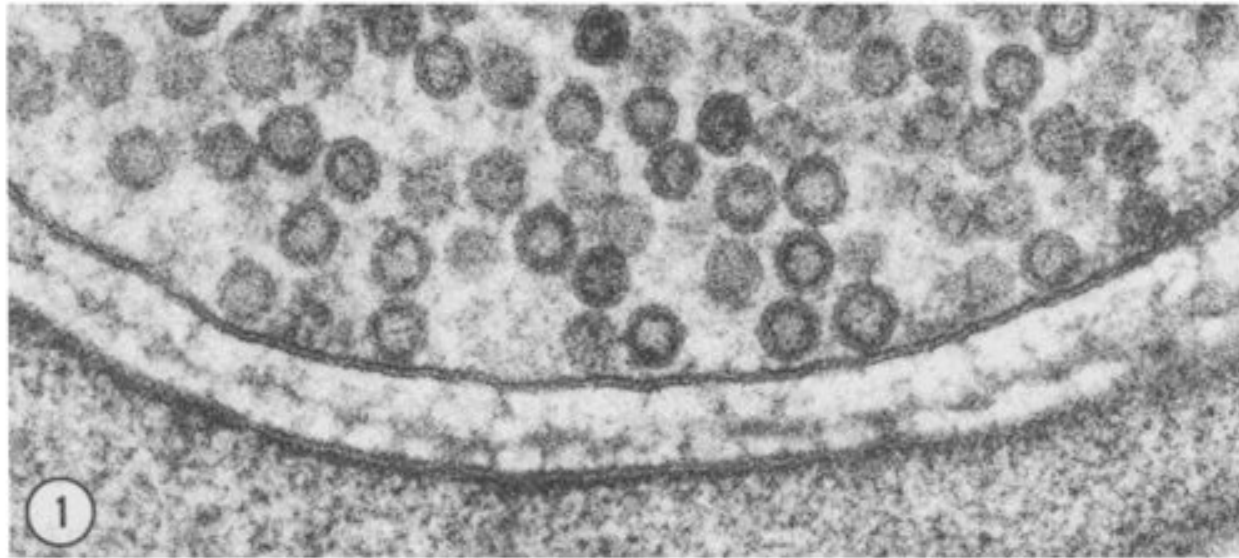
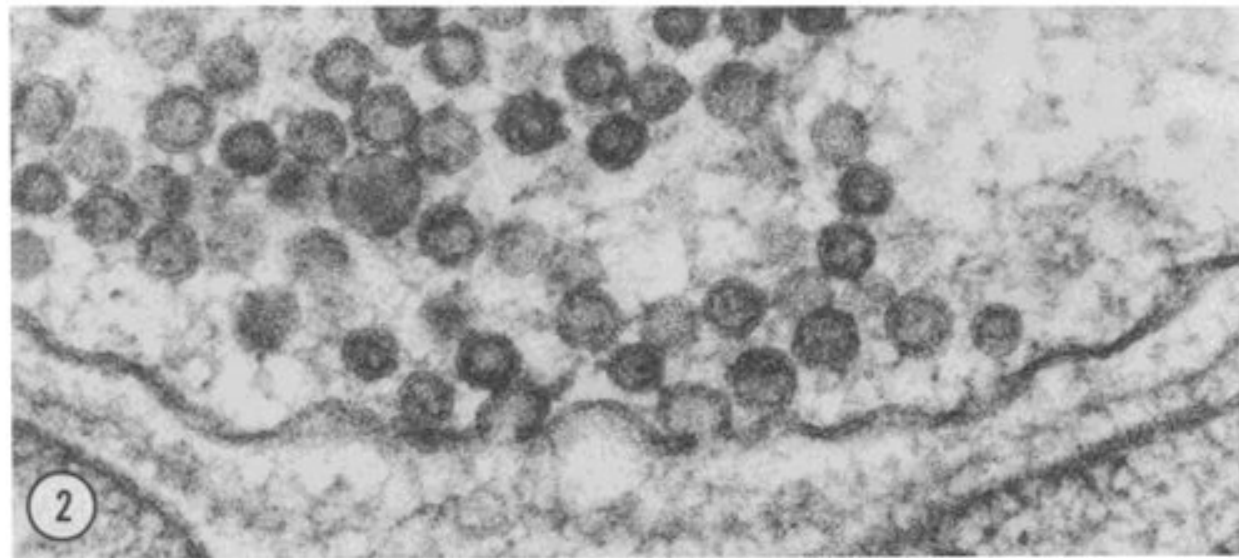


Tiny Bubbles (“Synaptic Vesicles”) at Nerve Endings Store Chemical Neurotransmitters and Release Them (“Membrane Fusion”) when the Electrical Signal Arrives

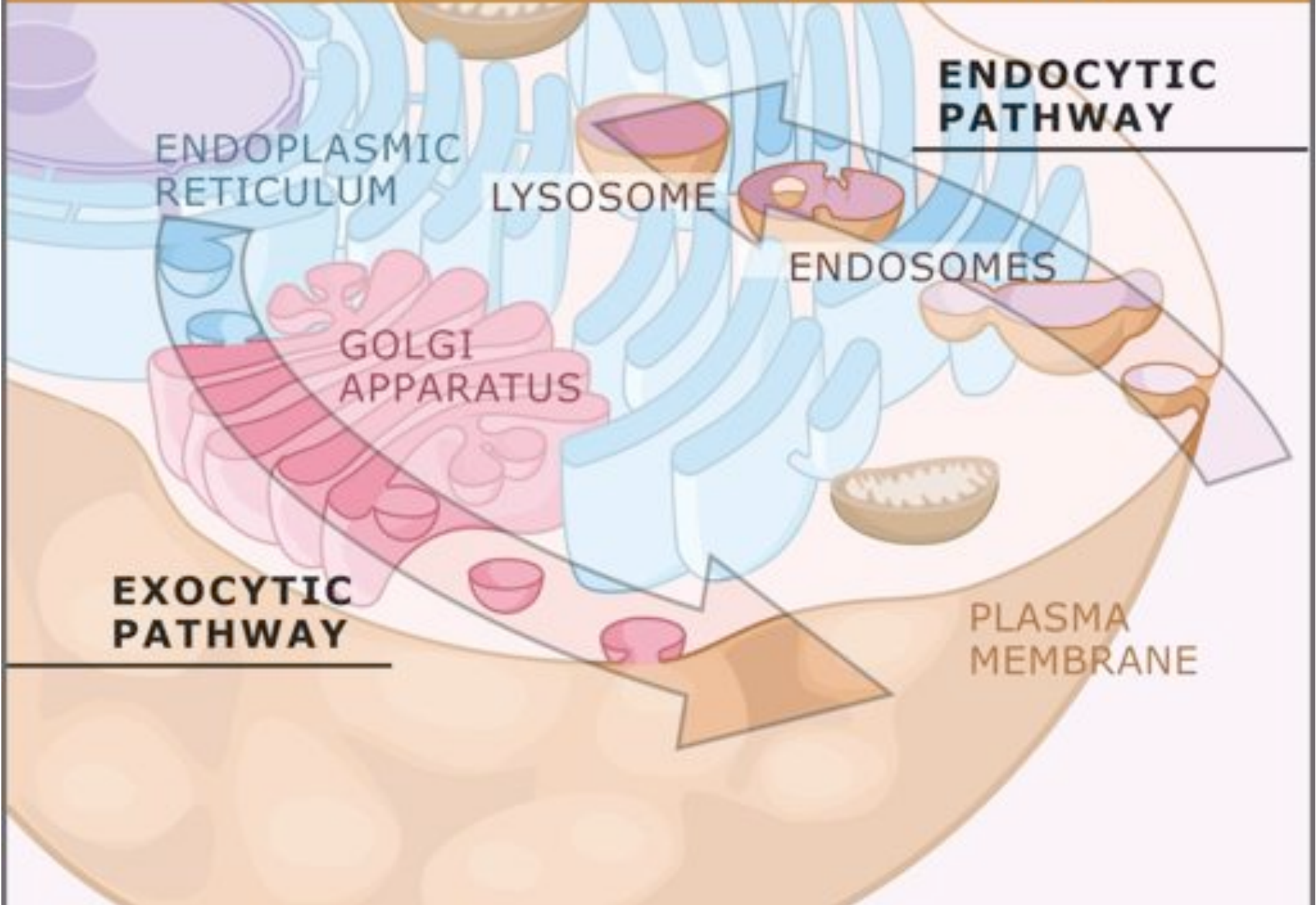


Fixed at
rest

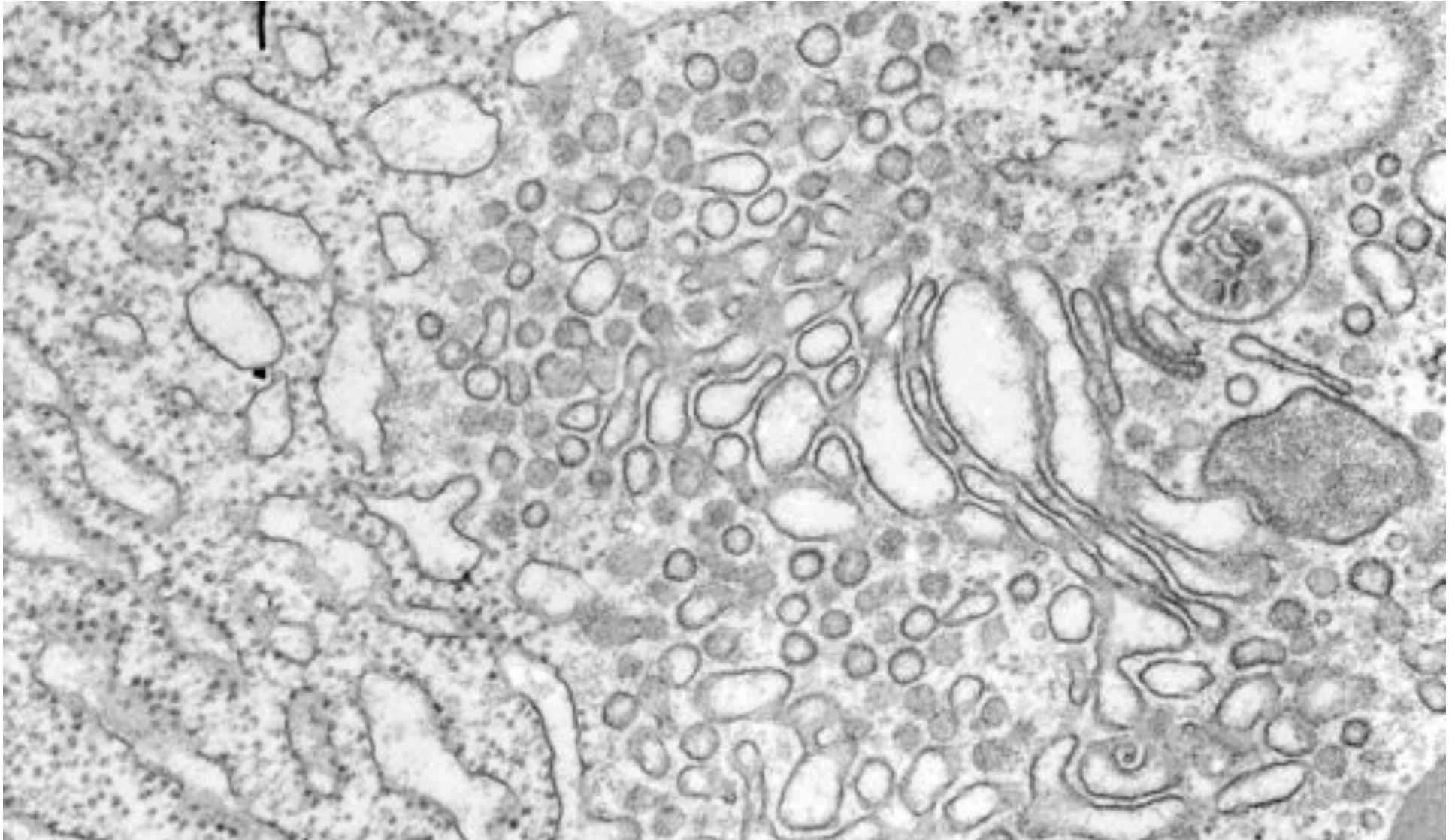


Fixed
5ms
after
stimulation

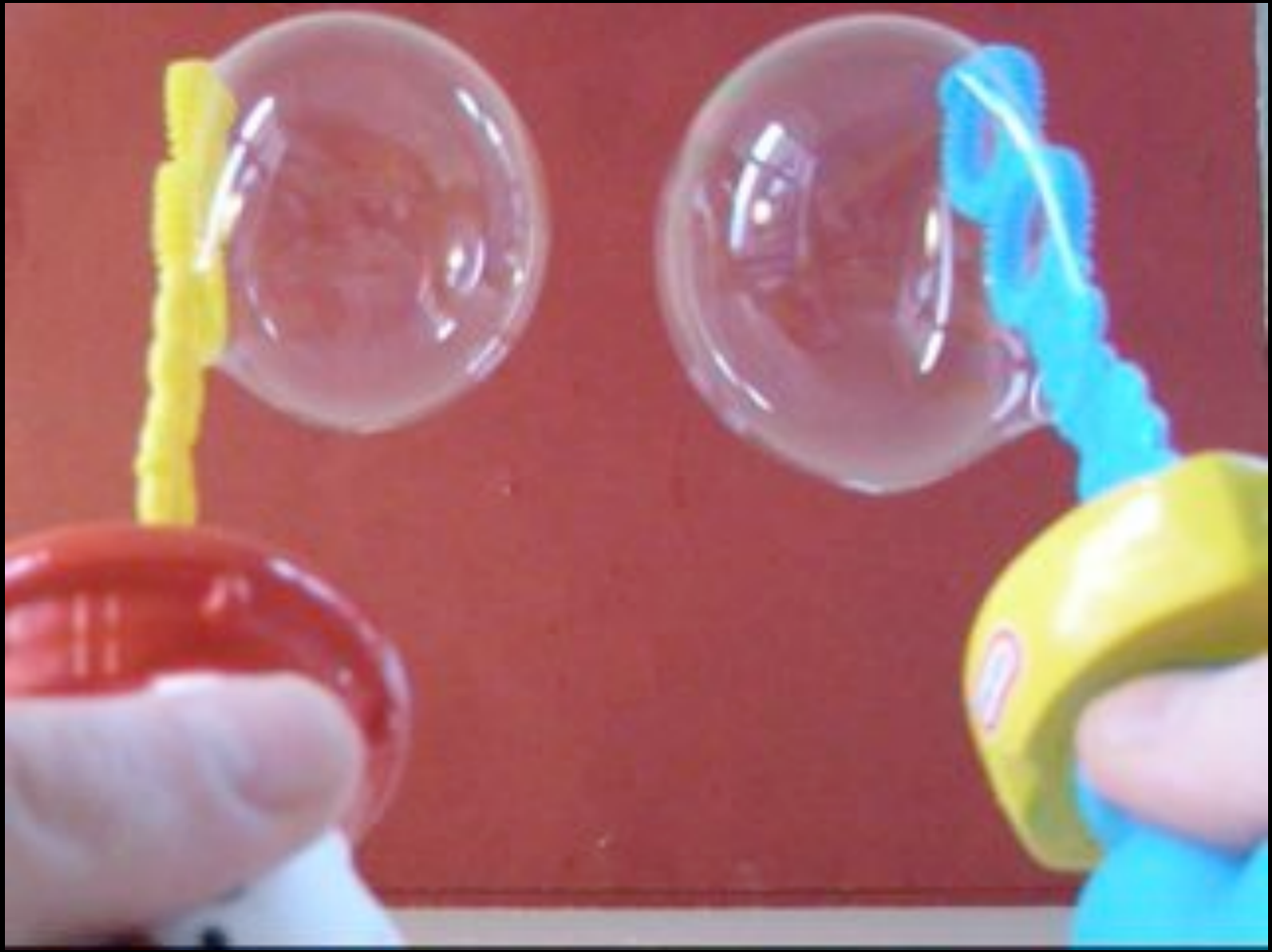
The exocytic and endocytic pathways



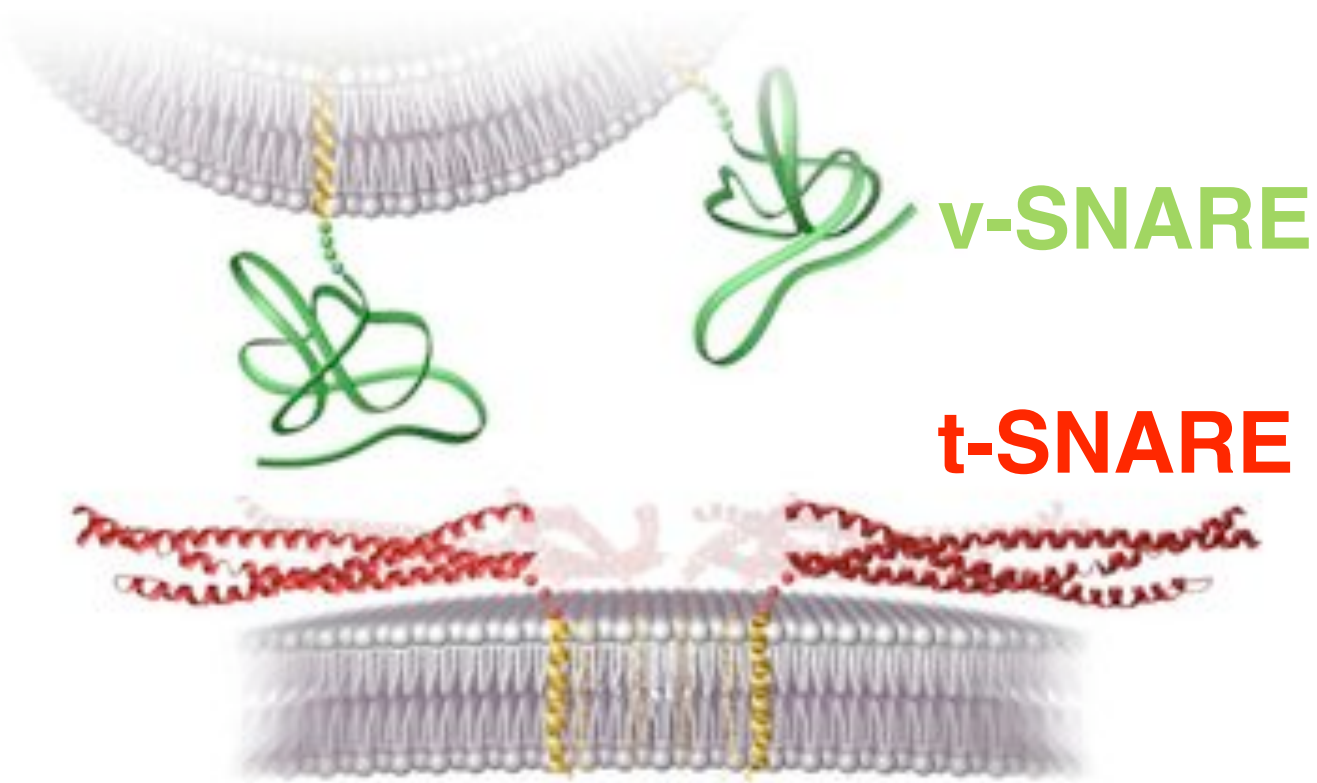
Membrane Fusion is a Universal Process



Similar Tiny Vesicle “Bubbles” Carry Enzymes and Other Cargo Around in the Cell

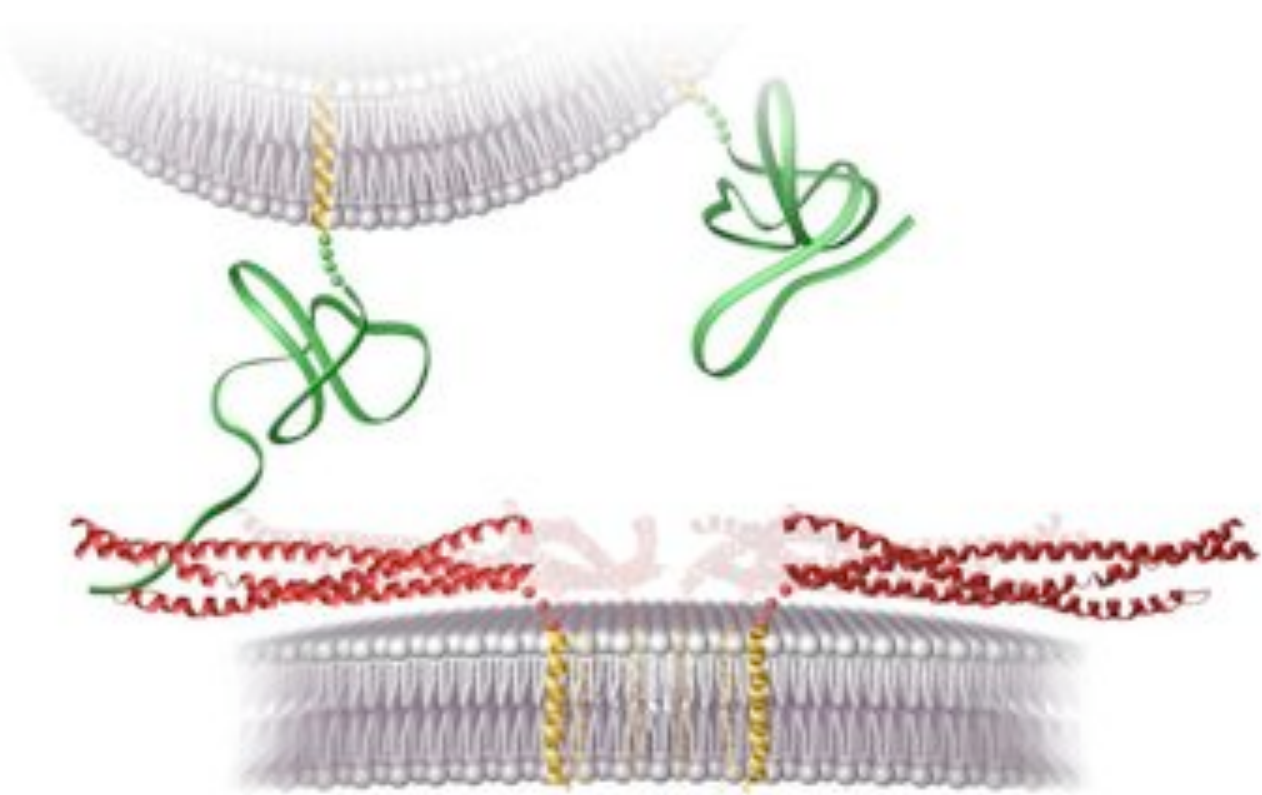


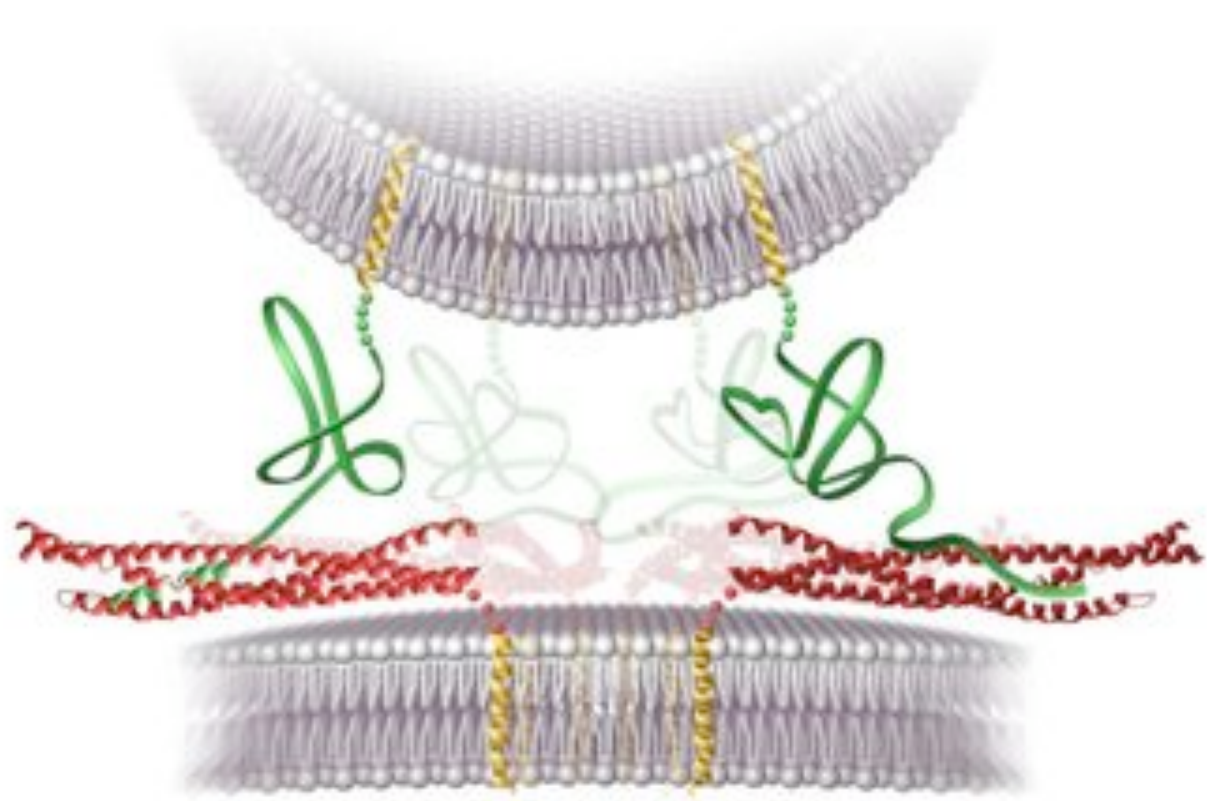
Synaptic Vesicle Containing Neurotransmitter

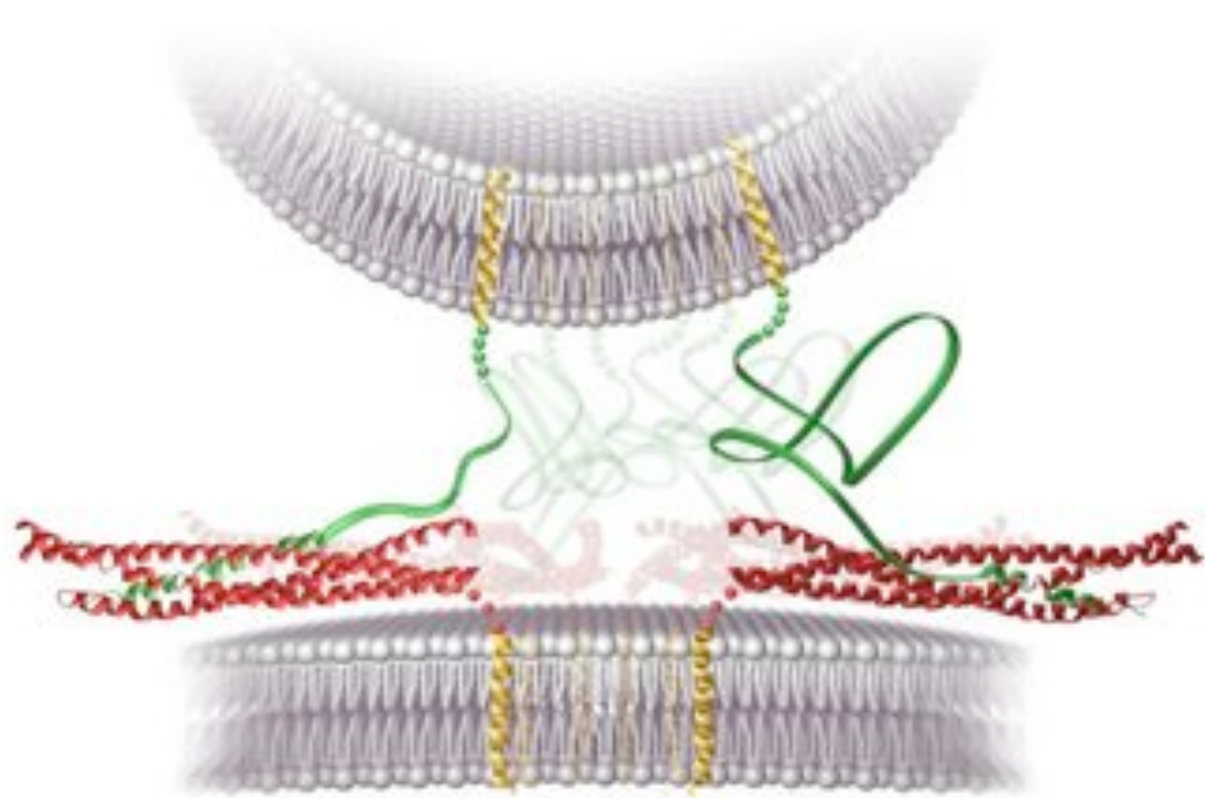


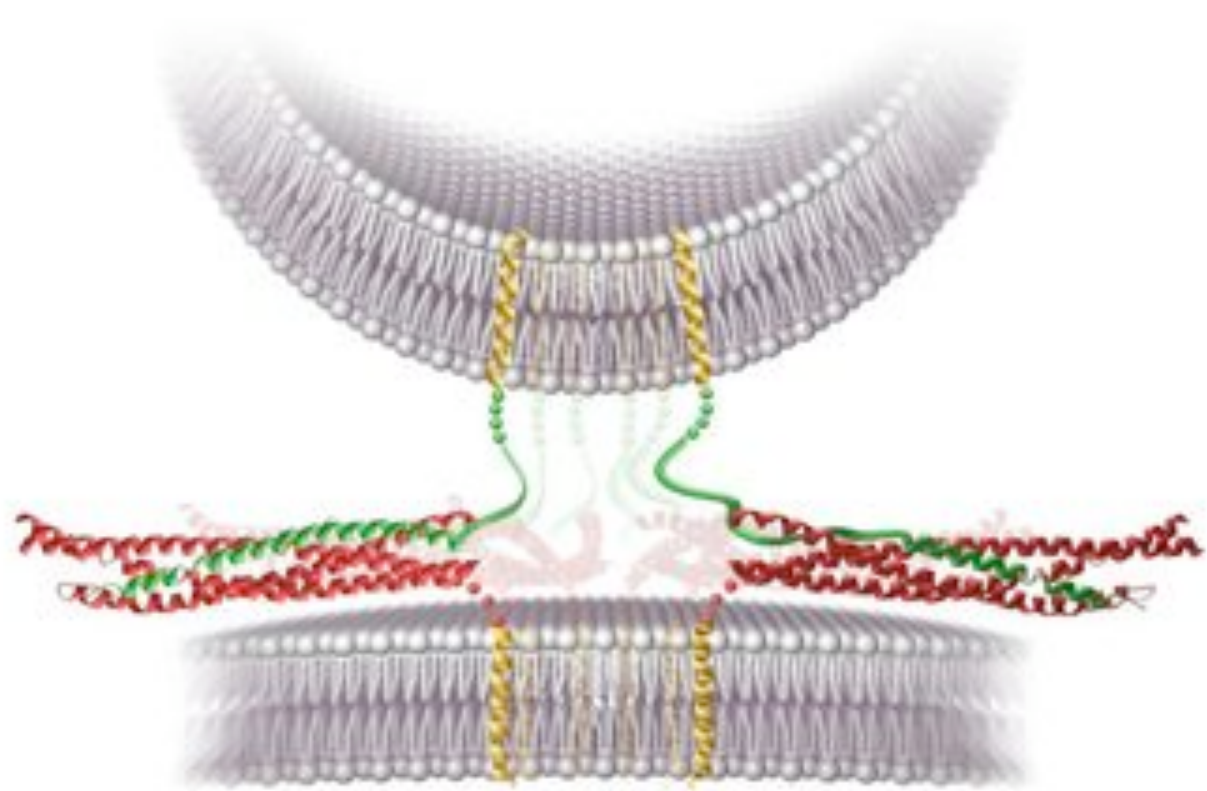
Outer Membrane of Nerve Cell

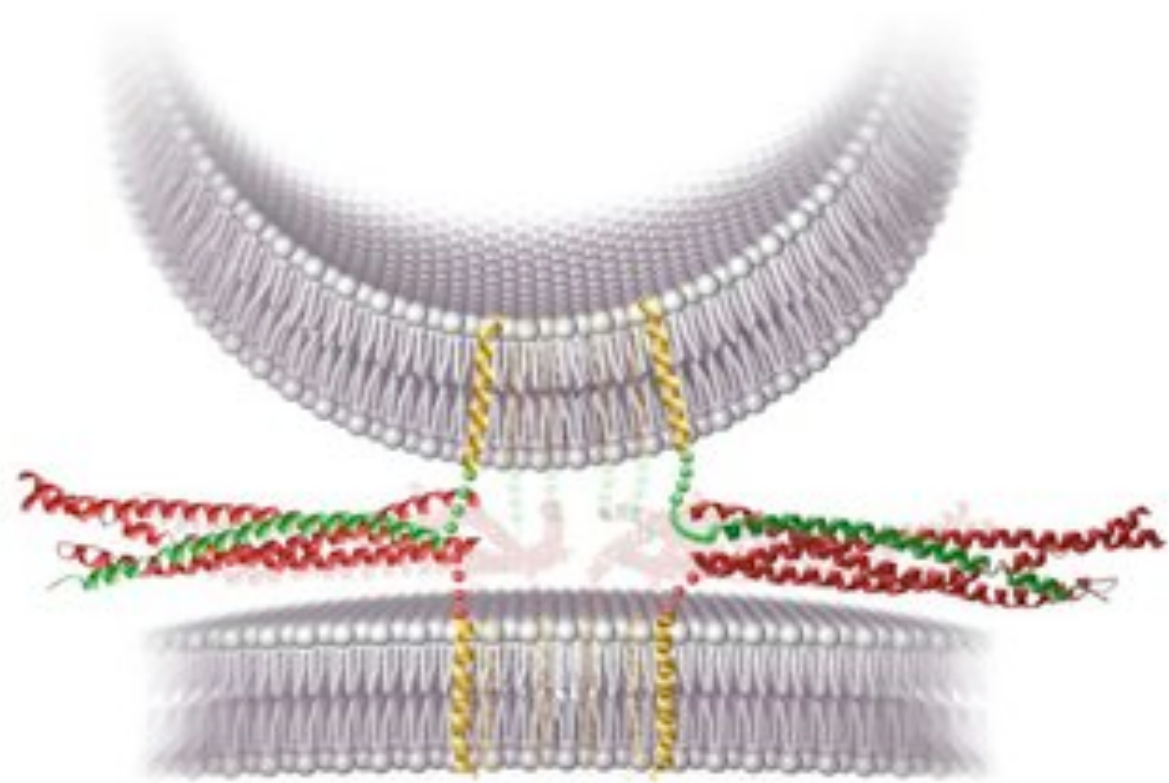
SNARE Proteins Link Up to Fuse Membranes

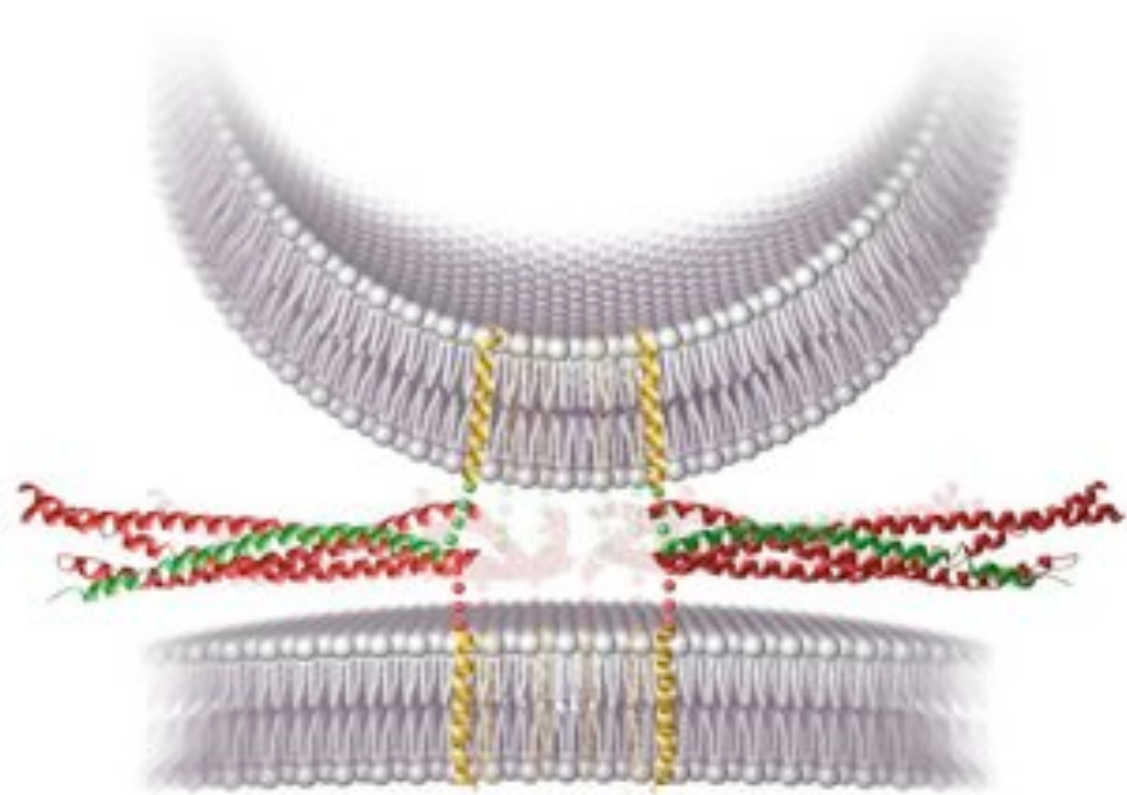


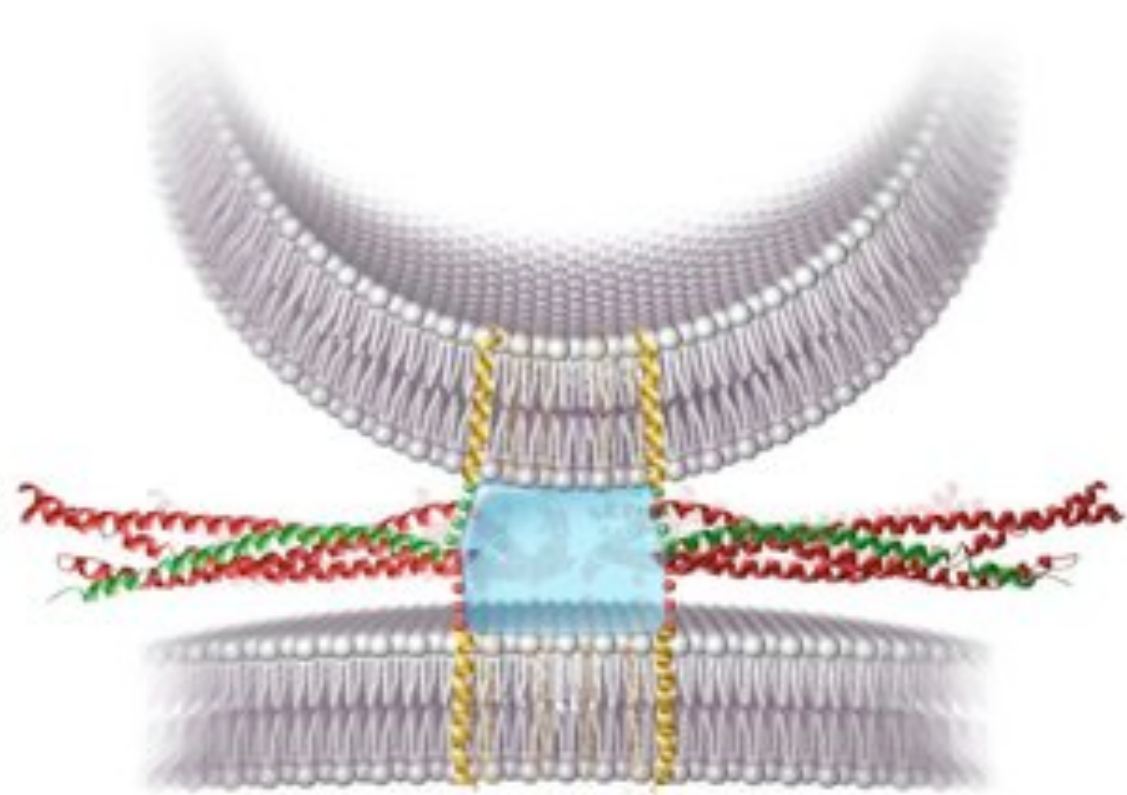




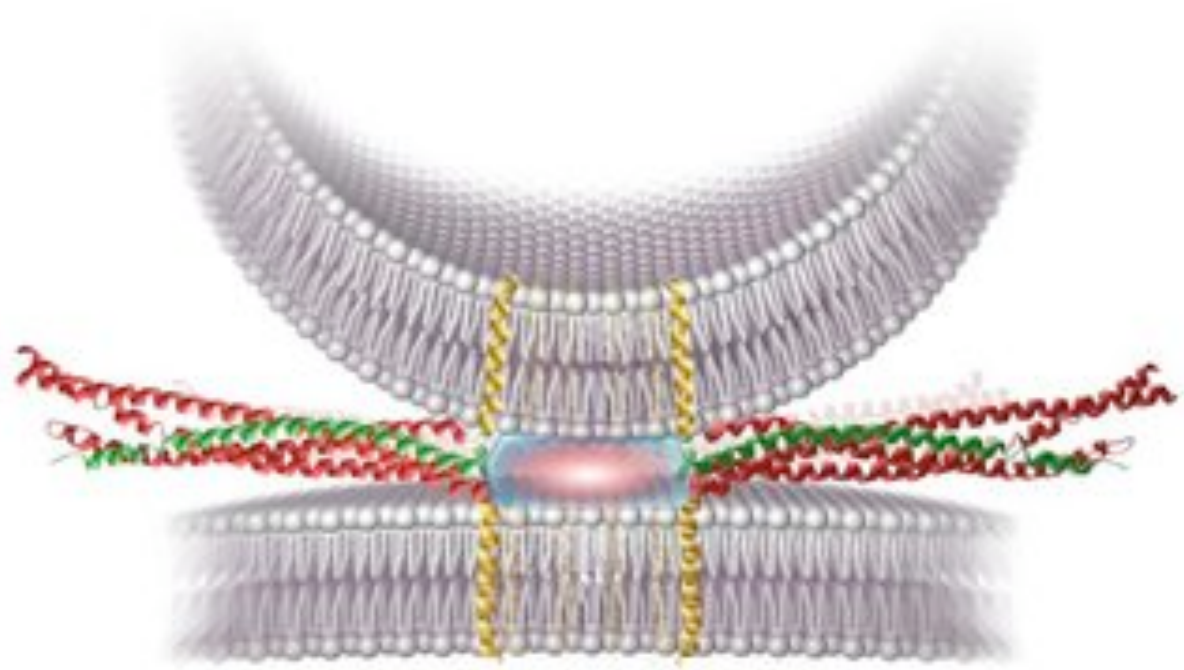


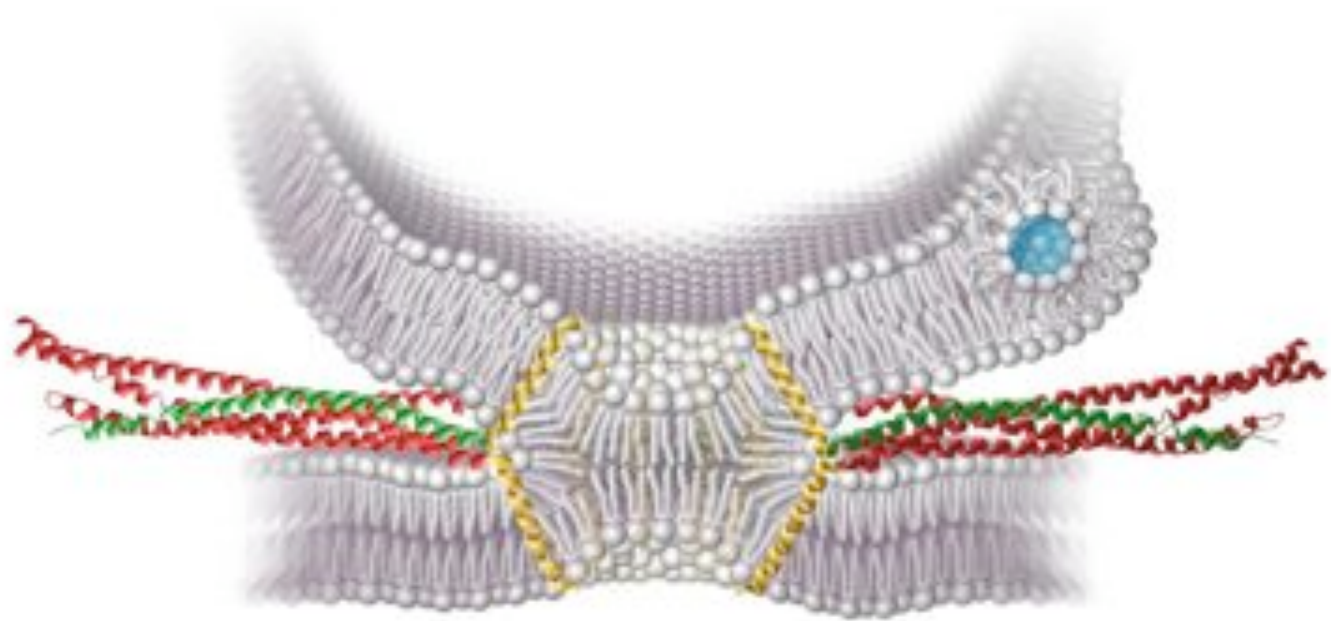


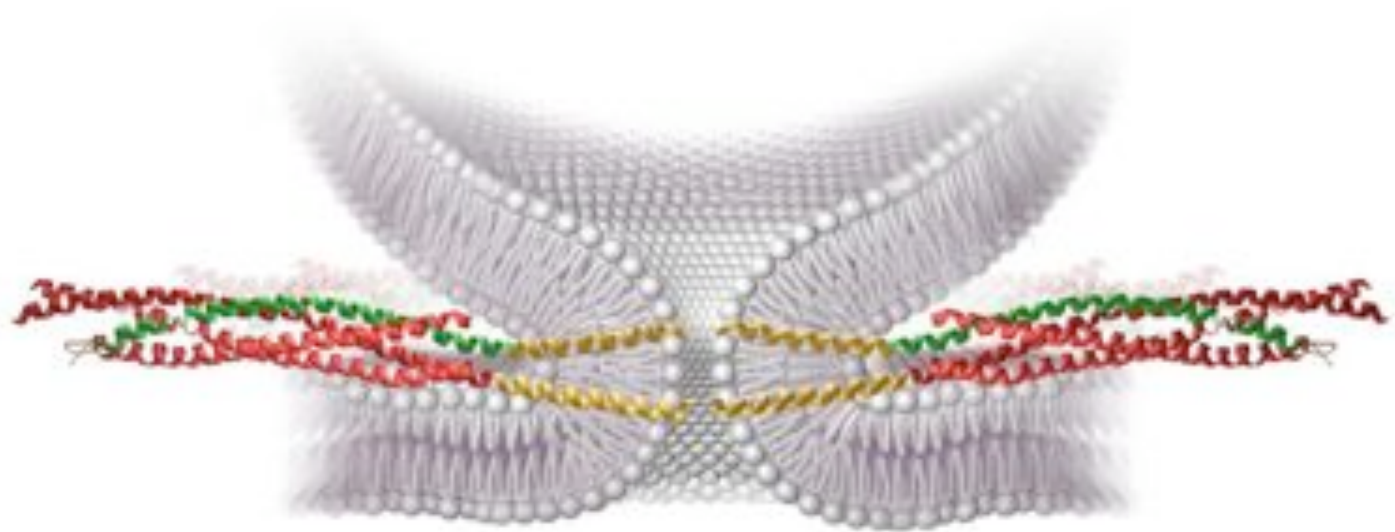










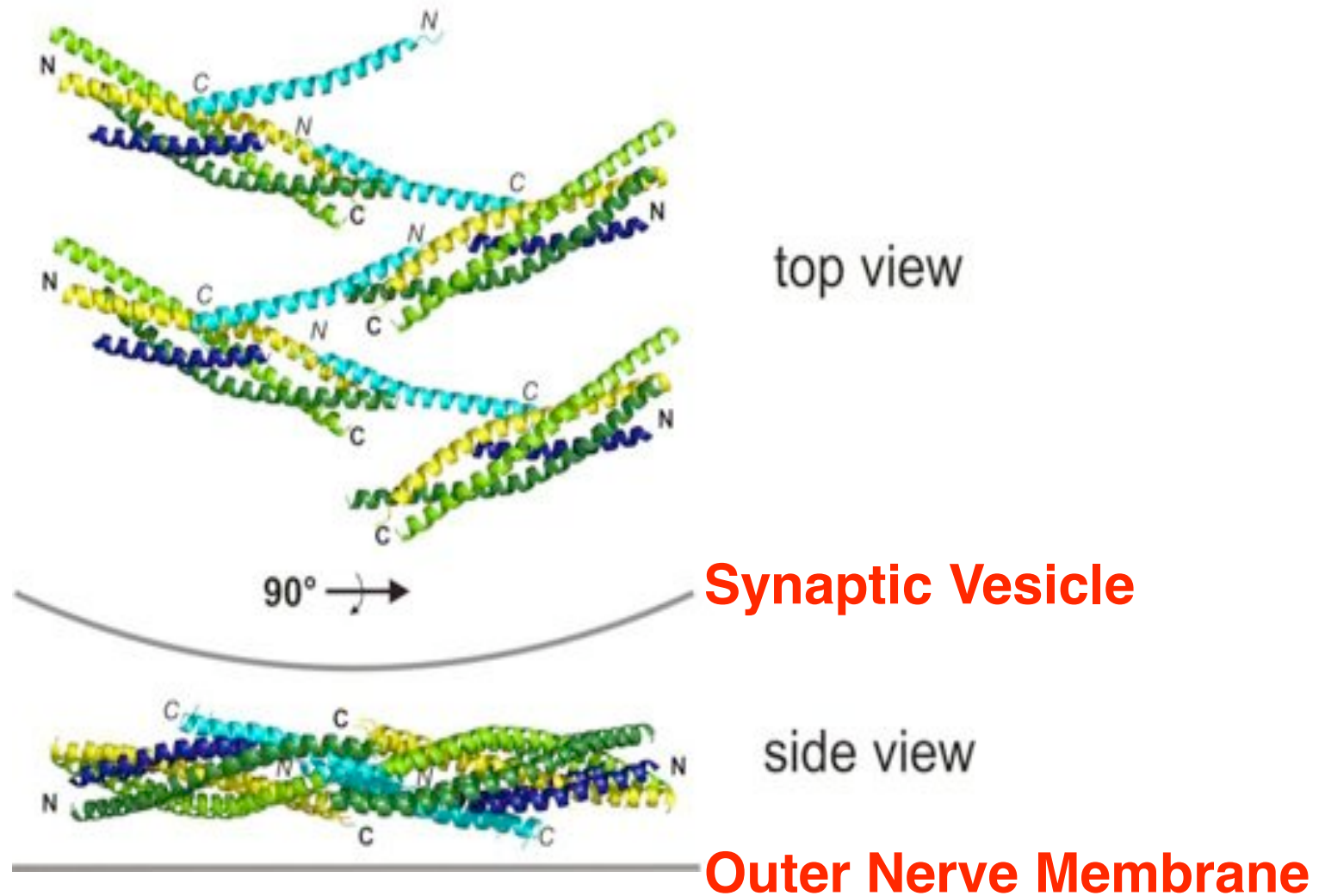


Precise Timing of Neurotransmitter Release is Fundamentally Needed for All Brain Function



But ... SNAREs Fuse Membranes Automatically

A Special “Clamping” Protein Embraces the SNAREs and Prevents Premature Release of Neurotransmitters



Special Acknowledgement of Key Contributors

Erik Fries	Reconstitution of intracellular transport (1980)
William Balch	Vesicle budding/fusion in cell-free assay (1984)
Lelio Orci (U Geneva)	Discovery of coated vesicles/budding mechanism
Benjamin Glick	Discovery of NSF (1987)
Marc Block & Felix Wieland	Purification of NSF (1988)

Vivek Malhotra & Lelio Orci	NSF required for membrane fusion (1988)
Duncan Wilson	Universal fusion machinery: NSF=sec18 (1989)
Douglas Clary	Discovered/purified SNAP (1990)
Thomas Söllner	Discovered SNARE complex (1993)
Thomas Weber	SNAREs alone mediate fusion (1998)
James McNew	Tested SNARE Hypothesis (2000)
Claudio Giraudo	The clamp for synaptic transmission (2006)

Background: Rothman Laboratory at Stanford University (1987)