Information Transfer via Vesicles in Cells

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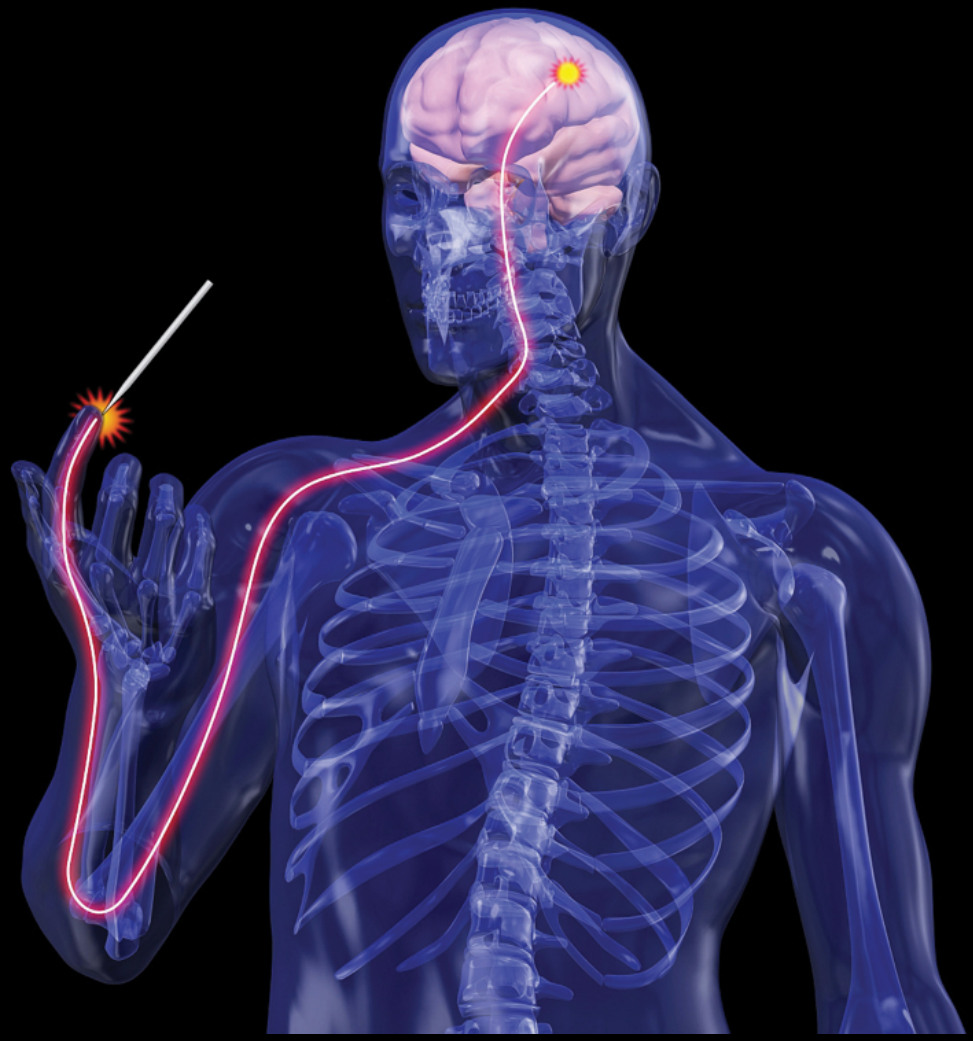
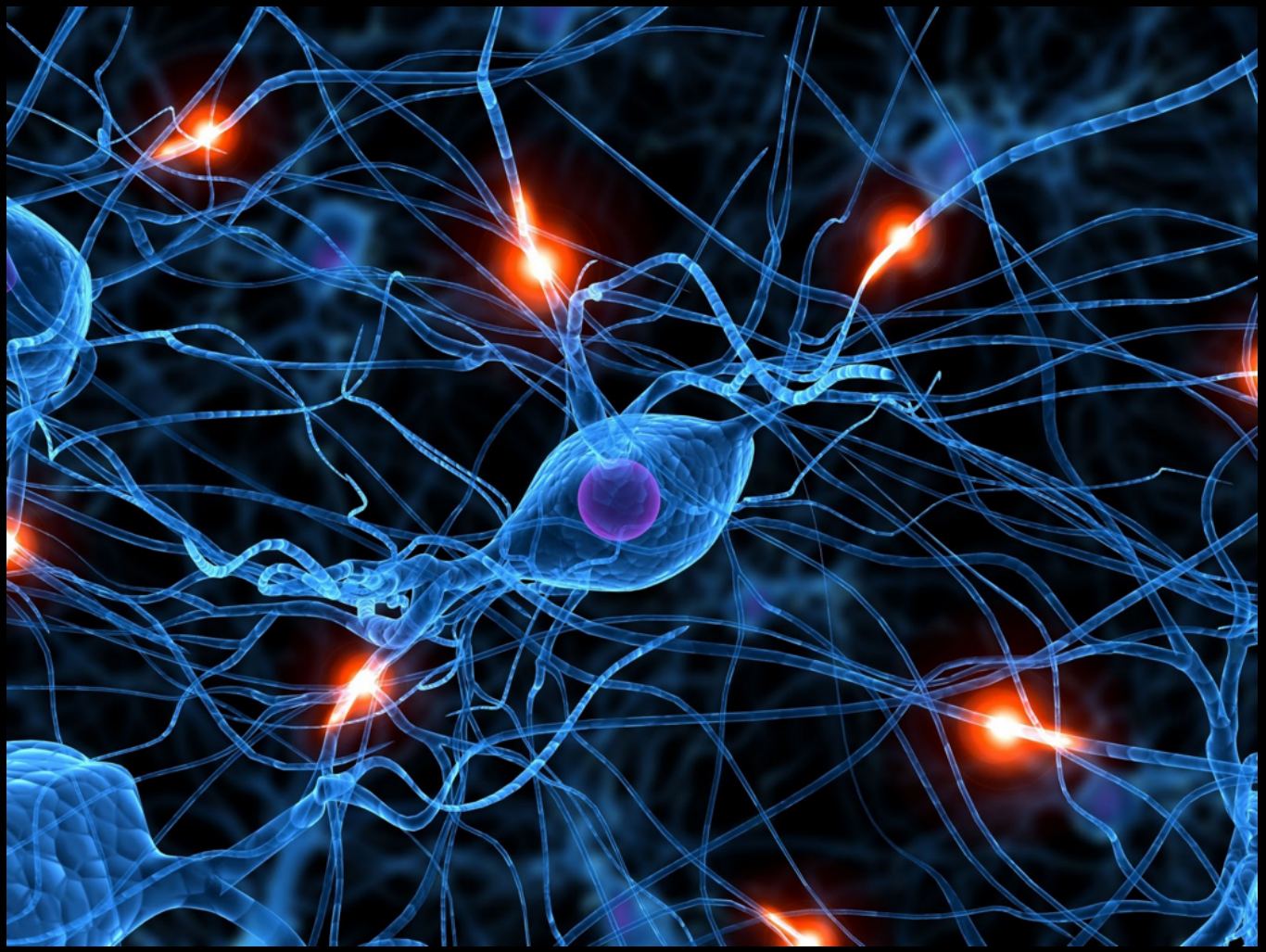
How do we perceive any sensation ?

Information is transferred by electrical signals within neurons and by chemical signals across neurons

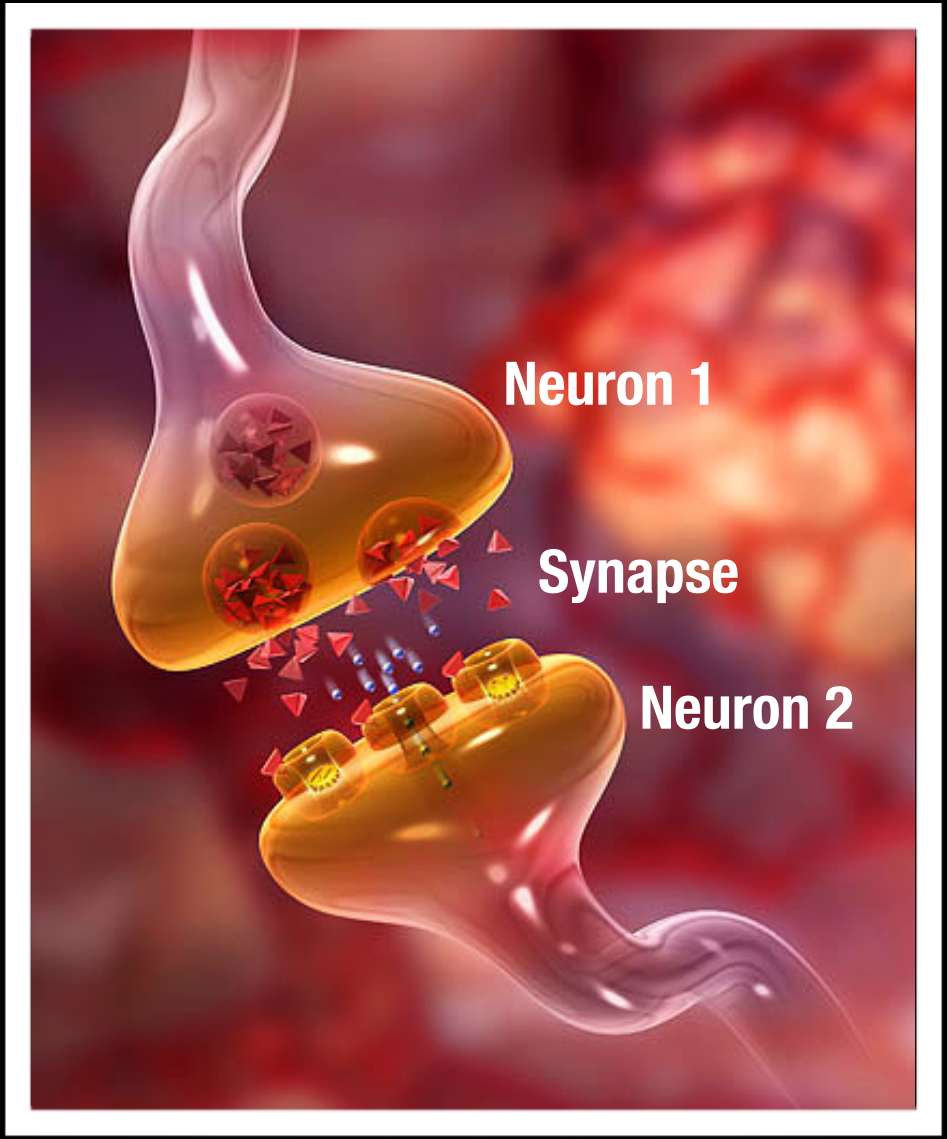


The Brain

A vast (~a billion) collection of neurons interconnected and communicating with each other via chemical signals



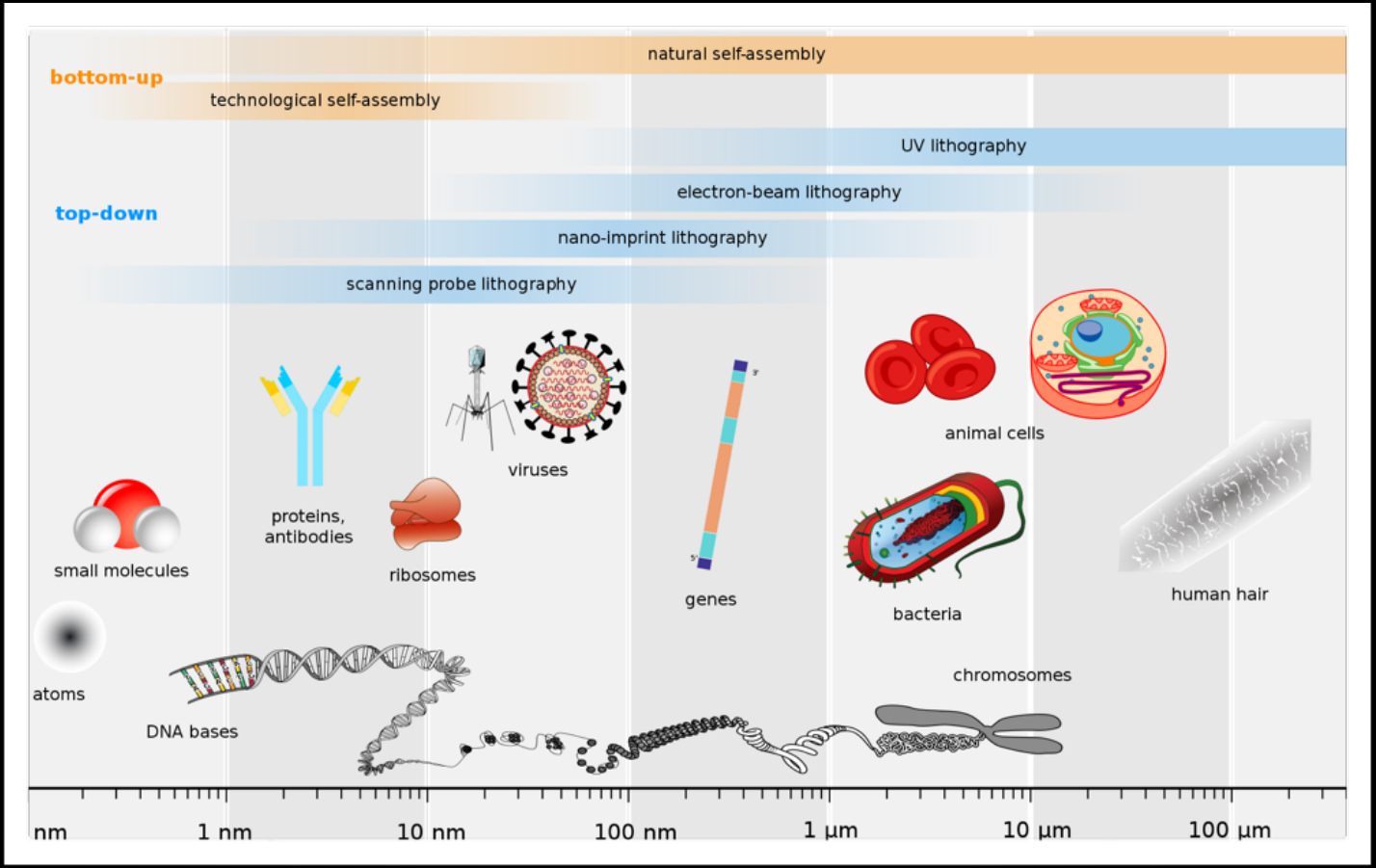
The Synapse



A physical barrier for interneuronal communication

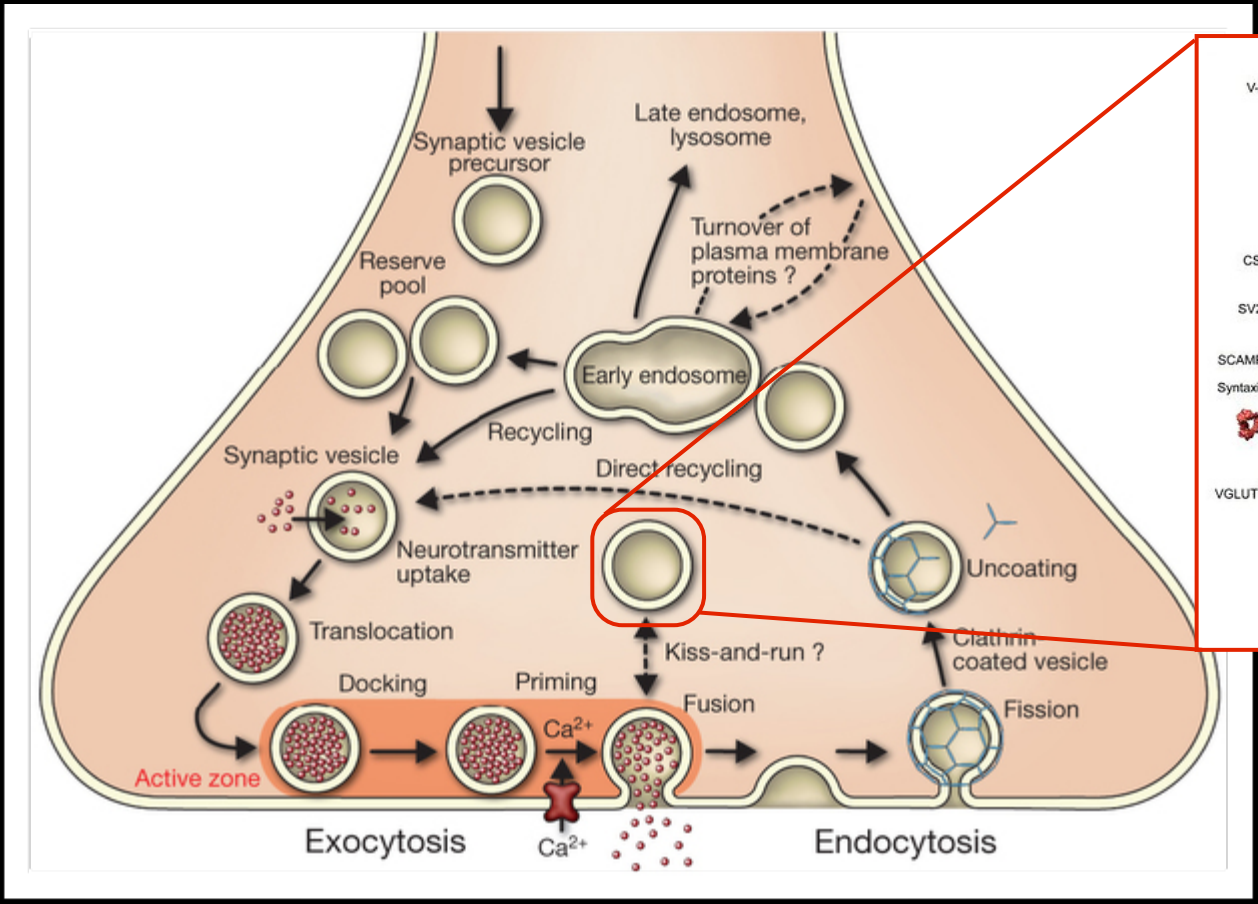
Signals across neurons are transferred via vesicles filled with neurotransmitters called synaptic vesicles

Length Scales Relevant to Biology

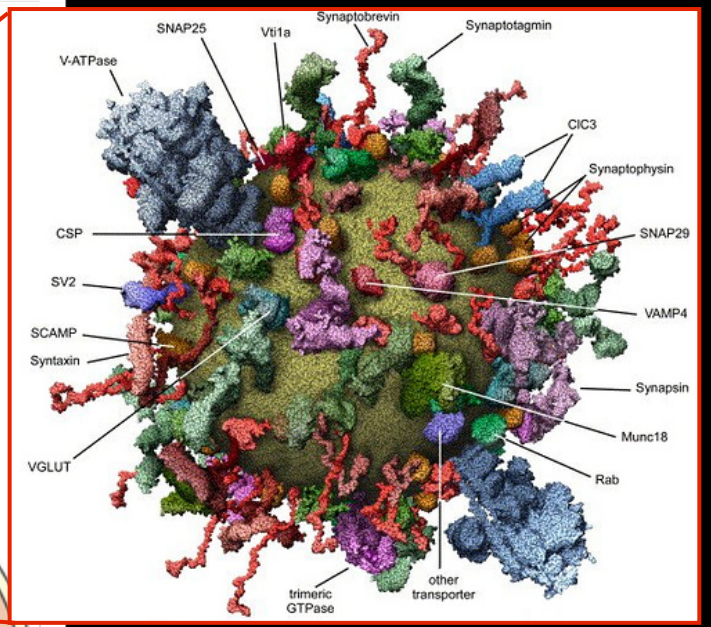


Schematic of a Synaptic Bouton - the tip of a neuron

Chemical signals are generated in the form of neurotransmitter filled synaptic vesicles which fuse with the cell boundary to release neurotransmitters by a process called ‘exocytosis’ and are regenerated by a process called ‘endocytosis’



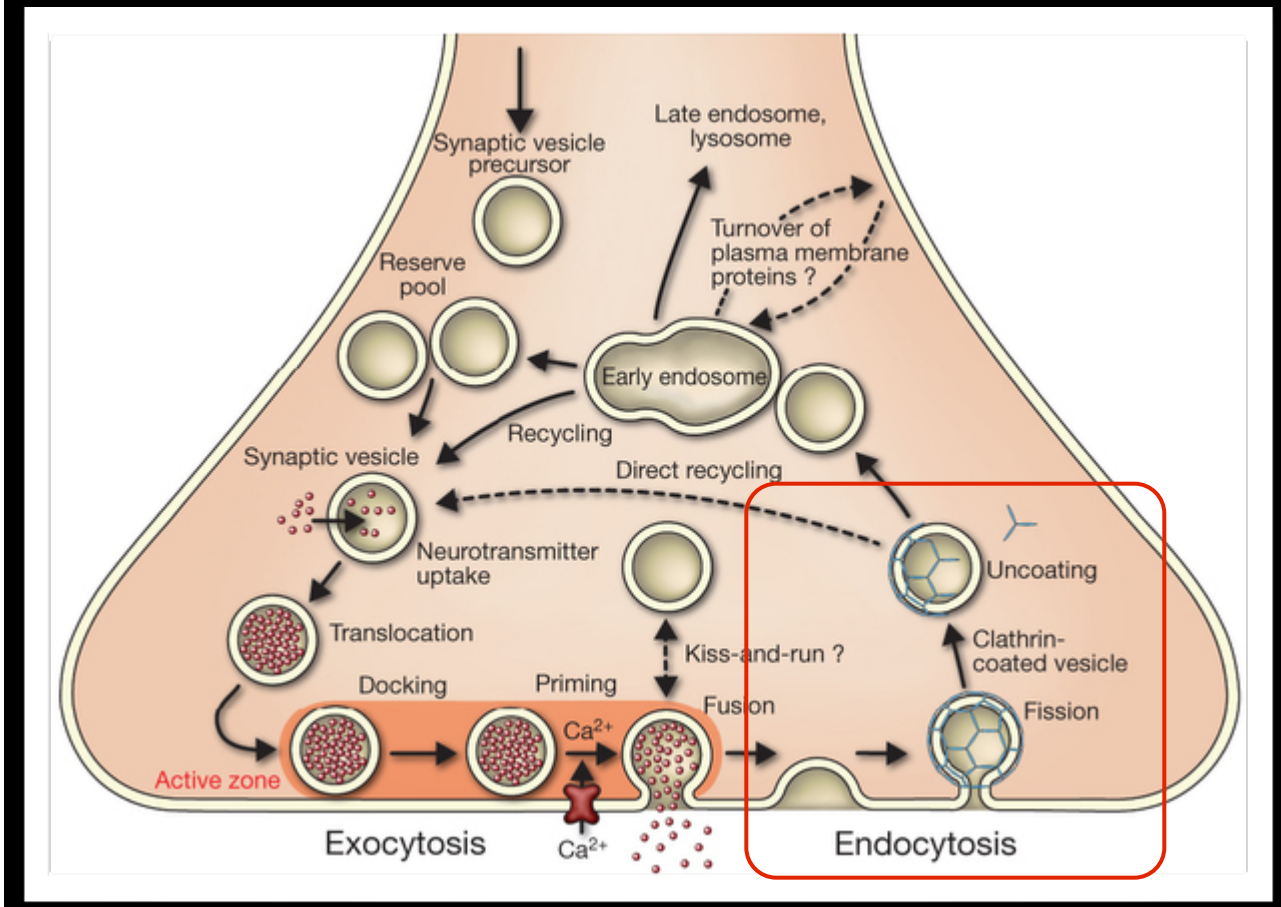
A Synaptic Vesicle



50 nanometers

Formation of Synaptic Vesicles

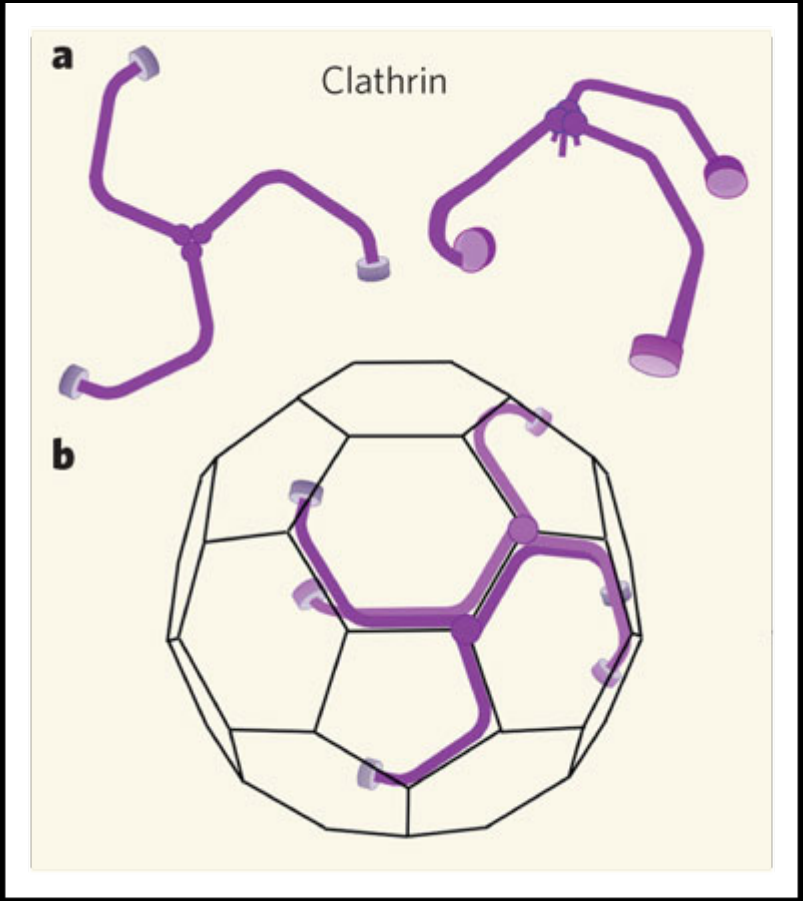
Birth of synaptic vesicles relies on a process called clathrin-mediated endocytosis



Clathrin-mediated Endocytosis

Clathrin is a protein that has a tendency to come together to form a polyhedral structure

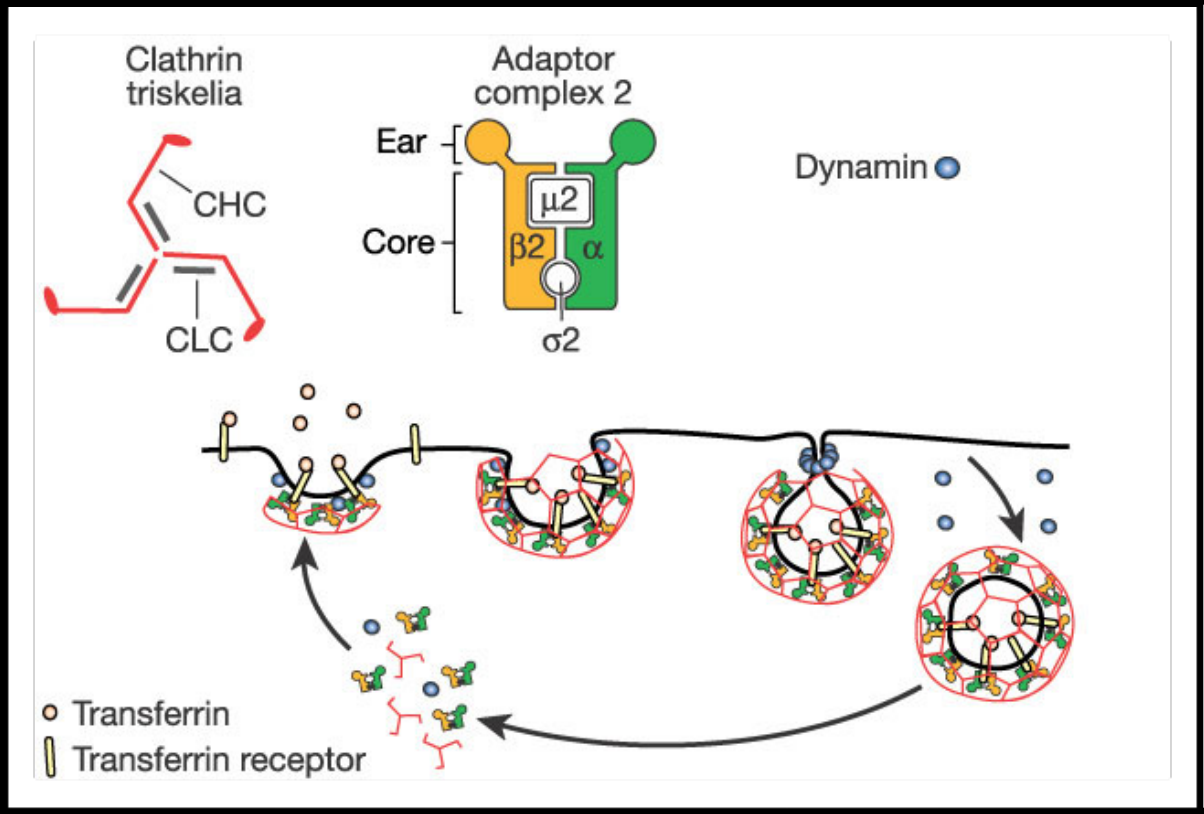
This coming together leads to growth of a scaffold that contributes to budding of vesicles from the cell boundary

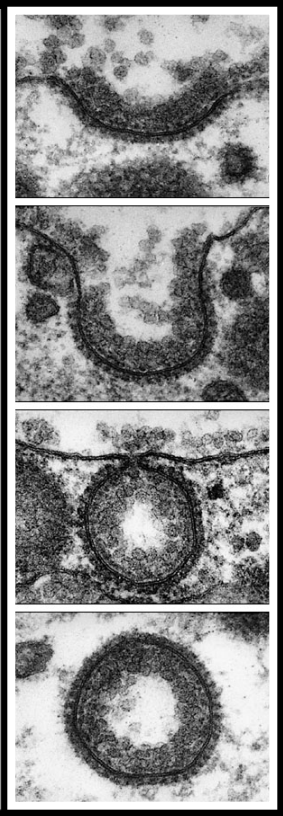


Budding and Fission of Clathrin-coated Pits

Clathrin-mediated endocytosis is a highly conserved process that in the brain is specialized to generate synaptic vesicles

In other cells, the same process contributes to nutrient uptake and regulation of cell surface display of receptors





Clathrin self-assembly generated a shallow pit

Further self-assembly generated a deeper membrane bud

Deeply invaginated buds are release by a process of membrane fission

We Study Budding and Fission of Clathrin-coated Pits

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Understanding cellular processes by reconstitution

The watchmaker's paradigm

Anyone who's owned a watch would agree that this little machine is a marvelous creation. Some may admire it as it ticks undisturbed in its protective casing. But like the watchmaker, those curious to know how it functions so precisely to maintain time are taken by an irresistible desire to open the back cover and dismantle the many small gears and springs. When put back together and the watch ticks as before, the 'watchmaker kinds' are overcome by a sense of gratification and humility in having finally understood how this little machine works.

Cells are like watches and molecules inside them are the gears and springs that have evolved to coordinate and catalyze reactions necessary for growth and survival of cells. But unlike watches, we don't quite know which molecules function as gears or springs. Moreover, experimental intervention to understand a single process in a complex machine like the cell can very often be confounded by global effects on cell growth and survival - akin to how the watch would stop working if any one of its many gears or springs are tampered.

Cells transport soluble and membrane proteins across organelles in membrane bound vesicles - a process that is termed vesicular transport. This process is necessary to generate cellular organelles and maintain their identity throughout the lifespan of the cell. When applied to cellular processes, the watchmaker's paradigm of learning by putting pieces back together to recreate function is termed biochemical reconstitution. We utilize this approach to understand the mechanism of vesicular transport and our efforts are guided by inputs from observing this process in living cells and rational design principles.

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