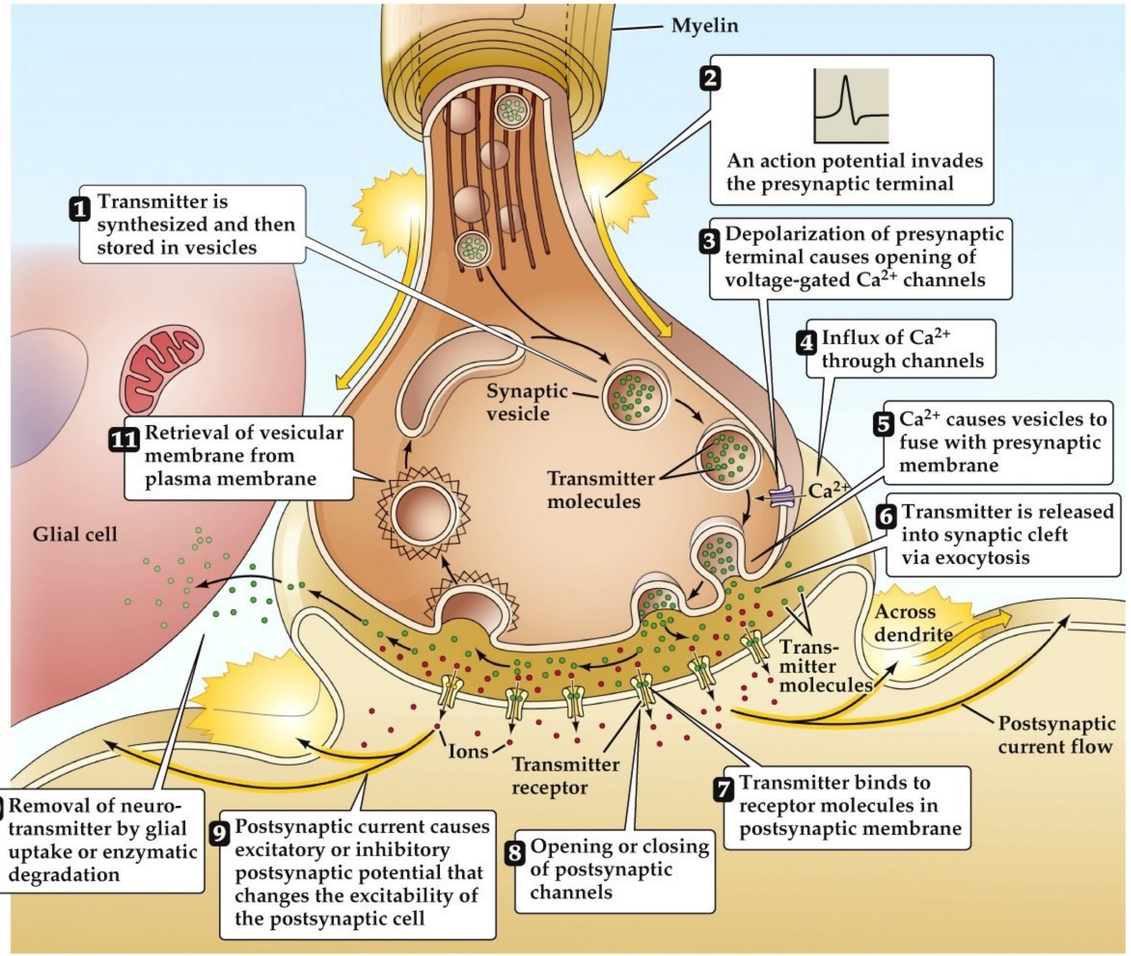


SynapseWeb, Kristen M. Harris, PI

Speaker notes

- synapse, Gray type 1 is asymmetrical synapse. Usually excitatory synapse. Spherical vesicles.
- synapse, Gray type 2 is symmetrical synapse. Usually inhibitory synapse. Elongated vesicles.

Synaptic transmission



Neuroscience 6e Fig. 5.4

Speaker notes

- Action potential in the presynaptic neuron opens voltage-gated Ca^{2+} channels
- Ca^{2+} influx raises $[Ca^{2+}]i$ in the nerve terminal
- Elevated $[Ca^{2+}]i$ triggers the fusion of synaptic vesicles to the plasma membrane of the presynaptic neuron and exocytosis
- Neurotransmitter is released into the synaptic cleft where it diffuses about
- Neurotransmitter binds to specific neurotransmitter receptors in the postsynaptic neuron causing ion channels in that cell to open or close
- The neurotransmitter is inactivated and/or removed from the synaptic cleft (active transport into presynaptic neuron or glial cells or both)
- The vesicular membrane is recovered by endocytosis and recycled

neurotransmitter receptors :

- direction action through ligand gated channels
- indirect action through G protein coupled receptors

The steps of synaptic transmission

1. **Neurotransmitter synthesized** and/or packaged into vesicles
2. **Action potential** enters the presynaptic terminal
3. **Voltage-gated calcium channels** open because of depolarization
4. **Calcium influx** occurs rapidly. Ca^{2+} concentration difference is 1000x across the cell membrane
5. **Vesicles fuse** with membrane because of calcium flux
6. **Neurotransmitter release** into synaptic cleft
7. **Neuroransmitter binds** to receptors on postsynaptic cell
8. **Postsynaptic ion channels** open or close
9. **Postsynaptic current** flux occurs across post-synaptic cell membrane
10. **Neurotransmitter removed** from synaptic cleft by enzymatic degradation or glial cell uptake
11. **Vesicle membrane** recycled via endocytosis

Speaker notes

No notes on this slide.

The discovery of the neurotransmitter acetylcholine

- Otto Loewi– wanted to figure out how stimulation of vagus nerve caused the heart to slow down
  - Vagus nerve (cranial nerve X) has both sensory and motor axons. Regulates heartbeat
- Loewi transfered a solution generated from one heart to slow down another heart even without stimulation
- Demonstrated a diffusible substance was released upon stimulation

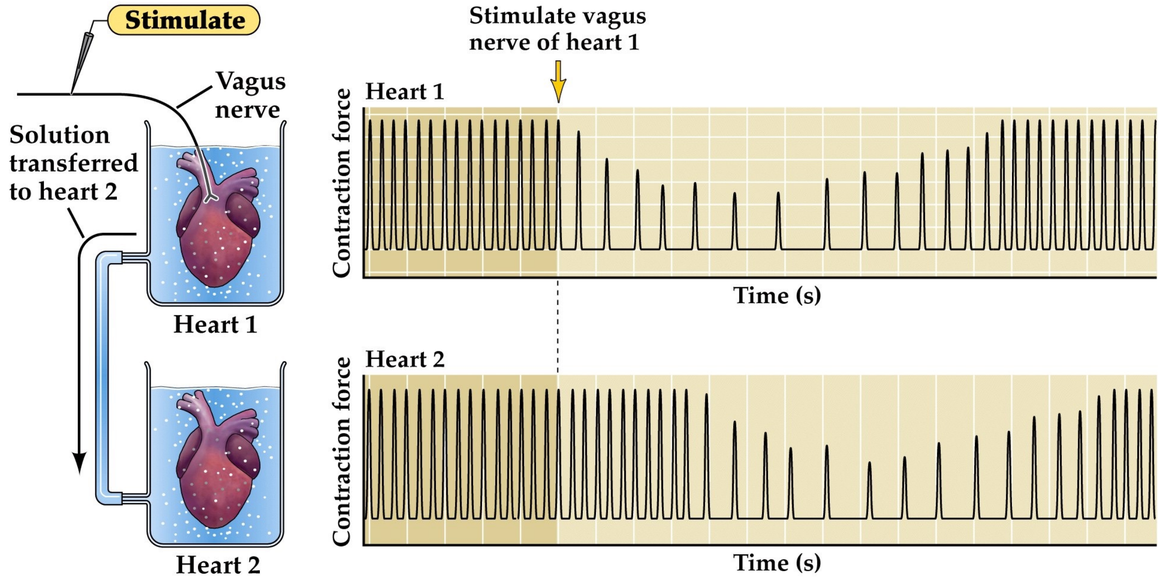
Speaker notes

Vagus nerve (/ˈveɪgəs/ vay-gəs)
: responsible for many things
: heart rate, gastrointestinal peristalsis, sweating, and some muscle movements in the mouth, including speech (via the recurrent laryngeal nerve)
: supplies motor parasympathetic fibers to all organs except the supra-renal (adrenal) glands, from the neck down to the second segment colon
: historically called the pneumogastric nerve
: is the tenth cranial nerve : regulates parasympathetic control of the heart and digestive tract
: vagus nerves are paired but often referred as singular
: has some afferent fibers that innervate the inner portion of the outer ear
: afferent fibers in vagus nerve innervating the pharynx, responsible for gag reflex

vagus nerve skeletal muscles controlled by vagus nerve include:

- Cricothyroid muscle
- Levator veli palatini muscle
- Salpingopharyngeus muscle
- Palatoglossus muscle
- Palatopharyngeus muscle
- Superior, middle and inferior pharyngeal constrictors
- Muscles of the larynx (speech).

The discovery of acetylcholine



Neuroscience 5e Fig. 5.4 Neuroscience 5e Fig. 5.4

Speaker notes

Otto Loewi, 1921

Free acetylcholine acts on **muscarinic receptors** which **hyperpolarize** the cells of the SA node and slow the conduction of the action potential through the AV node. This slows heart rate. Acetylcholine also decreases Ca2+ influx which lowers the heart's force of contraction.

This figure no longer is in 6e of textbook.

The discovery of acetylcholine

Otto Loewi (Austrian)– on the discovery of vagus nerve substance:

> *"In the night of Easter Saturday, 1921, I awoke, turned on the light, and jotted down a few notes on a tiny slip of paper. Then I fell asleep again. It occurred to me at six o'clock in the morning that during the night I had written down something most important, but I was unable to decipher the scrawl. That Sunday was the most desperate day in my whole scientific life. During the next night, however, I awoke again, at three o'clock, and I remembered what it was. This time I did not take any risk; I got up immediately, went to the laboratory, made the experiment on the frog's heart, described above, and at five o' clock the chemical transmission of nervous impulse was conclusively proved."*

Speaker notes

No notes on this slide.

Acetylcholine (ACh) shown to be the vagus factor

- Sir Henry Dale purified ACh (1914) and showed that it is vagus nerve substance
- Can apply ACh to muscle and evoke an end plate potential (EPP)
- Henry Dale and Otto Loewi shared Nobel prize (1936):

> *"for their discoveries relating to chemical transmission of nerve impulses"*

Speaker notes

- ACh action has same pharmacology as vagus nerve substance in that it is sensitive to curare (a plant poison that kills by preventing muscle contraction). Competes with curare for receptor binding
  - Curare used as a paralyzing poison by South American indigenous peoples for hunting that causes respiratory asphixiation (diaphragm muscle paralysis) in prey
  - Curare is a plant alkaloid that is a competitive and reversible inhibitors of nicotinic acetylcholine receptor (nAChR)

Formal criteria that define a neurotransmitter

1. Must be present in the presynaptic neuron
2. Must be released in response to a depolarization and be Ca^{2+} dependent
3. Must have specific receptors localized on the post-synaptic cell

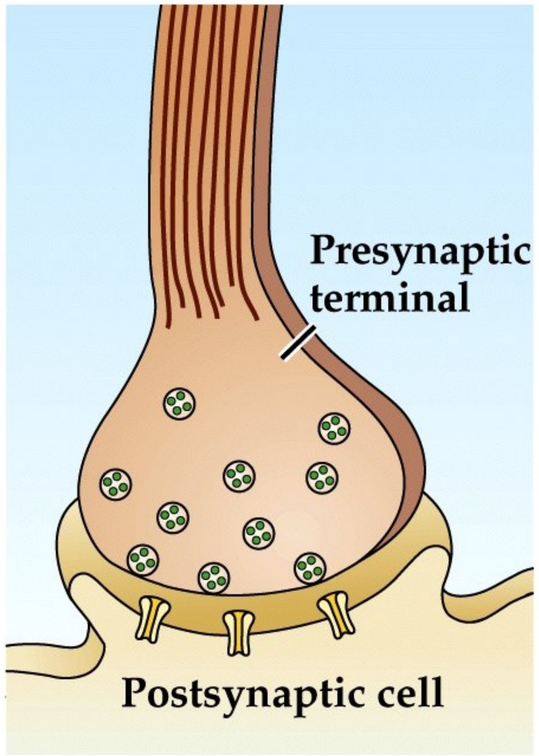
- Note– It does not have to function uniquely as a neurotransmitter (it may have other functions). e.g. glutamate, glycine, ATP

Speaker notes

There are a few criteria that define a neurotransmitter...

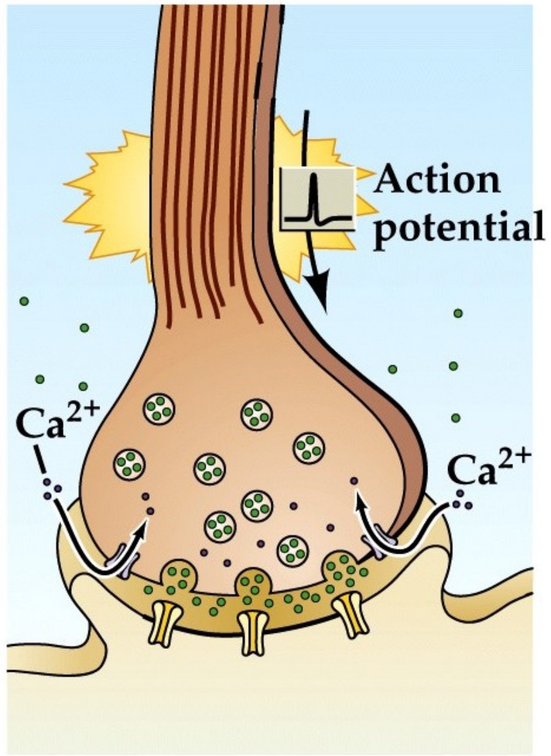
Criteria that define a neurotransmitter

present in presynaptic cell



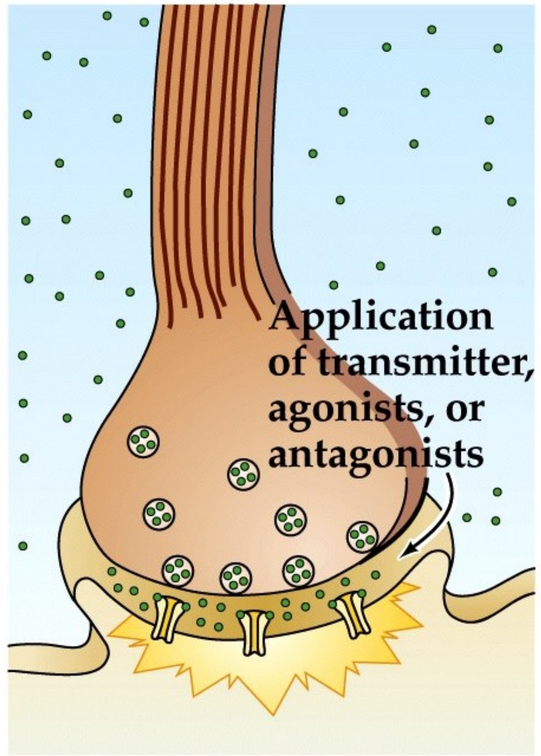
Neuroscience 5e Box 5A

calcium dependent release



Neuroscience 5e Box 5A

specific receptors on post-synaptic cell



Neuroscience 5e Box 5A

Speaker notes

Criteria depicted here

It depends on how you count, but maybe 30 - 100 different molecule types, with 10 of them doing 99% of the work. More than 100 different neurotransmitters have been identified.

There are two main broad categories of neurotransmitters: "Small molecule" neurotransmitters (glutamate, GABA, acetylcholine, biogenic amines (dopamine, serotonin, noradrenaline, and histamine)) and neuropeptides (opioid peptides, substance P). ATP/purines and unsaturated fatty acids like endocannabinoids (anandamide, 2-AG) also can act as neurotransmitters.

Synaptic transmission is quantal

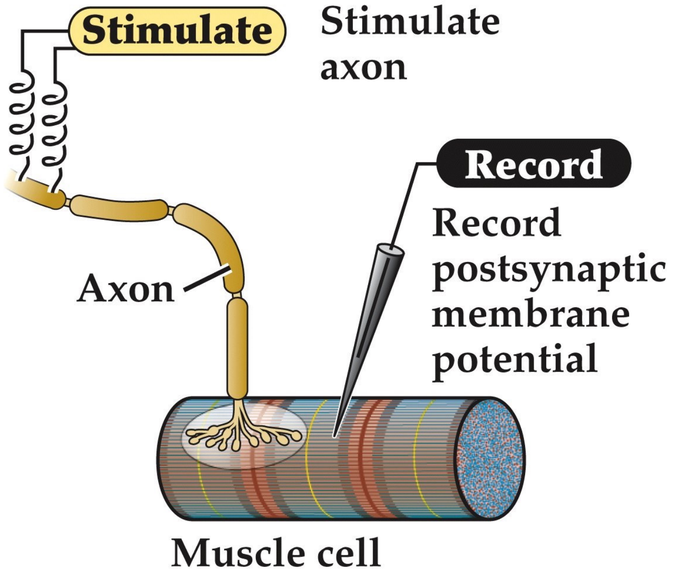
- Synaptic transmission is quantal (composed of discrete units)
- The initial evidence was obtained from studying the release of acetylcholine at neuromuscular junctions
- The synapses between spinal motor neurons and skeletal muscle are simple, large, and peripherally located. Easy to study
  - These motor synapses form structures at the neuromuscular junction called **end plates**. This is where the action happens

Speaker notes

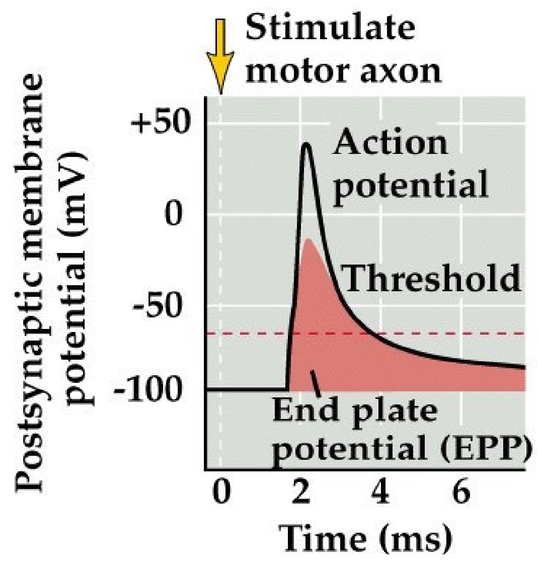
How have we come to learn about the properties of chemical synaptic transmission?

End plate potential

A presynaptic action potential releases a lot of ACh, opening channels in the muscle cell. The resulting depolarization in the muscle cell at the neuromuscular junction is called an end plate potential (EPP).



Neuroscience 6e Fig. 5.5



Neuroscience 6e Fig. 5.5

Speaker notes

Muscle fibers are excitable cells. They are multinucleated myocytes. They too generate action potentials.

End plate potentials evoked by motor neuron stimulation almost are almost always above threshold and result in an action potential along the muscle fiber.

It is the synaptic potential at the neuromuscular junction.

motor unit is a motor neuron's axon terminals and all the skeletal muscle fibers it innervates (10 for extraocular muscles, 1000 for thigh muscles). Motor pool is a bunch of motor units of same fiber type.

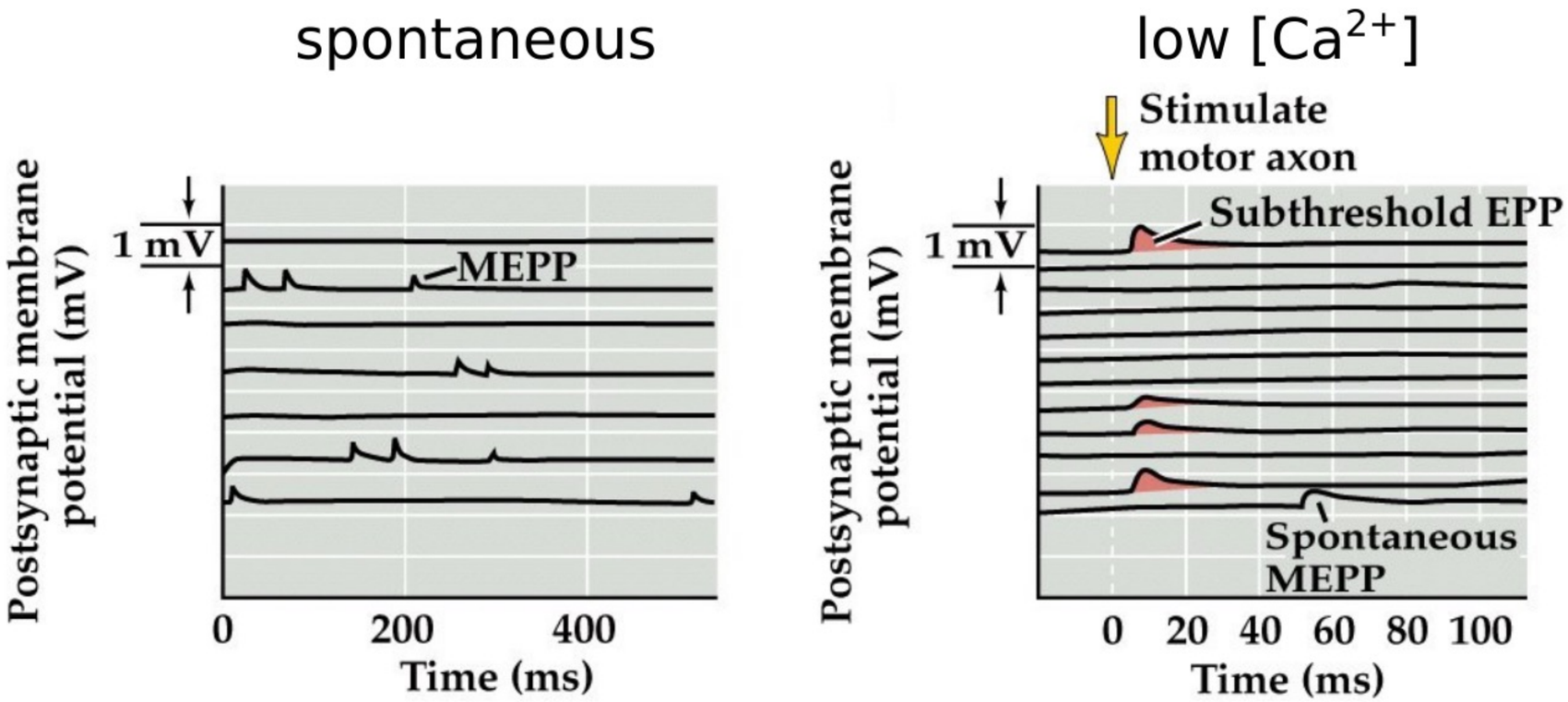
Miniature end plate potentials (MEPPs)

- Spontaneous changes in potential even in the absence of an action potential
- Same shape as EPPs but smaller (1 mV vs 50+ mV)
- Sensitive to agents that block ACh receptors
- Removing Ca^{2+} from media reduces EPPs to MEPPs
- Thus EPPs are a bunch of MEPPs added up

Speaker notes

No notes on this slide.

Spontaneous MEPPs and subthreshold EPPs evoked in low [Ca2+] have similar amplitudes



Neuroscience 6e Fig. 5.5; from Fatt and Katz *J Physiol* 1952

Speaker notes

0.5mV depolarizations.

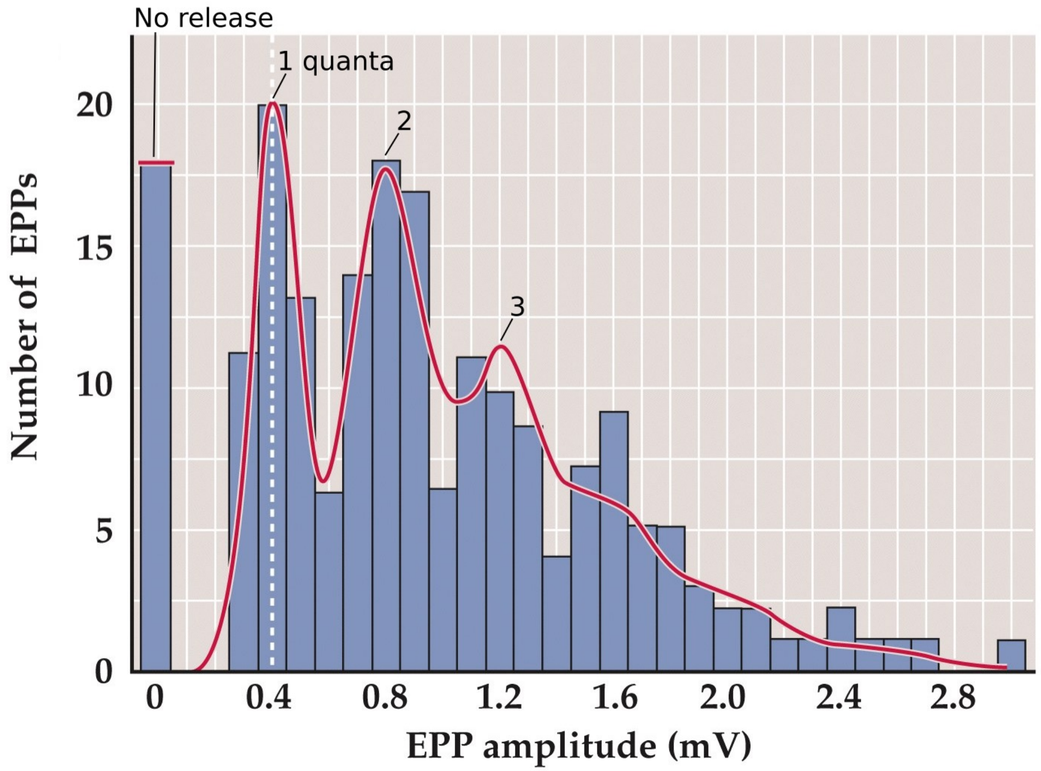
- in the absence of stimulation there is spontaneous postsynaptic membrane transients called minature EPPs. Small amplitude.
- Bath in low calcium and stimulate you get small subthreshold EPPs that are about the same size as the MEPPs.
- Examination of the muscle membrane potential at high gain reveals small, spontaneous depolarizations. These are miniature end plate potentials (MEPPs)

This work was on frog neuromuscular junc in 1950s but subsequent investigations have demonstrated these synaptic properties for all chemical synapses studied to date.

Quantal neurotransmission

- Lowering [Ca^{2+}] reduces the amount of total transmitter (no. of vesicles) released by an AP
- Here [Ca^{2+}] is so low that *often* presynaptic APs fail to release any ACh. But sometimes APs will release 1 to 6 quanta
- The distribution of stimulated EPPs in low [Ca^{2+}] has multiple modes (several local maxima). Multiples of the smallest EPP amplitude (e.g. 0.4 mV)

Histogram of EPP amplitudes in low [Ca^{2+}]



Neuroscience 6e Fig. 5.6; Boyd and Martin *J Physiol* 1955

Speaker notes

If you measure the amplitudes of these small low calcium EPPs and plot their distribution, e.g. this histogram here you can see a certain statistical distribution that indicates these amplitudes fall into discrete steps or quanta showing that the smallest amplitude ones that are about the same size as the spontaneous MEPPs must be result of neurotransmitter release from single synaptic vesicles.

Poisson statistics used to analyse independent occurence of unitary events. Red curve shows what the distribution would expected to be if neurotransmitter release is quantal, made up of discrete message packets (vesicles) made of multiples of MEPP amplitudes (e.g. 0.4 mV)

quantum, quanta (wn, noun)
: ((physics) the smallest discrete quantity of some physical property that a system can possess (according to quantum theory))

Quantal neurotransmission

- The **MEPP is the quantal event of neurotransmission**. It represents the postsynaptic response to the release of a single vesicle of neurotransmitter
- The EPP is the result of the synchronized release of many vesicles. It is the sum of many MEPPs
- Bernard Katz, Nobel prize (1970)

Bernard Katz

Speaker notes

No notes on this slide.

One MEPP = one synaptic vesicle

- Synaptic vesicles are full of neurotransmitter
- In motor neuron one vesicle contains approximately 10,000 molecules of neurotransmitter
- About the same amount needed to invoke an MEPP

Speaker notes

No notes on this slide.

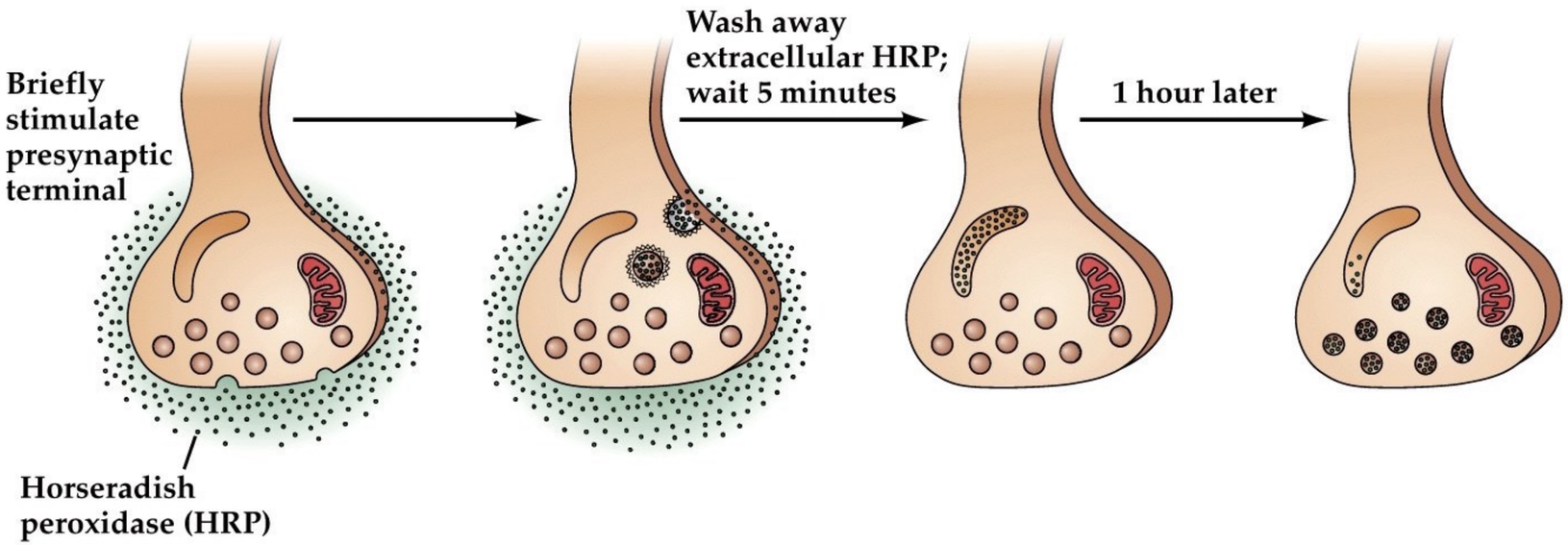
Synaptic vesicles recycle

- All that vesicle fusion– why doesn’t the membrane keep growing and growing?
- Synaptic vesicle membranes get recycled quickly
- Are endocytosed in clathrin coated vesicles which fuse to endosome and bud off again

Speaker notes

Can use a pulse chase experiment to show this -->

Local recycling of synaptic vesicles in presynaptic terminals



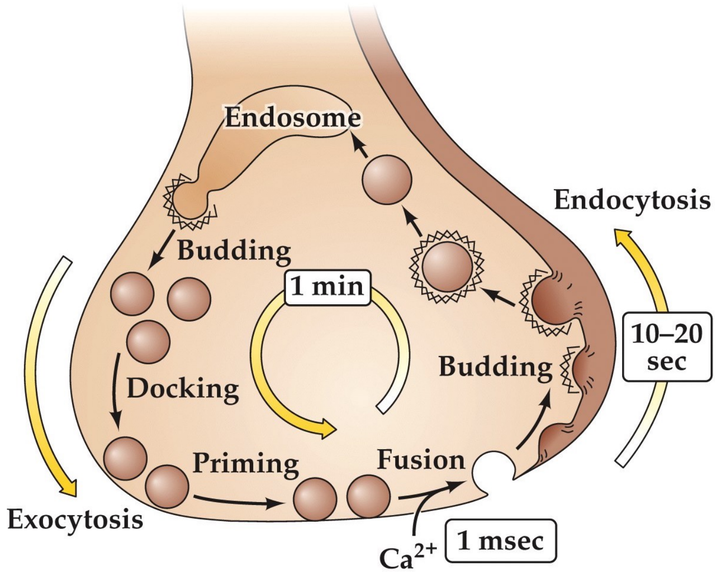
Neuroscience 6e Fig. 5.8

Speaker notes

Pulse chase experiments by Heuser and Reese, 1973. HRP enzyme forms dense reaction product, can be visualized easily in electron microscopy.

Clathrin has a unique three arm structure that forms little geodesic dome coverings around membrane segments and dynamin forms a ring that pinches or 'buds' off the vesicle.

Local recycling of synaptic vesicles in presynaptic terminals



Neuroscience 6e Fig. 5.8, 5e Fig. 5.9

Speaker notes

No notes on this slide.

Calcium is required for synaptic vesicle fusion

- Voltage clamping shows that there is an inward Ca^{2+} flux in presynaptic cells that is voltage dependent
- Ca^{2+} can be visualized entering cell after depolarization
- Injection of Ca^{2+} into the presynaptic neuron can drive a post-synaptic potential
- Chelating Ca^{2+} in the presynaptic cell can inhibit post-synaptic potential

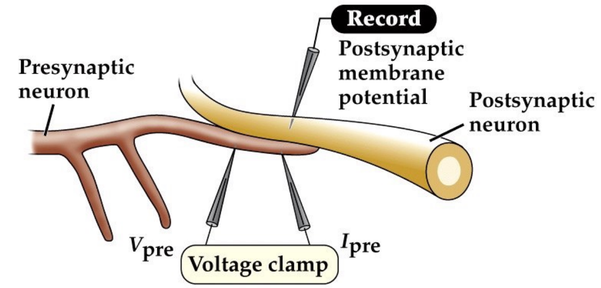
Speaker notes

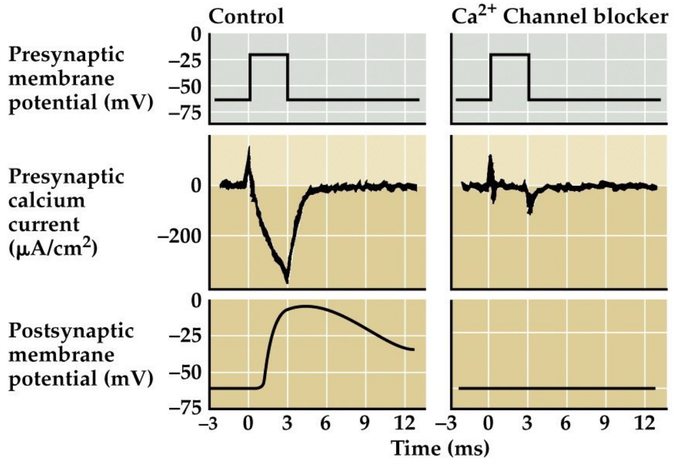
Calcium flux is essential for chemical synaptic neurotransmission.

The role of calcium

- If extracellular Ca^{2+} is removed or Ca^{2+} entry is blocked, there will be no release
- Voltage-gated Ca^{2+} channels in the presynaptic membrane provide Ca^{2+} to trigger the release of neurotransmitter

Voltage-clamp presynaptic neuron and block Na^{+}/K^{+} currents with TTX/TEA





Neuroscience 6e Fig. 5.9, 5e Fig. 5.10; from Augustine and Eckert *J Physiol* 1984

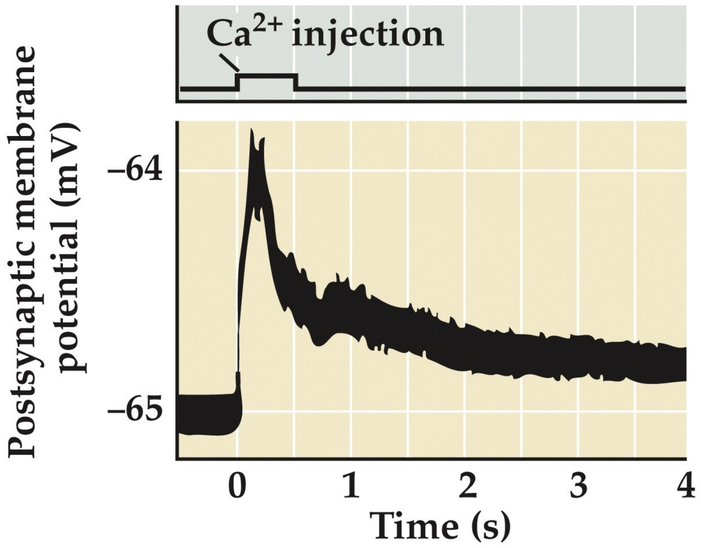
Speaker notes

experiment done in giant squid (Augustine and Eckert 1984)

The role of calcium

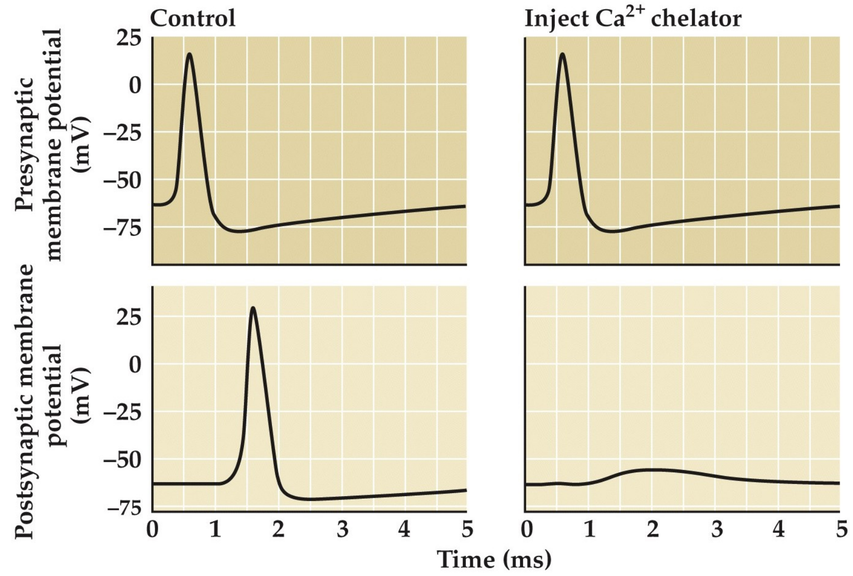
- Intracellular injection of Ca^{2+} into the presynaptic terminal will stimulate release
- Intracellular injection of Ca^{2+} chelator will inhibit release

microinjection of Ca^{2+} into presynaptic terminal



Neuroscience 6e Fig. 5.10; from Smith et al. *J Physiol* 1993, Miledi *Proc R Sci Lon B* 1973

microinjection of Ca^{2+} chelator BAPTA into presynaptic terminal



Neuroscience 6e Fig. 5.10; from Adler et al *J Neurosci* 1991

Speaker notes

- microinjection of Ca^{2+} into squid giant axon presynaptic terminal (Miledi, 1973)
- microinjection of Ca^{2+} chelator BAPTA into squid giant axon presynaptic terminal (Adler et al, 1991)

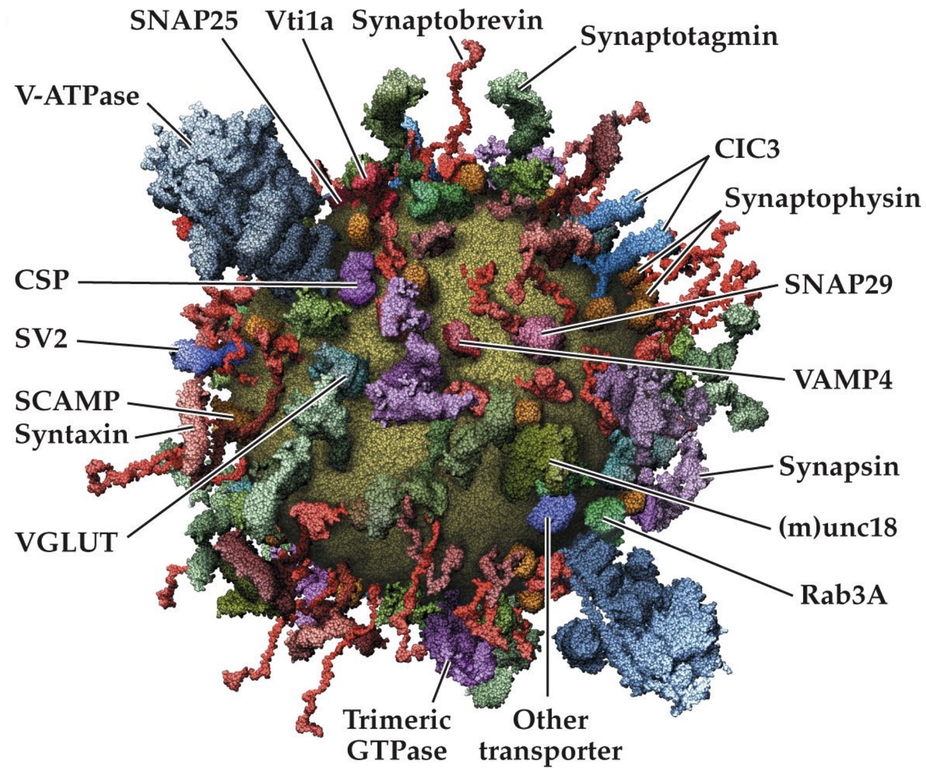
Fluorescent dye that binds calcium (Smith et al 1993)

squid giant axon contacts the contractile muscular mantle responsible for water expulsion and squid jet propulsion

Many proteins are involved in synaptic vesicle cycling

- Many specific proteins have been isolated from presynaptic terminals
- Some of these proteins are required for different steps of vesicle cycling: budding, docking, priming, fusion

Molecular model of a synaptic vesicle



Neuroscience 5e Fig. 5.13; from Takamori *Cell* 2006

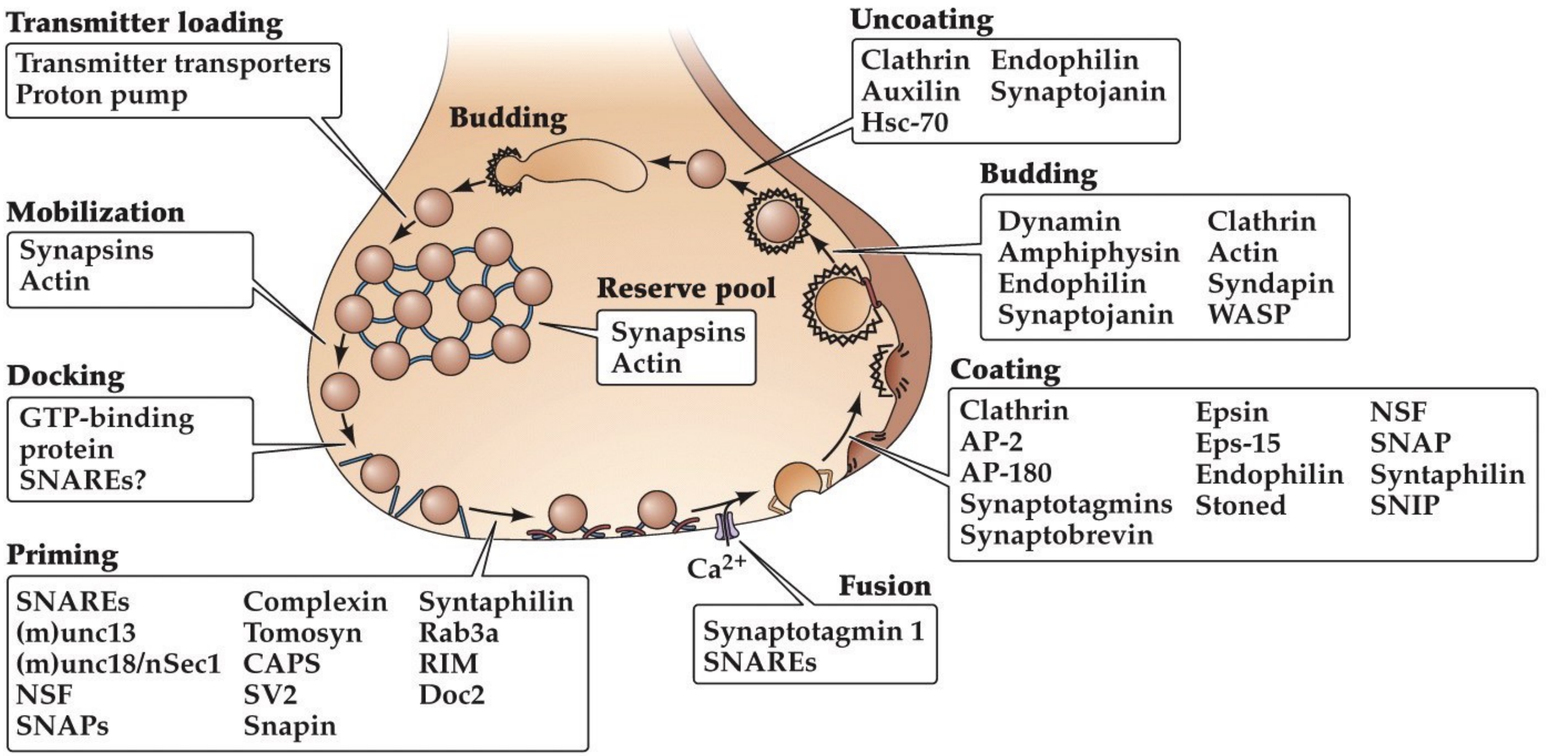
Speaker notes

Model after Takamori et al 2006

Don't memorize this.

Presynaptic proteins implicated in synaptic vesicle cycling

The vesicle trafficking cycle



Neuroscience 5e Fig. 5.13

Speaker notes

NSF: ATPase NSF important for fusion of vesicle with membranes of the golgi apparatus. NEM sensitive fusion protein.

snaps: soluble NSF-attachment proteins

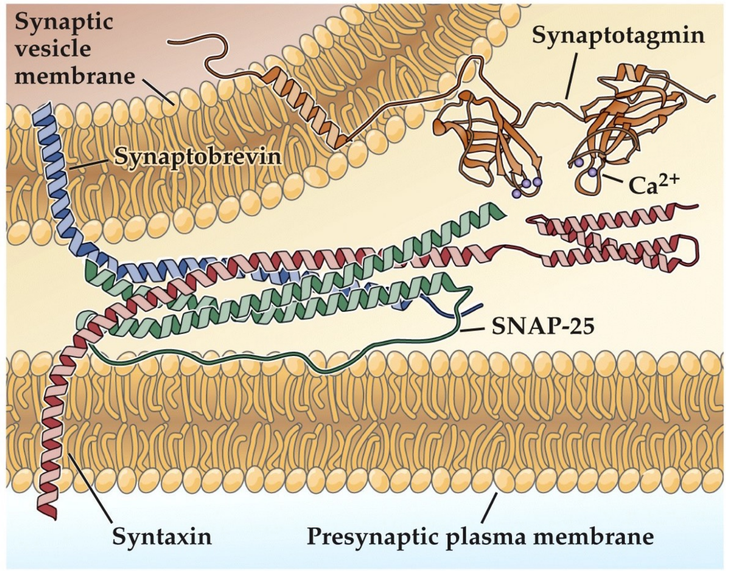
snares: SNAP receptors

Model after Takamori et al 2006

Molecular mechanisms of synaptic vesicle exocytosis

- **SNARES** ('SNAP' receptors) tether the vesicle to plasma membrane
  - SNAP-25 is a plasma membrane SNARE that regulates the assembly of two other SNAREs
  - Syntaxin is a plasma membrane SNARE
  - Synaptobrevin is a vesicle SNARE
- **Synaptotagmin** is a vesicle Ca^{2+} sensor and helps trigger vesicle fusion

Vesicle bound to plasma membrane



Neuroscience 6e Fig. 5.12; based on Sutton *Nature* 1998, Madej 2014

Speaker notes

Many proteins specific to presynaptic terminals have been isolated. These proteins are required for different steps of vesicle cycling: budding, docking, priming, fusion.

Just know there are is a calcium sensitive protein called synaptotagmin and that there are proteins like SNAREs that help dock and pinch membranes together

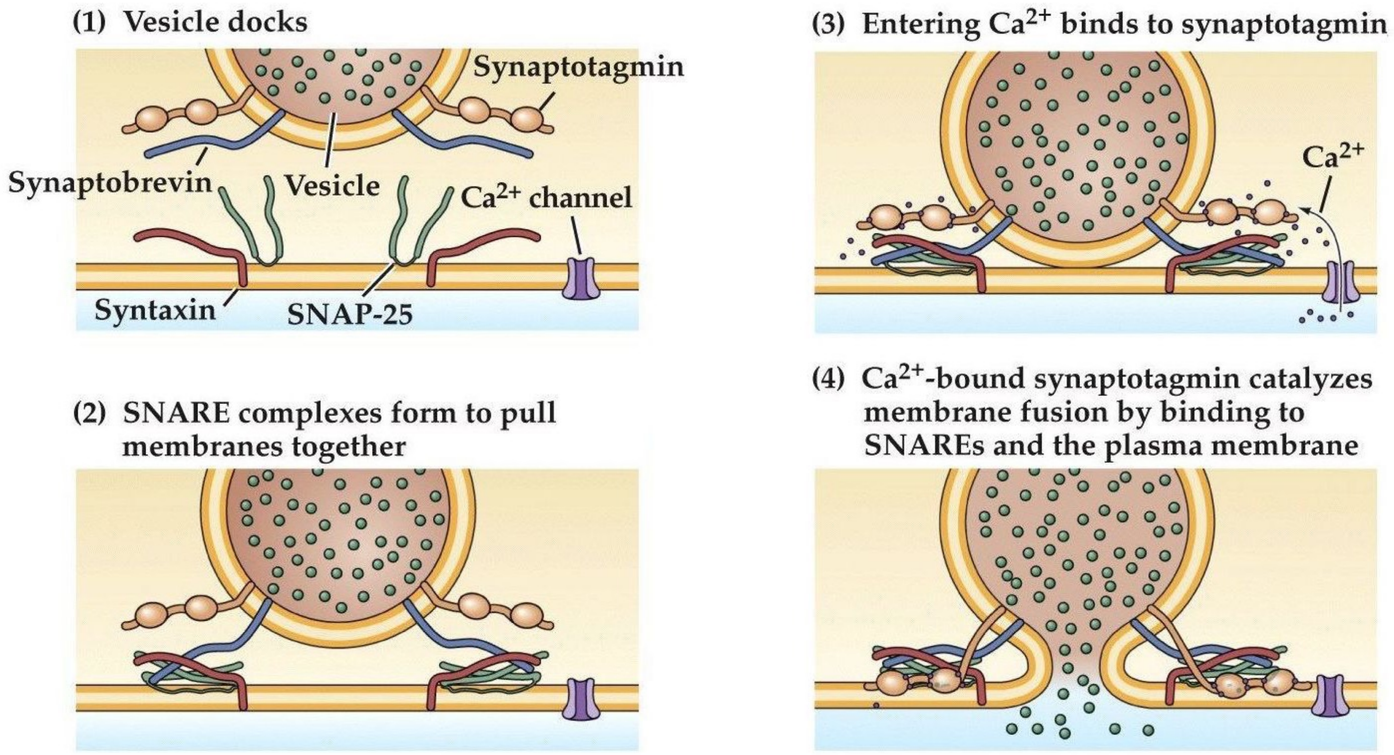
NSF
: NEM-sensitive fusion protein (orig found to be important for fusion of vesicles with membranes of Golgi apparatus) : ATPase

SNAPs
: soluble NSF attachment proteins

SNARES
: 'SNAP receptors'

Model based on crystal structure work for SNAP25 from Sutton 1998, Madej 2014, Zhou *Nature* 2015

Molecular mechanisms of synaptic vesicle exocytosis



Neuroscience 6e Fig. 5.12, 5e Fig. 5.14

Speaker notes

Model based on crystal structure work for SNAP25 from Sutton 1998, Madej 2014, Zhou *Nature* 2015

Vesicle proteins are the targets of many toxins

- Tetanus toxin– cleaves synaptobrevin
- Botulinum toxins– cleave syntaxin and snap25 (causes botulism)
- alpha-latrotoxin– black widow causes a massive exocytosis of vesicles. Somehow bypasses Ca^{2+} requirement, likely affecting synaptotagmin

Speaker notes

- cleavage of SNARE proteins inhibits acetylcholine release
- botulinum toxins specifically cleave SNAREs, preventing synaptic vesicles from docking and fusing with plasma membrane
- blocking release of acetylcholine results in flaccid paralysis of muscles (typical of botulism)
- https://en.wikipedia.org/wiki/Botulinum_toxin
- tetanus toxin cleaves the synaptobrevin SNARE protein within spinal cord interneurons. This results in less inhibition of spinal cord motor neurons giving rise to muscle hyperexcitation and "tetanic" contractions

Thus two definitions for tetanus from wordnet, one referring to the bacterial toxin and one referring to a hyperexcitable phenotype in muscle tissue:

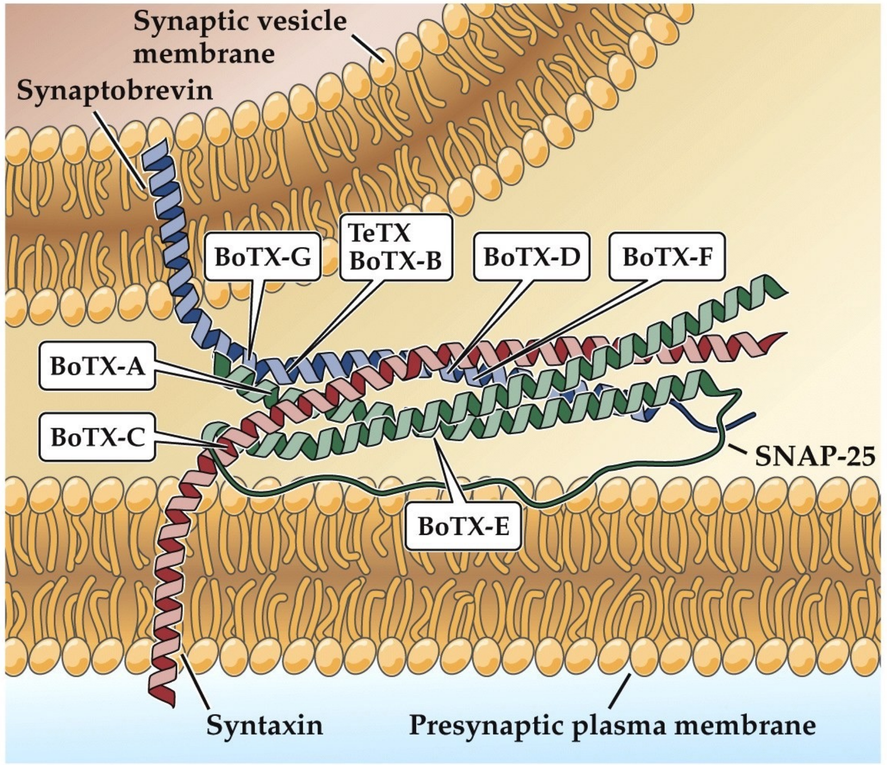
tetanus (wn, noun)
: an acute and serious infection of the central nervous system caused by bacterial infection of open wounds; spasms of the jaw and laryngeal muscles may occur during the late stages
: a sustained muscular contraction resulting from a rapid series of nerve impulses

Thus in animal physiology when discussing sustained excitation of muscle tissue, it may be referred as "tetanic" stimulation or a muscle "in tetanus".. even when there is no tetanus toxin.

Synaptic vesicle toxins

Tetanus toxin and botulinum toxins act by cleave synaptic SNARE proteins, preventing exocytosis.

SNARE protein sites cleaved by tetanus and botulinum toxins



Neuroscience 5e Box 5B, see also Clinical Application 6e p. 99-100

Speaker notes

Tetanus toxin and botulinum toxins are all from *Clostridium* bacteria.

Synaptic transmission summary video

Neuroscience 5e Animation 5.1

Speaker notes

No notes on this slide.